Clinical Neurophysiology xxx (xxxx) 1–12

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com

Reorganization of pragmatic language networks in patients with temporal lobe epilepsy

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ARTICLE INFO

Keywords:
Metaphor
Connectivity
Network
Plasticity
Refractory
Temporal lobe epilepsy

ABSTRACT

Objective: To investigate the neural networks involved in idiomatic expressions (IE) comprehension in healthy controls and patients with drug-resistant temporal lobe epilepsy (TLE), with a functional magnetic resonance imaging (fMRI) task.
Methods: Thirty-two patients with TLE (left or right) and seventeen healthy controls were evaluated. Activated nodes in the fMRI task were defined as Regions of Interest (ROIs) for a posterior functional connectivity analysis.
Results: All participants completed the task successfully. We found a bilateral fronto-temporal network, lateralized to the right, during IE processing in the overall sample. Compared to controls, patients additionally activated frontal, temporal, and insular areas in both hemispheres. Controls exhibited fewer connections but greater inhibitory connectivity, while the opposite (more connections and increased excitatory connectivity) occurred in patients. Compared to controls, TLE patients recruited additional brain areas on top of the expected bilateral frontotemporal network. The connectivity analysis revealed that controls exhibited more effective inhibitory connectivity, with more modular ROIs. In contrast, patients demonstrated greater excitatory connectivity.
Conclusion: The results suggest compensatory neural recruitment in additional areas in TLE during IE comprehension.
Significance: Exacerbated connections in TLE may reflect the need to recruit alternative regions, resulting in higher costs and lower efficiency of the neural network.

1. Introduction

Temporal lobe epilepsy (TLE), the most frequent focal epilepsy, is often linked to a range of cognitive symptoms. Around 50 % of patients with TLE present language impairment (Dabbs et al. 2009; Bell et al. 2011; Allone et al. 2017; Chang et al. 2017; Rodríguez-Cruces et al. 2018; Balter et al. 2019; Reyes et al. 2019). The underlying neurobiological substrate of language comprises a network of regions in the dominant hemisphere (usually the left), interconnected by peri- and extra-sylvian white matter tracts. Ictal and interictal discharges can modify these neural networks, among others (Berl et al. 2005; Gaillard et al. 2007; Bell et al. 2011; Bonilha et al. 2012; Allone et al. 2017; Pasquini et al. 2022), often leading to language alterations in TLE (Catani et al. 2005; Upadhyay et al. 2008; Poeppel et al. 2012; Price 2012; Caverzasi et al. 2014; Allone et al. 2017; Balter et al. 2019).

Although numerous studies have shown greater language impairment in patients with left (L)TLE compared to those with right (R)TLE (Busch et al. 2005; Raspall et al. 2005; Keary et al. 2007), there is increasing evidence highlighting that patients with RTLE may have language difficulties as well (Bell et al. 2001; Bonilha et al. 2012; Roger et al. 2020). Language disorders in RTLE have often been attributed to medication effects (Husebye et al. 2020; Besag and Vasey 2021), as a consequence of the early onset (Hermann et al. 2001; Oyegbile et al. 2004) or to a high frequency of the seizures (Sass et al. 1992; Stewart et al. 2014). However, it is possible that underlying neuronal connectivity abnormalities in LTLE and RTLE could explain language impairment.

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https://doi.org/10.1016/j.clinph.2024.12.012
Accepted 9 December 2024
1388-2457/© 20XX

Deficits in structural components of language, such as syntax, semantics, phonology, and morphology have been consistently studied in TLE, overshadowing the disruptions of other language subdomains such as pragmatics. Pragmatic language has a profound impact on speakers and listeners interaction, which goes beyond the linguistic components (Bara et al. 1999; Martin and McDonald 2003). Being able to adapt language expressions to the listener, context, and the situation is essential for successful communication (Bobrow and Bell 1973; Cacciari and Glucksberg 1994; Bishop and Baird 2001; Small 2008; Van Overwalle 2009). The notion of *pragmatic* (or *figurative*, or *non-literal*) language refers to expressions whose meaning is different from the sum of the meaning of their words, such as metaphors, idiomatic expressions, ironies, and jokes. Anatomically, the comprehension of this type of language involves frontotemporal areas in both cerebral hemispheres, with a slight predominance of the right one (Bambini et al., 2016, 2011; Bendersky et al., 2021; Cacciari and Tabossi, 2014, 1988; D'Ouakil, 2012; Gibbs Jr, 2008; Kempler et al., 1988; Nunberg et al., 1994; Papagno et al., 2002). According to the DSM-5, individuals with *pragmatic or social communication disorder* present difficulties in verbal and nonverbal communication for social purposes, which diminishes their ability to communicate effectively, participate socially, maintain social relationships, or otherwise get a successful performance academically or occupationally (American Psychiatric Association 2014). Sometimes the disability can be extremely subtle. They may seem socially inept and misinterpret the intentions of others, or their language may seem odd in an inconsistent way. Research on language impairments in epilepsy generally uses neuropsychological tests that mostly assess nomination and fluency, and do not usually measure pragmatic language (Sass et al. 1992; Bell et al. 2001; Hermann et al. 2001; Oyegbile et al. 2004; Busch et al. 2005; Raspall et al. 2005; Keary et al. 2007; Bonilha et al. 2012; Stewart et al. 2014; Roger et al. 2020).

Deficits in non-literal language have been found in several conditions, such as autism spectrum disorder, even when controlling for IQ (Coulson and Van Petten 2007; Vulchanova et al. 2015; Chahboun et al. 2016), schizophrenia (Titone and Connine 1999; Thoma and Daum 2006; Kircher et al. 2007; Saban-Bezalel and Mashal 2017; Rapp et al. 2018; Rossetti et al. 2018) or injuries to the right hemisphere (Kempler et al. 1988; Winner and Gardner 1993; Cheang and Pell 2006; Johns et al. 2008; Abusamra et al. 2009; Ferré et al. 2012; Lomlomdjian et al. 2017), among others. They have also been reported in patients with epilepsy, particularly in the right hemisphere (Lomlomdjian et al. 2017).

Individuals with TLE are prone to displaying atypical patterns of language representation within the brain, which likely reflects functional adaptations in response to the injury. Due to the long duration of the disease in drug-resistant epilepsy, the (re)organization of these networks is of great interest to understand the functioning of pre-surgical language and its hemispherical dominance, as well as to estimate the risk of post-surgical language impairment (Balter et al. 2019; Kaestner et al. 2020). It has been proposed that the activity of drug-resistant epilepsy gradually affects the structure and function of the brain, and these alterations may change or redirect language pathways to the non-dominant hemisphere during development (Duchowny et al. 1996; Engel 1998; Janszky et al. 2006). In a recent paper of our group, we found that patients with drug-resistant left and right TLE recruited additional nodes in both hemispheres when decoding prosody besides the putative areas. Noteworthy, both groups obtained similar accuracy and reaction times in the task (Elizalde Acevedo et al. 2022).

Drug-resistant epilepsy usually requires resective surgery as a treatment, and after the intervention up to 60 % of patients become seizure-free (Engel 1998; Wiebe et al. 2001). Possible sequelae of surgery are language disorders, reported in 30 to 50 % of these patients, despite thorough presurgical brain mapping to avoid them (Katz et al. 1989; Langfitt and Rausch 1996; Davies et al. 1998; Bell et al. 2000; Sabsevitz et al. 2003). In contrast to traditional anterior temporal lobectomy, selective amygdalohippocampectomy aims to retain functional tissue, potentially lowering associated risks. Nevertheless, data indicates that this safeguarding impact on cognitive results lacks statistical significance, implying that the extent of the resection might not serve as a reliable outcome predictor (Balter et al. 2019).

The selection of patients with TLE was based on the one hand, on the fact that it is the most common of focal epilepsy, in which the epileptogenic zone can be clearly defined. On the other hand, the hippocampus, parahippocampus, and related areas are part of several networks associated with different cognitive tasks, including pragmatic language. It is acknowledged that temporal regions (Bendersky et al. 2021) play a fundamental role in cognitive tasks related to idiomatic expressions. These activities are considered among the most complex within language (Catani and Bambini 2014), as they involve multiple cognitive functions and, consequently, activate specific brain areas such as the fusiform gyrus, pars triangularis, middle frontal gyrus, prefrontal cortex, and right parahippocampal gyrus (Rankin et al. 2009; Geranmayeh et al. 2014; Castellucci et al. 2022; Mouga et al. 2022). It is not surprising to consider the possibility of a network affected by refractory temporal epilepsy that may successfully carry out a pragmatic language comprehension task when exhibiting activations and connectivity between these regions in a non-conventional manner.

Language organization in TLE surgery candidates is studied with invasive intracarotid amobarbital (ICA) and non-invasive methods (e.g., fMRI). Lateralization, assessed with ICA or fMRI, categorizes dominance in the left, right, or both hemispheres (Binder et al. 2011; Janecek et al. 2013). fMRI also provides information about the intrahemispheric organization with high spatial resolution. Despite typical left hemisphere dominance, TLE patients (Berl et al. 2014) and healthy controls (Knecht et al. 2002) show a continuum of laterality rather than discrete categories (Fig. 1). The unconventional organization of lan-

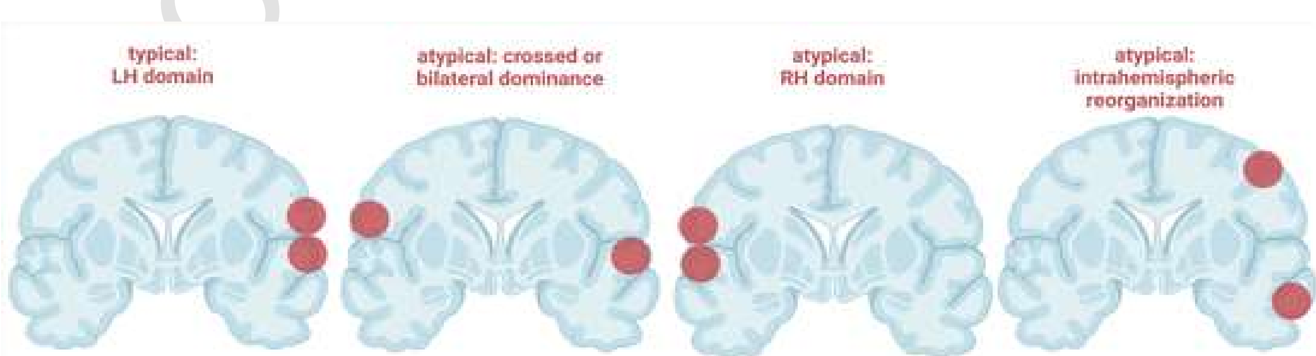

Fig. 1. Atypical language reorganization.

guage in individuals with epilepsy has traditionally been conceived following three general patterns: The first is a *right-hemisphere domain*, with central networks of language perception and production putatively located in the left hemisphere shifting towards the right hemisphere, most often to homologous regions (Gaillard et al. 2002; Gaillard et al. 2004; Thivard et al. 2005; Gaillard et al. 2007; Hamberger and Cole 2011; Baciu and Perrone-Bertolotti 2015). A second pattern of atypical organization is *crossed or bilateral dominance*, meaning that only some language subdomains move towards the right hemisphere, with some others preserved in the left (Baciu et al. 2003; Thivard et al. 2005; Lee et al. 2008; Hamberger and Cole 2011; Baciu and Perrone-Bertolotti 2015). For example, a frontal region of language production may be lateralized to the right, but a temporal region of language perception may be lateralized to the left. The third pattern of atypical organization involves *intrahemispheric reorganization*, wherein language regions relocate within the same hemisphere, particularly if it overlaps with the epileptogenic zone. These shifts frequently occur adjacent to the typical language zones, like the perisylvian cortex in the frontal and temporal lobes (Bell et al. 2002; Brázdil et al. 2003; Mbwana et al. 2008; Hamberger and Cole 2011; Baciu and Perrone-Bertolotti 2015) (Fig. 1).

