Comprehension of concrete and abstract words in patients with selective anterior temporal lobe resection and in patients with selective amygdalo-hippocampectomy

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Abstract

The role of the anterior temporal lobe (ATL) in semantic memory is now firmly established. There is still controversy, however, regarding the specific role of this region in processing various types of concepts. There have been reports of patients suffering from semantic dementia (SD), a neurodegenerative condition in which the ATL are damaged bilaterally, who present with greater semantic impairment for concrete concepts than for abstract concepts, an effect known as reversal of the concreteness effect. This effect has previously been interpreted as reflecting degraded visual-perceptual features of objects due to damage to the inferior temporal lobes such as is observed in SD. Temporal lobe atrophy in SD, however, is bilateral even if it usually predominates to the left ATL, and it has been found to extend beyond the ATL, throughout the temporal lobes including medial and posterior temporal lobe regions. The question therefore remains whether greater impairment for concrete concepts results from damage to the ATL or from damage to the visual association cortex, and if unilateral damage can produce such a deficit.

The aim of the present study was to investigate the processing of concrete and abstract words in rare patients who underwent a selective ATL surgical resection, and to compare their performance with that of patients with selective medial temporal lobe damage sparing the ATL region. Seven patients with a selective unilateral anterior temporal resection (ATL), 15 patients with a selective unilateral amygdalo-hippocampectomy (SeAH), and 15 healthy age- and education-matched controls underwent detailed neuropsychological assessment and carried out a semantic similarity judgement task evaluating their comprehension of concrete and abstract words. Results showed that both ATL and SeAH groups were significantly impaired on the semantic task relative to the control group. Within the patient groups, however, comprehension of concrete words was significantly more impaired than that of abstract words in the ATL group, while comprehension of abstract and concrete words was

equally affected in the SeAH group. Results of this study suggest that the ATL region may play a critical role in processing concrete concepts, and that the reversal of the concreteness effect observed in ATL patients may result from damage to a categorical organization underlying the representation of concrete concepts.

1. Introduction

Semantic memory (SM) concerns general world knowledge, acquired over a lifetime and shared by a same cultural group. It includes for instance knowledge about objects, people and places, as well as knowledge about facts, concepts and language. Semantic disorders occur in various neurological conditions such as semantic dementia (SD) (Bonner et al., 2009; Breedin, Saffran, & Coslett, 1994; Lambon Ralph, Lowe, & Rogers, 2007; Noppeney et al., 2007; Snowden, Goulding, & Neary, 1989; Warrington, 1975), Alzheimer's disease (AD) (Giffard et al., 2001; Grossman et al., 2003; Joubert et al., 2010), herpes simplex encephalitis (Lambon Ralph et al., 2007; Noppeney et al., 2007; Warrington, 1984), and temporal lobe epilepsy (Glosser, Salvucci, & Chiaravalloti, 2003). Typically, SD is considered the neurological condition in which progressive semantic impairment is the most selective, often sparing other cognitive domains for some time, at least in the early stage of the disease. Thus, SD has represented a clinical model of considerable interest in recent years, and has bolstered our understanding of the cognitive architecture and neural basis of SM.

One topic of particular interest in the study of SM and semantic disorders has been the apparent dissociations reported between the processing of concrete concepts (tangible entities such as objects, people and places that we experience via our senses and that are typically highly imageable) vs. abstract concepts (purely linguistic concepts that are poorly imageable). Such dissociations have been reported in behavioural and functional neuroimaging experiments in the healthy subject, as well as in brain-damaged populations. For instance, the classical concreteness effect (CE) is a robust behavioural phenomenon that has been observed in neurologically healthy subjects in a variety of tasks (e.g. naming, memory, semantic judgement, lexical decision tasks) and which consists in faster and more accurate processing for concrete concepts than for abstract concepts (see Paivio, 1991 for a review) . Enhancement of this effect has also been reported in certain neurological conditions such as

AD, aphasia, or deep dyslexia (Franklin, Howard, & Patterson, 1995; Jefferies, Baker, Doran, & Ralph, 2007), such that abstract words were processed even more poorly relative to concrete words in these patients as compared to healthy subjects. There have been less frequent reports of patients who show the reverse pattern: more impaired comprehension of concrete concepts than abstract concepts. This unusual pattern of semantic impairment, referred to as a *reversal of the concreteness effect* (RCE), has been documented in patients who suffered lesions to the anterior and inferior portions of the temporal lobes, most often within the context of SD (Breedin et al., 1994; Cipolotti & Warrington, 1995b; Loiselle et al., 2007; Macoir, 2009; Papagno, Capasso, & Miceli, 2009; Warrington, 1975; Yi, Moore, & Grossman, 2007). Some authors have even suggested that the RCE is the norm in SD (Grossman & Ash, 2004). This relative difficulty with concrete words has been interpreted as reflecting the deterioration of visuoperceptual knowledge about objects, associated with atrophy of the left inferior temporal cortex (Yi et al., 2007). The RCE in SD patients is consistent with the clinical presentation of these patients, who appear to be most impaired with concrete concepts such as objects, animals, as well as familiar and famous people, but who show in contrast relatively well-preserved language comprehension (at least in the early stages), perhaps reflecting greater preservation of abstract knowledge. However, other authors have not found any difference between concrete and abstract concepts in SD and suggested that the RCE was an anomalous finding due to a reporting bias or lack of control of variables such as frequency (Jefferies, Patterson, Jones, & Lambon Ralph, 2009). Hoffman et al. (2011) also did not find a RCE in SD. In fact, they found the reverse pattern in a group of SD patients (i.e. concrete words were better preserved than abstract words), and suggested that two stimulus factors were critically important in the tasks employed: word frequency and imageability. They suggested that previously-reported cases of RCE may actually be due to the use of higher frequency words to probe abstract knowledge and to the fact that these studies employed less robust imageability manipulations.

Typically, SD is associated with relatively circumscribed atrophy of the inferior and anterior portions of the temporal lobe, predominating in the left hemisphere (Hodges, Patterson, Oxbury, & Funnell, 1992). Although the role of the anterior temporal lobes (ATL) in SM is now widely accepted, the specific role of this region remains disputable. On the one hand, tenants of the distributed plus hub hypothesis suggest that the ATL region supports the most central and amodal hub of semantic knowledge (Lambon Ralph, Cipolotti, Manes, & Patterson, 2010; Patterson, Nestor, & Rogers, 2007) and that this region plays a critical role in abstract as well as concrete knowledge (Jefferies et al., 2009). Such a view is compatible with the idea that the RCE is not a typical feature of SD.

