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Semantic memory and Alzheimer's disease:
A normative, neuropsychological and fMRI study

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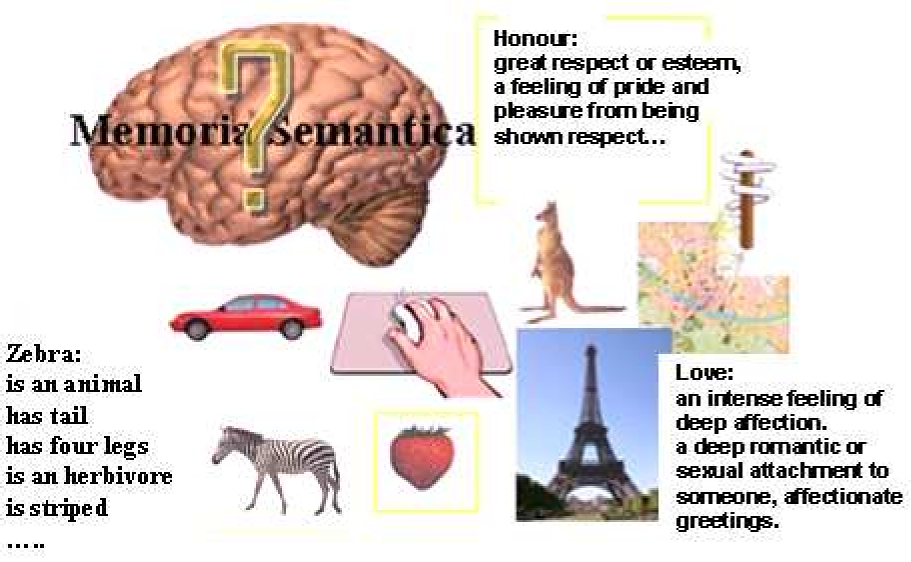
PART III

Chapter 1: Semantic memory



Which is the capital of France? What is a zebra? How does a computer mouse work? And what is love?

Every day of our life we use a huge amount of information related to the world that surrounds us; most of the time we deal with it in a simple way, with no need of any particular effort or commitment. Our brain is sometimes conceived to be similar to a box that is supposed to be filled in with an apparent infinite number of old and new mental concepts, well organized in order to be quickly retrieved when needed. In several pathological conditions this organization is affected, and many studies report cases of neurological patients who show a very remarkable disability in their daily life because of this dysfunction.

- Patterson and co-workers (2007) reported that when they asked one of their patients “to name a picture of a zebra, she replied: “It’s a horse, ain’t it?” Then, pointing to the stripes, she added, “But what are these funny things for?”

- A patient described by Chertkow and co-workers (1990) was able to name a picture of a zebra and to correctly answer questions that uniquely identified the animal (e.g. is the zebra striped?). However, at the same time the patient incorrectly answered many basic questions

> concerning the animal ("Do zebras meat eat?", "Do they live in Africa?"). When the patient could not answer the identification questions concerning an animal, then he was also unable to name the picture of the same animal.
>
> More surprisingly, there are cases of patients who have an impairment for a particular class of objects, for example patient HELGA, who "showed a disorder relating to processing of knowledge about animate objects (animals and fruits and vegetables) in the presence of spared knowledge of inanimate objects" (Mauri et al., 1994).
>
> Martin & Fedio (1983), describing the performances on several tasks of a group of patients compared to healthy controls, reported that "single-word comprehension was impaired, except when judgments of affective meaning were required".

Tulving (1972) has perhaps provided the most overarching definition of semantic memory as a mental thesaurus, i.e. the organized knowledge a person possesses about words and their meaning, and relations among them. Semantic memory refers to our general knowledge of objects, meaning of the words, facts and persons (Tulving, 1972). It has a central role in many cognitive processes, such as production and understanding of language skills and the recognition of objects. It is essential in daily life: we continuously use a large amount of knowledge that enables us to interact with the world around us, permitting us to know that a zebra is an animal with four legs, that eats only plants and has stripes, that Paris is the capital of France, how to use a computer mouse and that hope is a feeling of expectation and desire, and so on. Consequently, a semantic memory impairment results, as in the examples above, in a very remarkable disability actions (Bier et al., 2010). It is generally assumed that this knowledge is mostly shared across individual of a given culture (Patterson et al., 2007). However, individuals differed largely in "the things that they know" (Saffran, 2000), leading to individual and gender differences (Funnell & DeMornay Davies, 1996).

Important questions in semantic memory research concern the way in which the concepts are organized and represented in the mind and how they can be affected following brain damage, showing many different patterns of deterioration. Even semantic memory involves both abstract and concrete concepts, the former have been only rarely investigated.

Researchers from different several disciplines, including cognitive psychology, psycholinguistic, neuropsychology and neuroscience, have contributed to the understanding of the organizational principles of the semantic system. In particular, evidences deriving from neuropsychological studies represent a fundamental source of knowledge. In the last decades, advances in brain imaging technology (especially functional Magnetic Resonance Imaging, fMRI, and Positron Emission Tomography, PET) have improved our understanding of the functional organization of the semantic memory. While studies of brain damage strongly depend from the cerebral regions affected by pathology, neuroimaging studies allow to explore the functional organization of the semantic system in the brain in healthy individuals. Although important goals have been reached, many questions are still to be solved. In some cases, the results coming from clinical studies do not seem immediately to agree with those coming from neuroimaging studies.

1.1 Semantic memory impairments

Many clinical studies have been giving a huge contribution in identifying the neural systems which are responsible for the storage of knowledge, being the only source of information until few years ago. Neuropsychological studies conducted on patients with specific conceptual knowledge impairments have been a useful source of data for addressing issues about the organization of the knowledge in the human brain. Different forms of brain damage can lead to semantic memory disorders, leading to a general disorder of conceptual information about objects and to category-specific deficits. The most common aetiology is herpes simplex encephalitis (HSVE, Warrington and Shallice, 1984), but other focal aetiologies include cerebro-vascular accident (Caramazza & Shelton, 1998), and traumatic injury (Rosazza et al., 2003). Much work has been with neurodegenerative conditions such as Alzheimer's disease (AD, Chertkow & Bub, 1990; Hodges, Salmon & Butters, 1992) and semantic dementia (Snowden et al., 1989; Hodges et al., 1992).

A generalised semantic impairment. In a seminal report, Warrington (1975) described three cases of progressive deterioration of semantic memory. Despite largely preserved cognitive and language functions outside the realm of semantic knowledge, the patients performed poorly on tests of picture naming and definition, word to picture naming and property verification, in which patients were asked questions such as "is it a bird?" or "is it heavy?". In contrast to test that required basic level classification, the patients were able to process the superordinate label for many of the items. Warrington argued for in favour of the hierarchical categorization model of semantic memory proposed by Collins and Quillian (1969), but provided evidence to constrain it concerning the direction of processing trough the hierarchy. A general (not category specific) and progressive deterioration of semantic memory has been subsequently reported in similar cases, defined as semantic dementia (Hodges et al., 1992, Snowden et al., 1989). Semantic dementia (SD) patients show a selective decline of semantic memory, consequent to the degeneration of the anterior temporal lobes (Patterson et al., 2007). A progressive loss of the expressive and receptive vocabulary and an initial and relative sparing of the other cognitive functions are common characteristics of this pathology. Deficits include impaired object naming (with errors typically consisting of semantic errors – retrieving the name of another object from the same category, or retrieval of a superordinate category name), impaired generation of the names of objects within a superordinate category, and an inability to retrieve information about object properties – including sensory-based information (shape, colour) and functional information (motor-based properties related to the object's use, or other kinds properties). The impairment is not limited to stimuli presented in a single modality, like vision, but rather extends to all tasks probing object knowledge regardless of stimulus presentation modality (visual, auditory, tactile) or format (words, pictures) and all categories. The performance obtained at semantic tests is generally determined by the severity of the disease, the familiarity and typicality of the stimuli used and the specificity of information required by the task. Broad levels of knowledge are often preserved, while specific information is impaired. Longitudinal studies investigating types of errors in picture naming show clearly this pattern of semantic degradation. While in the first stage of disease patients made semantically related naming errors (horse for zebra, as the patient reported above) in the later stages the errors become more general (animal for zebra). A similar pattern of semantic memory loss has been documented in patients with Alzheimer's disease (Martin & Fedio, 1983; Gonnermann et al., 2004). Semantic memory impairments in AD are discussed chapter 3.

The vast majority of these works focused on the concrete concepts. Crutch and Warrington (2006) investigated the existence of comparable gradual degradation of semantic memory for abstract concepts. They showed this effect both in AD and SD patients, suggesting that the partial degradation could be considered a general characteristic of a degraded knowledge base, not restricted to concrete concepts only (see chapter 3 part III).

The Living – Non Living dissociation. In addition to the generalised impairment reported above, some aspects of semantic memory can be selective impaired, providing a unique opportunity to understand how semantic memory is organised. Patients with category-specific semantic deficits present with disproportionate or even selective impairments for one semantic category compared to other semantic categories. Category-specific deficits refer to the semantic-lexical level, and are not specific for modality of input and output, although patients can also show deficits at the presemantic level (see Mahon & Caramazza, 2009). Also in this case, as reported above, patients have more difficulties in distinguishing among basic level concepts than among superordinate categories. The most common dissociation involves living (animals, fruits and vegetables) and non living entities (tools, vehicles, furniture). However a dissociation between abstract and concrete concepts has been also reported (see below). The seminal report by Warrington and Shallice (1984) raised a great deal of interest in the possibility that patients with semantic deficits could show a selective deficit for a particular semantic category or domain. The authors described four patients with semantic impairments due to HSVE, which were evident on a range of tests. Importantly, the patients showed a differential impairment in their knowledge of items from the semantic domains comprising living and nonliving concepts, with the former at floor and the latter near ceiling in one patient (JBR) and very high in the other (SBY). Several cases have been subsequently reported, and in most of these the living entities domain is more impaired than artifacts (Barbarotto, Capitani, Spinnler, & Trivelli, 1995; Caramazza & Shelton, 1998), such as in the case of the patient Helga (Mauri et al., 1994) reported above. A poorer performance on artefacts than on living things has been also reported (Cappa et al., 1998; Sacchett & Humphreys, 1992; Warrington & McCarthy, 1987). More than a hundred case of category specific semantic impairment have been reported and, according to a recent review (Capitani et al., 2003), the most common finding is greater impairment for the living category. Capitani et al. (2003) reported that on 79 case studies, 61 showed a disproportionate deficit for Living entities and 18 for artefacts. Since reports seemed to show that category-specific impairments tended to affect living concepts most commonly, researchers began to investigate whether the very existence of these impairments could be explained by poorly matched stimulus materials. This is because studies in healthy participants have demonstrated that living and nonliving concepts differ along several dimensions such as familiarity, frequency, visual complexity (Funnell & De Mornay Davies, 1996, Snodgrass & Vanderwart, 1980) and several others (see chapter 2, 3 and 4). It is possible, therefore, that living and non living items do not differ conceptually, but that living things are merely more difficult to retrieve for a damaged system.

