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Impaired acquisition of new words after left temporal lobectomy despite normal fast-mapping behavior



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ABSTRACT

Word learning has been proposed to rely on unique brain regions including the temporal lobes, and the left temporal lobe appears to be especially important. In order to investigate the role of the left temporal lobe in word learning under different conditions, we tested whether patients with left temporal lobectomies (N=6) could learn novel words using two distinct formats. Previous research has shown that word learning in contrastive fast mapping conditions may rely on different neural substrates than explicit encoding conditions (Sharon et al., 2011). In the current investigation, we used a previously reported word learning task that implemented two distinct study formats (Warren and Duff, 2014): a contrastive fast mapping condition in which a picture of a novel item was displayed beside a picture of a familiar item while the novel item's name was presented aurally ("Click on the numbat."); and an explicit encoding (i.e., control) condition in which a picture of a novel item was displayed while its name was presented aurally ("This is a numbat."). After a delay, learning of the novel words was evaluated with memory tests including three-alternative forced-choice recognition, free recall, cued recall, and familiarity ratings. During the fast-mapping study condition both the left temporal lobectomy and healthy comparison groups performed well, but at test only the comparison group showed evidence of novel word learning. Our findings indicate that unilateral resection of the left temporal lobe including the hippocampus and temporal pole can severely impair word learning, and that fast-mapping study conditions do not promote subsequent word learning in temporal lobectomy populations.

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1. Introduction

Word learning is a critical and commonplace part of human life from infancy through old age, but the neural bases of this ability are still being investigated. Brain regions important for word learning are likely to be concentrated in the left hemisphere given normative left lateralization of related abilities including speech, naming, verbal learning, and semantic memory (Damasio et al., 2004; Frisk and Milner, 1990; Jones-Gotman et al., 1997; Manns et al., 2003; Miceli et al., 1991; Milner, 1972; Tranel, 1991). Another consideration for localization is that word learning requires memory for arbitrary associations of phonology, visual representations, and semantic knowledge. Thus, word learning might be expected to rely on left-hemisphere brain regions that contribute to declarative memory for facts and events such as the medial temporal lobe (MTL) or relational binding such as

http://dx.doi.org/10.1016/j.neuropsychologia.2015.11.016 0028-3932/© 2015 Elsevier Ltd. All rights reserved. hippocampus (Eichenbaum and Cohen, 2001, 2014; Gabrieli et al., 1988; Scoville and Milner, 1957; Squire et al., 2004). However, recent findings suggest that incidental association of novel items and novel phonology (*fast mapping*) may promote word learning without relying on the MTL or hippocampus (Sharon et al., 2011) while offering preliminary evidence that the neural substrate of this learning is left temporal pole. When considering localization of word learning to left MTL, left temporal pole, or both, a critical missing datum is whether left-lateralized temporal lobe lesions including both structures are sufficient to impair word learning by any means. We addressed this question by evaluating word learning by explicit encoding or by fast mapping in patients with left anterior temporal lobe resections including left hippocampus, MTL, and temporal pole.

Neural systems that support word learning must encode associations between *arbitrary* combinations of phonology, imagery, orthography, and meaning (Duff and Brown-Schmidt, 2012). Although the formation of arbitrary relations has been theorized to depend on the hippocampus (Davachi and Dobbins, 2008;







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Fig. 1. Task phases (A) and trial sequence of study (B) and 3AFC recognition (C) phases (labels between B and C are relevant for both). (A) Task phase sequence for the protocol (see Section 2). (B and C) All study and test trials began with central fixation followed by display onset, audio instruction playback (including a critical orienting word), and a response phase. Eye movements were monitored during all trials, and we used the critical target word (crit.) onset event to anchor timecourse analyses of eye movements (see Section 2). (B) Fast mapping (FM) and explicit encoding (EE) study formats were similar, but in the EE study format (bottom) only 1 uncommon item was presented, while in the FM study format (top) 2 items were presented and a choice was required. (C) 3AFC recognition test format was the same after FM and EE encoding. Adapted from Warren and Duff (2014).

Eichenbaum and Cohen, 2001; Ranganath, 2010), hippocampal contributions may not be necessary for word learning under certain conditions such as fast mapping (Sharon et al., 2011). Fast mapping describes the on-line association of a novel word with a novel object or property (Carey and Bartlett, 1978) (Fig. 1B). The ability to learn words from fast-mapping exposure has been studied extensively in children (Bion et al., 2013; Carey and Bartlett, 1978; Friedrich and Friederici, 2011; Gershkoff-Stowe and Hahn, 2007; Halberda, 2006; Horst and Samuelson, 2008; Spiegel and Halberda, 2011; Vlach and Sandhofer, 2012) and to a lesser extent in neurologically healthy adults (Greve et al., 2014; Halberda, 2006; Markson and Bloom, 1997). Two lines of evidence have converged to suggest that the hippocampus may not be necessary for word learning by fast mapping. First, young children have sometimes been shown to learn from fast mapping (Carey and Bartlett, 1978; Halberda, 2006; Spiegel and Halberda, 2011) despite the relatively slow maturation of hippocampal memory system (Bauer, 2005; Overman et al., 1996). Second, across two studies (Merhav et al., 2014; Sharon et al., 2011) a total of three severely amnesic adults with MRI-confirmed bilateral hippocampal damage (cases E.C., Sh.B., and D.A.) were shown to learn novel words studied in a fast mapping format. Although learning by fast mapping has not always been reproduced in healthy children (Bion et al., 2013; Friedrich and Friederici, 2011; Gershkoff-Stowe and Hahn. 2007: Horst and Samuelson. 2008: Vlach and Sandhofer, 2012) or adult amnesic patients (Smith et al., 2014; Warren and Duff, 2014) the implication of the Sharon et al. (2011) and Merhav et al. (2014) findings is that learning by fast mapping may exercise a non-hippocampal system that is sufficient to support learning of arbitrary relations.