While in healthy population the left hemisphere is usually dominant for language, in patients with epilepsy the atypical organization of language can follow several patterns in a continuum of laterality. LH: left hemisphere, RH: right hemisphere.

Throughout the history of neurology, understanding the links between cognitive functions and brain structures has required finding dissociations. This helps to establish causality: if altering a brain structure affects a function, that structure is assumed to have a causal role in the affected cognitive domain. This is why epilepsy serves as a model for comprehending the mind-brain relationship (Jackson 1880). Currently, individuals with drug-resistant epilepsy, especially those with long chronicity, may give rise to structural or functional atypical neural networks (Alba-Ferrara et al. 2018). Functional connectivity refers to the statistical relationship or temporal correlation that exists between two or more brain areas that are anatomically distinct or located at a certain distance from each other in terms of neurophysiological activity (Whitfield-Gabrieli and Nieto-Castanon 2012). Inter-hemispheric language reorganization can be attributed to changes mediated by transcallosal connections, whereas intra-hemispheric language reorganization is explained by changes in collateral connections (Hamberger and Cole 2011; Tzourio-Mazoyer et al. 2017; Balter et al. 2019). Notably, presurgical patients have shown a curious pattern wherein there is heightened connectivity among limbic regions in proximity to the impaired hippocampus (referred to as the hippocampal paradox), alongside diminished connectivity in various cortical areas distant from it (Bonilha et al. 2012; Leyden et al. 2015; Kaestner et al. 2020).

In short, language comprises different components and functionalities that can be reorganized together or independently. Pragmatic language in healthy controls (CTRL) depends on a bilateral fronto-temporal network, with a slight predominance of the non-dominant hemisphere (Bambini et al., 2016, 2011; Bendersky et al., 2021; Cacciari and Tabossi, 2014; D'Ouakil, 2012; Elizalde Acevedo et al., 2022; Gibbs Jr, 2008; Kempler et al., 1988; Nunberg et al., 1994; Papagno et al., 2002). Pragmatic skills are sometimes difficult to evaluate in patients with chronic epilepsy and associated cognitive impairment, but many patients have no cognitive impairment, have minimal or no memory compromise, and manage to maintain an adequate neurocognitive status. This compensation possibly depends on a reorganization with greater recruitment of accessory areas and the creation of new connections. The reorganization of networks for this specific type of language in patients with TLE has not yet been studied. Since some of these patients are candidates for epilepsy surgery, it is important to know these compensatory networks recruited so as not to harm them.

2. Materials and methods

2.1. Participants

2.1.1. Inclusion criteria

All participants signed an informed consent to participate in the study, which was evaluated by the Ethics Committee of the Hospital El Cruce and Hospital Roffo, according to the declaration of Helsinki. All participants complied with the current guidelines for fMRI research, had to be able to solve the paradigms before being scanned, and could perform a fMRI of 30 min. In addition to the demographic variables (sex and age), the variable of years of education (in the whole sample) was collected (Table 1). Participants did not receive financial compensation for their participation in the study, only travel expenses were refunded.

2.1.1.1. Patients with left and right temporal lobe epilepsy. Patient selection was carried out in the Epilepsy Center of "Hospital El Cruce Nestor Kirchner" (EC-HEC), the main referral center for adult epilepsy patients in the public health system, from the City and Province of Buenos Aires. About 75 % of the patients of the EC-HEC have pharmacoresistant epilepsy. We selected thirty-two patients with mesial temporal lobe epilepsy (as it is one of the most common medically intractable seizure disorders). A mesial TLE origin was considered if seizures arose in the hippocampus, amygdala, and/or entorhinal cortex. Sixteen patients diagnosed with drug-resistant LTLE, and sixteen patients diagnosed with RTLE were recruited. All of them were candidates for unilateral temporal lobectomy. The diagnostic algorithm involved a video-EEG to identify the epileptogenic zone and to distinguish epileptic crisis from psychogenic non-epileptic seizures. The criteria for inclusion encompassed having at least one distinct clinical episode supported by concurrent ictal irregularities visible in the EEG, validated through video-EEG monitoring, and diagnosed according to the ILAE nomenclature (Berg et al. 2010; Scheffer et al. 2016). The time from the onset of epilepsy was recorded in the group of patients (Table 1). Also, patients with TLE were assessed with additional cognitive tests: WMS-IV and WAIS-IV (Wechsler 2002), normalized for the Argentine population, and adjusted for age and education.

2.1.1.2. Control group. A CTRL group of seventeen subjects from 18 to 40 years, was matched by age and sex. Participants were selected based on the absence of any prior neurological or psychiatric disorders and either normal vision or corrected-to-normal vision.

2.1.2. Exclusion criteria

Patients who did not complete all diagnostic steps, did not sign informed consent, or had an IQ of 70 or below on the Wechsler IQ Test (Wechsler 2002) were excluded. Additionally, patients with bilateral TLE or those in whom the laterality of their epileptic seizures could not be determined were not included, as well as patients with severe, extensive, bilateral lesions (e.g., tuberous sclerosis), as connections are likely to be altered at various points.

Table 1
Demographic data.

Number of Subjects	CTRL17	LTLE16	RTLE16	*p*
Sex (F/M)	7/10M (SD)	8/8M (SD)	11/5M (SD)	
Age	34.87 (7.88)	31.43 (7.97)	28.56 (7.44)	0.082 (1)
Years of education	17.26 (5.03)	11.41 (2.84)	12.75 (2.98)	0.001 (1)
Epilepsy onset	–	13 (9.35)	12 (4.85)	0.069 (2)

CTRL, healthy controls; LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; M. mean; S.D., standard deviation. (1) One-way ANOVA, (2) two samples t-test. Significant differences between the CTRL group with the RTLE and LTLE groups were found in the years of education. In both cases, the patients groups did not differ between themselves.

2.2. Neuropsychological and mental health evaluation

In addition to evaluating manual dominance using the Edinburgh questionnaire – to evaluate hemispheric dominance and obtain additional information on lateralization (Oldfield 1971) – the following tests were applied to rule out cognitive impairment: *Direct/Inverse Digit span* from the Wechsler Memory Scale (WMS-IV) (Weschler and Stone 1945) WAT (Word Accentuation Test), in Spanish (Del Ser et al. 1997). Moreover, all participants completed the Spanish version of the Beck Depression Inventory (Brenlla and Rodríguez 2006) and the Anxiety State and Trait Inventory in Spanish (Buela-Casal et al. 2011) as well as a SCID (First et al. 1999) interview to rule out the presence of current mental disorder (Table 2).

2.3. fMRI

2.3.1. Stimuli: Understanding idiomatic expressions (IE) in Spanish

The fMRI paradigm was adapted from a task created by Papagno (Papagno and Caporali 2007) and Proverbio (Proverbio et al. 2009), in which a sentence had to be matched to a word with a related meaning. The Spanish version of the task has already been validated by our research group, at the behavioral level and in the fMRI setting (Lomlomdjian et al. 2017; Bendersky et al. 2021). The stimuli for the study comprised a total of 120 idiomatic expressions and 120 literal sentences. These idiomatic expressions were carefully selected based on their common usage in Argentina. Each of the idiomatic and literal expressions was matched with four potential target word options: i) the correct one corresponding to the idiomatic or literal meaning, ii) an option that was semantically related to the main structure of the sentence, and iii) two options that were unrelated to the expression's meaning. As an example, for the idiomatic expression "*The artist kicked the bucket*," the target options included *death-football-food-city*. In this case, the first two options were connected to the expression's meaning, while the latter two were unrelated. For the literal expression "*The player kicked the ball*," the target options were *action-accident-score-passion*. In this instance, the first and third options were relevant to the literal meaning of the sentence.

During the task, each sentence appeared at the top of the screen, while the target options were positioned at the bottom. Participants were guided to read and comprehend the meaning of the idiomatic or literal expressions and then choose the option that most accurately represented it by a key press. To familiarize themselves with the task, participants underwent a preliminary run involving twenty trial rounds before entering the scanning session.

The stimuli, whether figurative or literal, comprised straightforward sentences (subject-verb-object) characterized by a uniform and unbiased structure at the beginning. However, the concluding key structure, unique to each stimulus, varied and dictated the intended meaning (specific word or group of words). The sentence predictability was assessed through an inquiry conducted by a panel of six neurolinguistics (Lomlomdjian et al. 2017; Bendersky et al. 2021). Although sentences in this study were not divided into parts for display, the length of the initial and key structures of each sentence was balanced across different types of stimuli. For more information regarding the task and stimuli see Bendersky et al. (2021).

Stimuli were presented every 4.5 s (with a 4-second display time) in an event-related design, featuring a jittered ISI of $\bar{x} = 500$ *ms* $\pm$ *300. The entire run lasted 5 min and 21 s, while the full session was approximately 25 min long. A total of 214 volumes corresponding to the task, along with four dummy scans, were acquired. The dummy scans, not shown in the figure, were collected during the first 6 s of the run.*

2.3.2. Image acquisition

Structural and functional MRI data for the entire brain were acquired using a 3.0 Tesla Siemens Trio MRI scanner. A T1-weighted localizer scan was performed to generate nine images (three levels of cuts in three different orientations) to verify head placement. Subsequently, full-brain MRI scans were conducted using (1) a 2D multislice spoiled T1 sequence and (2) a 3D T1 sequence (MPrage). The 3D T1 data was collected in the sagittal plane with a TR of 2 ms, TE of 3.7 ms; an inversion angle of 80°, a field of view (FOV) of 214 × 214 mm, and a matrix size of 240 × 240. Phase encoding was done in the anteroposterior direction and from left to right, with a slice thickness of 128 mm, Nav = 1 (number of signal averages), voxel dimensions of 0.89 × 0.89 × 1.0 mm^3, acquisition bandwidth of 191.5 Hz/pixel, and parallel imaging with a SENSE factor of 8. The images were reconstructed using an intra-plane interpolation factor of 2 for each dimension.

The functional images were acquired through a sequence sensitive to BOLD contrast. Two Hundred Forty-One volumes were acquired, each one following the orientation AC-PC (anterior-posterior commissure). Each slice had a resolution of 64 × 64 pixels, and a voxel size of 3.75 × 3.75 × 4 mm^3, with no spacing between slices, and was acquired in an interleaved sequence. The volumes were recorded with a repetition time of 1.5 s, echo time of 35 ms, and a radiofrequency pulse angle of ninety degrees. Two Hundred Forty-One whole brain volumes (4 dummy scans) were acquired at the beginning of the run. The entire run lasted 5:21, and the full session had a duration of around 25 min (Fig. 2).

Stimuli were presented using a laptop with E-prime 3.0 stimulus delivery software (Psychology Software Tools, Pittsburgh, PA) every 4 s in an event related design, with a jittering of ±500 ms, previously proven to be accurate for this kind of experiments (Rossell et al. 2003; Spengler et al. 2009; Wolf et al. 2012). The order of test trials and jitter intervals were optimized using optseq software (https://surfer.nmr.mgh.harvard.edu/optseq/) Using a back-projection system during the fMRI session, participants viewed stimuli via a mirror attached to the head coil. Responses were obtained using a magnet compatible system. The scanner was started 6 s before the behavioral task began to allow for steady state magnetization to be achieved; the resulting initial four scans were discarded. A single run was acquired for this paradigm.

2.3.3. Image processing

Data was processed following the steps of previous work (Alba-Ferrara et al. 2016; Bendersky et al. 2021). Image preprocessing and statistical analyses were performed using the SPM12 software package

Table 2
General neuropsychological evaluation results.