Following robust demonstrations of category-specificity (e.g. Hillis & Caramazza, 1991), a logical progression for research was to find the neuroanatomical correlates of such behaviors. Gainotti (2000) compared the lesions of a large number of published cases of patients with category specific deficits. He found a consistent relationship between site of lesion and the semantic category impaired. When patients showed selective problems with living things, the lesions were bilateral (but asymmetric, usually larger on the left) and involved the anterior, mesial and inferior parts of the temporal lobes. In contrast, patients with a category-specific impairment for nonliving things had unilateral lesions, particularly involving the frontoparietal areas of the dominant hemisphere.

Brambati et al (2006) showed that the naming accuracy in patients with neurodegenerative diseases for living items (animals and fruits) correlated with gray matter volume in the medial portion of right anterior temporal lobe, while naming accuracy for living items (household items, vehicles, and manipulable objects) correlated with the left posterior middle temporal gyrus. More recently, Capitani et al. (2009) found that in patients with posterior cerebral artery infarctions a disproportionate semantic deficit for fruits and vegetables is associated to a lesion in the intermediate portion of the fusiform gyrus.

Many functional imaging studies have attempted to assess whether various brain regions are differentially active for concepts from different domains in healthy participants. Results have not been entirely consistent across studies, probably because the studies used a different tasks, different stimuli, and different experimental designs (but see chapter 4).

Abstract – concrete dissociation. Most of the research following the first studies of Warrington et al. (1975; Warrington & Shallice, 1984) concerned concrete concepts, despite the fact that, in the seminal report in 1975, Warrington described that abstract and concrete knowledge may be selectively impaired (Warrington, 1975). Patient AB showed a better performance on concrete than on abstract words, while patient EM showed the opposite trend (not significant at statistical level), namely a better performance on abstract words (see Warrington, 1975)[1]. A better performance for concrete items, known as concreteness effect, is a common and robust finding reported both in healthy subjects (deGroot, 1989; James, 1975; Kroll & Merves, 1986; Paivio, 1991) and in neurological patients that generally show an exaggeration of this effect, such as in patients with aphasia and with deep dyslexia (Coltheart et al., 1980; Goodglass et al., 1969; Jefferies et al., 2007) and SD (Jeffereis et al., 2009). As we report in Chapter 3 (part III) only a limited number of studies have investigated the abstract domain of knowledge in AD patients, reporting a poorer performance for abstract than for concrete words (Rissenberg & Glanzer, 1987; for this issue see chapter 3 part III). Some investigators found a better performance for abstract words in respect to the concrete ones in HSVE (Sirigu et al., 1991; Warrington & Shallice, 1984), in SD (Bonner et al., 2009; Breedin et al., 1994; Cipolotti & Warrington, 1995; Loiselle et al., 2007; Macoir, 2009; Papagno et al., 2007; 2009, Reilly et al., 2006, 2007a, 2007b; Warrington, 1975; Yi

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[1] Note that Warrington reported that only for high frequency words no differences were detected between concrete and abstract words in both patients. For low frequency items, AB showed a significantly better performance on concrete than on abstract words, while patient EM showed the opposite trend. "However by analysis of the total pool of words to which the responses of AB and EM did not correspond, it can be shown that the pattern of correct responses to concrete and abstract words is significantly different in the two patients".

et al., 2007), and in patients with focal lesions (Bachoud-Lévi & Dupoux, 2003; Marshall, Chiat, Robson, & Pring, 1996; Marshall et al., 2001; Warrington, 1981).

An open debate concerns the reverse of the concreteness effect reported in patients with semantic dementia. On one hand, based on the evidences reported in literature, Ash and Grossmann (2004) proposed that a better performance on abstract words is a typical pattern in SD. Several authors suggested that the reversal of the concreteness effect is due to the loss of visual/perceptual knowledge in SD, because of the anatomical distribution of the pathology in visual association cortex; all these patients sustained damage to one or both temporal lobes (Bonner et al., 2009; Breedin et al., 1994; Yi et al., 2007). Nevertheless, the patient described by Papagno et al. (2009) performed better on visual than on non visual properties, and showed a reversal of the concreteness effect. The authors supposed that this effect is generally associated with an involvement of the left anterior temporal lobe (Papagno et al., 2009). In contrast, Bonner et al. (2009) showed an association with damage to the right temporal pole, but they used verbs as stimuli to asses the reversal of the concreteness effect, while the patient described by Papagno et al. showed no differences between abstract and concrete verbs. In contrast, Jeffereis et al. (2009) showing a better performance on more imageable concepts with respect to less imageable ones in a group of 11 SD, suggested that the reversal of the concreteness effect could be an exceptional finding in these patients. In favour of this hypothesis they report that Yi et al (2007) for example, showed the reversal of the concreteness effect in SD only for verbs, but not for nouns. Still, Bonner et al. (2009) highlighted that the findings reported by Jefferies et al. could be biased by the fact that abstract words were longer than the concrete ones.

1.2 Theories concerning concrete concepts

The first model concerning the representation of semantic memory posits a hierarchical organization (Collins & Quillian, 1969; 1972). General and specific information is supposed to be stored at different levels of the network. Although the idea of a strict hierarchy was abandoned by Collins and Loftus (1975), this network model has formed the basis of much subsequent cognitive research in semantic memory, and has inspired many theories concerning its organization. Feature-based theories of semantic memory assume explicitly that concepts are composed of "smaller elements of meaning", subordinate elements, or features (McRae, de Sa, & Seidenberg, 1997; Rosch, 1973; Smith & Medin, 1981). In this framework, categories arise from the similarity or the overlap of these features. The feature comparison model (Smith et al., 1974) assumes that concepts are represented as a combination of “defining” and “characteristic” attributes. However an important criticism is that it is not possible to identify the defining attributes for all meanings (Fodor, 1980). More recently a featural approach has derived from neuropsychological (Allport, 1985; Warrington & Shallice, 1984) and from computational neuroscience (e.g. Farah & McClelland, 1991). In this approach, features are not abstract, but grounded (to some extent) in perception and action. Many authors, as discussed below, assume that concepts can vary according to the role of different types of features, such as sensorial or motor (e.g., Barsalou, Simmons, Barbey & Wilson, 2003; Cree & McRae, 2003; Damasio et al., 2004; Gallese & Lakoff, 2005; Rogers et al., 2004; Vigliocco et al., 2004). In addition to the type of feature, models of semantic memory also take into account a number of properties of features that determines the conceptual structure. One of the key relations between semantic properties is correlation, the degree to which features co-occur together (Garrard et al., 2001a; McRae et al., 1997). In addition, distinctiveness concerns degree to which particular features within a concept are shared by other members of the same category. Connectionist models assume that knowledge is instantiated in neural networks, where a node represents single features, and concepts are represented as patterns of activation across a large set of features. Early models were based on small and arbitrary set of features, but more recently models have adopted larger set of features collected empirically. In these studies healthy subjects are asked to generate attributes of concepts in response to their name (Garrard et al., 2001a; McRae et al., 1997; McRae & Cree, 2002; Cree & McRae, 2003; McRae et al., 2005; Vinson & Vigliocco, 2002, see also for abstract concepts Barsalou & Wiemer Hastings, 2005) or to the corrinsponding picture (Mechelli et al., 2006). While these definitions are not considered as a literal record of semantic representations, they are considered to represent a window to semantic representations (McRrae et al., 1997). Using the generated definition, the analysis of conceptual structure can be conducted according to many variables, and comparisons can be made of the distribution of these variables across semantic categories and broader domains.

Although categorization has been explored in much developmental psychology (Mandler, 1992) and cognitive psychology models (Collins & Quillian, 1969), neuropsychological demonstrations of dissociations between different semantic categories has renewed interest in how category may be represented in the brain. Following the demonstration of a number of regularities across patients, in terms of the concepts that tend to be impaired or spared together, it has become necessary for theories concerned with the organization of semantic memory to be constrained by the evidence coming from patients with these types of impairment. A number of theories of semantic memory organization have been proposed to account for the category-specific semantic deficits.

Here we separate them in three broad groups of theories. The first group proposes a semantic system organized by different types of knowledge (different modality), while the second proposes a semantic system organized by category. Both share the assumption that deficits are due to a differential or selective damage to the neural substrate upon which the impaired category of items depends. The third view, based on the correlated structure principle, does not involve segregated semantic representations. It proposes that semantic memory is a system that represents statistical regularities in the co-occurrence of object properties in the world. Some theoretical proposals are trying to council some of the previous theories, putting forward new models in which different modality specific information is combined into abstract representations in an modal semantic junction level, through the identification of modality-specific regularities during perception and action (e.g. the Distributed-plus-Hub View, Patterson et al, 2007). Finally, it is important to underline the fact that not all the authors agree with the idea that category-specific deficits are genuine, that is they are generated by a disproportionate loss of the characteristics connected to concepts that belong to the most impaired categories. Some authors, indeed, support the idea that category specific deficits are an epiphenomenon caused by an intrinsic difficulty in elaborating concepts belonging to the affected categories. As a result, whenever the cognitive resources decrease, the impairment becomes more evident for those concepts which are more difficult to elaborate (for further details see chapter 2, 3 and 4).

Sensory/Functional Theory. In order to account for the category-specific deficits Warrington and Shallice (1984) formulated the Sensory/Functional Theory (SFT), based on the assumptions that semantic memory is constituted by different modality-specific subsystems. SFT proposed the existence of two types of semantic knowledge: the sensory (colour, sound, smell) and the functional attributes (usefulness, value); the first is considered to be more important for the representation and identification of living things, the latter for identifying nonliving objects. The theory explains the category-specific deficits in terms of damage to the crucial information necessary to identify the category of a concept or to distinguish between members of that category. Because our representations of living things are more dependent on perceptual than functional attributes, they will be more degraded when there is a damage to the store of perceptual information, whereas man-made objects will be more affected by damage to the functional properties which are critical to their meanings (Warrington and McCarthy, 1983; Warrington and Shallice, 1984). An influential early connectionist network was developed by Farah & McClelland (1991) to model the dissociation shown in HSVE patients between their knowledge of living and nonliving concepts. The authors demonstrated that category-specificity could emerge following damage to a system that was organized according to sensory-functional knowledge type, rather than category per se. They asked healthy participants to underline the sensory and functional attributes from dictionary definitions and found that living things had a seven times more sensory than functional attributes, whereas these relative proportions were more equal for nonliving concepts. When these weightings were included in the representations of concepts in the connectionist network, damage to sensory units caused deficits for living things whereas damage to functional knowledge caused greater impairment for nonliving things. Caramazza and Shelton (1998) criticized the modality through which the authors derived the semantic properties, because the functional properties of living things were underestimated. In addition, criticisms to the Sensory-Functional Theory mainly come from studies of patients that show deficits in identifying living beings, with equivalent impairment for both perceptive and functional/associative knowledge (Blundo et al., 2006; Caramazza & Shelton, 1998; Laiacona et al., 1993; Laicona & Capitani, 2001; for a review see Capitani et al., 2003). In addition, the observation of patients with more severe deficits of visual/perceptive knowledge compared to functional/associative knowledge in absence of deficits for the living category (Lambon-Ralph et al. 1998; Miceli et al., 2001;) cannot be reconciled with Warrington et colleagues' predictions. Finally, the theory is not able to explain the case of patients with greater deficits for fruits/vegetables than animals (Samson & Pillon, 2003; Hart et al., 1985) as well as the case of patients with greater deficits for animals than for fruits/vegetables categories (e.g., Blundo et al., 2006; Caramazza & Shelton, 1998). The Sensory-Functional Theory is not able to explain all the clinical evidences reported in literature.

