

Cognitive and anatomic double dissociation in the representation of concrete and abstract words in semantic variant and behavioral variant frontotemporal degeneration



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ABSTRACT

We examine the anatomic basis for abstract and concrete lexical representations in semantic memory by assessing patients with focal neurodegenerative disease. Prior evidence from healthy adult studies suggests that there may be an anatomical dissociation between abstract and concrete representations: abstract words more strongly activate the left inferior frontal gyrus relative to concrete words, while concrete words more strongly activate left anterior-inferior temporal regions. However, this double dissociation has not been directly examined. We test this dissociation in two patient groups with focal cortical atrophy in each of these regions, the behavioral variant of Frontotemporal Degeneration (bvFTD) and the semantic variant of Primary Progressive Aphasia (svPPA). We administered an associativity judgment task for abstract and concrete words, where subjects select which of two words is best associated with a given target word. Both bvFTD and svPPA patients were significantly impaired in their overall performance compared to controls. While controls treated concrete and abstract words equally, we found a category-specific double dissociation in patients' judgments: bvFTD patients showed a concreteness effect (CE), with significantly worse performance for abstract compared to concrete words, while svPPA patients showed reversal of the CE, with significantly worse performance for concrete over abstract words. Regression analyses also revealed an anatomic double dissociation: The CE is associated with inferior frontal atrophy in bvFTD, while reversal of the CE is associated with left anterior-inferior temporal atrophy in svPPA. These results support a cognitive and anatomic model of semantic memory organization where abstract and concrete representations are supported by dissociable neuroanatomic substrates.

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1. Introduction

Central to the question of how semantic concepts are organized in the brain is the debate of whether abstract and concrete word categories have distinct representations. While concrete words have referents with sensory-motor features, abstract words refer to concepts that primarily exist within the mind and via language (Hale, 1988). However, it is uncertain if this concrete-abstract distinction has a basis in the neuroanatomic representation of these categories.

Two historically dominant theories of concrete and abstract word representation are the dual-coding theory and the context availability hypothesis. The dual-coding theory proposes that,

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while both abstract and concrete words have linguistically-based representations, only concrete words have additional visually-based representations that draw from their physical referents (Paivio, 1989, 1991). Indeed, concrete words tend to have more predicate features associated with them than abstract words, and these features facilitate word knowledge and recognition (Recchia and Jones, 2012; Hill et al., 2014). The richness of concrete feature representations offers an explanation for the concreteness effect (CE)-the tendency for individuals to be more accurate and faster when identifying concrete words compared to abstract words. The dual-coding view is closely aligned with more current theories of semantic memory related to grounded cognition. These theories propose that sensory-motor features in part underlie conceptual knowledge, and that neural systems associated with sensory-motor processing help support lexical processing (Barsalou, 2008; Binder and Desai, 2011). Thus, the representations of both abstract and concrete concepts are hypothesized to be supported by language regions in the perisylvian areas of the left hemisphere. However, only concrete word processing receives additional

support from the inferior temporal cortex and surrounding regions associated with high level visual processing and the representation of visual-perceptual and object feature knowledge (Chao et al., 1999; Martin et al., 1995, 2007; Miyashita, 1993). In support of these perspectives, evidence from functional imaging studies show that recognition of concrete words activates extensive areas associated with visual feature and object processing, including the inferior temporal cortices, and the fusiform and parahippocampal gyri (Mellet et al., 1998; Sabsevitz et al., 2005; Wang et al., 2010).

An alternative view is the context availability hypothesis, which posits that word knowledge and recognition depend in part on the associated context (Schwanenflugel et al., 1988). Because concrete referents have physical or temporal existence, these words appear in a more consistent and relatively narrow set of contexts. In comparison, abstract words tend to be more semantically diverse than concrete words, appearing in a larger variety of contexts, and with more variations in their meaning. For example, the general meaning of the word “honor” is high respect or reputation, but the specific meaning can change depending on context: “honor” can refer to a privilege, as in “it is my honor”; an achievement, as in “graduated with honors”; or a title, as in “your Honor, I object”. The need to select from different possible interpretations may explain why abstract words can take longer to identify than concrete words, especially when context is minimal. Moreover, relevant context has been shown to facilitate the recognition of abstract words, so that they are processed as quickly as concrete words (Schwanenflugel and Shoben, 1983; van Hell and De Groot, 1998). Similarly, abstract word comprehension, more than concrete, is supported by accessing closely semantically associated words (Crutch and Warrington, 2005; Crutch et al., 2009). Because of this reliance on context, abstract words may partially depend on executive functioning and semantic control to regulate meaning selection. In support of this view, imaging studies in healthy adults demonstrate that the processing of abstract words activates the inferior frontal gyrus (Hoffman et al., 2010; Wang et al., 2010), an area thought to be involved in semantic control (Moss et al., 2005; Thompson-Schill et al., 1997) and in the integration of contextual information (Hoffman et al., 2015).

