

When the zebra loses its stripes: semantic priming in early Alzheimer's disease and semantic dementia

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Summary

Patients suffering from Alzheimer's disease (AD) or semantic dementia (SD) both exhibit deficits on explicit tasks of semantic memory. Semantic priming (SP) paradigms provide a very pure and precise *implicit* measurement of semantic memory impairment, and a previous study of AD (Giffard et al., 2002) using one such paradigm revealed that AD patients in the initial stages of semantic deterioration presented an abnormally large priming effect (hyperpriming) in a category-coordinate condition, compared with controls. This astonishing phenomenon could stem from the specific loss of distinctive attributes that make it possible to distinguish between semantically close concepts, while attributes shared by different concepts belonging to a given category remain intact. To test this hypothesis and compare the degradation of semantic memory in AD and SD, we devised an SP paradigm in which word pairs had either a category-coordinate or an attribute relationship. In accordance with our hypothesis, we distinguished between shared (*duck-feathers*) versus distinctive attributes (*zebra-stripes*) and close (*tiger-lion*) versus distant (*elephant-crocodile*) category-coordinate relationships. This paradigm, together with two explicit semantic memory tasks (picture-naming and categorization), was administered to 16 AD and 8 SD patients and 30 elderly control subjects. The AD patients, at the very beginning of semantic deterioration, only displayed impaired SP effects in the distinctive attribute condition, whereas in the SD patients, who had more severe semantic deterioration, we observed an extinction of SP effects in both attribute conditions. In SD patients, we also report hyperpriming effects in both category-coordinate conditions. Our results suggest that semantic memory impairment follows the same course in both AD and SD, affecting distinctive attributes first and then shared ones. In accordance with distributed models of semantic memory, the loss of distinctive attributes leads to a confusion between close concepts and it is this which causes the transient hyperpriming phenomenon.

Abbreviations

AD = Alzheimer's disease; ANOVA = analysis of variance; DRS = dementia rating scale; MMSE = mini-mental state examination; RT = reaction time; SD = semantic dementia; SOA = Stimulus-Onset Asynchrony; SP = semantic priming.

1 Introduction

Semantic memory disorders are a defining feature of semantic dementia (SD) and also occur in Alzheimer's disease (AD), where they can be observed even at a very early stage of the illness (Adlam et al., 2006; Chételat et al., 2005). AD patients display impaired abilities in object naming (Hodges et al., 1992b), verbal fluency (Salmon et al., 1999) and definition (Hodges et al., 1996; Lambon-Ralph et al., 1997). Patients often produce semantic field errors which are either hierarchically or intra-categorically related to the target word (Hodges et al., 1991; Martin and Fedio, 1983). Moreover, a number of studies of AD patients have reported a loss of knowledge of the specific attributes of concepts that constitute their meaning (Chan et al., 1997; Chertkow and Bub, 1990; Garrard et al., 2001; Martin, 1992). Using a finely-tuned methodology, Garrard et al. (2005) reported a differential vulnerability between distinctive attribute (e.g. the zebra's stripes) and shared ones (e.g. four legs). Distinctive attributes, which are specific to one particular concept, were more vulnerable than attributes shared by numerous exemplars of a given category.

SD defines a clinical syndrome characterised by a severe semantic memory disorder. This causes loss of vocabulary and general knowledge, contrasting with a relative preservation of episodic memory, perceptual skills and nonverbal problem-solving abilities (Hodges et al., 1992a). Patients may also exhibit deficits in recognizing faces, objects, smells, tastes and nonverbal environmental sounds (Bozeat et al., 2000; Luzzi et al., 2007; Snowden et al., 2004). SD patients' performances reflect a gradual loss of the features of semantic representations that enable discrimination to take place, ultimately leading to their complete extinction (Hodges et al., 1995). SD is theoretically important because it provides a relatively pure model for exploring the cognitive organization of semantic memory.

Observations of AD and SD patients support the view that the loss of semantic knowledge reflects a bottom-up hierarchy, with specific features being the most vulnerable

and superordinate information being preserved the longest (Hodges et al., 1992a; Warrington, 1975). This pattern of semantic deterioration does not mean that the hierarchy is explicitly matched by the semantic network. Distributed models hold that knowledge of higher-order structures (categorical and superordinate) is an emergent property of a distributed network of more fine-grained components (Masson, 1995; Plaut and Booth, 2000). The underlying cognitive structure of such a network can thus be reduced to an overlapping organization of discrete featural elements. Higher-order knowledge is supported by information that is shared by the members of a given category (shared attributes), whereas exemplar-level knowledge consists of information that is unique to a single member (distinctive attribute). The loss of distinctive attributes therefore causes close concepts to merge. Concepts gradually come to be supported solely by shared properties, thus allowing only category or prototypical representations to emerge.

Explicit semantic tasks are characterized by the intentional, non-automatic and even effortful processing of semantic information, and some authors have argued that impaired performances reflect inefficient access to relatively intact semantic knowledge (Hartman, 1991; Nebes et al., 1989; Nebes, 1994; Ober and Shenaut, 1988). For this reason, one of the methods that is increasingly being used to assess semantic memory in dementia is the single-word semantic priming (SP) paradigm. The SP effect is attested by a faster reaction time (RT) and/or greater accuracy when the target (*'giraffe'*) is preceded by a semantically associated prime (*'zebra'*) rather than an unrelated one (*'table'*) (Neely, 1977). SP effect relies on automatic processes; this allows semantic memory to be assessed implicitly, thus minimizing the intervention of non-semantic cognitive processes. However, in some conditions (see below), attentional controlled processes are sometimes involved (Posner and Snyder, 1975; Neely, 1991).

