Overreliance on Thematic Knowledge in Semantic Dementia: Evidence From an Eye-Tracking Paradigm

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Abstract

Objective: The present study explored two types of semantic relationships in semantic dementia (SD), that rely on functionally and neuroanatomically distinct semantic systems (taxonomic vs. thematic).

Method: We used the visual world paradigm coupled with eye-movement recordings, to gain an implicit, fine-grained and dynamic measure of semantic processing. Nine patients with SD and 15 healthy controls performed a simple word-to-picture matching task in which they had to identify each target among semantically related (taxonomic or thematic) competitors and unrelated distractors.

Results: We demonstrated different patterns of gaze fixations between patients with SD and controls: while patients with SD and controls were similarly sensitive to competition from taxonomically-related pictures, patients with SD were far more sensitive than controls to thematically-related competitors before identifying the targets. Moreover, most of the confusion errors made by patients with SD involved taxonomic distractors rather than thematic ones.

Conclusions: We interpreted these findings as reflecting a semantic disequilibrium in SD, with increasing over-reliance on thematic knowledge as taxonomic knowledge gradually deteriorates. We concluded that thematic relationships constitute a set of residual semantic knowledge and that their exaggerated activation in SD might certainly deserve further explorations to determine their specific role in this disease and notably, their influence on patients' abilities to deal with daily living activities.

Keywords: semantic dementia; taxonomic system; thematic system; semantic disequilibrium; eye-tracking paradigm

Significance Statements:

This study provides evidence that patients with semantic dementia (SD) differentially identify two types of semantic relationships (namely, taxonomic and thematic relationships) in comparison to controls, with an over-reliance on thematic knowledge.

This points to the existence of residual semantic knowledge in SD and that the patients might excessively rely on these relationships between objects to compensate for the erosion of the other types of semantic knowledge.

Finally, this work raises the question of how such exaggerated activation of thematic knowledge may benefit patients' daily living abilities and also suggests that the role played by thematic knowledge in daily living abilities is underestimated in this disease.

1. Introduction

Semantic dementia (SD) is a rare neurodegenerative disease (Belliard, Merck, Jonin, & Vérin, 2013; Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000; Gorno-Tempini et al., 2011; Landin-Romero, Tan, Hodges, & Kumfor, 2016; Neary et al., 1998; Snowden, Goulding, & Neary, 1989) associated with temporal lobe atrophy, often bilateral but predominantly on the left side (Chan et al., 2001; Hodges, Patterson, Oxbury, & Funnell, 1992). If SD is also currently considered as the semantic variant of primary progressive aphasia (Gorno-Tempini et al., 2011; Mesulam, 2001; Mesulam, Grossman, Hillis, Kertesz, & Weintraub, 2003), the syndrome largely exceeds the language disorders (Botha & Josephs, 2019). Its cognitive profile is characterized by a gradual and selective loss of conceptual knowledge, responsible for limited vocabulary in speech, poor comprehension, and deficits in the identification of objects and persons in different input modalities (Bozeat et al., 2000; Luzzi et al., 2007; Péron et al., 2015; Snowden, Thompson, & Neary, 2012; Snowden et al., 2017). Language remains fluent and well-structured, without any phonological or grammatical errors, and only subtle abnormalities in the syntactic structure of speech have been reported (Meteyard & Patterson, 2009). In the early stages of the disease, the SD syndrome is also characterized by spared general intellectual ability, day-to-day memory (Adlam, Patterson, & Hodges, 2009; Irish et al., 2016) and visuoperceptual abilities. In spite of their massive semantic deficit, patients with SD remain relatively independent in some activities of daily living (Bier et al., 2013; Bier & Macoir, 2010) and show preserved technical reasoning/mechanical problem solving abilities (Baumard et al., 2019; Baumard et al., 2016; Hodges, Bozeat, Lambon Ralph, Patterson, & Spatt, 2000).

Considering the semantic disruption in SD, some studies have demonstrated dissociations in the type of semantic features impacted by the disease. Many of them found that functional/contextual features were more robust than other features, notably

visuoperceptual features (Lambon Ralph, Patterson, Garrard, & Hodges, 2003; Merck et al., 2014; Moss, Tyler, Patterson, & Hodges, 1995; Tyler & Moss, 1998). For example, Merck et al. (2014) demonstrated a significant effect of contextual/functional priming (e.g., *camel* priming *desert*), but not of visuoperceptual priming (e.g., *ostrich* priming *neck*) on lexical decisions in patients with SD, whereas controls showed the opposite pattern. Moreover, the dissociation between the two features increased as the disease progresses.

Visuoperceptual features have been shown to be a core determinant of taxonomic relationships, whereas contextual/functional features underlie thematic relationships (Denney, 1975; Estes et al., 2011; Lin & Murphy, 2001; McRae et al., 1997, 2005; Medin & Ortony, 1989). Taxonomic and thematic relationships refer to two different ways of semantically grouping objects (see Mirman, Landrigan, & Britt, 2017 for a recent review). Taxonomic relationships group objects according to their similarity and bring together objects that share features, with an important weight of visuoperceptual features (Kalénine et al., 2009) (e.g., both *daisy* and *nenuphar* have petals). In contrast, thematic relationships group objects based on their complementarity in events and bring together objects that belong to the same spatial and/or temporal context (e.g., *hammer* and *nail* have complementary roles in a DIY event). Therefore, the differential status of visuoperceptual and contextual/functional features in SD may reflect a *semantic disequilibrium* between taxonomic and thematic relationships in the disease.

The cognitive and cerebral organization of taxonomic and thematic relationships has been differentially addressed in theoretical models of semantic memory. The “hub and spoke” model of semantic cognition (Lambon Ralph, 2014; Lambon Ralph, Cipolotti, Manes, & Patterson, 2010; Patterson et al., 2007; Rogers et al., 2004) considers that the anterior temporal lobe (ATL) is the core region of a single convergence zone (the “hub”) that brings together various modality-specific information from different sensory, motor and linguistic

regions (the "spokes") into an amodal and coherent stored representation. Accordingly, this model assumes subtle rather than substantial differences between taxonomic and thematic processing since both taxonomic and thematic knowledge would be represented within a single, unified semantic system that heavily relies on the ATL (Lambon Ralph, Jefferies, Patterson, & Rogers, 2017; Rice, Hoffman, & Lambon Ralph, 2015). In Jackson et al. (2015)'s study, for instance, the authors showed only weak differences in the neural substrates involved in taxonomic and thematic processing, which were considered to reflect graded differences in task difficulty. At odds with the influential "hub and spoke" assumption, another theoretical view claims instead that taxonomic and thematic knowledge relies on two distinct semantic systems based on evidence for partially but substantial distinct neural bases between the two processing (Kalénine et al., 2009; Liu, Han, Zhang, & Li, 2019; Schwartz et al., 2011; Xu et al., 2018). Taxonomic processing has been found to activate bilateral visual association areas (cuneus and lingual gyrus, Brodmann area 18; Kalénine et al., 2009), in addition to ATL regions (Lewis, Poeppel, & Murphy, 2015; Schwartz et al., 2011; Xu et al., 2018). By contrast, thematic relationships have been found to be associated with the posterior temporoparietal cortex, which is known to be involved in motion, action and spatial processing (de Zubicaray, Hansen, & McMahon, 2013; Kalénine & Buxbaum, 2016; Mirman & Graziano, 2012a; Schwartz et al., 2011; Xu et al., 2018). In healthy adults, empirical data suggest that taxonomic and thematic systems are co-activated (Landrigan & Mirman, 2018; see Mirman, Landrigan, & Britt, 2017; Xu, Qu, Shen, & Li, 2019) and may compete with one another (Maguire, Brier and Ferree, 2010). In Maguire et al. (2010)'s study featuring event-related spectral perturbation analyses, the authors demonstrated that theta power increases over right frontal areas for thematic versus taxonomic relationships, and alpha power increases over parietal areas for taxonomic versus thematic relationships. They suggested that the increase in alpha power is the consequence of inhibiting thematic processing to make way

for taxonomic processing. The "hub and spoke" model and the "two systems" model of semantic memory make relatively different assumptions regarding the pattern of deficits in taxonomic and thematic knowledge in SD. In this disease, neural damage follows a rostrocaudal gradient in the temporal lobes as the disease progresses, with the anterior parts being more severely and rapidly affected than the posterior ones (Brambati et al., 2015; Bright, Moss, Stamatakis, & Tyler, 2008; Chan et al., 2001; Desgranges et al., 2007; La Joie et al., 2014; Leyton, Britton, Hodges, Halliday, & Kril, 2016). Therefore, the "two systems" model would predict that patients with SD may differentially rely on two competing semantic systems, exhibiting poor taxonomic processing and over-reliance on thematic knowledge when processing object concepts. The "hub and spoke" model would rather expect poor processing of both taxonomic and thematic relations, with only subtle differences between the two types of knowledge.

To directly test these assumptions, we investigated the implicit processing of taxonomic and thematic semantic relationships in SD. We adopted an eye-tracking protocol, in order to gain an implicit, fine-grained and dynamic measure of semantic processing (Mirman & Magnuson, 2009). This technical approach was recently used in patients with SD to highlight abnormalities in taxonomic processing. Seckin et al. (2016) recorded eye-movements during a word-to-picture matching task in nine patients with SD and six patients with other primary progressive aphasia syndromes. This study only focused on taxonomic relationships. The patients with SD showed abnormal increases in the number of fixations and the amount of time spent on taxonomically-related competitors. In particular, they oriented their gaze back and forth between taxonomically-related items for a longer time before identifying the target. Findings support the hypothesis that the taxonomic impairment in SD may be reflected by greater errors in target identification and/or longer-lasting semantic competition with taxonomic distractors during word-to-picture matching. From a

methodological perceptive, the authors recommended examining eye movements to highlight subtle disturbances in the processing engaged by patients that are not always detectable in target identification performance and may be reflected in incidental, online semantic processing. Faria, Race, Kim and Hillis (2018) also used an eye-tracking paradigm with a word-to-picture matching task to identify early markers of SD and enhance understanding of patients' semantic disturbances. Compared with 11 patients with other primary progressive aphasia syndromes, the eight patients with SD produced a far higher proportion of fixations on unrelated foils, reflecting the uncertainty of their responses. The study also featured conditions in which foils were taxonomically or thematically related. The authors mentioned that the patients with SD produced more errors than patients with other variants of primary progressive aphasia in the semantic "coordinate"/taxonomic condition (e.g., horse-cow) and in the "schematically"/thematic condition (e.g., horse-saddle) than other variants of primary progressive aphasia. Furthermore, both the patients with SD and the patients with a logopenic variant of primary progressive aphasia looked longer at the semantically related objects than at the unrelated ones. Unfortunately, the eye movement patterns of the patients with SD in these semantic conditions were not reported and the eye-movements were not compared between groups separately in the taxonomic and the thematic conditions. Together, previous studies point to abnormalities in the pattern of fixations of SD patients when identifying a target object among semantically-related distractors. Although they stressed the relevance of using eye-tracking in order to finer assess semantic disturbances in an implicit manner, the distinction between taxonomic and thematic knowledge has never been directly addressed in such protocols in SD. We therefore applied an eye-tracking protocol which, combined with a statistical approach allowing changes in gaze behavior to be analyzed over time, has been successfully used to compare the amplitude and time course of implicit taxonomic and thematic processing in both healthy participants and other patients with cognitive impairments