If a non-hippocampal word-learning system existed, plausible neural substrates would include several regions located in the left hemisphere. Functional neuroimaging studies have shown that new word learning causes increased activity in left frontal, temporal, and parietal regions (Binder et al., 2009). In particular, new word learning has been shown to activate left hippocampus (Breitenstein et al., 2005; Davis et al., 2009) while naming performance activates left temporal pole (Grabowski et al., 2001). Paralleling and extending these neuroimaging findings, neuropsychological studies have established that the left MTL and hippocampus are necessary for normal verbal memory (Frisk and Milner, 1990; Jones-Gotman et al., 1997; Milner, 1972) and that portions of the left anterior, lateral, and ventral temporal lobe are necessary for normal naming (Damasio et al., 2004). More specifically, the left lateral temporal lobe has a well-established role in the storage and use of names with an anterior–posterior gradient ranging from individual persons and proper names to various object categories (e.g., musical instruments, tools, animals) (Damasio et al., 2004). Of particular relevance to the current study, impaired word learning has been reported in a case study of a patient with damage to the left anterior temporal lobe (Tranel, 1991) following a traumatic brain injury (TBI), but word-learning by non-TBI patients has not been systematically evaluated.

The necessity of the left anterior temporal lobe for learning new words has been studied neuropsychologically (Sharon et al., 2011; Tranel, 1991), but patients who have undergone left temporal lobectomy (TL) offer an untapped opportunity for research in this domain. Surgical resection of regions including the hippocampus, temporal lobe cortex, and temporal pole can sometimes remediate pharmaceutically-resistant temporal lobe epilepsy. Following resection, TL patients are often neuropsychologically normal except for selective deficits on tests of naming and (frequently but not uniformly) verbal memory (Gleissner et al., 2004; Ojemann and Dodrill, 1985; Rausch et al., 2003; Saykin et al., 1995). Also, TL patients often report subjective difficulty with learning new names. This potential for a selective deficit in learning new names suggests that TL patients may be particularly informative when studying tasks thought to rehabilitate word learning abilities. Conditions found to benefit word learning by such TL patients could potentially be applied to other populations with neurological word-learning and naming deficits including older adults (Connor et al., 2004) and patients with dementias including Alzheimer's (Bayles and Tomoeda, 1983). Meanwhile, interventions that did not promote word learning in TL patients with relatively preserved cognitive abilities would be predicted to be of little use for populations with more severe impairments.

In this neuropsychological investigation, we evaluated the contributions of the left anterior temporal lobe, including hippocampus and temporal pole, to word learning in two conditions. We studied on-line performance of fast-mapping and word learning from fast-mapping in a group of patients with left temporal lobectomy (N=6) and healthy normal comparisons (N=6). Our methods replicated a previous study of fast mapping in severely amnesic patients with bilateral hippocampal damage (Warren and Duff, 2014): after initial assessments of familiarity, novel words were studied under fast-mapping or explicit encoding conditions; afterward, memory for the novel words was thoroughly assessed with tests of free recall. 3-alternative forcedchoice (3AFC) recognition, cued recall, and familiarity ratings. We also recorded eve movements at study and 3AFC recognition in order to assess whether there was any covert evidence of learning not expressed in overt behavior. Based on previous findings from severely amnesic patients with bilateral hippocampal damage (Smith et al., 2014; Warren and Duff, 2014) and from patients with unilateral left hippocampal or left temporopolar damage (Sharon et al., 2011), we hypothesized that TL would cause impairments in all forms of word learning. Thus, we predicted that TL patients would show deficits in the ability to learn novel words in either study condition as reflected in explicit measures of memory. Additionally, we predicted that implicit measures of memory (i.e., eye movements) would demonstrate that TL patients did not show evidence of prior exposure to novel word-object associations.

2. Methods

2.1. Participants

We recruited patients with a history of early onset epilepsy and subsequent left unilateral temporal lobectomy ("TL"; N=6; 5F, 1M) and healthy normal comparison participants ("NC": N=6) who were individually matched to the TL participants on sex, age, and education. The TL participants were recruited from the Patient Registry from the University of Iowa Department of Neurology (henceforth, "the registry"). In accordance with their enrollment in the registry, the patients were free of histories of intellectual limitation, learning disability, psychiatric disease, and dementia, and they all had focal, stable lesions. Additionally, we applied the following inclusion criteria: early-onset epilepsy (< 5 years); leftlateralized language abilities (as determined by Wada testing); left temporal lobectomy in adulthood (> 18 years); interval of at least one year since TL surgery; and relatively intact neuropsychological status on measures of language, naming, and memory. Early-onset epilepsy cases were preferred in order to ensure relatively homogeneous, albeit epilepsy-disrupted, childhood development for all participants. Relatively preserved cognitive abilities were preferred because this sample appeared to offer the best opportunity for remedial intervention. Demographic and neuropsychological data were obtained from a database of the registry and are summarized in Table 1. NC participants were recruited from Iowa City and the surrounding communities. All participants completed informed consent and were treated in accordance with the Declaration of Helsinki. Participants were remunerated for their time.

The TL participants all had previous diagnoses of epilepsy. Mean age of first seizure for the group was 20.5 months (S. D.=13.5) and the mean age of surgical resection was 41.0 years (S. D.=13.3). Handedness, measured with the Geschwind-Oldfield Questionnaire, indicated 5 TL subjects were fully right-handed (+100) and one TL subject with majority right-handed preference (+15). TL participants had standard left hemisphere language dominance as determined by pre-surgical Wada testing.

In general, participants had relatively intact cognition, memory, and language abilities. TL participants did not have significant disruptions in language (i.e., no aphasia). None had significant memory impairment, reflected in the fact that each participant scored similarly on normative tests of general intellectual ability and memory (i.e., ≤ 25 point difference between each patient's WAIS full-scale IQ and WMS general memory index). Naming performance was numerically low (mean=52.8, S.D.=2.5) but within normative limits for all participants (Kaplan et al., 1983). Scores on the WMS auditory delay index and the AVLT delayed recall test were normal for all TL participants. Two TL participants (2246 and 2403) had relatively low scores on one measure of visual delayed memory (WMS visual delayed index) but were within the normal range on another (Rey-Osterrieth Complex Figure Task).