According to distributed models of semantic memory, concepts are represented by patterns of activity spread across a large number of interconnected units, with related concepts having similar patterns of activity. When a target word is processed, the network starts from the pattern that has just been created by processing the prime. This pattern is more similar to the target's representation when the prime is related to the target than when it is unrelated. Semantic priming occurs because the prime and target are closer to each other in a high-dimensional semantic space than unrelated primes and targets (Masson, 1995; McRae and Boisvert, 1998; Plaut and Booth, 2000).

In AD, several group studies have been performed, but these have yielded contradictory results (for reviews see, Giffard et al., 2005; Ober, 2002), showing either impaired (Ober and Shenaut, 1988; Salmon et al., 1988; Silveri et al., 1996), equivalent (Nebes et al., 1984; Ober et al., 1991) or even, paradoxically, increased priming effects (hyperpriming) (Balota et al., 1999; Balota and Duchek, 1991; Bell et al., 2001; Chertkow et al., 1989; Nebes et al., 1989) compared with controls. Some authors have reported a combination of no priming and normal priming effects (Albert and Milberg, 1989; Bushell and Martin, 1997; Glosser et al., 1998), others both normal priming and hyperpriming (Giffard et al., 2001; Margolin et al., 1996; Shenaut and Ober, 1996). First, methodological differences have to be considered to understand these disparities particularly those modifying the processing level (intervention or not of attentional mechanisms; See Glosser and Friedman, 1991). In AD, hyperpriming effects were reported in attentional controlled (Shenaut and Ober, 1996) and in automatic non-attentional SP paradigms (Giffard et al., 2001; 2002) but they could be the result of different mechanisms. In attentional controlled conditions, a high proportion of related words pairs is used and subjects who are encouraged to take into account the prime and had a long time between the onset of the prime and the target (Stimulus-Onset Asynchrony SOA) could develop attentional strategies such as expectancy mechanism. This mechanism consisting in

generating a list of predicted targets facilitates the processing of expected targets and inhibits recognition of unexpected ones. AD patients who present impaired divided attention, working memory and inhibition processes would have an adverse effect on both generating predicted targets and processing the targets that did not fit with the expected response. Such difficulties lead to particularly long RTs in the unrelated condition compared to normal subjects magnifying the difference between unrelated and related primes RT. Automatic SP paradigms minimize the intervention of non semantic cognitive processes among which attentional mechanisms. In such conditions hyperpriming effects were interpreted as a facilitated process of related prime to target occurring in the context of semantic network deterioration (Giffard et al., 2001; 2002). However, to minimize attentional processing, automatic SP paradigms methodology has to fulfil very strict criteria (Posner and Snyder, 1975; Neely, 1991) that could be invoked to explain that some studies failed to report hyperpriming effects with short SOA. In addition, the clinical heterogeneity of the populations being investigated has undoubtedly contributed to these disparities.

In a previous longitudinal study with a very controlled methodology to minimize attentional processes, we demonstrated that SP effects fluctuate according to the level of semantic deterioration and the semantic relationship between prime and target (Giffard et al., 2002). Thus, in an attribute condition (*duck-feathers*), the SP effect steadily dwindles, whereas in a category-coordinate condition (*snail-slug*), the priming effect increases abnormally (hyperpriming) before declining. Our highly-controlled methodology allowed us to conclude that this pattern of priming reflects changes in semantic memory which can be accounted for by distributed network models of semantic memory. In these models, category structure is based on similarity, i.e. the degree to which semantic features overlap. Thus, although close concepts such as ‘zebra’ and ‘giraffe’, which belong to the same category, share a large number of attributes (‘African’, ‘mammal’ ‘four legs’, ‘wild’), they can normally

be distinguished by one or two specific attributes (e.g. the zebra's stripes and the giraffe's long neck). We showed that hyperpriming in the category-coordinate condition reflects the loss of attributes and suggested that this phenomenon could simply be due to the loss of the distinctive ones first. However, as we did not manipulate the types of attributes (shared vs. distinctive), we were unable to test this assumption.

SP studies in SD are rarer and have concerned only a few patients (Moss et al., 1995; Nakamura et al., 2000; Tyler and Moss, 1998). In a single-case longitudinal study, Tyler and Moss (1998) reported that SP effects in Patient AM were preserved longer in attribute conditions (functional and perceptual) than in categorical ones (category coordinates and category labels), thus arguing against the hierarchical assumption. Using semantically-related words with a coordination relationship, Nakamura et al. (2000) failed to observe any SP effect at all in 3 SD patients compared with 3 elderly control subjects. This result, in keeping with Moss et al.'s findings (Moss et al., 1995; Tyler and Moss, 1998) concerning the category-coordinate relationship, attests to a storage deficit in SD.

Rogers and Friedman (2008) recently assessed SP effects in both AD and SD for three types of semantic relationships: attributes (*couch-fabric*), category coordinates (*cherry-apple*), and category superordinates (*walnut-wood*). SD patients showed no SP effects for any semantic relationship. Although this result was consistent with the profound semantic impairment of SD patients, it gave few clues as to how the semantic network deteriorates. AD patients exhibited normal superordinate priming, but reduced category-coordinate priming and no attribute priming, reflecting a partially impaired semantic network. Moreover, this pattern of results supported the hypothesis of bottom-up deterioration in semantic memory, affecting the most fine-grained knowledge first. Although the authors did not report any hyperpriming effect, it is worth noting that hyperpriming is a transient phenomenon which flares up at the very onset of semantic deterioration (Giffard et al., 2002; 2008), whereas the

patients described by Rogers and Friedman (2008) already demonstrated obvious semantic deterioration.