Here we investigate the cognitive and anatomical representation of abstract and concrete words, and evaluate our results in the context of grounded cognition and context availability theories. To assess semantic memory, subjects participated in a two-alternative forced-choice task, where they were asked to select which of two nouns best associates with a target noun; half of trials were composed of abstract nouns, and half were concrete. We examine semantic processing in two patient groups with atrophy to regions implicated in object feature processing and in semantic control: patients with semantic variant primary progressive aphasia (svPPA) and with behavioral variant frontotemporal degeneration (bvFTD), respectively. We test concrete word knowledge in svPPA, a form of primary progressive aphasia characterized by impaired confrontation naming and poor word comprehension (Hodges and Patterson, 2007; Mesulam et al., 2003). This patient group presents with profound atrophy to the anterior inferior temporal cortex (Amici et al., 2007; Grossman et al., 2004; Libon et al., 2013; Mion et al., 2010; Rogalski et al., 2011). Poor concrete knowledge in svPPA has been previously observed, with several studies showing a reversal of the CE-selectively worse concrete word knowledge and recognition, compared to abstract (Warrington, 1975; Breedin et al., 1994; Bonner et al., 2009, 2015; Macoir, 2009). While this is not seen in all studies (Jefferies et al., 2009; Hoffman et al., 2013a), differences in impairment are possibly due to variability in the location and progression of atrophy in svPPA (Bright et al., 2008; Hoffman et al., 2012). We directly assess the relationship between relative difficulty with concrete word knowledge and atrophy to the inferior temporal gyrus in svPPA. We also compare svPPA

performance to that of bvFTD patients, a social disorder typified by social disinhibition, apathy, and personality changes. Importantly, these patients present with impaired executive functioning along with frontal lobe atrophy (Rascovsky et al., 2011). While bvFTD is not typically associated with impaired semantic knowledge, this may be due in part to the design of standard semantic memory assessments, whose stimuli largely consist of concrete words (e.g. Boston Naming Test, Kaplan et al., 2001; and Pyramids and Palm Trees Test, Howard and Patterson, 1992). If executive functioning and semantic control processes are important for abstract meaning selection, we expect impaired processing for abstract words to be found in bvFTD, and we expect this to relate to atrophy of the inferior frontal gyrus in these patients.

2. Materials and methods

2.1. Subjects

Participants were 12 right-handed, English speakers that were diagnosed with svPPA and 18 patients diagnosed with bvFTD, based on the consensus diagnostic criteria outlined by Gorno-Tempini et al. (2011) and Rascovsky et al. (2011), respectively. We compared the performance of these patients with 18 healthy older adult controls. Of the 12 svPPA patients, 10 also had co-occurring mild behavioral symptoms. Co-occurrence of behavioral symptoms with svPPA is typical, and is representative of the svPPA spectrum. None of the 18 bvFTD patients were mixed cases. Demographic features of all three groups are outlined in Table 1. These data show that all groups are matched for age and education, and that svPPA and bvFTD patients do not significantly differ in disease duration.

Table 2 summarizes performance on standard language and neuropsychological measures for both patient groups, including the mini-mental state exam (MMSE), FAS version of the Controlled Oral Word Association Test (FAS), Pyramids and Palm Trees (PPT; using both picture and word stimuli), Boston Naming Test (BNT), Digit Symbol Substitution, Visual-Verbal Test, and Neuropsychiatric Inventory (NPI). An abbreviated version of these tests was administered, and total scores are listed in Table 2, shown in parenthesis by the test name. Compared to healthy older adults, bvFTD patients were significantly impaired on all measures while svPPA patients were significantly impaired on all measures except for Digit Symbol, Visual-Verbal, and NPI. Direct comparisons of svPPA and bvFTD patients demonstrated different patterns of impairment: Although patient groups revealed no significant difference on their MMSE scores, svPPA patients showed significantly greater impairment than bvFTD patients for measures involving lexical knowledge, including PPT and BNT. In contrast, bvFTD patients were significantly more impaired than svPPA patients for executive functioning and flexibility measures, including Digit Symbol and Visual-Verbal tasks, and for the NPI behavioral scale.

2.2. Associativity judgment task

To evaluate processing of abstract nouns compared to concrete nouns, subjects participated in a two-alternative, forced-choice associativity judgment task. Subjects were presented with a target word on the top half of a computer screen, and were asked to select which of the two words on the bottom half of the screen is best associated with the target word. The two choices were between a high-associativity word and a foil-word, and the positions of the two word choices were counter-balanced so that the correct choice for each category was equally distributed on the left and the right. Of the 60 probed triads, half were concrete and half were abstract. Participants could take as much time as needed to make

Table 1
Demographic data.

	svPPA		bvFTD		Controls		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F	p
Age (years)	62.9	9.24	63.9	7.38	68.6	9.38	n.s.	
Education (years)	15.3	2.34	16.3	2.79	15.6	3.01	n.s.	
Disease duration (months)	52.9	30.69	59.2	38.87	–	–	n.s.	

