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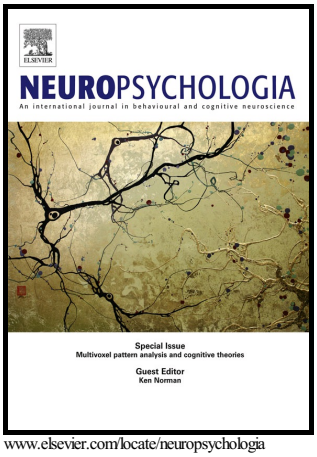

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Distinct progression of the deterioration of thematic and taxonomic links in natural and manufactured objects in Alzheimer's disease

Isabelle Simoes Loureiro and Laurent Lefebvre

Cognitive psychology and neuropsychology unit, Institute of health sciences and technologies, University of Mons

Correspondence: Isabelle Simoes Loureiro, Cognitive psychology and neuropsychology unit, University of Mons (UMONS), Place du Parc, 18, 7000, Mons. Email: isabelle.simoesloureiro@umons.ac.be

Abstract

Taxonomic and thematic relationships are core elements of lexico-semantic networks. However, the weight of both links differs in semantic memory, with distinct support for natural and manufactured objects: natural objects tend to be more taxonomically identified while manufactured objects benefit more from the underlying thematic relationships. Alzheimer's disease (AD) causes early semantic memory impairment characterized by a category-specific deterioration, where natural objects are more sensitive to the disease than manufactured objects. However, relatively few studies have examined the progressive deterioration of specific thematic versus taxonomic relations in both categories of objects in AD. To better understand semantic memory disorganization in AD and analyze the potential interaction effect between the category (natural/manufactured), the condition (thematic/taxonomic) and AD, we will investigate the lexico-semantic network in 82 AD patients (divided into three groups depending on their global cognitive deterioration and their performance in a preliminary semantic knowledge questionnaire (mild (AD1), moderate (AD2) and advanced (AD3) stages of semantic knowledge alteration). The experimental protocol contains two tasks: an implicit semantic priming paradigm and an explicit card-sorting test that uses the same items, equally divided between natural and manufactured objects. Results show a distinct taxonomic and thematic evolution pattern with early taxonomic deterioration. Natural objects are also more vulnerable to the disease. Lastly, there is an interaction effect between the category and the condition in the priming task indicating that natural objects are more taxonomically organized and manufactured objects benefit more

from both thematic and taxonomic organizations, reinforcing the idea of the robustness of this category. The theoretical accounts of these observations will be discussed in detail.

Keywords: semantic memory, semantic priming, Alzheimer's disease, taxonomic links, thematic links, category-specific deterioration

1. Introduction

Alzheimer's disease (AD) is the most common neurodegenerative disease. Its neuropsychological picture is dominated by an early and massive breakdown of memory processes. While episodic memory deterioration characterized by difficulties in learning new information is the predominant symptom in AD, semantic memory impairment is also found relatively early. Semantic memory includes decontextualized knowledge as general culture elements, as well as words and their meanings. The progressive deterioration of the lexico-semantic system has been the subject of many investigations (Adlam, Bozeat, Arnold, Watson & Hodges, 2006; Au, Chan & Chiu, 2003; Binetti et al., 1995; Giffard et al., 2001; Hodges & Patterson, 1995; Laisney, Desgranges, Eustache & Giffard, 2010). This deterioration can occur early (Chertkow, Bub, Cosgrove & Dixon, 1993; Rico Duarte, Jiménez, Syssau & Launay, 2004) with heterogeneous inter-individual impairment (Chainay, 2005; Simoes Loureiro & Lefebvre, 2015). Even today, the processes underlying semantic deficits are still a matter of debate. While some researchers argue that semantic deficit symptoms reflect access difficulties, others posit that there is deterioration in memory. Current data suggest the temporal succession of the two pathological events: first, access disorders, and then conceptual impairment.

In order to understand the semantic memory content and interactions, researchers have developed different theories. Collins & Loftus' (1975) lexico-semantic model of spreading-activation is widely used to explain semantic priming effects. Every concept may be defined by semantic attributes. While some attributes may be shared between several concepts, others are more specific. Specific links develop between concepts sharing common semantic features. During the presentation of a concept, activation spreads automatically and progressively, connected nodes of the concept can vary in strength and length.

In this lexico-semantic network, thematic and taxonomic links are both particularly salient types of connections. Two "thematically linked" concepts share a spatio-temporal context link without belonging to the same category (e.g. rabbit-carrot) and two "taxonomically linked"

concepts belong to the same ordinate category (e.g. carrot-tomato). Both kinds of connections are built early in the lexico-semantic network of children (Arias-Trejo & Plunkett, 2013; Rämä, Sirri & Serres, 2013) and remain prominent in the lexico-semantic system of adults. However, the weights of these two kinds of relationships seem different, the thematic network dominating the taxonomical network (Chen et al., 2014). Indeed, several semantic priming experimental studies have demonstrated either a thematic priming effect but no taxonomic priming effect (Bouaffre & Faïta-Ainseba, 2007; Sass, Sachs, Krach & Kircher, 2009) or a thematic priming which is more dominant than the taxonomic priming effect (Moss & Tyler, 1995; Shelton & Martin, 1992). For Maguire, Brier & Ferree (2010), taxonomic and thematic systems may be distinct and complementary but they can also compete. Neuronal activation has shown a reverse activation pattern underlying taxonomical or thematic processing.

In the same vein, the hypothesis of a category-specific organization has been proposed. Warrington and Shallice (1984) put forward the idea that natural and manufactured concepts are processed differently within the semantic network. Their "sensory-functional theory" asserted that the organization of the semantic network depends on modality-specific subsystems. The processing of different categories of objects thus depends on the internal information of the category. The 'natural objects' category (fruits, vegetables, animals…) might be based on visuo-perceptual information while the 'manufactured objects' category (furniture, tools, vehicles…) was preferentially based on functional/thematic links. Concepts could therefore be categorized based on objects' salient features. Explanatory theories based on Warrington and Shallice's sensory-functional hypothesis have focused on dissociating natural objects from manufactured ones.

