Resolving Cross-modal Semantic Interference among Object Concepts Requires Medial Temporal Lobe Cortex

Chris B. Martin[1]*, Danielle M. Douglas[2]*, Louisa L. Y. Man[3], Rachel N. Newsome[4], Ryan A. Kretschmar[1], Haley Park[4], Hira M. Aslam[4], and Morgan D. Barense[4,5]

Abstract

■ The ability to flexibly categorize object concepts is essential to semantic cognition because the features that make two objects similar in one context may be irrelevant and even constitute interference in another. Thus, adaptive behavior in complex and dynamic environments requires the resolution of feature-based interference. In the current case study, we placed visual and functional semantic features in opposition across object concepts in two categorization tasks. Successful performance required the resolution of functional interference in a visual categorization task and the resolution of visual interference in a functional categorization task. In Experiment 1, we found that patient D. A., an individual with bilateral temporal lobe lesions, was unable to categorize object concepts in a context-dependent manner. His impairment was characterized by an increased tendency to incorrectly group objects that were similar on the task-irrelevant dimension, revealing an inability to resolve cross-modal semantic interference. In Experiment 2, D. A.'s categorization accuracy was comparable to controls when lures were removed, indicating that his impairment is unique to contexts that involve cross-modal interference. In Experiment 3, he again performed as well as controls when categorizing simple concepts, suggesting that his impairment is specific to categorization of complex object concepts. These results advance our understanding of the anterior temporal lobe as a system that represents object concepts in a manner that enables flexible semantic cognition. Specifically, they reveal a dissociation between semantic representations that contribute to the resolution of cross-modal interference and those that contribute to the resolution of interference within a given modality. ■

INTRODUCTION

Semantic memory allows us to think about and categorize concepts according to multiple criteria. For example, we can group "electric drill" with "hammer" when task demands emphasize knowledge of functional features, or with "hairdryer" when task demands emphasize knowledge of sensory features, such as prototypical shape. The fact that a given feature will be relevant in some contexts and irrelevant in others establishes a need to flexibly resolve interference. Otherwise, cross-modal interference can cause categorization errors, such as incorrectly grouping "electric drill" with "hairdryer" rather than "hammer" when function matters but form does not. One prominent perspective suggests that this flexibility reflects interactions between a system of semantic representation and a system of cognitive control (Lambon Ralph, Jefferies, Patterson, & Rogers, 2017). In the current neuropsychological single-case study, we aimed to better understand the functional properties of the system of representation, with a particular focus on structures in the temporal lobe. Specifically, we asked whether neocortical structures in the medial temporal lobes (MTLs) represent the semantic

information that critically enables the resolution of cross-modal semantic interference.

Evidence from multiple lines of research suggests that MTL cortex contributes to the resolution of interference in multiple task contexts. For example, individuals with damage that affects perirhinal cortex (PRC) are susceptible to interference in perceptual discrimination tasks involving pictures of objects with high visual feature overlap (Inhoff et al., 2019; Barense et al., 2012; Barense, Henson, Lee, & Graham, 2010; Barense et al., 2005; Lee et al., 2005; see Ferko et al., 2022; O'Neil, Cate, & Köhler, 2009, for convergent neuroimaging data in neurologically healthy participants). PRC lesions also result in an impoverished ability to resolve interference among objects and object concepts with a high degree of semantic feature overlap (Wright, Randall, Clarke, & Tyler, 2015; Kivisaari, Tyler, Monsch, & Taylor, 2012; Noppeney et al., 2007; Moss, Rodd, Stamatakis, Bright, & Tyler, 2005; see Liuzzi et al., 2019; Clarke & Tyler, 2014; Bruffaerts et al., 2013; Tyler et al., 2013, for convergent neuroimaging data). These deficits can be understood through the lens of theoretical models that situate PRC at the apex of an object processing pathway in inferior occipitotemporal cortex (Clarke & Tyler, 2015; Kravitz, Saleem, Baker, Ungerleider, & Mishkin, 2013; Taylor, Devereux, & Tyler, 2011; Graham, Barense, & Lee, 2010; Taylor, Moss, Stamatakis, & Tyler, 2006; Murray & Bussey, 1999). On these accounts, PRC

[1]Florida State University, Tallahassee, [2]Mount Allison University, Canada, [3]Queens University, Canada, [4]University of Toronto, Canada, [5]Rotman Research Institute, Canada
*Indicates equal contributions.

represents objects and object concepts as unique conjunctions of features that can be used to resolve interference in experimental contexts that involve high feature overlap. Impairments emerge when these comparatively complex representations are compromised, and performance is driven by low-level feature information represented elsewhere in the brain, such as more posterior areas in the ventral visual stream.

Although object information in MTL cortex is thought to be multidimensional (Lehky & Tanaka, 2016; Suzuki & Naya, 2014; Ranganath & Ritchey, 2012), it is unclear whether it contributes to the flexible resolution of interference across semantic modalities. However, findings from a recent fMRI study suggest that it may be well suited to do so. Specifically, a representational similarity analysis of neural activity patterns evoked by thinking about object concepts revealed that PRC was the only region in the entire brain that simultaneously captured semantic similarities at the level of sensory features (e.g., prototypical shape, size, texture, color) and nonsensory features (e.g., functional, contextual, and encyclopedic; Martin, Douglas, Newsome, Man, & Barense, 2018). Thus, activity patterns in this region simultaneously reflected the visual similarity between "electric drill" and "hairdryer," and the functional similarity between "electric drill" and "hammer." This result was obtained across task contexts that biased participants toward processing either visual or functional information in semantic memory and controlling for the fact that these kinds of features tend to covary across stimuli. Importantly, although visual and functional information always simultaneously shaped the representational structure of activity in PRC, information from the task-relevant modality had the strongest influence. That is to say, semantically based visual information best explained neural similarity in the visual task context, whereas information pertaining to functional features best explained neural similarity in the functional task context. This pattern of results suggests that PRC integrates semantic features from different modalities, and that its representational structure is flexibly modulated by task demands (see Lambon Ralph et al., 2017; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997, for related discussion). As such, PRC has a unique representational capacity to variably enable categorization of "electric drill" with either "hairdryer" or "hammer" depending on contextual factors.

In the current study, we asked whether an individual (patient D. A.; Figure 1) with temporal lobe damage could flexibly resolve cross-modal semantic interference in categorization tasks that used concrete object concepts as stimuli. On each trial, participants were presented with a trial-unique referent concept and asked to select either a visual or functional match from a four-alternative array. In the visual categorization task, the referent (e.g., "electric drill") was visually but not functionally similar to the target (e.g., "hairdryer") and functionally but not visually similar to a lure (e.g., "hammer"). In the functional categorization task, the referent (e.g., "electric drill") was functionally but not visually similar to the target (e.g., "hammer") and visually but not functionally similar to a lure (e.g., "hairdryer," Figure 2). With this design, successful categorization performance required the resolution of functional interference in a visual categorization task and the resolution of visual interference in a functional categorization task. In both cases, our stimulus set was carefully developed to ensure that visual and functional features were not confounded across concepts. We hypothesized that if multidimensional object representations in MTL cortex are required for cross-modal interference resolution, then D. A. would be impaired on our categorization task. We predicted that this impairment would manifest as an elevated tendency to incorrectly select lures. We also predicted that D. A. would perform as well as control participants when the lures were removed from each four-alternative array (Figure 5), indicating that MTL cortex plays a particularly important role in resolving interference rather than a more general role in semantic categorization. Lastly, we predicted that D. A. would also perform as well as controls when categorizing simple concepts (e.g., letters or numbers, Figure 6) with interference that varied along a single dimension, which can be resolved based on low-level features represented outside of the MTL (Barense et al., 2012).