An alternative account, which is consistent with the RCE reported in a series of articles on SD (Breedin et al., 1994; Cipolotti & Warrington, 1995b; Macoir, 2009; Papagno et al., 2009; Warrington, 1975; Yi et al., 2007), postulates that the ATL region may play a greater role in processing certain types of concepts such as highly imageable concepts. For example, Yi and colleagues (2007) found a RCE in SD and suggested that the relative difficulty with concrete words in some SD patients may be interpreted as reflecting the deterioration of visual-perceptual knowledge involved in object recognition, associated with underlying atrophy in the left inferior temporal cortex. According to this view, there would be less of an impact on abstract nouns because they depend much less on visual/sensory knowledge. Bonner and colleagues study (2009) reported a similar RCE in six SD patients and found that the semantic deficit for concrete concepts correlated with atrophy in the right ATL region. As in the previous study, they suggested that the RCE stemmed from degraded visual-perceptual representations of objects due to damage to the visual association cortex (ventral stream). However, as the authors point out, this view is not necessarily incompatible with the distributed plus hub hypothesis, since the latter also stipulates that perceptual characteristics are represented in modality-specific association cortices. Therefore, greater impairment for concrete concepts may arise from a combination of damage to the ATL (the hub) which results in a multimodal semantic impairment, and damage to the visual association cortex which leads to impaired visual feature representations of objects (Bonner et al., 2009). Posterior temporal regions such as the occipito-temporal region (i.e. fusiform gyrus) are indeed damaged in SD (Desgranges et al., 2007; Nestor, Fryer, & Hodges, 2006), making this hypothesis plausible.

Although atrophy in SD was usually considered to be circumscribed to the ATL region, there is now strong evidence showing that the pattern of atrophy is more widespread than initially thought: Grey matter atrophy in SD is found not only in the temporal neocortex (temporal pole, and inferior, middle and superior temporal gyri), but also in the hippocampus, amygdala, parahippocampal gyrus, as well as in the fusiform gyrus (Chan et al., 2001; Desgranges et al., 2007; Good et al., 2002; Gorno-Tempini et al., 2004; Mummery et al., 2000; Rogers et al., 2006). Atrophy in the left insula, anterior cingulate cortex, thalamus and caudate nucleus has also been reported (Desgranges et al., 2007; Gorno-Tempini et al., 2004). Some studies have even demonstrated that the pattern of medial temporal lobe atrophy in SD is indistinguishable from that found in AD (Nestor et al., 2006). Therefore, even though atrophy may predominate in the ATL, it is clearly not restricted to this region and thus it is difficult to determine whether the RCE reported by several groups in SD patients results from damage to this region, from damage to the visual association cortex, or from a combination of both.

In order to address this issue, the current study examined in patients with very selective ATL damage, whose lesions did not extend caudally to occipito-temporal lobe regions. The first aim of this study was to explore the role of the ATL region in processing concrete relative to abstract words in these patients. More specifically, we sought to determine if patients with selective ATL damage showed an RCE similar to that reported in studies of SD patients. In order to achieve this goal, we recruited a group of rare patients who had undergone a selective unilateral ATL resection, a second group of patients who had undergone a selective resection of the hippocampus and amygdala (which did not encroach upon the ATL region), and a group of healthy control subjects matched for age and level of education. The three groups of participants underwent a semantic judgment task of concrete and abstract words, in addition to a detailed neuropsychological assessment. Our hypothesis was that patients with selective ATL damage, but not patients with selective damage to the hippocampus and amygdala, would be more impaired at understanding concrete vs. abstract words when compared to healthy controls.

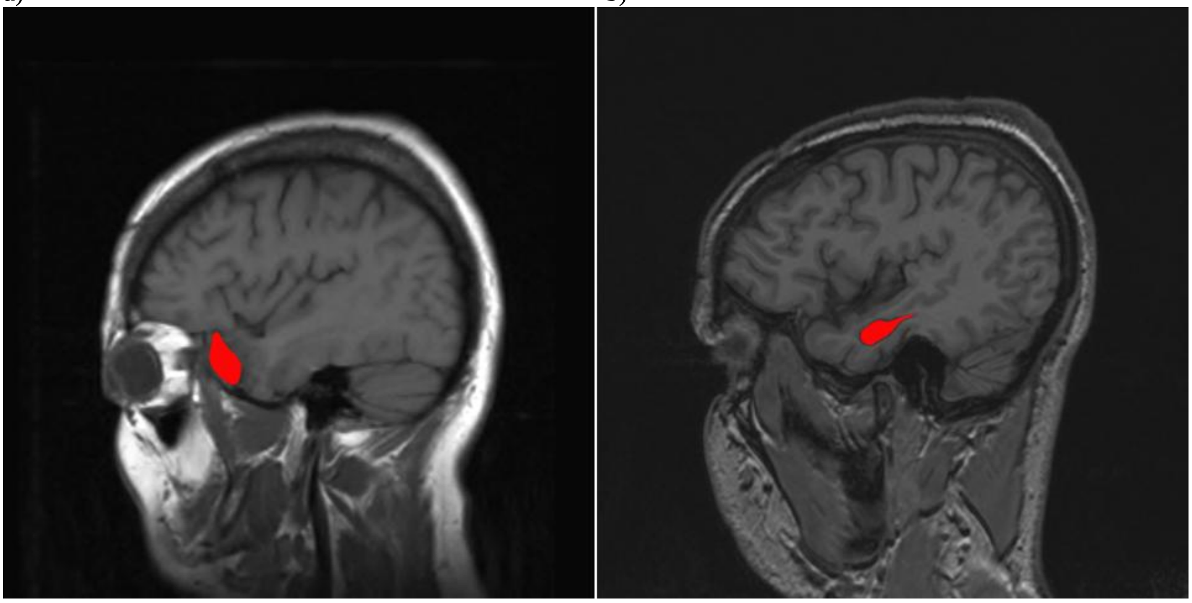
2. Methods

2.1. Subjects

A total of 22 French speaking patients were recruited from the Neurology Unit of Notre-Dame Hospital and from the Montreal Neurological Institute and Hospital in Montreal, all referred by a neurologist or neurosurgeon. The patients selected had undergone either type of surgery: (i) a selective unilateral amygdalo-hippocampectomy (SeAH), or (ii) a selective unilateral anterior temporal resection, rostral to the head of the hippocampus and excluding the amygdala. The SeAH surgery consisted of the resection of the following structures: the amygdala, the hippocampus, and the anterior portion of the parahippocampal gyrus (including the entorhinal cortex, perirhinal cortex and uncus). In the ATL resection, the temporal pole (Brodmann area - BA 38) was completely or partially removed. The resection covered the anterior portions of the inferior, middle and superior temporal gyri (BA 20, 21, and 22, or T3, T2, and T1, respectively). Resection was on average 4.5 cm posterior to the tip of the temporal pole although this varied across patients. Resection did not affect the fusiform gyrus (T4) in any of the patients. This point is important to point out since recent studies have shown that the anterior portion of the fusiform gyrus may play a significant role in semantic memory (Mion et al., 2010; Binney et al., 2010). Also, ATL resection did not extend posteriorly into the occipito-temporal gyrus (including the posterior portion of the fusiform gyrus). Both groups of patients in the current study are quite rare since the classical surgery in temporal lobe epilepsy usually consists in the resection of the temporal pole as well as a portion of the amygdalo-hippocampal complex. Finally, there were no overlapping regions in the resections of both groups of patients. Figure 1 shows examples of both types of resection in two of our patients. All patients: 1) were aged between 18 and 65 years old; 2) had no history of other neurological condition; 3) had no history of psychiatric disorder; 4) had normal or corrected-to-normal visual acuity; 5) had a normal IQ; 6) were left hemisphere language-dominant such as determined by intracarotid amobarbital (Wada) testing, cortical stimulation and/or neuropsychological evaluation; 7) were native or perfectly fluent French speakers.