The aim of the present study was to improve our understanding of the nature of the semantic memory deterioration and, by extension, of the hyperpriming phenomenon in AD and SD. To explore SP effects stemming from different semantic relationships, we constructed a highly-controlled paradigm derived from that developed by Giffard et al. (2001; 2002; 2003) with a new set of stimuli, distinguishing between shared (*duck-feathers*) and distinctive attributes (*zebra-stripes*), as well as between close (*tiger-lion*) and distant (*elephant-crocodile*) category-coordinate concepts. Because they are less well-represented in the semantic network, distinctive attributes may be more sensitive to semantic deterioration than the shared attributes of concepts. Thus, we assumed that, at the very first stage of semantic deterioration, only distinctive attributes would be lost, thus extinguishing the SP effect in this condition. At the same time, hyperpriming would occur in the close category-coordinate condition. Shared attributes would be preserved longer than distinctive ones, thus inducing normal priming effects in this condition. Furthermore, as distinctions can still be made even after some distinctive attributes have been lost, distant category-coordinate concepts would still produce normal SP effects. As semantic deterioration progressed, shared attributes would be lost, too, and there would be a reduction in SP for all the semantic relationships. Given their semantic impairment, we expected both AD and SD patients to exhibit this pattern of SP effects at the first stage of the disease, although as so few group studies have been conducted, little is known about the SP effects in SD. Moreover, as Rogers and Friedman (2008) failed to find an SP effect in SD for any of the semantic relationships they tested, their results precluded any comparison between patterns of semantic deterioration in AD and SD.

2 Material and methods

2.1 Participants

All participants were French native speakers and had a minimum level of education equivalent to the '*certificat d'études primaires*', a diploma that is generally obtained at ~ 14 years, following 8 years of primary education. None of the participants had a history of alcoholism, head trauma, or neurological or psychiatric illness. All subjects gave their written informed consent to the study, which was approved by the local ethics committee. They underwent a neurological examination and an extensive routine neuropsychological assessment. No abnormality other than atrophy was found on the MRI scans. For each patient, the selection was made according to a codified procedure, in French approved centres, by senior neurologists (VDLS and SB) whose main activity is the diagnosis and follow-up of patients suffering from neurodegenerative disorders. Neuropsychologists and speech therapists contributed to the diagnosis. Patients with AD were selected on the basis of the NINCDS-ADRDA criteria (McKhann et al., 1984), while patients with SD were selected according to the consensus diagnostic criteria of Neary et al. (1998) and Hodges et al. (1999). The mini-mental state examination (MMSE; Folstein et al., 1975) and the dementia rating scale (DRS; Mattis, 1976) were used to assess the level of cognitive impairment of each participant. For each group, the illness was at an early stage of dementia (MMSE > 20) and had been diagnosed within the previous twelve months. Twenty-four patients and 30 healthy volunteers were recruited. Patients had to be capable of fully understanding the instructions and/or performing an SP training session (see below). Finally, the initial diagnoses were confirmed by a clinical and neuropsychological follow-up of the patients, who were re-examined between 1 and 3 years after their first consultation.

2.2 Stimuli

To construct our set of stimuli for the SP paradigm, we had to select prime/target word pairs with one of four different semantic relations: shared (*duck-feather*) versus distinctive attribute (*zebra-stripes*) or close (*tiger-lion*) versus distant category-coordinate (*elephant-crocodile*). We also selected pairs of unrelated words (*glass-shark*) and word/pseudoword pairs (*horse-hiction*). To create word pairs that were associatively and semantically related, we administered two restricted verbal association tasks to students, in two separate sessions. In the first task, students ($n = 129$) had to produce the first word in the category that came to mind in response to 116 inductor words. In the second task, in order to select properties that could be expressed in a single word, the students ($n = 104$) had to produce the first attribute that came to mind in response to each inductor word.

Pairs in the category-coordinate condition were divided into two subcategories, according to their semantic distance from the prime: first- and second-order associations (words with the highest frequency of occurrence, i.e. the words cited most often during the restricted verbal association task) were classified as semantically close pairs (*tiger-lion*), while fourth- and fifth-order associations (words with the lowest frequency of occurrence) were classified as semantically distant pairs (*elephant-crocodile*) (Richards and Chiarello, 1995). Concerning the pairs in the attribute condition, the distinctiveness of the attributes was assessed on a five-point scale by 23 young subjects (mean age: 24.5 ± 1.2). Attributes with a mean score below 2.6 were deemed to be shared (*elephant-legs*) and those with a mean score above 3.4, distinctive (*zebra-stripe*). In this way, we created a large set of 584 prime/target pairs, wherein the target was either a category-coordinate-related word or an attribute of the prime.