(Kalénine, Mirman, & Buxbaum, 2012; Kalénine, Mirman, Middleton, & Buxbaum, 2012; Mirman & Graziano, 2012a; Mirman & Graziano, 2012b; Mirman & Magnuson, 2009). The protocol uses the visual world paradigm (VWP) and involves a very simple word-to-picture matching task. Participants are instructed to locate a target picture corresponding to an auditory word, and while they are doing so, their eye movements are recorded. The time course of gaze fixations on the different pictures in the display is assumed to reflect semantic competition effects, in that distractor pictures that are semantically related to the target may compete for attention and induce longer gaze fixations than semantically distant or unrelated pictures during the process of target identification. Importantly, this protocol can highlight both reduced/delayed (reflecting impaired semantic activation) and increased/earlier (reflecting exaggerated semantic activation) semantic competition in patients (Kalénine, Mirman, & Buxbaum, 2012). It may thus be best suited to contrasting distinct types of semantic relationships in patients.

Taking into account previous indirect arguments supporting the possibility of the semantic disequilibrium between taxonomic and thematic knowledge in SD, we expected the patients with SD to exhibit an over-reliance on thematic knowledge compared to controls. This mechanism should be reflected in their gaze behavior by greater and/or earlier thematic competition from thematic distractors before correct target identification. In contrast, patients with SD should show taxonomic blurring. This deficit may be directly visible in greater confusion errors and/or in later, longer-lasting competition with taxonomic distractors before correct target identification.

2. Materials and methods

2.1 Participants

The protocol was approved by the ethics committee of Lille University. The

experiment was conducted in accordance with the Declaration of Helsinki (1964, 2013) and with the current French legislation (Huriet Act, 1988). All participants gave their written informed consent before being included in the study. Their demographic and clinical features are set out in Table 1.

2.1.1 Patients with SD

Nine patients fulfilling the diagnostic criteria for SD (Neary et al., 1998) were included in this study. They also fulfilled diagnostic criteria for semantic variant of primary progressive aphasia (svAPP, Gorno-Tempini et al., 2011). However, we preferred to retain the terminology of semantic dementia in this study, given the current criticisms of the terminology of svAPP which focuses on the language symptoms and excludes patients with primarily nonverbal semantic disorders (Botha & Josephs, 2019). The participants with SD were recruited at the memory clinic of Rennes University Hospital from 2016 to 2018. All of them were right-handed and had no history of neurological or psychiatric disorders, or drug or alcohol use. Their physical neurological examination was unremarkable. They all presented the typical clinical features of SD: a history of complaints about worsening comprehension deficits, anomia, and difficulty identifying objects and/or persons, reflecting a predominant and distressing loss of conceptual knowledge, contrasting with the relative preservation of perceptual abilities and day-to-day memory. Day-to-day memory was assessed at the clinical level by the ability to evoke recent events (i.e., family events, programs of the last days, walks…), to recall recent exams and the date and context of the previous medical consultation. Speech was still fluent, without any phonological or syntactic errors. All the patients with SD underwent a comprehensive neuropsychological battery, in addition to the word-to-picture matching task with an eye-tracking paradigm. This battery consisted of assessments of their general cognitive functioning (Raven's Coloured Progressive Matrices; Raven, Raven, & Court, 1998; Dementia Rating Scale, DRS; Mattis, 1976; Mini Mental State

Examination, MMSE; Folstein, Folstein, & McHugh, 1975), nonverbal episodic memory (The Doors visual recognition task; Baddeley, Emslie, & Nimmo-Smith, 1994; Delayed recall condition of the Rey–Osterrieth Complex Figure Test–Form A; Osterrieth, 1944), and working memory (Digit Span Forward and Backward, Wechsler Adult Intelligence Scale Revised, WAIS-R; Wechsler, 1981). Language skills and semantic knowledge were assessed by regular and irregular word reading, the single-word repetition subtest of the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1972), the oral syntactic comprehension subtest of the Montreal-Toulouse protocol (MT 86; Joanette, Nespoulous, & Roch Lecours, 1998), and the GRECO neuropsychological semantic battery (BECS-GRECO; Merck et al., 2011), which assesses the integrity of the same 40 items (20 biological entities and 20 manufactured entities) in a picture-naming task and verbal and visual semantic matching tasks. Finally, visuoperceptual performance was also measured (copy condition of the Rey–Osterrieth Complex Figure Test–Form A; Embedded Figures subtest of the Protocole d'Evaluation des Gnosies Visuelles, PEGV; Agniel, Joanette, Doyon, & Duchein, 1992; Benton Facial Recognition Test; Benton et al., 1994).

Almost all the patients (8/9) performed normally on Raven's Coloured Progressive Matrices, but the majority was impaired on the DRS (8/8) and MMSE (7/9). These results were to be expected, given the large number of items involving vocabulary and comprehension in these two general cognitive functioning scales, making them not entirely reliable in assessing overall cognitive functioning in SD (Merck et al., 2017). Regarding each DRS-subscale, only one patient scored below the normal range (SD3) on the attentional subscale. On the initiation/perseveration subscale, all the patients were impaired and 6/8 patients scored below the normal range on the conceptualization subscale. Deficits in these two last subscales were essentially due to the involvement of lexical-semantic abilities. All the patients performed normally on construction subtests. Finally, on memory subtest, more

than half of the patients (5/8) exhibited abnormal scores. Day-to-day memory appeared relatively preserved at the clinical level, whereas patients failed on one of the two episodic/anterograde memory tasks. Only two patients scored below the normal range on one of the digit spans of working memory. The assessment of language abilities and semantic knowledge showed a surface dyslexia when reading irregular words in 5/9 patients, but there were no errors when reading regular words. None of the patients were impaired on isolated word repetition. Oral syntactic comprehension was impaired in 2/9 patients. All patients exhibited compromised naming abilities and scored below the normal range on both the verbal and visual semantic matching tasks (BECS-GRECO). Based on the total scores on this semantic battery, four patients could be considered to have a mild level of semantic impairment (SD1, SD2, SD4, SD8) and the five others a moderate level (SD3, SD5, SD6, SD7, SD9). Finally, visuoperceptual performance was normal for all patients (see Table 2 for individual performance on this neuropsychological battery).

Neuroimaging (MRI scans) revealed atrophy, predominantly in the temporal lobes. This atrophy was bilateral for one patient (SD5), bilateral but more pronounced on the left side in five patients (SD2, SD3, SD4, SD6, SD9), and bilateral but more pronounced on the right side in three patients (SD1, SD7, SD8). Seven patients (SD1, SD2, SD3, SD4, SD6, SD8, SD9) underwent a test for a cerebrospinal fluid (CSF) biomarker of Alzheimer's disease, which showed that they all had a negative Alzheimer's status (cut-off applied : *Index IATI = Aβ (1-42)/(240 + 1.18 x H-Tau)* > 1.2 and *p-Tau* < 60 pg/mL, Engelborghs et al., 2008; *Aβ (1-42)/Aβ (1-40)* > 0.05, Wiltfang et al., 2007).

2.1.2 Healthy controls

We recruited 15 healthy older adults (see Table 1 for their demographic data). All were native French speakers. They, too, underwent an extensive interview beforehand to ensure that they had no history of neurological or psychiatric disorders, or drug or alcohol use. All

these control participants were included after undergoing a short screening assessment to rule out any overall cognitive impairment (all DRS scores were above the cut-off point; Pedraza et al., 2010) or lexical semantic disorder (all scores were above the cut-offs on the BECS-GRECO subtests, Merck et al., 2011; mean picture-naming score = 38.67 ± 1.23, range = 36-40; mean verbal semantic matching score = 39.73 ± 0.59, range = 38-40; mean visual semantic matching score = 39.67 ± 0.62, range = 38-40; mean 6-item verbal semantic questionnaire score = 236.53 ± 1.81, range = 233-239). Almost all the controls (14/15) were right-handed, and the remaining one was ambidextrous.

Controls were matched with the patients for age [$t(22) = 0.641$, $p = 0.528$], sex [$\chi^2(1) = 0.296$, $p = 0.586$] and years of education [$t(22) = -0.528$, $p = 0.603$]. Controls exhibited a higher level of general cognitive functioning on the DRS scale than patients [$t(21) = -4.608$, $p = 0.002$] (see Table 1).

2.2 Experimental materials and design

2.2.1 Stimuli

Stimuli were 468 color pictures of objects. Some of these pictures (254/468) were taken from a revisited version of Snodgrass and Vanderwart's object pictorial set, improved with color and texture (see Rossion & Pourtois, 2004). The remaining 214 came from OpenClipArt. The 468 pictures were divided into five main sets: 26 target items, 26 taxonomic competitors, 26 thematic competitors, 26 semantically unrelated but visually similar items (see the list of items in Supplemental Materials), and 364 semantically unrelated and visually nonsimilar items. Unrelated but visually similar items were selected as sharing a close shape to the target, with the same orientation, dimension or color. Similarity in low-level visual features was calculated using the FSIM Toolbox (Zhang et al., 2011) and confirmed that these items presented a higher visual similarity with the target than the other unrelated and visually nonsimilar items [$t(25)$, all ps < 0.05]. Moreover, the taxonomic

competitors were as visually similar to the target as the unrelated but visually similar items [$t(25)= -0.388$, $p = 0.701$], whereas the thematic competitors tended to be visually less similar to the target than the unrelated but visually similar items [$t(25) = -1.856$, $p = 0.075$].

Among the 26 target items, 12 were biological entities and 14 were artifacts.