Figure 1. Post-surgery MRI of a patient with ATL resection (a) and of a patient with SeAH resection (b).

a) b)



Using this set of criteria, 15 SeAH and 7 ATL were tested. Most patients had undergone surgery in order to treat their pharmacologically resistant temporal lobe epilepsy (17), while the others had a tumour resection (5). A control group consisting of 15 healthy adults strictly matched for age and education was also recruited in this study. Demographic and clinical information are summarized in Table 1. Our study was approved by the Notre-Dame Hospital and by the Montreal Neurological Institute and Hospital Research Ethics Boards. All participants gave signed informed consent prior to the experiment.

Table 1

Group demographics and clinical information

	Controls (n = 15)	**ATL** (n = 7)	**SeAH** (n = 15)
Age, years	42,5 (14,4)	34,0 (13,6)	40,3 (14,9)
Education, years	13,5 (2,1)	14,1 (2,2)	12,8 (2,6)
Gender (male/female)	7 / 8	4 / 3	8 / 7
Handedness (right/left)	13 / 2	6 / 1	13 / 2
Injured hemiphere (right/left)	-	4 / 3	9 / 6
Aetiology (epilepsy/tumour)	-	2 / 5	15 / 0
Years post-surgery	-	4,0 (3,0)	4,9 (2,9)

Results are presented in Mean and S.D. in parentheses. *p* values for group effects were not significant for age, education, and years post-surgery.

N.B. Among those patients who underwent surgery in order to treat temporal lobe epilepsy (17), 12 were seizure-free at the time of evaluation, including 4 who were also medication free. Among the patients who were not seizure-free, 3 had relatively good seizure control, while a second surgery was being considered for the last 2.

2.2. Neuropsychological assessment

All patients and control participants underwent a comprehensive neuropsychological assessment as part of this study. Episodic verbal memory was assessed with the Logical Memory I and II subtests of the Wechsler Memory Scale-III (WMS-III; Weschler, 2001). Visual memory was assessed using the immediate and delayed recall (20 min) conditions of the Rey complex figure (Rey, 1960). The picture version of the Pyramids and Palm Trees Test (Howard & Patterson, 1992) and the Information subtest of the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) were employed as tests of general semantic memory. Language was assessed using the 15-item version of the Boston Naming Test (Calero, Arnedo, Navarro, Ruiz-Pedrosa, & Carnero, 2002), as well as with the Letter (P) and Category (animals) fluency tests (Cardebat, Doyon, Puel, Goulet, & Joanette, 1990). It is worth mentioning that the Boston Naming Test as well as the categorical fluency test could also be representative of semantic memory abilities. Executive functions were evaluated using the Stroop-Victoria Test (Regard, 1981) and the Trail Making Test (Reitan, 1955). Short-term and working memory were evaluated using the forward and backward span subtests of the WMS-III (Weschler, 2001). Visuoconstructive abilities were tested using the copy of the Rey-Osterrieth Figure (Rey, 1960). Lastly, Benton's Facial Recognition Test was used to evaluate facial visuoperceptual abilities (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). Table 2 summarizes the results of the neuropsychological assessment for each group.

Table 2

Results of the neuropsychological assessment

	Controls (n = 15)	**ATL** (n = 7)	**SeAH** (n = 15)	*p* value for the Kruskal-Wallis test group effect
Memory				
Logical Memory I and II (WMS-III)				
Immediate free recall (75)	53,0 (6,0)[a, c]	35,7 (11,8)[a]	36,8 (10,6)[c]	$p < 0.01$
Delayed free recall (50)	33,5 (6,4)[a, c]	21,3 (7,5)[a]	19,7 (9,1)[c]	$p < 0.01$
Rey-Osterrieth Immediate recall (36)	21,8 (4,7)	16,7 (6,9)	16,8 (6,5)	Ns
Rey-Osterrieth Delayed recall (36)	20,7 (6,1)	15,7 (6,9)	15,9 (6,1)	Ns
Semantic knowledge				
Pyramids and Palm Trees Test (52)	50,4 (1,1)[a]	48,0 (1,9)[a, f*]	49,6 (1,7)[f*]	$p < 0.05$
Information (WAIS-III) (28)	20,4 (3,2)[d*]	16,6 (5,9)	14,1 (7,3)[d*]	$p < 0.05$
Executive functions/working memory				
Stroop-Victoria Test (sec)				
Part A (color dots)	11,2 (2,0)	13,0 (4,1)	12,3 (2,6)	Ns
Part B (words)	13,87 (3,1)	16,9 (6,7)	14,7 (2,6)	Ns
Part C (interference)	20,4 (4,7)	27,4 (14,7)	22,4 (7,2)	Ns
Trail Making Test (sec)				
Part A	32,3 (10,3)	32,9 (12,7)	29,8 (7,9)	Ns
Part B	57,7 (23,2)	63,3 (19,5)	61,1 (29,4)	Ns
Digit span forward (WAIS-III)	11,3 (1,6)	9,7 (2,4)	10,7 (3,0)	Ns
Digit span backward (WAIS-III)	9,3 (2,5)[b*]	6,3 (2,1)[b*]	8,2 (3,0)	$p < 0.05$
Processing Speed				
Digit Symbol (WAIS-III) (133)	75,9 (16,4)	74,3 (10,4)	66,3 (16,3)	Ns
Language				
Boston Naming Test (15)	14,7 (0,6)[a, c]	12,4 (1,7)[a]	12,6 (2,1)[c]	$p < 0.01$
Verbal fluency "P" in 2 min	28,1 (6,2)[a, c]	16,7 (6,6)[a]	20,2 (5,2)[c]	$p < 0.01$
Category fluency "animals" in 2 min	35,13 (8,1)[b, c]	24,4 (7,5)[b]	24,7 (9,5)[c]	$p < 0.01$
Visuoconstructional abilities				
Rey-Osterrieth Figure - Copy (36)	33,7 (0,8)[b]	31,7 (2,3)[b]	31,9 (2,7)	$p < 0.05$
Visuoperceptual abilities				
Benton's Facial Recognition Test (54)	50,5 (2,3)[b, c]	46,9 (4,5)[b]	47,4 (3,1)[c]	$p < 0.05$