METHODS

Experiment 1: Categorization of Object Concepts with Cross-modal Semantic Interference

Participants

We tested two memory-impaired individuals with different lesion profiles, as well as 21 age- and education-matched
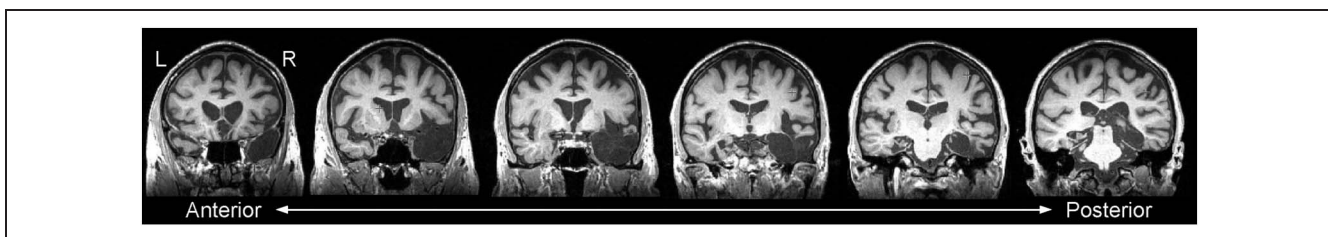
Figure 1. D. A.'s brain lesion. Coronal slices from a T1-weighted MRI (MPRAGE) illustrating complete loss of right medial and anterior temporal lobe structures and selective loss of left MTL structures.
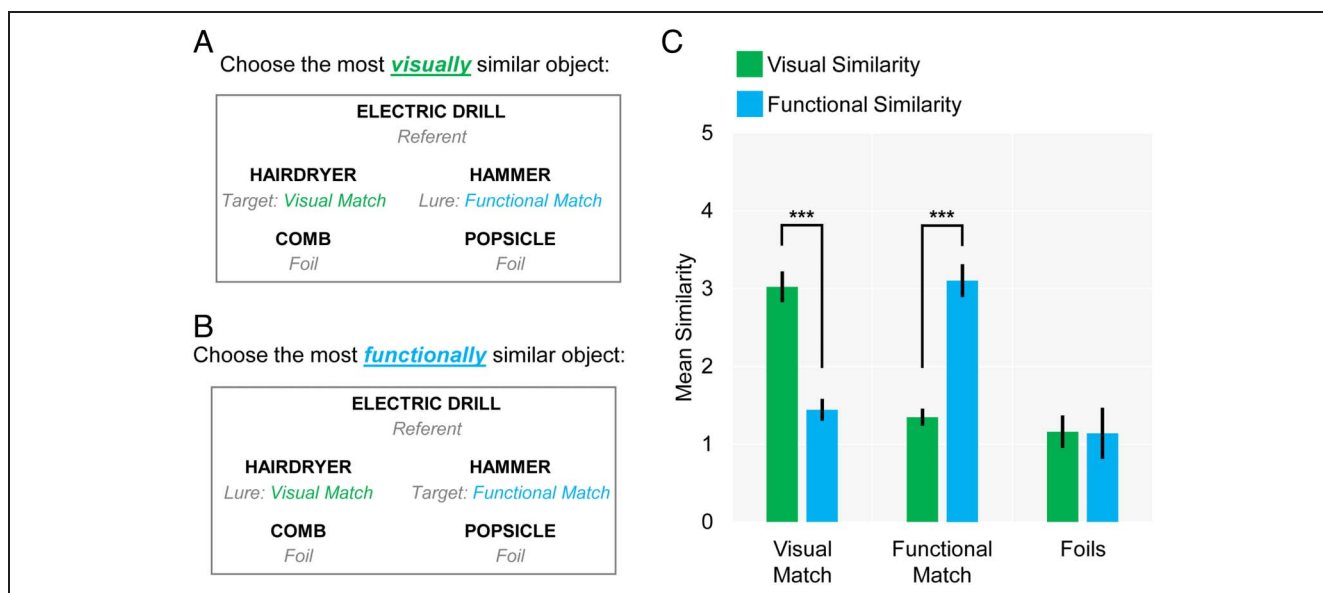
Figure 2. Categorization tasks and normative stimulus data. (A) In the visual categorization task context, participants were instructed to choose the alternative that was visually most similar to the referent. (B) In the functional categorization task context, participants were instructed to choose the alternative that was functionally most similar to the referent. (C) Normative similarity ratings from an independent sample of healthy control participants ($n = 17$). Pairwise ratings were obtained between trial-unique referent concepts and each alternative (i.e., visual match, conceptual match, foils). Participants rated visual and functional similarities separately. Ratings ranged 1–5, with higher values indicating greater similarity.

control participants. All participants received either monetary compensation or course credit. Written consent was obtained from each participant, and the study was approved by the research ethics board at the University of Toronto and Baycrest Hospital.

Patient D. A. Patient D. A. is a right-handed man with 17 years of education. He was 64 years of age at the time of testing. An extensive description of his case history and neuroanatomical lesion profile has been described previously (Olsen et al., 2013; Rosenbaum et al., 2008; Westmacott, Black, Freedman, & Moscovitch, 2004). D. A. developed amnesia after contracting herpes simplex viral encephalitis in middle age. He sustained extensive damage to the right MTL and anterior temporal lobe, with near complete ablation of PRC, entorhinal cortex, parahippocampal cortex, amygdala, the hippocampus, and temporopolar cortex (Figure 1, Table 1). Further right hemisphere volume loss was observed in posterior temporal, ventral frontal, and occipital regions. In the left hemisphere, D. A. has focal damage in the MTL, with

an additional small lesion in middle temporal gyrus (Rosenbaum et al., 2008). Considered together, D. A. has bilateral MTL damage, right-lateralized damage to the medial and lateral extent of the temporal pole, and a largely intact left temporal pole (both medial and lateral). This lesion profile presents an opportunity to ask whether structures comprising the MTL and/or right temporal pole contribute to the resolution of cross-modal semantic interference. Above chance performance on our categorization task would suggest that the left temporal pole, which figures prominently in relevant neurocognitive theories of semantic cognition (Lambon Ralph et al., 2017; Pobric, Jefferies, & Ralph, 2010; Patterson, Nestor, & Rogers, 2007), can support this aspect of cognition.

Patient H. C. Patient H. C. is a right-handed woman with 14 years of education. She was 27 years of age at the time of testing. H. C. has developmental amnesia attributed to congenital hippocampal damage caused by hypoxia during a premature birth (Rosenbaum, Gao, et al., 2014; Rosenbaum, Gilboa, & Moscovitch, 2014; Olsen et al.,

Table 1. MTL Volume Relative to Age-matched Controls (*z*-Scored)

	PRC		Entorhinal Cortex		Parahippocampal Cortex		Hippocampus	
	Left	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*
D. A.[a]	−9.75	−7.12	−6.65	−6.02	−4.00	−3.13	−4.14	−5.19
H. C.[b]	0.23	1.10	−0.57	−0.84	2.25	1.85	−3.14	−3.04

[a] Ryan et al. (2013).

[b] Olsen et al. (2013).

2013; Rosenbaum et al., 2011; Vargha-Khadem et al., 2003). A detailed volumetric assessment indicates that her hippocampi are 30% smaller than what is typical of age-matched controls, with most pronounced reductions in the anterior extents (Table 1). The mammillary bodies and anterior fornices were absent, and anterior thalamic nuclei were significantly reduced. Although her perirhinal and parahippocampal cortices show abnormal shape, it is unclear whether these morphological differences impact on behavior. H. C.'s overall brain volume was within the normal range (Rosenbaum, Gao, et al., 2014; Rosenbaum, Gilboa, et al., 2014; Olsen et al., 2013). Looking across patients, D. A. has bilateral damage to all MTL structures as well as the right temporal pole, whereas clear damage in H. C. is more focally limited to the hippocampus. Thus, if D. A. is impaired on a categorization task that requires the resolution of cross-modality interference but H. C. is not, then we can conclude that this aspect of cognition critically requires extrahippocampal MTL cortex (i.e., PRC, entorhinal cortex, and parahippocampal cortex) and/or the right temporal pole.

