Table e-1. fMRI evidence

First author, y	Class	Group Size	Subject Characteristics	Brain Function Localized	fMRI task	Outcome Measures	Results/Complications/Comments	IAP
				LANGUAGE STUDIES				
Adcock et al., 2003[e19]	III	19	L TLE = 12 (8 w/MTS; 4 w/other) R TLE = 7 (4 w/MTS; 3 w/DNET)	language	Verbal fluency / visual fixation	Agreement w/IAP fMRI repeatability	“Good” agreement between fMRI and IAP in language lateralization but fMRI “more sensitive” to bilateral language lateralization Correlation between fMRI studies in language lateralization r=0.65; p<0.0001	Incomplete description
Arora et al., 2009[e15]	II	40*	L hemispheric = 24 R hemispheric = 16	language	Reading sentence comprehension Auditory sentence comprehension Verbal fluency	Agreement w/IAP Comprehensive language panel (3 tasks)	*not all participants had all tasks 31 w/IAP (concordant w/fMRI reading comprehension task in 83.9%; w/auditory comprehension task in 83.3%; w/verbal fluency in 76.9%); conjunction analysis – 91.3% agreement between fMRI and IAP	Complete description provided
Benke et al., 2006[e20]	III	68	R TLE = 28 (24 medial; 4 neocortical); variable etiologies combined L TLE = 40 (31 medial; 9 neocortical); variable etiologies combined	language	SDTD (adapted from Binder et al., 1996)	Agreement w/IAP	R TLE – 89.5% L TLE – 72.5%	Complete description provided
Binder et al., 1996[e21]	III	22	NL MRI = 13 L T “sclerotic changes” = 4 T L cavernoma = 2 L hemispheric encephalomalacia = 3	language	SDTD	Agreement w/IAP	Correlation coefficient with IAP r = 0.96	Complete description provided
Binder et al., 2010[e22]	II	67	L ATL = 30 R ATL = 37	language memory	SDTD, scene encoding/scrambled scene pairs	Language lateralization vs. hippocampal activation as predictors of surgical outcome	Preoperative language lateralization correlated with postoperative verbal memory change (multiple measures and multiple ROIs). Hippocampal activation asymmetry was strongly related to side of seizure focus and to IAP memory asymmetry but was unrelated to verbal memory outcome (all p>0.05).	Complete description provided
Bonelli et al, 2012[e36]	II	44	L TLE = 24 (all HS) R TLE = 20 (all HS)	language	Verbal fluency vs. crosshair fixation (rest)	4 months verbal fluency and naming outcomes	Pre-op better naming correlated with better LH and LF activation. In LTLE, stronger LF activation predicted greater post-resection decline; post-resection performance depended on greater RF shift. In RTLE better post-resection performance was associated with greater LF and LH activation.	N/A
Chlebus et al., 2007[e23]	III	15	L TLE = 12 (11 w/MTS) R TLE = 3 (2 w/MTS)	language	Letter fluency vs. rest	Agreement w/IAP	Correlation coefficient with IAP r = 0.94 for Broca’s area	Complete description provided
Deblaere et al., 2004[e24]	I	20*	L MTS = 8; L lesion (T neocortical) = 3 R MTS = 5; R lesion (T neocortical) = 2 NL MRI = 2	language	Word chain task vs. counting	Agreement w/IAP	Agreement between IAP and fMRI = 100% including 2 with atypical language lateralization *17 available for comparison but not clear which patients had IAP	Complete description provided
Ellmore et al., 2010[e25]	III	23	L TLE = 19 R TLE = 4 17/23 w/TLE; 4/23 with seizure onset other than medial temporal	language	Four language tasks: naming of line drawings, naming of faces, action naming, word stem completion	Prediction of seizure and language lateralization	After a multiple comparison correction three variables were found to have significant and independent predictive power for determining Wada outcome: Broca's area fMRI activity, handedness, and the DTI of AF. Test of predictive power based on a model using all three variables was correctly classified the dominant hemisphere in 22 of 23 (95.6%) patients based on Wada outcome.	Only minimal IAP details provided
Gaillard et al., 2002[e8]	II	30*	L hemispheric focus = 18 R hemispheric focus = 121 2 NL MRI, 12 MTS (which side?); rest other lesions/abnormalities	language**	Naming to description / patterns of dots	Agreement w/IAP	*21 available for comparison between IAP and fMRI **Inter-rater agreement between fMRI readers 0.71-0.77 (Cramer V) 22/25 IAP and fMRI congruent 3/25 IAP and fMRI partially congruent	Only minimal IAP details provided