Table 2
Language and neuropsychological data for patient groups.

Task (total possible)	svPPA		bvFTD		t-test	
	Mean	SD	Mean	SD	t	p
MMSE (30)	20.67	6.95	23.63	5.71	n.s.	
Digits backward (8)	4.00	1.00	3.86	2.12	n.s.	
FAS (86)	17.70	9.92	19.38	13.53	n.s.	
PPT picture (26)	18.11	4.23	22.67	4.03	2.51	0.021
PPT word (26)	16.88	3.98	22.08	3.42	3.13	0.006
Boston naming (30)	5.22	4.24	25.43	3.13	13.17	0.000
Digit symbol (93)	43.80	15.19	26.54	10.24	3.26	0.004
Visual-verbal (20)	18.60	1.17	15.44	4.10	2.90	0.009
NPI (70)	17.43	12.58	33.30	18.90	2.16	0.044

their selection. Based on ratings obtained from the MRC database, we matched stimulus materials across both abstract and concrete conditions for frequency and familiarity (all p -values > 0.1), and for numbers of sight vocabulary words. We also assessed each triad for concreteness and semantic diversity based on ratings presented in Brysbaert et al., 2014; Hoffman et al., 2013b, to ensure that the concrete stimuli used were more concrete ($F(1,58)=197.3$, $p < 0.001$) and less semantically ambiguous ($F(1,58)=15.72$, $p < 0.001$) than the abstract stimuli.

2.3. Imaging methods and procedures

Subsets of svPPA ($n=9$) and bvFTD patients ($n=14$) agreed to participate in the imaging component of this study. These patient subsets were not significantly different from the rest of the patient groups on performance for the associativity task or the neuropsychological measures (all p -values > 0.1). Participants underwent T1 magnetic resonance imaging (MRI) to examine grey matter atrophy. A T1-weighted three-dimensional spoiled gradient-echo sequence was acquired on one of two Siemens 3.0 T Trio scanners using an eight-channel head coil with TR=1620 ms, TE=3 ms, flip angle=15°, matrix=192 × 256, slice thickness=1 mm, and in-plane resolution=0.9 × 0.9 mm. A covariate was included in the imaging analysis to remove any potential scanner effect on the analysis. Imaging was acquired within an average of 114 days of the associativity judgment task. Imaging was also collected on an independent group of 34 healthy seniors, who were age and education matched to both patient groups.

Images were normalized to a standard space and segmented using the PipeDream interface (<http://sourceforge.net/projects/neuropipedream/>) to the ANTs toolkit (<http://www.picsl.upenn.edu/ANTs/>). Grey matter probability (GMP) images were calculated and were transformed into Montreal Neurological Institute (MNI) space and down-sampled to 2mm³ resolution. Images were smoothed using a 2-mm full-width half-maximum (FWHM) Gaussian kernel to minimize individual gyral variations. GMP for both svPPA and bvFTD patient groups was determined relative to controls in SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8>) using a whole-brain voxel-wise analysis with a threshold of $p < 0.001$ (controlled for multiple comparisons with false

discovery rate), and a minimum cluster size of 100 voxels. The multiple regressions module in SPM8 related grey matter atrophy for each patient group to task accuracy, and the difference between task performance for concrete words and for abstract words, constrained to regions of grey matter atrophy. Regression analyses were accepted as significant using a height threshold of $p < 0.05$ (uncorrected) and a minimum cluster size of 50 voxels.

3. Results

3.1. Cognitive results

3.1.1. Overall accuracy for Associativity task

Mean overall performance in the associativity task is shown in Fig. 1. A univariate ANOVA revealed a significant effect of patient group (svPPA, bvFTD, Control) on accuracy ($F(2,45)=17.83$, $p < 0.001$). Compared to healthy controls, accuracy was significantly impaired for both svPPA ($F(28)=56.27$, $p < 0.001$) and bvFTD ($F(34)=22.40$, $p < 0.001$). Overall accuracy was not significantly different between svPPA and bvFTD patients.

3.1.2. Concrete vs. abstract accuracy

An ANOVA with a 2 (Condition: Abstract, Concrete) × 3 (Group: svPPA, bvFTD, Control) repeated-measures design showed that, while there was no main effect of condition ($p=0.465$), there was a significant Condition × Group interaction ($F(2,45)=7.25$, $p=0.002$). For bvFTD patients, performance was significantly worse for abstract words compared to concrete words ($t(17)=2.35$, $p=0.031$). This CE was reversed for svPPA patients, whose