Tyler & Moss (1997) and Gonnerman, Andersen, Devlin, Kempler & Seidenberg (1997) introduced other concepts such as distinctiveness and intercorrelation which made the differentiation of the two categories of objects possible. The distinctiveness and intercorrelation theory refers to the fact that shared properties (e.g. the common features of a category such as legs for animals) may be more intercorrelated in the category of natural objects while distinct properties (e.g. features present only for a reduced sample among the members of a category, such as blades for tools) may be more often and more robustly intercorrelated for manufactured objects (Durrant-Peatfield, Tyler, Moss & Levy, 1997; Randall, Moss, Rodd, Greer & Tyler, 2004; Tyler, Moss, Durrant-Peatfield & Levy, 2000). According to Tyler and Moss (1997), natural objects possess shared perceptual attributes that are more intercorrelated with functional features (e.g. the legs used by animals to walk). By

contrast, distinct perceptual attributes (e.g. zebra stripes) are less intercorrelated and thus more vulnerable. In the domain of manufactured objects, distinct perceptual attributes are strongly intercorrelated with functional features (e.g. the blade of a knife to cut) while shared perceptual attributes are less intercorrelated. However, functional features have a higher frequency of occurrence than shared perceptual attributes in the domain of natural objects (Garrard, Ralph, Hodges & Patterson, 2001; McRae & Cree, 2001). In sum, manufactured objects are more resistant to cognitive deterioration because their distinct perceptual attributes are more strongly intercorrelated with a function and because the shared perceptual attributes, even if they are less intercorrelated, have a higher frequency of occurrence. Recent research has put forward the idea that natural objects are *perceptually* and *taxonomically* organized while manufactured objects are *thematically* organized (Bonthoux and Kalénine, 2008). Silveri, Daniele, Giustolisi & Gainotti (1991) were the first to show category-specific deficits in AD patients. Using a naming task, they observed that AD patients produced better results for manufactured objects than for natural objects. These results were later confirmed (Garrard et al., 2001; Zannino, 2002). Other studies have failed to find any disequilibrium in semantic deficit in both categories (Gonnerman et al., 1997; Hodges, Salmon & Butters, 1992) (for a review, see the introduction by Hernández, Costa, Juncadella, Sebastián-Gallés & Reñé, 2008). These differences may arise from different experimental paradigms (Hernández et al., 2008; Humbert & Chainay, 2006) or from the use of specific statistical tests (Laws, Gale, Leeson & Crawford, 2005). To date, it has generally been accepted that, in AD, the deterioration of conceptual elements of natural and manufactured domains follows a differentiated deterioration profile. Gonnerman (1997) and his team found that while manufactured objects progressively and linearly deteriorated, the 'animals' category followed a different curve of deterioration defined by irregular alteration: although a few concepts of this category appear to be preserved in the mild stage of the disease, they are soon subject to major deterioration. The findings by Devlin, Gonnerman, Andersen & Seidenberg (1998) confirm that there is a significantly faster deterioration for natural objects over the course of AD but only in cases where there is no initial preservation.

In order to understand the importance of thematic and taxonomic relationships and further explain the origin of category-specific impairment in AD, we propose a semantic priming procedure in a naming task and a card-sorting task. Semantic priming is an experimental paradigm that is particularly appropriate for examining semantic links in memory. It consists in presenting a prime before asking subjects to process the target. It enables subjects to

manipulate the relations between the prime and the target and to compare the quality of thematic and taxonomic relationships. Many researchers who have worked on this protocol agree that presenting semantically linked primes diminishes the reaction time to target processing. This phenomenon is described as "semantic priming". According to Giffard, Desgranges & Eustache (2005), when the semantic priming procedure respects certain methodological conditions, it makes it possible to obtain an implicit measure of semantic memory and minimize the intervention of factors other than semantic ones. Recent research using semantic priming in AD has shown that there is a progressive loss of semantic knowledge, with a hyperpriming effect (abnormal increase in semantic priming), in coordinate taxonomic conditions only in the mild stage of AD. This surprising effect may represent the degradation of distinct attributes of the concepts (Giffard et al., 2002; Laisney, Giffard & Eustache, 2004; Martin, 1992). Hyperpriming in AD occurs in a context of difficult semantic differentiation between the target and the prime and may be explained by an effect comparable to repetition priming where the prime and the target are similar, producing an even greater priming effect.

Our work aims to implicitly and explicitly investigate the distinct deterioration of taxonomic and thematic links, category-specific impairment and the interaction of these variables according to the evolution of AD. We claim that when the semantic memory has not completely deteriorated (massive semantic deterioration is defined in this study by the disappearing of the semantic priming effects), condition and category effects should interact with groups. Early taxonomic network damages should appear in the mild stage of AD. Moreover, natural objects should be more precociously altered in AD compared to manufactured objects. Finally we posit that, as the alteration of the thematic and taxonomic links of natural and manufactured objects distinctly evolves, the taxonomic links of natural objects and the thematic links of manufactured objects should be more resistant to semantic disturbance.

2. Method

2.1. Participants

The participants were recruited through retirement homes from the central region of Belgium. They were all native French speakers. The socio-cultural level was determined using Poitrenaud's test (Hugonot-Diener, 2007). The majority of participants had obtained a primary education certificate (six years of schooling) (see table 1). Subjects or their legal

representatives signed a written research consent form for the study. Individuals who had experienced problems with alcoholism, strokes, epilepsy, cerebrovascular accidents, neurological or psychiatric backgrounds were systematically excluded from the study. The emergence of depressive affects in the Geriatric Depression Scale (Yesavage et al., 1997) was also a criterion for exclusion. None of the participants had uncorrected auditory or visual difficulties. Visual/diagnostic performances were assessed by subjects' ability to name a set of 15 pictures. Patients showing significant difficulties in recognizing the items were also excluded.