Gaillard et al., 2004[e16]	II	26	L MTS = 7 L lesion = 3 R MTS = 7 R lesion = 2 MRI NL = 7 (R T or FT = 3; L T or FT = 4)	language	Three tasks: verbal fluency, reading and auditory comprehension	Agreement w/IAP	21/25 fMRI and IAP agreed in LI 3/25 partial disparity between fMRI and LI 1/25 failed IAP Agreement between raters Cramer V = 0.93 for all three tasks vs. Cramer V = 0.72 for any single task	Complete description provided
Gutbrod et al., 2012[e26]	II	20	12 w/epilepsy 8 w/tumors	language	Letter-decision, rhyme-decision, synonym-decision, sentence-decision	Agreement w/IAP and interrater agreement	Interrater agreement was 0.90 for IF and 0.97 for ST activations; correlation with IAP was 0.86 for sentence and 0.89 for synonym task	Complete description provided
Janecek et al., 2013[e57]	I	229	91 RT onset 97 LT onset 41 Extra-T onset	language	SDTD, scene encoding/scrambled scene pairs	Agreement w/IAP	Discordant results in 14%; discordance highest in the “bilateral” group; the only factor that predicted discordance was the degree of atypical language lateralization; Discordant results in 14%	Complete description provided

Jones et al., 2011[e27]	II	51	34 w/epilepsy 17 w/brain tumors (based on Table 5)	language	Covert word generation, rhyming, passive listening	Agreement with IAP lateralization	Correlation between objective measure of language lateralization and LI score was r^2=0.46. 59 enrolled; Some patients received fMRI twice and some tasks were repeated "at the discretion of the MR technologist"; some had incomplete IAP	Only minimal IAP details provided
Kamada et al., 2007[e28]	III	117*	*87 with various lesions underwent IAP, fMRI and MEG (tumors, vascular lesions, etc.)	language	Two tasks: VGT (control: words played backwards) and abstract/concrete words categorization (dots)	Agreement w/IAP	90.1% agreement with fMRI verb generation Abstract/concrete words categorization task – "unsuitable for language mapping"	Complete description provided
Ota et al., 2011[e30]	II	28	13 – epilepsy (8 LTE; 5 RTE) 13 – brain tumors 2 - AVM	language	*Kana* reading task	Agreement w/IAP (and other non-invasive measures)	In left lateralized language; 95% sensitivity and 87.5 specificity; 3 patients were right-lateralized by IAP – no fMRI concordance	Not provided
Rodin et al., 2013[e31]	II	20	Mixed onset and pathology w/typical distribution for pediatric epilepsy	language	Panel of 7 language tasks	Agreement with IAP (7), ESM (17) and both (4)	IAP – 57% concordance in F and 43% in T regions (visual analysis; lower with LI use) using fMRI and ESM data; there were no discordant cases	Complete description provided
Rutten et al., 2002[e32]	III	18	L hemispheric = 16 (10 w/MTS; 6 with other lesions) R TLE = 2	language	Battery of 4 tasks: VGT, verbal fluency, picture naming, sentence comprehension	Agreement w/IAP	A combined task analysis and use of anatomically pre-defined volumes-of-interest led to LI calculation. The combined task analysis was, retrospectively, more robust than any given task. Concordance was found in 10/11 left-IAP, 3/4 bilateral IAP, and 2 of 3 right-IAP patients. Best agreement with verb generation fMRI	Complete description provided
Sabbah et al., 2003[e33]	III	20	L hemispheric = 11 (L TLE = 6) R hemispheric = 9 (R TLE = 7)	language	Two semantic fluency paradigms	Agreement w/IAP	Agreement in LI in 19/20 patients. This includes 7/8 right dominant patients. The one incongruent case was correctly lateralized but weaker than pre-defined threshold.	Complete description provided
Sabsevitz et al., 2003[e34]	III	56	L TLE = 24 R TLE = 32	language	SDTD	Agreement w/IAP Language outcome	Agreement between IAP and fMRI r>0.65 for all measures (all p<0.001) fMRI LI was 100% sensitive and 73% specific for post-surgical naming decline	Complete description provided
Szaflarski et al., 2008[e18]	II	38*	L medial temporal = 8 L temporal (presumably neocortical) = 3 L extra-temporal = 2 R medial temporal = 9 R temporal (presumably neocortical) = 4 R extratemporal = 1 Bitemporal = 1	language	SDTD and VGT	Agreement w/IAP Compare VGT and SDTD	*28/38 underwent IAP Both tasks generated laterality indices using pre-defined regions-of-interest. The LI index for SDTD and VGT correlated with IAP (r=0.65 and r=0.735, each p<0.001, respectively) This included 5 atypical IAP results.	Complete description provided