	CTRL	LTLE	RTLE	*One-Way* ANOVA
	M *(SD)*	M *(SD)*	M *(SD)*	*p*
Edinburgh	89.33 % (17.09)	83 % (18.92)	92.14 % (13.11)	0.312
Digit Span[a]	11.81 (2.92)	7.46 (3.41)	6.75 (1.71)	0.000
WAT[a]	5.38 (2.59)	9.67 (3.51)	9.29 (5.81)	0.000
BDI[b]	2.81 (3.12)	11.41 (8.20)	7.35 (8.49)	0.008
STAI-S	13 (5.64)	13.50 (7.69)	15.75 (10.55)	0.667
STAI-T	17.07 (8.06)	20 (12.19)	19.16 (12.04)	0.779

CTRL, healthy controls; LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; M, Mean; S.D., standard deviation; WAT, Word Accentuation Test (number of errors); Edinburgh, Manual dominance; BDI, Beck Depression Inventory; STAI-S, State-Trait Anxiety Inventory-State; STAI-T, State-Trait Anxiety Inventory-Trait.

[a] Difference between the CTRL, with the RTLE and the LTLE groups was significant at $p < 0.001$ (One-Way ANOVA test, Bonferroni post hoc test). The patients groups did not differ between themselves.

[b] Difference between the LTLE with the CTRL, group was significant at $p < 0.05$ (One-Way ANOVA test, Bonferroni post hoc test). The patients groups did not differ between themselves.

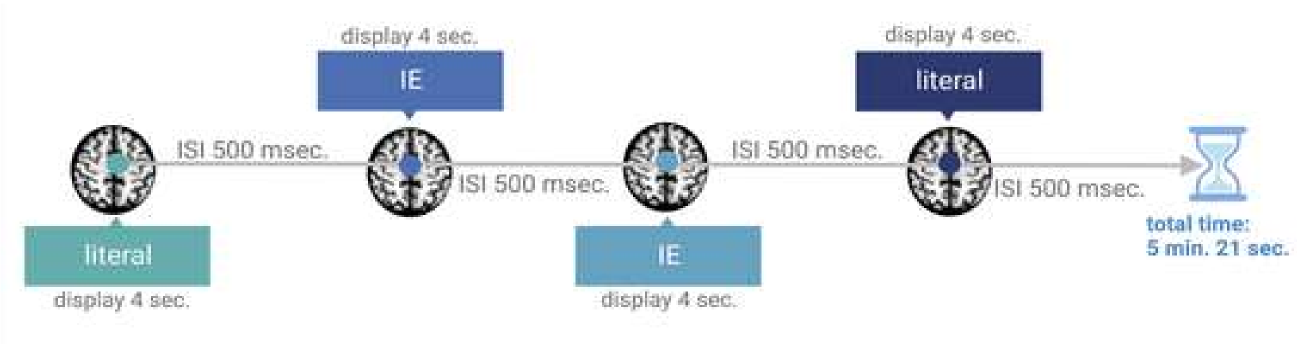

Fig. 2. Image acquisition and stimuli exposure with an event related design.

(https://www.fil.ion.ucl.ac.uk/spm, Wellcome Department of Cognitive Neurology). The functional images were subjected to geometric distortion correction and motion correction. The structural images were co-registered to the mean unwarped and motion corrected functional image for each subject and segmented into gray and white matter images. Functional and structural gray matter images were normalized to Montreal Neurological Institute (MNI) space, and volumes were smoothed with a Gaussian kernel of 8 mm (FWHM). Individual statistics were computed using a general linear model approach as implemented in SPM (Friston et al. 1994; Friston 2003), and a 128 s high-pass filter was used to remove non-physiological slow signal shifts. A random effects analysis was conducted for group averaging and population inference. One image per contrast was computed for each subject from a design matrix that included estimated individual movement parameters as regressors in addition to literal or IE sentence task conditions as explanatory variables. To explore regions specifically activated by IE and literal sentences, t-contrast analysis (SPM12) was performed.

2.3.4. Contrast

A random effects analysis was performed using an established neuroimaging software package (SPM12) to compute contrast image for each participant. Subsequently, we compared two different experimental conditions using t-tests. To correct for multiple comparisons and control the family-wise error rate, we employed a Monte Carlo simulation procedure. This approach leverages the fact that under the null hypothesis of no true activation, the probability of observing large contiguous clusters of activated voxels systematically decreases. Each simulation consisted of 1000 iterations using a 3D matrix representing the brain volume. For each iteration, the voxel values were assigned random numbers drawn from a normal distribution. The spatial extent of any resulting clusters was then calculated. Based on this null distribution of cluster sizes, a threshold was determined such that only clusters larger than this extent would be considered statistically significant at $p < 0.05$, corrected. The locations of significant activations were subsequently identified by an experienced neuroanatomist, who provided labels for the specific gyri and Brodmann areas involved.

2.4. Connectivity analysis

2.4.1. Preprocessing connectivity

Functional and anatomical data were preprocessed using a flexible preprocessing pipeline (Whitfield-Gabrieli and Nieto-Castanon 2012; Nieto-Castanon 2020) including realignment with correction of susceptibility distortion interactions, slice timing correction, outlier detection, direct segmentation, and MNI-space normalization, and smoothing. Functional data were realigned using SPM realign & unwarp procedure, where all scans were co-registered to a reference image (first scan of the first session) using a least squares approach and a six parameter (rigid body) transformation and resampled using b-spline interpolation. Temporal misalignment between different slices of the functional data (acquired in interleaved Siemens order) was corrected following SPM slice timing correction (STC) procedure, using sinc temporal interpolation to resample each slice BOLD timeseries to a common mid-acquisition time. Potential outlier scans were identified using ART as acquisitions with framewise displacement above 0.9 mm or global BOLD signal changes above 5 standard deviations, and a reference BOLD image was computed for each subject by averaging all scans excluding outliers. Functional and anatomical data were normalized into standard MNI space, segmented into grey matter, white matter, and CSF tissue classes, and resampled to 2 mm isotropic voxels following a direct normalization procedure using SPM unified segmentation and normalization algorithm with the default IXI-549 tissue probability map template. Last, functional data were smoothed using spatial convolution with a Gaussian kernel of 8 mm full width half maximum (FWHM).

2.4.2. Denoising connectivity

Additionally, functional data underwent denoising through a standard pipeline. This process involved regressing out various potential confounding effects, including white matter timeseries (10 CompCor components), CSF timeseries (5 CompCor components), motion parameters along with their first-order derivatives (12 factors), outlier scans (below 48 factors), session and task effects with their first-order derivatives (8 factors), and linear trends (2 factors) within each functional run. Following this, bandpass frequency filtering was applied to the BOLD timeseries, targeting frequencies between.01 Hz and 0.1 Hz. CompCor noise components from white matter and CSF were estimated by analyzing the average BOLD signal and the largest principal components orthogonal to the BOLD average, motion parameters, and outlier scans within each subject's eroded segmentation masks. Based on the number of noise terms considered in this denoising approach, the effective degrees of freedom for the BOLD signal post-denoising were estimated to range from 137.5 to 169.9, with an average of 160.5 across all subjects.

2.4.3. Group-level analyses were performed using a generalized psychophysiological interactions

For each voxel, a separate generalized PsychoPhysiological Interaction (gPPI) analysis was conducted, with the first-level connectivity measures for that voxel serving as dependent variables (one independent sample per subject and one measurement per task or experimental condition, if applicable), and group or subject-level identifiers acting as independent variables (Nieto-Castanon, 2020). Hypotheses at the voxel level were tested using multivariate parametric statistics, incorporating random effects across subjects and covariance estimation from multiple measurements. Statistical inference was performed at the cluster level, where clusters were defined as groups of contiguous voxels. These cluster-level inferences were based on parametric statistics derived from Gaussian Random Field theory. Results were considered significant using a combined approach of a voxel-level threshold with $p < 0.001$ for cluster formation and corrected p-FDR < 0.05 for cluster size. Based on the results obtained from the analysis in SPM12 we defined the Regions of Interest (ROIs) for further CONN Toolbox analysis. ROIs were defined anatomically using the default atlas used in CONN (a combination of the Harvard-Oxford and AAL atlas). For CTRLs, we traced the connectivity of the left operculum, left and right fusiform gyrus, left pars triangularis, left and right angular gyrus, and right superior temporal gyrus. For patients with RTLE, the connectivity of the left operculum, left medial frontal gyrus, left inferior occipital gyrus, right superior middle gyrus, right medial temporal gyrus, right frontal pole, right precentral gyrus, and right anterior superior temporal gyrus was tracked down. For patients with LTLE, we traced the connectivity of the left medial frontal gyrus, left and right precentral gyrus, left and right angular gyrus, right inferior occipital gyrus, right medial temporal gyrus, right superior temporal gyrus, and right fusiform gyrus. Once the ROIs were delimited, positive connections (probability of a region becoming active increases when the ROI is activated) and negative connections (probability of a region becoming deactivated increases when the ROI is activated) were compared.

3. Results

3.1. Behavioral results

All three groups successfully completed the task. Two One-Way ANOVAs showed that there were no significant differences between groups in accuracy. Nevertheless, reaction times were significantly higher in RTLE and LTLE compared to CTRL (Table 3).

3.2. SPM results

3.2.1. Activations in the whole sample

An analysis encompassing the entire sample and collapsing the three groups revealed cortical activity network for IE in comparison to literal sentences within specific regions, including both the bilateral frontal cortex (which encompassed the pars triangularis of the inferior frontal gyrus in both hemispheres and the pars orbitalis of the left inferior frontal gyrus), the right middle frontal gyrus, and the left superior frontal gyrus. This heightened activity further extended to prefrontal areas BA 9 and 10, as well as the posterior segment of the superior temporal gyrus in both hemispheres. Additionally, increased activity was detected in the right anterior insula, and within the left hemisphere, in regions like the supramarginal/angular gyrus and the fusiform gyrus (Table 4, and Figure 3).

Activation of each group during the language task in fMRI. From top to bottom of the figure, the activations of all groups are represented together (Full Sample), the activation of LTLE compared to CTRL (LTLE-CTRL), and the activation of RTLE compared to CTRL (RTLE-CTRL).

Table 3
Overview of the behavioral results of the IE task.

	CTRL M (SD)	LTLE M (SD)	RTLE M (SD)	*One-way ANOVA p*
Accuracy	62 % (27)	47 % (18)	47 % (21)	0.089
Reaction Time*	2206 (887)	3029 (282)	3083 (369)	0.001

CTRL, healthy controls; LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; S.D., standard deviation.
*significant differences between the CTRL group, and the RTLE and LTLE groups were found in the reaction time.

Table 4
Overview of results obtained during IE vs. literal sentences contrast ($p < 0.005$).

Region label	*hemisphere*	*BA*	*k*	*Z*	*Peak (MNI coordinates)*		
					x	*y*	*z*
Fusiform	L	37	303	3.49	−34	−46	−20
MFG	R	9	57	3.41	10	48	28
Parahippocampal	R	36	397	3.29	18	−42	−11
Prefrontal	L	10	220	3.21	−14	42	−6
Prefrontal	R	9	136	2.81	22	38	26
IFG Triangularis	L	45	126	2.70	−28	22	12

References: R, right; L, left; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; T, peak level; k, cluster size in the number of voxels; MNI, Montreal Neurological Institute.