The task involved a total of 216 trials: 52 critical trials, 52 composed filler trials, and 112 unrelated filler trials. In each trial, four pictures were simultaneously displayed. In critical trials, the target was the reference object (e.g., *bell*), displayed with a competitor object that was taxonomically (e.g., *whistle*) or thematically (e.g., *church*) associated with the target, an object that was semantically unrelated but visually similar to the target (e.g., *knight's helmet*), and an object that was semantically, visually and also phonologically unrelated to both the target and the competitor and that was different between the thematic and the taxonomic conditions (e.g., *raccoon* or *lobster*). The two other sets of trials were designed to avoid any anticipatory strategy, so that participants would not be able to guess which object was the target based on prior exposure. In the composed filler trials, the pictures used for the critical trials were rearranged so that either the taxonomic or the thematic competitor became the target. Unrelated filler trials featured novel pictures that were unrelated to each other. Altogether, each target, taxonomic competitor, thematic competitor and unrelated similar object appeared three times. Unrelated nonsimilar objects were displayed twice (when they were selected as targets) or once (when they were never used as a target).

Concerning the presentation of the trials, two pseudorandomized orders were established to avoid the targets appearing in the same position twice or in consecutive trials. Targets that were first presented with their taxonomic competitor in Trial order 1 were first presented with their thematic competitor in Trial order 2, and vice versa. The two orders were counterbalanced across participants. Trials were divided into three fixed blocks, to allow participants to take short breaks.

Targets, taxonomic competitors, and thematic competitors were matched on several confounding variables, based on Rossion and Pourtois (2004)'s normative data and the Lexique database (New et al., 2004). No significant differences were found between the three types of items on either naming accuracy, naming latency, familiarity, age of acquisition, lexical frequency, name agreement, imagery agreement, or visual complexity [for all one-way ANOVAs $F(2,77)$, all $ps > 0.125$,]. Among this pictorial set, we selected pictures sharing taxonomic and thematic relationships in accordance with the definition of the two semantic relationships used in Mirman and Graziano (2012a)'s study: "taxonomically related pairs were members of the same category and thematically related pairs frequently participated in an event or scenario and were not members of the same category". We verified that all picture-pairs were correctly categorized as either taxonomic or thematic by at least two of three independent raters. We also controlled for semantic variables. The semantic similarities between the targets and their competitors were calculated using the Latent Semantic Analysis databank (LSA @ CU Boulder: http://lsa.colorado.edu/). Taxonomic and thematic competitors did not differ on semantic similarity to their targets [$t(25) = 0.231$, $p = 0.819$]. The associative strength between the targets and their competitors was also measured in an additional group of 20 young adults (mean age = 25.6 ± 2.9 years, range = 20-31). Targets were presented with each distractor separately. Participants were instructed to rate the strength of the semantic association on a 7-point scale ranging from 1 (*Not associated at all*) to 7 (*Very strongly associated*) between the target and the distractor. Again, no significant differences were observed between the taxonomic and thematic competitors [$t(25) = 0.712$, $p = 0.483$; taxonomic : mean = 5.5 ± 0.7; thematic : mean = 5.7 ± 0.9]. Target and unrelated non similar distractors were judged as poorly semantically related in the taxonomic and the thematic conditions [$t(25) = 1.029$, $p = 0.313$; in the taxonomic condition, unrelated nonsimilar distractors: mean = 1.3 ± 0.3; in the thematic condition, unrelated nonsimilar

distractors: mean = 1.2 ± 0.3]. Unrelated but visually similar distractors (remaining the same across the two conditions) were less semantically associated to the target than both taxonomic and thematic competitors [respectively, $t(25) = 15.097$, $p < 0.001$ and $t(25) = 13.436$, $p < 0.001$; unrelated but visually similar distractors: mean = 2.5 ± 0.9].

The relative visual saliency of the four pictures (i.e., target, competitor, unrelated but visually similar, unrelated and visually nonsimilar objects) in each critical display was determined using the Saliency Toolbox (Walther & Koch, 2006). No differences were visible in the saliency rank between the four types of pictures, in each condition [critical trials with taxonomic competitor: $\chi^2(9) = 5.54$, $p = 0.785$; critical trials with thematic competitor : $\chi^2(9) = 11.08$, $p = 0.271$]. This means that the low-level visual properties of the four types of pictures have the same potential to capture visual attention. Finally, there were no significant differences in the distribution of the four types of objects in each corner of the screen / area of interest (AOI; see definition below in Subsection 2.3 “Data analysis”), between conditions or pseudorandomized orders [for all $\chi^2(9)$, all ps > 0.153].

The task also included a training session composed of eight representative trials featuring combinations of eight novel pictures, which made it possible to adjust the sound volume for each participant and make sure that the instructions were well understood. This training could be repeated as many times as necessary for each participant.

2.2.2 Apparatus

A Tobii T60 eye-tracker embedded in a 17-inch TFT monitor with a maximum resolution of 1280 x 1024 pixels was used to record gaze position and duration. Tobii Studio version 3.3.0 software (Stockholm, Sweden) was used for the recordings and the calibration process. The eye-tracker has a 60-Hz sampling rate (every 16.67 ms) and a spatial resolution below 0.5°.

2.2.3 Procedure

Each participant was seated in front of the eye-tracker, at a distance of approximately 60 cm. All the pictures were resized so that their width and height did not exceed 200 pixels. In each trial, four pictures were simultaneously displayed, with one in each of the four corners of the computer screen, so that they had a subtended visual angle of 8° (height) and 11° (width). Before starting the experiment, all participants underwent a five-point calibration. Once the calibration procedure has been validated, the eye tracking recording could begin.

Each participant was informed that their eye movements would be recorded. They were instructed to look at screen, to avoid moving their face and hiding their eyes. They did not receive any additional instruction about a particular way to move their eyes, except during the calibration phase. The procedure was close to the one used in Kalénine, Mirman, Middleton, et al. (2012) and in Kalénine, Mirman and Buxbaum (2012). Participants saw a central fixation cross (100 x 100 pixels) for 1000 ms, followed by a preview of the four-picture display lasting 1000 ms. A red circle (200 x 200 pixels) was displayed in the center of the screen for the last 250 ms of this preview, to draw participants' visual attention back to a neutral central location. This was followed by the word-picture matching phase, which lasted for 5000 ms, starting from the auditory word onset. Participants were instructed to click with the mouse on the picture that corresponded to the word they heard (Fig. 1). As in the passive version of the Mirman & Graziano (2012b)'s study, trials had a fixed duration. Yet a click response was required in order to assign a clear motor goal to the task, instead of only instructing the participants to simply look at the target. The fixed duration of each trial avoided eliminating trials from the gaze data analysis because of potential clumsily clicks before word onset.

2.3 Data analysis

2.3.1 Mouse clicks

Accuracy was expressed as correct mouse clicks on the critical trials and was analyzed

using logistic mixed-effect models with Group (patients, controls) and Condition (taxonomic, thematic) as fixed effects and Condition as random slopes for participants.

At a more qualitative level, we also analyzed for each participant the distribution of the errors produced between four different types: no response, confusion error with a competitor, confusion error with an unrelated picture, misclick (*i.e.*, a clumsily click before the word onset or out of areas of interest defined for each pictures).

Reaction times (RTs) were expressed in milliseconds and were only analyzed for correct responses on critical trials. To ensure the normality of the distribution, RTs were log transformed. Log-transformed RTs were analyzed using linear mixed-effect models with Group (patients, controls) and Condition (taxonomic, thematic) as fixed effects and Condition as random slopes for participants.

Mixed-effects models were fitted using the *glmer* and *lmer* functions of the lme4 package (Version 1.1-21) in R (Version 3.5.1.). Likelihood ratio tests (LRT) for fixed effects were computed in order to provide an overall measure of the effect size of the model. For linear mixed-effect models (RTs), significance *F* tests of fixed effects on each time term were obtained using the ANOVA function of the LmerTest package (Version 3.1-0). *P* values for *F* tests on fixed effects and *t* tests on parameter estimates of the model were calculated based on Satterthwaite's' approximations.

2.3.2 Fixation data averaging

We defined four areas of interest (AOIs), corresponding to 400 x 300 pixel quadrants in each corner of the computer screen. Fixations inside one of these AOIs were classified as object fixations, whereas fixations outside these AOIs were classified as nonobject fixations. For each 16-ms sample of a given trial, fixations could either be 1 (object fixations) or 0 (nonobject fixations). For each trial for each participant, the number of samples on each AOI was computed over 50-ms time bins. Sample data at the trial level was then averaged over

trials in order to provide an estimate of the time course of fixations on the target, competitor, and unrelated objects. Data from filler trials were excluded from the analysis. Only critical trials where the target image was correctly identified by the participant in both the taxonomic and thematic conditions were considered for gaze analyses.

2.3.3 Growth curve analysis of fixation data

We used growth curve analysis, a multilevel modeling method that has proven successful in analyzing gaze data over time (Kalénine, Mirman, Middleton, et al., 2012; Mirman, 2014; Pluciennicka, Wamain, Coello, & Kalénine, 2016), to test how SD impacts taxonomic and thematic semantic competition during object identification. At Level 1, changes in the proportion of fixations as a function of time were modeled using fourth-order orthogonal polynomials. The intercept term reflected the overall height of the fixation curve, the linear term reflected the slope of the curve, the quadratic term reflected the central inflection of the curve, and the cubic and quartic terms reflected inflections at the extremities of the curve. In brief, the intercept captured changes in semantic competition amplitude, whereas the other time terms captured changes in semantic competition timing. The effects of the factors of interest on the fixation curve were added as fixed effects to the model at Level 2. The random effect structure captured variations in the shape of the overall fixation curve between participants (random intercepts) and individual differences in the semantic competition effect (random slopes).

Using the grow curve analysis approach, two sets of mixed-effect models were conducted on the gaze data during word-to-picture matching after target word onset:

a) *Analysis of fixations on the target object as a function of group and condition*. This model aimed at comparing target identification fixation curves between groups and conditions once the target word had been delivered. This was an additional assessment of the performance in target identification. Fixed effects of the model at Level-2 corresponded to

Group (controls, patients) and Condition (taxonomic, thematic) and their interaction. In particular, we wanted to evaluate the Group x Condition interaction on the linear term, which would indicate variations in the slope of target identification between groups and conditions (see Lee, Middleton, Mirman, Kalénine, & Buxbaum, 2013 for a similar evaluation).

b) *Analysis of fixations on the distractor objects as a function of group and condition: assessment of the "semantic competition effects"*.

The first full model aimed at verifying whether semantic competition effects were modulated by group and condition. Fixed effects of the model at Level-2 corresponded to Object Relatedness (C for competitors, i.e., semantically-related distractors, US for unrelated but visually similar distractor, and UN for unrelated non similar distractor), Condition (taxonomic, thematic), Group (patients, controls), and their interactions. Object relatedness did not involve the target, as semantic competition is classically evaluated by comparing the fixation time courses of related versus unrelated distractors. We expected a 3-way interaction between Object Relatedness, Group, and Condition on the intercept and/or on the time terms.