NC participants completed the Weschler Test of Adult Reading (WTAR) (Wechsler, 2001) to measure their verbal abilities. The NC group's WTAR standard scores were within normative expectations (mean=109.8, S.D.=6.6, range=105–123) as were their WTAR-estimated WAIS-III verbal IQ (VIQ) scores (mean=107.3, S. D.=4.8, range=104–117). WTAR-estimated NC VIQ scores did not differ significantly from the LTL group's VIQ scores [T(10)=2.108, p=0.061].

Neuroanatomically, TL participants had nearly uniform resections of the head and body of the left hippocampus. The hippocampal tail was completed resected in several TL participants and exhibited substantial atrophy in the others. The extent of resection in the remainder of the left temporal lobe varied between patients. All TL resections were traced in a common space according to the MAP-3 method (Damasio and Frank, 1992) and overlapped for voxelwise comparison (Fig. 2A). At the level of anatomical parcels

Table 1

Demographic and neuropsychological information for the left temporal lobectomy (TL) group. Test scores indicating impairment ≥ 2 SDs below normative expectations for age are *italicized*. Abbreviations: Age, age in years at time of test; Hand, handedness from +100 (fully right-handed) to -100 (fully left handed); Edu., formal education in years; DX, age at first seizure in years (to 2 decimal places); Sur, age at TL resection in years; Chr., chronicity, age in years since resection; FSIQ, WAIS IV full-scale IQ: VCI, WAIS IV verbal comprehension index; PRI, WAIS IV perceptual reasoning index; DS, WAIS IV digit span subtest; BVRT, Benton Visual Retention Test, errors; GMI, WMS III general memory index; ADI, WMS III auditory delayed index; VDI, WMS III visual delayed index; AVLT, Rey Auditory Verbal Learning Task, words recalled on trial 5 and after 15-min. delay; CFT, Rey-Osterrieth Complex Figure Task, scores for copy and 30-min. delay phases; BNT, Boston Naming Task. For further information regarding these neuropsychological instruments consult Lezak et al. (2012).

ID	Age	Sex	Hand	Edu.	DX	Sur.	Chr.	FSIQ	VCI	PRI	DS	BVRT	GMI	ADI	VDI	AVLT	CFT	BNT
2023	51	М	100	16	1.00	30	21	113 ^a	110 ^a	116 ^a	14 ^a	3	100	105	112	9/8	33/19	53
2246	68	F	15	20	0.83	53	15	116	107	109	15	2	91	94	72	13/8	31/17	54
2403	55	F	100	12	2.00	41	14	93	89	92	12	4	88	97	72	11/10	31/12	57
2555	42	F	100	12	0.42	30	12	96	85	94	9	4	91	94	94	13/9	30/22	52
3166	39	F	100	16	3.00	31	8	100	102	107	8	1	93	83	112	11/8	36/25	50
3472	65	F	100	13	3.00	61	4	105	93	107	11	9	88	92	84	13/7	27/14	51
Mean	53.3		85.8	14.8	1.71	41.0	12.3	103.8	97.7	104.2	11.5	3.8	91.8	94.2	91.0	11.7/8.3	31.3/18.2	52.8
SD	11.8		34.7	3.1	1.13	13.3	5.9	9.2	10.2	9.3	2.7	2.8	4.4	7.1	18.2	1.6/1.0	3.0/4.9	2.5

^a For 2023, equivalent WAIS III scores are shown.



Fig. 2. Lesion extent in the TL group (A) and behavioral results (B–E). For B–E, bars show group means and whiskers are s.e.m. (A) Lesion extent was traced in a common template space for each TL participant, then summed to create these left-hemisphere overlap maps (from top, perspectives are lateral, medial, and bottom). Lesions were concentrated in the anterior left temporal lobe (red region, see color scale). Also see **Figs. S1 and S2**. (B) Left panel: both groups performed FM well above chance at study, and there were no between-group differences. Right panel: in the 3AFC recognition task, the NC group performed well above chance, but the TL group performed significantly less well and not better than chance. Neither EE nor FM study affected recognition in TL patients. (C) Left panel: free recall of unfamiliar items was poor for all groups, but the TL group averaged fewer than one recalled item. Right panel: free recall of familiar items was better than that of unfamiliar items for both groups, and both groups recalled more familiar items in the FM condition than the EE condition. The lack of between-group differences in this phase shows that the TL group was not globally amnesic. (D) Left panel: cued recall based on a novel visual exemplar of a studied item was above zero for the NC group, while the TL group did not recall any words on average. Right panel: adding a verbal cue improved performance of the NC group, but the TL group was statistically greater for the NC group; EE and FM encoding produced similar numerical results.

defined by gyral anatomy (Fig. S1 and Table S1) it was evident that on average the TL resections included the majority of the gray matter in the anterior portions of all temporal gyri except the superior temporal gyrus, and that the temporal pole was also frequently and extensively resected or disconnected. Illustrations of individual lesion extent in MAP-3 space are provided in Fig. S2.

2.2. Equipment

Tasks were visually displayed on a 21-in. LCD monitor (Multi-Sync 2190UXi, NEC Corporation of America, Irving, TX) at a distance of 550 mm. Behavioral responses were made verbally or with a computer mouse. During study and recognition phases, participants placed their head in a padded chinrest/headrest apparatus, and saccadic eye movements were monitored with a sampling rate of 1000 Hz using an EyeLink 1000 remote infrared camera system (SR Research Ltd., Ontario). Gaze position was calibrated to be accurate to within 1° of visual angle. Audio and video were recorded with a Flip camera (Cisco Systems, San Jose, CA).

2.3. Procedure

Our within-subjects experimental design was intended to thoroughly evaluate familiarity ratings, free recall, recognition memory, and cued recall performance in two different experimental conditions: fast mapping (FM) and explicit encoding (EE). Participants completed the protocol twice (once in each study format) separated by at least 1 month (mean=129.5 days, S. D.=62.9 days). One participant (2403) was tested on two consecutive days due to limited availability. The order of condition administration was fixed by design (i.e., FM in the first session and EE in the second). Two non-overlapping item sets were assigned to different study conditions for different participants. Counterbalancing was designed to control for item effects between participants by ensuring that the sets of items that were assigned to the FM condition (e.g., set A) and EE condition (e.g., set B) for one participant were reversed for the next participant (i.e., set B for FM, set A for EE). TL participants and their matched comparisons completed the same counterbalancing conditions. Interactive computerized tasks were implemented in Matlab 2007b (The Mathworks, Inc., Natick, MA) using the Psychophysics Toolbox (Brainard, 1997).