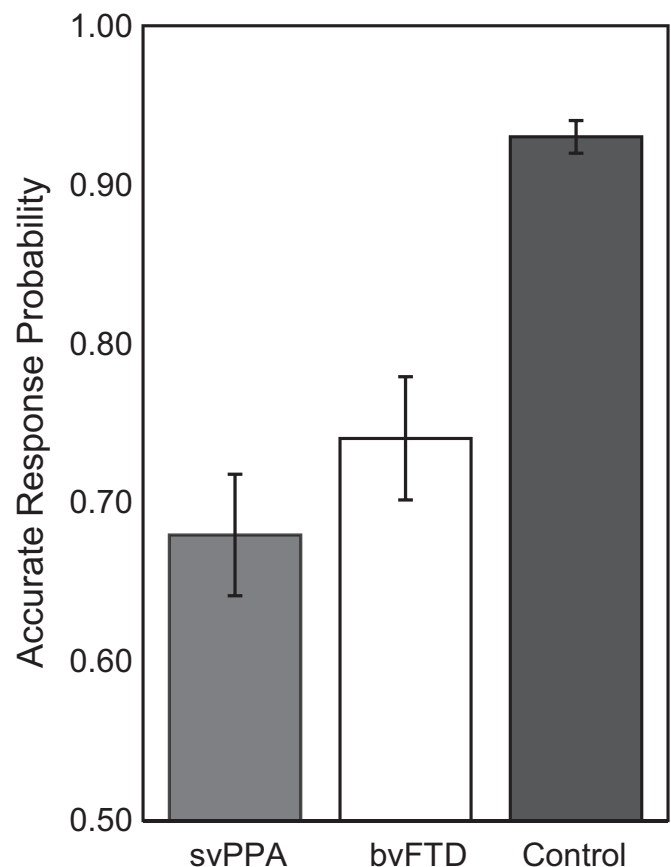


Fig. 1. Associativity Task Accuracy. The proportion of correct associations made for each word triad. Error bars represent standard error of the mean. Total accuracy for each group: svPPA (grey), bvFTD (white), and control (black).

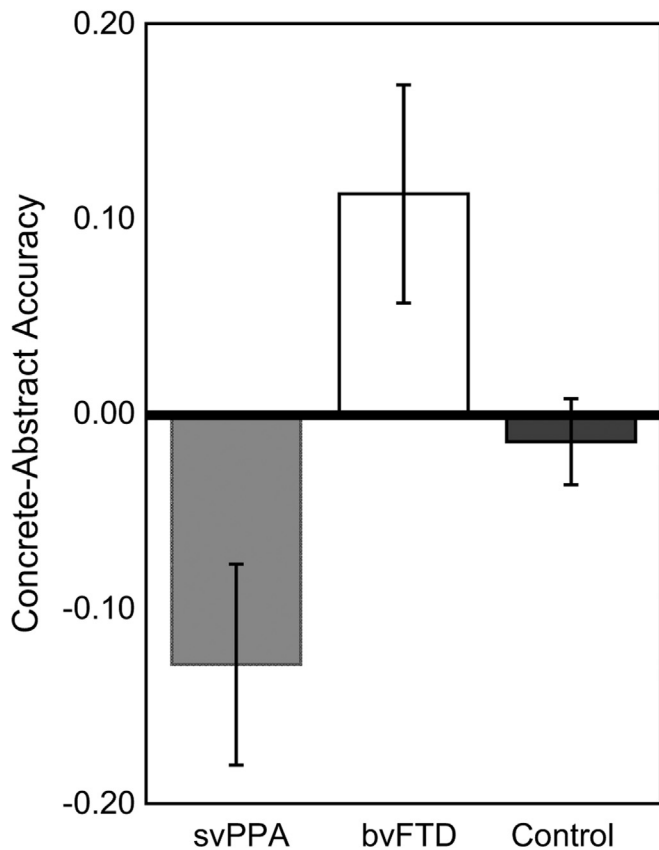


Fig. 2. Magnitude of the Concreteness Effect (CE). The normed accuracy for concrete words minus abstract words, or the magnitude of CE. Negative values indicate a reversal of the CE. svPPA patients are plotted in grey, bvFTD in white, and control in black. Error bars represent standard error of the mean.

accuracy was significantly worse for concrete words compared to abstract words ($t(11)=2.37$, $p=0.037$). There was no significant difference between concrete and abstract words for Controls.

To measure the magnitude of the CE for each group, accuracy for abstract words was subtracted from the accuracy for concrete words, and then divided by total accuracy (Fig. 2). A univariate ANOVA revealed a significant effect of patient group on the adjusted difference score ($F(2,45)=6.64$, $p=0.003$). svPPA patients had a significantly greater reversal of the CE than bvFTD patients

($F(28)=8.98$, $p=0.006$) and Controls ($F(28)=5.29$, $p=0.029$). By comparison, bvFTD patients showed a greater CE than Controls ($F(34)=4.46$, $p=0.042$).