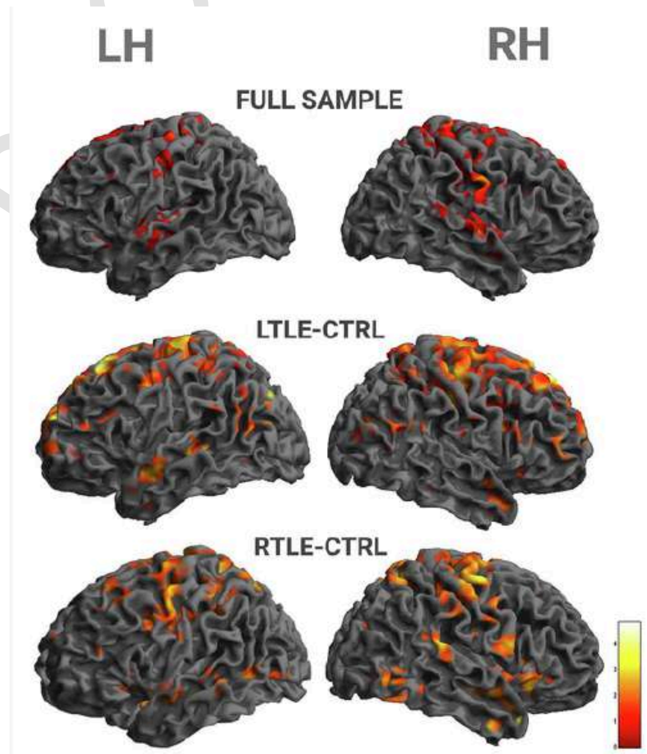

Fig. 3. Overview of every comparison result obtained during IE >Literal contrast ($p < .001$).

3.2.2. CTRL group

The contrast CTRL minus TLE (right and left together) showed no differences, however, when performing the reverse comparison, additional activations were found in the angular and fusiform gyrus, bilaterally; in the right dorsolateral prefrontal cortex (BA 9) and superior temporal gyrus; and in the left dorsolateral prefrontal cortex (BA 46) and IFG-pars orbitalis (BA 47) (See Supplementary material).

3.2.3. Patients with LTLE compared to CTRL

Patients with LTLE presented more extensive activations of the prefrontal gyrus than CTRLs, predominantly on the left hemisphere (Table 5, and Fig. 3). Additional activations were found in other language-related areas such as the right supramarginal and in the angular gyrus in both hemispheres, as well as in the left lateral temporal cortex (STG and MTG).

Table 5
Overview of the results obtained comparing LTLE vs CTRL ($p < 0.05$).

Region label	*hemisphere*	*BA*	*kE*	*Z*	*Peak (MNI coordinates)*		
					x	*y*	*z*
Precentral	L	8	18,994	4.27	−8	40	50
Precentral	R	8	614	3.19	36	4	−32
STG	L	22	413	2.68	−54	−28	−2
MTG	L	21	1607	3.15	−56	−6	−16
Supramarg	R	40	82	2.92	64	−44	28
Angular	R	39	82	1.76	56	−52	32
Angular	L	39	73	2.82	−32	−80	36
Inferior Occipital	R	19	86	2.37	40	−80	24

References: R, right; L, left; STG, superior temporal gyrus; MTG, middle temporal gyrus; Supramarg, supramarginal gyrus; T, peak level; k, cluster size in the number of voxels; MNI, Montreal Neurological Institute.

3.2.4. Patients with RTLE compared to CTRL

Compared to CTRL, RTLE activated additional frontotemporal areas in the RH: STG and MTG, PMA/SMA, prefrontal, precentral, and MFG, and in the supramarginal gyrus. In the LH, weaker activations were found in the anterior MFG, inferior occipital gyrus, and pars opercularis of the IFG (Table 6 and Fig. 3).

3.3. Functional connectivity results

Our findings showed different patterns of abnormal connectivity in epilepsy patients (Fig. 4): Patients with TLE obtained more positive connections (red dots) than the CTRL. The CTRLs showed more negative connections (blue dots) than the patients with RTLE and LTLE. RTLE had a more widespread inter and intrahemispheric network, with additional recruitment and connectivity of areas not activated or moreover, deactivated by CTRL. Connectivity abnormalities in LTLE were less pronounced and predominantly intrahemispheric. To visualize the specific connectivity results for each ROI, please refer to the supplementary material.

Connectivity of the ROIs for each group during the language task in fMRI. The red points represent positive connectivity, indicating a greater probability of activation in one ROI when another ROI is activated. The blue points represent negative connectivity, signifying a lower probability of activation in other ROIs when one ROI is activated. The lines connecting the points represent the correlation between areas. FP, Frontal Pole; FUS, Fusiform Gyrus; IO, Inferior Occipital Gyrus; MFG, Middle Frontal Gyrus; OP, Pars Opercularis; PHIP, Parahippocampal; PREC, Precuneus; SMG, Supramarginal Gyrus; STA, Superior Temporal Gyrus, Anterior Part; STG, Superior Temporal Gyrus; TR, Pars Triangularis.

Table 6
Overview of the results obtained comparing RTLE vs CTRL (FWE $p < 0.05$).

Region label	*hemisphere*	*BA*	*kE*	*Z*	*Peak (MNI coordinates)*		
					x	*y*	*z*
STG	R	22	164	2.89	64	−38	20
MTG	R	21	164	1.99	66	−44	6
PMA-SMA	R	6	136	2.63	60	6	18
Prefrontal	R	8	99	2.18	26	28	44
Supramarg	R	40	108	2.16	58	−32	44
Precentral	R	4	24	2.14	62	−8	36
MFG	R	9	101	2.10	24	38	30
Anterior MFG	L	46	57	2.06	−40	38	20
Inferior occipital	L	19	64	1.95	−16	−94	0
IFG opercular	L	44	19	1.95	−40	6	6

References: R, right; L, left; STG; superior temporal gyrus; MTG, middle temporal gyrus; MFG: middle frontal gyrus; IFG: inferior frontal gyrus; Supramarg, supramarginal gyrus; PMA-SMA, premotor area-supplementary motor area; T, peak level; k, cluster size in the number of voxels; MNI, Montreal Neurological Institute.

4. Discussion

The present study aimed to investigate the neural circuit underlying pragmatic language comprehension in patients with chronic epilepsy of the right and left temporal lobes, as compared to healthy CTRLs, using a behavioral task in fMRI. Subsequently, differences in functional connectivity were explored within each specific sample. From the behavioral data, it was observed that all three groups performed the IE similarly (Table 3), but differences in fMRI activation emerged (Fig. 3 and Tables 4, 5, and 6), which became more pronounced in the analysis of functional connectivity (see Fig. 4 and supplementary material CONN). We found distinct connectivity patterns between the CTRL and TLE groups. Our results show that patients with drug-resistant TLE have bilateral, temporal and extratemporal functional connectivity alterations. These alterations may be indicative of the cerebral plasticity present in epilepsy.

4.1. Representation of idiomatic expressions and their working network

Given the importance of IE during social communication, it is necessary to reveal the working network that organizes the subfunction of pragmatic language. Although functional connectivity in this psychophysiological interaction does not directly inform about the directionality of the connection and the network is composed of several nodes, the literature offers us some hints to integrate our findings into a mechanistic model of IE neural processing. For a better understanding of the working network, some nodes that show activation but belong to another cognitive function (e.g., primary visual cortex) will be omitted.

Network processing pragmatic language, including the fusiform gyrus (FusG), middle frontal gyrus (MFG), prefrontal cortex (PFG), posterior parahippocampal region (PHG), parahippocampal gyrus (Phipp), and pars triangularis (Tri). In patients with TLE, language functions can be reconfigured and redistributed to contralateral homologous areas (for both right and left hemisphere). These changes reflect how TLE affects language processing.

IE processing seems to start in (1) the fusiform gyrus, involved in the visual processing of language, which is coupled with the pars triangularis to capture the crucial semantic and grammatical aspects for identifying idiomatic expressions, detecting the frequency and familiarity of words (Schaffler et al. 1994). Colloquial semantics play a significant role in the identification of idiomatic expressions. If a culturally unfamiliar synonym is used, the phrase may lack the intended pragmatic sense (e.g., saying 'crack the ice' is different from 'break the ice'). Moving on, (2) the pars triangularis captures the sentence grammatical structure. Both areas (1 & 2) show high positive connectivity – they activate simultaneously – with adjacent white matter and association areas. The (3) middle frontal gyrus, associated with verbal and non-verbal semantics,(Castellucci et al. 2022) couples with the pars triangularis and fusiform gyrus to identify IE. On the other hand, the prefrontal cortex plays a broad role in cognition and learning, (Geranmayeh et al. 2014) associated with IE identification and specifically related to task execution. PFC may monitor and decide whether to ignore the literal meaning and focus on the figurative one, or not. Lastly, (4) the right parahippocampal gyrus is linked to adding social context – involved in object memory – to a situation and it could be a crucial key not only in interpreting idiomatic expressions but also in understanding humor or sarcasm in communication (Rankin et al. 2009) (Fig. 5). A recent study has detected deactivation in the parahippocampal gyrus in persons with autism (Mouga et al. 2022), identifying the zone as a key area for making sense of social context. In the CONN analysis, the posterior parahippocampal region showed only negative connectivity (low probability of presenting activity with other areas at the same moment), suggesting that it may work with greater independence. While it is possible to hierarchically order some of these mentioned zones – e.g., the fusiform gyrus involved in visual processing would activate before the right parahippocampal gyrus – at some point, it can be inferred that all these

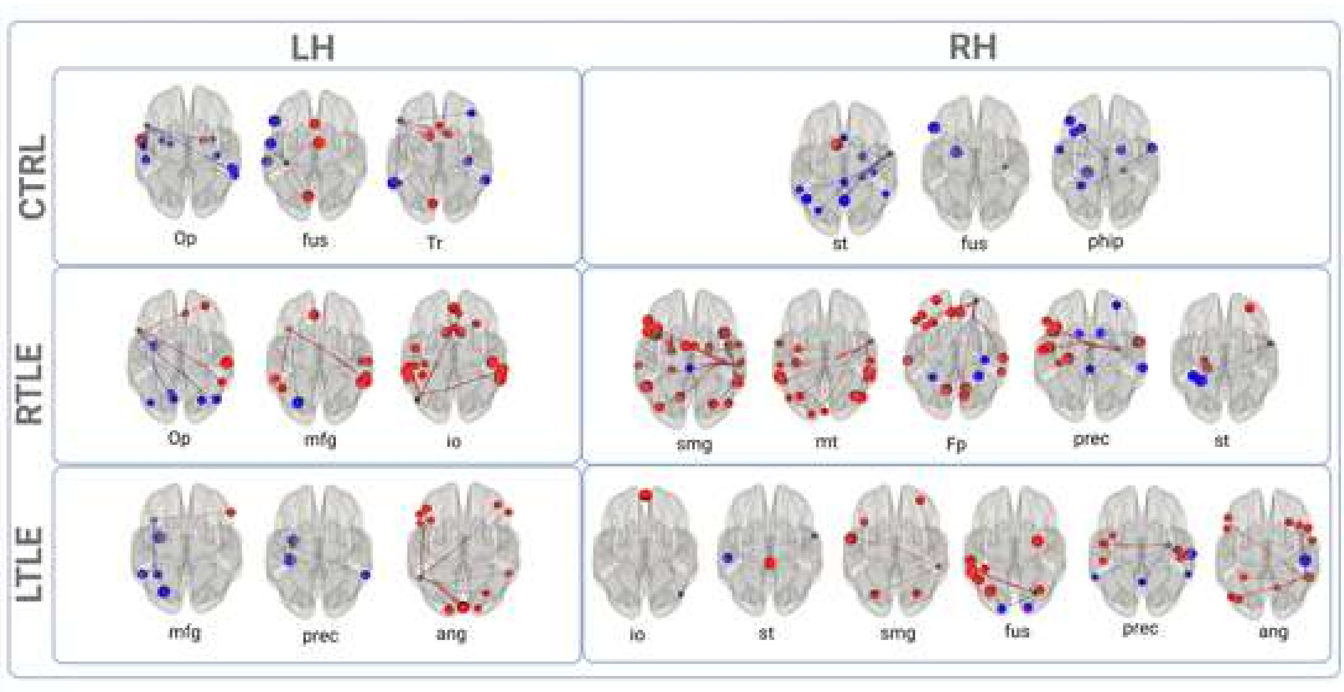

Fig. 4. Functional connectivity of CTRL, RTLE & LTLE.