Our experimental protocol (see Fig. 1) replicated that of Warren and Duff (2014). Participants first rated their familiarity with a set of common and uncommon words (rating scale was 1–6: 1 = not at all familiar; 6=very familiar) and provided brief verbal descriptions of familiar words. Next, a study phase that varied in format according to condition (FM or EE) was completed. In the FM condition (Fig. 1B, top), two items were displayed, one novel and one common. Aural instructions were presented on each trial using the following carrier phrase: "Click on the ..." followed by the name of the novel item. In the EE condition (Fig. 1B, bottom), one novel item was displayed and accompanied by the following aurally-presented sentence: "This is $a(n) \dots$ " followed by the name of the novel item. In both conditions, trials ended when the participant clicked on an item. 24 critical study trials were presented in each condition along with 8 catch trials in which both the target and lure items were common. All trials were presented twice: in the FM condition, a different common item was paired with the target item on the second presentation and the display position of the target item was reversed.

After the study phase, free recall for all studied items was tested immediately and again after a filled 30-min. delay (nb. the delay task was visuoperceptual and is not reported here). Following the delayed free recall test a three-alternative forcedchoice (3AFC) recognition task was administered (Fig. 1C). During each 3AFC trial. 3 studied novel items were presented along with aural instructions using the following carrier phrase: "Click on the ..." followed by the name of one studied novel item. 3AFC test trials ended when the participant clicked on an item. Target position was balanced across the right, left, and bottom display positions, and all studied items were used as targets. Following the 3AFC recognition phase, a cued recall phase was administered in two rounds: first, novel visual exemplars of all studied novel items were presented and participants were asked to name the item aloud; second, the same exemplars were presented again, now accompanied by a verbal cue (i.e., the first phoneme of the item's name) if necessary. Finally, after the cued recall phase, the familiarity of each word was assessed again as before.

Originated by Warren and Duff (2014), this protocol employed a large number of memory tasks with the goal of thoroughly and accurately characterizing any word learning that occurred during the session. We tested familiarity with common and uncommon words at the beginning of each experimental session in order to: first, determine whether participants had a relatively intact basic vocabulary (all did); and second, ensure that participants did not have pre-experimental familiarity with the uncommon words (any uncommon words familiar to a given participant were excluded from analysis). We tested familiarity with the same words at the end of the session to evaluate whether intra-experimental exposure to uncommon words affected familiarity. We tested free recall of words immediately after the study phase to determine whether participants had explicit, immediate memory for the studied words and again after a 30-min delay to measure the durability of memory across time. We tested recognition for studied uncommon words in a 3AFC paradigm as an explicit measure of memory for the relationship between aurally-presented words and visual images. Finally, we tested the generalizability of recently-learned words to novel exemplars in visually-cued and visually-and-aurally-cued recall tasks in order to test the flexibility of new learning.

2.4. Analysis

Data were aggregated using Matlab 2007b, Python 2.7, and Python's pandas library. Data were analyzed and graphed using R 3.2.0 software and its nlme, multcomp, lattice, and Cairo libraries.

Analyses were broadly similar to those described in Warren and Duff (2014). Data belonged to two broad categories: behavioral responses and eye movements. Overt behavioral responses included familiarity ratings, referent selection (only in the FM study phase), free recall, cued recall, and 3AFC recognition. Response times were collected during the study and 3AFC phases and were measured from the end of the auditory stimulus. Eye movement data complemented behavioral responses in the FM study phase and the 3AFC phase. All of our analyses used repeated-measures ANOVA tests implemented as linear mixed-effect (LME) models with participants entered as a random effect. We tested planned comparisons using linear contrasts applied to the LME models (reported using the normally-distributed *Z* value), and p values were corrected for multiple comparisons (indicated by p_c ; α =0.05) using a single-step method (Bretz et al., 2010). Effect size calculations used a variant of Cohen's *d* that adjusts for small sample sizes (Grissom and Kim, 2012) and which we report as d_{adj} .

2.4.1. Behavioral measures

Word familiarity: changes in familiarity ratings (post-rating minus pre-rating) were calculated for all words unfamiliar to each participant and averaged within participants. These mean change scores were analyzed using a repeated-measures ANOVA. Participants were a random effect and study condition was a withinsubjects fixed effect (levels: FM and EE). Group membership (levels: TL or NC) was a between-subjects fixed effect. FM study: Referent selection performance was summarized as proportion correct (i.e., number of correct responses/number of responses) and analyzed using a simple ANOVA with group membership as the sole factor. Free recall: Number of words recalled (unfamiliar and familiar) was analyzed using a similar repeated-measures ANOVA but included a delay factor (levels: pre- or post-delay). Cued recall: Number of words recalled was analyzed using another similar repeated-measures ANOVA, but included a cue-type factor (levels: visual only or visual and verbal). 3AFC recognition: proportion correct was analyzed using a repeated-measures ANOVA with a within-subjects factor for study condition and a betweensubjects group membership factor. Response time: Response time (RT) for correct trials was analyzed in the same manner as other behavioral measures for both the study and 3AFC recognition phases. For all performance measures, the repeated-measures ANOVA was supplemented by planned comparisons between groups and (where possible) versus chance performance. Several post-hoc analyses suggested by reviewers were also conducted and are described in the results section.