Results are presented in Mean and S.D. in brackets.
[a] $p < 0.01$ between control group and ATL patient group.
[b] $p < 0.05$ between control group and ATL patient group.
[c] $p < 0.01$ between control group and SeAH patient group.
[d] $p < 0.05$ between control group and SeAH patient group.
[e] $p < 0.01$ between ATL group and SeAH patient group.
[f] $p < 0.05$ between ATL group and SeAH patient group.
* Ns with Bonferroni Correction (0,05/3), $p > 0.0167$

2.3. Semantic memory test

2.3.1. Stimuli

To evaluate semantic knowledge of concrete and abstract words, a semantic similarity judgement task composed of 100 triplets (50 concrete and 50 abstract) was developed. Each triplet was composed of two nouns with a very similar meaning and a third semantically irrelevant noun. Lexical frequency of words was taken from the French Lexical Database Lexique 3.01 (New, Pallier, Brysbaert, & Ferrand, 2004; http://www.lexique.org/) while word imageability was taken from the University of Ottawa OMNILEX database (OMNILEX: A Computerized Database on the French Lexicon; http://www.omnilex.uottawa.ca/; Desrochers, 2006). Examples of concrete and abstract triplets are illustrated in Appendix.

Concrete and abstract triplets were matched for frequency of use (counts per million). The mean overall frequency of abstract and concrete word lists was matched so that no significant difference emerged between the two lists [t (98) = .568, p = .571; mean triplet frequency for concrete nouns = 13.98, S.D. = 10.82]; mean triplet frequency for abstract nouns = 15.01, S.D. = 6.94). Moreover, mean frequencies of each word list within the triplet lists of abstract and concrete nouns were matched. The concrete and abstract triplet word lists were each composed of three lists: S1 (synonym 1), S2 (synonym 2) and F (foil). Mean frequency of the S1 concrete word list and of the S1 abstract word list was matched, so that no significant difference emerged between both lists [t (98) = .593, p = .555; mean frequency S1 concrete list = 13.59, S.D. = 14.94; mean frequency S1 abstract list = 15.21, S.D. = 12.08]. Similarly, mean frequency of the S2 concrete word list and of the S2 abstract word list was matched [t (98) = .400, p = .690; mean frequency S2 concrete list = 13.45, S.D. = 20.16); mean frequency S2 abstract list = 14.98, S.D. = 18.11]. Finally, there was no significant difference in mean frequency between the list of concrete foils and the list of abstract foils [t

(98) = .016, *p* = .987; mean frequency F concrete list = 14.88, S.D. = 15.58; mean frequency F abstract list = 14.84, S.D. = 11.17].

Word lists were also controlled for imageability, based on the assumption that concrete words should be easily picturable, while abstract words should not (Breedin et al., 1994; Macoir, 2009). The only norms available for word imageability in Quebec French are found in the OMNILEX Database (Desrochers, 2006). Imageability values were available for 249 of the 300 nouns forming our experimental triplets and ranged from 1 to 7, where 1 was most abstract and 7 was most concrete. The difference between the mean triplet imageability values was significant [t (57) = 29.65, $p < .001$; mean of 5.61 (0.29) and 2.97 (0.39) for concrete and abstract nouns, respectively].

2.3.2. Procedure

One hundred triplets (50 triplets consisting of concrete words and 50 triplets consisting of abstract words) were presented to each participant in this study. At first, the experiment was preceded by a practice session consisting of three items. Both the practice and experimental tasks were administered on a computer using E-prime software (version 1.2, Psychology Software Tools Inc., Pittsburgh, USA). Participants were simultaneously presented with three written nouns aligned vertically in the center of the screen. Stimulus presentation was pseudo-randomized so that the correct response was equally distributed across the three possible positions (top, center, bottom). The presentation of abstract and concrete word triplets was intermixed and pseudo-randomized across participants. Each word occurred only once during the experiment. A fixation cross first appeared in the middle of the screen for 500msec to signal the start of each trial and stimuli remained onscreen until a response was given.

Participants were told that they would see three words simultaneously on a computer screen and that two of these words were very close in meaning. They were instructed to identify, using the appropriate computer key, the word that was most different from the two other semantically-related words. Participants were asked to indicate their choice by pressing one of three designated keys (1, 2, or 3) on the keyboard corresponding to the position of the word on the screen (top, center, and bottom, respectively).

2.4. Statistical analysis

2.4.1. Demographic and clinical data

A Kolmogorov-Smirnov test was first performed and showed that all demographic variables had a Gaussian distribution and the assumption homogeneity of variance was met. Thus, one-way analyses of variance were carried out on the demographic variables for the three groups. Additional t-tests for Equality of Means were also carried out to confirm these results. A Mann-Whitney U-test was performed for *Years post-surgery* due to a non-normal distribution in the ATL group.

2.4.2. Neuropsychological data

A Kolmogorov-Smirnov test was first performed and showed that for most neuropsychological tests at least one of the three groups did not show a Gaussian distribution. Therefore, data were analyzed using non-parametric statistics. A Kruskal-Wallis H-test was first carried out. When the analysis revealed significant differences, post hoc analyses were run using Mann-Whitney U-tests.

2.4.3. Experimental task

A Kolmogorov-Smirnov test was first performed and showed that for most neuropsychological tests at least one of the three groups did not show a Gaussian distribution. Therefore, data were analyzed using non-parametric statistics. A Kruskal-Wallis H-test was first carried out. When the analysis revealed significant differences, post hoc analyses were run using Mann-Whitney U-tests.

For the purpose of statistical comparison, the standard deviation approach (Damasio, Tranel, Grabowski, Adolphs, & Damasio, 2004) was used. Patients' performance was converted into z-scores derived from the mean performance and standard deviation of the healthy control group (number of SDs above or below control subjects' mean). This method gives a representation of the relative degree of impairment of patients, rather than performance being expressed in terms of percentage of accuracy. For instance, a patient showing identical performance on abstract and concrete word triads expressed in percentage (e.g. 85%) may have different z-score values due to differences in standard deviations (e.g. $z = -2.1$ for abstract vs. $z = -1.3$ for concrete triads). Performance was considered impaired if it was 1.96 SDs or more below the control mean (type 1 error, $p = .05$, two-tailed, Holdstock et al., 2002). This method has been widely used (Barbeau et al., 2004; Bonner et al., 2009; Damasio et al., 2004).

Prior to converting the raw percentage correct score of all patients into z-score values, we ensured that there were no ceiling effects in healthy controls. Performance of the control group, expressed in terms of percentage correct response, was similar on concrete (M = 92.7%, S.D. = 3.75) and abstract (M = 91.5%, S.D. = 5.15) triads and no ceiling effect was observed.