Neuropsychological profiles.   Results from extensive neuropsychological batteries administered to D. A. and H. C. have been reported previously (Ryan, Moses, Barense, & Rosenbaum, 2013; Kwan, Craver, Green, Myerson, & Rosenbaum, 2013; Rabin, Braverman, Gilboa, Stuss, & Rosenbaum, 2012; Rosenbaum et al., 2011; Rosenbaum et al., 2008; Westmacott et al., 2004; Vargha-Khadem et al., 2003). We include these data here to provide a comprehensive picture of their cognitive performance. We also administered a series of new assessments to D. A., including the Weschler Abbreviated Scale of Intelligence (WASI) Similarities subtest, the Vividness of Visual Imagery Questionnaire (VVIQ; Marks, 1973), the Verbalizer–Visualizer Questionnaire (VVQ; Richardson, 1977), a 64-item semantic battery (Bozeat, Ralph, Patterson, Garrard, & Hodges, 2000), and the word and the picture versions of the Camel and Cactus Test (Bozeat et al., 2000). H. C. was unable to complete these tasks because of time constraints.

Although D. A. has severe anterograde and graded retrograde amnesia, his cognitive abilities are otherwise largely intact (Table 2). He has above-normal intelligence and normal perceptual, verbal, and executive functions. D. A.'s performance on semantic memory assessments was mixed (Table 2 and 3). Relative to normative data (Garrard, Carroll, Vinson, & Vigliocco, 2004; Bozeat et al., 2000), D. A. was within the normal range at picture naming (Picture Naming, Table 3), category comprehension (Category Comprehension, Table 3), and matching objects based on their semantic relatedness (word and picture version of Camel and Cactus Test, Table 3). However, his ability to name objects based on either a functional or perceptual description was impaired (Naming to Description, Table 3). There was no hint of category-specific impairments (e.g., living vs. nonliving) on any task. This pattern suggests that D. A. may have a subtle semantic

memory impairment. Lastly, D. A. is able to visualize objects as well as healthy controls, as indicated by data from the VVIQ and VVQ (VVIQ: D. A. = 38, control mean = 28.3 ± 8.4; VVQ verbal: D. A. = 7, control mean = 7.8 ± 1.0; VVQ visualizer: D. A. = 9, control mean = 8.6 ± 1.2).

Healthy control participants.   Twenty-one neurologically healthy individuals were recruited from the University of Toronto and surrounding community for Experiment 1. Eight healthy older adults were yoked to D. A. (five men; mean age = 64.7 years, *SD* = 2.12 years, range = 62–68 years; mean years of education = 16.50, *SD* = 1.41). Thirteen healthy young adults were yoked to H. C. (12 women; mean age = 21.54 years, *SD* = 5.08 years, range = 17–34 years; mean years of education = 13.69, *SD* = 1.55). All control participants were native English speakers screened for a history of neurological disorders. Older participants completed the Montreal Cognitive Assessment (Nasreddine et al., 2005) to ensure overall cognitive well-being.

Stimuli

Five hundred words referring to concrete object concepts were used as stimuli. See https://osf.io/ht86r/ for the complete stimulus set and corresponding normative data. These were systematically divided into 100, five-word sets (i.e., pentads). Each pentad consisted of a referent word and four alternative words that varied in kind and degree of similarity to the referent (Figure 2A–B). One alternative was visually very similar to the referent but only minimally similar in terms of function (i.e., visual match). This concept served as a target in the visual categorization task and a lure in the functional categorization task. A second alternative was functionally very similar to the referent but only minimally similar in terms of visual features (i.e., functional match). This concept served as a target in the functional categorization task and a lure in the visual categorization task. The two remaining alternatives were unrelated to the referent and served as foils. One foil was functionally similar to the visual match, and the other was visually similar to the functional match. Foils were included to maximize interference among object concepts within each pentad and to prevent participants from using an elimination strategy when responding.

Initial stimulus selection was based on experimenter intuition. We then quantified within-pentad similarities using ratings data obtained from an independent sample of 17 cognitively and neurologically healthy participants (8 women, mean age = 26.8 years, range = 22–30 years). Participants made pairwise judgments regarding the degree of visual and functional similarity between the referent and each of the alternatives using a 5-point Likert scale (Figure 2C). These ratings were obtained using pairwise stimulus presentations, without any overt reference to the pentad structure. After collapsing ratings data across all four alternatives, mean visual similarity with referents did not differ from mean functional similarity with referents,

Table 2. Neuropsychological Profiles

	D. A.	H. C.		D. A.	H. C.
Intelligence (WAIS-R)			Anterograde Memory		
Full Scale IQ	117 (87%)	106 (66%)	WMS-R[b]		
Verbal IQ	121 (92%)	104 (61%)	General Memory	74 (5%)	49 (<1%)
Performance IQ	106 (66%)	106 (66%)	Verbal Memory	74 (5%)	–
AM-NART	117 (87%)	101 (53%)	Visual Memory	81 (37%)	–
			Logical Passages I	84 (15%)	4 (3%)
			Logical Passages II	45 (1%)	0 (1%)
			Visual Reprod. I	7 (19%)	4 (2%)
			Visual Reprod. II	0–2 (1%)	2 (1%)
Executive Function			ROCF		
Letter Fluency	8 (25%)	11 (69%)	Copy (/36)	35	36
TMT A	–	0.69 (76%)	Immediate Recall	–	<20 (1%)
TMT B	–	−0.23 (41%)	Delayed Recall	27 (1%)	<20 (1%)
WAIS-R Digits	13 (84%)	13 (84%)	WRMT Words	21/50	–
WCST Cat.	6/6	6/6	WRMT Faces	25/50	–
WCST Persev. Resp.	−0.5 (31%)	–			
Language and Semantic Knowledge			CVLT		
WAIS-R Vocab.[a]	12 (75%)	11–12 (69%)	Acquisition	9 (1%)	38 (11%)
WASI Similarities	48 (42%)	–	Short Delay	−4 (1%)	−4 (1%)
BNT (/60)	56	58	Long Delay	−4 (1%)	−3 (1%)
Semantic Fluency	12 (75%)	>14 (>94%)	Recognition	−4 (1%)	−2 (1%)
Visual Perception					
Line Orient.	26/30	24/30			

H. C. completed the [a]WASI and [b]WMS-III. D. A. data sourced from Olsen et al. (2013), Rosenbaum et al. (2008), and Westmacott et al. (2004). H. C. data sourced from Kwan et al. (2013), Rabin et al. (2012), and Rosenbaum et al. (2011). AM-NART = American National Adult Reading Test; BNT = Boston Naming Test; CVLT = California Verbal Learning Test; ROCF = Rey Osterrieth Complex Figure; Persev. Resp. = Perseverative Response; TMT = Trail-Making Test; WAIS-R = Wechsler Adult Intelligence Scale–Revised; WASI = Weschler Abbreviated Scale of Intelligence; WCST = Wisconsin Card Sorting Test; WMS-R = Weschler Memory Scale–Revised; WRMT = Warrington Recognition Memory Test; % = percentile rank.

$F(1, 16) = 0.53, p = .48, \eta_p^2 = .03$. In line with the objectives of our initial stimulus selection, visual matches were more than twice as similar to the referents in the visual modality than they were in the functional modality, $t(16) = 6.60, p < .001, d = 1.60$, and functional matches were more than twice as similar to the referents in the functional modality than they were in the visual modality, $t(16) = 6.67, p < .001, d = 1.62$. Importantly, mean degree of similarity between visual matches and referents did not differ from that of functional matches and referents, $t(16) = 0.43$, p = .68, Cohen's $d = 0.10$, but there were numerical differences among these relationships within a given pentad.