2.4.2. Eye-movement measures

Fixations were defined using two criteria: if eye position was accurately detected while eye velocity and acceleration were both less than their respective thresholds (30°/s. and 8000°/s², respectively), the eye was deemed to be engaged in a fixation (else saccade or blink). We measured the position and timing of fixations to displays during the study and 3AFC test phases of our protocol. We analyzed these fixation data at three different levels. First, whole-display measures included number of fixations and time spent fixating a display. Second, we divided the displays into rectangular regions of interest (ROIs) bounding the images and coded each ROI for content (e.g., target item, competitor item) and for response (i.e., selected or non-selected). ROI measures then included the proportion of time spent fixating each ROI and the number of fixations to each ROI. Finally, we extended our ROI analysis by locking the time of eye movements to specific trial events. We analyzed data at each level as described below.

During FM study, fixation time and number of fixations were summarized by averaging across trials to obtain per-participant values. We analyzed those data using a simple ANOVA with a single, between-subjects group membership factor (levels: TL and NC) to evaluate group differences, followed by planned comparisons. 3AFC fixation time and number of fixations were analyzed using a repeated-measures ANOVA with a within-subjects study condition factor (levels: EE or FM) and planned comparisons.

Measures of proportion fixation time were calculated by determining the fixation time to each ROI, and then dividing those per-ROI fixation time values by the sum of all ROI fixation time values (i.e., the quotient was a proportion of total fixation time across ROIs). In the FM study phase, each trial contained 2 ROIs: the ROI containing the target image; and the ROI containing the competitor image. With only 2 ROIs, values of proportional fixation time were constrained and we limited our analyses to correct



Fig. 3. On-line eye-movement measures of both groups were similar during study (A), but differed at 3AFC test (B and C) reflecting within-session word learning by the NC group. Points and lines indicate group mean proportion fixation time (PFT) per 500 ms time bin (shading shows 95% confidence intervals) anchored to the onset of the critical word (Crit. Onset Time = 0). B and C plot the same 3AFC recognition test eye-movement data differently to emphasize specific patterns of viewing over time. (A) During correct FM study trials, a *selection effect* was evident for both groups – viewing of the selected target increased after playback of the critical word. (B) Withinsession word learning by the NC group increased their viewing of target items versus competitors whether selected (left) or not (right) while the TL group did not. Left, top: the NC group showed a temporally-localized increase in proportion fixation time to selected targets (black) versus selected competitors (gray). Left, bottom: the TL group did not selections (*: PFT Target > PFT Comp., p < 0.05). Right, top: meanwhile, the NC group viewed non-selected items similarly. (C) Increased viewing of correctly-selected targets by the NC group at test appeared to be an on-line expression of prior learning, while the TL group showed similar viewing of selected items whether correct or incorrect. Left, *correct trials*: Both groups viewed selected target items (black) more later in the trial. Right, *incorrect trials*: The TL group (bottom) also showed steadily increased viewing of incorrectly-selected competitor items (gray) later in incorrect trials. However, the NC group (top) differed, showing increased viewing of non-selected items later in the trial, notably the non-selected target (red). Thus, within-session word learning appeared to the on-line egned viewing of non-selected items later in the trial, notably the non-selected target (red). Thus, within-session word learning appeared to the web version of this atticle.)

trials and the selected-target ROI. We analyzed these data using a simple ANOVA with a single group-membership factor and planned comparisons. In the 3AFC test phase, each trial contained 3 ROIs (only one of which could be selected): the ROI containing the target image, and 2 ROIs containing competitor images. We analyzed these data using a repeated-measures ANOVA with a between-subjects group-membership factor (levels: TL and NC) and within-subjects factors representing ROI type (levels: target or competitor), selection (levels: selected and non-selected), and study condition (levels: EE or FM) along with planned comparisons. This ANOVA was applied separately to data from both correct trials and incorrect trials. Following examples from prior work (Hannula et al., 2007: Warren and Duff, 2014) correct trials were isolated in order to evaluate whether viewing of target items differed between groups and conditions over time without the potential confound of substantially different response latencies for correct vs. incorrect responses. Fixation data from incorrect trials were submitted to a parallel analysis in order to evaluate evidence for non-conscious influence of name learning expressed covertly in eye movements (Warren and Duff, 2014).

We analyzed proportional fixation-time measures time-locked to the onset of the critical target word ("crit", Fig. 1B and C). A 6-s. epoch including the critical event was analyzed, stretching from 2 s. before playback began to 4 s. after. The 6-s. epoch was split into 12 500-ms. timebins, and these timebins were a within-subjects factor. *Study*: fixation data from the FM condition within the ROI of correctly-selected targets were analyzed (EE displays contained only one item). Group membership was a between-subjects factor. *3AFC recognition*: study condition (levels: FM or EE) was added as a within-subjects factor. Additionally, ROI was added a within-subjects factor for separate analyses of selected ROI data (levels: selected-target and selected competitor) and non-selected ROI data (levels: non-selected target, non-selected competitor/ miss, and non-selected competitor/hit).

3. Results

3.1. Study phase: fast-mapping (referent selection) behavior

Both the TL and NC groups performed very well in the FM study phase (Fig. 2B, left) and did not differ from one another [Z=0.309, p=0.946]. Both groups accurately selected the uncommon item at rates near ceiling (TL, mean prop. correct=0.971, SEM=0.010; NC, mean=0.964, SEM=0.020) and performed almost perfectly on catch trials in which the target and lure items were both common items (TL group was perfect; NC group missed 1 trial total of 96 possible). Response times did not differ between groups, study conditions, or in the interaction of these factors [each *F* (1,10) < 2.371, each p > 0.155].

3.2. Study phase: eye movements

The NC and TL groups showed similar viewing of selected targets during FM study trials, viewing selected targets more later in the trial (Fig. 3A). Analysis of the timecourse of proportional fixation time by the TL and NC groups to the selected target ROI during correct FM study trials (timelocked to the onset of the critical word) did not show any between-group differences [*F*(12, 109)=1.029, p=0.428]. However, across all participants there were significant differences between the proportion of fixation time spent in the selected-target ROI between timebins [*F*(12,109)=240.433, p < 0.001]. This effect is attributable to both groups fixating the selected-target ROI more later in the trial, a *selection effect* that was significant for both groups soon after the critical word [NC, 0–500 ms, *Z*=5.291, p_c < 0.001; TL, 500–1000 ms, 5.413,

 $p_c < 0.001$]. Importantly, neither group differed from chance viewing in the 1000 msec. prior to the presentation of the critical word [each Z < 2.4, each $p_c > 0.2$] suggesting no bias in attention to either item.