Beyond Sensory/Functional Theory. Several variants of the SFT have been subsequently proposed (Borgo & Shallice, 2001; Humphreys & Forde, 2001; Martin, Unterleider, & Haxbury, 2000). For instance, Humphreys and Forde (2001) assume that living things are more visually similar than non living things. A damage to areas processing visual structural description is suggested to result in n a more severe impairment for living things, which are characterized by more perceptual crowding among their structural descriptions. According to Borgo and Shallice (2001) the "sensory quality categories", including living things, non edible materials, liquids, and edible substances, depend differentially from colour and texture information. However Laiacona and colleagues (2003) reported a patient who had spared knowledge of sensory-quality categories with the exception of L.

As the binary distinction between sensory and functional features proposed by SFT seems to bee too simple to capture all the different category-specific deficits, some authors suggested that several dimensions may be important in distinguishing between different categories, on the basis of feature generation tasks with healthy subjects, (Cree & McRae, 2003). Two relatively large scale studies, including over 400 concepts were conducted by Cree & McCrae (2003) and Vinson *et al.* (2003). The concept definitions generated by the participants were analyzed for the type of features included. The two studies used two slightly different classifications of feature types (Cree & McCrae, 2003; Vinson *et al.*, 2003). Vinson et al. (2003) found that visual features (e.g. color, form) were more important for animals and fruits and vegetables (although less so) but far less important for most non living categories. Nonvisual perceptual (e.g. taste and texture) were important for fruits and vegetables and clothing compared to other categories. Non living categories were far more reliant on functional features than living categories, a pattern that was also reflected in the quantity of motoric features than living categories.

Cree and McRae (2003) asked to generate definitions for 541, classified in nine knowledge types of features: colour, visual parts and surface properties, visual motion, smell, sound, tactile, taste, function, and encyclopaedic. When hierarchical cluster analyses of features were performed, they found that three semantic domains could be differentiated: animals, fruits and vegetables, and nonliving categories. Features types that were important for, and separated creatures from the other domains included visual-motion features (they engage in self-initiated actions) but not their function. They were more defined by visual colour features than NL but less than fruits and vegetables. In contrast Nonliving things were defined by their function/ motor features and not by their visual motion features. Fruits and vegetables while forming a distinct cluster did cluster with NL at late stage on analysis. They were differentiated on the basis of their visual colour and taste features, while being low in visual motion and visual part. They tend to cluster with NL due to their possession of function (we peel, cook and eat them). These studies show that semantic categories may emerge from knowledge of feature types, and that feature type is an important part of conceptual knowledge. Cree and McRae (2003) found that no single knowledge type was capable of explaining the entire category trend reported in category literature, but rather an interaction between all of them. Importantly, the authors argue that a knowledge type analysis provide any insight into the finding that L deficits are far more common than NL deficits.

Many neuroimaging studies have focused on determining in which areas of cortex these different semantic features may be represented (Martin et al., 2001; Martin et al., 2007; Marques et al., 2008; see also chapter 4). Neuropsychological and functional imaging studies have shown that relevant information about an object (such as visual, auditory, olfactory, motor and linguistic) are partially stored in the same or near the sensory and motor systems activated during the acquisition of that information (e.g., Boronat et al., 2005; Gainotti, 2004; Gonzalez et al., 2006; Martin, 2007; Perani et al., 1995; Simmons, Martin, & Barsalou, 2005; Tettamanti et al., 2005; see

Martin, 2007; but see Mahon & Caramazza, 2008). For example, Martin et al. (1995), asked subject to generate colour and action words in response to objects names. While both activated a common network of areas, generating colour words activated ventral temporal cortex, while generating action activated a posterior region in the middle temporal gyrus. The region of the fusiform gyrus activated by colour condition was near to regions known to be active in colour perception (Chao & Martin, 1999). The middle temporal activation for "action" was located near the regions active during motion perception. Hauk et al. (2004) showed that reading words denoting actions specific for tongue, finger and leg activated the same regions in the premotor cortex also activated when subjects moved tongue, finger and leg. Based on those types of studies the Sensory-Motor Property Theory (Martin et al., 2000) assumes that semantic categories are represented in the same sensory motor areas responsible of their acquisition. In addition to sharing the same predictions as the SFT for living entities, this model suggests that identifying manipulable non living things depends from intact knowledge about how to use them (see chapter 4). Mahon and Caramazza (2008) suggested that the evidence coming from apraxic patients who are impaired in using objects, but can name the same object and recognise its pantomime are not in agreement with this theory. These data, indeed, suggest that the integrity of the motor processes is not necessary to name and recognise the use of objects. However, a recent study in a group of unilateral stroke patients (Mahon et al., 2007) suggests that action knowledge associated with objects is relevant for successful identification of the objects. The authors documented a relationship between performance in object identification and object use only in patients with lesions involving the parietal cortex, but not in patients without parietal involvement.

Domain-Specific Hypothesis. Caramazza & Shelton (1998) have proposed the Domain-Specific Hypothesis, which considers semantic categories as the principal element of organization of the conceptual system. Categorical organization is considered to result from evolutionary pressures that have shaped a few mechanisms, specialized in distinguishing, perceptively and conceptually, different categories of objects. Following this hypothesis, only those functional systems, evolutionary relevant for the survival and the reproduction of an individual can be considered as relevant. Different semantic categories are then represented in innate, specialized, functionally dissociable neuronal circuits. These authors suggested that a tripartite distinction is evident in pattern of impairments, as animals, fruit and vegetables and tools can be damaged independently. This is largely based on a single case, EW, who had a selective impairment for animals relative to plants and artefact (Caramazza & Shelton, 1998) and on cases with a selective deficit for fruit and vegetables and not animals (e.g., Hart et al., 1985). In addition, for each category both visual/perceptive information and functional/associative information are stored together and the category-specific deficits are not determined by a selective deficit of recovery of a particular kind of knowledge (Caramazza & Sheldon, 1998). This hypothesis can explain cases with a disproportionate deficit for living things and an *equivalent* impairment for visual/perceptual and functional/associative knowledge. However, whereas the dissociation between animals and plants is fully compatible with the categorical account, inanimate entities such as musical instruments are not related to any evolutionarily relevant distinction and thus do not fit this explanation. Thus, the Domain-Specific theory cannot account for patients that show dissociation which do not reflect the evolutionary categories predicted by the theory (Siri et al., 2003). In addition, it cannot account for the association of deficits for L and some categories of NL such as musical instrument (Basso et al., 1988) as it predicts that damage to the store for animals should leave the store for artefacts intact (unless anatomical proximity allows both system to be damaged, but more one than the other). In order to overcome these limitations, some authors have proposed alternative solutions, suggesting that both domain and feature type are involved in the organization of conceptual knowledge (Mahon & Caramazza 2003; Miceli et al., 2001). Mahon and Caramazza (2009) proposed The Distributed Domain-Specific Hypothesis (see also the Domain-Specific Sensory-Motor Hypothesis, Mahon & Caramazza, 2008). Extending the original Domain Specific theory, the authors suggested that both "object domain and a distributed network of modality-specific representations constrain the organization of conceptual knowledge of objects". They assume that the domain remains the first principle of organization, but within each domain there is a specialization reflecting different modalities. In this way, different subsystems process different properties, for example for living things there is one subsystem for visual motion and one for affective properties. Functional connectivity plays an important role in relatin information deriving form different subsystems(different types of information).

Correlated structure accounts. Proponents of a correlated structure accounts argue for a single semantic store in which structure emerges from the distribution of features across categories (Caramazza et al., 1990). Connectionist models have provided valuable ways of specifying in explicit terms the internal structure of concepts. In this framework, the semantic system is a single, highly distributed network, in which all concepts are represented as patterns of activation over many units corresponding to semantic properties or features. Each concept therefore has a specific structure, which is determined by the set of features that it activates and relation among those features. These models enable the exploration of the effects of representational structure on the behavior of neural systems under damage, and predict that severity of brain damage is a major determinant of category-specificity. The Organised Unitary Content Hypothesis (OUCH: Caramazza et al., 1990) does not propose separate stores for perceptual and functional knowledge, but argues that all types of knowledge are stored in a single amodal semantic system. The model takes account of the degree of feature intercorrelations within concepts, and evidence that members of a category share many features in common. The bundles of intercorrelated properties are differentially distributed in categories of living and nonliving things, and the semantic space is not homogenous but “lumpy”- some regions are densely packed and others are sparsely occupied. The denser regions represent concept domains characterized by highly correlated properties, and these are most likely to correspond to living concepts. Focal damage can therefore lead to a category-specific deficit if it affects a region of semantic space where such similar concepts are stored. This leads to the prediction that semantic categories with highly correlated properties are more likely to be damaged as a category, and this is in line with the demonstration that deficits for living concepts are by far the most common. While OUCH can account for almost any pattern of category-specific deficit found, this is by virtue of its being underspecified in terms of conceptual structure and semantic organization (Caramazza & Shelton, 1998). Since the OUCH model, other accounts have emerged which consider correlation to be an important factor in determining conceptual structure, but also include other factors. The model proposed by Devlin et al. (1998) considers three differences in the representational structure of the living and nonliving domains: living concepts have a higher ratio of sensory to functional features than nonliving concepts; living things have a higher proportion of correlated feature pairs than nonliving things; and in addition, living concepts are more likely to share features with one another whereas artefacts are more likely to be composed of idiosyncratic features. All these assumption have been implemented in a connectionist model. When the model was progressively lesioned, smaller amounts of damage caused greater difficulty in naming NL. With greater damage, the ability to name L began to decline sharply so that the reverse dissociation occurred. This was explained with reference to the shared features of L which can support performance with small amounts damage as they can fill in missing features on the basis of knowledge about correlation, but as damage increases, this shared features structure becomes a liability and whole groups of interconnected features are lost and the network lacks the critical mass of activation to support L identification. Due to artifacts being represented by distinctive features primarily, they are not affected by these dynamics of a degrading system and therefore the models ability to differentiate them, declines in a linear fashion (see also chapter 3). An alternative account is the Conceptual Structure Account (CSA: Tyler et al., 2000), that which is similar in many aspects to the model put forward by Devlin et al. (1998). Like that account it is based on the notion that L tend to have many shared properties, and these also tend to be strongly correlated. The distinctive properties of L that allow them to be distinguished tend to be weakly correlated with other properties and so are vulnerable to damage. In contrast NL tend to have fewer properties in total, and these properties are relatively more distinctive but not shared across members of the category. These differences in properties across the domains were supported by data generated in a feature norming study using normal participants. In contrast to other correlation based model (Devlin et al., 1998; McRae et al., 1997) the CSA stresses the importance of differential form-function correlations for conceptual structure and Tyler et al. argue that for artifacts, distinctive features enter into such correlation, while shared features are involved for L. In fact, non living distinctive perceptual features co-occur with distinctive functional information (e.g. sews-cuts). In contrast, for living things, while shared perceptual features co-occur with biological functional information (e.g. has eyes-seeing), distinctive perceptual features are not correlated with functional ones (e.g. has stripes for zebra). It follows that, when a system is damaged, the distinctive properties of artefacts and the shared properties of L will be more robust by virtue of these correlations, leading to opposite predictions with respect to Devlin et al model. In addition CSA does not consider knowledge type (feature modality) to be important in determining category specificity. These models are particularly suitable to account for the patterns of progressive loss of conceptual knowledge observed in neurodegenerative diseases, such as in Alzheimer's disease (see chapter 3). However a number of studies failed to confirm the predictions of both models (Duarte et al., 2009; Garrard et al., 1998; Zannino et al., 2002).