3.2. Imaging results

We examined regions of significant atrophy in grey matter for patients with svPPA (Fig. 3, Panel A) and bvFTD (Fig. 3, Panel B) compared to controls. Patients with svPPA showed significant atrophy in the temporal lobes, and this atrophy was more evident in the left hemisphere. There was modest extension of atrophy into the insula and orbital frontal cortex. Patients with bvFTD demonstrated significant atrophy compared to controls, primarily in the frontal lobe regions. There was modest temporal lobe atrophy in bvFTD, more evident in the right hemisphere.

To determine how atrophy in both patient groups affected semantic knowledge, we performed regression analyses relating overall task performance to grey matter probability. For svPPA patients, task performance was related to atrophy in the left inferior and superior temporal lobe (Table 3). For bvFTD patients, task performance related to broad bilateral atrophy of the lateral and medial frontal lobe (Table 4).

To identify the anatomical regions supporting abstract and concrete word representations, we examined regression analyses relating atrophy to the adjusted difference score between abstract and concrete accuracy in svPPA and bvFTD. We related atrophy to the difference score to remove the effects of shared properties between concrete and abstract word processing, such as retrieval or phonetic decoding. Fig. 4 depicts how the CE in bvFTD patients and the reversal of the CE in svPPA relate to the regions of atrophy for these patient groups. For svPPA patients, reversal of the CE was associated with atrophy of the left inferior, middle, and superior temporal lobe (see Table 3). For bvFTD patients, the CE was associated with bilateral atrophy of the inferior frontal gyrus and the insula (see Table 4). There was no significant association between atrophy and the CE in svPPA, nor the reversal of CE and bvFTD.

4. Discussion

This study revealed an anatomical double disassociation between abstract and concrete word representations by examining single word semantic deficits in svPPA and bvFTD. While controls showed equally accurate performance for concrete and abstract

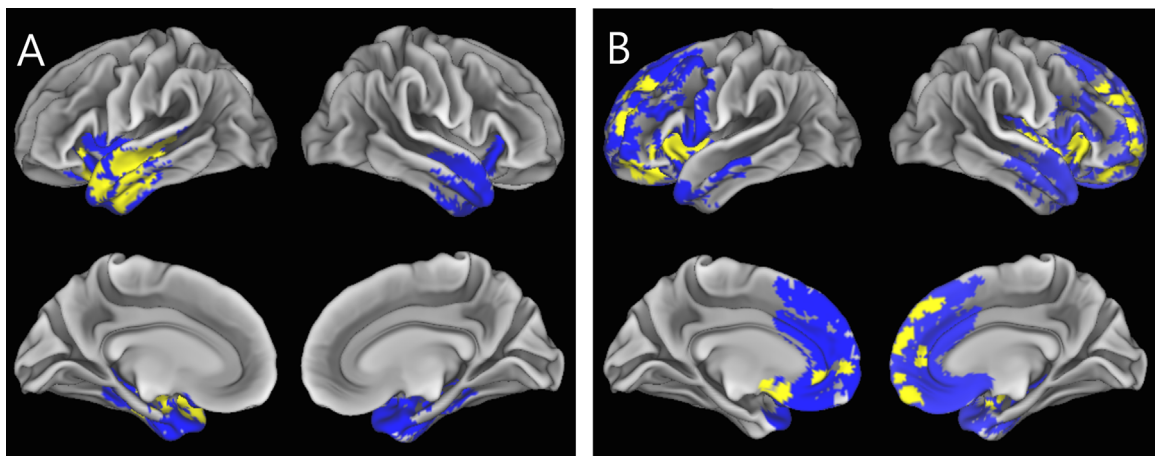


Fig. 3. Regions of significantly reduced grey matter and regression with behavioral performance. Panel A: in svPPA. Blue and yellow regions indicate areas of grey matter atrophy in svPPA compared with control patients. Yellow only regions indicate areas in svPPA patients where more severe atrophy is significantly associated with worse task performance. Panel B: in bvFTD. Blue and yellow regions indicate areas of grey matter atrophy in bvFTD compared with control patients. Yellow only areas indicates regions in bvFTD patients where more severe atrophy is significantly associated with worse task performance.

Table 3
Regressions of task performance with grey matter atrophy in svPPA.

	MNI Coordinates					
svPPA	BA	x	y	z	Z score	Cluster size (voxels)
Grey Matter Atrophy, svPPA < Control						
Left Parahippocampal Gyrus	36	−28	−6	−36	Inf	5196
Right Inferior Temporal Gyrus	20	42	−10	−38	7.27	2387
Right Orbitalfrontal Gyrus	11	12	18	−16	5.19	185
Regression of Task Accuracy with Grey Matter Atrophy						
Left Superior Temporal Gyrus	38	−46	10	−26	3.62	390
Left Inferior Temporal Gyrus	20	−46	0	−40	3.60	563
Left Inferior Temporal Gyrus	20	−40	−24	−26	3.28	98
Regression of the Reversal of Concreteness Effect with Grey Matter Atrophy						
Left Inferior Temporal Gyrus	20	−42	2	−40	3.23	118
Left Middle Temporal Gyrus	21	−66	−8	−18	3.14	135
Left Superior Temporal Gyrus	22	−46	−12	−2	3.89	164