3.3. 3AFC associative recognition: behavior

In the 3AFC recognition phase, the NC group showed clear evidence of learning the names of the novel items after the FM and EE study conditions while the TL group performed near chance in both study conditions (Fig. 2B, right). Specifically, there was a significant main effect of group [F(1, 10) = 85.829, p < 0.001] and planned comparisons indicated that the NC group performed better than the TL group in both study conditions (FM condition, Z=3.738, $p_c=0.001$; EE condition, Z=5.573, $p_c<0.001$). Within groups, no recognition differences were found between the FM and EE conditions (each Z < 2.0, each $p_c > 0.3$). Only the NC group performed significantly above chance (FM, Z=7.058, $p_c < 0.001$; EE, Z = 9.432, $p_c < 0.001$): the TL group never differed from chance performance (each Z < 1.8, each $p_c > 0.3$). Previous studies have indicated that FM study may produce less robust recognition performance than EE study (Coutanche and Thompson-Schill, 2014; Merhav et al., 2014; Sharon et al., 2011), and we observed this pattern in a post-hoc test of NC group 3AFC recognition [onetailed T-test (EE > FM), T(5) = 2.202, p = 0.039]. Response times did not differ between groups, study conditions, or in the interaction of these factors [each *F*(1,10) < 1.416, each *p* > 0.323].

This paradigm has previously been reported in a study of a severely amnesic group of patients with bilateral hippocampal damage (Warren and Duff, 2014), and in a *post-hoc* test we directly contrasted the 3AFC recognition performance of the two patient groups. After FM exposure, the performance of the two groups was numerically similar (amnesic mean=0.427, TL mean=0.425) and statistically indistinguishable [T(12)=0.031, p=0.976]. The same qualitative pattern was observed after EE exposure [amnesic mean=0.387, TL mean=0.414, T(12)=0.430, p=0.675].

3.4. 3AFC associative recognition: eye movements

The eye movements of the NC and TL groups differed during 3AFC recognition suggesting that correct 3AFC responses by the TL group were guided by chance rather than by knowledge (Fig. 3B andC). There was no significant effect of FM versus EE study condition in the timecourse of eye movements at test [F(1,206)] = 0.616, p=0.433], nor was there evidence of a significant interaction between group, timebin, and study condition [F(11,206)]= 0.616, p=0.814] so data from the FM and EE conditions were collapsed. Analysis of the timecourse of proportion of fixation time by the TL and NC groups to selected ROIs during correct and incorrect test trials (timelocked to the onset of the critical word) showed different patterns for the two groups. The TL group showed evidence of a selection effect during correct and incorrect test trials that was evident in above-chance viewing of the selected ROI after the critical word [timebin 1000-1500 ms, each Z > 3.0, each $p_c < 0.025$] (Fig. 3B, bottom left), but the proportion of viewing to selected target and competitor ROIs never differed significantly within a timebin [each Z < 1.5, each $p_c > 0.7$]. The NC group showed a selection effect for selected target ROIs [timebin 0-500 ms, Z=3.320, p_c =0.011] (Fig. 3B, top left), but no selection effect for selected competitor ROIs [each Z < 2.7, each $p_c > 0.08$]. Additionally, NC viewing of selected target ROIs during correct trials was greater than viewing of selected competitor ROIs during incorrect trials later in the trial [timebin 3500–4000 ms, Z > 2.779, $p_c=0.028$]. A complementary viewing effect was observed in NC group viewing of non-selected target ROIs in incorrect trials. Specifically, the NC group viewed non-selected target ROIs more than non-selected competitor ROIs late in 3AFC trials [timebins 3000–3500 and 3500–4000 ms, each Z > 2.8, each $p_c < 0.025$] (Fig. 3B, top right) potentially indicating some knowledge of the target's identity even when a non-target item was eventually selected. The TL group did not show this effect, viewing non-selected targets no differently than non-selected competitors [each Z < 2.2, each $p_c > 0.22$] (Fig. 3B, bottom right). Together, the NC group's significant reduction in viewing of incorrectly-selected competitors and significant increase in viewing of incorrectly-rejected targets suggest that their 3AFC responses were strongly influenced by learning during the study phase. Inversely, the lack of either effect in the TL group's eye movement data suggests that most of their 3AFC responses were guesses and not influenced by learning.

3.5. Free recall

The NC group was able to recall some unfamiliar names immediately after study and following a delay while the TL group had poor recall for unfamiliar names (Fig. 2C, left). However, the NC and TL groups had similar recall for familiar names after both the FM and EE study conditions (Fig. 2C, right). Notably, there were no differences in pre- and post-delay free recall performance for items that were unfamiliar [F(1,30) = 1.324, p = 0.259] or familiar [F(1,30)=2.004, p=0.167] so only post-delay free recall was analyzed for both types of items. Item familiarity influenced recall performance [F(1,30)=50.612, p<0.001] and interacted with study condition [F(1,30) = 5.124, p = 0.031], prompting separate consideration of familiar and unfamiliar items. For unfamiliar items, there was a significant effect of group [F(1, 10)=6.183,p=0.032], but no main effect or interaction with study condition [each F(1,10) < 1.7, each p > 0.20]. In planned comparisons the NC group recalled significantly more unfamiliar items than the TL group in the EE condition (Z=2.795, p_c =0.033) but not in the FM condition (Z=1.808, p_c =0.326). A different pattern was observed for familiar items: there was a significant main effect of study condition [F(1,10) = 11.395, p = 0.007]; but there was no effect of group [F(1,10)=0.877, p=0.371]. We attributed the increased number of familiar items recalled in the FM condition to the additional familiar items presented as lures. Consistent with this proposition, a supplemental analysis that replaced the number of items recalled with the proportion of studied items recalled showed that the proportion of familiar items recalled after FM study was significantly less than after EE [main effect of study condition: F(1,10) = 56.471, p < 0.001]. Regardless, the lack of a group difference for recall of familiar items in either study condition provides evidence that the TL group was not globally amnesic for verbal information.