The Distributed-plus Hub View. Rogers, Patterson and colleagues (2004, 2007) assumed that the distributed brain regions and connections between them proposed by sensory motor theory are not sufficient to explain the neural basis of semantic memory and have proposed the existence of a unique and amodal convergence zone or hub that unifies information coming from sensory-motor systems. Starting from studies of patients with semantic dementia, the authors individuated the neural basis of the hub in the anterior temporal lobe. They suggested that the formation of unique concepts, starting from modality-specific information, requires the presence of a semantic hub, which represents an amodal and unitary semantic store, across all modalities and all categories. According to this model, a central amodal semantic system maps modality-specific perceptual information into an abstract semantic representation. These semantic representations can then be used for generalization of stored information to novel items, as well as for the addition of new information to already stored representations of familiar objects. This central junction supports the generalization of concepts that have semantic relations but that, at the same time, have only a few properties in common. In addition some factors, such as the number of semantic representations proximal to the property to be recovered and the level of condivision between semantic neighbours, could determine the production of a deficit for living things (Rogers et al., 2004). The Distributed-plus Hub View is an innovative approach that seems to be suitable to overcome the dichotomy between modal and amodal models. Several evidences support this model, in particular those derived from neuropsychological studies with SD patients. A recent study with healthy subjects using repetitive Transcranial Magnetic Stimulation (rTMS) has shown that the stimulation of the ATL leads to a generalized slowing in semantic tasks, both verbal and non verbal, but not in equally demanding non semantic tasks (Pobric et al., 2007). Functional neuroimaging studies seem less consistent in supporting the role of the anterior temporal lobe (ATL) in semantic processing, in that several fMRI failed to show activations in the ATL. However, it has been reported that methodological factors, as the semantic task used (Rogers et al., 2006), fMRI artefact (Devlin et al., 2000; 2002; Visser et al., 2009), and the statistical threshold (Visser et al., 2009) could account for these data. However the role of ATL is not still clear. For example, a recent study has shown a selective activation of the anterior temporal lobes once information about people (not about tools or buildings) was acquired, and these areas were functionally connected to a wider network, generally engaged by social cognition tasks (Simmons et al., 2009). A problem for the Distribute Plus Hub model arises from cases of SD patients who showed a better performance for abstract than concrete words (Papagno et al., 2007, 2009; but see Bonner et al., 2009 for a recounciling view). In fact these evidences suggest that ATL stores concrete but not abstract concepts, contrary to the assumption of an amodal region that makes a critical contribution to all types of concept, irrespective to the category. The data are however not univocal, because recently both neuropsychological and rTMS studies have shown that both abstract and concrete concepts are supported by the ATL (Jefferiers et al., 2009; Pobric et al., 2009).

1.3 Theories concerning abstract concepts

It is still a matter of debate whether abstract and concrete concepts are represented in the same way, as the definition of what is concrete and what is abstract is quite vague. In general, what is abstract is defined on the basis of not being concrete (Crystal, 1995).

The majority of studies concerning semantic memory has considered only concrete concepts. However exceptions derive from neuropsychological studies showing a double dissociation between abstract and concrete concepts. On one hand a better performance on concrete concepts can be explained by different theories, because abstract concepts have less features (Plaut & Shallice, 1991), less availability of the context information (Schwanenflugel & Shoben, 1983), and are represented only verbally (Paivio, 1986). For these theories, however, it is not easy to account for the reversal of the concreteness effect. Some authors have suggested that a better performance on abstract than concrete words in patients with semantic dementia or HSVE is in agreement with the sensory motor theory, in that it could be due to the loss of visual/perceptual features knowledge (Bonner et al., 2009). However, there are studies not supporting this hypothesis (see Papagno et al., 2009).

It has been suggested that theories based only on sensory-motor representations of the external experience to represent knowledge are not able to represent abstract concepts (e.g. Mahon & Caramazza, 2008; Dove, 2009). Some attempts tried to overcome these limitations.

According to the Conceptual Metaphor Theory, abstract concepts are grounded metaphorically in embodied and situated knowledge. The concrete conceptual domain of knowledge is used to describe the abstract conceptual domain (Lakoff & Johnson 1980; 1999; Gibbs, 1994; see Barsalou for a review, 2008). In this view, learning and representation of abstract concepts in the mind/brain is grounded in the learning and representation of concrete knowledge, which in turn is grounded in our bodily experience of the world. Although some studies showed that metaphors play a role in the conceptualization of some abstract domains (Gibbs, 2006), the role that it assumes in the representation of abstract concepts remains unclear.

Barsalou and Wiemer-Hastings (2005) suggested that in addition to sensory motor information also internal states, such as meta-cognition and affect, constitute important sources for the representation of knowledge, especially for abstract concepts. They showed that an important difference between abstract and concrete concepts is which situations are more salient for the two types of words. In their study subjects were asked to generate features for abstract, concrete and “intermediate” words. They found that abstract concepts focus on social event and introspective contents, and to a lesser extent on physical setting. Thus, abstract concepts are grounded in simulations of introspective experience and situations (e.g., Barsalou, 1999; Barsalou & Wiemer-Hastings, 2005). This theory, however, is not able to account for all abstract words in their variety.

The role played by linguistic experience in abstract words acquisition should also be considered. In fact, the meaning of some abstract words is not exhausted by experiential information only, as it requires also information that can be acquired through language (see Andrews & Vigliocco, 2009). The meaning of a word can be acquired perceptually, linguistically or by a combination of both (see Della Rosa et al., 2010; Wauters et al., 2003;). It has been demonstrated that concepts vary along a continuum, from the purely experiential to the purely linguistic. Concrete words are acquired mainly through experience, while the meaning of abstract words is tightly bound to language and acquired later (Della Rosa et al., 2010).

Alternatively, some models have proposed that knowledge is represented in terms of linguistic context-vectors, focusing exclusively upon linguistic data. According to the Hyperspace Analogue to Language (HAL, Burgess & Lund, 1997) and the Latent Semantic Analysis (LSA, Landauer & Dumais, 1997) our knowledge is organized in a propositional way, and that the meaning of a concept/word depends on lexical co-occurrence and semantic relatedness. These models extract and represent the meaning of words, basing on statistical computations applied to a large corpus of existing texts. This hypothesis is motivated by the fact that words that behave similarly within a language (in terms of statistical co-occurrence) are also often conceptually related (Landauer & Dumais, 1997; Burgess & Lund, 1997). However, these models failed to account for how any kind of knowledge acquired can be related to the world (see Andrews & Vigliocco, 2009).

Although the contribution of experiential and linguistic data has been considered independently, both are important to the semantic representations of concepts. A combination of both sources of knowledge, which are not mutually exclusive, could represent a promising way to elaborate a theory of semantic memory representing both abstract and concrete words (for a computational model in this direction see Andrews et al., 2009).

The first attempt to be considered is the Dual Code Theory (Paivio, 1971) a mixed approach, in which language and simulation work together to produce human cognition (e.g., Barsalou, Santos, Simmons, & Wilson, 2008; Barsalou, 2010). This theory claims that there is a dual coding system, responsible for the storage of the semantic representations related to concepts. One is grounded in information derived from our perceptual experience, while the other is based on verbal information derived from language. According to this position, the differences between abstract and concrete concepts can be ascribed to the different availability of the two systems for concrete concepts (perceptual and verbal) with respect to abstract ones (only verbal). More recently Barsalou et al (2008) proposed the Language and Situated Simulation Theory (LASS). LASS is based on the assumption that representations and processing of the concepts rely on multiple systems, including both language and situated simulation. These two systems interact continuously in order to form conceptual processing, and with different mixtures depending from stimuli and task conditions. When a word is presented, both linguistic and simulation systems become active. While the activation of the linguistic system peaks earlier, because the representations of linguistic forms are more similar to the presented word, situated simulation is more delayed and deeper. In LASS theory, the meaning resides primarily in the simulation systems. Evidences supporting LASS theories derive from behavioural (Solomon & Barsalou, 2004; Santos et al., in press) and fMRI studies (Simmons et al., 2008). For example, in a property generation task subjects generated first words linguistically related to the cue, such as associated word and words phonologically or morphologically related to the cue. Later the subjects generated aspects of situations, such as setting information, mental states and physical properties (Santos et al., in press).

Vigliocco et al. (2009) suggested that both experiential (sensory, motor, and affective) and linguistic (verbal associations arising through patterns of co-occurrence as well as syntactic information derived from the general linguistic context in which words appear) information contribute to the representations of the meaning of both concrete and abstract concepts. Concrete and abstract word meanings differ in the types and proportions of experiential and linguistic information. Concrete concepts are characterized by a statistical preponderance of sensorimotor information, while abstract words are characterised by a statistical preponderance of affective and linguistic information. Evidence in favour to the fact that emotional content contributes to the representation and processing of abstract concepts is derived from a study with healthy subjects, in which the authors demonstrated that abstract words have a processing advantage over concrete words, and this advantage was due to the emotional content, greater in abstract than in concrete concepts (Kousta et al., in press; see chapter 2).