To check that the targets in these pairs were understandable, unambiguous and recognizably French, with homogeneous RTs and a low proportion of errors, we constructed a simple lexical decision task featuring 584 targets and 584 pseudowords. The latter, which

were all pronounceable, were constructed by changing one letter per syllable but maintaining the orthographic structure of the French language. Nineteen healthy and right-handed elderly people (mean age: 68.8 years \pm 1.5) had to decide as quickly as possible whether the letter strings constituted a French word or not. The task was computerized (Superlab 1.68, Cedrus Corporation, Phoenix, Arizona, USA) and run individually. Stimuli were presented in the centre of the screen and measured 2.5 cm high. During each trial, the subject saw a fixation point on the screen lasting 200 ms, followed by a letter string. Subjects were instructed to respond as fast as possible. If they recognized a French word in the letter string, they had to press the 'yes' key with their dominant hand. If the letter string meant nothing to them, they had to press the 'no' key with their other hand. The target remained on the screen until a response was made. In order to minimize loss of attention and tiredness, the task was divided into four blocks and separated by a few minutes' interval. In each block, a randomized distribution of the stimuli was the same for all subjects. Blocks were counterbalanced between the subjects. In order to familiarize themselves with the task, subjects performed a training block. All words and pseudowords giving rise to more than a 6% classification error were removed from the target list.

Finally, for each semantic relationship condition (close vs. distant category-coordinate, shared vs. distinctive attribute), we selected 18 word pairs (presented in appendix) whose targets had a mean RT ranging between 650 and 950 ms. To check that the RT differences between the related and unrelated conditions were due to semantic relationships, for each pair of semantically related words (4 conditions x 18 pairs; $n = 72$), we chose a matched pair of semantically and associatively unrelated words whose target had the same mean RT as the related pair's target when presented without its prime. There were no differences between the 8 conditions in terms of target mean RT or prime and target, mean word length (number of letters) and mean lexical frequencies (Lexique 3.05, New et al., 2004). We also selected 216

other word pairs without any semantic relationship. These pairs were used to assess the subjects' processing times. Thus, out of all the word pairs ($n = 360$), 20% were semantically related ($n = 72$) and 80% were unrelated ($n = 72$ matched + 216 non-matched). These proportions helped to prevent expectancy about the nature of the target. To construct the lexical decision task for the priming paradigm, we created 360 pairs with words as primes and pseudowords as targets. The likelihood of encountering a word versus a pseudoword in the target position was 50%, thereby minimizing the intervention of postlexical attentional processes (Neely, 1991).

2.3 Semantic priming procedure

The SP procedure was derived from Giffard et al. (2001; 2002; 2003). Stimuli were presented using Superlab 2.0 software (Cedrus Corporation, Phoenix, Arizona, USA), which allows RTs to be measured within 1 ms. During each trial, the subject saw a fixation point on the screen lasting 500 ms, followed by a prime word displayed for 200 ms. Thereafter, the screen remained empty for 50 ms before the target appeared. SOA was 250 ms, which was too short for the subject to anticipate the nature of the target (Lecardeur et al., 2007; Neely, 1977). There was a 1,000 ms inter-stimulus interval between each trial. In order to promote task automaticity, subjects were instructed to respond solely for the target and as fast as possible. If they recognized a French word in the letter string, they had to press the 'yes' key with their dominant hand. If the letter string meant nothing to them, they had to press the 'no' key with their other hand. The target remained on the screen until a response was made, in order to avoid patients responding at random.

In order to minimize loss of attention and tiredness, the task was divided into eight blocks lasting ~5 minutes each and separated by a few minutes' interval. The different types of pairs (related, unrelated and pseudoword) were evenly distributed across the blocks. Unrelated

pairs were placed in the same block as their matched related pairs. In each block, the pseudo-randomized distribution of the stimuli was the same for all subjects and respected the following constraints: there were never more than 3 occurrences of a word or pseudoword target in a row, related pairs never occurred at the beginning of a block, and related pairs of words were evenly spaced within the block. Blocks were counterbalanced between the subjects. In order to familiarize themselves with the task, subjects performed a training block made up of 30 practice trials without any semantic related words. Instructions were repeated until they were fully understood.

2.4 Explicit assessment of semantic memory

The semantic knowledge of 99 concepts corresponding to the words included in the SP paradigm either as primes or targets was assessed by means of explicit semantic memory tasks. Picture-naming and categorization tasks at three levels of the semantic hierarchy (superordinate category (living vs. manmade), category (plant, animal or object) and subcategory (fruit, tree, flower, cereal or vegetable)) were administered to the subjects in a separate session following the SP paradigm. In the categorization tasks, they had to read words and select the corresponding category from a list placed in front of them. Scores were converted into a percentage of correct responses.

2.5 Statistical analysis

One-way analyses of variance (ANOVA) were carried out to compare the demographic and clinical data of the three groups of subjects.

With respect to the lexical decision task, accuracy was close to ceiling in all groups (mean respectively 99%, 98.6% and 97.5% for Controls, AD and SD patients) so only reaction times (RT) data were analysed. Analyses of RTs were based on correct responses only. However, in order to ensure that performances on the lexical decision task were not

influenced by extreme scores, in each condition, response latencies exceeding 3 standard deviations above each participant's mean were treated as outliers, and the mean calculated again. First, we performed a Group (Controls, AD patients and SD patients) x Link (related vs. matched unrelated) x Type of relationship (distinctive attribute, shared attribute, distant category-coordinate and close category-coordinate) ANOVA on raw data with Link and Type of relationship as repeated-measures. To take into account baseline differences that may occur between patient and control groups transformed scores were computed and a similar Group x Type of relationship analysis was performed. These scores were computed as follow. For each semantic relationship condition (shared attributes, distinctive attributes, distant category-coordinates and close category-coordinates) and for each subject, SP effects based on differences of RT (i.e., raw mean RT for the related condition – mean RT for the matched unrelated condition) are expressed as a percentage of the mean RT for the non-matched related condition (SP effect divided by the mean RT for the non-matched unrelated condition x 100). Before conducting this second analysis, we tested SP effects in each group and type of relationship by using one sample t-tests. These ANOVAs were followed by post-hoc comparisons using Post-hoc analyses using Fisher's Least Significant Difference (LSD) tests to compare group means.