Table 4
Regressions of task performance with grey matter atrophy in bvFTD.

bvFTD	MNI Coordinates				Z score	Cluster size (voxels)
	BA	x	y	z		
Grey Matter Atrophy, bvFTD < Control						
Left Anterior Prefrontal Cortex	10	−10	46	−6	6.76	15,165
Left Middle Temporal Gyrus	21	−64	−10	−14	4.68	129
Left Inferior Temporal Gyrus	20	−52	0	−36	5.82	387
Right Inferior Temporal Gyrus	20	42	−12	−28	5.24	108
Regression of Task Accuracy with Grey Matter Atrophy						
Left Anterior Prefrontal Cortex	10	−8	56	2	3.15	75
Left Middle Frontal Gyrus	11	−30	48	−12	3.27	117
Left Superior Frontal Gyrus	9	−20	40	40	3.37	88
Left Subcallosal Gyrus	25	−4	12	−16	3.52	381
Right Middle Frontal Gyrus	10	26	58	14	3.43	68
Right Caudate	48	12	2	18	3.30	314
Right Middle Frontal Gyrus	11	28	54	−14	3.21	205
Regression of the Concreteness Effect with Grey Matter Atrophy						
Left Inferior Frontal Gyrus	47	−30	46	−14	3.23	193
Right Insula	13	40	10	−8	3.16	408

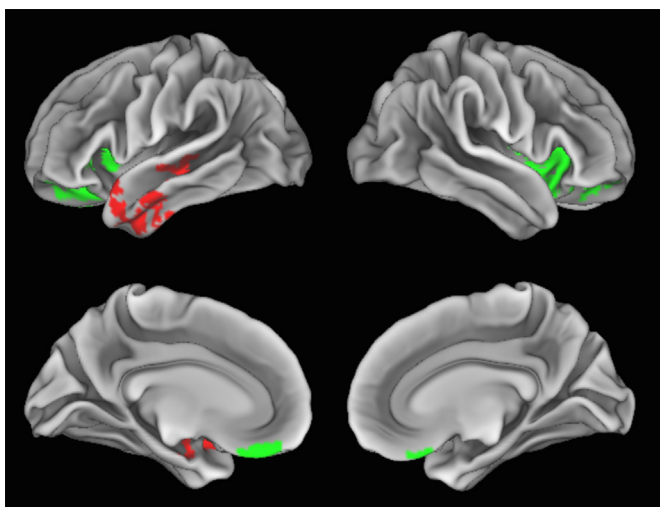


Fig. 4. Regression of grey matter probability with reversal of the CE for svPPA and CE bvFTD. Red indicates areas of atrophy that significantly correlate with the Reversal of Concreteness Effect-better knowledge for abstract words-in svPPA patients. Green indicates areas of atrophy that significantly correlate with the Concreteness Effect-better knowledge for concrete words-in bvFTD patients. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

words, bvFTD patients demonstrated significantly worse performance for abstract words, and svPPA patients were significantly worse for concrete than abstract words, showing a reversal of the CE. We related this dissociation in performance to regions of grey matter atrophy in these patients. In svPPA, the reversal of the CE was related to atrophy in an area of high-level visual processing, the left anterior-inferior temporal cortex. In bvFTD the CE was related to bilateral inferior frontal atrophy, a region important for semantic control. Thus, we observe a cognitive and anatomic double dissociation for concrete and abstract word categories. We discuss cognitive performance and the anatomic associations in each group below, and relate these observations to theories of semantic memory.

4.1. svPPA

Also known as semantic dementia (Hodges et al., 1992), svPPA is associated with impaired confrontation naming and poor word comprehension (Hodges and Patterson, 2007; Mesulam, 2003). While svPPA is often characterized by a global impairment in semantic memory (Patterson et al., 2007), several studies have described individual cases (Breidin et al., 1994; Macoir, 2009) and groups of patients (Reilly et al., 2006; Yi et al., 2007; Bonner et al., 2009, 2015) with worse performance on concrete words relative to abstract words. This reversal of the CE is an extension of

Warrington (1975) initial observations of semantic dementia. Although this is not seen by all investigators (Jefferies et al., 2009; Hoffman et al., 2013a), such discrepancies may be due to differences in the svPPA populations that are sampled, specifically due to variance in the course, extent, and stage of disease (Bright et al., 2008; Rohrer et al., 2008). One possibility is that semantic impairment in svPPA is initially amodal, but as disease spreads posteriorly through the ventrolateral temporal lobe, words with rich visual features are progressively more impaired (Hoffman et al., 2012). Alternatively, early atrophy of the visual association cortex in the inferior temporal lobe may lead to an initial impairment for concrete words with rich visual features in svPPA, but disease progression toward more superior and posterior regions in the temporal lobe (Brambati et al., 2009) can result in lexical deficits for other sensory modalities. Likewise, disease progression in svPPA may compromise connectivity with other brain regions important for semantic memory, leading to a multimodal semantic memory deficit (Agosta et al., 2010; Bonner and Price, 2013). Such an account is compatible with the results we report here, though further longitudinal work is needed to chart disease location and progression of atrophy to concrete word knowledge. Nonetheless, evidence suggests that the extent of disease to the inferior lateral temporal gyrus likely determines the severity of concrete word impairment in svPPA. This is supported by functional imaging studies in controls, which indicate that concrete word knowledge depends on visual and object features, related to visual association regions in the inferior temporal gyrus, fusiform gyrus, and supporting areas (Binder et al., 2005; Mellet et al., 1998; Wang et al., 2010; Bonner et al., 2015).