The control group comprised 33 healthy elderly subjects with normal cognitive functioning demonstrated by a mini mental state examination (MMSE) superior to 28; this score is associated with the absence of abnormal cognitive complaints in the elderly.

The experimental group was composed of AD patients, diagnosed by a doctor or neurologist based on National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann et al., 1984). Patients with neurodegenerative diseases with a different etiology from AD were excluded. Participants who did not wish to take part in the study were also excluded. Patients were allowed to take medication such as cholinesterase inhibitors or antidepressants but the dosage had to be stable before the beginning of the study.

AD patients were allocated to three groups according to the MMSE consensual limits defined by the GRECO (Hugonot-Diener, Barbeau, Michel, Thomas-Antérion & Robert, 2008): AD1 group comprised AD participants with MMSE scores superior to 20 (mild stage); AD2 group consisted of subjects with MMSE scores between 16 and 19 (moderate stage); and AD3 group was composed of patients with MMSE scores largely inferior to 16 (advanced stage). The stage of the disease was then confirmed by the Global Deterioration Scale (GDS) developed by Reisberg, Ferris, de Leon, and Crook (1982).

For each participant, a complementary evaluation using a semantic knowledge questionnaire (SKQ) (Simoes Loureiro & Lefebvre, 2015) ensured that, beyond general cognitive efficiency, patients included in the same group presented a homogeneous semantic knowledge level. In the SKQ, 30 items were associated with four questions investigating superordinate (Q1: question about general superordinate aspects; Q2: question about the intracategorical level) and subordinate (Q3: question about perceptual attributes; Q4: question about functional/thematic attributes) levels. For each question, multiple options were proposed.

Each error was counted. For each group of participants, subjects demonstrating results significantly different from the group's mean result (extreme value defined by more than 1.5 times the interquartile range, in accordance with the Tukey boxplot (1977)) were excluded from the study. While no subject was removed from the control group, five AD patients were excluded from the initial sample (three from the AD1 group and two from the AD3 group). 82 AD participants were chosen to participate in the study (AD1: N=28; AD2: N=26; AD3: N=28).

The mean number of errors at SKQ differed significantly between groups (F=50.614; p= or <.001) except for the post hoc comparisons based on Bonferroni's test between AD1 and AD2 (p=.120).

All the groups were paired according to socio-cultural level (χ^2=2.440; p =.486) and age (F=2.117; p=.102). The features of the groups are described in Table 1.

Table 1: Clinical and demographical features of the groups
AD patients and the control group's mean and standard deviation for age, MMSE and the number of errors at SKQ

	Control group N=33 (19♀)	AD1 group N=28 (25♀)	AD2 group N=26 (24♀)	AD3 group N=28 (27♀)
Age	82.64 (σ=5.867)	86.36 (σ=4.923)	83.65 (σ=6.729)	83.68 (σ=6.110)
Education level	7 SCL1 ; 16 SCL2 ; 7 SCL3 ; 3 SCL4	1 SCL1 ; 18 SCL2 ; 7 SCL3 ; 2 SCL4	0 SCL1 ; 21 SCL2 ; 4 SCL3 ; 1 SCL4	2 SCL1 ; 15 SCL2 ; 7 SCL3 ; 4 SCL4
MMSE	29.12 (σ=.781)	23.11 (σ=2.347)	17 (σ=1.131)	11.89 (σ=2.266)
SKQ (mean number of errors)	2.3 (σ=1.591)	12.61 (σ =6.130)	19.27 (σ=8.938)	34.46 (σ=18.085)

SCL1= no degree of certificate of professional competence; SCL2= primary school certificate or certificate of professional competence + primary school certificate or some secondary education attendance; SCL3: attendance of the last three years of secondary education without the certificate; SCL4= completion of the secondary school leavers' examination or higher school level

2.2. Material and method

The experimental protocol was conducted in two sessions: the first comprised an implicit investigation task of thematic and taxonomic links in semantic memory (semantic priming paradigm) and the second an explicit card-sorting task. The same pictures were used in both tasks.

2.2.1. Semantic priming paradigm

The semantic priming paradigm is an intra-modal procedure: tasks consist in naming a target-picture while ignoring a prime-picture.

2.2.1.1. Stimuli of the semantic priming paradigm

The stimuli of the semantic priming paradigm were designed according to four conditions: two related conditions (taxonomic and thematic) and two control conditions (unrelated and neutral). In each condition, 22 pictures (11 naturals and 11 manufactured) appeared as picture-targets. The related pairs (taxonomic and thematic) constituted 20% of the experimental protocols (22 pictures * 2 conditions (thematic and taxonomic) = 44 pairs) (cfr appendix 1). The remaining 80% were composed of prime-target pairs in the control condition (22 pictures * 2 control conditions = 44 pairs + 132 prime-target filler pairs = 176 pairs). This repartition (20% of interest pairs and 80% of control and fillers pairs) helped prevent expectancy strategies (Laisney et al., 2011). In sum, 220 items were presented. A break was automatically proposed after approximately 40 pictures had been shown to avoid cognitive overload (five blocks). No target appeared twice within one block. The order of block presentation was counterbalanced with three semi-random orders of presentation. In order to familiarize subjects with the task, the first 15 pairs presented were training pairs.

2.2.1.1.1. Creation of pairs of interest

To maximize the chances of correct naming in AD patients, target-pictures were selected on the basis of the items from Bonin, Peereman, Malardier, Méot & Chalard (2003) and Chalard, Bonin, Méot, Boyer & Fayol (2003) with age of acquisition (AoA) inferior or equal to 55 months. Indeed, an AoA effect associated with a frequency effect has been demonstrated in naming tasks for AD patients (Lymperopoulou, Barry & Sakka, 2006). To create the prime-target pairs, three pre-tests were realized.