As the main objective of the study was to assess the effect of SD on the processing of two distinct types of relationships, we then compared the shape of the semantic competition effect between patients with SD and controls in the taxonomic condition on the one hand, and in the thematic condition on the other hand (see Mirman & Graziano, 2012a, for a similar approach to the comparison of patients with anterior or posterior stroke). In each semantic condition, a mixed-effect model was conducted with Object relatedness (C, US, and UN), Group (patients, controls), and the Object relatedness x Group interaction as fixed effects[1]. The interaction between Object relatedness and Group, reflecting the impact of the pathology on taxonomic and thematic semantic competition, was the critical fixed effect evaluated in

[1] Lmer structure of Level-2 models tested in the taxonomic and thematic conditions: model < -lmer(fixation~(intercept+linear+quadratic+cubic+quartic) * (Group*Object) + (intercept+linear+quadratic+cubic+ quartic|Subject) + (intercept+linear+quadratic+cubic+ quartic|Subject:Object).

each condition. In each condition, we expected to observe main effects of Object Relatedness evaluating semantic competition effects and/or interactions between Group and Object relatedness. Main effects of Group on fixation curves (independently of Object Relatedness) were possible but not informative.

Linear mixed-effect models of fixation data were fitted using restricted maximum likelihood estimation using the lmer function of the lme4 package (Version 1.1-21) in R (Version 3.5.1.). Likelihood ratio tests (LRT) for fixed effects were computed in order to provide an overall measure of model fit improvement after adding the factors of interest to the model. Significance *F* tests of fixed effects on each time term were obtained using the ANOVA function of the LmerTest package (Version 3.1-0). *P* values for *F* tests on fixed effects and *t* tests on parameter estimates of the model were calculated based on Satterthwaite's' approximations. Post-hoc paired comparisons (Tukey's adjusted) were provided, when relevant, using the emmeans package (Version 1.3.4).

3. Results

No trial had to be excluded because of a lack of gaze data (track loss or off-screen samples). For each critical trial, we recorded 7-216 on-screen samples for controls (mean = 123 ± 36), and 1-182 on-screen samples for the patients with SD (mean = 80 ± 37).

3.1 Mouse click data

3.1.1 Accuracy

The logistic mixed-effect model of accuracy data (LRT: $\chi^2(3) = 26.46$, $p < 0.001$) showed a significant main effect of Group [Estimate = -2.766, SE=0.534, z = -5.183, $p < 0.001$] as patients with SD were significantly less accurate (mean = 83.55 ± 15.71%, range = 57.77-98.08%) than controls (mean = 99.10 ± 1.76%, range = 94.23-100%). The effects of Condition [Estimate = 0.361, SE=0.527, z = 0.684, $p = 0.494$] and the Group x Condition

interaction [Estimate = 0.116, SE=1.054, z = 0.110, p = 0.912] did not reach significance (see detailed accuracy in each condition in Table 3).

Analysis of the distribution of the four different types of errors produced by each participant showed that patients with SD produced mainly *no responses* (mean = 38.28 ± 32.20% of their total errors) and *confusion errors with competitors* (mean = 34.35 ± 39.86% of their total errors). They made a lower proportion of *confusion errors with unrelated pictures* (mean = 8.10 ± 9.56% of their total errors) and *misclicks* (mean = 19.27 ± 32.86% of their total errors). A comparison of the proportions of confusion errors between the two types of competitors indicated that patients with SD made significantly more confusions with taxonomic competitors (31.81% of total errors) than with thematic competitors (9.1% of total errors) [$\chi^2(1) = 5.662$, $p = 0.017$]. For controls, errors essentially consisted in *misclicks* (mean = 15.56 ± 35.34% of their total errors). They produced very few *confusion errors with competitors* (mean = 2.22 ± 8.61% of their total errors), *confusion errors with unrelated pictures* (mean = 2.22 ± 8.61% of their total errors), or *nonresponses* (mean = 6.67 ± 25.82% of their total errors). No differences were found on the proportions of confusion errors between the two types of competitors in the control group [$\chi^2(1) = 0.875$, $p = 0.349$].

3.1.2 RTs

The linear mixed-effect model on log-transformed RTs (LRT: $\chi^2(3) = 15.01$, p = 0.002) revealed a significant main effect of Group [$F(1,44.84) = 15.501$, $p < 0.001$] as controls were faster (mean = 1795.83 ± 428.12 ms) than patients with SD (mean = 2378.63 ± 702.84 ms). The effects of Condition [$F(1,44.84) = 0.417$, $p = 0.521$] and the Group x Condition interaction [$F(1,44.84) = 0.367$, $p = 0.548$] did not reach significance (see detailed RTs in each condition in Table 3).

3.2 Fixation data

Trials where participants clicked on the incorrect picture were excluded from the

fixation analyses. In addition, in order to keep the item sets strictly equivalent at the individual level between the thematic and taxonomic conditions, we only considered critical trials where the target was correctly identified by the participant in both conditions (i.e., 78% of patient data and 98% of control data). Analyses of gaze data after word onset were performed on a 1000 ms time window starting 100 ms after word onset (minimum time required to plan and execute a saccade driven by the auditory prompt). Importantly, the time window was identical for the two groups and the two conditions, and included the rise of target fixation curves to their asymptote (see Fig. 2).

3.2.1 Target identification after word onset

Adding the different fixed effects to the model of target fixations after word onset improved the model fit of the data overall (LRT: $\chi^2(19) = 102.25$, $p < 0.001$). *F* tests of fixed effects only showed a main effect of Group on the intercept term [$F(1, 22.40) = 24.67$, $p < 0.001$] and on the linear term [$F(1, 22.51) = 25.31$, $p < 0.001$]. After word onset, patients with SD looked overall less at the target than controls (estimate patients-controls = -0.32, SE = 0.08, t = -3.91, $p < 0.001$) and their target identification curve showed a slower rise than controls (estimate patients-controls = -1.09, SE = 0.30, t = -3.62, $p < 0.001$). There were no main effect of Condition [$F(1, 25.17) = 1.40$, $p = 0.249$] and no Group x Condition interaction [$F(1, 25.17) = 0.363$, $p = 0.552$]. The slower (although correct) visual identification of the target in patients with SD was therefore equivalent between the taxonomic and thematic conditions.

3.2.2 Semantic competition effects after word onset

Adding the different fixed effects to the model of distractor fixations after word onset improved the model fit of the data overall (LRT: $\chi^2(59) = 129.06$, $p < 0.001$). *F* tests of fixed effects highlighted an interaction between Object Relatedness, Group, and Condition on the intercept [$F(2, 113.38) = 4.12$, $p = 0.019$]. The amplitude of semantic competition effects was

indeed modulated by the semantic condition and the pathology. The interaction between Object Relatedness, Group, and Condition was not evidenced on the time terms. The 3-way interaction was then decomposed by evaluating the Object Relatedness x Group interaction model in each condition.

Taxonomic condition

Figure 3 shows the model fit of the fixation data for the taxonomic condition (LRT: $\chi^2(29) = 76.17$, $p < 0.001$). *F* tests of fixed effects on the intercept term showed no significant main effect of Object Relatedness [$F(2, 55.37) = 1.78$, $p = 0.177$] and no significant interaction between Object Relatedness and Group [$F(2, 55.37) = 0.73$, $p = 0.487$]. However, the comparisons of interest between related distractors and the two possible unrelated distractor baselines highlighted that irrespective of group, there were more fixations overall on taxonomic competitors than on unrelated nonsimilar distractors [estimate C - UN = 0.09, $SE = 0.42$, $t = 2.18$, $p = 0.033$]. In contrast, the difference between taxonomic competitors and unrelated but visually similar distractors was not significant [estimate C - US = 0.037, $SE = 0.42$, $t = 0.87$, $p = 0.386$]. The only other significant effect involving object relatedness (either alone or in interaction with group) was a main effect of object relatedness on the quartic term [$F(2, 65.09) = 3.35$, $p = 0.041$], reflecting differences between related and unrelated fixation curves at their extremities, regardless of group. The full results are reported in Table 4. An illustration of the time course of the taxonomic competition effect in the patient and control groups is provided in Figure 4.

Thematic condition

Figure 5 shows the model fit of the fixation data for the thematic condition (LRT: $\chi^2(29) = 91.17$, $p < 0.001$). *F* tests of fixed effects on the intercept term showed no main effect of Object Relatedness [$F(2, 49.72) = 0.24$, $p = 0.785$] but highlighted an interaction between Object relatedness and Group [$F(2, 49.72) = 4.83$, $p = 0.012$]. The interaction

revealed that the amplitude of the competition effect (i.e., overall difference in fixation proportion between competitor and unrelated distractors) was greater in the SD group than in the control group, both when the fixation proportion on the thematic competitor was compared with fixation proportion on the unrelated nonsimilar distractor [estimate (C - UN for patients) - (C - UN for controls) = 0.14, *SE* = 0.05, *t* = 2.74, *p* = 0.009] and when it was compared with the fixation proportion on the unrelated but visually similar distractor [estimate (C - US for patients) - (C - US for controls) = 0.13, *SE* = 0.05, *t* = 2.64, *p* = 0.011]. There were no other significant effects involving object relatedness, either on its alone or in interaction with group. The full results are reported in Table 4. Figure 6 clearly illustrates the greater thematic competition encountered by patients as compared to controls[2].