In conclusion, it seems that a single principle of organization and a single source of knowledge are not sufficient to explain entirely the organization of the semantic memory, including both abstract and concrete concepts.

1.4 Outline

The main aim of this work is to investigate the organization of semantic memory, and its degradation in patients with Alzheimer's disease. Accordingly, the following chapters report a normative (Chapter 2), a neuropsychological (Chapter 3) and a functional-Magnetic-Resonance-Imaging (*f*MRI, Chapter 4) studies, aiming to provide novel methodological tools, as well as resulting empirical evidences, to this important issue.

After reviewing available knowledge on the organization of semantic memory (Chapter 1), I describe the construction and standardization of two new batteries of semantic memory tests, concerning concrete and abstract concepts respectively, on healthy subjects (Chapter 2). These tools entail a number of advantages over the existing alternatives, in that they control for several variables that are known to influence subjects' performance. In addition, this study represents an important way to overcome the lack of Italian standardized tests assessing semantic memory.

In Chapter 3 I describe the application of these two batteries to the investigation of three different crucial aspects of semantic memory impairments in Alzheimer's disease, namely, the semantic degradation at feature level and its relation with picture naming performance, the presence of the Living and Non Living dissociation, and the status of abstract knowledge.

In Chapter 4 the results of an *f*MRI study are shown, aiming to add further evidence to the neural bases of semantic memory, and particularly the issue of category-specificity, employing stimuli carefully controlled for several confounding variables on healthy elderly individuals.

Finally, in Chapter 5 the findings are briefly summarized and discussed in terms of their contribution to the issue of the organization of semantic memory.

Chapter 2: The assessment of semantic memory: a normative study

2.1 General introduction

Studies of patients with semantic memory impairments have contributed enormously to understanding of the organization of conceptual knowledge in the human brain. Several forms of neurological disorders, both focal, such as herpes simplex encephalitis, stroke, or head injury, and neurodegenerative disease, such as Alzheimer's disease and semantic dementia, can lead to different semantic memory impairments. An heterogeneous picture of the semantic deficits within or across these different patient types, characterized by a general disorder of conceptual knowledge or by a selective impairment of different semantic categories as abstract words (Warrington, 1975; 1981), biological entities (McCarthy & Warrington, 1991; Warrington & Shallice, 1984) or manmade artefacts (Warrington & McCarthy, 1987; 1983), has been reported.

As the majority of research into semantic representation has focused on how concrete concepts are represented and processed, neglecting the abstract ones, also neuropsychological assessment has addressed almost exclusively questions relating only to concrete knowledge impairments (e.g. artefacts and animals), although not without problems (e.g. Laws, 2005).

Semantic memory deficits are frequent, and a variety of clinical tasks are commonly used to asses them. However, its evaluation is not always straightforward. A poor performance on semantic tasks can be secondary to deficits involving other cognitive abilities that interact with semantic memory (Chertkow, Whatmough, Saumier, & Duong, 2008). For example, different processes could be responsible of a disorder on picture naming, a quick and easy-to-administer test largely used in the assessment of semantic memory. If a patient is enable to name the picture of a zebra and no further information are available, we can suppose that it could be due to a purely visual processing problems, or to the loss of the concept "zebra" and its features (e.g. "has stripes") from his semantic memory or to a difficulty accessing the sound form of words (Saumier & Chertkow, 2002). Thus, assessing semantic memory it is undoubtedly important to evaluate the integrity of visual input to semantic memory using tests such as matching two pictures of an object that are depicted from different viewpoints, copying simple geometric figures and discriminating between real and unreal objects. In addition tests, as deciding whether or not a spoken utterance or a written-letter sequence is a word, are generally used to assess the integrity of word representations (Chertkow et al., 2008). As impairments may result from degradation of a particular sensory modality of input or output, and not from the loss of semantic information (Ratcliffe & Newcombe, 1982; Shallice, 1988), the principle underlying evaluation of semantic memory is the assessment of knowledge using different modalities of input and output. Tests traditionally used to assess semantic memory integrity for concrete concepts include:

- Category fluency, that refers to the ability to retrieve words within a category, e.g. animal, fruit etc.
- Picture naming or confrontation naming, in which subject is asked to name the picture presented; items may be graded for familiarity (Graded Naming Test; McKenna & Warrington, 1983), for frequency (Boston Naming Test; Kaplan, Goodglass, & Weintraub, 1983), or for typicality (LOST, Adlam, Patterson, Rogers et al., 2006b),
- Naming to description, in which subject is asked to name an item after a verbal description
- Generation of verbal definitions, in which subjects is asked to describe\provide a definition of a concept
- Verification of semantic attribute questions, in which subject is asked to answer questions concerning attributes of concepts
- Sorting pictures of objects or words, in which subject is asked to sort pictures or words at different levels of specificity, generally at superordinate, category, and subordinate levels
- Word picture matching, a word comprehension task in which the subjects is asked to point to the picture, among foils, named by the examiner
- Tests of associative semantics, in which the subject is asked to match a stimulus with one of two alternative pictures, an example is the Pyramids and Palm Trees test (PPT; Howard & Patterson, 1992)

“A pattern of consistency over testing sessions, together with item specific failure on a range of tests, suggests semantic memory impairment” (Garrard, Perry and Hodges, 1997). Several of these tasks are generally included in semantic memory batteries, used to investigate semantic memory deficits for concrete concepts (Adlam et al., 2010; Hodges, Salmon, & Butters, 1992a; Hodges, Patterson, Oxbury, et al., 1992b; Laiacona et al. 1993; Moreno et al., 2005). Actually the most known is the Cambridge Semantic test battery (Adlam et al., 2010; Adlam et al., 2006b; Hodges et al., 1999; Hodges & Patterson, 1995; Hodges et al., 1992b). From the original version (Hodges et al., 1999; Hodges & Patterson, 1995) different updates have been made changing the number of stimuli and the tasks adopted (for example including or not the generation of verbal definitions). The most recent version is based on 64 items and 5 different tests including production and comprehension tasks: category fluency; picture naming of line drawings; word–picture matching, sorting of pictures and words and the Camel and Cactus Test (CCT), a measure of semantic association (Bozeat, Lambon Ralph, Patterson, Garrard, & Hodges, 2000). CCT has been designed along the principles of the most known Pyramids and Palm Trees test (PPT, Howard & Patterson 1992); however CCT resulted more sensitive to mild semantic impairments (Adlam et al., 2010). This battery has been extensively used in the assessment of semantic memory impairment in patients with neurodegenerative diseases, as Alzheimer's Disease and semantic dementia. In addition other specific tests of non-verbal semantic knowledge were developed for this purpose, as the Object knowledge task, assessing associative information, functional knowledge and use of objects (Adlam, Bozeat, Arnold et al., 2006a); the Color selection task (concerning the selection of the correctly coloured animal or object), the Object selection task (concerning the selection of the correct object or animal from two alternatives, where one is altered, e.g. an elephant with normal-sized rather than large ears) and the Enviroment sound Test (regarding matching of object pictures to their characteristic sounds, Bozeat, Lambon Ralph, Patterson et al., 2000; Hodges & Patterson, 2007). The semantic battery created by Laiacona et al. (1993b) is the only battery actually used in Italy. The battery consists of 3 tasks, all using the same 60 stimuli: picture naming, word picture matching, a questionnaire on semantic features of the concepts. Later versions included a category fluency and a Reality Decision Task, in which subject is asked to discriminate between real and unreal objects (Barbarotto, Capitani, Spinnler et al., 1995; Laiacona, Capitani, & Barbarotto et al., 1997). This battery has been particularly used to investigate the dissociation between living and non living entities.

The assessment of abstract concepts impairments results more complex. As the majority of theoretical accounts, also neuropsychological assessment has focused on the differences between concrete and abstract domains. Thus, the tests generally used adopt both abstract and concrete words, in that they are arranged to investigate the abstract concrete dissociation.

Verbal modality is generally the only used, in that it is naturally rather difficult to represent abstract concepts into pictorial material. However the evaluation requires both production and comprehension tasks. Examples of production tasks include:

- Category fluency (e.g. for abstract domain: positive and negative feelings, Papagno, Capasso, & Miceli, 2009)
- Free association task, in which subject is asked to report the first word that come to mind associated to the presented word or to report all the words that come in mind in a minute (Vesely, Bonner, et al., 2007)
- Word definition in which subject is asked to give the most complete definition of concepts (Breedin, Saffran & Coslett, 1994; Macoir, 2009; Papagno et al., 2009; Warrington, 1975)
- Picture description-based tasks, in which subject is asked to describe the image presented (Crutch & Warrington, 2003)

- Naming on verbal definition (Rissemberg & Glanzer, 1987; for a particular version see Marshall et al., 1996).

An example of naming on definition task for both abstract and concrete concepts is represented by the Italian test created by Novelli and co-workers (1986). The subject is asked to produce the name corresponding to 38 definitions (28 of concrete words and 10 of abstract words) orally presented by examiner. In case of failure, the subject is asked to select his response among three words (the target and two semantic foils). The use of tasks with a multiple choice presentation format could minimized the patients' difficulty with naming production or lexical retrieval as in a naming to verbal definition (Warrington, McKenna & Orpwood, 1998; Yi, Moore, & Grossman, 2007).

Examples of comprehension tasks include:

- Multiple-choice, naming-to-description Task that varies between studies for the number of distracters proposed (Yi et al., 2007), in some cases the choice is only one and the patient is asked to decide whether or not the word is appropriate for the definition (Papagno et al., 2009)
- Synonymy tasks, in which subject is presented with triplets of words from the same semantic category and asked to indicate the word least related in meaning to the other two (Breedin et al. 1994; Macoir, 2009; Papagno et al., 2009). In a different version the subject is asked to choose among two\three options the item semantically similar (Jefferies, Patterson et al., 2009; Concrete and Abstract word Synonym Test, Warrington et al., 1998) or more associated (Marshall et al., 1996) to the stimulus presented. In a further variant 3 different levels of synonymy comprehension are assessed (Crutch & Warrington, 2006).
- Concrete/abstract spoken word-to-picture matching, in which subject is asked to point to one of four pictures that matches with the word named by the examiner (Crutch & Warrington, 2007; Macoir, 2009; Shallice & Coughlan, 1980), in some case the picture is only one and the subject is asked to decide whether or not the picture matches with the word (Marshall et al., 1996). A recent version has been developed only for abstract words (Kunisue et al., 2007; Uno et al., 2003).