The Kolmogorov-Smirnov test was used in order to determine if the z-scores of concrete and abstract triads had a Gaussian distribution and if homogeneity of variance was met. Paired sample t-tests were performed in order to compare z-score values between concrete and abstract word triads in both ATL and SeAH patient groups. This allowed us to determine within each group if one word category was more impaired than the other.

Finally, as in the Bonner and colleagues study (2009), we also used another measure which consisted in subtracting concrete from abstract z-scores. In addition, a Kolmogorov-

Smirnov test was performed in order to determine if the difference (abstract z-score minus concrete z-score) had a Gaussian distribution and if homogeneity of variance was met. An independent samples t-test was then carried out on this last variable. We used an alpha level of 0.05 for all statistical tests and applied Bonferroni corrections when necessary, i.e. for possible alpha inflation due to multiple comparisons.

2.4.4. Post-hoc analyses

An important number of studies have suggested that left- or right-hemispheric lesions may have a differential impact on the comprehension of abstract and concrete concepts. In fact, hemispheric distinctions have long been considered to be a main variable accounting for differences between concrete and abstract word comprehension (Chiarello, Senehi, & Nuding, 1987; Collins & Frew, 2001; Dhond, Witzel, Dale, & Halgren, 2007; Fiebach & Friederici, 2003; Kahlaoui & Joanette, 2006; Kounios & Holcomb, 1994; Rainville, Goulet, & Joanette, 1995; Shibahara & Lucero-Wagoner, 2002; Villardita, Grioli, & Quattropani, 1988). Therefore, additional analyses were carried out on the three z-score variables (abstract, concrete, abstract-concrete) as a function of hemispheric lesion (left or right), irrespective of the anatomical locus of lesion (ATL or SeAH). A Kolmogorov-Smirnov test was carried out and showed that the mean z-score value for abstract concepts in the right-hemisphere-damaged group did not have a Gaussian distribution. Therefore, data were analyzed with non-parametric Mann-Whitney U-tests.

3. Results

3.1. Demographic and clinical data

As illustrated in Table 1, there was no significant difference between our three groups in terms of age [F (2, 34) = .76, p = .48] or education [F (2, 34) = .58, p = .57]. This is important considering the impact of education of semantic knowledge. The two patient groups did not differ in terms of number of years post surgery (i.e., years between the evaluation and operation dates; $U = 41.0$, $z = -0.82$, $p = .45$).

3.2. Neuropsychological tests

Each patient group differed significantly from the control group on measures of verbal anterograde memory, language and visuoperceptual processing. However, none of the patient groups differed from the control group on tests of visual memory, executive functions nor processing speed. Measures on which the ATL group but not the SeAH group differed statistically from the control included the Pyramids and Palm Trees Test and copy of the Rey-Osterrieth Figure. More importantly, however, when the patient groups were compared directly, they did not differ on any neuropsychological measure. Thus, our two patient groups were overall equivalent in terms of neuropsychological performance, although the ATL group showed poorer performance on a measure of semantic memory. Results of the neuropsychological assessment are reported in Table 2.

3.3. Experimental task

Individual raw scores of ATL and SeAH patients as well as mean percentage score of controls are presented in Table 3, expressing percentage correct responses for abstract and concrete triads. Results indicate that performance of healthy controls was equivalent on concrete and abstract triads (concrete: M=92.7, s.d.=3.8; abstract: M=91.5, s.d.=5.2) and that there were no ceiling effects.

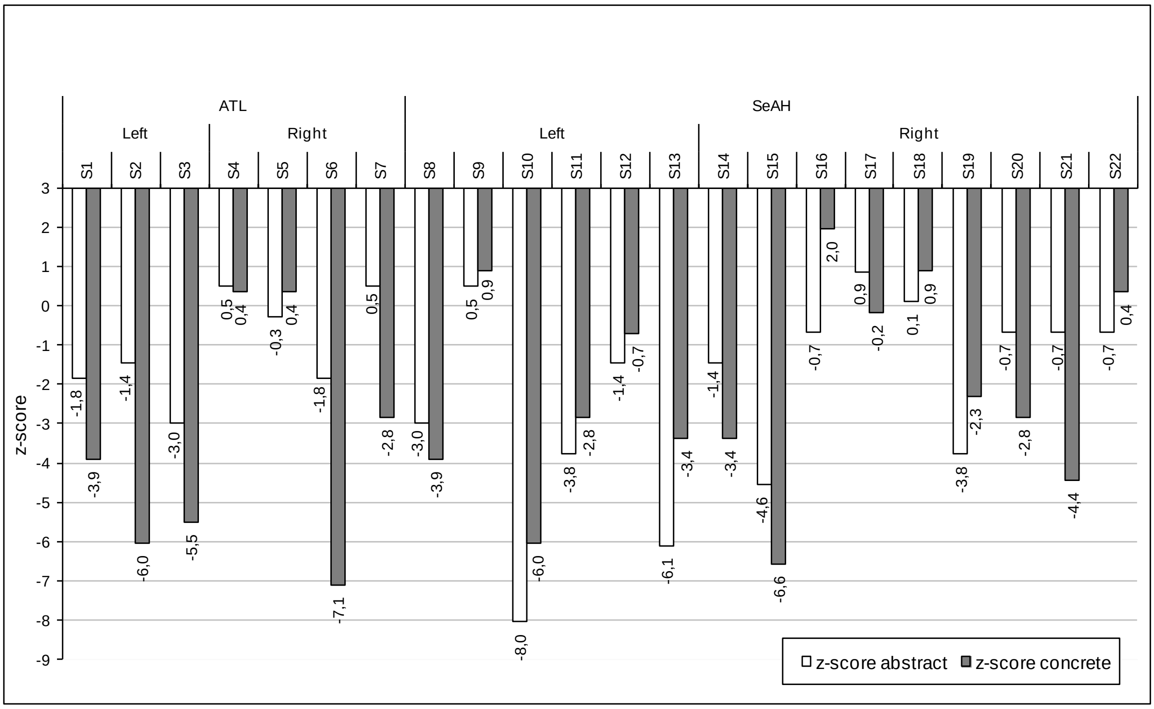
Table 3

Individual raw scores of patients and mean performance of the control group on abstract and concrete triads

		% correct answers abstract triads	% correct answers concrete triads
Controls	Mean (s.d.)	91.5 (5.2)	92.7 (3.8)
Left ATL	S1	82	78
	S2	84	70
	S3	76	72
Right ATL	S4	94	94
	S5	90	94
	S6	82	66
	S7	94	82
Left SeAH	S8	76	78
	S9	94	96
	S10	50	70
	S11	72	82
	S12	84	90
	S13	72	82
Right SeAH	S14	84	80
	S15	68	68
	S16	88	100
	S17	96	92
	S18	92	96
	S19	72	84
	S20	88	82
	S21	88	76
	S22	88	94