Regarding the explicit semantic memory tasks, a one-way ANOVA was used to compare the three groups' picture-naming performances, and a Group (Controls, AD patients and SD patients) x Semantic levels (superordinate category, category and subcategory) ANOVA with Semantic levels as repeated measures was performed on categorization performances.

3 Results

3.1 Demographic data and general cognitive assessment

There were no differences between the AD, SD and control groups for age and educational level, but a significant group effect was found for the MMSE and DRS scores, with significantly lower scores for both patient groups compared with controls, but no significant difference between the scores of the AD and SD patients (Table 1).

3.2 Reaction times in lexical decision task

3.2.1 Raw data

Means and standard deviations of RTs of the related and matched unrelated conditions are presented in table 2. A Group x Link x Type of relationship ANOVA showed a significant Group effect [$F(2, 51) = 6.86, p < .003$], a significant Link effect [$F(1, 51) = 55.83, p < .0001$] and a significant Type of relationship effect [$F(3, 153) = 2.32, p < .004$]. Group x Link interaction was significant [$F(2, 51) = 6.72, p < .003$], Group x Type of relationship was significant [$F(6, 153) = 2.32, p < .04$], Link x Type of relationship [$F(3, 153) = 10.2, p < .0001$] and Group x Link x Type of relationship was also significant [$F(6, 153) = 3.19, p < .006$]. Post-hoc analyses indicated that, in the controls, there were no significant differences between related and matched unrelated RTs in the distinctive attribute, shared attribute, distant category-coordinate conditions (all $p > .20$) and a significant difference in the close category-coordinate condition ($p = .01$). In the AD patients, post-hoc analyses indicated no significant difference between the related and matched unrelated RTs in the distinctive attribute condition ($p > .35$) whereas the differences were significant in the shared attribute ($p < .04$), distant category-coordinate ($p < .03$) and close category-coordinate ($p < .0001$) conditions. In the SD patients, post-hoc analyses indicated no significant

differences between related and matched unrelated RTs in both attribute conditions (all $p > .25$) while these differences were significant in both category-coordinate conditions (all $p < .002$).

3.2.2 Transformed scores

In the control group, the SP effects were significant in all the semantic relationship conditions: close category-coordinate [$t(29) = 5.58, p < .0001$], distant category-coordinate [$t(29) = 2.47, p = .02$], shared attribute [$t(29) = 2.99, p = .006$] and distinctive attribute [$t(29) = 3.35, p = .002$].

In the AD patients, the SP effects were significant in both the close category-coordinate [$t(15) = 4.27, p = .0006$] and distant category-coordinate conditions [$t(15) = 4.41, p = .0005$], as well as in the shared attribute condition [$t(15) = 3.78, p = .002$], though not in the distinctive attribute one [$t(15) = .45, p = .658$].

In the SD patients, the SP effects were significant in both the close category-coordinate [$t(7) = 2.86, p = .018$] and distant category-coordinate conditions [$t(7) = 3.07, p = .024$], but not in the shared attribute [$t(7) = .91, p = .392$] or distinctive attribute conditions [$t(7) = .28, p = .785$].

A Group \times Type of semantic relationships showed a significant group effect [$F(2,51) = 5.60, p = .006$], a significant semantic relationship effect [$F(3,153) = 9.94, p < .0001$] and a significant interaction [$F(6,153) = 2.35, p = .033$].

Post-hoc analyses indicated that, in the close category-coordinate condition, the SP effect did not differ significantly between controls (7.24%) and AD patients (10.46%, $p = .32$), although there was a significant difference between controls and SD patients (25.46%, $p < .0001$), as well as between AD and SD patients ($p = .001$). In the distant category-coordinate condition, although the SP effect did not differ between controls (3.59%) and AD

patients (6.57%, $p = .177$), it was significantly higher in SD patients (12.68%) compared with controls ($p = .029$), though not compared with AD patients ($p = .356$). In the shared and distinctive attribute conditions, there was no significant difference between the three groups (all $p > .391$). In the control group, there was no significant difference between any of the semantic relationship conditions (all $p > .169$). In the AD group, the only significant difference was between the close category-coordinate and distinctive attribute conditions ($p = .011$; all other $p > .135$). In the SD group, SP was significantly higher in the distant coordinate condition than in all the other conditions (all $p < .014$).

Results on transformed scores are reported in Fig. 1.

3.3 Explicit assessment of semantic memory

3.3.1 Picture-naming task

A one-way ANOVA revealed a significant group effect (Controls, AD and SD patients) for the picture-naming score [$F(1,51) = 42.77, p < .0001$]. SD patients' performances (52.39% correct responses) were lower than those of both controls (85.05%, $p < .0001$) and AD patients (79.79%, $p < .0001$). AD patients' performances, however, did not differ significantly from those of controls ($p = .062$).

3.3.2 Categorization tasks

A two-way ANOVA (three groups (AD, SD and controls) x three semantic levels (superordinate category, category and subcategory)) showed a significant group effect [$F(2,152) = 58.17, p < .0001$], a significant semantic level effect [$F(2,152) = 117.64, p < .0001$] and a significant group x semantic level interaction [$F(4,152) = 10.05, p < .0001$]. SD patients' performances were lower than those of both controls and AD patients for each level of categorization (all $p < .005$), whereas AD patients' performances only differed significantly from those of controls for the subcategory level ($p = .0001$).