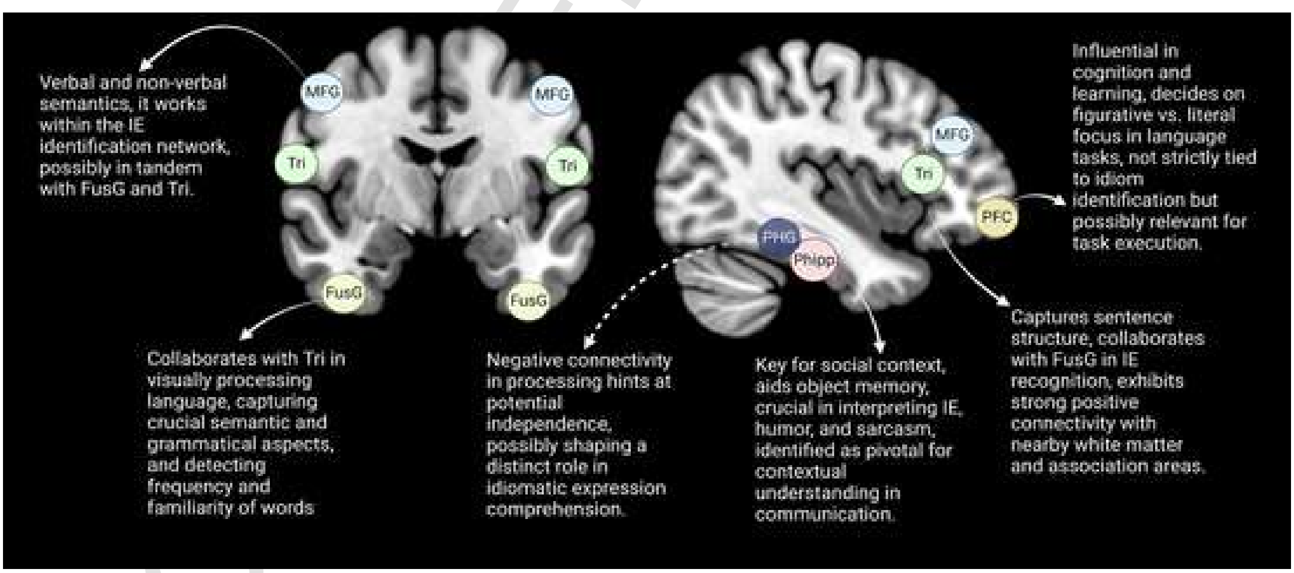

Fig. 5. Pragmatic language processing network.

zones work together as nodes but processing different information. Certain areas, such as the fusiform gyrus, are thought to relate to primary processing, and thus it may process the stimuli before the nodes in charge of high level cognitive operations. Our results demonstrate that these ROIs work interconnected, contributing to the holistic understanding of idiomatic expressions. Our analysis poses challenges associated with determining temporality in functional connectivity analysis, necessitating the formulation of a hypothesis about the sequential order of activations in understanding the activation time-course of different brain regions contributes to the overall comprehension of idiomatic expressions during social communication. Therefore, an interdependent network model allows us to comprehend the reorganization of the neural circuitry in LTLE. It should be noted that, compared to TLE patients, the CTRL group presented a smaller set of activated areas, but with higher Z values compared to the patients.

4.2. Pragmatic language in TLE

Language is supported by a large, flexible cerebral network distributed within and across hemispheres, that due to the long duration of refractory epilepsy, may be reorganized to maintain functionality. A high incidence of atypical language representation in TLE has been described (Goldmann and Golby 2005; Bonelli et al. 2012).

TLE patients showed activation patterns similar to CTRL individuals, albeit more widespread and with positive rather than negative connectivity. Patients were capable of compensating for the damage caused by chronic epilepsy (lasting over 15 years) or long-term medication, but they required connecting a greater number of nodes to achieve successful performance. The TLE groups exhibited a more extensive set of activations, with a tendency toward regions in the right hemisphere, especially in patients with LTLE. On the other hand, the RTLE presented activations similar to LTLE but with more positive inter- and intrahemispheric connectivity. The RTLE group also recruited areas involved in pragmatic language processing. While the STG is typically associated with phonological tasks in CTRL individuals, its damage in epilepsy leads to word naming problems (Sone et al. 2022). The middle temporal gyrus (MTG), involved in word association tasks (Barnett et al. 2014), was also activated. Another area that showed activation was the angular gyrus, a key area for semantic processing and word comprehension, as well as reasoning and social cognition (Seghier, 2013). Additional activations were found in other regions, such as the precuneus, which connects language zones through the superior longitudinal fasciculus, the frontal pole connected by the uncinate fasciculus, or the inferior occipital sulcus connected by the inferior fronto-occipital ventrolateral fasciculus (Binding et al. 2022). Lastly, activations in our epilepsy patients were found in some putative language or working memory related areas, such as prefrontal cortex, SMA or PMA, zones that exhibit high connectivity with hippocampal and parahippocampal areas (Laufs et al. 2014).

Patients with LTLE recruited additional lateral temporal areas in the left hemisphere, suggesting intrahemispheric reorganization; while RTLE patients also activated mirrored language-related areas in the right hemisphere, such as the supramarginal and angular gyri, and in the fusiform gyrus. The overlapping recruitment of these regions indicates the involvement of various systems that support pragmatic language, which are activated when the primary network is compromised. A comparable reorganization was observed in patients with stroke (Saur 2006). This phenomenon has been reported in patients with epilepsy regarding naming or verbal fluency, located in the main language areas (Bell et al. 2002; Hamberger and Cole 2011; Berl et al. 2014; Tzourio-Mazoyer et al. 2017). A previous work of our group reported plasticity in areas related to prosody in epilepsy patients (Elizalde Acevedo et al. 2022). Our present results showed that pragmatic language areas were remodeled as well.

4.3. Comparison of CTRL and TLE

Perhaps, modular models successfully explain the brain correlates of cognitive functions under normal conditions, but once plasticity mechanisms are triggered by a lesion (structural or functional), connectionist models seem more accurate to describe spread-out neural networks recruited to perform a task. Participants with RTLE showed a significantly stronger positive correlation compared to the CTRL– in the SMG, STG, MTG, and angular gyrus. Instead, CTRL use a more succinct network to perform the task. Despite the impact of the disease, patients with RTLE managed to reorganize brain activity.

Regarding the phenomenon of reorganization, it is worth considering that studies by Hamberger (2011) hypothesize that TLE patients have an intrahemispheric reorganization of language functions if it began before the critical window of plasticity before the age of five. In contrast, our study includes patients with an average of around 10 years since the onset of epilepsy. This could be related to the signs of interhemispheric reorganization observed in connectivity results, particularly in how TLE patients exhibit positive connectivity – more activity correlated with other language-related zones but in the opposite hemisphere –compared to CTRL individuals.

Unlike aphasic syndromes, the brain's organization of pragmatic language has not been extensively researched, even in healthy individuals. In cases of epilepsy and similar conditions, deficits can arise following damage to either the left or right hemisphere (whether structural or functional), due to the engagement of various intra- and interhemispheric regions in the processing of pragmatic language. Pragmatic language consists of words that can mean something different from the literal sum of their (semantic and syntactic) components (Gibbs Jr 2008; Rapp et al. 2012; Reyes-Aguilar et al. 2018). This idea allows us to understand the processing of IE as a juxtaposition of different cognitive abilities involving language, perception, memory, emotions, and executive functions.

Due to its dependence and connection with the organization of general semantics (as a suprasegmental function), it is expected that pragmatic language reorganizes in other areas that can also carry out an IE task. This supports the notion that the lateralization of language functions may be more relative than absolute in epilepsy (Friederici and Alter 2004).

Much of the literature on fMRI and epilepsy treats language as a unified and indivisible entity that either shifts to the right hemisphere or remains lateralized to the left. However, language consists of various components and distinct subdomains that may reorganize either collectively or independently: some aspects of it may reorganize while others do not, so it is important to assess different language components, as pragmatics besides evaluating the hemispheric specialization for nomination or verbal fluency. Moreover, given the complexity of the language network, and the interindividual variability, personalized patterns of reorganization should be assessed for those patients undergoing brain surgery.

Our results show that there is a wide reorganization of the pragmatic language network in patients with chronic temporal lobe epilepsy, not only in LTLE but in RTLE as well. This is not surprising, as the pragmatic network in healthy subjects includes frontotemporal areas in both hemispheres. Nevertheless, the reorganization of language function differed between patients with RTLE and LTLE. Recent investigations about connectivity in patients with unilateral epileptogenic zones showed that lesions on either the left or right side may lead to distinct and specific effects on cerebral connectivity (Neudorf et al. 2020). In patients who will be surgically treated, it is of keen interest to understand pre-surgical language function and to estimate the risk for post-surgical language decline. In a broader sense, brain mapping of language before surgery serves two primary objectives: (a) to elucidate language networks and to establish hemisphere specialization, and (b) to pinpoint areas susceptible to surgical intervention, whose removal could result in aphasia or other language-related deficits.

Measures of broadly distributed, bilateral functional global networks have predictive power for postsurgical outcomes (Audrain et al. 2018). For patients with epilepsy, examining language networks with fMRI during different tasks provides a valuable chance to investigate the variability in the organization and reorganization of language.

5. Conclusion

The present study utilized fMRI to investigate the comprehension of IE, a subfunction of pragmatic language in patients with drug-resistant TLE compared to a CTRL group. The results revealed significant differences in neural activation patterns and connectivity between the two groups during an IE comprehension task. For the CTRL group, IE comprehension primarily engaged a bilateral frontotemporal network, lateralized to the right hemisphere. These individuals exhibited greater inhibitory connectivity and more modular activations, suggesting an efficient and economical process for pragmatic language comprehension. In contrast, TLE patients demonstrated more widespread neural activation, involving frontal, temporal, and insular areas in both hemispheres. This additional activation suggests compensatory neural recruitment due to epilepsy. Additionally, these patients exhibited greater excitatory connectivity and more connections between brain regions, possibly indicating the need to utilize alternative brain areas for pragmatic language comprehension. However, this trade-off may involve higher neural costs and lower overall efficiency—potentially reflected in RTs—during IE processing.

This study provides valuable insights into the neural mechanisms underlying IE comprehension in patients with drug-resistant TLE and healthy individuals. These findings may have important implications for the design of interventions and therapies aimed at improving language processing in patients with this neurological condition.

Author contributions

All authors have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design analysis, writing, or revision of the manuscript and have any conflict of interest to disclose.

B. Elizalde Acevedo drafted the first version of the manuscript and carried out data recollection, analysis, and interpretation of the results.

S. Kochen assisted with participant recruitment and revised the manuscript critically.

L. Alba-Ferrara & M. Bendersky designed the study and revised the manuscript critically for important intellectual content.

Funding

The research did not receive any specific grant.

Uncited references

Cacciari and Tabossi (2014b), Gibbs (2008), Schaffler et al. (1994), Seghier (2013a), Seghier (2013b), Slotnick and Schacter (2004).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2024.12.012.

References

Abusamra, V., Côté, H., Joanette, Y., Ferreres, A., 2009. Communication impairments in patients with right hemisphere damage. Life Span Disabil. 12 (1), 67–82.

Alba-Ferrara, L., Müller-Oehring, E.M., Sullivan, E.V., Pfefferbaum, A., Schulte, T., 2016. Brain responses to emotional salience and reward in alcohol use disorder. Brain Imaging Behav. 10 (1), 136–146. https://doi.org/10.1007/s11682-015-9374-8.