The creation of thematic and taxonomic primes was based on a first pre-test where 20 healthy adults were asked to provide a word belonging to the same category as a target-word in order to create taxonomic primes, and a spatio-temporal word associated with but belonging to a different category in order to create thematic primes. Participants were asked to provide the word that best represented the relationship between the two conditions. The words had to be nouns (no verbs or adjectives) and they had to be picturesque. The associations most frequently quoted (first order of association) were retained. When pairs were phonologically similar (sharing more than one phoneme) or when the target could be confounded with the primes of other items (e.g.: “table-chair”-“chair-table”), a second order of association (the second most frequently quoted item of the pre-test) was chosen.

To ensure that the final set of selected items correctly reflected the taxonomic or thematic relationship, a second pre-test consisting in judging thematic or taxonomic strength was administered to a sample of 33 healthy elderly subjects. These subjects differed from the experimental group recruited in nursing homes (age: m=82.06, σ=6.344). Pictures were presented in corresponding pairs. The task consisted in judging the strength of the thematic or taxonomic relationship between two pictures on a scale ranging from 0 to 5. There were significant differences between the evaluation of the thematic and taxonomic links. As expected taxonomic pairs favored taxonomic links (z=-2.4; p= .014) and thematic pairs favored thematic links (z =-4.074; p= .001).

Verbal association norms for the retained items were collected in order to control the verbal association strength between thematic and taxonomic pairs (prime-target). Indeed, when two words maintained a strong verbal association, the semantic link and the priming effect were all the more important (Laisney et al., 2010). The method used drew on the studies by Glosser, Friedman, Grugan, Lee & Grossman (1998). Pairs whose verbal associations (outliers) were either too strong or too weak were suppressed. 22 pairs were selected. There were no significant differences between the mean of verbal associations for taxonomic and thematic pairs (U=193.5; p=.402). The intervention of lexical processing between the two conditions was thus under control and the mechanisms used were mainly semantic.

The targets that were to be named had a mean AoA of 38.7 months (σ=7.5). The mean familiarity evaluated in 33 healthy adults was 4.05 (σ=0.85). The comparison of frequency (Lexique 380, New, Pallier, Ferrand & Matos, 2001) between natural and manufactured objects was non-significant for movie frequency (t=-1.515 ; p=.145). Both categories were comparable with regard to AoA (t=.487; p=.632), familiarity (t=-1.581; p=.130), picture variability (t=-.988; p=.335), word length (t=-.689; p=.498) and verbal associations for thematic (t=.264; p=.795) and taxonomic pairs (t=.422; p=.677).

2.2.1.1.2. Neutral and unrelated primes

The introduction of a neutral prime in the experimental paradigm makes it possible to better quantify the facilitation and inhibition effects. Facilitation is a process defined by slower reaction times with regard to target processing when preceded by a related prime, compared to a neutral prime. Inhibition is the increase in reaction time with regard to target processing when neutral and unrelated conditions are compared.

A pre-test involving 20 adults allowed us to highlight that a neutral prime containing a set of geometrical shapes evokes less meaning than degraded pictures. The primes in the related condition for manufactured objects were also used as primes in the unrelated condition for naturals objects and vice versa. This counterbalance ensured that the priming effect in the related condition actually depended on thematic or taxonomic links rather than on the nature of the primes.

2.2.1.2. Methodological conditions

The stimuli were presented on an ASUS laptop. The recording of participants' verbal productions began when the target appeared. Short SOA (250ms) were used to prevent expectancy strategies (Neely, 1977; Lecardeur et al., 2007). Each "prime-target pair" respected the following methodological criteria: blank for 150 ms, then a mask (a series of hash keys) for 50 ms, followed by the prime for 200 ms. The mask then reappeared for 50 ms before the picture-target was presented until the subject named it. The mask procedure (before and after the prime) was identical to the one used by Ferrand, Segui & Grainger (1996). The masked priming technique makes it possible to reduce the visibility of the prime (Evett & Humphreys, 1981) and guarantees the automaticity of the task. This is useful in the priming paradigm in picture naming or lexical processing (Bajo, Puerta-melguizo & Macizo, 2003). It also guarantees that there is no visual recovery between the prime and the target (Ferrand & Grainger, 1992).

At the end of the priming task, subjects were invited to name or describe the 66 primes (22 thematic, 22 taxonomic and 22 unrelated) in order that the priming efficacy might be assessed. Only the items whose primes were recognized were considered for analysis.

2.2.2. Card-sorting task

The semantic card-sorting task is used to assess the existent semantic relationships in an explicit investigation of the semantic system. In this task, the same stimuli as those used in the priming paradigm were presented (11 naturals and 11 manufactured). Each target was presented and associated with its taxonomic, thematic and unrelated picture. The subject was asked to sort the stimuli in accordance with the strength of the connection with the target picture. The instructions were to indicate the first picture "that corresponded perfectly with the target", followed by the picture "that corresponded well with the target" and finally the picture "that did not correspond with the target".

2.2.3. Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics 21. For the priming paradigm, the analysis focused on reaction times (RT), which were extracted manually using Audacity. Only correct productions were taken into account. Outlier RT (more than two standard deviations from the mean) for each subject and for each condition were deleted to ensure that the performances were not influenced by extreme scores. The percentage of missing data, due to outliers and errors, was 3.7% for the control group, 12.5% for the AD1 group, 14.6% for the AD2 group and 20.29% for the AD3 group. The RT were transformed into priming proportions to reduce the impact of the processing speed. As the RT in the unrelated and neutral conditions did not differ, priming effects were expressed as a proportion, comparing related and unrelated RT in accordance with Balota, Watson, Duchek, and Ferraro's (1999) procedure, which has also been used in more recent works (Laisney et al., 2011; Merck et al., 2014) : (mean unrelated RT-mean related RT)/(mean unrelated RT)*100. The score obtained was a priming proportion effect based on the unrelated condition.