Procedure

Participants completed our semantic categorization task in one of two contexts. In the visual task context, they were asked to indicate which object concept among the four alternatives was most visually similar to the referent (Figure 2A). Participants were explicitly told that "visually similar" refers to the object concept (i.e., prototypical visual form), not the orthography of the word. In the functional task context, they were asked to select the object concept that was most functionally similar to the referent (Figure 2B). The task contexts were blocked, such that each participant completed 50 consecutive trials in one

Table 3. D. A.'s Semantic Memory Profile

	D. A.	Healthy Controls
Picture Naming[a] (/64)	98.44%	97.3% (2.5%)
Category Comprehension[a] (/64)	100.00%	99.5% (0.8%)
Camel and Cactus Pictures[a] (/64)	84.38%	88.9% (12.1%)
Camel and Cactus Words[a] (/64)	85.94%	92.3% (9.8%)
Naming to Description Perceptual[b] (/64)	67.19%***	84.4% (3.1%)
Living (/32)	68.75%	–
Nonliving (/32)	65.63%	–
Naming to Description Functional[b] (/64)	79.69%*	89.2% (3.8%)
Living (/32)	81.25%	–
Nonliving (/32)	78.13%	–

[a] Bozeat et al. (2000), $n = 14$.

[b] Garrard et al. (2004), $n = 20$.

* $p < .05$, $t(19) = 2.78$, $z_{CC} = 2.54$.

*** $p < .001$, $t(19) = 6.02$, $z_{CC} = 5.5$.

task context and then completed the remaining 50 trials in the other task context. Given the nature of D. A.'s and H. C.'s memory impairments, task-specific instructions were presented on screen for every trial. Block order and assignment of pentads to task condition were counterbalanced across control participants, and pentad order was randomized within each block. To facilitate comparison, D. A. and H. C. completed the visual task context block first, although trial order was randomized for each. All participants completed three practice trials with feedback at the beginning of each block to ensure task comprehension. Blocks were separated by a 2-min rest period. The task was self-paced, and participants responded using keyboard buttons mapped to four locations on screen: upper left (A), bottom left (Z), upper right (K), and bottom right (M). Brightly colored stickers marked response buttons to remind participants of key locations. The experiment was implemented in E-Prime (Psychology Software Tools).

D. A. completed the experimental task twice to ensure that his performance was stable and could not be explained by an inability to understand the task demands. Sessions 1 and 2 were separated by 5 months, a delay that reflected constraints to his availability. In Session 1, D. A. responded using a button press, whereas Session 2 involved verbal responses that required a logical explanation for each decision. Verbal responses were obtained to ensure that any deficits were not because of D. A. confusing the response button mappings and to ensure that we gave him the opportunity to clarify any confusion he might have about the task instructions. Note that for this reason, we were unable to obtain measures of RT in Session 2. Anecdotally, we note that in Session 2, D. A. often read the on-screen instructions aloud to himself before making

a response, including on trials for which he endorsed an incorrect alternative. Moreover, he never expressed any confusion about the task instructions. These behaviors suggest that D. A.'s errors are unlikely to reflect an inability to remember or understand the task demands.

Results

Experiment 1: Accuracy. We compared D. A.'s and H. C.'s categorization performance to their respective control group using Crawford's *t* test, a conservative analysis for single-case studies (Crawford & Howell, 1998). Effect sizes were estimated using case–control *z* scores (zCC; Crawford, Garthwaite, & Porter, 2010). These analyses revealed significant impairments in D. A.'s performance in both the visual and functional categorization task contexts for Session 1 (visual task: $t(7) = -8.35$, $p < .001$, zCC $= -7.81$; functional task: $t(7) = -8.43$, $p < .001$, zCC $= -7.88$; Figure 3A) and Session 2 (visual task: $t(7) = -4.21$, $p = .001$, zCC $= -3.94$; functional task: $t(7) = -8.43$, $p < .001$, zCC $= -10.55$; Figure 3A). The magnitude of D. A.'s deficit was striking. His visual categorization task accuracy fell 7.81 (Session 1) and 3.94 (Session 2) standard deviations below the control mean, and his functional categorization task accuracy fell 7.88 (Session 1) and 10.55 (Session 2) standard deviations below the control mean. In stark contrast, H. C.'s performance did not differ from her control group in either task context (visual task: $t(12) = -0.28$, $p = .39$, zCC $= .26$; functional task: $t(12) = -0.56$, $p = .29$, zCC $= .53$). With respect to RTs, both D. A. and H. C. responded as quickly as participants in their respective control groups (D. A. visual task: $t(7) = 0.07$, $p = .47$, zCC $= -.07$; D. A. functional task: $t(7) = -0.11$, $p = .46$, zCC $= .10$; H. C. visual

task: $t(12) = 0.77$, $p = .23$, zCC $= -.72$; H. C. functional task: $t(12) = 0.93$, $p = .18$, zCC $= -.87$). Together, these findings indicate that D. A. was unable to accurately categorize object concepts in the presence of cross-modal semantic interference. Raw and summarized data for all experiments can be accessed at https://osf.io/ht86r/.

Experiment 1: Error analysis. In a key test of our hypothesis, we next examined the nature of D. A.'s categorization errors to determine whether they reflected an inability to resolve cross-modal semantic interference (Figure 3B–C). If this were the case, we would expect a disproportionate number of errors to be an endorsement of the lure rather than either of the foils. Indeed, D. A.'s errors were not evenly distributed across incorrect alternatives; nearly all errors involved selection of a lure. In other words, he would incorrectly choose the functional match in the visual categorization task context, and the visual match in the functional categorization task context. This pattern of results contrasts sharply with that observed in H. C., whose errors were distributed evenly across lures and foils. Together, these results suggest that D. A. is unable to resolve cross-modal semantic interference.

Experiment 1: Trial-level difficulty analysis. Although mean visual and functional similarities were statistically equated between referent versus target and referent versus lure comparisons, there was considerable numerical variability within pentads. Targets were numerically more similar to referents than were lures on some trials, and lures were numerically more similar to referents than were targets on other trials. This allowed us to ask whether D. A.'s impairment was driven by a tendency to choose the alternative that was most similar to the referent

irrespective of task demands. To this end, we quantified difficulty on a trial-by-trial basis using normative data obtained from the independent sample of participants that rated the similarities among object concepts within each pentad. Difficulty was calculated as the difference score between overall referent versus lure similarity and overall referent versus target similarity [i.e., (referent vs. lure visual similarity + referent vs. lure functional similarity) − (referent vs. target visual similarity + referent vs. target functional similarity)]. Positive difference scores were obtained when the lure was more similar to the referent than was the target, and negative difference scores were obtained when the target was more similar to the referent than was the lure. Thus, from the perspective of interference resolution, trials with positive values were more difficult than those with negative values. If D. A.'s impairment was driven by difficulty rather than resolving cross-modality interference per se, then his incorrect trials should be biased toward more difficult trials.