Alba-Ferrara, L., Kochen, S., Hausmann, M., 2018. Emotional prosody processing in epilepsy: some insights on brain reorganization. Front Hum Neurosci. 12 (March), 1–11. https://doi.org/10.3389/fnhum.2018.00092.

Allone, C., Lo Buono, V., Corallo, F., Pisani, L.R., Pollicino, P., Bramanti, P., Marino, S., 2017. Neuroimaging and cognitive functions in temporal lobe epilepsy: a review of the literature. J Neurol Sci. 381, 7–15. https://doi.org/10.1016/j.jns.2017.08.007. https://linkinghub.elsevier.com/retrieve/pii/S0022510X17304926.

American Psychiatric Association. 2014. DSM-5. Manual Diagnostico y estadistico de los trastornos mentales(DSM 5).:50–59.

Audrain, S., Barnett, A.J., McAndrews, M.P., 2018. Language network measures at rest indicate individual differences in naming decline after anterior temporal lobe resection. Hum Brain Mapp. 39 (11), 4404–4419. https://doi.org/10.1002/hbm.24281.

Baciu, M., Perrone-Bertolotti, M., 2015. What do patients with epilepsy tell us about language dynamics? A review of fMRI studies. Rev Neurosci. 26 (3). https://doi.org/10.1515/revneuro-2014-0074.

Baciu, M.V., Watson, J.M., McDermott, K.B., Wetzel, R.D., Attarian, H., Moran, C.J., Ojemann, J.G., 2003. Functional MRI reveals an interhemispheric dissociation of frontal and temporal language regions in a patient with focal epilepsy. Epilepsy Behav. 4 (6), 776–780. https://doi.org/10.1016/j.yebeh.2003.08.002. https://linkinghub.elsevier.com/retrieve/pii/S152550500300204X.

Balter, S., Lin, G., Leyden, K.M., Paul, B.M., McDonald, C.R., 2019. Neuroimaging correlates of language network impairment and reorganization in temporal lobe epilepsy. Brain Lang. 193, 31–44. https://doi.org/10.1016/j.bandl.2016.06.002.

Bambini, V., Gentili, C., Ricciardi, E., Bertinetto, P.M., Pietrini, P., 2011. Decomposing metaphor processing at the cognitive and neural level through functional magnetic resonance imaging. Brain Res Bull. 86 (3–4), 203–216. https://doi.org/10.1016/j.brainresbull.2011.07.015.

Bambini, V., Bertini, C., Schaeken, W., Stella, A., Di Russo, F., 2016. Disentangling metaphor from context: an ERP study. Front Psychol. 7, 559. https://doi.org/10.3389/fpsyg.2016.00559.

Bara, B.G., Bosco, F.M., Bucciarelli, M., 1999. Developmental pragmatics in normal and abnormal children. Brain Lang. 68 (3), 507–528. https://doi.org/10.1006/brln.1999.2125.

Barnett, A., Marty-Dugas, J., McAndrews, M.P., 2014. Advantages of sentence-level fMRI language tasks in presurgical language mapping for temporal lobe epilepsy. Epilepsy Behav. 32, 114–120. https://doi.org/10.1016/j.yebeh.2014.01.010.

Bell, B.D., Davies, K.G., Hermann, B.P., Walters, G., 2000. Confrontation naming after anterior temporal lobectomy is related to age of acquisition of the object names. Neuropsychologia 38 (1), 83–92. https://doi.org/10.1016/s0028-3932(99)00047-0.

Bell, B.D., Hermann, B.P., Woodard, A.R., Jones, J.E., Rutecki, P.A., Sheth, R., Dow, C.C., Seidenberg, M., 2001. Object naming and semantic knowledge in temporal lobe epilepsy. Neuropsychology 15 (4), 434–443. https://doi.org/10.1037/0894-4105.15.4.434.

Bell, B., Hermann, B., Seidenberg, M., Davies, K., Cariski, D., Rosenbek, J., Woodard, A., Rutecki, P., Bishop, M., 2002. Ipsilateral reorganization of language in early-onset left temporal lobe epilepsy. Epilepsy Behav. 3 (2), 158–164. https://doi.org/10.1006/ebeh.2002.0322.

Bell, B., Lin, J.J., Seidenberg, M., Hermann, B., 2011. The neurobiology of cognitive disorders in temporal lobe epilepsy. Nat Rev Neurol. 7 (3), 154–164. https://doi.org/10.1038/nrneurol.2011.3.

Bendersky, M., Lomlomdjian, C., Abusamra, V., Elizalde Acevedo, B., Kochen, S., Alba-Ferrara, L., 2021. Functional anatomy of idiomatic expressions. Brain Topogr. 34 (4), 489–503. https://doi.org/10.1007/s10548-021-00843-3.

Berg, A.T., Berkovic, S.F., Brodie, M.J., Buchhalter, J., Cross, J.H., van Emde, B.W., Engel, J., French, J., Glauser, T.A., Mathern, G.W., et al., 2010. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE commission on classification and terminology, 2005-2009. Epilepsia 51 (4), 676–685. https://doi.org/10.1111/j.1528-1167.2010.02522.x.

Berl, M.M., Balsamo, L.M., Xu, B., Moore, E.N., Weinstein, S.L., Conry, J.A., Pearl, P.L., Sachs, B.C., Grandin, C.B., Frattali, C., et al., 2005. Seizure focus affects regional language networks assessed by fMRI. Neurology 65 (10), 1604–1611. https://doi.org/10.1212/01.wnl.0000184502.06647.28.

Berl, M.M., Zimmaro, L.A., Khan, O.I., Dustin, I., Ritzl, E., Duke, E.S., Sepeta, L.N., Sato, S., Theodore, W.H., Gaillard, W.D., 2014. Characterization of atypical language activation patterns in focal epilepsy. Ann Neurol. 75 (1), 33–42. https://doi.org/10.1002/ana.24015.

Besag, F.M.C., Vasey, M.J., 2021. Neurocognitive effects of antiseizure medications in children and adolescents with epilepsy. Paediatr Drugs. 23 (3), 253–286. https://doi.org/10.1007/s40272-021-00448-0.

Binder, J.R., Gross, W.L., Allendorfer, J.B., Bonilha, L., Chapin, J., Edwards, J.C., Grabowski, T.J., Langfitt, J.T., Loring, D.W., Lowe, M.J., et al., 2011. Mapping anterior temporal lobe language areas with fMRI: a multicenter normative study. Neuroimage 54 (2), 1465–1475. https://doi.org/10.1016/j.neuroimage.2010.09.048.

Binding, L.P., Dasgupta, D., Giampiccolo, D., Duncan, J.S., Vos, S.B., 2022. Structure and function of language networks in temporal lobe epilepsy. Epilepsia 63 (5), 1025–1040. https://doi.org/10.1111/epi.17204.

Bishop, D.V., Baird, G., 2001. Parent and teacher report of pragmatic aspects of communication: use of the children's communication checklist in a clinical setting. Dev Med Child Neurol. 43 (12), 809–818. https://doi.org/10.1017/s0012162201001475.

Bobrow, S.A., Bell, S.M., 1973. On catching on to idiomatic expressions. Mem Cognit. 1 (3), 343–346. https://doi.org/10.3758/BF03198118.

Bonelli, S.B., Thompson, P.J., Yogarajah, M., Vollmar, C., Powell, R.H.W., Symms, M.R., McEvoy, A.W., Micallef, C., Koepp, M.J., Duncan, J.S., 2012. Imaging language networks before and after anterior temporal lobe resection: results of a longitudinal fMRI study. Epilepsia 53 (4), 639–650. https://doi.org/10.1111/j.1528-1167.2012.03433.x.

Bonilha, L., Nesland, T., Martz, G.U., Joseph, J.E., Spampinato, M.V., Edwards, J.C., Tabesh, A., 2012. Medial temporal lobe epilepsy is associated with neuronal fibre loss and paradoxical increase in structural connectivity of limbic structures. J Neurol Neurosurg Psychiatry. 83 (9), 903–909. https://doi.org/10.1136/jnnp-2012-302476.

Brázdil, M., Zákopčan, J., Kuba, R., Fanfrdlová, Z., Rektor, I., 2003. Atypical hemispheric language dominance in left temporal lobe epilepsy as a result of the reorganization of language functions. Epilepsy Behav. 4 (4), 414–419. https://doi.org/10.1016/S1525-5050(03)00119-7.

Brenlla, M.E., Rodríguez, C.M., 2006. Adaptación argentina del Inventario de Depresión de Beck (BDI-II). BDI-II Inventario de depresión de Beck.:11–37.

Buela-Casal, G., Guillén-Riquelme, A., Seisdedos Cubero, N., 2011. Cuestionario de ansiedad estado-rasgo: Adaptación española. Madrid: TEA Ediciones.

Busch, R.M., Frazier, T.W., Haggerty, K.A., Kubu, C.S., 2005. Utility of the Boston naming test in predicting ultimate side of surgery in patients with medically intractable temporal lobe epilepsy. Epilepsia 46 (11), 1773–1779. https://doi.org/10.1111/j.1528-1167.2005.00300.x.

Cacciari, C., Glucksberg, S., 1994. Understanding figurative language. In: Gernsbacher, M.A., editor. Handbook of psycholinguistics. Academic Press. p. 447–477.

Cacciari, C., Tabossi, P., 2014b. Idioms. Cacciari C, Tabossi P, Cacciari C, editors. Psychology Press.

Cacciari, C., Tabossi, P., 1988. The comprehension of idioms. J Mem Lang. 27 (6), 668–683. https://doi.org/10.1016/0749-596X(88)90014-9.

Cacciari, C., Tabossi, P., 2014. Idioms: Processing, structure, and interpretation. Psychology Press.