4. Discussion

The present study investigated residual semantic knowledge in SD, focusing on two semantic systems (taxonomic vs. thematic) that rely on at least partially distinct neuroanatomical substrates. Using a highly sensitive paradigm (i.e. visual world paradigm coupled with eye-movement recording) to implicitly measure the activation of semantic processing, we demonstrated different patterns of gaze fixations for patients with SD versus controls during a word-to-picture matching task. For correct trials, whereas controls only exhibited a competition effect for taxonomically related pictures, patients with SD were far more sensitive than controls to thematically related competitors before identifying the targets. Overall, this pattern of results is consistent with the hypothesis of a semantic disequilibrium between the two semantic relationship systems, predicting overuse of thematic relationships as the disease progresses and as the taxonomic relationship system collapses. In the present

[2] The pattern of results remained the same after excluding the two patients with low scores on the MMSE, confirming that the semantic competition profile of patients with SD was not related to their poor general cognitive functioning, as least as assessed by MMSE-like scales.

study, eye movements revealed an abnormal reliance on thematic processing in patients compared with controls, reflecting the semantic disorganization in SD. Although the breakdown in taxonomic relationships did not directly show up in the gaze data of the SD group, it clearly appeared when analyses focused on patients' accuracy in that condition. The patients with SD produced a significantly higher rate of confusion errors with the taxonomic distractors (31.81% of total errors) than with the thematic ones (9.1% of total errors). The extinction of distinctive visuoperceptual attributes may have been responsible for these confusions between two objects belonging to the same taxonomic category. This line of interpretation has been put forward to explain the hyperpriming effects observed in patients with SD or Alzheimer's disease (Giffard et al., 2001; Giffard et al., 2002; Laisney et al., 2011). For example, *tiger* abnormally primes *lion*, because the tiger has lost its *stripes* and the lion its *mane*, meaning that the remaining, spared features are shared by both entities and overlap completely, thus leading to confusion between the two concepts. Moreover, according to Seckin et al. (2016), taxonomic blurring leading to errors in favor of taxonomic associates in word-object matching is a hallmark symptom of SD. Using an eye-tracking paradigm during a word-to-picture matching task, these authors demonstrated an abnormally increased number of fixations on taxonomically related competitors in patients with SD until late during the identification process, compared with both controls and patients with other primary progressive aphasia syndromes. At first sight, this result might seem to be at variance with our finding, since we did not observe any significant difference in the gaze pattern of patients with SD and controls in the taxonomic condition. However, our methodological choices are certainly responsible for these apparent discrepancies. We should recall that the trials where participants clicked on the incorrect picture were removed from our gaze fixation analyses, to ensure that the two kinds of competition effect were strictly comparable. To better capture all the processing engaged by the patients with SD when performing the word-to-picture

matching task, gaze fixations need to be considered together with accuracy. Thus, the taxonomic blurring mentioned by Seckin et al. (2016) appeared in our results through the greater number of taxonomic confusion errors in the SD group. In Seckin et al. (2016)'s study, there were far more (16) objects presented in the array and pictures were displayed in shades of gray. This choice of display may have favored the significant taxonomic blurring observed in all the participants (including controls), by strengthening the visual similarity confusions between objects belonging to the same taxonomic category, especially Fruit & Vegetables. For this category, several studies have underlined the importance of color knowledge to correct identification (Connolly, Gleitman, & Thompson-Schill, 2007; Crutch & Warrington, 2003; Warrington & McCarthy, 1987). Taxonomic relationships are well known to rely on shared features between concepts (McRae et al., 1997, 2005; Mirman et al., 2017), especially visuoperceptual features (Estes, Golonka, & Jones, 2011; Kalénine et al., 2009). Our findings are aligned with the specific contribution of visuoperceptual features in taxonomic relationships, as the competition effect for the taxonomic distractors only appeared when taxonomically-related objects were compared with unrelated, visually nonsimilar objects. The effect failed to reach significance when fixations on taxonomically-related objects were contrasted with semantically unrelated but visually similar objects. By contrast, the competition effect was not modulated by the type of unrelated object baseline when competitors were thematically related to the target.

Critically, the main finding of the present study concerned the thematic condition, where patients with SD exhibited a greater semantic competition effect than controls. Why did patients exhibit this exaggerated thematic activation? Before answering this question, it should be mentioned that a particular status of thematic knowledge in SD has also been recently reported by Merck et al. (2019) with an explicit forced-choice picture-matching task. In this study, 10 participants with SD were compared to 10 participants with Alzheimer's

disease (AD) and 20 healthy controls. Participants were instructed to explicitly identify thematic versus taxonomic relationships. The authors demonstrated that the performance of the two groups of patients differed in the taxonomic condition but not in the thematic condition. They also indicated that the particular status of thematic relationships in SD was even stronger for artifact concepts. Nonetheless, the authors acknowledged that their explicit task could be contaminated by additional mechanisms, such as the intervention of executive functions. Although these mechanisms may not be entirely responsible for the relatively preserved identification of thematic relationships observed in the SD group, the intervention of non-semantic cognitive functions could partially account for the semantic matching performance of the SD patients. Besides, this explicit task generated a ceiling-effect in healthy controls, preventing from precise comparisons of the thematic and taxonomic processing between patients with SD and controls. In the present study, we adopted an eye-tracking protocol to investigate the processing of taxonomic and thematic semantic relationships at an implicit level in order to bypass such methodological shortcomings.

To explain the particular status of thematic knowledge in SD, several behavioral and neurophysiological arguments support the assumption that thematic processing is faster, less effortful, and therefore preferred over taxonomic processing (Kotz, Cappa, von Cramon, & Friederici, 2002; Lawson, Chang, & Wills, 2017; Lin & Murphy, 2001; Sachs et al., 2008; Sass, Sachs, Krach, & Kircher, 2009). Furthermore, taxonomic processing reportedly requires more cognitive resources than thematic processing (Maguire et al., 2010; Savic, Savic, & Kovic, 2017). Others studies nuanced this assumption by incriminating the strength of the semantic relationships rather than the type of semantic relationships (Geller, Landrigan, & Mirman, 2019; Thompson et al., 2017) as the cognitive control requirement is mainly determined by the strength of the semantic relationship. Thus, one possible explanation is that our patients with SD simply displayed an over-reliance on the easiest form of semantic

processing (i.e., for thematic relationships) and/or on the stronger semantic relationships. This line of interpretation would be consistent with the "hub and spoke" semantic framework (Lambon Ralph, 2014; Lambon Ralph et al., 2010; Patterson et al., 2007; Rogers et al., 2004). The "hub and spoke" model predicts relatively subtle distinctions between taxonomic and thematic processing, as it states that a single and unified semantic system, relying on the anterior temporal lobes, would underlie the two kinds of semantic relationships (Jackson et al., 2015; Lambon Ralph et al., 2017; Rice et al., 2015). Nevertheless, this interpretation seems relatively unlikely, as we carefully controlled and matched conditions on the strength of the semantic association between targets and competitors as well as on several potential confounding variables in the two conditions (i.e., linguistic variables, semantic similarities, visual saliency of pictures; see Section 2 "Materials and methods"). Moreover, controls were less sensitive than patients with SD to thematically related competitors, and there is no reason to believe that controls would have gone for the more demanding (taxonomic) semantic process rather than the less demanding (thematic) one. We therefore believe that the profile exhibited by patients with SD points to differences between taxonomic and thematic processing that go beyond task difficulty and sustain the assumption of two anatomically and functionally distinct semantic systems that are differentially affected in SD. This interpretation is consistent with another important line of evidence supporting the notion of at least partially distinct neural mechanisms for taxonomic and thematic relations (de Zubicaray, Hansen, & McMahon, 2013; Kalénine & Buxbaum, 2016; Kalénine et al., 2009; Lewis, Poeppel, & Murphy, 2015; Mirman & Graziano, 2012a; Schwartz et al., 2011; Xu et al., 2018). In particular, several neuroimaging studies in healthy controls and lesion-symptom mapping studies in patients have demonstrated that, compared with taxonomic relations, which mostly rely on the anterior temporal lobe (ATL), thematic relations recruit posterior regions around the temporoparietal junction (de Zubicaray et al., 2013; Kalénine & Buxbaum,

2016; Kalénine et al., 2009, Mirman & Graziano, 2012a; Schwartz et al., 2011; Xu et al., 2018). In Mirman & Graziano (2012a)'s study, the visual world paradigm coupled with eye-movement recordings was proposed to stroke participants with aphasia. Interestingly, participants with damage of left hemispheric posterior regions (Brodmann area 39 surrounding temporo-parietal cortex regions) exhibited reduced thematic competition effects, while they yielded a taxonomic competition effect comparable to controls. This posterior-lesioned group with aphasia presented the opposite pattern of thematic competition effects to that exhibited by our patients with SD. As the temporoparietal junction is known to be relatively spared in SD in contrast to the strong anterior temporal lobe damage (Brambati et al., 2015; Bright, Moss, Stamatakis, & Tyler, 2008; Chan et al., 2001; Desgranges et al., 2007; La Joie et al., 2014; Leyton, Britton, Hodges, Halliday, & Kril, 2016), the dissociation between their posterior-lesioned group and our patients with SD offers supplementary arguments in favor of distinct neural mechanisms supporting taxonomic and thematic processing. Besides, this allows ascertaining that the Visual World Paradigm is a particularly suitable approach for highlighting dissociations between semantic processes. The results from this study thus nicely complement the present findings and support the assumption of a key role of the posterior temporoparietal cortex for thematic processing.

Hurley, Mesulam, Sridhar, Rogalski, and Thompson (2018) recently added another area to the brain network involved in thematic processing, as they found that the performance of patients with SD on a picture-based thematic verification task was correlated with the cortical thickness of the right ATL. They also observed that the most salient difference between patients with higher versus lower performance was atrophy in the right ATL. Nonetheless, Figure 3 of their paper (p. 97) suggests that patients with poorer scores on thematic verification presented more extensive brain abnormalities, including in the temporoparietal junction. This raises the question of whether this correlation with the right ATL was actually a

reflection of more pronounced atrophy spreading to both the contralateral and posterior areas, as previously shown in longitudinal studies in SD (Brambati et al., 2015; Kumfor et al., 2016).

A convincing line of interpretation for the over-reliance on thematic knowledge reported in patients with SD is the hypothesis of a semantic disequilibrium, as it has been inferred from previous findings such as in Merck et al. (2014)'s study. This hypothesis states that the two semantic processes are held in balance, with the spared process (thematic processing in SD) taking over from the impaired one (taxonomic processing in SD). The notion of a balance between two types of semantic relationship has earlier been posited by Kalénine, Mirman and Buxbaum (2012), who found a negative correlation between the implicit processing of thematic relations (e.g., *broom-dustpan*) and relations of general functional similarities (e.g., *broom-sponge*) in patients with stroke. Further support for the notion of a semantic disequilibrium may come from the observation of interconnection abnormalities between the caudal and rostral parts of the temporal cortex in SD (Acosta-Cabronero et al., 2011). Combining measures of atrophy, hypometabolism and white-matter abnormalities, these authors postulated that changes in feedback neurons along the ventral stream can explain the deterioration in semantic knowledge in SD. In their model, the predominantly efferent projections from the damaged temporal lobe (arcuate and uncinate) degenerate, while predominantly afferent projections (inferior longitudinal fasciculus) to this region are relatively preserved. Assuming that the taxonomic system mostly relies on the rostral part of the temporal cortex, whereas the neural bases of the thematic system are more caudal, a disturbance in neural feedback would affect the remote modulation of one system over another. Furthermore, our results open the question of a possible dynamic semantic reorganization at the brain level. Recently, adaptive changes in SD have been claimed by Battistella et al. (2019) to explain the increased functional connectivity between the inferior

frontal gyrus and the superior portion of the angular gyrus, compared to heathy controls. The authors concluded to an up-regulation of the dorsal pathway in response to the degeneration of the anterior temporal lobes. To some extent, such up-regulation of the dorsal pathway could fit with the over-reliance on thematic knowledge reported in the patients with SD.