We found mixed results in both task contexts (Figure 4). Visual inspection of difficulty distributions for correct and incorrect trials reveals that D. A.'s poor categorization performance does not simply reflect a tendency to select the alternative that is most similar to the referent. For the visual task, the trials on which D. A. was correct were numerically more difficult than were the trials on which he was incorrect in Session 1 (mean correct $= 0.23 \pm 0.18$ *SEM*, mean incorrect $= -0.68 \pm 0.19$ *SEM*). One-sample t tests (all two-tailed) revealed that the mean difficulty for correct trials did not differ significantly from zero, $t(28) = 1.24$, $p = .23$, but that it did for incorrect trials, $t(20) = -3.72$, $p < .001$. The opposite pattern of results was obtained in Session 2. Correct trials were numerically
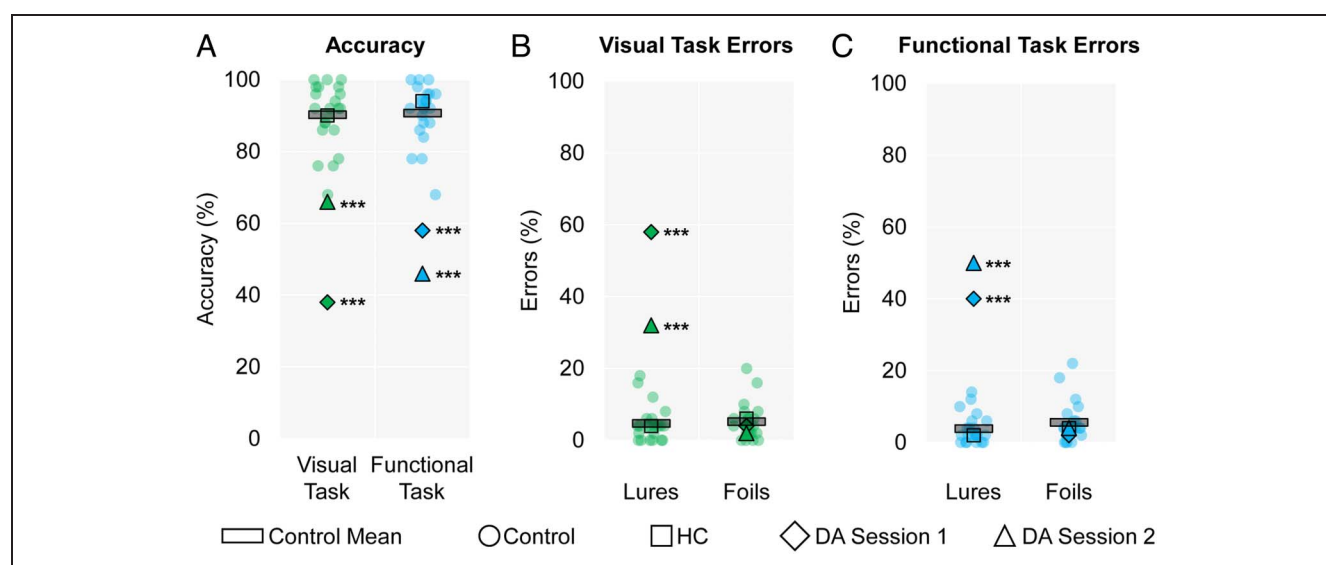
Figure 3. Experiment 1 categorization performance. (A) Overall accuracy. (B) Percentage of trials on which participants incorrectly endorsed a lure in the visual task context, for example, indicating that "electric drill" is visually more similar to "hammer" than it is to "hairdryer." (C) Percentage of trials on which participants incorrectly endorsed a lure in the functional task context, for example, indicating that "electric drill" is functionally more similar to "hairdryer" than it is to "hammer." ***$p < .05$ for D. A.
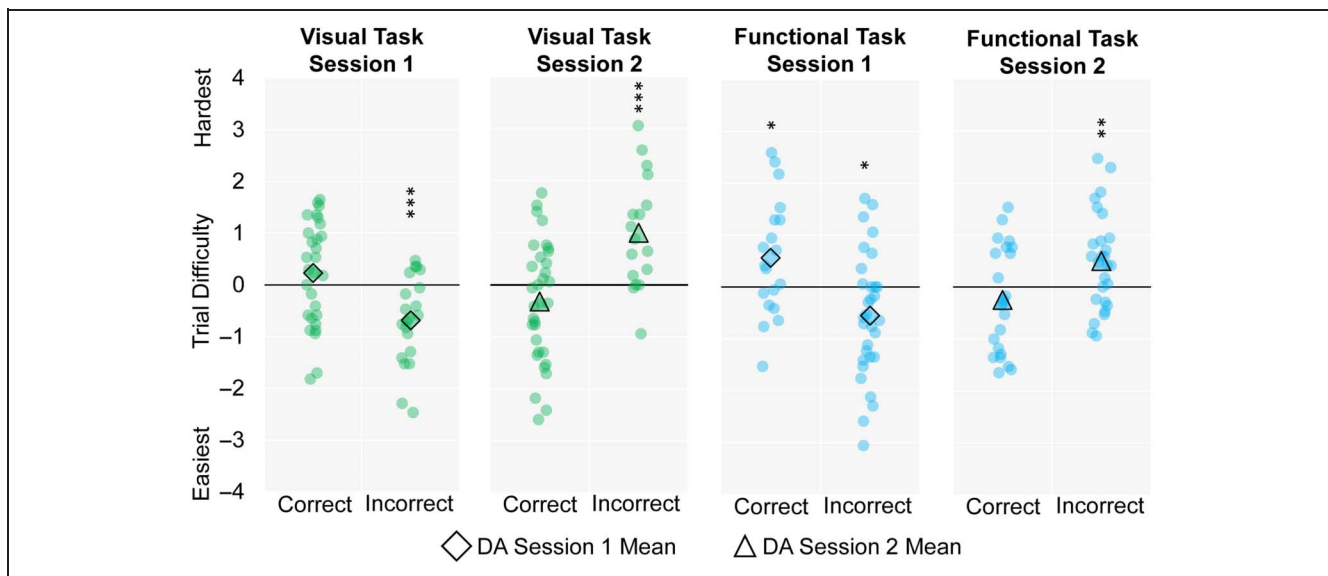
Figure 4. Trial-wise difficulty for D. A.'s correct and incorrect responses in Experiment 1. (A) Difficulty is quantified as a difference score between referent-lure overall similarity and referent-target overall similarity. Positive values correspond to trials for which the lure is more similar to the referent than is the target, resulting in an increased demand to resolve cross-modal interference. Individual data points correspond to separate trials. Difficulty values for each task in each session were compared against zero using two-tailed, one-sample t tests. $*p < .05$, $**p < .01$, $***p < .001$.

less difficult than were the trials on which he was incorrect (mean correct = -0.32 ± 0.19 *SEM*, mean incorrect = 1.00 ± 0.27 *SEM*). Mean difficulty for correct trials did not differ from zero, $t(32) = -1.60$, $p = .12$, but it did for incorrect trials, $t(16) = 3.82$, $p < .001$. Accuracy was positively correlated with difficulty in Session 1 (Spearman's $r = .42$, $p < .01$) and negatively correlated with difficulty in Session 2 (Spearman's $r = -.47$, $p < .001$). For the functional task, D. A.'s correct trials were numerically more difficult than were his incorrect trials in Session 1 (mean correct = 0.56 ± 0.26 *SEM*, mean incorrect = -0.55 ± 0.21 *SEM*). Mean difficulty differed significantly from zero for both correct, $t(18) = 2.17$, $p < .05$, and incorrect trials, $t(30) = -2.57$, $p < .05$. The opposite pattern of results was obtained in Session 2. Correct trials were numerically less difficult than were the trials on which he was incorrect (mean correct = -0.25 ± 0.21 *SEM*, mean incorrect = 0.50 ± 0.18 *SEM*). Mean difficulty for correct trials did not differ from zero, $t(22) = -1.17$, $p = .26$, but it did for incorrect trials, $t(26) = 2.78$, $p < .01$. Accuracy was positively correlated with difficulty in Session 1 (Spearman's $r = .41$, $p < .01$) and negatively correlated with difficulty in Session 2 (Spearman's $r = -.32$, $p < .05$). Overall, these results suggest that D. A. has a complex semantic memory deficit that is not systematically related to task difficulty.