Woermann et al., 2003[e35]	III	100	L hemispheric = 82 (63 w/TLE) R hemispheric = 18 (11 w/TLE)	language	Word generation vs. rest	Agreement w/IAP	Overall discordance between fMRI and IAP LI was 9%. In patients with left extra-temporal epilepsy it was 25%. False categorization was 3% for L TLE and 25% (4/16) L extra-temporal epilepsy. 3/29 atypical IAP were falsely categorized by fMRI.	Minimal description of IAP
				MEMORY STUDIES				
Binder et al., 2008[e44]	II	122	L ATL = 60 R ATL = 62	verbal memory	SDTD	Postsurgical memory	50% of postsurgical memory outcome was explained by NPT 10% by fMRI	IAP of language or memory did not contribute
Binder et al., 2010[e22]	II	67	L ATL = 30 R ATL = 37	language memory	SDTD, scene encoding/scrambled scene pairs	Language lateralization vs. hippocampal activation as predictors of surgical outcome	Preoperative language lateralization correlated with postoperative verbal memory change (multiple measures and multiple ROIs). Hippocampal activation asymmetry was strongly related to side of seizure focus and to IAP memory asymmetry but was unrelated to verbal memory outcome (all p>0.05).	Complete description provided
Bonelli, S et al., 2010[e12] **(subset from this study was published earlier – Powell et al., 2007 thus older study not included)**	II	72*	L TLE = 41 (40 w/MTS; 1 cavernoma) R TLE = 31 (28 w/MTS; 1 cavernoma; 1 dysplasia; 1 DNET)	memory	Encoding of faces, pictures, and words (event related)	Verbal and visual memory	Preoperative memory fMRI was the strongest predictor of postoperative verbal and visual memory decline; *54 had surgery	N/A
Bonelli et al, 2013[e38]	II	46	25/26 LHS 16/20 RHS	memory	Encoding of faces, pictures, and words (event related)	Verbal and visual memory	LTLE: greater pre-operative posterior H activation was associated with better post-resection verbal memory outcome; greater post- then preoperative activation was associated with worse outcome. RTLE: this was not observed. Conclusion – reorganization to the posterior temporal lobe pre-resection predicts good post-resection	N/A

							outcome. Post-surgical reorganization does not imply better performance.	
Cheung et al., 2009[e45]	II	17	L TLE = 9 (7 w/MTS; 1 glioma, 1 cavernoma) RTLE = 8 (3 w/MTS; 4 with lesions, 1 normal)	memory	Novel visual scene encoding vs. visual fixation	Postsurgical memory	Preoperative fMRI activation was associated with postoperative memory outcomes	N/A
Deblaere et al., 2005[e39]	III	17	L TLE = 7 R TLE = 9	memory	Picture encoding/recall	Agreement w/IAP	Correlation (p<0.001) between R TLE IAP and fMRI but not L TLE (p>0.1)	Complete description provided
Dupont et al., 2010[e41]	II	25	R MTLE = 14 L MTLE = 11 (23 with unilateral lesions "mostly MTS"; one with bilateral lesion and one with no lesion)	memory	Three fMRI tasks – the most important one was delayed memory recognition	Agreement w/IAP and postsurgical memory outcome	No correlation between fMRI and IAP LI in 19/25 patients (p=0.152) Pre-to-post surgery change in verbal memory correlated with L fMRI activation during delayed recognition (p=0.009) and pre-op verbal memory score (p<0.001). Delayed recall task predictive of verbal memory outcomes after left temporal lobectomy but not predictive of non-verbal memory outcomes after right temporal lobectomy. Overall fMRI better than IAP in predicting outcome after left temporal lobectomy.	Complete description provided
Frings et al., 2008[e46]	II	22*	L TLE = 12 (7 w/MTS; 5 w/other pathologies) R TLE = 10 (6 w/MTS; 4 w/other pathologies)	memory	Visual spatial memory/ visual size comparison	Postsurgical memory	*available in 15 patients Correlation between postsurgical verbal learning deterioration and ipsilateral resection (rho = 0.49; p<0.05)	N/A