3.6. Cued recall

The NC group recalled several items on average in the cued recall task and benefitted from a supplemental verbal cue, while the TL group recalled few items and did not show similar benefits (Fig. 2D). There were significant main effects of group [F(1,10)= 12.681, p=0.005] and cue type [F(1,30)=11.499, p=0.002] along with an interaction of those factors [F(1,30)=4.814, p=0.036]. There were no significant main effects of study condition [F(1,30)=0.637, p=0.431] or its interactions [each F(1,30) < 1.5, each p > 0.24]. Collapsing across study condition, the NC group recalled more items than the TL group in both the visual cue condition and the visual-and-verbal cue condition (each Z > 2.7, each p_c < 0.05) (Fig. 2D left and right, respectively).

3.7. Familiarity

At the beginning of the session, both groups rated item

familiarity using a 1–6 scale (not at all familiar to very familiar). Both groups rated common items as very familiar (each group mean > 5.8) and uncommon items as very unfamiliar (each group mean < 1.4). This difference in familiarity ratings between common and uncommon items was significant [F(1,34)=4883.261, p < 0.001] and there was no evidence of group differences [F(1,10)=0.036, p=0.853] or an interaction [F(1,34)=0.913, p=0.346].

At the end of the session, changes in the familiarity of unfamiliar words were assessed with a second familiarity rating phase. The NC group showed a larger change in familiarity ratings than the TL group [F(1,10)=5.623, p=0.039] and there was no effect of study condition overall or in interaction with study condition [each F(1,10) < 0.55, each p > 0.49] (Fig. 2E). Planned contrasts of rating changes versus zero indicated that the NC group significantly increased their familiarity ratings in both study conditions (each Z > 4.9, each $p_c < 0.001$) while the TL group increased their familiarity ratings in the EE condition (Z=2.711, p_c =0.043) but not the FM condition (Z=2.069, $p_c=0.204$). Numerically, the familiarity rating change for the TL group was approximately half that observed in the NC group in both conditions. A post-hoc test of the numerical difference between the TL group's FM and EE familiarity rating changes indicated that the difference was statistically significant [T(5)=3.110, p=0.027] although the effect size was relatively small, $d_{adj} = 0.232$. As a point of comparison, the corresponding difference in the NC group's ratings was not significant [T(5)=0.301, p=0.776] and the effect size was similar to that of the TL group, $d_{adi} = 0.182$.

4. Discussion

In this neuropsychological study, we evaluated the necessity of left temporal lobe for normal fast mapping and word learning. We observed that a group of TL patients and their matched healthy comparisons were able to successfully perform a fast-mapping task by selecting a novel referent in response to a novel word However, the TL group did not show significant evidence of learning unfamiliar words in subsequent explicit tests of memory or in eye movement measures while the NC group showed evidence of learning in many different explicit tests after both study conditions. These results are of particular interest because in contrast to previous studies of severely amnesic patients (Merhav et al., 2014; Sharon et al., 2011; Smith et al., 2014; Warren and Duff, 2014) the TL patients were not globally amnesic for verbal information but proved to be severely impaired at learning new names despite normal on-line responses in the fast-mapping study phase. These findings address an important unresolved issue by demonstrating that left temporal lobe lesions including the left hippocampus and left temporal pole are sufficient to impair word learning without altering on-line responses to novel words. In so doing, these results also reinforce a previously characterized relationship between naming and verbal memory processes supported by left temporal lobe regions including temporal pole and hippocampus, respectively.

The neuropsychological status and task performance of the TL group in our study was broadly congruent with expectations based on previous descriptions of temporal lobectomy samples (Gleissner et al., 2004; Ojemann and Dodrill, 1985; Rausch et al., 2003; Saykin et al., 1995). Pre-experimentally, the normal but numerically reduced naming performance of the current TL group was typical of other TL patients and clinical epilepsy populations, although less exaggerated than in some reports. Verbal memory performance was better preserved in the current group than previous reports would have predicted. We speculate that some degree of developmental reorganization may have been possible

for TL participants in the current group given the early onset of their seizure activity, but we also note that presurgical WADA testing indicated left-lateralized language function for all TL participants. The TL group's neuropsychological characteristics were reflected in their task performance: common object naming ability was sufficiently spared to support normal fast mapping performance; verbal memory for familiar words was relatively spared as shown in free recall; but unfamiliar words were remembered poorly if at all, as shown in both free recall and 3AFC recognition. In short, the sample of TL patients recruited for this study showed a selective neuropsychological deficit for learning new words after controlled laboratory exposure.

Our novel findings are broadly congruent with the larger literatures of word learning, word knowledge, and naming which have frequently associated these abilities with left temporal lobe. Left temporal pole has been implicated as a critical substrate of naming and conceptual knowledge by neuropsychological and functional neuroimaging studies (Damasio et al., 2004; Davis et al., 2009; Grabowski et al., 2001; Visser et al., 2010). Correlational neuroimaging evidence has also related left hippocampus and left MTL to normal word learning performance (Breitenstein et al., 2005; Davis et al., 2009). Sharon et al. (2011) previously reported that damage to left hippocampus and left temporal pole was sufficient to disrupt word learning under FM and EE conditions in a single neurological patient (patient A.A.), an outcome that was consistent with an earlier report of impaired word learning by a patient following traumatic left temporal lobe damage (Tranel, 1991). Our study supports and extends these findings through methodological refinements and use of a larger sample of patients with joint left hippocampal and left temporopolar damage. Importantly, presurgical Wada testing of the current patient sample demonstrated their uniform left lateralization of language functions while previous studies have typically relied on normative assumptions regarding language lateralization.