The normality of distribution of the four groups was evaluated using the Kolmogorov-Smirnov test. All the distributions used in the following analyses were normal, except for the raw reaction times (RRT). Therefore, ANOVA analysis was not conducted on the RRT. The problem of RRT abnormality in priming is well-known, and has been detailed in the work of Laisney et al. (2011). In the present study, the priming effects were calculated using the Student's t-test on the RRT because 1) the distributions for each group for the RRT in thematic, taxonomic and unrelated conditions were normal and 2) parametrical and non-parametrical tests gave convergent results.

Repeated-measures ANOVA were performed on the transformed reaction times. Post hoc tests were undertaken using Student's t-tests with Bonferroni's correction (p value adjusted with Bonferroni's correction). Secondly, to test the *a priori* hypothesis on condition and category-specific deterioration, *a priori* t-tests were conducted. Bonferroni's corrections were applied for multiple Student's t-test comparisons and for pre-planned comparisons (level of significance adjusted for six group comparisons: .05/6 =.008).

Results

3.1. Semantic priming

3.1.1 Raw Reaction Times

The mean RT for each group and condition are reported in table 1. In the control group, the semantic priming effect was significant in the thematic condition (t=-2.941; p=.006) but not in the taxonomic condition (t=-1.509; p=.141) (comparison between related and matched unrelated RT). In the AD1 and AD2 groups, the semantic priming effect was significant in both conditions, thematic (AD1: t=-4.956; p<.001; AD2: t=-6.187; p<.001) and taxonomic (AD1 t=-5.601; p<.001; AD2: t=-5.838; p<.001). In the AD3 group, the semantic priming effects disappeared in both conditions (taxonomic: t=-1.499; p=.145; thematic: t=-.122; p=.904).

Table 1: Mean reaction times (RT) and standard deviation by group and condition

	Mean RT in taxonomic condition		Mean RT in thematic condition		Mean RT in unrelated condition		Mean RT in neutral condition	
Control	885,16	(σ=213,61)	876,86	(σ=248,95)	915,67	(σ=311,46)	872,32	(σ=231,77)
MA1	1028,89	(σ=190,58)	1056,26	(σ=221,52)	1142,55	(σ=213,20)	1067,77	(σ=247,71)
MA2	1225,55	(σ=378,07)	1208,96	(σ=355,36)	1393,51	(σ=410,96)	1285,19	(σ=422,01)
MA3	1615,03	(σ=736,875)	1693,01	(σ=904.643)	1686.54	(σ=743.99)	1769,30	(σ=1168,53)

3.1.2. Transformed reaction times

To ensure that the priming proportion, based on transformed reaction times, significantly differed from zero in each condition and each group, one-sample t-tests were performed (comparisons between related versus unrelated transformed scores). In the control group, the semantic priming effect was significant in the thematic condition (t=3.390; p=.002) but not in the taxonomic condition (t=1.757; p=.088). In the AD1 and AD2 groups, the semantic priming effect was significant in both conditions, thematic (AD1: t=5.701; p<.001; AD2: t=6.071; p<.001) and taxonomic (AD1 t=6.487; p<.001; AD2: t=6.892; p<.001). In the AD3 group, the semantic priming effect disappeared in both conditions (taxonomic: t=1.238; p=.226; thematic: t =.602; p=.552).

Repeated measures ANOVA with ‘conditions’ (thematic vs. taxonomic) and ‘categories’ (natural vs. manufactured) as within-subject factors, and ‘groups’ (control, AD1, AD2, AD3) as between-subject factors were computed on transformed reaction times. The results showed a significant group effect (F= 6.801; p<.001), a significant condition effect (thematic/taxonomic) (F=15.566; p<.001) and a significant category effect (naturals/manufactured) (F=11.722; p=.001). An interaction effect appeared between ‘category’ and ‘condition’ (F=8.010; p=.006).

Considering the hypothesis, and the fact that the semantic priming effects completely disappeared in the AD3 group demonstrating the significant semantic deterioration, the same ANOVA was conducted excluding this AD3 group. These data-driven post hoc results were analyzed with caution. A group effect (F=13.765; p<.001), a condition effect (F=27.216; p<.001), and a category effect (F=35.701; p<.001) were all obtained, as were interaction effects between 'category' and 'condition' (F=28.732; p<.001) and between 'condition' and 'groups' (F=7.356; p=.001).

Post hoc analyses were conducted for the groups, condition and category comparisons (Student's t-tests with Bonferroni's correction). Results showed that the control group and the AD2 group differed significantly (t=-3.67; p=.002) as well as the AD2 and AD3 groups (t=3.307; p=.008). In contrast, the AD1 and AD2 groups (t=.07; p=1.0) did not differ. The taxonomic priming proportion was significantly higher than the thematic priming proportion (t=.3.662; p<.001). The priming proportion for natural and manufactured objects differed significantly (t=-3.338; p=.001). Manufactured objects displayed a higher priming proportion than natural objects. For natural objects, taxonomic priming favored object retrieval compared to thematic priming (t=-5.273; p<.001). In contrast, for manufactured objects, there was no difference in thematic or taxonomic priming (see figure 1).