Another important aspect that must be considered in the assessment of semantic memory is that several variables influence the performance on lexical-semantic tasks both in healthy subjects and in patients. Parameters like frequency, familiarity, age of acquisition, tipicality can be considered as a measure of the difficulty of the concepts (Sartori et al., 2005). For example, high-frequency words are retrieved more quickly and accurately than low-frequency ones (McRae, Jared, & Seidenberg, 1990), and are generally more resistant to brain damage (Cuetos et al., 2008;

Hodges, Salmon, & Butters, 1992). Highly familiar and highly typical items are named more accurately (Funnell & Sheridan, 1992) and familiarity predicts naming performance in semantic dementia (Hirsch & Funnell, 1995; Lambon Ralph, Graham, Ellis, and Hodges, 1998). Words acquired earlier in life are recognised faster (Barry, Morrison, & Ellis, 1997) and resulted more resistant to deterioration (Cuetos et al., 2008; Cuetos et al., 2005; Forbes-McKay, Ellis, Shanks, & Venneri, 2005; Silveri et al., 2002) than those acquired later.

In addition these and several other parameters necessitate to be accounted for specifically when the impairment involves only specific categories of concepts (e.g. living-non living and abstract-concrete dissociations). The tests described above vary considerably with respect to the degree and amount of control of the variables tied to the stimulus sets employed. In Italy few published norms exist (Barca et al., 2002; Dell'Acqua et al., 2000; Della Rosa et al., 2010; Miceli et al., 2000; Viggiano et al., 2004), complicating the construction of tools able to detect the genuineness of the category dissociations. Furthermore, no explicit criteria exist for the number or the type of tasks to use for the assessment of category-specific deficits (see Laws & Sartori, 2005).

Clearly, for semantic memory tests to be used effectively in clinical practice, normative data indicating healthy performance levels need to be established. Even if many tests have been described, they are generally ad hoc test used for experimental studies only. Very few are standardized, and this is particularly true in Italy, where the normative data are available only for the semantic battery of tests created by Laiacona et al. (1993) and the three tests of Novelli and co-workers (1987; see also Italian norms for PPT, Gamboz et al., 2009).

In this study we introduce and standardize two new batteries of tests for the assessment of semantic memory impairments, one concerning concrete concepts (CaGi), the other the abstract ones (DeCAbs). The new batteries have some advantages over the existing alternatives in that they control for several variables that are known to influence the subjects' performance.

In addition this study represents an important way to overcome the lack of Italian standardized tests assessing semantic memory.

2.2 Construction and standardization of a new battery investigating concrete concepts

The loss of concrete knowledge has been addressed by several studies. As reported above, several forms of neurological disorders can lead to semantic memory impairments. A general and progressive deterioration of semantic memory has been reported in patients with neurodegenerative diseases, such as semantic dementia and Alzheimer's disease (Hodges, Graham, & Patterson, 1995; Hodges et al., 1992a; Martin & Fedio, 1983; Warrington, 1975). A crucial observation is that semantic memory impairments may involve only specific categories of objects. The most studied dissociation concerns living (L) and non living (NL) entities, with the former more frequently impaired than the latter (Capitani et al., 2003, see chapter 1). Both focal damage, such as herpes simplex encephalitis, stroke, or head injury, and diffuse brain pathology, as in Alzheimer's disease, may result in category-specific deficits.

Some authors have actually proposed that category effects are spurious consequences of stimuli artifact, and several factors have been identified in predicting category dissociations. Living things may be more vulnerable than non living things because they are associated to lower values of concept familiarity (Funnel & Sheridan, 1992) and word frequency, and with higher values of visual complexity (Stewart, Parkin, & Hunkin, 1992). In addition, living things are more semantically similar than non living things and consequently more easily confused (Cree & McRae 2003; McRae & Cree, 2002; Sartori & Lombardi, 2004). The role of semantic distance or similarity as a factor accounting for category specificity has been specified in a recent study by Zannino et al. (2006a; 2006b). They demonstrated that the disadvantage on living items observed in patients with Alzheimer's disease disappeared when semantic distance was taken in account. Sartori and Lombardi (2004) reached the same conclusions by introducing a new semantic variable. Based on their features norms, they calculated semantic relevance, "a measure of the contribution of semantic features to the core meaning of the concept" (Sartori & Lombardi, 2004). Highly relevant features allow to identify a concept and to discriminate it from other similar members of the same category. The features of the semantic representations of L were on average characterized by lower level of relevance, and consequently were more difficult to retrieve. Using a naming to verbal description task, the authors demonstrated that the impairment for L items both in Alzheimer patients and in a patient suffering from herpes simplex encephalitis, disappeared when stimuli were matched for semantic relevance.

The manipulability of objects may also influence the identification of stimuli. In particular, non manipulable objects were identified more quickly than manipulable ones when they were matched for familiarity; however the reverse pattern was found for items not matched for familiarity (Filliter et al., 2005). As suggested by the authors, these findings may indicate that the selection of items, combined with a lack of control of the familiarity, may in general favour NL, in that tools and animals are the most frequently used stimuli among those categories. However, the definition of manipulability is still unclear. In fact, there are at least two ways to interact with objects: grasping them or using them, so we could distinguish between grasping gestures associated with using an object for its intended purpose (functional manipulability) and those used to pick up an object (volumetric manipulability) (Bub et al., 2008). The results obtained by Filliter and co-workers refer to the volumetric manipulability.

The age of acquisition of a concept may also favour the processing of living items (Silveri et al., 2002). In addition living items are also more imaginable, have fewer lexical alternatives and a higher name agreement (Albanese et al., 2007) and are typically rated as having more emotional content than non living items (Brousseau et al., 2004).

Finally it is important to highlight that several other variables may influence lexical-semantic tasks, such as typicality (Garrard et al., 2001a) and number of features (Pexman, Lupker, & Hino, 2002).

From this summary of the relevant literature it is clear how difficult it is to test empirically the genuineness of the category specific deficits, because to the best of our knowledge none of the currently available semantic tests controls for all the confounding variables described above. Several studies have been carried out, varying considerably with respect to the degree and amount of control exerted upon combinations of variables tied to the stimulus sets employed, thus yielding contradictory results. Although some studies show category specific deficits when controlling for confounding factors (e.g. Laiacona et al.,1997; Martinaud, 2009), others report no category specific deficits (e.g. Tippett 1996, 2007). In particular it is interesting to note that Tippet and co-workers (2007) showed in the same group of patients with Alzheimer’s disease three different patterns of deterioration (a better performance on LT items than on NL, the opposite pattern and no difference between the two domains) on the basis of different stimulus selection (for similar evidences see also Sartori and Lombardi, 2004). On the other hand, however, Hillis and Caramazza (1991) described two patients showing respectively a greater impairment for L than NL and viceversa, using the same stimuli and task.

As reported above, semantic memory batteries are generally used to investigate semantic memory deficits for concrete concepts (Adlam et al., 2010; Moreno et al., 2005). An example is the Cambridge Semantic test battery (Adlam et al., 2010; Hodges et al., 1999; Hodges & Patterson, 1995). Although in the first version stimuli were not balanced for any confounding variables, the last version consists of two subset of stimuli selected in order to match living and non living things respectively for age of acquisition and for familiarity. This battery however does not take into account several of the factors which have been shown to affect performance, i.e. semantic relevance, semantic distance and so on.

The semantic battery created by Laiacona et al. (1993b) is the only standardized battery actually used in Italy. Variables such as name agreement, image agreement, visual complexity, familiarity, frequency and prototipicality of the stimuli are available, although the last one derived from non Italian norms (from Battig & Mountag, 1969, see Laiacona et al., 1993b), notwithstanding that this is culturally dependent parameter. In addition the approach used to derive the features for the questionnaire, a task of the battery, was not carried out in a systematic manner through the collection of features norms on normal subjects.

The aim of this study was to develop and standardize a new battery of semantic memory tests (CaGi), in order to assess the status of semantic memory in different neurological conditions and to overcome some of the limitations of existing tests, through both an empirically derived corpus of semantic features and rigidly controlling for different confounding variables which were identified as the possible undermining cause of category specific effects.

2.2.1 Test construction

We started from a set of 82 concepts (44 living and 38 non living things, see Appendix A.1) selected from previous database in order to obtain the values of confounding variables for both words (Dell'Acqua et al., 2000) and for colored images (Viggiano et al., 2004) and to be representative of different living and non living categories. Values of variables such as visual complexity (defined as "the amount of details and intricacy of lines and edges in the picture), Visual Familiarity (defined as "how frequently you come in contact with the stimulus, both in a direct way running into a real exemplar of the object and in a mediated way, seeing it represented in the media, as newspapers, TV or others") and Name Agreement were taken from Viggiano et al (2004), while the Word Frequency, Familiarity and Age of Acquisition from Dell'Acqua et al (2000).

Values of arousal, emotional valence were taken from normative study described below .

2.2.1.1 Norms for Familiarity, typicality, volumetric and functional manipulability

We conducted 4 different ratings in order to obtain normative data on Familiarity, typicality, volumetric and functional manipulability.

All of the subjects included in the norming studies were native Italian speaker and had normal or corrected-to-normal vision. For all the four ratings, the instructions were provided in written Italian and subjects were tested individually under the supervision of an experimenter. Each participant's responses were coded and saved as EXCEL files. We first examined their responses to ensure that each participant had understood the instructions and completed the rating adequately. We used two different criteria in order to exclude participants. The first was to exclude subjects who used the same response (for example 7) more than 85% of the total of responses for each list. The second took in account subjects' scores that were more than 2,5 standard deviations away from the groups average for each item.

Familiarity.- Although familiarity norms obtained by Dell'Acqua et al (2000) refers to concept familiarity, participants were asked to rate the familiarity of the concepts represented by black and white pictures. In order to avoid any confounding results, in that we use colored pictures, we have decided to collect norms for the familiarity of the 82 concepts.

30 subjects (mean age= 21,37 sd=0,81, 14 males, 16 females) were asked to rate the 82 concepts on a familiarity (FAM) scale. Two different list versions were created and the order of the words within every list was randomized. The familiarity (FAM) scale ranged from 1 to 7 in which 1 indicated unfamiliar and 7 indicated familiar. The instructions were based largely on those used by Della Rosa et al. (2010) who collected norms on 417 Italian words (see Appendix A.2). The data for 4 participants were discarded. In addition we computed the correlation of our variable with the other normative data previously collected by Dell'Acqua et al (2000) and Della Rosa et al (2010), in this last case 71 of the 82 stimuli used were in common. We found high significant correlations ($r=0,71$, $p<0,001$ with Dell'Acqua et al' stimuli; $r=0,802$, $p<0,001$ with Della Rosa database).

Typicality, volumetric and functional manipulability.- Norms for typicality, volumetric and functional manipulability were collected on the same sample of 16 subjects (8 males). The age of the subjects ranged from 55 and 85 years (age 64,43 ± 9,10). Only in the typicality rating, data for one participant were discarded as a result of failure to follow instructions.