Based on the current findings in TL patients and previous findings from patients with bilateral hippocampal damage, we speculate that the left hippocampal damage common to these samples may be sufficient to produce deficits in word learning by explicit encoding (Merhav et al., 2014; Sharon et al., 2011) or by any means (Smith et al., 2014; Warren and Duff, 2014). This would be consistent with an acknowledged role played by the hippocampus in binding together arbitrarily related stimuli (Davachi and Dobbins, 2008; Eichenbaum and Cohen, 2001; Ranganath, 2010). While previous reports that word learning was rescued by fast mapping in three patients with bilateral hippocampal damage (Merhav et al., 2014; Sharon et al., 2011) weigh against this account, failures to demonstrate extrahippocampal word learning by fast mapping in independent laboratories (Smith et al., 2014; Warren and Duff, 2014) suggest that the phenomenon may be more complex or more fragile than is currently understood. Application of the current methodology to neuropsychological cases with isolated left hippocampal damage could potentially address our speculative prediction. Damage to other left temporal lobe regions including left temporal pole may also be sufficient to produce severe deficits in word learning (Sharon et al., 2011; Tranel, 1991), and neuropsychological studies of patients with focal damage would be very informative. Alternatively, testing of a substantially larger patient group might support a voxelwise lesion symptom analysis (Rorden and Karnath, 2004) of wordlearning phenomena that would parallel previous efforts which targeted naming abilities (Damasio et al., 2004).

We observed that fast-mapping behavior was normal in the TL group despite their lack of word learning. This suggests that the neural substrates of fast-mapping behavior were preserved. In this vein, it is notable that previous work has shown that bilateral hippocampal damage or more extensive damage to the medial

temporal lobes can produce mild impairments in fast-mapping behavior (Warren and Duff, 2014). These dissociations between intact fast-mapping behavior and deficits in learning following successful fast-mapping highlight the importance of distinguishing one from the other in research designs and interpretation of findings (Bion et al., 2013; Carey, 2010; McMurray et al., 2012; Warren and Duff, 2014). However, this distinction between the act of fast mapping and any corresponding word-learning process that begins with that action has been sometimes overlooked in cognitive neuroscience investigations which have adapted fast mapping methods. Concerns over ambiguity in reporting have prompted some researchers to describe fast-mapping performance as "referent selection" to prevent confusion (McMurray et al., 2012). Whatever terms are used, accurate descriptions of these behaviorally dissociable abilities are critical for unambiguous communication between researchers.

Regarding the neural substrates of fast mapping behavior, we suggest that successful fast-mapping behavior requires the coordinated deployment of many cognitive processes that have widespread neural bases. A partial list of such processes (and their roles) would include: visual perception (item discrimination); auditory perception (word discrimination); visual memory (identify novel item); auditory memory (identify novel word); naming (naming familiar items); and executive functions (response selection, decision-making). We hypothesize that damage to brain regions supporting one or more of these processes could potentially disrupt fast mapping performance. The large number of component processes will make it challenging to identify regions that might be uniquely associated with and necessary for fastmapping behavior. Candidate regions might be identified based on correlational functional neuroimaging data related to word learning and fast mapping performance (Atir-Sharon et al., 2015; Davis et al., 2009; Merhav et al., 2015), and those candidate regions could be evaluated neuropsychologically.

In the current study, one piece of evidence suggesting that the TL group may have acquired some information about unfamiliar words was the increase in their familiarity ratings during the test session. This change in familiarity could have been driven by repeated exposure to the unfamiliar words during various phases of the session (e.g., 3AFC recognition, cued recall) in addition to the study-time exposure. However, we cannot apply the same explanation to the small but statistically significant advantage of the explicit encoding format over the fast-mapping encoding format for this measure in the TL group. This effect could be attributable to meaningful differences in the two encoding conditions, but we note the modest effect size (see Section 3) and the unique directionality of this outcome among our findings.

Our study had some limitations. As in many neuropsychological investigations, our sample sizes were relatively small owing to strict inclusion criteria (see Section 2), but enforcing these criteria yielded a TL group with relatively homogenous profiles and performance. Meanwhile, homogeneity in the resection of left hippocampus combined with resection or surgical disconnection of the left temporal pole in the TL group limited our ability to draw conclusions about the respective contributions of these two regions. On this topic, Sharon et al. (2011) reported one case (patient K.S.) with relatively focal left temporal pole damage who had word learning impairments despite fast-mapping study, and functional neuroimaging studies have provided correlational evidence consistent with the hypothesis that left temporal pole is necessary for word learning by fast mapping (Atir-Sharon et al., 2015; Merhav et al., 2015). Returning to the current patient sample, the history of epilepsy shared by all TL participants could potentially have contributed to deficits in name learning. These factors limit the specificity of our conclusions, but we note that the current TL group normative performance on a had naming standard

neuropsychological test (albeit numerically below average; see Table 1) suggesting that their real-world word learning performance was relatively unaffected by the disease process prior to resection. Additionally, at least one patient with a history of epilepsy and a unilateral right temporal lobe resection (patient M.E.) has been reported to have normal word learning following fast mapping (Merhav et al., 2014) which suggests that a history of epilepsy does not preclude rapid word learning. Subsequent research with TL patients might attempt to recruit non-resected patients with a history of epilepsy as an additional comparison or adopt a longitudinal strategy to study the same patients before and after TL resection.

In summary, we found that participants with left temporal lobe resections including left hippocampus and left temporal pole exhibited profound deficits in the learning of new words whether by explicit encoding or fast mapping. These findings are consistent with prior work but extend those findings methodologically by using careful inclusion criteria and collecting eye movement data to evaluate any covert expressions of learning. Meanwhile, the TL group was unimpaired when responding to a novel word in a contrastive learning context. In contrast to findings from amnesic patients (Smith et al., 2014; Warren and Duff, 2014) the TL group did not show global memory deficits, instead demonstrating normal recall of familiar words after a 30-min delay while memory for unfamiliar words was selectively impaired. This pattern of spared and impaired performance on a free-recall test is novel to our knowledge and may reflect unique contributions of left temporal lobe to memory for novel but not familiar words. Further investigation of the neural substrates of word learning could explore this speculative relationship further and potentially contribute to improved rehabilitation techniques for populations with wordlearning deficits.

Author contribution

D.E.W., D.T., and M.C.D. designed research; D.E.W. and M.C.D. performed research; D.E.W. analyzed data; D.E.W., D.T., and M.C.D. wrote the paper.

Conflicts of interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.neuropsychologia. 2015.11.016.

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