Our findings in svPPA further implicate visual association cortices in concrete word processing. We observed that svPPA patients are more impaired for concrete words than abstract words, and that reversal of the CE is associated with grey matter atrophy in the left temporal cortices, including the inferior temporal and ventral temporal gyri. While svPPA patients can present with surface dyslexia, the stimuli were composed of an equal number of sight vocabulary words for concrete and abstract conditions, and this would not account for the difference in performance. These results support the hypothesis that visual features are especially important for the representation of concrete words. Still, many concrete concepts are multi-modal, with salient auditory, tactile, or motor features. It is beyond the scope of the present study to assess to what extent other sensory regions are also involved in concrete word representations, and additional work is needed to probe the multi-modal feature knowledge of concrete object concepts. For example, auditory feature knowledge associated with concrete words may be represented in part in auditory association cortex (Pandya and Yeterian, 1985), and disease in posterior-superior temporal regions may be associated with deficits for words that are relatively dependent on auditory feature knowledge (Bonner et al., 2012). In our study, this region exhibited a relatively modest extent of atrophy in svPPA, and regression analysis implicated a small area of the anterior-superior temporal lobe.

4.2. bvFTD

Unlike svPPA, bvFTD patients demonstrated a significant CE, showing more difficulty with abstract than concrete lexical concepts. Patients with bvFTD are typically characterized by atrophy involving medial, dorsolateral, inferior and orbital regions of the frontal lobe. bvFTD typically presents as a disorder of social comportment and personality, with associated disinhibition, ritualistic behavior, apathy, poor insight, impoverished empathy, and limited executive functioning (Rascovsky et al., 2011). Though bvFTD is not typically characterized as a language disorder, several studies have

observed deficits in discourse (Ash et al., 2006), sentence (Ash et al., 2006; Charles et al., 2013; Williams et al., 2015) and lexical processing (Libon et al., 2009).

We found that bvFTD patients are impaired overall on the lexical associativity judgement task compared to controls, and that this deficit is significantly worse for abstract than concrete items. Poor executive functioning in bvFTD can compromise working memory, processing speed, and mental flexibility of these patients. However, these effects on performance for our task should be minimal, since the stimuli remained available during the entire period of judging a stimulus triad, performance was untimed, we did not observe perseveration during task performance, and patients exhibited only mild dementia, with an average MMSE of 23.6. Moreover, it is unlikely that these factors could explain the category-specific deficit for abstract stimuli we observe, since an identical procedure was used for the concrete stimuli.

We are not aware of previous studies examining abstract word processing in bvFTD, and we argue that the lexical semantic deficit in bvFTD observed in this study is due in large part to their relative difficulty with abstract words. Traditional measures of lexical semantic knowledge like visual confrontation naming (e.g. Boston Naming test) and semantic associativity judgments (e.g. Pyramid and Palm Trees test) use concrete stimuli, and bvFTD patients typically demonstrate relatively preserved performance on these measures. Accordingly, we observed more accurate performance on these traditional measures in bvFTD than svPPA. In the present study, we found instead that bvFTD patients are relatively impaired for abstract words compared to concrete words. Moreover, regression analyses related poor abstract word knowledge in bvFTD to atrophy in the inferior frontal gyrus and insula bilaterally. These findings are in agreement with fMRI studies of healthy controls that show recruitment of inferior frontal cortex in response to abstract words (Hoffman et al., 2010; Wang et al., 2010). The inferior frontal gyrus has been shown to be important for tasks requiring semantic control and selection (Moss et al., 2005; Thompson-Schill et al., 1997), and this may be critical for words that have multiple, subtly nuanced meanings, like abstract words (Schwanenflugel et al., 1988).

bvFTD patients' atrophy extended somewhat into the superior temporal lobe, and we cannot rule out that subtle modality-specific associations of concrete words are compromised in bvFTD. However, regression analyses did not demonstrate a significant association between superior temporal atrophy and overall performance on this associativity judgment measure, nor did we find a significant association between atrophy and worse performance for concrete words (reversal of the CE). Instead, we found that a relative deficit for abstract words compared to concrete words is associated with bilateral inferior frontal disease in these patients.