Our finding of preserved thematic knowledge was also congruent with prior reports incriminating some semantic knowledge as being responsible for the astonishing functional abilities in SD (see Bier et al., 2013; Bier & Macoir, 2010; Péron et al., 2015). Some of those studies highlighted the critical role of contextual information (Bozeat, Lambon Ralph, Patterson, & Hodges, 2002; Buxbaum, Schwartz, & Carew, 1997; Hodges et al., 2000), also underscored in the notion of *functional-contextual contiguity* in Lauro-Grotto, Piccini, and Shallice (1997; see definition on p. 616). Nevertheless, our results go beyond these proposals, given the exaggerated activation of thematic relationships we observed in patients with SD. These patients might excessively rely on these relationships between objects to compensate for the erosion of the other types of semantic knowledge. This raises the question of how such exaggerated activation of thematic knowledge benefits patients' daily living abilities. It also suggests that the role played by thematic knowledge in daily living abilities is underestimated in this disease.

We acknowledge that the small sample size of patients with SD is one limitation of this study, owing to the rarity of this disease. Nevertheless, we believe that this first finding of over-reliance on thematic relationships in SD offers promising research perspectives on semantic memory and may also offer a novel guideline in the construction of future rehabilitation programs in SD.

Moreover, we did not find the expected thematic competition effect in controls, although it was not the focus of the present study. The reasons for this absence of thematic competition effect in controls remain unclear. Thematic competition effects in healthy adults tend to be

relatively small (e.g., Mirman & Graziano, 2012b) and may be very sensitive to methodological details. In the present study, we chose to introduce an unrelated but visually similar distractor in the display to control for the effect of visual similarity. We can speculate that the presence of a visually similar distractor may have reduced and erased the thematic competition effect in controls. Participants may orient their attention on object features differently depending on the type of distractors in the display (see Ruotolo, Kalénine, & Bartolo, 2019). This limitation does not impact the main finding reported in this study, as patients with SD were still more sensitive to thematic competition, consistent with an over-reliance on thematic knowledge. Yet it suggests carefully selecting methodological details when assessing thematic competition in the visual world paradigm. In particular, it may be important to balance the need to control for visual similarity with the risk to fail detecting thematic competition effects.

In conclusion, we found that patients with SD were far more sensitive than controls to thematic relationships in a word-to-picture matching task. This finding indicates an over-reliance on thematic knowledge in SD, and supports the assumption of a semantic disequilibrium in the disease. Accordingly, we argue that this residual semantic knowledge – exaggeratedly activated in SD - plays an as yet underestimated role in patients' ability to deal with daily living activities.

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	Healthy controls		Patients with semantic dementia (SD)	
Sex (male; female)	5;10		4;5	
	Mean (standard deviation)	**Range**	**Mean (standard deviation)**	**Range**
Age in years	68.5 (5.3)	58-77	69.8 (3.9)	65-77
Education in years	11.7 (3.5)	7-20	10.9 (3.5)	7-17
DRS /144	139.8 (2.8)*	134-144*	109.2 (18.6)*	72-131*
Disease duration in years			3.7 (1.8)	1-6
AD biomarker status				Negative: 7 Not done: 2
Side of temporal atrophy (L = left; R = right)				5 L > R 3 R > L 1 R = L

Table 1. Participants' general demographic and clinical features.

Note. * Significant difference between patients with SD and controls; DRS: Dementia Rating Scale; AD: Alzheimer's disease.

Tests		Patients with semantic dementia (SD)									
	Cut-off at 5%	**Mean (standard deviation)**	**SD1**	**SD2**	**SD3**	**SD4**	**SD5**	**SD6**	**SD7**	**SD8**	**SD9**
General cognitive functioning											
Mini-Mental State Examination, MMSE (/30)	*26*	20.22 (7.56)	26	28	**12**	**22**	**23**	**4**	**23**	**24**	**20**
Raven's Coloured Progressive Matrices (/36)	*15*	25 (7.30)	22	34	**14**	26	26	33	33	19	18
Dementia Rating Scale (/144)	*136*	109.25 (18.64)	**124**	**131**	**72**	**102**	**123**	-	**106**	**115**	**101**
Attention subscale (/37)	*32*	34,13 (2.03)	34	36	**31**	32	35		37	35	33
Initiation/perseveration subscale (/37)	*31*	22,13 (5.69)	**21**	**29**	**11**	**21**	**28**		**19**	**25**	**23**
Construction subscale (/6)	*4*	6 (0)	6	6	6	6	6		6	6	6
Conceptualization subscale (/39)	*33*	29 (7.60)	38	37	**14**	**26**	**30**		**31**	**31**	**25**
Memory subscale (/25)	*21*	18 (5.55)	25	23	**10**	**17**	24		**13**	**18**	**14**
Nonverbal episodic memory											
Delayed recall of Rey-Osterrieth complex figure–Form A (/36)	*5*	8.36 (7.02)	15	21	-	**2,5**	**6**	-	**6**	**6**	**2**
The Doors visual recognition task: Part A (/12)	*8*	6.89 (2.67)	**5**	12	**4**	8	8	8	**7**	**7**	**3**
The Doors visual recognition task: Part B (/12)	*5*	4 (1)	5	**4**	-	-	-	**3**	-	-	-
Working memory											
Digit Span Forward (WAIS-R) (/9)	*4*	5.44 (1.13)	7	6	5	6	7	4	5	5	4
Digit Span Backward (WAIS-R) (/8)	*3*	3.67 (1.58)	5	5	**2**	3	6	**1**	4	3	4
Language and semantic knowledge											
Irregular word reading test (/18)	*17*	15.78 (2.17)	**14**	18	**15**	17	18	**12**	**14**	**16**	18
Regular word reading test (/18)	*17*	18 (0)	18	18	18	18	18	18	18	18	18
Isolated word repetition test (Boston Diagnostic Aphasia Examination) (/10)	*9*	9.78 (0.36)	10	10	10	10	10	9	10	9,5	9,5
Oral comprehension subtest of the Montreal-Toulouse protocol - MT 86 (/38)	*33*	32.44 (7.99)	37	38	**20**	36	36	**17**	37	35	36
Naming task (BECS-GRECO) (/40)	*35*	11.89 (11.54)	**27**	**28**	**1**	**12**	**5**	**2**	**4**	**25**	**3**
Verbal semantic matching task (BECS-GRECO) (/40)	*38*	29.56 (3.91)	**32**	**35**	**25**	**29**	**27**	**27**	**31**	**35**	**25**
Visual semantic matching task (BECS-GRECO) (/40)	*38*	29.78 (4.99)	**34**	**36**	**24**	**30**	**29**	**36**	**23**	**31**	**25**
BECS-GRECO total score-sum of the 3 tasks (/120)	*111*	71.22 (18.50)	**93**	**99**	**50**	**71**	**61**	**65**	**58**	**91**	**53**
Level of the overall semantic impairment (Mild: 1; Moderate: 2; Severe: 3)			1	1	2	1	2	2	2	1	2
Visuoperceptual abilities											
Benton Facial Recognition Test (/54)	*38*	44.56 (3.13)	47	41	43	47	47	45	41	49	41
Protocole d'Evaluation des Gnosies Visuelles Embedded figure task (/36)	*30*	35.22 (0.83)	35	36	34	34	36	36	36	35	35
Copy of Rey-Osterrieth complex figure (/36)	*29*	33.11 (2.52)	33	31	29	30	35	35	35	34	36

Table 2. Neuropsychological data for each of the nine patients with semantic dementia. Scores in bold were below the normal range.
Note. WAIS-R: Wechsler Adult Intelligence Scale-Revised.

Participants	Measures	Taxonomic condition	Thematic condition
Patients with semantic dementia	Accuracy (%) Mean (standard deviation)	81.2 (18.09)	85.9 (14.52)
	RT (ms) Mean (standard deviation)	2532.53 (382.67)	2395.36 (436.84)
Healthy controls	Accuracy (%) Mean (standard deviation)	98.97 (2.28)	99.23 (1.59)
	RT (ms) Mean (standard deviation)	1798.96 (173.27)	1798.23 (168.07)

Table 3. Performance in the taxonomic and thematic conditions.
Accuracy is expressed as the percentage of correct mouse clicks. Reaction times (RTs) are expressed in milliseconds and were calculated by averaging RTs for correct mouse clicks.

Taxonomic condition			
Terms	Group	Object	Group x Object
Int	$F(1, 28.37) = 0.08$, $p = 0.78$	$F(2, 55.37) = 1.78$, $p = 0.18$	$F(2, 55.37) = 0.73$, $p = 0.49$
Lin	**$F(1, 23.31) = 4.23$, $p = 0.05$**	$F(2, 47.98) = 1.09$, $p = 0.34$	$F(2, 47.98) = 0.40$, $p = 0.67$
Quad	$F(1, 40.94) = 0.01$, $p = 0.92$	$F(2, 62.97) = 0.89$, $p = 0.42$	$F(2, 62.97) = 0.33$, $p = 0.72$
Cub	$F(1, 31.04) = 0.96$, $p = 0.34$	$F(2, 53.78) = 0.17$, $p = 0.84$	$F(2, 53.78) = 1.13$, $p = 0.33$
Quar	$F(1, 53.84) = 0.11$, $p = 0.74$	**$F(2, 65.09) = 3.35$, $p = 0.04$**	$F(2, 65.09) = 1.99$, $p = 0.14$
Thematic condition			
Terms	Group	Object	Group x Object
Int	$F(1, 22.27) = 2.46$, $p = 0.13$	$F(2, 49.72) = 0.24$, $p = 0.78$	**$F(2, 49.72) = 4.83$, $p = 0.01$**
Lin	**$F(1, 30.01) = 3.19$, $p = 0.08$**	$F(2, 54.72) = 0.45$, $p = 0.64$	$F(2, 54.72) = 1.05$, $p = 0.36$
Quad	$F(1, 50.35) = 0.06$, $p = 0.81$	$F(2, 61.58) = 0.82$, $p = 0.44$	$F(2, 61.58) = 2.02$, $p = 0.14$
Cub	$F(1, 46.35) = 0.65$, $p = 0.42$	$F(2, 65.11) = 0.75$, $p = 0.48$	$F(2, 65.11) = 0.94$, $p = 0.39$
Quar	$F(1, 66.00) = 0.36$, $p = 0.55$	$F(2, 66.00) = 1.87$, $p = 0.16$	**$F(2, 66.00) = 2.57$, $p = 0.08$**