Castellucci, G.A., Kovach, C.K., Howard, M.A., Greenlee, J.D.W., Long, M.A., 2022. A speech planning network for interactive language use. Nature 602 (7895), 117–122. https://doi.org/10.1038/s41586-021-04270-z.
Catani, M., Bambini, V., 2014. A model for social communication and language evolution and development (SCALED). Curr Opin Neurobiol. 28, 165–171. https://doi.org/10.1016/j.conb.2014.07.018.
Catani, M., Jones, D.K., ffytche, D.H., 2005. Perisylvian language networks of the human brain. Ann Neurol. 57 (1), 8–16. https://doi.org/10.1002/ana.20319.
Caverzasi, E., Papinutto, N., Amirbekian, B., Berger, M.S., Henry, R.G., 2014. Q-ball of inferior fronto-occipital fasciculus and beyond. PLoS One 9 (6). https://doi.org/10.1371/journal.pone.0100274.
Chahboun, S., Vulchanov, V., Saldaña, D., Eshuis, H., Vulchanova, M., 2016. Can you play with fire and not hurt yourself? A comparative study in figurative language comprehension between individuals with and without autism spectrum disorder. PLoS One 11 (12), 1–24. https://doi.org/10.1371/journal.pone.0168571.
Chang, Y.-H.-A., Kemmotsu, N., Leyden, K.M., Kucukboyaci, N.E., Iragui, V.J., Tecoma, E.S., Kansal, L., Norman, M.A., Compton, R., Ehrlich, T.J., et al., 2017. Multimodal imaging of language reorganization in patients with left temporal lobe epilepsy. Brain Lang. 170, 82–92. https://doi.org/10.1016/j.bandl.2017.03.012.
Cheang, H.S., Pell, M.D., 2006. A study of humour and communicative intention following right hemisphere stroke. Clin Linguist Phon. 20 (6), 447–462. https://doi.org/10.1080/02699200500135684.
Coulson, S., Van Petten, C., 2007. A special role for the right hemisphere in metaphor comprehension? Brain Res. 1146, 128–145. https://doi.org/10.1016/j.brainres.2007.03.008.
D'Ouakil, B.G., 2012. Foundations of language. Thought. 15 (3), 534–535. https://doi.org/10.5840/thought1940153101.
Dabbs, K., Jones, J., Seidenberg, M., Hermann, B., 2009. Neuroanatomical correlates of cognitive phenotypes in temporal lobe epilepsy. Epilepsy Behav. 15 (4), 445–451. https://doi.org/10.1016/j.yebeh.2009.05.012.
Davies, K.G., Bell, B.D., Bush, A.J., Hermann, B.P., Curtis Dohan, F., Jaap, A.S., 1998. Naming decline after left anterior temporal lobectomy correlates with pathological status of resected hippocampus. Epilepsia 39 (4), 407–419. https://doi.org/10.1111/j.1528-1157.1998.tb01393.x.
Del Ser, T., González-Montalvo, J.I., Martínez-Espinosa, S., Delgado-Villapalos, C., Bermejo, F., 1997. Estimation of premorbid intelligence in Spanish people with the word accentuation test and its application to the diagnosis of dementia. Brain Cogn. 33 (3), 343–356. https://doi.org/10.1006/brcg.1997.0877.
Duchowny, M., Jayakar, P., Harvey, A.S., Resnick, T., Alvarez, L., Dean, P., Levin, B., 1996. Language cortex representation: effects of developmental versus acquired pathology. Ann Neurol. 40 (1), 31–38. https://doi.org/10.1002/ana.410400108.
Elizalde Acevedo, B., Olano, M.A., Bendersky, M., Kochen, S., Agüero Vera, V., Chambeaud, N., Gargiulo, M., Sabatte, J., Gargiulo, Á., Alba-Ferrara, L., 2022. Brain mapping of emotional prosody in patients with drug-resistant temporal epilepsy: An indicator of plasticity. Cortex 153, 97–109. https://doi.org/10.1016/j.cortex.2022.04.014.
Engel, J., 1998. Etiology as a risk factor for medically refractory epilepsy: a case for early surgical intervention. Neurology 51 (5), 1243–1244. https://doi.org/10.1212/WNL.51.5.1243.
Ferré, P., Fonseca, R.P., Ska, B., Joanette, Y., 2012. Communicative clusters after a right-hemisphere stroke: are there universal clinical profiles? Folia Phoniatr Logop. 64 (4), 199–207. https://doi.org/10.1159/000340017.
First, M., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1999. Entrevista clínica estructurada para los trastornos del eje I del DSM-IV: SCID-I. Masson.
Friederici, A.D., Alter, K., 2004. Lateralization of auditory language functions: a dynamic dual pathway model. Brain Lang. 89 (2), 267–276. https://doi.org/10.1016/S0093-934X(03)00351-1.
Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.-P., Frith, C.D., Frackowiak, R.S.J., 1994. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp. 2 (4), 189–210. https://doi.org/10.1002/hbm.460020402.
Friston, K.J., 2003. 01. Introduction: Experimental design and Statistical Parametric Mapping. SPM Introduction.:599–632. 10.1016/B978-012693019-1/50024-1.
Gaillard, W.D., Balsamo, L., Xu, B., McKinney, C., Papero, P.H., Weinstein, S., Conry, J., Pearl, P.L., Sachs, B., Sato, S., et al., 2004. fMRI language task panel improves determination of language dominance. Neurology 63 (8), 1403–1408. https://doi.org/10.1212/01.WNL.0000141852.65175.A7.
Gaillard, W.D., Berl, M.M., Moore, E.N., Ritzl, E.K., Rosenberger, L.R., Weinstein, S.L., Conry, J.A., Pearl, P.L., Ritter, F.F., Sato, S., et al., 2007. Atypical language in lesional and nonlesional complex partial epilepsy. Neurology 69 (18), 1761–1771. https://doi.org/10.1212/01.wnl.0000289650.48830.1a.
Gaillard, W.D., Balsamo, L., Xu, B., Grandin, C.B., Braniecki, S.H., Papero, P.H., Weinstein, S., Conry, J., Pearl, P.L., Sachs, B., et al., 2002. Language dominance in partial epilepsy patients identified with an fMRI reading task. Neurology. 59(2):256 LP – 265. 10.1212/WNL.59.2.256.
Geranmayeh, F., Wise, R.J.S., Mehta, A., Leech, R., 2014. Overlapping networks engaged during spoken language production and its cognitive control. J. Neurosci. 34 (26), 8728–8740. https://doi.org/10.1523/JNEUROSCI.0428-14.2014.
Gibbs, Jr, R.W., 2008. The Cambridge handbook of metaphor and thought. Cambridge University Press.
Goldmann, R.E., Golby, A.J., 2005. Atypical language representation in epilepsy: implications for injury-induced reorganization of brain function. Epilepsy Behav. 6 (4), 473–487. https://doi.org/10.1016/j.yebeh.2005.03.012.
Hamberger, M.J., Cole, J., 2011. Language Organization and Reorganization in Epilepsy. Neuropsychol Rev. 21 (3), 240–251. https://doi.org/10.1007/s11065-011-9180-z.
Hermann, B.P., Bell, B., Seidenberg, M., Woodard, A., 2001. Learning disabilities and language function in epilepsy. Epilepsia 42, 21–23. https://doi.org/10.1046/j.1528-1157.2001.00507.x.
Husebye, E.S.N., Gilhus, N.E., Spigset, O., Daltveit, A.K., Bjørk, M.H., 2020. Language impairment in children aged 5 and 8 years after antiepileptic drug exposure in utero - the Norwegian Mother and Child Cohort Study. Eur J Neurol. 27 (4), 667–675. https://doi.org/10.1111/ene.14140.
Jackson, J.H., 1880. On right or left-sided spasm at the oonset of epileptic paraxysms, and on crude sensation warnings. And Elaborate Mental States. Brain. 3 (2), 192–206. https://doi.org/10.1093/brain/3.2.192.
Janecek, J.K., Swanson, S.J., Sabsevitz, D.S., Hammeke, T.A., Raghavan, M.E., Rozman, M., Binder, J.R., 2013. Language lateralization by fMRI and Wada testing in 229 patients with epilepsy: rates and predictors of discordance. Epilepsia. 54(2):314–322. 10.1111/epi.12068.
Janszky, J., Mertens, M., Janszky, I., Ebner, A., Woermann, F.G., 2006. Left-sided interictal epileptic activity induces shift of language lateralization in temporal lobe epilepsy: an fMRI study. Epilepsia 47 (5), 921–927. https://doi.org/10.1111/j.1528-1167.2006.00514.x.
Johns, C.L., Tooley, K.M., Traxler, M.J., 2008. Discourse impairments following right hemisphere brain damage: a critical review. Lang Linguist Compass. 2 (6), 1038–1062. https://doi.org/10.1111/j.1749-818X.2008.00094.x.
Kaestner, E., Balachandra, A.R., Bahrami, N., Reyes, A., Lalani, S.J., Macari, A.C., Voets, N.L., Drane, D.L., Paul, B.M., Bonilha, L., et al., 2020. The white matter connectome as an individualized biomarker of language impairment in temporal lobe epilepsy. Neuroimage Clin. 25, 2019. https://doi.org/10.1016/j.nicl.2019.102125.
Katz, A., Awad, I.A., Kongy, A.K., Chelune, G.J., Naugle, R.I., Wyllie, E., Beauchamp, G., Lüders, H., 1989. Extent of resection in temporal lobectomy for epilepsy. II. Memory changes and neurologic complications. Epilepsia 30 (6), 763–771. https://doi.org/10.1111/j.1528-1157.1989.tb05336.x.
Keary, T.A., Frazier, T.W., Busch, R.M., Kubu, C.S., Iampietro, M., 2007. Multivariate neuropsychological prediction of seizure lateralization in temporal epilepsy surgical cases. Epilepsia 48 (8), 1438–1446. https://doi.org/10.1111/j.1528-1167.2007.01098.x.
Kempler, D., Van Lancker, D., Read, S., 1988. Proverb and idiom comprehension in Alzheimer disease. Alzheimer Dis Assoc Disord. 2 (1), 38–49. https://doi.org/10.1097/00002093-198802010-00005.
Kircher, T.T.J., Leube, D.T., Erb, M., Grodd, W., Rapp, A.M., 2007. Neural correlates of metaphor processing in schizophrenia. Neuroimage 34 (1), 281–289. https://doi.org/10.1016/j.neuroimage.2006.08.044.
Knecht, S., Flöel, A., Dräger, B., Breitenstein, C., Sommer, J., Henningsen, H., Ringelstein, E.B., Pascual-Leone, A., 2002. Degree of language lateralization determines susceptibility to unilateral brain lesions. Nat Neurosci. 5 (7), 695–699. https://doi.org/10.1038/nn868.
Langfitt, J.T., Rausch, R., 1996. Word-finding deficits persist after left anterotemporal lobectomy. Arch Neurol. 53 (1), 72–76. https://doi.org/10.1001/archneur.1996.00550010090021.
Laufs, H., Rodionov, R., Thornton, R., Duncan, J.S., Lemieux, L., Tagliazucchi, E., 2014. Altered fMRI connectivity dynamics in temporal lobe epilepsy might explain seizure semiology. Front Neurol. 5 (SEP). https://doi.org/10.3389/fneur.2014.00175.
Lee, M.C., Zambreanu, L., Menon, D.K., Tracey, I., 2008. Identifying brain activity specifically related to the maintenance and perceptual consequence of central sensitization in humans. J Neurosci. 28 (45), 11642–11649. https://doi.org/10.1523/JNEUROSCI.2638-08.2008.
Leyden, K.M., Kucukboyaci, N.E., Puckett, O.K., Lee, D., Loi, R.Q., Paul, B., McDonald, C.R., 2015. What does diffusion tensor imaging (DTI) tell us about cognitive networks in temporal lobe epilepsy? Quant Imaging Med Surg. 5 (2), 247–263. https://doi.org/10.3978/j.issn.2223-4292.2015.02.01.
Lomlomdjian, C., Múnera, C.P., Low, D.M., Terpiluk, V., Solís, P., Abusamra, V., Kochen, S., 2017. The right hemisphere's contribution to discourse processing: a study in temporal lobe epilepsy. Brain Lang. 171, 31–41. https://doi.org/10.1016/j.bandl.2017.04.001.
Martin, I., McDonald, S., 2003. Weak coherence, no theory of mind, or executive dysfunction? Solving the puzzle of pragmatic language disorders. Brain Lang. 85 (3), 451–466. https://doi.org/10.1016/s0093-934x(03)00070-1.
Mbwana, J.S., Berl, M.M., Ritzl, E.K., Rosenberger, L., Mayo, J., Weinstein, S., Conry, J.A., Pearl, P.L., Shamim, S., Moore, E.N., et al., 2008. Limitations to plasticity of language network reorganization in localization related epilepsy. Brain 132 (2), 347–356. https://doi.org/10.1093/brain/awn329.
Mouga, S., Duarte, I.C., Café, C., Sousa, D., Duque, F., Oliveira, G., Castelo-Branco, M., 2022. Parahippocampal deactivation and hyperactivation of central executive, saliency and social cognition networks in autism spectrum disorder. J. Neurodev. Disord. 14 (1), 9. https://doi.org/10.1186/s11689-022-09417-1.
Neudorf, J., Kress, S., Gould, L., Gibb, K., Mickleborough, M., Borowsky, R., 2020. Language lateralization differences between left and right temporal lobe epilepsy as measured by overt word reading fMRI activation and DTI structural connectivity. 107467. Epilepsy Behav. 112. https://doi.org/10.1016/j.yebeh.2020.107467.
Nieto-Castanon, A., 2020. Handbook of functional connectivity Magnetic Resonance Imaging methods in CONN. Hilbert Press. https://www.hilbertpress.org/link-nieto-castanon2020.
Nunberg, G., Sag, I.A., Wasow, T., 1994. Idioms. Language (Baltim). 70 (3), 491–538.
Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9 (1), 97–113. https://doi.org/10.1016/0028-3932(71)90067-4.
Oyegbile, T.O., Dow, C., Jones, J., Bell, B., Rutecki, P., Sheth, R., Seidenberg, M., Hermann, B.P., 2004. The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. Neurology 62 (10), 1736–1742. https://doi.org/10.1212/01.wnl.0000125186.04867.34.
Papagno, C., Caporali, A., 2007. Testing idiom comprehension in aphasic patients: the