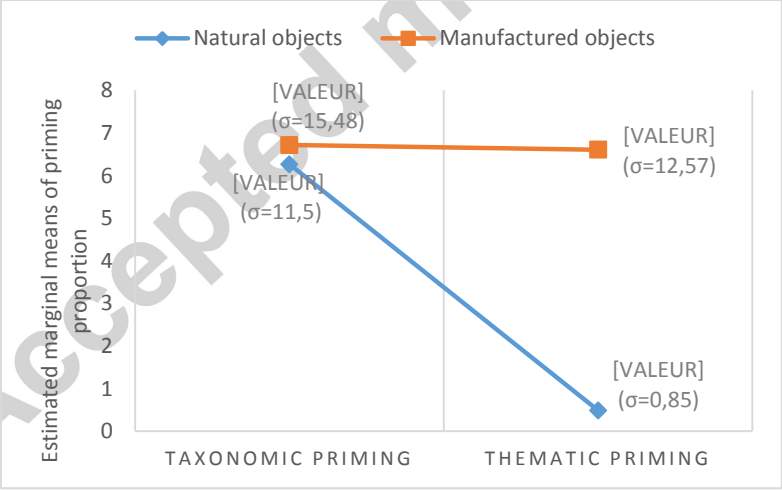

Fig. 1. Means of priming proportion in thematic and taxonomic condition for natural and manufactured objects

Considering the hypothesis and the 'group*condition' interaction, *a priori* t-tests were conducted. Results showed that the AD1 group differed from the control group for the taxonomic (t=2.909; p=.004) but not for the thematic condition (t=2.237; p=.027). Indeed, the AD1 group demonstrated a high increase in the taxonomic priming effect. There was no difference between the AD1 and AD2 groups (thematic condition: t=.263; p=.793; taxonomic

condition: t=.855; p=.394). The AD2 and AD3 groups differed significantly for both the taxonomic (t=-3.014; p=.003) and thematic (t=-2.786; p=.006) conditions, with a considerable priming-effect decrease noted for the AD3 group (see figure 2).

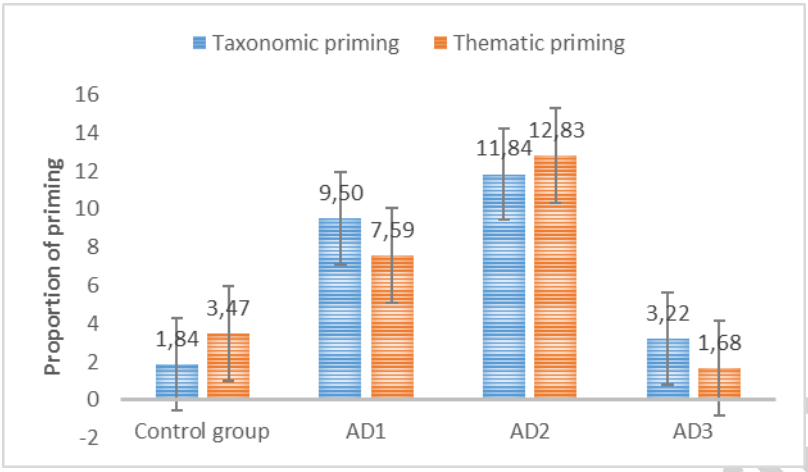

Fig. 2. Taxonomic versus thematic priming expressed as a proportion according to groups. The proportion is the result of the following formula: mean unrelated RT-mean related RT)/ (mean unrelated RT)*100. Errors bars represent standard errors.

Although the group*category interaction effect was non-significant, an *a priori* hypothesis on the category-specific deterioration in AD meant that pre-planned *a priori* t-tests were carried out. There was no difference between natural and manufactured object processing for the control group (F=2.506; p=.123) and the AD3 group (F=97.254; p=.568). However, differences appeared between both categories of objects for the AD1 (D=18.889; p<.001) and AD2 group (D=10.054; p=.004) with a higher priming proportion for manufactured objects.

To control the sex variable, complementary analysis was conducted contrasting men and women in the control group. They displayed comparable thematic (t=.572; p=.572) and taxonomic priming effects (t=.216; p=.831) as well as similar priming effects for processing natural (t=-.395; p=.696) and manufactured objects (t=.844; p=.405).

3.2. Card sorting task

The mean number of first choices ("the picture that corresponded perfectly with the target") for thematic, taxonomic and unrelated relationships was analyzed using a repeated-measures ANOVA with two categories (natural vs. manufactured) and three choices of sorting (taxonomic, thematic and unrelated).

Results indicated an effect of the "choice of sorting" (F=392.592; p<.001), as well as an interaction effect for "group*choice of sorting" (F=7.471; p<.001). No group effect (F=.685; p=.563) nor category (natural vs. manufactured) effect (F=2.608; p=.014) on the choice of sorting was observed.

A one-way ANOVA showed a trend toward significance during the intergroup comparisons for thematic choices (F=4.120; p=.008) and significant differences for taxonomic choices (F=9.492; p<.001) and unrelated choices (F=15.938; p<.001).

Post hoc tests (Bonferroni) highlighted that the AD1 group differed significantly from the control group for thematic (I-J =-3.104; p=.004) and taxonomic choices (I-J=3.233; p=.001) but not for unrelated choices. Indeed, an increase in thematic choices for the AD1 group compared to the control group was observed. The opposite was observed for taxonomic choices, which decreased in the AD1 group. The results were similar for the AD2 group. The differences did not attain the threshold of significance for the comparison between groups AD1 and AD2, nor between groups AD2 and AD3 except for unrelated choices, which increased progressively between AD2 and AD3 groups (I-J=-1.655; p=.001) (see figure 5).

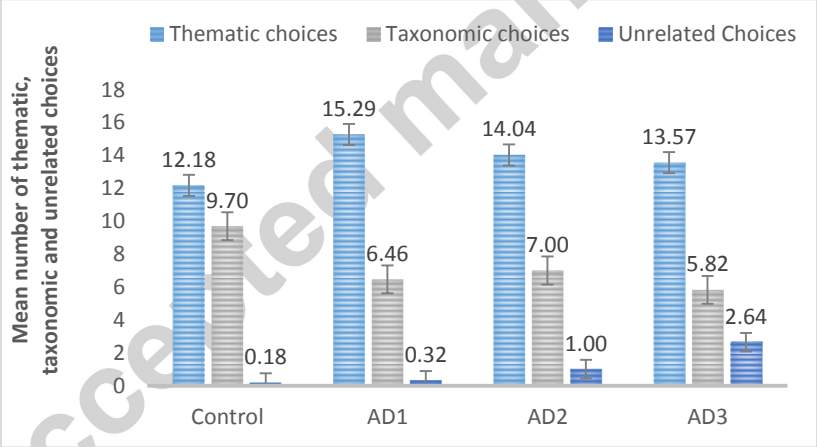

Fig. 5. Mean number of taxonomic, thematic and unrelated choices by group.