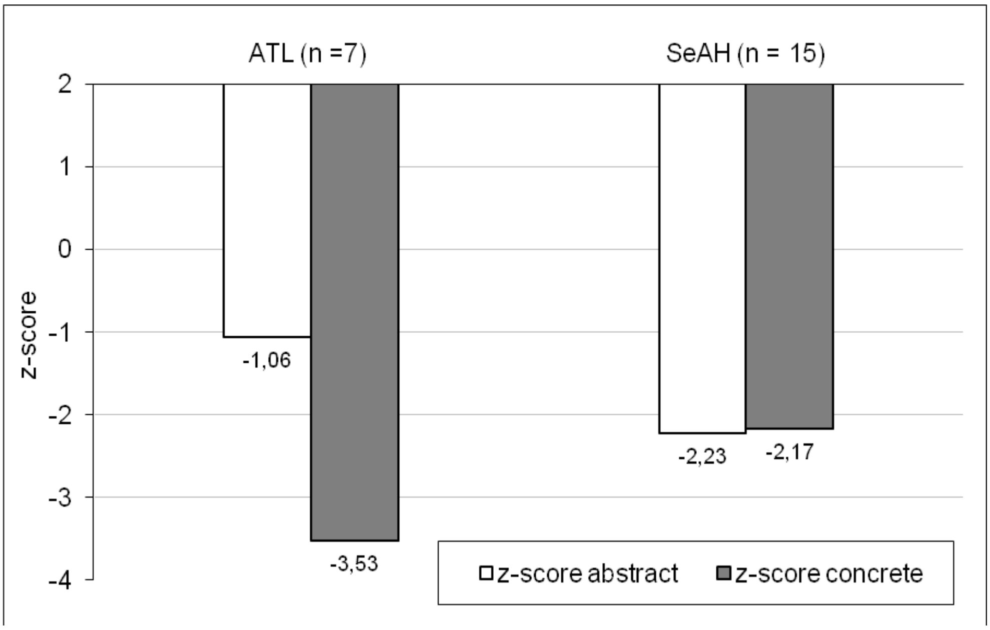
When looking at z-score results of participants on an individual basis, using the cut-off z-score of -1.96, we found significantly impaired performance in 6/15 SeAH patients (40.0%) and in 1/7 ATL patients (14.3%) on abstract triads, while 9/15 SeAH patients (60.0%) and 5/7 ATL patients (71.4%) were significantly impaired on concrete triads. Individual z-scores for each participant are presented in Figure 2.

Fig. 2: Individual z-scores on abstract and concrete triads



Mean z-score for the ATL group was -3.53 (S.D. = 2.99) for concrete triads and -1.06 (S.D. = 1.33) for abstract triads. The difference between concrete and abstract triads in the ATL group was significant [*t* (6) = 3.00; *p* = .02]. Mean z-score for the SeAH group was -2.24 (S.D. = 2.63) for concrete triads and -2.23 (S.D. = 2.58) for abstract triads. The difference between concrete and abstract triads in the SeAH group was not significant [*t* (14) = 0.24; *p*= .98]. Results are presented in Figure 3.

Figure 3: Mean z-scores for each group on abstract and concrete triads



Moreover, the abstract minus concrete z-scores (revealing contrasting performance between concrete and abstract words) of the SeAH group (M = 0.012, S.D. = 1.92) and the ATL group (M = 2.47, S.D. = 2.17) differed significantly [t (20) = -2.68; p = .014], indicating that the decrement in concrete noun comprehension (relative to abstract noun comprehension) was significantly worse in the ATL than in the SeAH group. This decrement in performance can also be seen in Table 3 where individual scores of patients are expressed in percentage correct response.

3.4. Post-hoc results

Post-hoc analyses were performed to further examine the impact of the side of lesion, in addition to the type of resection, on comprehension of concrete and abstract nouns. Since the number of patients in each group was too small to perform adequate statistical analyses, we first report qualitatively the proportion of patients with impaired scores in each subgroup of left- and right-brain-damaged patients. For abstract triads, we found significantly impaired performance in 5/9 (55.6%) left-hemisphere-damaged (LHD) patients (1/3 ATL and 4/6 SeAH) and in 2/13 (15.4%) right-hemisphere-damaged (RHD) patients (0/4 ATL and 2/9 SeAH). Regarding concrete triads, 7/9 (77.8%) LHD (3/3 ATL and 4/6 SeAH) and 7/13 (53.8%) RHD patients (2/4 ATL and 5/9 SeAH) were significantly impaired (see Figure 2 for individual z-scores).

When side of lesion was considered irrespective of the type of resection (the number of subjects was sufficient in this case to carry out analyses), further analyses revealed that the difference between LHD patients (mean z-score = -3.61, S.D. = 2.35) and RHD patients (mean z-score = -1.98, S.D. = 2.89) for concrete triplets was not significant. However, the difference between LH-damaged patients (mean z-score = -3.13, S.D. = 2.60) and RH-damaged patients (mean z-score = -0.97, S.D. = 1.62) for abstract triplets was found to be significant (U = 25.5, z = -2.22, p = .025).

4. Discussion

The main goal of the present study was to investigate if patients with selective ATL lesions were more impaired at understanding concrete words than abstract words, when compared to patients with selective medial temporal lobe lesions and healthy controls. Our hypothesis was that the semantic impairment would be more pronounced for concrete words than for abstract words in the ATL group but not in the SeAH group. In accordance with this hypothesis, ATL patients were found to be significantly more impaired at processing concrete than abstract nouns, while no such difference was found in SeAH patients and in the control group. The SeAH group, in contrast to controls, was equally and significantly impaired on both abstract and concrete word comprehension. When the performance of patients was examined on an individual basis, the RCE was found in the majority of ATL patients. These results suggest that the ATL region has a significant role in the processing of concrete words, despite the absence of lesions to the visual association cortex. Moreover, results of this study also indicate that a unilateral temporal lobe lesion (ATL or SeAH) is sufficient to cause a significant semantic impairment.

4.1. Theoretical explanations of the reversal of the concreteness effect in ATL patients

Crutch and colleagues proposed the *differential structural framework theory*" (Crutch, 2006; Crutch, Connell, & Warrington, 2009; Crutch, Ridha, & Warrington, 2006; Crutch & Warrington, 2004, 2005, 2007, 2010), which suggests that the semantic organization of concrete and abstract concepts differs qualitatively. This approach is largely based on the study of patients with refractory access dysphasia or deep dyslexia. According to this view, abstract concepts would be represented in an associative neural network whose organization relies primarily on semantic associations in a more gist-like than categorical manner. Associated words are frequently seen in the same sentence or observed together in the real world (e.g. "In order to maintain <u>peace</u> and <u>justice</u>, the <u>judge</u> has to apply the <u>law</u>") but are not synonymous (Crutch & Warrington, 2005) and do not belong to the same semantic category. Alternatively, concrete concepts are assumed to be categorically organized and processed along a similarity-based system (e.g. lion, tiger and leopard). Items belonging to the same category are similar because of their numerous shared features (e.g. big claws, big teeth, big animal, furry, dangerous, roar, hunt, eat meat). In our view, this system may be primarily, but not only, organized along visual and perceptual characteristics with other related concepts. It may allow individuals to quickly categorize and make useful deductions about new stimuli in the environment. Moreover, Crutch and Warrington (2005) insist on the relative rather than absolute distinction between the associative and categorical representational framework. In other words, the similarity- and associative-based systems are not mutually exclusive.