For the typicality rating, participants viewed the 82 pictures in randomized order (4 different list versions were created), and were instructed to judge how typical each picture was within the corresponding category by saying a value on the scale from 1 to 7, in which 1 indicated *not typical* and 7 indicated *highly typical*. The instructions for typicality were based largely on those used by Dell'Acqua et al (2000, see appendix A.3).

For manipulability ratings participants were asked to rate the 82 concepts both on functional and volumetric scales. The two scales identify two ways to interact with objects, grasping gestures associated with using an object for its intended purpose (functional manipulability) and those used to pick up and move an object (volumetric manipulability) (Bub et al., 2008). Two lists of 82 words were created, where each word was rated on both scales and the order of the lists for each variable was randomized across subjects (two lists were created for functional manipulability and other two lists were created for volumetric manipulability). The scales for functional manipulability and for volumetric manipulability ranged from -3 to +3 in which -3 indicated respectively *no action association* or *cannot hold in hand and move* and +3 indicated respectively *high action association* or *can hold in hand and move.* The instructions for functional and volumetric manipulability were largely based on those used by previous investigators (Rueschemeyer et al., 2010; see appendix A.4, A.5). In this case, lists were distributed and participants were permitted to stop the rating at any time and restart at another time as long as they continued and handed in the list within a three day's time. The two manipulability scales (functional and volumetric) correlate significantly with each other ($r=0,547$, $p<0,005$).

Semantic feature production norms. 20 Italian subjects took part in the study (10 females; age mean=24,25 , sd=3,05; years of education mean=16,55, sd=1,60). The instructions were based on those used by McRae et al (2005) to collect their semantic features production norms (see appendix A.6). The subjects were asked to list as many features as possible in order to describe 82 concepts (44 living and 38 non living things). Examples of different types of features were provided. The sequence of concepts presentation was randomized for each subject.

The data were analyzed according to the criteria for feature categorization proposed by McRae et al. (1997). Quantifiers were removed, disjunctive proprieties, adjective-noun and verb-noun proprieties were divided, synonyms were collapsed together and lemmatization was performed. From the 4608 features obtained, idiosyncratic proprieties generated by fewer than 3 participants were excluded.

All the 1911 remaining features were classified into one of eight knowledge types: corresponding to Visual (visual–color, visual–parts and surface properties, and visual–motion), Smell, Sound, Tactile, Taste, functional/motor (regarding how people interact with objects) Taxonomic and Encyclopedic information (corresponding to all the other types of knowledge e.g. associative relationship with a concept). The first five types are also labeled as sensorial, the last three as non sensorial.

For each feature we computed:

1) Dominance or production frequency as the number of participants who listed a specific feature for a specific concept (between 1 and 20; Ashcraft, 1978; Garrard, et al., 2001a; McRae et al., 2005)
2) Frequency as the number of concepts in which a given feature appears (in respect to each category and to all concepts of database)
3) Two different measures of Distinctiveness:
    a) Distinctiveness as “the inverse of the number of concepts in which the feature appears in the norms” (Devlin et al.,1998; McRae et al. 2005) as the number of concepts in which the semantic feature appears divided by the total number of concepts in the database
    b) Distinctiveness as “the proportion of concepts within a category for which the feature in question was generated” (Garrard et al. 2001a).
4) Semantic relevance as non liner combination between dominance and distinctiveness (1) (see Mechelli et al., 2006; Sartori & Lombardi, 2004)

For each concept we computed:

1) Number of features
2) Semantic relevance mean, as the mean of semantic relevance values of all features for each concept.
3) semantic relevance sum, as the sum of semantic relevance values of all features for each concept.
4) Two different measures of Semantic distance as in Zannino (2006a)
    a) Semantic distance between each pair of concepts belonging to the same category, this index has been demonstrated to be important in tasks such as word–picture matching task (Zannino et al., 2006a).
    b) Semantic distance between each concept and the centroid of the relative semantic category, this index has been demonstrated to be important in identifying a concept as required in tasks such as picture-naming task (Zannino et al., 2006a).

From the 82 stimuli, 48 concepts were selected. The stimuli were divided into 24 living things (6 land animals, 6 birds, 6 fruits, 6 vegetables) and 24 non living things (6 furniture, 6 kitchen item, 6 tools, 6 clothing; see appendix B.1).

The stimuli were matched across the two domains for visual complexity (p=0,2), Visual Familiarity (p=0,08), Name Agreement (p=0,18) Word Frequency (p=0,1), Familiarity (from

Dell’Acqua database, p=0,62), Age of Acquisition (p=0,25), number of letters (p=0,14), Semantic Distance between concepts and centroids (p=0,61) Semantic Relevance mean (p=0,09), semantic relevance sum (p=0,16), arousal (p=0,76), emotional valence (p=0,1), volumetric manipulability (p=0,14). On the other hand, it was impossible to match for FAM, functional manipulability, number of features and typicality. Living things were associated with lower values of FAM , higher values of typicality and number of features than Non Living things (p<0,05).

2.2.2 Test description

The battery is composed of five different sub-tests, all including the same 48 stimuli described above. The sequence of presentation is randomized for each task.

Naming of coloured photographs. The subject is asked to name all the 48 stimuli (see appendix B.2 for an example of the stimuli used and for instructions). The stimuli were matched across domains for semantic distance (calculated between each concept and the centroid of the relative semantic category, see above; p=0,61). Less frequent names given by subjects are also accepted as a correct response if in the original norms (Viggiano et al., 2004) they are reported as the most frequent non dominant names listed by at least the 10% of the control subjects. The accepted names are shown in appendix B.2. Scoring is obtained attributing one point for each correct response (range 0-48).

Naming in response to an oral description. The subject is asked to name each of the 48 stimuli after a verbal definition (see appendix B.3 for instructions). For each concept a description is provided made of the two sensorial and two non sensorial semantic features with higher values of semantic relevance. Summed relevance for living and nonliving is matched (p=0,85). Less frequent names were classified as correct if three naive colleagues judged them as consistent with the description (see appendix B.3). One point is given for each correct response (range 0-48). Ex: *It is a fruit, it is yellow, it has half-moon shape, it is eaten by monkeys*

Word-picture matching test. The subject is asked to point at a target picture among other stimuli in response to a spoken word (see appendix B.4 for an example and for instructions).
For each concept three pictures are presented: 1 target and 2 foils taken from the same semantic category. Semantic distance of the pair of foils and relative target is matched between living and

non living (p=1) as well as the sum of semantic distance values of the two foils and target of each trial (p=0,99). The foils were then divided in: foils more similar to the target (one for each trial) and foils less similar to the target (one for each trial). The similarity was computed on the bases of the difference in terms of semantic distance between the foils for each target. There is no difference between living and non living things for both types of foils (more similar, p=0,81; less similar, p=0,94). The position of the targets is balanced among trials. One point is given for each correct response (range 0-48). An example of the test is shown in appendix B.4.

Picture sorting at four levels. The subject is asked to sort the 48 pictures (see appendix B.5 for instructions) according to 4 different levels:

1. General Superordinate: The subject is asked to sort the 48 stimuli into one pile for living items and in another pile for non living ones.
2. Category Superordinate: The subject is given the 24 living items and asked to sort them into the appropriate category (12 vegetables vs. 12 animals) followed by the 24 non living (12 tools and 12 not tools).
3. category: The subject is given the 12 vegetables items and asked to sort them into the appropriate sub category (fruits vs. vegetables) followed by the 12 animals (6 land animals vs. 6 birds), 12 tools (6 kitchen items vs. 6 not kitchen items), 12 not tools (6 furniture vs. 6 clothes).
4. Subordinate: The subject is given the 6 pictures of each sub-category which he is asked to sort according to binary choice (e.g. for fruits– it is eaten with the peel or not).

A general and a level scoring can be computed. In the first case one point is given for each correct response (range 0-15). In the latter the scoring is classified on the bases of the different levels considering for each the different number of stimuli.

Free generation of features and sentence verification. This task is divided in two sessions, in the first the subject is asked to say everything she knows about each concept; in the second session she is asked to answer questions related to the features she has not generated (see appendix B.6). Ten features were selected for each concept from the collected norms. The following criteria were used to selected the features for each concept:

1. 4 features with higher semantic relevance, of which2 shared (1 sensorial and 1 non sensorial) and 2 distinctive (1 sensorial and 1 non sensorial)
2. 4 features with lower semantic relevance, of which2 shared (1 sensorial and 1 non sensorial) and 2 distinctive (1 sensorial and 1 non sensorial)

3. 1 with higher and 1 with lower value of semantic relevance (different from those described above) independently of sensoriality or distinctiveness

Sometimes it was not possible to have every combination for each concept, so the following criteria were followed: relevance was considered first, then distinctiveness and at the end sensoriality. The median of the distribution of the values of semantic relevance of the features for each concept was used as cut-off in order to classify features with high (>= median) and low (<median) values of semantic relevance. Semantic relevance was matched between living and non living (p=0,8).

In order to classify the features as distinctive or shared we calculated the median of the distribution of the values of distinctiveness (calculated as in Garrard et al., 2001a) for each category. Features with a value of distinctiveness at or upper than median were considered shared, features with a value of distinctiveness lower than the median value were considered distinctive. However every feature classified as distinctive appears in 1 or 2 concepts at most (only 4 features appear in 3 concepts). Values of frequency and distinctiveness are made available.

Each question includes a correct and an incorrect choice. For questions at the subordinate level we used features that could be true for concepts belonging to the same superordinate category. The position of the correct feature is balanced among stimuli. An example is shown in appendix B.6.

Scoring: free generation and sentence verification are scored independently, however for both one point is given for each correct feature (for sentence verification range 0-480).

2.2.3 Battery standardization

2.2.3.1 Methods

Subjects

106 healthy subjects took part to the study (53 females, see appendix C.1). Their mean age was 55 (SD = 17,8, range 25 - 84 years) and the years of education mean was 11,35 (SD = 4,43; range 2 - 22). The distribution of demographic data is shown in appendix C.1. Subjects with past or present neurological or psychiatric illnesses or a corrected score less than 24 at Mini Mental State Examination (Folstein et al., 1975) were excluded.

Procedures

The battery was administered to all participants in two different sessions. The sequence of presentation of the items was randomized for each test. All subtests were administered and scored as described above.

Data analyses

For each test different simple linear regression studies were performed in order to asses which demographic variables age, years of education (or their transformations) and gender were to be included in the final models in that more effective in reducing the residual variance. A multiple regression was then carried out to generate the prediction equation. For each test score we obtained correction coefficients and correction grids were then derived to adjust the original score adding or subtracting the contribution of the significantly influencing variables. Following the Equivalent Scores method used by Capitani et al. (1987) we classified the adjusted scores into five categories. An equivalent score of 0 indicates a performance lower than the outer 5% based on non-parametric tolerance limits; the score 4 is ascribed to values higher than median value; 1, 2 and 3 are intermediate scores.