Janecek et al, 2013[e17]	I	229	L TLE = 97 R TLE = 91 Extra-temporal (L and R) = 41	language	SDTD	Agreement w/IAP	Discordant rates were observed in 14% with 8% in patients w/L language lateralization, 40% in bilateral, and 33% in right. FMRI contributed to 22-26% of variance in LI data while IAP contributed 2-5% - most of variance in the data is accounted for by fMRI.	Complete description available
Jokeit et al., 2001[e42]	III	30	L TLE = 16 (10 w/MTS; 6 w/other pathologies) R TLE =14 (7 w/MTS; 7 w/other pathologies)	memory	Home walking task / counting odd numbers back	Memory asymmetry prediction and agreement with IAP*	fMRI predicted memory asymmetry correctly in 90% of patients; # of activated fMRI L hippocampal voxels correlated in L TLE with L IAP score (p<0.01) and R hippocampal voxels with Rey Complex Figure (p<0.05) *14 patients bilateral IAP; 4 patients unilateral IAP	Partial description of IAP
Koylu et al., 2008[e29]	III	26	L TLE = 14 (13 w/medial temporal onset) R TLE = 12 (no information on the make-up of this group)	language memory	SDTD (adapted from Binder et al., 1997)	Postsurgical outcomes	L TLE: Activation in L MTL correlates positively with preoperative verbal memory ability. Activation in R MTL correlates positively with preoperative and postoperative verbal memory ability. R TLE: Activation in R MTL correlates positively with preoperative and postoperative verbal memory.	*all participants were left hemispheric for language by IAP but description of IAP or comparison with fMRI not done; multiple tests done w/o correction for multiple comparisons
Mechanic-Hamilton et all., 2009[e13] **(subset from this study was published earlier – Rabin et al., 2004 thus older study not included)**	III	49	L TLE = 21 R TLE = 24 Bilateral = 4 Lesional or non-lesional TLE (patients with tumors, vascular lesions, prior TBI or extra-temporal epilepsy were excluded) *patients split between 1.5 and 3T scanners	memory	Scene encoding / scrambled scene pairs	Agreement w/IAP Postsurgical outcomes	Hippocampal fMRI asymmetry vs. IAP – no correlation Medial temporal ROI – correlated with IAP (r=0.59; p=0.001) Left TLE: Preoperative activation in left MTL during scene encoding is negatively correlated with pre-to-post change score on a scene encoding recognition task. Preoperative MTL activation is NOT correlated with change on any standard verbal or nonverbal neuropsychological measures. Right TLE: FMRI activation in MTL was not related to any postoperative outcome measures. This conflicts with a previous smaller study by the same group (Rabin et al. 2004), which had suggested that activation in the MTL predicts postop scene encoding ability in both left and right TLE patients.	No IAP description
Sidhu et al., 2015[e40]	II	50	L TLE = 23 R TLE =27	memory	Encoding of concrete nouns (Event related)	Post-resection NPT outcome	LTLE: increasing L LI was associated with increasing post-resection verbal memory decline (r=0.44; p=0.037); RTLE – no effect. Post-resection outcomes: LTLE – L activations predicted post-surgical memory decline; RTLE – L IFG activations predicted post-resection decline.	N/A
Vannest et al., 2008[e43]	III	23	L hemispheric = 11 (5 w/MTLE) R hemispheric = 12 (6 w/MTLE)	memory	Scene encoding / scrambled scene pairs	Memory lateralization and Agreement with NPT	For L hemispheric focus memory shifted to the R and for R hemispheric focus memory shifted to the L on several measures (p<0.05). Several significant (p<0.05) relationships between fMRI and NPT reported.	N/A
Wagner et al., 2007[e47]	II	21	L TLE = 11 (all HS) R TLE = 10 (all HS)	memory	Word pairs encoding	Functional connectivity and postsurgical outcome	Task-correlations between hippocampus and cortical areas was higher in those who subsequently had worse verbal learning (p<0.05).	N/A

Abbreviations: AF = arcuate fasciculus; ATL = anterior temporal lobe epilepsy; DNET = dysembryoplastic neuroepithelial tumor; DTI = diffusion tensor imaging; IAP = intracarotid amobarbital procedure; LI = laterality index; MTLE = medial temporal lobe epilepsy; MTS = medial temporal sclerosis; NPT = neuropsychological testing; ROI = region of interest; SDTD = semantic decision / tone decision; TLE = temporal lobe epilepsy; VGT = verb generation task.

Citations provided from full-length guideline, published as a data supplement at Neurology.org.