Experiment 2: Categorization of Object Concepts without Interference

We next conducted a second experiment to better understand the nature of D. A.'s semantic categorization deficit. Specifically, we asked whether his impairment was specific

to resolving semantic interference or whether it reflected a more general problem with understanding how object concepts relate to one another. We hypothesized that if D. A.'s poor performance on Experiment 1 was driven by an inability to resolve interference, then removing lures from the four alternative arrays would result in performance that is comparable to that of controls. This manipulation also allowed us to examine whether D. A.'s impairment was driven by the accumulation of feature-based interference across trials rather than within trials. Removing lures from each pentad minimized within-trial interference but does not necessarily reduce any potential interference that may emerge across trials. It is particularly important to rule out this possibility given that cross-trial interference can negatively impact discrimination in individuals with MTL damage (Barense et al., 2012; McTighe, Cowell, Winters, Bussey, & Saksida, 2010).

Participants

D. A. and 11 neurologically healthy older adult participants (5 female) completed Experiment 2. Control participants were native English speakers, matched to D. A. for age, $t(7) = 1.32$, $p = .11$, $M = 68.75$, $SD = 3.85$, zCC = -1.24, and education, $t(7) = -0.71$, $p = .25$, $M = 14.50$, $SD = 3.74$, zCC = 0.67, and had not previously completed Experiment 1. All control participants were recruited from the Toronto community and provided written consent and received monetary compensation for their time. This study was approved by the research ethics board at the University of Toronto and Baycrest Hospital.

Stimuli and Procedure

Experiment 2 was procedurally identical to Experiment 1 but differed at the level of interference within each pentad (Figure 5A–B). Specifically, lures were removed and replaced with a third foil that was unrelated to the referent object. In other words, only one object, the target, was semantically similar to the referent.

Results

In contrast to D. A.'s poor performance on Experiment 1, he performed as well as control participants when cross-modal semantic interference was eliminated from each trial (Figure 5C). This was true of the visual task, $t(7) = -0.42$, $p = .34$, zCC = 0.39, and the functional task, $t(7) = 0.54$, $p = .30$, zCC = -0.51. Thus, D. A. was able to correctly categorize object concepts based on their visual and functional features when there was no need to resolve interference. His intact performance on this task also weighs against the possibility that the impairment revealed in Experiment 1 reflected an accumulation of feature-based interference across trials, but rather reflects interference within a specific pentad. Ultimately, these data suggest that cortical structures within the MTL and/or right temporal pole make necessary contributions to categorization of complex object concepts only when task demands require resolution of interference.

Experiment 3: Categorization of Simple Concepts with Within-modal Interference

Experiment 1 revealed that D. A. was unable to categorize object concepts based on their visual or functional similarities in the presence of cross-modal semantic interference. Experiment 2 revealed normal performance when interference was removed, suggesting that his impairment does not reflect a more general inability to categorize object concepts. In a final experiment, we sought to determine whether D. A.'s impairment specifically reflects an inability to resolve cross-modal interference among complex object concepts. To this end, we administered two additional semantic categorization tasks that involved simple concepts with interference at the level of features from the same modality rather than across modalities. The concepts were letters and numbers that differed from one another along a single dimension (i.e., ordinal position; for related work, see Dixon, Bub, & Arguin, 1997; Arguin, 1996). Previous research in humans and non-human primates has demonstrated that individuals with MTL cortex damage are able to make perceptual discriminations between simple stimuli that vary along a single dimension, such as shapes that differ in size or luminance (Lee, Levi, Davies, Hodges, & Graham, 2007; Barense et al., 2005; Buckley, Booth, Rolls, & Gaffan, 2001). This pattern is consistent with the notion that PRC differentially represents the high-level feature conjunctions that define complex objects (Graham et al., 2010; Murray & Bussey, 1999). As such, we predicted that D. A. would perform as well as controls on these tasks because performance does not require complex object representations.

Participants

Experiment 3 was conducted in the same experimental session as Experiment 2, with the same group of participants. All participants provided written consent and received monetary compensation for their time. This study was approved by the research ethics board at the University of Toronto and Baycrest Hospital.
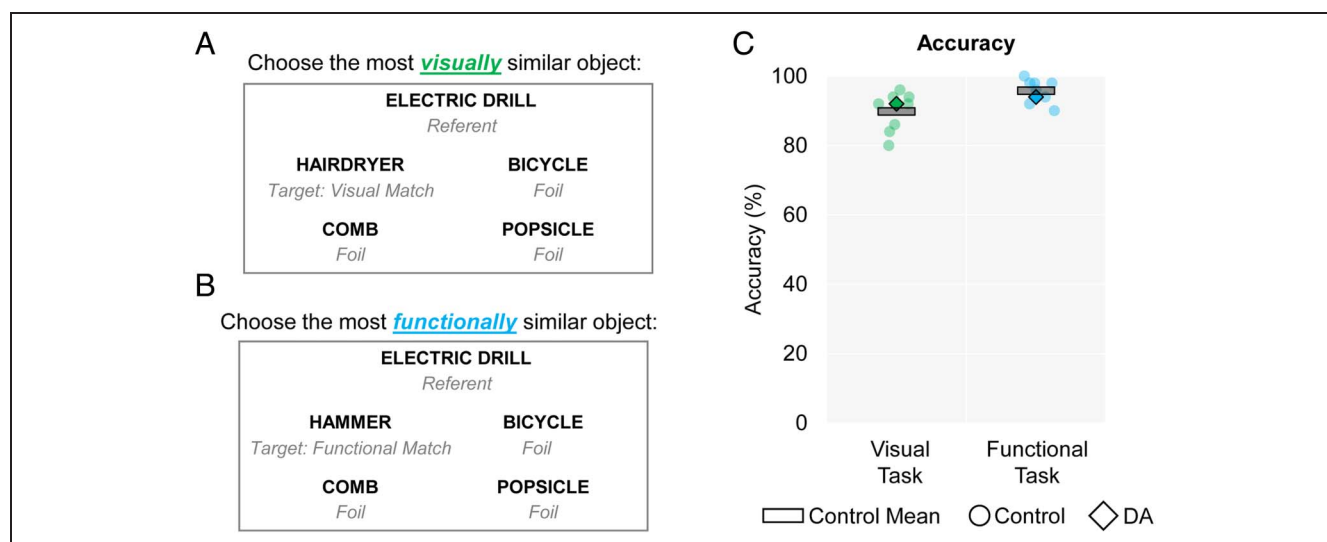
Figure 5. Experiment 2 tasks and categorization performance. (A) Visual categorization task without critical lures. (B) Visual categorization task without critical lures. (C) Overall accuracy.
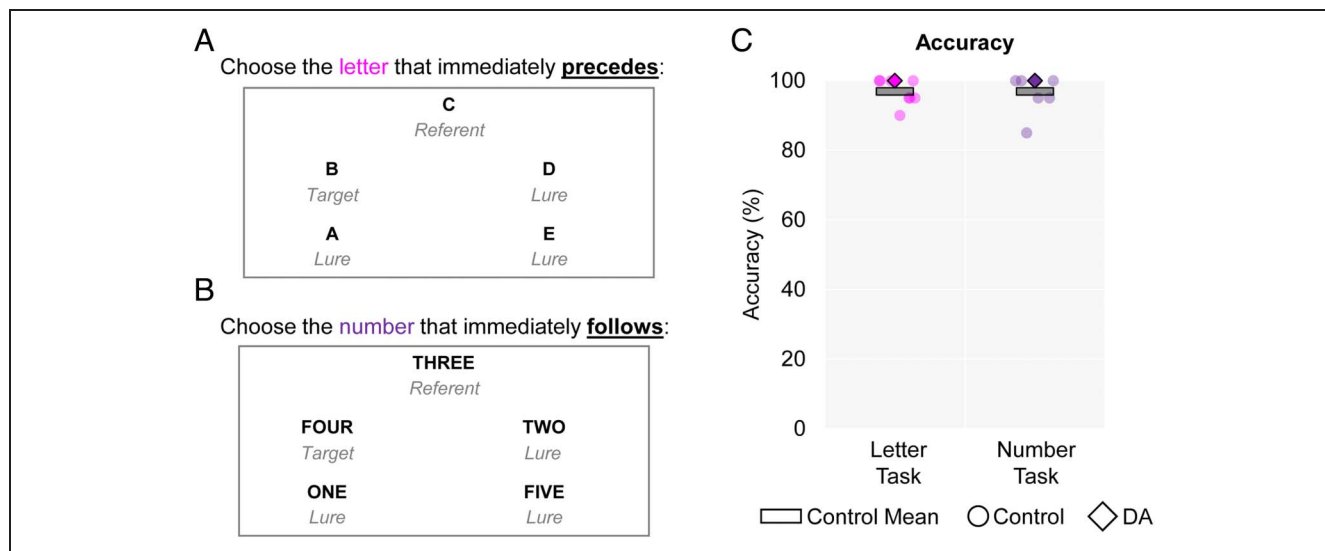
Figure 6. Experiment 3 tasks and categorization performance. (A) Letter categorization task. (B) Number categorization task. (C) Overall accuracy.