Thematic sorting was dominant compared to taxonomic sorting in all AD groups (AD1: t=-7.962; p<.001; AD2: t=-5.870; p<.001; AD3: t= 9.527; p<.001). The control group did not present this preference (t =-1.705; p=.098).

3. Discussion

The objective of this research was to contribute further to the understanding of the disorganization of semantic memory in AD. Many studies have highlighted the importance of thematic and taxonomic links in the lexico-semantic network during semantic memory

development in children or in adults. While the deterioration of semantic memory in AD is today well-known, the deterioration of the lexico-semantic network deserves further attention. The category-specific deficit that shows more significant alteration of natural objects than manufactured objects in AD has been repeatedly observed and there have been many attempts to explain this alteration. Recent research suggests that natural objects are more taxonomically organized and manufactured objects benefit more from thematic organizations (Kalénine et al., 2009).

Our results are consistent with the idea that 1) the deterioration of thematic and taxonomic links follows a distinct evolution, with an earlier alteration of taxonomic links compared to thematic links, 2) the deterioration of the semantic attributes of natural objects is more significant than the deterioration of manufactured objects in AD patients in mild and moderate stages of the disease, and 3) the organization of natural objects is underpinned by a more specific taxonomic organization while manufactured objects seem to be both taxonomically and thematically organized.

Both experimental tasks suggest an earlier deterioration of taxonomic links compared to thematic links. Indeed, in the semantic priming protocol, we observed that subjects from the AD1 group differed significantly from subjects in the control group in the taxonomic condition but not in the thematic condition. There was a taxonomic hyperpriming effect in AD1 subjects that seemed to persist in AD2 subjects. This corroborates the results of previous studies that have demonstrated that AD patients in the mild stage name items more rapidly when they are preceded by a taxonomic prime. Some authors (Laisney et al., 2011) argue that when the prime and the target no longer semantically differ due to concepts attributed to loss, AD patients benefit from a faster reaction time in the taxonomic condition compared to the unrelated condition. Our results were consistent with the studies described above. We believe that the loss of specific attributes induces a taxonomic disconnection demonstrated by hyperpriming which is consistent with bottom-up deterioration of semantic memory in AD (Hodges et al., 1992). Indeed, if a concept loses its attributes, it becomes an undifferentiated exemplar of a category. If the rooster and the dog lose their attributes, they become two similar concepts, belonging to the same category of animals. Activation is faster because there are fewer specific links and the most robust links (animals, natural objects) persist.

Likewise, results from the card-sorting test are consistent with early taxonomic deterioration. Indeed, from the onset of the disease, subjects produced more thematic choices than subjects

in the control group, to the detriment of taxonomic choices. In our opinion, this considerable support shows that the taxonomic system deteriorates. Indeed, if the loss of specific attributes materializes through a hyperpriming effect in a semantic priming task, it is not surprising that, in the card-sorting task, which requires conscious retrieving of the links, alteration is manifested through a decrease in taxonomic choices. From a clinical point of view, the comments of AD patients with regard to the taxonomic associates also maintained the explicit loss of categorization links ("*none of that has anything to do with the picture*", "*the two do not go together*"). However, we cannot exclude a task effect. Indeed, some authors have suggested that choices can be constrained by experimental conditions (see Blaye & Bonthoux, 2001). Finally, the increase in the number of unrelated choices observed in the advanced stage of the disease is a strong indicator of semantic memory disorganization.

The priming task also confirmed that the thematic network was more resistant to semantic deterioration. Indeed, thematic priming did not differentiate control subjects from early AD patients, suggesting that thematic links are less vulnerable to semantic disturbance in AD. In contrast, the AD1 and AD2 groups did not show a different taxonomic/thematic pattern in semantic priming or in the card-sorting task. The progression of the disease (AD3) considerably reduced priming effects in the taxonomic and thematic conditions. The suppression of hyperpriming effects observed was synonymous with an increase in semantic deterioration in the disease. When knowledge is more substantially impaired, hyperpriming is replaced by a normal priming effect or a hypopriming effect (Humbert and Chainay, 2006). We indeed observed a considerably reduced priming pattern in our AD3 subjects compared with the AD1 and AD2 groups. However, our results were inconsistent with studies that have found that priming effects completely disappear, suggesting a partial preservation of the tested concepts in AD3 subjects. It is worth noting that the targets used in our protocol were early acquired items with high frequency. We can thus postulate that words acquired early are better preserved in AD (Frouin et al., 2014).

Similar to the results found by Giffard et al. (2001) and Humbert & Chainay (2006), we observed that the profile of priming effects evolved in a specific way over the course of semantic alteration. Our study found a distinct evolution of taxonomic and thematic priming. While the taxonomic network was affected early, the thematic system only showed evidence of disturbance at a more advanced stage. Taxonomic and thematic networks thus seem relatively independent. This is consistent with Maguire, Brier and Ferrée (2010), who argue that thematic and taxonomic systems are two parallel and distinct systems.

We also observed, in consistency with the literature, that AD deteriorated natural concepts earlier than manufactured concepts (Warrington & Shallice, 1984; Humbert & Chainay, 2006). Different processing in terms of more significant priming for manufactured objects compared to natural objects was observed. This phenomenon appeared in the priming procedure in the AD1 group and persisted in the AD2 group before disappearing in the AD3 group. The disequilibrium between natural and manufactured objects, unobserved in the control group, clearly demonstrated that the representation of the items in these two categories in the lexico-semantic network evolved differently during the course of the disease. Our results replicate those of Humbert & Chainay (2006), i.e., that the benefit in priming is more important for AD in manufactured-objects processing. Like them, we interpret this effect as reflecting a better preservation of these types of objects. Indeed, when the deterioration of attributes was restricted, a hyperpriming effect appeared (Giffard et al., 2001), and when the deterioration was more advanced, this effect disappeared (Humbert & Chainay, 2006).