effects of task and idiom type. Brain Lang. 100 (2), 208–220. https://doi.org/10.1016/j.bandl.2006.01.002.
Papagno, C., Oliveri, M., Romero, L., 2002. Neural correlates of idiom comprehension. Cortex 38 (5), 895–898. https://doi.org/10.1016/S0010-9452(08)70065-0.
Pasquini, L., Di Napoli, A., Rossi-Espagnet, M.C., Visconti, E., Napolitano, A., Romano, A., Bozzao, A., Peck, K.K., Holodny, A.I., 2022. Understanding language reorganization with neuroimaging: how language adapts to different focal lesions and insights into clinical applications. Front Hum Neurosci. 16 (February). https://doi.org/10.3389/fnhum.2022.747215.
Poeppel, D., Emmorey, K., Hickok, G., Pylkkänen, L., 2012. Towards a new neurobiology of language. J. Neurosci. 32 (41), 14125–14131. https://doi.org/10.1523/JNEUROSCI.3244-12.2012.
Price, C.J., 2012. A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. Neuroimage 62 (2), 816–847. https://doi.org/10.1016/j.neuroimage.2012.04.062.
Proverbio, A.M., Crotti, N., Zani, A., Adorni, R., 2009. The role of left and right hemispheres in the comprehension of idiomatic language: an electrical neuroimaging study. BMC Neurosci. 10, 116. https://doi.org/10.1186/1471-2202-10-116.
Rankin, K.P., Salazar, A., Gorno-Tempini, M.L., Sollberger, M., Wilson, S.M., Pavlic, D., Stanley, C.M., Glenn, S., Weiner, M.W., Miller, B.L., 2009. Detecting sarcasm from paralinguistic cues: anatomic and cognitive correlates in neurodegenerative disease. Neuroimage 47 (4), 2005–2015. https://doi.org/10.1016/j.neuroimage.2009.05.077.
Rapp, A.M., Mutschler, D.E., Erb, M., 2012. Where in the brain is nonliteral language? A coordinate-based meta-analysis of functional magnetic resonance imaging studies. Neuroimage 63 (1), 600–610. https://doi.org/10.1016/j.neuroimage.2012.06.022.
Rapp, A.M., Felsenheimer, A.K., Langohr, K., Klupp, M., 2018. The comprehension of familiar and novel metaphoric meanings in schizophrenia: a pilot study. Front Psychol. 8. https://doi.org/10.3389/fpsyg.2017.02251.
Raspall, T., Doñate, M., Boget, T., Carreño, M., Donaire, A., Agudo, R., Bargalló, N., Rumià, J., Setoain, X., Pintor, L., et al., 2005. Neuropsychological tests with lateralizing value in patients with temporal lobe epilepsy: reconsidering material-specific theory. Seizure 14 (8), 569–576. https://doi.org/10.1016/j.seizure.2005.09.007.
Reyes, A., Kaestner, E., Bahrami, N., Balachandra, A., Hegde, M., Paul, B.M., Hermann, B., McDonald, C.R., 2019. Cognitive phenotypes in temporal lobe epilepsy are associated with distinct patterns of white matter network abnormalities. Neurology 92 (17), e1957–e1968. https://doi.org/10.1212/WNL.0000000000007370.
Reyes-Aguilar, A., Valles-Capetillo, E., Giordano, M., 2018. A quantitative meta-analysis of neuroimaging studies of pragmatic language comprehension: in search of a universal neural substrate. Neuroscience 395, 60–88. https://doi.org/10.1016/j.neuroscience.2018.10.043.
Rodríguez-Cruces, R., Velázquez-Pérez, L., Rodríguez-Leyva, I., Velasco, A.L., Trejo-Martínez, D., Barragán-Campos, H.M., Camacho-Téllez, V., Concha, L., 2018. Association of white matter diffusion characteristics and cognitive deficits in temporal lobe epilepsy. Epilepsy Behav. 79, 138–145. https://doi.org/10.1016/j.yebeh.2017.11.040.
Roger, E., Pichat, C., Torlay, L., David, O., Renard, F., Banjac, S., Attyé, A., Minotti, L., Lamalle, L., Kahane, P., et al., 2020. Hubs disruption in mesial temporal lobe epilepsy. A resting-state fMRI study on a language-and-memory network. Hum Brain Mapp. 41 (3), 779–796. https://doi.org/10.1002/hbm.24839.
Rossell, S.L., Price, C.J., Nobre, A.C., 2003. The anatomy and time course of semantic priming investigated by fMRI and ERPs. Neuropsychologia 41 (5), 550–564. https://doi.org/10.1016/S0028-3932(02)00181-1.
Rossetti, I., Brambilla, P., Papagno, C., 2018. Metaphor comprehension in schizophrenic patients. Front Psychol. 9 (MAY), 1–15. https://doi.org/10.3389/fpsyg.2018.00670.
Saban-Bezalel, R., Mashal, N., 2017. Comprehension and hemispheric processing of irony in schizophrenia. Front Psychol. 8. https://doi.org/10.3389/fpsyg.2017.00943.
Sabsevitz, D.S., Swanson, S.J., Hammeke, T.A., Spanaki, M.V., Possing, E.T., Morris, G.L., Mueller, W.M., Binder, J.R., 2003. Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. Neurology 60 (11), 1788–1792. https://doi.org/10.1212/01.WNL.0000068022.05644.01.
Sass, K.J., Sass, A., Westerveld, M., Lencz, T., Novelly, R.A., Kim, J.H., Spencer, D.D., 1992. Specificity in the correlation of verbal memory and hippocampal neuron loss: dissociation of memory, language, and verbal intellectual ability. J Clin Exp Neuropsychol. 14 (5), 662–672. https://doi.org/10.1080/01688639208402854.
Saur, D., 2006. Dynamics of language reorganization after stroke. Brain 129 (6), 1371–1384. https://doi.org/10.1093/brain/awl090.
Schaffler, L., Luders, H.O., Morris, H.H., Wyllie, E., 1994. Anatomic Distribution of Cortical Language Sites in the Basal Temporal Language Area in Patients with Left Temporal Lobe Epilepsy.
Scheffer, I.E., French, J., Hirsch, E., Jain, S., Mathern, G.W., Moshé, S.L., Perucca, E., Tomson, T., Wiebe, S., Zhang, Y.-H., et al., 2016. Classification of the epilepsies: new concepts for discussion and debate-special report of the ILAE classification task force of the commission for classification and terminology. Epilepsia Open. 1 (1–2), 37–44. https://doi.org/10.1002/epi4.5.
Seghier, M.L., 2013a. The angular gyrus. Neuroscientist 19 (1), 43–61. https://doi.org/10.1177/1073858412440596.
Seghier, M.L., 2013b. The angular gyrus: multiple functions and multiple subdivisions. Neuroscientist. 19 (1), 43–61. https://doi.org/10.1177/1073858412440596.
Slotnick, S.D., Schacter, D.L., 2004. A sensory signature that distinguishes true from false memories. Nat Neurosci. 7 (6), 664–672. https://doi.org/10.1038/nn1252.
Small, S.L., 2008. The neuroscience of language. Brain Lang. 106 (1), 1–3. https://doi.org/10.1016/j.bandl.2008.05.004.
Sone, D., Ahmad, M., Thompson, P.J., Baxendale, S., Vos, S.B., Xiao, F., Tisi, J., McEvoy, A.W., Miserocchi, A., Duncan, J.S., et al., 2022. Optimal surgical extent for memory and seizure outcome in temporal lobe epilepsy. Ann Neurol. 91 (1), 131–144. https://doi.org/10.1002/ana.26266.
Spengler, S., von Cramon, D.Y., Brass, M., 2009. Was it me or was it you? How the sense of agency originates from ideomotor learning revealed by fMRI. Neuroimage 46 (1), 290–298. https://doi.org/10.1016/j.neuroimage.2009.01.047.
Stewart, C.C., Swanson, S.J., Sabsevitz, D.S., Rozman, M.E., Janecek, J.K., Binder, J.R., 2014. Predictors of language lateralization in temporal lobe epilepsy. Neuropsychologia 60, 93–102. https://doi.org/10.1016/j.neuropsychologia.2014.05.021.
Thivard, L., Hombrouck, J., Tézenas du Montcel, S., Delmaire, C., Cohen, L., Samson, S., Dupont, S., Chiras, J., Baulac, M., Lehéricy, S., 2005. Productive and perceptive language reorganization in temporal lobe epilepsy. Neuroimage 24 (3), 841–851. https://doi.org/10.1016/j.neuroimage.2004.10.001.
Thoma, P., Daum, I., 2006. Neurocognitive mechanisms of figurative language processing-evidence from clinical dysfunctions. Neurosci Biobehav Rev. 30 (8), 1182–1205. https://doi.org/10.1016/j.neubiorev.2006.09.001.
Titone, D.A., Connine, C.M., 1999. On the compositional and noncompositional nature of idiomatic expressions. J Pragmat. 31 (12), 1655–1674. https://doi.org/10.1016/S0378-2166(99)00008-9.
Tzourio-Mazoyer, N., Perrone-Bertolotti, M., Jobard, G., Mazoyer, B., Baciu, M., 2017. Multi-factorial modulation of hemispheric specialization and plasticity for language in healthy and pathological conditions: a review. Cortex 86, 314–339. https://doi.org/10.1016/j.cortex.2016.05.013.
Upadhyay, J., Silver, A., Knaus, T.A., Lindgren, K.A., Ducros, M., Kim, D.S., Tager-Flusberg, H., 2008. Effective and structural connectivity in the human auditory cortex. J. Neurosci. 28 (13), 3341–3349. https://doi.org/10.1523/JNEUROSCI.4434-07.2008.
Van Overwalle, F., 2009. Social cognition and the brain: a meta-analysis. Hum Brain Mapp. 30 (3), 829–858. https://doi.org/10.1002/hbm.20547.
Vulchanova, M., SaldaÃ±a, D., Chahboun, S., Vulchanov V., 2015. Figurative language processing in atypical populations: the ASD perspective. Front. Hum. Neurosci. 9 (February):1–11. 10.3389/fnhum.2015.00024.
Wechsler, D., 2002. Test de inteligencia para adultos, III. WAIS. Paidós.
Weschler, D., Stone, C.R., 1945. Instruction manual for the Weschler Memory Scale. Psychological Corps, New York.
Whitfield-Gabrieli, S., Nieto-Castanon, A., 2012. Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. Brain Connect. 2 (3), 125–141. https://doi.org/10.1089/brain.2012.0073.
Wiebe, S., Blume, W.T., Girvin, J.P., Eliasziw, M., 2001. A Randomized, controlled trial of surgery for temporal-lobe epilepsy. N. Engl. J. Med. 345 (5), 311–318. https://doi.org/10.1056/NEJM200108023450501.
Winner, E., Gardner, H., 1993. Metaphor and irony: Two levels of understanding. In: Metaphor and Thought. Cambridge University Press. p. 425–444.
Wolf, R.C., Grön, G., Sambataro, F., Vasic, N., Wolf, N.D., Thomann, P.A., Saft, C., Landwehrmeyer, G.B., Orth, M., 2012. Brain activation and functional connectivity in premanifest Huntington's disease during states of intrinsic and phasic alertness. Hum Brain Mapp. 33 (9), 2161–2173. https://doi.org/10.1002/hbm.21348.