4 Discussion

In this study, we used an automatic SP paradigm with a very controlled methodology minimizing the intervention of non-semantic cognitive processes. Such a procedure is particularly relevant to investigate the integrity of the semantic memory network in patients with semantic knowledge retrieval and attentional mechanisms deficits. To further explore the semantic deterioration and to confirm previous results (Giffard et al., 2001; 2002), we devised an SP paradigm in which word pairs had either a category-coordinate or an attribute relationship, but we also distinguished between shared (*duck-feathers*) versus distinctive attributes (*zebra-stripes*) and close (*tiger-lion*) versus distant (*elephant-crocodile*) category-coordinate relationships. Furthermore, we proposed this paradigm to two different patient populations, AD and SD.

We based our interpretation on transformed data that did not follow the traditional procedure consisting in conducting the analysis and interpreting the raw data first. Contrary to SP data expressed as a percentage, raw data for almost all groups and conditions did not fit with normal distributions. This deviation from normality could modify the statistical results, especially when group sizes are unequal, as is the case in our study. In the results section, we reported an omnibus ANOVA on raw data, but preferred not to go further in the discussion of these results. Additional non-parametric analyses on raw data were carried out. Wilcoxon matched-pairs signed-ranks tests contrasting RTs between related and unrelated matched conditions indicated significant differences for all types of semantic relationship in the control group (all $p \leq .01$). In the AD group, the differences were significant (all $p \leq .01$), except between the distinctive attribute and the unrelated matched condition ($p = .88$). In the SD group, the differences were significant between the coordinate (both close and distant) and the unrelated matched conditions (both $p < .05$), but not between the attribute (both shared and distinctive) and the unrelated matched conditions (both $p \geq .20$). Overall, these results are

identical to those of the one-sample *t* tests conducted on the transformed SP effects in each group and type of relationship. These results confirm the risk of using an incorrect description of RTs distributions. In addition, these results reinforce the validity and usefulness of the percent priming method (Giffard et al., 2001; 2002). This procedure is commonly used (Ober, 2002) and produces comparable results to other data transformation procedures (Giffard et al., 2003).

As expected, we reported longer RTs for both groups of patients. The cognitive slowing can be at the origin of hyperpriming effects (Nebes et al., 1989): a subject with very long RTs has more chances of showing a larger decrease in RT when the prime is followed by a semantically related target and thus leads to an increase of the SP effect. A relation between increased semantic priming effects in raw scores (difference between mean RT in related vs. non-related condition) and the cognitive slowing linked to normal aging has already been reported (Giffard et al., 2003). SP expressed as a proportion of a mean RT in a non-related condition for each subject takes into account the differences of cognitive speed processing between control and patients groups. Hence, this transformation procedure proves to be particularly relevant to compare these two populations.

In previous studies (Giffard et al., 2001; Giffard et al., 2002), we reported hyperpriming effects in a close category-coordinate condition in AD patients and suggested that this phenomenon is due to the loss of distinctive attributes. In the present study, we observed AD patients with minor semantic deterioration. We observed an extinction of SP in the distinctive attribute condition, while the SP effect remained normal in the shared attribute and category-coordinate conditions (distant and close). We compared these SP effects with those in SD patients with more severe semantic deterioration, as assessed by the explicit semantic tasks. SD patients presented not only an extinction of SP effects in both attribute conditions but also a hyperpriming effect in both category-coordinate conditions. These observations suggest that

the semantic deterioration follows the same course in both AD and SD patients, beginning with the loss of distinctive attributes.

We studied SP effects in AD patients who were at the early stage of the disease, as indicated by their scores on the general cognitive scales (MMSE and DRS). We only observed impaired performances on the categorization task at a subordinate level of the semantic hierarchy. This result underlines the relative preservation of semantic memory in the AD patients included in our study. Even though the task difficulty may have contributed to this result, this pattern of performances (impaired subordinate categorization with preserved superordinate categorization) is consistent with bottom-up semantic deterioration, hitting fine grained knowledge first. Consistent with this idea, AD patients only presented an extinction of the SP effect in the distinctive attribute condition.

Our failure to observe a hyperpriming phenomenon in the category-coordinate conditions could be explained by the fact that the AD patients were at a less severe stage of the disease (mean MMSE = 25.4 ± 2.6) than those studied by Giffard et al. (2001) (mean MMSE = 20.78 ± 3.9). In accordance with the mild severity of the disease, AD patients in our study presented a very slight semantic deterioration as confirmed by their close to normal explicit semantic memory performances. The patients observed by Rogers and Friedman (2008) also suffered from mild AD (mean MMSE = 21.5) but it's important to notice that they were selected to demonstrate a substantial degree of semantic impairment on an explicit semantic battery. One could hypothesize that at this stage of the semantic deterioration, the transient period allowing the hyperpriming effect is over and SP effect decreases in the category-coordinate condition. In a short SOA condition, Shenault and Ober (1996) did not report hyperpriming effects in a category-coordinate condition for patients with mild dementia (mean MMSE = 21.5). First, hyperpriming as the result of the semantic deterioration is a transient phenomenon that did not agree with the large scale of the dementia severity observed in this study (scores from 12 to

28). In addition, they used a 50% pairs of related words that could compromise the automatic nature of the task. Attentional process could appear and biased RTs of the patients. Previous studies in AD have reported a lack of any SP effect when the target is an attribute of the prime (Giffard et al., 2002; Giffard et al., 2008; Rogers and Friedman, 2008), arguing in favour of a deterioration in this type of semantic knowledge. In our study, we manipulated the type of attribute in order to demonstrate that attributes are affected to deferring degrees, according to their distinctiveness. In line with our hypothesis, distinctive attributes proved to be the most sensitive to semantic deterioration. This differential vulnerability of distinctive attributes compared with shared ones has already been reported in AD (Alathari et al., 2004; Garrard et al., 2005). In a connectionist framework, shared and distinctive attributes vary in the degree to which they are coactivated. Shared attributes frequently co-occur, making them more resilient to the effects of brain damage (Devlin et al., 1998). Conversely, distinctive attributes, which are not often activated, are more vulnerable.