It was also observed that the priming condition produced different effects according to the category of objects. Indeed, we found that thematic priming induced a different pattern of activation, benefiting manufactured objects but very few natural objects. This interaction effect between the category of objects and the type of semantic relationships has already been presented by Kalénine et al. (2009): taxonomic relationships are identified faster for natural objects and thematic relationships are processed faster for manufactured objects. Moreover, our results are partially consistent with those of Kalénine et al. (2009): natural objects effectively benefit from taxonomic rather than thematic priming. However, we found no dissociation for manufactured objects: both priming conditions increased the processing speed. These observations attest that there is a distinct organization in both categories of objects. Natural objects seemed to rely predominantly on the taxonomic network. This seems to indicate not pathology but, rather, the intrinsic organization of the category of natural objects as the imbalance already appears in the control group and is further maintained in AD1 and AD2 patients. By contrast, manufactured objects benefited from both taxonomic and thematic priming in a similar manner. These findings are inconsistent with existing literature. Indeed, for Kalénine et al. (2009), manufactured objects should benefit more from the thematic condition. We failed to observe any distinction between the taxonomic and thematic condition for manufactured objects. We believe that this might be explained by the robustness of manufactured concepts, as proposed by Tyler and Moss (1997). Indeed, manufactured objects are more robust than natural objects because their distinctive perceptual attributes are

strongly intercorrelated with functional aspects, and shared perceptual attributes possess a higher frequency of occurrence (Cree & McRae, 2003; Garrard et al., 2001; McRae & Cree, 2001). In our study, taxonomic relationships between manufactured objects indeed presented shared perceptual attributes between the members of the category as the construction material (e.g. the fabric for the pair "pants-skirt" belonging to the category of clothes or the bricks for the pair "house-castle" belonging to the category of real property). This sharing of perceptual attributes could explain the unexpected taxonomic priming for manufactured objects and emphasize the aforementioned robustness of this category of objects.

4. Conclusion

In conclusion, this study sheds new light on semantic impairment in AD. It clearly shows preserved priming effects, even though these differ from the control group. This attests early lexico-semantic network disorganization. The deterioration observed is consistent with the alteration of attribute concepts in the early stage of the disease and a more general impairment in the advanced stages. The category of manufactured objects seems less fragile than the category of natural objects. Lastly, it seems that natural objects have benefited little from thematic priming that has been essentially sustained by taxonomic aspects.

To our knowledge, this study is the first to show a progressive distinctive pattern of thematic and taxonomic alteration in AD patients, with a better preservation of thematic aspects in the early stages of the disease. In 2014, Merck, Jonin, Laisney, Vichard & Belliard investigated visuo-perceptual links (defined as a central element of taxonomic relationships) and contextual/functional (interpreted as thematic) in a priming task in semantic dementia. However, no similar study has yet been conducted with AD patients. Finally, this study supports the idea that semantic loss in AD does not follow a linear pattern with possible stagnation of thematic and taxonomic disturbance between the AD1 and AD2 groups. Indeed, our different semantic investigations coincide to show the equivalence of these two groups, even if the global cognitive functioning measured with MMSE is different.

The results presented should nevertheless be viewed with caution. A few limitations can be highlighted. First, the study population was primarily composed of women. While this reflects the field reality, it questions the possibility of generalizing these results to men. However, a comparison between men and women showed that reaction times in taxonomic and thematic priming as well as in natural and manufactured object processing were identical in the control group. We can thus postulate that this variable has no impact in our experimental groups.

Also, all the participants were very old which limits somewhat the interpretability of the findings. Indeed, cognitive changes above 80 years of age are common. However, the including of a control group of healthy old people allowed controlling difficulties during normal aging. We also believe that varying the choice of experimental items - for which many psycholinguistic variables were controlled - could provide avenues for further research. For instance, varying AoA could define distinct priming patterns, demonstrating a retrogenesis effect (Reisberg, 2002). Similarly, the protocol used in this research could be administered to children. Indeed, the priming procedure in naming has already been used with children and has shown a distinct developmental pattern (Perraudin & Mounoud, 2009). This would enable us to compare involutionary and evolutionary patterns of the lexico-semantic network and provide new elements for the understanding of the construction and deconstruction process in semantic memory.

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Appendix 1

Stimuli of the semantic priming paradigm : 11 manufactured and 11 natural objects targets associated with their primes in the taxonomic and thematic condition.

Manufactured targets	Taxonomic primes	Thematic primes	Natural targets	Taxonomic primes	Thematic primes
Plane	Helicopter	Sky	Cow	Sheep	Milk
Bottle	Glass	Wine	Carrot	Tomato	Rabbit
Truck	Car	Road	Horse	Donkey	Saddle
Key	Padlock	Keyhole	Dog	Rooster	Bone
Knife	Fork	Bread	Finger	Toe	Ring
Spoon	Plate	Soup	Flower	Plant	Vase
Lamp	Candle	Desk	Moon	Star	Rocket
House	Castle	Garden	Hand	Arm	Glove
Watch	Clock	Wrist	Moutain	Volcano	Snow
Pants	Skirt	Leg	Fish	Shark	Aquarium
Train	Bus	Rail	Ear	Mouth	Phone

Highlights

- The deterioration of thematic and taxonomic links follows a distinct evolution in Alzheimer's disease, with an earlier alteration of taxonomic links compared to thematic ones

- The deterioration of the semantic attributes of natural objects is more significant than the deterioration of manufactured objects in AD patients in mild and moderate stages of the disease

- The organization of natural objects is underpinned by a more specific taxonomic organization while manufactured objects seem to be both taxonomically and thematically organized