Table 4. Full results of the *F* tests on the fixed effects of the model in the taxonomic and thematic conditions. The main effects of Group and Object relatedness, as well as the Group x Object relatedness, were evaluated on the different time terms describing the fixation curve (Int: intercept, Lin: linear, Quad: quadratic, Cub: cubic, Quar: quartic). Values in bold indicate that the results are significant or tend to be significant

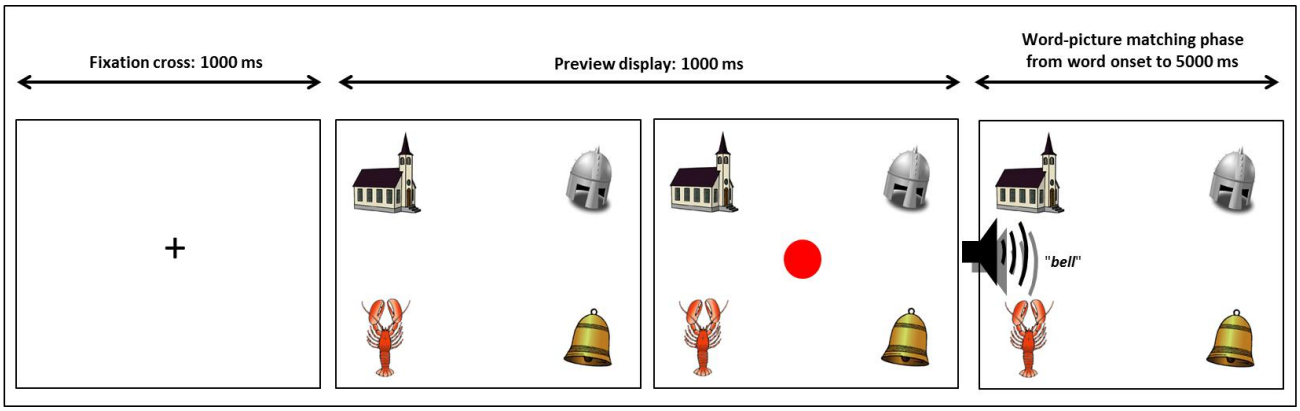

Figure 1

Illustration of the procedure used in this eye-tracking paradigm. In this example of a trial, the target ("bell") is presented with a thematic competitor ("church"), a visually similar but semantically unrelated object ("knight's helmet") and a visually dissimilar and semantically unrelated object ("lobster"). The target word was orally delivered after the preview display.

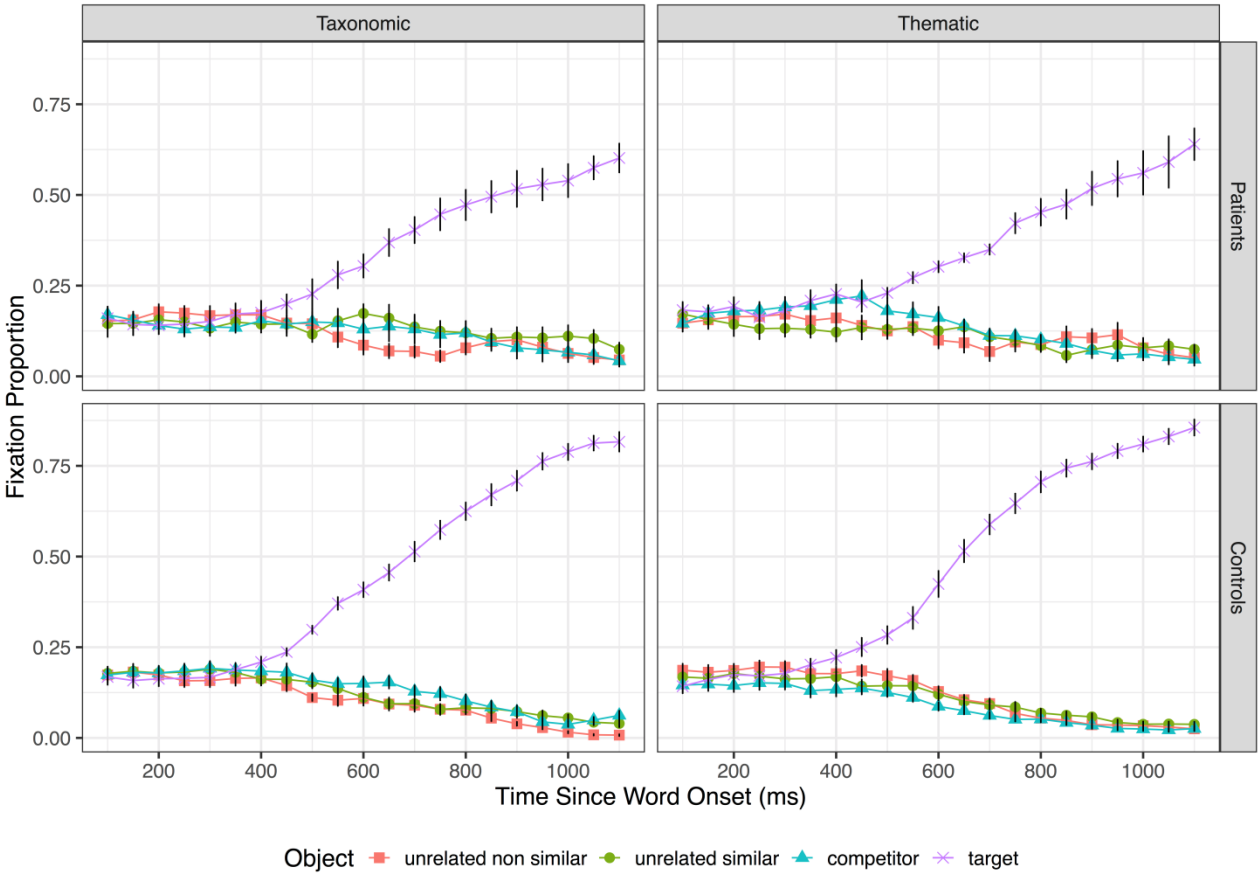

Figure 2

Gaze data for the competition window (100-1100 ms after word onset). The graph shows the mean fixation proportion (and standard errors for participants) as a function of time, object (target, competitor, unrelated similar, unrelated nonsimilar), group (patients, controls), and condition (taxonomic, thematic).

Error bars represent standard error of the mean.

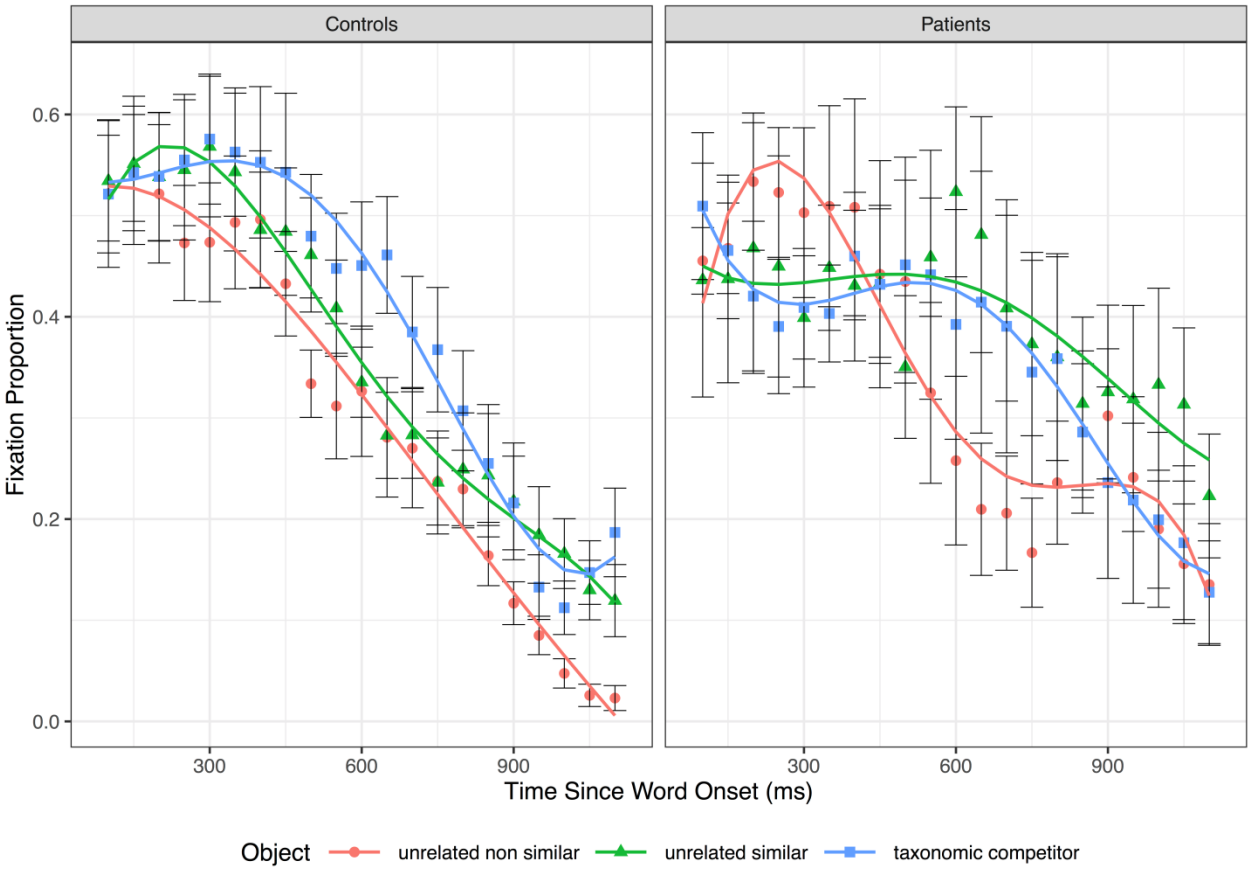

Figure 3

Model fit (lines) of the fixation data (points) of patients and controls in the taxonomic condition. Statistical tests highlighted greater fixations on the taxonomic competitor (blue square) than on the unrelated nonsimilar distractor (red circle), regardless of group.

Error bars represent standard error of the mean.