4.3. Theories of semantic memory

While both grounded cognition and context availability hypotheses offer theoretical insights into our behavioral and anatomical results, neither theory alone can fully explain our observations. Theories like grounded cognition and dual-coding propose that lexical semantic processing is facilitated by the sensory and motor features associated with that word, and that concrete words have more visual predicate-features which support their processing. Our results in svPPA show that relatively decreased knowledge for concrete words, compared to abstract, relates to reduced grey matter of the anterior-inferior temporal lobe, as well as the middle and superior temporal lobe. Compared to abstract words, concrete words are thought to be more dependent on visual object feature knowledge, and prior research has related the anterior-inferior temporal gyrus to the representation of object and feature knowledge (Bonner and Price, 2013; Patterson et al., 2007).

However, other evidence suggests that the left anterior temporal lobe is more specifically related to linguistic processes, such as lexical retrieval and word comprehension, rather than semantic processes, which encompass both verbal and non-verbal representations of objects (Mesulam et al., 2013). If the left anterior temporal lobe were dedicated to linguistic representations, we would have expected that abstract concepts—which are theorized to be primarily linguistic in nature—would be supported by this region, more so than concrete words. We should therefore have seen a concreteness effect related to this region. Instead, we see the reverse pattern, with atrophy of the anterior temporal lobe in svPPA patients associated with poor concrete word comprehension, and a reversal of the concreteness effect. These results suggest that concrete concepts may depend in part on multimodal sensory-motor features, including the role of the inferior temporal gyrus related to visual feature knowledge and the superior temporal gyrus in auditory feature knowledge.

However, in addition to poor performance for concrete words in svPPA, we also observed a deficit for abstract word processing in bvFTD related to atrophy in regions associated with executive processing and semantic control. The dual-coding theory asserts that abstract concepts are limited to verbal, linguistic-based representations alone (Paivio, 1991). This theory would implicate the mental lexicon in the left hemisphere in abstract word processing, particularly per-Sylvian regions that include left posterior superior temporal cortex, but this area that was not implicated in our analyses. Thus, our findings—poor abstract word processing in bvFTD relating to reduced grey matter in bilateral frontal regions—contradict the assumptions of the dual-coding theory. From the perspective of grounded cognition, representations of abstract words are thought to depend on oblique sensory-motor associations (e.g. “justice” is loosely associated with a courtroom and a judge’s robes). However, grounded cognition predicts no specific role for the frontal lobe or executive processing in abstract word comprehension, and therefore does not offer an explanation of our results in bvFTD.

We hypothesize that our observations in bvFTD are best interpreted from the perspective of the context availability hypothesis. This theory proposes that the comprehension of abstract words is more dependent on constraining context, compared to concrete words. This is because abstract words have extensive variations in meaning and are encountered in more varied contexts. Abstract words are therefore hypothesized to require executive control processes to correctly select word meaning. This serves to incorporate surrounding context or to inhibit irrelevant, alternative meanings. The inferior frontal gyrus is associated with this function (Thompson-Schill et al., 1997), and accordingly, our results suggest that impaired abstract word processing in bvFTD is related to grey matter atrophy in the inferior frontal gyrus. The role of the insula is unclear. This region may be related to an emotional component of abstract lexical representations, to be examined in future work. Nevertheless, context availability theory alone cannot easily explain the deficit for concrete words in svPPA. Together, our results in svPPA and bvFTD appear to be consistent with a combination of grounded cognition and context-availability theories.

Several caveats should be kept in mind when considering our findings. First, although focal neurodegenerative conditions affecting these brain regions are uncommon, we studied a relatively small number of patients with an average interval of 3.7 months between administration of the associativity task and imaging. Further, participants in this study were relatively mild in disease severity, and additional work is needed with more impaired patients who have more extensive disease. Second, tasks other than associativity judgment may be informative, such as investigating context availability directly by manipulating the contextual constraint of abstract words, or by studying grounded cognition with

words dependent on auditory feature knowledge in these patients. Our stimuli were neither purely concrete-visual nor purely abstract, and we did not investigate subtler, secondary features that may be associated with words. We also limited our investigation to nouns to eliminate the potential confounds of grammatical class, and there should be further investigation of how word class interacts with concreteness. Finally, our focus has been on the dissociable anatomical representations of concrete and abstract concepts. However, our exploration of the regions involved in abstract and concrete lexical processing is not exhaustive. The fact that both patient groups show some impairment in their stronger modality—abstract for svPPA and concrete for bvFTD—indicates that other semantic processing systems are involved. With these caveats in mind, our findings of cognitive and anatomic double dissociations are consistent with a model of lexical semantic representation that distinguishes in part between concrete words involving sensory-motor representations and abstract words involving semantic control, and associates these representations with partially distinct brain regions – visual association cortex in the left anterior-inferior temporal lobe and inferior frontal cortex, respectively.

Conflicts of interest

The authors have no conflicts of interest to report.

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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.2016.02.025>.

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