Stimuli and Procedure

The categorization tasks were procedurally identical to those from Experiment 1. Letters were used as stimuli in Experiment 3A (e.g., "c"; Figure 6A) and numbers were used as stimuli in Experiment 3B (e.g., "three"; Figure 6B). The alternatives varied in degree of similarity to the referents in terms of ordinal proximity in either the alphabet or on a standard number line (e.g., "a," "b," "d," "e"; "one," "two," "four," "five"). In both categorization tasks, participants were asked to choose the alternative that immediately preceded the referent in one 50-trial block (e.g., "b" or "two" for the letter and number preceding task, respectively) and the alternative that immediately followed the referent in a second 50-trial block (e.g., "d" or "four" for the letter and number following task, respectively).

Results

D. A. performed as well as healthy controls on both the letter and number categorization task (Figure 6C; letter preceding task: $t(7) = -0.58, p = .29$, zCC = 0.54; letter following task: $t(7) = -0.77, p = .23$, zCC = 0.72; number preceding task: $t(7) = -0.77, p = .23$, zCC = 0.72; number following task: $t(7) = -0.38, p = .36$, zCC = 0.35). In other words, in contrast to his poor performance on Experiment 1, D. A. performed as well as controls on a nearly identical task using simple stimuli that varied along a single dimension (i.e., ordinal proximity). This pattern of results suggests that D. A.'s impairments on Experiment 1 cannot be attributed to a general inability to resolve semantic interference. Rather, his deficit is specific to categorization of complex object concepts in the presence of cross-modal interference. This outcome is consistent with the notion that structures in the MTL represent objects as complex conjunctions of features that span multiple kinds of knowledge.

DISCUSSION

Semantic memory allows us to categorize the concept "electric drill" with either "hammer" or "hairdryer" depending on task demands. To better understand how this cognitive flexibility is achieved, we asked participants to categorize object concepts based on their semantic knowledge of visual or functional features. Our stimulus set was developed to ensure that accurate categorization required the resolution of cross-modal semantic interference (i.e., resolve visual interference in a functional categorization task context or resolve functional interference in a visual categorization task context). In Experiment 1, we found that D. A., an individual with diffuse right temporal lobe damage and left MTL damage, was impaired at resolving cross-modal interference. This impairment manifested as an increased tendency to incorrectly group concepts that shared task-irrelevant features. For example, he would mistakenly claim that "electric drill" is functionally more similar to "hairdryer" than it is to "hammer," or that "electric drill" is visually more similar to "hammer" than it is to "hairdryer." Importantly, this pattern of results could not be attributed to differences in difficulty across trials. Evidence obtained in Experiment 2 suggests that his impairment is restricted to situations that require the resolution of semantic interference rather than a general inability to access and use semantic knowledge. Findings from Experiment 3 further revealed that his impairment is more specifically restricted to situations that require the resolution of cross-modal semantic interference among complex object concepts. Together, these results suggest that D. A. has a complex and previously undocumented semantic memory impairment.

Our findings provide novel neuropsychological evidence that implicates the anterior temporal lobe in the resolution of cross-modal semantic interference. We revealed this link using a carefully developed stimulus set that controlled for the otherwise typical co-occurrence of visual

and functional semantic features across objects. Specifically, we used targets and lures that were either visually similar to a referent concept or functionally similar to a referent concept. Importantly, visually similar concepts were minimally related at the level of functional features, and functionally similar concepts were minimally related at the level of visual features. This careful stimulus configuration allowed us to characterize the role of the temporal lobe in resolving cross-modal semantic interference after controlling for the often-confounded relationship between visual and functional features. In Experiment 1, participants categorized these concepts using either visual or functional similarity as a grouping criterion. Thus, accurate performance required the prioritization of task-relevant features and inhibition or filtering of task-irrelevant features. Our key finding was that patient D. A., an individual with episodic amnesia stemming from temporal lobe damage, was unable to accurately categorize objects irrespective of task demands. Effectively, all of his errors involved an endorsement of lures, indicating that he was not able to successfully resolve cross-modal semantic interference. This result is consistent with previous research that has linked structures in the anterior temporal lobe to the resolution of interference within a single modality. For example, findings from research in patients as well as neuroimaging have revealed a role for PRC in the resolution of visual interference in perceptual discrimination tasks (Inhoff et al., 2019; Barense et al., 2005, 2010, 2012; Lee et al., 2005) and functional or encyclopedic interference in semantic discrimination task (Kivisaari et al., 2012; Noppeney et al., 2007; Moss et al., 2005). Importantly, our findings from D. A. deepen our understanding of the functional characteristics of the anterior temporal lobe by linking it to cross-modal interference resolution.

It is generally thought that complex semantic cognition, including the process of resolving interference, reflects an interaction between a system of cognitive control and a system of semantic representation (Chen, Lambon Ralph, & Rogers, 2017; Lambon Ralph et al., 2017; Binder & Desai, 2011; Thompson-Schill et al., 1997). Within this framework, the control network, situated in frontal and temporoparietal cortex, exerts influence over the system of representation to prioritize task-relevant information. Although characterizing the precise nature and functional neuroanatomy of the representational system has been a matter of contention, structures in the anterior temporal lobe are thought to be critically important (Martin, 2007, 2016; Mahon, 2015; Kiefer & Pulvermüller, 2012; Patterson et al., 2007). Here, we have shown that damage to this system of representation can produce a complex semantic memory impairment that is apparent only when there is cross-modal competition between the visual and functional properties of object concepts. D. A. performed well on our semantic categorization tasks when there was no competition (Experiment 2), suggesting that he can access and use semantic knowledge to guide decision making

under some circumstances. This result is consistent with the observation that he generally performs well on most, but not all, standardized neuropsychological assessments of semantic memory (Tables 2 and 3), and neither reports nor appears to have semantic impairments in his day-to-day life. He also performed well on a semantic categorization task that used simple concepts as stimuli and required the resolution of interference from within a given domain (Experiment 3). This overall pattern of results sheds new light on the anterior temporal lobe system of semantic representation. Specifically, it reveals a potentially important dissociation between semantic representations that contribute to the resolution of interference between cross-modal features and those that contribute to the resolution of interference from within a given modality. If performance on these tasks across the three experiments, which vary in complexity, were predicated on the same neural representations, then D. A. should have performed either equally well or equally poorly in all experiments administered in the current investigation.