Contrary to our hypothesis, the extinction of the SP effect in the distinctive attribute condition did not coincide with the appearance of hyperpriming in the close category-coordinate condition in AD patients. This does not, however, invalidate the theory that the hyperpriming phenomenon stems from the loss of distinctive attributes. Assuming that more than one distinctive attribute is generally necessary to isolate one concept from the other members of its category, the loss of just one distinctive attribute could be sufficient to reduce the SP effect in the distinctive attribute condition but not enough to generate confusion between two close concepts (i.e. hyperpriming in the close category-coordinate condition). Hyperpriming may well occur as semantic network breakdown progresses and several distinctive attributes of prime and target concepts disappear.

The SD patients displayed impaired performances on every component of the explicit semantic memory assessment. As already reported, explicit semantic memory tasks reveal a

more severe semantic deficit in SD than in AD, even when SD patient' general cognitive performances are comparable to those of AD (Rogers et al., 2006). It is important to note that although the SD patients included in the present study were not yet severely affected, they displayed SP effects neither in the distinctive attribute condition nor in the shared attribute one. This result is consistent with our hypothesis that, in patients with a higher degree of semantic impairment than that of the AD group, the shared attributes would be affected, too. In addition, this finding and those of earlier studies (Moss et al., 1995; Nakamura et al., 2000; Rogers and Friedman, 2008; Tyler and Moss, 1997) support the view that the SP paradigm provides an effective means of highlighting disruption of the central semantic network. The absence of SP in the attribute conditions contrasts with a significant SP effect observed in both category-coordinate conditions. This result contradicts Tyler et al.'s findings (Moss et al., 1995; Tyler and Moss, 1998) and supports the assumption of hierarchical semantic deterioration in SD. At first glance, one might conclude that the SP patients' performances in the category-coordinate conditions also contradicted Rogers and Friedman's results (2008). Once again, however, considering the progressive nature of semantic deterioration, it is important to note differences in disease severity between the patient groups in these two studies. While the mean MMSE score of the SD patients in Rogers and Friedman's study was approximately 22, we investigated patients with a more minor general cognitive impairment (mean MMSE = 24.9 ± 2.1).

As expected, the SP effect in the close coordinate category condition observed in SD patients was greater (hyperpriming) than that observed in the control group. In the SD patients, we highlighted the co-occurrence of extinction of SP effects in the distinctive attribute and hyperpriming in the close category-coordinate. Even though they had lost many of their distinctive attributes and, in the case of some of them, a large proportion of their shared ones, too, the concepts were sufficiently well-preserved and distinguishable to produce

an SP effect in the category-coordinate condition. This confirms an important characteristic of the distributed network model. The fact that knowledge is distributed across many components of the network allows concepts to be evoked even if many of their attributes have been destroyed. However, this disruption of the semantic network does have an impact on SP, producing a greater effect than that observed in healthy subjects. As distinctive properties are lost, the distinction between close category-coordinate concepts therefore becomes less and less marked. As some authors have suggested (Giffard et al., 2001; Giffard et al., 2002; Martin, 1992), while hyperpriming is not the same as repetition priming, it may bear certain similarities to it. The difference between SP effects in the attribute and category-coordinate conditions proves that the hyperpriming phenomenon is not due to cognitive slowing or an intentional process, but rather to semantic impairment.

Considering the distant category-coordinate condition, we also observed an unexpected hyperpriming effect. This could be due to the substantial loss of shared properties, as reflected in the absence of SP in the shared attribute condition. However, this hyperpriming effect was smaller than that observed in the close category condition as the distant category-coordinate concepts were sufficiently semantically distant for them to remain distinct, in spite of the overlap generated by the loss of properties.

Overall, we observed changes in SP effects in early AD and SD, reflecting the onset of semantic deterioration. This deterioration was confirmed by performances on picture-naming by SD patients and on categorization at the lower level of the semantic hierarchy by both patient groups. In accordance with our hypothesis concerning changes in SP effects as semantic deterioration progresses, discrepancies between the AD and SD groups can be ascribed to differences in their degree of semantic impairment. Patterns of SP effects indicate that the gradual deterioration in semantic memory follows the same course in both AD and SD. As indicated by the SP effects observed in the AD groups, the deterioration affects

distinctive attributes first, then shared ones. In the early stages of semantic deterioration, concepts begin to be impaired and the closer ones become blurred. With the progression of semantic deterioration and the loss of shared attributes, higher levels of semantic knowledge are affected, too. This hierarchical semantic deterioration was confirmed by the pattern of performances by AD and SD patients on the categorization tasks.

In the light of both these results and those of our previous studies (Giffard et al., 2001; Giffard et al., 2002), we can assume that, as the semantic deterioration progresses, SP effects undergo similar changes in both AD and SD (see Fig. 2 for details). Thus, like SD patients, AD patients display reduced SP effects in the shared attribute condition and an increased SP effect when the prime and target are category-coordinate concepts - all the more so when they are close. In SD patients, the extensive loss of attributes means that the semantic network is too severely impaired for there to be any SP effect in either category-coordinate condition. Finally, the semantic deterioration ends in the extinction of SP effects in all conditions. A longitudinal follow-up study would help to confirm this hypothesis regarding the fine-grained dynamics of semantic disorders in degenerative pathologies.