Therefore, any concept may be represented in both systems in uneven proportions, with more or fewer connections which also vary in strength.

Even though Crutch and colleagues did not propose an explicit explanation for the RCE, Macoir (2009) recently suggested, based on this model, that the RCE could be explained by a greater degradation of hierarchically-structured categorical connections which are more important in the representation of concrete concepts, than of associative connections which are more involved in abstract concept representations. Hence, it is possible that beyond a degradation of the visual-perceptual features of objects, it is the categorical organization itself that is damaged in patients with ATL lesions. In our view, the differential structural framework theory thus offers a very plausible account of the RCE reported in this study as well as in previous studies. The ATL region may represent a critical neuroanatomical site underpinning the processing of concrete concepts, which are mainly (but not only) tributary of this categorical organization. This hypothesis remains to be tested in future studies.

4.2. Neuroanatomical explanations of the reversal of the concreteness effect

Recent neuroanatomical interpretations have been proposed to account for the greater difficulty observed in some patients in processing concrete relative to abstract words. According to the *sensory-motor approach*, concrete concepts are represented under sensory-perceptual and motor-action features (Barsalou, 2008; Bonner, Ash, & Grossman, 2010; Martin, 2007; Pulvermuller, 2005). This approach stipulates that the degradation of visual-perceptual feature knowledge, which is crucial in the processing of concrete concepts, is at least partly responsible for the RCE. The inferior temporal lobes are part of the ventral visual stream and are important in the processing of features such as shape and color, involved in object recognition (Ungerleider & Mishkin, 1982). Hence, damage to this region may account for the RCE in SD patients and for the exacerbation of the semantic deficit for concrete, imageable objects. In addition, the RCE in SD may also arise from additional damage to the ATL, leading to the multimodal semantic deficit observed in SD (Bonner et al., 2009).

An alternative view is the *distributed plus hub hypothesis*, which emphasizes the crucial role of the ATL in semantic memory (Patterson et al., 2007). In view of the fact that this region is primarily affected in SD, a condition which causes a slowly progressive and central breakdown of semantic knowledge, and because the ATL have extensive connections with modality-specific cortical areas, the ATL are believed to be the plausible substrate for the *hub*, where concepts are assumed to be processed at an abstract, amodal level. Therefore, according to the distributed plus hub hypothesis, the sensory-perceptual and motor-action features of a concept in semantic memory converge and are integrated in the ATL to form an amodal conceptual representation (Patterson et al., 2007; Rogers, Lambon Ralph, Garrard et al., 2004; Rogers, Lambon Ralph, Hodges, & Patterson, 2004). The ATL region thus underpins a single semantic store that is critical for understanding all types of stimuli, including concrete and abstract words (Jefferies et al., 2009; Lambon Ralph et al., 2010; Pobric, Jefferies, & Ralph, 2010). Jefferies and colleagues (2009) did not observe an RCE effect in their study with SD patients and argued that the RCE may be an anomalous finding that could be due to a lack of control of variables such as word frequency (Jefferies et al., 2009). Similarly, Hoffman & Lambon Ralph (2011) found an advantage for concrete words over abstract words in SD patients and proposed that inadequate control of word frequency and imageability may explain discrepancies between studies and may account for the RCE found in some previous studies of SD patients. According to some authors, the sensory-motor account is not incompatible with the distributed plus hub hypothesis since the semantic features that the hub integrates are mainly represented in perceptual and motor cortex regions, just as they are in the sensory-motor approach (Bonner et al., 2009).

In light of the current findings, the RCE documented in our ATL patients cannot be attributed to degraded visual perceptual features due to lesions to the associative visual cortex (Bonner et al., 2010; Yi et al., 2007). In fact, contrary to SD patients whose lesions typically extend to the fusiform gyrus and to the associative visual cortex (Nestor et al., 2006), lesions of the ATL group in this study were restricted to the anterior part of the temporal lobe and did not encroach upon the fusiform gyrus and the visual association cortex. Rather, results suggest that damage restricted to the ATL is sufficient to cause a disproportionate impairment for concrete words. Moreover, word frequency was strictly controlled in the present study, which makes it highly unlikely that a lack of control of this variable could account for the RCE that was observed in our ATL group. Our results therefore suggest that the ATL region may have a significant role in the semantic organization of tangible objects, which would rely primarily on a similarity-based system. This system may in turn be highly dependent on the visual features of the stimuli as well as those arising from other sensory modalities (e.g. auditory, haptic, etc) and, to a lesser extent, on verbal information.

4.3. Are unilateral lesions sufficient to cause a measurable semantic impairment?

According to the distributed plus hub hypothesis, bilateral lesions of the ATLs are necessary to result in a significant semantic impairment, i.e. the left and right ATL function together to support a redundant and thus robust system for semantic representations (Lambon Ralph et al., 2010). Therefore, a central, amodal hub of conceptual knowledge would be distributed across left and right ATLs "in a largely undifferentiated fashion" (Lambon Ralph et al., 2010; Patterson et al., 2007; Pobric, Jefferies, & Lambon Ralph, 2010). This view stemmed first from studies of SD patients with circumscribed bilateral ATL atrophy who showed semantic deficits across a variety of input modalities (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Bozeat, Lambon Ralph, Patterson, & Hodges, 2002; Bozeat et al., 2003;

Coccia, Bartolini, Luzzi, Provinciali, & Ralph, 2004; Lambon Ralph, McClelland, Patterson, Galton, & Hodges, 2001; Luzzi et al., 2007). This view also received support from studies which found that repetitive transcranial magnetic stimulation (rTMS) applied to the ATL can mimic “symptoms” of SD in healthy subjects (Pobric, Jefferies, & Lambon Ralph, 2007) and induces slowing either in a semantic verbal task (Lambon Ralph, Pobric, & Jefferies, 2008; Pobric, Jefferies, & Lambon Ralph, 2010) or in a non-verbal task (Pobric, Jefferies, & Lambon Ralph, 2010). These authors also showed using rTMS that the left and right temporal poles made a significant contribution to the semantic processing of both abstract and concrete words (Pobric, Lambon Ralph, & Jefferies, 2009). In sum, unilateral stimulation of either the left or right ATL was able to produce a mild yet measurable impairment, which is consistent with results of the present study. However, similar effects were found following left or right stimulation, suggesting a bilateral distribution of knowledge in the ATLs and fitting the notion of a single amodal semantic hub (Pobric, Lambon Ralph, & Jefferies, 2009).