One of the more important aspects of our results is the observation that D. A. was impaired when categorizing object concepts in the face of cross-modal interference (Experiment 1) but not when interference was removed (Experiment 2). We attribute this divergent outcome to an inability to resolve cross-modal interference rather than a more general semantic memory impairment that has compromised his ability to access and use concepts to guide decision making. It is important, however, to ask whether D. A.'s performance was intact in the absence of interference simply because the task was less difficult overall, with only one concept in the four alternative arrays being semantically related to the referent. Indeed, previous research in individuals with semantic dementia has shown that anterior temporal lobe damage is associated with the progressive loss of semantic knowledge with most notable cognitive deficits in difficult tasks that require discrimination based on fine-grained semantic knowledge (Patterson et al., 2007; Rogers et al., 2006). We addressed this possibility by quantifying trial-level difficulty in Experiment 1 and exploring whether the distributions of D. A.'s correct and incorrect categorization decisions revealed any systematic relationships between performance and requirement for fine-grained semantic access. Although results were mixed across test sessions, this approach revealed that D. A. performed well on some relatively difficult trials that involved the highest degree of cross-modal interference, and poorly on relatively easy trials that involved the lowest degree of cross-modal interference (Figure 4). This pattern of results suggests that D. A.'s semantic memory impairment does indeed reflect a compromised ability to resolve cross-modal interference irrespective of task difficulty.

It is important to note that D. A.'s lesion encompasses multiple structures in the temporal lobe, including bilateral PRC, parahippocampal cortex, entorhinal cortex, and hippocampus, as well as right-lateralized damage to

the temporal pole. This diffused lesion profile makes it challenging to draw firm conclusions regarding the neuroanatomical specificity of his semantic memory impairment. However, data from patient H. C. suggest that D. A.'s impairment does not reflect hippocampal dysfunction. Specifically, H. C., who has a bilateral MTL lesion that selectively affects the hippocampus, performed as well as healthy controls on the categorization task that required cross-modal interference resolution (Experiment 1, Figure 3). Both individuals are typically described as having episodic amnesia with otherwise intact cognitive function, including semantic memory. Our divergent results across patients reveal a complex form of semantic memory impairment that sheds new light on the functional roles of extrahippocampal temporal lobe structures. Ideally, our understanding of D. A.'s impairment could be further constrained through future research in which performance is compared across patients with selective lesions in MTL, lateral temporal lobe, or the temporal pole.

Although the current data do not directly reveal a role of any one brain region, we can ask whether D. A.'s impairment is strongly predicted by findings from other relevant lesion and neuroimaging studies. In other words, can we appeal to the known functional properties of the cortical areas encompassed by his lesion to constrain our interpretation of the current data and guide future investigations? We first consider PRC, which has previously been linked to performance on tasks that require participants to discriminate between objects that share many low-level features (Martin, Sullivan, Wright, & Köhler, 2018; Lacot et al., 2017; Clarke & Tyler, 2014; Martin, McLean, O'Neil, & Köhler, 2013; Yeung, Ryan, Cowell, & Barense, 2013; Barense et al., 2005, 2010, 2012; Kivisaari et al., 2012; Cowell, Bussey, & Saksida, 2010; Moss et al., 2005). Indeed, D. A.'s inability to resolve cross-modal semantic interference can be understood when viewed through the lens of our recent neuroimaging research (Martin, Douglas, et al., 2018). Specifically, we have shown that PRC uniquely supports the integration of cross-modal semantic knowledge with a multidimensional code that can be transiently reshaped across task contexts (Martin, Douglas, et al., 2018). Information represented in PRC captured the visual similarities between "electric drill" and "hairdryer" as well as the functional similarities between "electric drill" and "hammer," and it flexibly reshaped this similarity structure to match task demands. Importantly, no other cortical area expressed this multidimensionality, including those encompassed by D. A.'s large temporal lobe lesion. Instead, we found that semantic knowledge of visual features was selectively coded in lateral occipital cortex and knowledge of functional and contextual features was selectively coded in the temporal pole (Martin, Douglas, et al., 2018). These data suggest that PRC represents semantic information in a manner that might be particularly well-suited for resolving cross-modal interference, perhaps through interactions with a frontally mediated system of control (Lambon Ralph et al., 2017).

Given the fact that selective PRC damage is exceedingly rare (Bowles et al., 2007; Köhler & Martin, 2020), it will be important for future neuroimaging research to more directly test the suggestion that PRC makes unique contributions to the resolution of cross-modal semantic interference.

Considerable neuropsychological and neuroimaging research has revealed a role for lateral temporal cortex and the temporal pole in semantic memory (Chadwick et al., 2016; Peelen & Caramazza, 2012; Lambon Ralph, Pobric, & Jefferies, 2009; Patterson et al., 2007; Grabowski et al., 2001). However, we think it unlikely that damage to these cortical areas can explain the pattern of results obtained in D. A. Relevant neuropsychological evidence from the semantic dementia literature suggests that the left temporal pole, which is intact in D. A., is more strongly related to conceptual processing and the resolution of conceptual interference than the right temporal pole (Binney, Embleton, Jefferies, Parker, & Lambon Ralph, 2010; Galton et al., 2001; Mummery et al., 2000; Wiggs, Weisberg, & Martin, 1999; but see Snowden et al., 2018; Woollams & Patterson, 2018; Kumfor et al., 2016; Pobric et al., 2010; Lambon Ralph et al., 2009, for compelling evidence in favor of hemispheric equivalency). D. A. should not have presented with a profound semantic categorization impairment in the presence of cross-modal interference if the left temporal pole can support this specific kind of interference resolution. Moreover, our previous fMRI research revealed that the temporal pole represents object concepts in a manner that captures functional and contextual, but not visual, similarities among stimuli, suggesting that it is not particularly well-suited to efficiently enable simultaneous consideration of cross-modal similarities (Martin, Douglas, et al., 2018). Looking beyond temporopolar cortex, we are unaware of any evidence that has linked either parahippocampal cortex or entorhinal cortex to the resolution of semantic interference among object concepts (see Ranganath & Ritchey, 2012, for related review).

We have characterized D. A.'s semantic memory impairment as highly complex, selectively compromising his ability to resolve cross-modal interference. We revealed this deficit, in part, by tapping into semantic knowledge of visual features. However, this does not necessarily mean that D. A. has a visual impairment. Indeed, visual semantics may reflect an entirely propositional knowledge structure (i.e., "this is red" without having the property of redness). Nevertheless, it is interesting to consider findings from research in other patients with lesion profiles similar to D. A. Specifically, patients with PRC damage tend to be impaired on perceptual discrimination tasks that use pictures of objects with many shared visual features as stimuli (Bonnen, Yamins, & Wagner, 2021; Barense et al., 2012; Barense, Gaffan, & Graham, 2007; Lee et al., 2005). Such deficits are consistent with the notion that PRC represents objects as unique conjunctions of features. Moreover, they motivate the strong prediction that D. A. would be

impaired on a perceptual discrimination task, were we to test him.

In conclusion, we provide neuropsychological evidence that reveals a previously undocumented dissociation between the ability to resolve semantic interference across versus within a modality. Specifically, we found that patient D. A., an individual with anterior temporal lobe damage, was unable to flexibly categorize object concepts in a context-dependent manner when performance required cross-modal interference resolution. Although his brain damage extends beyond any one temporal lobe structure, his complex semantic memory impairment is most strongly predicted by theoretical models that attribute multidimensional object representation to PRC.

Data Availability Statement

All data and materials are available at https://osf.io/ht86r/.

Author Contributions

Chris B. Martin: Conceptualization; Formal analysis; Validation; Visualization; Writing—Original draft; Writing—Review & editing. Danielle M. Douglas: Conceptualization; Data curation; Formal analysis; Investigation; Writing—Original draft; Writing—Review & editing. Louisa L. Y. Man: Data curation; Investigation; Writing—Review & editing. Rachel N. Newsome: Conceptualization; Data curation; Investigation; Writing—Review & editing. Ryan A. Kretschmar: Data curation; Formal analysis. Haley Park: Data curation; Investigation. Hira M. Aslam: Data curation; Investigation. Morgan D. Barense: Conceptualization; Funding acquisition; Supervision; Writing—Review & editing.

Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience* (*JoCN*) during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance. The authors of this article report its proportions of citations by gender category to be as follows: M/M = .38; W/M = .23; M/W = .20; W/W = .20.

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