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Figures

Title for Fig. 1

Fig. 1 - Semantic priming effects expressed in percentages (mean and standard deviation) for each group (Controls, AD and SD) in the four semantic relationship conditions (distinctive attribute, shared attribute, distant category-coordinate and close category-coordinate).

Caption for Fig. 1

Rings represent a lack of priming effect (non-significant p -value reported by one-sample t -tests). Straight lines represent a significant difference between groups (Fisher's LSD post-hoc). A semantic priming effect significantly higher than those of controls represents a hyperpriming effect.

Title for Fig 2.

Fig. 2 - Schematic evolution of SP effects in relation to semantic memory deterioration in AD and SD (mild to moderate dementia): Extrapolation from present data and from the literature.

Caption for Fig 2.

Black lines illustrate the hypothetical evolution of the range of SP effects associated with the semantic memory deterioration in different semantic relationship conditions: close and distant category-coordinate, and shared and distinctive attribute (see Introduction). The grey area represents a mean normal priming effect. Extinction of priming is represented by lines under this area while hyperpriming is represented by lines up-above. The distribution of performances of AD and SD patients in the present study are shown on the figure. AD patients - who showed minor semantic deterioration - could be placed on the left part of the

axis representing semantic memory deterioration (AD patient oval). An extinction of SP is observed in AD patients in the distinctive attribute condition (see Results), confirming the relative vulnerability of distinctive attributes. However, the degree of the semantic deterioration in the present sample would not be enough to produce hyperpriming effects in line with the very slight semantic deterioration (see Discussion). SD patients of this study, who presented more severe semantic deterioration than their AD counterparts, could be placed further along the “Semantic memory deterioration” axis (SD patients oval). They presented a SP effect neither in the distinctive attribute condition nor in the shared attribute one and they simultaneously displayed a hyperpriming effect in the close category-coordinate one. Contrary to our hypothesis (dotted line), their SP effects in the distant category-coordinate condition (solid line) also increased, albeit to a lesser extent (see Results and Discussion).

Appendix – Word pairs (British English/American English translations) of the four related conditions of the semantic priming paradigm

Distinctive attribute	Shared attribute	Distant category-coordinate	Close category-coordinate
train – wagon (train – carriage/car)	pigeon – aile (pigeon – wing)	armoire – table (wardrobe – table)	cuillère – fourchette (spoon – fork)
bicyclette – guidon (bicycle – handlebars)	gorille – poil (gorilla – hair)	baleine – requin (whale – shark)	peigne – brosse (comb – hairbrush)
araignée – toile (spider – web)	botte – talon (boot – heel)	fourmi – cafard (ant – cockroach)	abeille – guêpe (bee – wasp)
sapin – aiguille (fir – needle)	brouette – roue (wheelbarrow – wheel)	assiette – bol (plate – bowl)	luge – traîneau (toboggan – sledge/sled)
chaussure – lacet (shoe – lace)	canard – plume (duck – feather)	homard – crevette (lobster – shrimp)	salopette – pantalon (dungarees – trousers)
cerf – bois (stag – woods)	casquette – tissu (cap – fabric)	chaise – banc (chair – bench)	fraise – framboise (strawberry – raspberry)

lunettes – monture	chat – moustache	laitue – endive	pastèque – melon
(glasses – frame)	(cat – whiskers)	(lettuce - chicory/endive)	(water melon – melon)
avion – aile	corbeau – bec	mouche – papillon	poney – cheval
(plane – wing)	(crow – beak)	(fly – butterfly)	(pony – horse)
chameau – bosse	pioche – manche	camion – tracteur	sandale – chaussure
(camel – hump)	(pick – handle)	(lorry/truck – tractor)	(sandal – shoe)
zèbre – rayure	ciseaux – lame	pâquerette – tulipe	sanglier – cochon
(zebra – stripe)	(scissors – blade)	(daisy – tulip)	(wild boar – pig)
biberon – tétine	tigre – griffe	clou – punaise	tasse – bol
(feeding-bottle – teat/nipple)	(tiger – claw)	(nail – drawing pin/thumbtack)	(cup – bowl)
lit – drap	pinceau – poil	vache – mouton	ail – oignon
(bed – sheet)	(brush – bristle)	(cow – sheep)	(garlic - onion)
crabe – pince	lézard – queue	couteau – scie	bureau – table
(crab – pincer)	(lizard – tail)	(knife – saw)	(desk – table)
cheval – sabot	palmier – tronc	pissenlit – marguerite	escargot – limace
(horse – hoof)	(palm tree – trunk)	(dandelion – daisy)	(snail – slug)

moulin – ailes	cerise – queue	pantalon – chemise	loup – chien
(windmill – blade)	(cherry – stem)	(trousers – shirt)	(wolf – dog)
éléphant – trompe	sauterelle – patte	cassis – fraise	collier – bracelet
(elephant – trunk)	(grasshopper – leg)	(blackcurrant – strawberry)	(necklace – bracelet)
panier – osier	citrouille – pépin	vase – verre	maïs – blé
(basket – wicker)	(pumpkin – pip/seed)	(vase – glass)	(corn – wheat)
escargot – coquille	peuplier – feuille	cerf – sanglier	foulard – écharpe
(snail – shell)	(poplar – leaf)	(stag – wild boar)	(foulard – scarf)