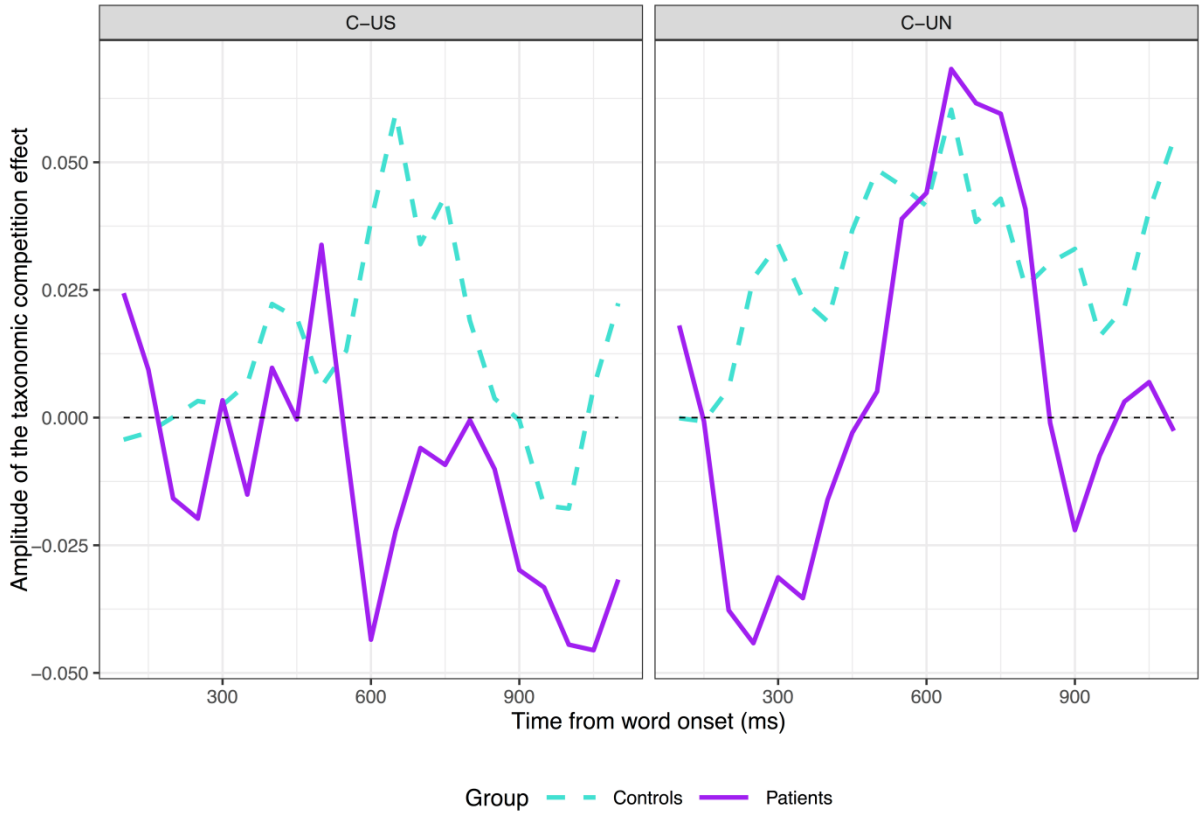

Figure 4

Taxonomic competition effect amplitude computed on raw fixation proportions (i.e. proportion fixation related - proportion fixation unrelated) as a function of time since word onset, unrelated distractor baseline (US, UN), and group (patients, controls).

Note. C: semantically related competitors, US: semantically unrelated but visually similar objects, and UN: semantically unrelated and visually nonsimilar objects.

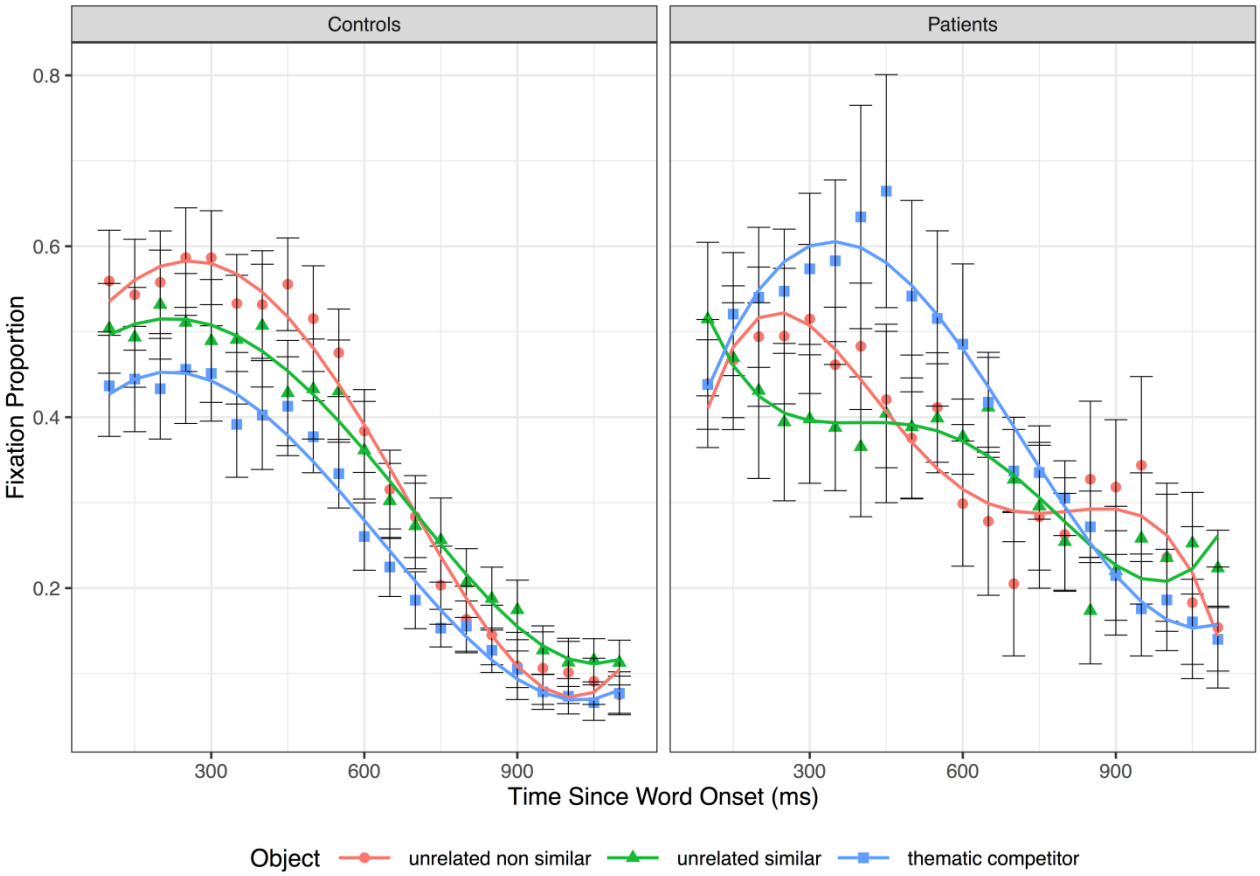

Figure 5

Model fit (lines) of the fixation data (points) of patients and controls in the thematic condition. Statistical tests highlighted greater fixations on the thematic competitor (blue square) than on either of the unrelated distractors (red circle or green triangle) in patients with SD compared to controls.

Error bars represent standard error of the mean.

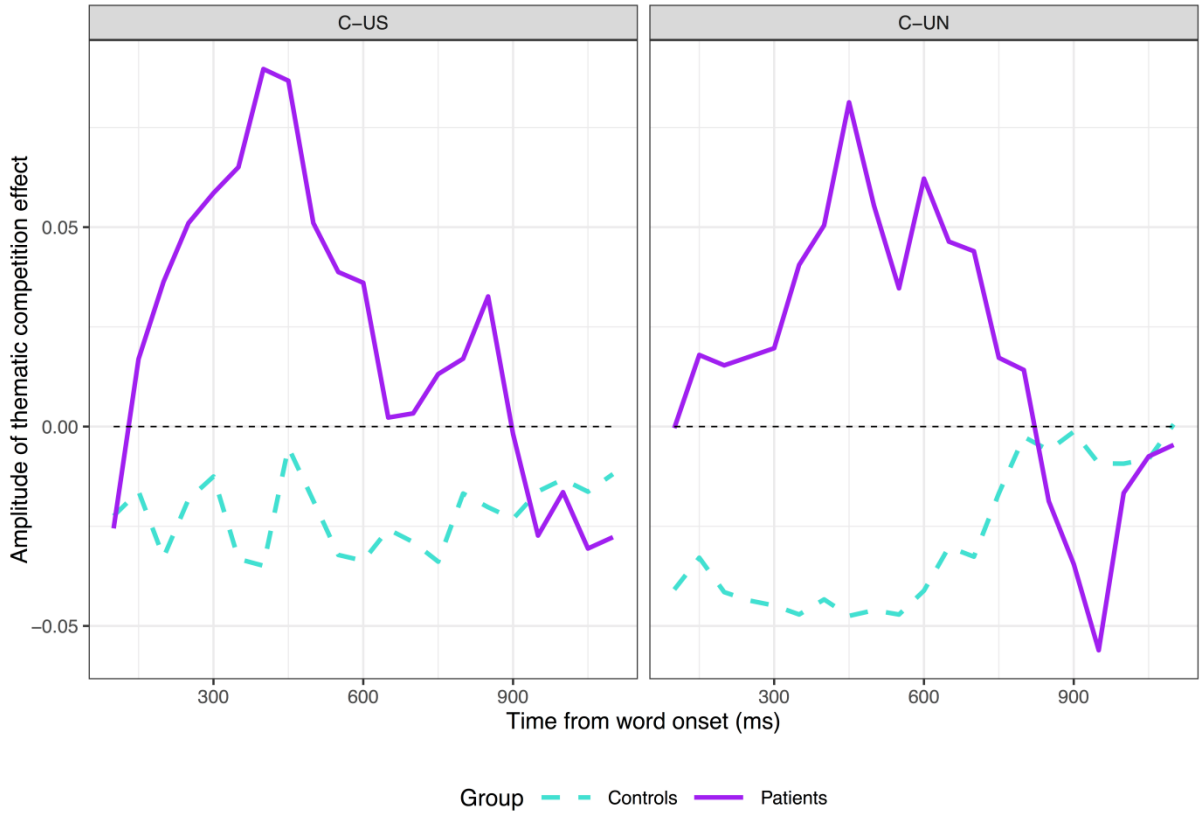

Figure 6

Thematic competition effect amplitude computed on raw fixation proportions (i.e. proportion fixation related - proportion fixation unrelated) as a function of time since word onset, unrelated distractor baseline (US, UN), and group (patients, controls).

Note. C: semantically related competitors, US: semantically unrelated but visually similar objects, and UN: semantically unrelated and visually nonsimilar objects.