Moreover, based on the observation that patients with a unilateral temporal lesion did not show any semantic disturbance, it was suggested that both ATLs need to be damaged for a semantic deficit to emerge (Lambon Ralph et al., 2010). Similar evidence comes from a recent study with acute stroke patients with unilateral anterior temporal pole damage, which also suggests that in order to act as a semantic hub for object meaning the anterior temporal lobe must be represented bilaterally. Isolated unilateral temporal pole damage is not sufficient to cause a significant word comprehension or naming deficit for objects (Tsapkini, Frangakis, & Hillis, 2011).

In contrast, 14 of the 22 patients with unilateral anterior temporal lobe lesions (ATL or SeAH) in the current study showed a significant semantic impairment (either for concrete words, abstract words or both). Therefore, results of the present study suggest that unilateral lesions of the anterior temporal lobe may be sufficient to cause a measurable semantic disturbance. One possible explanation to account for the fact that we observed semantic deficits in the majority of our patients may be that the semantic task used in the present study may have been more sensitive to detect semantic deficits because it necessarily engaged the similarity-based system. The semantic tasks carried out by patients with unilateral ATL damage in previous studies may possibly have depended less on this categorical organization and to a greater extent upon an associative system.

When the performance of patients with left vs. right temporal lesions was compared, we found that LHD patients (ATL and SeAH combined) were more impaired than RHD patients on abstract but not on concrete triads. More specifically, 56% of LHD patients vs. 15% of RHD patients were impaired on abstract triads, while 78% of LHD patients vs. 54% of RHD patients were impaired on concrete triads. These results seem to suggest a more specialized role of the left hemisphere for verbally-mediated abstract words, while concrete words appear to rely to a greater extent on both the hemispheres. Unfortunately, statistical analyses could not be carried out to compare left vs. right ATL and SeAH groups separately due to insufficient sample size. In conclusion, despite these differences between the dominant and the non-dominant hemispheres, one of the important findings of the present study is that abstract and concrete word processing as well as the RCE appear to be determined to a greater extent by intra-hemispheric differences rather than by inter-hemispheric differences.

4.4. Can medial temporal lesions cause semantic deficits?

A rather unexpected finding in this study was that SeAH patients showed significant semantic deficits, even though neither RCE nor classical CE emerged. These results may be explained by recent evidence suggesting that the hippocampus may play a role, to some extent, in retrieving the semantic representations of stimuli by providing complementary support to activation in the lateral temporal cortex, in response to task difficulty. For instance, Whatmough and Chertkow (2007) found that the speed with which subjects performed semantic memory tasks co-varied with the increase of regional cerebral blood flow in the hippocampus. Using a semantic categorization task in their functional MRI study, Tieleman and colleagues (2005) also found that in addition to activation found in the lateral temporal cortex, activation was observed in the left hippocampus and left parahippocampal gyrus when participants were doing the same task but at a more rapid rate. In another study, Gleissner and Elger (2001) reported that in patients with temporal lobe epilepsy, the subgroup with hippocampal sclerosis named fewer words on semantic fluency tasks relative to phonemic fluency tasks. This pattern was not observed in patients with other types of temporal lobe damage. Lastly, the anterior portion of the hippocampus may also be part of a network of anterior temporal lobe structures underlying semantic memory, which also include the perirhinal and entorhinal cortices, the temporal pole and the anterior fusiform gyrus (Barbeau et al., in press).

Another explanation is that the semantic deficits in the SeAH group may be due to the resection of a portion of the perirhinal cortex and amygdala. The role of the perirhinal cortex in semantic memory is presumably important (Barbeau et al., 2004; Davies, Graham, Xuereb, Williams, & Hodges, 2004). For example, this structure is implicated in object recognition (Holdstock, 2005), possibly more so when fine-grained discrimination is necessary (Buckley, 2005). Therefore, this subhippocampal region could be particularly involved in the processing of concrete concepts. Moreover, the amygdala could play a role in the representation of abstract concepts since it has been demonstrated that emotional information is important in the representation of these concepts (Kousta, Vigliocco, Vinson, Andrews, & Del Campo, 2011). Abstract concepts are especially more “emotionally valenced” than are concrete words (Kousta et al., 2011). A lesion of the amygdala could thus particularly disturb the processing of abstract concepts. In summary, the SeAH semantic deficits could be explained by the concomitant damage to the perirhinal cortex and amygdala.

Finally, aetiology of lesion should also be considered in interpreting these findings. In fact, all of the SeAH patients in the present study had undergone surgery in order to treat their pharmacologically resistant temporal lobe epilepsy. As pointed out by Lambon Ralph and colleagues (2010), semantic function is different in a patient with a long-standing seizure history vs. a patient who underwent a tumour resection for instance. In fact, several neuroanatomical changes occur in patients with long-standing epilepsy and this may give rise to mild semantic problems in these patients that may be present prior to surgery.

5. Conclusion

In summary, SeAH patients showed impaired concrete and abstract word comprehension, while ATL patients were only impaired on concrete word comprehension, when compared to healthy age- and education-matched controls. The reversal of the concreteness effect observed in the ATL group may be interpreted in terms of qualitative differences in the way concrete and abstract words are processed. Concrete words, particularly those belonging to well-defined semantic categories, may rely to a greater extent upon a similarity-based system highly dependent upon common perceptual features, while abstract words would rely on an associative-based system. The larger deficit for concrete words in the ATL group may thus result from a breakdown of the similarity-based system as well as an increased and abnormal reliance on the associative-based system. Results of this study also showed that patients with selective unilateral anterior temporal lobe lesion can present measurable semantic deficits. From an anatomical point of view, this study indicates that the ATL region may hold a critical role in processing concrete concepts. Finally, this study suggests that it is not so much the side but rather the site of lesion that matters most in explaining differential patterns of impairment in the comprehension of concrete and abstract words.

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Appendix

Examples of concrete and abstract triplets

	synonym 1	synonym 2	foil
Concrete triplets	abeille *bee*	guêpe *wasp*	moustique *mosquito*
	boeuf *ox*	taureau *bull*	chèvre *goat*
	caillou *stone*	roche *rock*	branche *branch*
	pipe *pipe*	calumet *peace pipe*	allumette *match*
Abstract triplets	blague *joke*	plaisanterie *prank*	accident *accident*
	origine *origin*	commencement *beginning*	déroulement *progress*
	oubli *forgetting*	omission *omission*	défaite *defeat*
	coutume *customs*	moeurs *habit*	exception *exception*