2.2.4 Results

Multiple linear regressions analysis revealed that all tests are influenced by age and/or education and sex. Naming, both in visual and verbal format, was influenced by age (respectively F(2,105)=22,821, p<0,001; t=-5,201, p<0,001 and F(2,105)=10,001, p<0,001; t=-2,732, p<0,001). A progressive decrease of performance is associated with lower values in age. Word-picture matching and Picture sorting were influenced only by education (respectively F(1,105)=4,318, p<0,001; t=2,074, p<0,05 and F(2,105)=7,265, p<0,005; t=3,094, p<0,005). Higher values of education impact positively on the performance of both tests. Finally, generation of features is the only test influenced by all the three variables (F(3,105)=9,361, p<0,001; age t=-2,804, p<0,005, sex t=2,018, p<0,01; education t=2,004, p<0,05), with better scores for female, higher values of education and lower values in age. Instead only age and education influenced feature verification (F(2,105)=9,361, p<0,001; age t=-3,180, p<0,005, education t=2,643, p<0,05). Younger and highly educated subjects had a better performance on this task. Correction grids and equivalent scores for each task are shown in appendix C2.

2.2.5 Discussion

We have developed and standardized a new tool, including 5 different tasks, in order to investigate semantic memory impairments through different input and output modalities using the same set of stimuli. Age, education and gender influenced differently the performance on semantic tasks. The availability of normative data permit the use of this battery in clinical assessment.

The collection of a new set of semantic features norms, on the base of feature based models of semantic representations (Garrard et al., 2005; McRae et al., 1997), allowed us to identify semantic features as sensorial or non sensorial (Garrard et al., 2001a), distinctive or shared (Garrard et al., 2001a; Tyler at al., 2000; Devlin et al., 1998), with high and low semantic relevance (Sartori & Lombardi, 2004).

The battery can be used to investigate the modality of semantic memory degradation in patients with neurodegenerative diseases at feature level. Longitudinal studies investigating types of errors in picture naming have shown a hierarchical pattern of semantic memory loss, characterized by a progressively generic response both in semantic dementia and in AD patients (Barbarotto et al., 1998; Gonnermann et el., 2004; Hodges et al., 1995). While in the first stage of disease patients made semantically related naming errors (horse for zebra), in the later stages the errors become more general (animal for zebra). This pattern is easily explained by feature-based models, suggesting a progressive loss of semantic features, in which distinctive properties of objects (that differentiate between closely related concepts, members of the same semantic category) are lost at earlier stages of the dementia, while shared properties (that give structure to semantic category) remain preserved for a longer time. A direct proof of a selective impairment of distinctive features at an early stage of Alzheimer's disease has been reported in a longitudinal study using a systematic approach based on empirical data at the feature level (Duarte et al., 2009; Garrard et al., 2005; see also Alathari et al., 2004). Some semantic priming studies are in line with these results (Giffard et. al, 2002; 2001; Laisney et al., 2011), revealing the same progression of semantic memory degradation in SD and AD, beginning with the loss of distinctive features (although a more severe semantic deterioration was present in SD).

The battery can be also used to investigate the presence of selective category deficits, in that the values of confounding variables are available. Different theories proposed a disproportionate degradation of semantic features for the impaired category. Warrington et al. (1984) proposed that the degradation of sensory features causes a deficit for living things, because these features are considered more prominent for living things. A reverse pattern, with a deficit for non living things, instead may occur for the degradation of the functional information. The conceptual structure account (CSA, Tyler et al., 2000) explains these phenomena in terms of feature distinctiveness and inter-correlation between perceptual–functional features between living and non living concepts. It is now well known that in order to verify the presence of category specific deficits confounding variables must be taken into account. However it is extremely difficult to tightly match multiple stimulus variables simultaneously in living-nonliving item sets. Typically, the stimuli obtained in this way result in a limited set of exemplars, which are often non representative of the living versus non-living dichotomy as encountered in the real world. In the present battery, the stimuli are matched for most of the confounding variables. However, some are only loosely matched. It has been documented that patients with Alzheimer's disease showed a deficit for living things when items were loosely matched for familiarity (with a p value from 0,5 to 0,15), with living items resulting slightly less familiar than nonliving items. When tightly matched stimuli were used, the effect disappeared (Tippet et al., 2007). To overcome this limitation we propose to carry out a regression analysis in order to examine category effects after partialling out the possible influence of the confounding variables (e.g., Laiacona et al., 1993; Perri et al., 2003; Zannino et al., 2002).

Another advantage of the battery is that it is based on colored photographs (Viggiano et al., 2004) while the majority of semantic memory studies used black and white drawings (Snodgrass & Vandervent, 1980). This could overcome to the ambiguity of some black and white drawings (Brousseau et al. 2004). In addition Zannino et al. (2007) showed how colored photographs with respect to line drawings improve the controls and Alzheimer patients' performance on LT items (see however Adlington et al., 2009 for contrasting evidence).

In conclusion, this battery allows the investigation of different input and output modalities using the same set of stimuli, in order to assess the presence of category specific deficits and the modality of semantic memory degradation in patients with neurodegenerative diseases.

2.3 Construction and standardization of a new battery to investigate abstract concepts

Knowledge concerning abstract concepts has been generally investigated only in comparison with concrete entities in the attempt to trace a dichotomy between these two domains. Indeed, several studies have reported that concrete words have a common cognitive advantage over abstract words, advantage known as concreteness effect (deGroot, 1989; James, 1975; Kroll & Merves, 1986; Paivio, 1991). Healthy subjects generally perform faster and more accurate on concrete words than on abstract words on a range of lexical and semantic tasks, as in lexical decision (Bleasdale, 1987; Kounios & Holcomb, 1994) and memory tasks (Paivio, 1991).

Different psycholinguistic variables have been proposed in order to quantify this difference between concrete and abstract concepts. The most important ones are: Concreteness (CNC), Imageability (IMG), Context availability (CA, that refers to the number of contexts in which a given word can be used), Familiarity (FAM), Age of Acquisition (AoA), Mode of Acquisition (MoA). All these variables have been investigated through rating procedures, in which subjects are asked to evaluate words with respect to each measure and to assign a score to each word, which represents a measure of a particular concept with respect to the specific variable (Altarriba, Bauer & Benvenuto, 1999; Della Rosa et al., 2010; Setti, Caramelli, 2005; Wauters, Tellings, van Bon & van Haaften, 2003; Wiemer-Hastings, Krug & Xu, 2001;).

According to the two dominant theories of the representation of concrete vs. abstract words, two variables seem to play a primary role and can account for the concreteness effect reported in many studies. According to the dual coding theory (e.g., Paivio, 1986) imageability (IMG) is a primary determinant of the difference between concrete and abstract words as the latter are less imageable. In accordance to the context availability hypothesis (Schwanenflugel et al., 1992) abstract words are more difficult to contextualize and are somehow disadvantaged with respect to concrete ones.

In addition concrete concepts are more familiar and are therefore associated with more propositions in long-term memory (deGroot, 1989; Kieras, 1978).

It has been suggested that the concreteness effect could arise from the ambiguity in the use of some psycholinguistic variables. A lot of studies assumed that concreteness and imageability tap into the same underlying theoretical construct. It has been documented that the two variables, although highly correlated, are not synonymous (Kousta et al., in press, 2009; Macoir, 2009). Kousta and co-workers (in press; 2009) highlighted the differences between the frequency distributions (based on MRC database values) of the two variables; whereas the concreteness distribution is bimodal, with two distinct modes for abstract and concrete words, the distribution of imageability is unimodal. In fact, concreteness classifies entities into two basic kinds: concrete concepts, that refer to something tangible that we are able to perceive through our senses, and abstract concepts, that refer to entities that we cannot perceive directly through our senses, while imageability ratings index a graded property that is meant to capture the differential association of words with sensory (primarily visual) properties. For example, some emotion concepts although non-concrete are rated with a high score in imageability (Altarriba et al., 1999; Paivio et al., 1968). However many authors use the two terms interchangeably (see also Really et al., 2006).

Not compatibly with the "dual-code" and "context-availability" hypothesis, the reverse of the concreteness effect, with a better performance on abstract concepts with respect to concrete ones, has been recently reported in healthy subjects (Kousta et al., in press; 2009). Kousta et al (in press) reported in lexical decision experiments, as well as in large scale regression analyses of data from the English Lexicon Project (ELP, Balota et al., 2007) that after controlling for imageability and context availability, in addition to a large number of other lexical and sublexical factors, abstract words have a processing advantage over concrete words. This surprising result contrasts with previous works showing a processing advantage for concrete over abstract words, difference that probably arises due to lack of control in previous works of other important lexical factors which also affect lexical processing (most notably imageability but also familiarity). Crucially, they found that this residual advantage for abstract over concrete words could be accounted for in terms of differences in affective associations (both valence and arousal) of the words. Abstract words are more emotionally valenced than concrete words. They concluded suggesting that emotional content contributes to the representation and processing of abstract concepts. In particular they sustained that experiential information is central to the representation of both concrete and abstract words, attributing a foundational role to sensorimotor information for concrete words and to affective information for abstract words. These results are in accordance with previous evidences that suggested as abstract concepts and word meanings are grounded in introspective states (mental and affective; Barsalou & Wiemer-Hastings, 2005). Both evidences represent important clues in understanding the organization of abstract knowledge.

Some investigators tried to shed light on the organization of the abstract domain of knowledge, postulating a possible categorical organization (Setti & Caramelli, 2005; Altarriba et al., 1999) for abstract concepts as for concrete ones or claiming that differences may exist between abstract concepts, independently from the specific categories. The existence of categories of abstract concepts remains still an open question. While in the concrete domain we generally discriminate between living and non-living categories (see above), a number of studies have focused on the identification of categories within the abstract domain. Some studies put forward the idea of the existence of a categorical organization for abstract knowledge as well. Altarriba and

Bauer (1999) were the first to note the distinctiveness of emotion concepts, showing the distinct characteristics in respect to abstract and concrete concepts. Emotion words resulted less concrete and higher in IMG and CA than other abstract words. In addition emotion words differed from concrete and abstract ones in a free recall task and in a lexical decision task with a priming paradigm. These results have been interpreted by the authors as an evidence that concrete, abstract and emotions words belong to different domains, and in particular that emotion words differed from the other abstract words, disagreeing with what is usually assumed. Influenced by these interesting results, Setti and Caramelli (2005) tried to provide evidence for the existence of other categories in the abstract domain, inferring some clues for their organization. They considered four domains of abstract knowledge (emotions, cognitive processes, states of self and nominal kinds) in order to check whether are differentiated along on CNC, IMG, CA and abstractness (ABS) dimensions. They showed that different categories of abstract knowledge differ with respect to these variables.

Differently from a categorical framework, it has been hypothesised that a variability inside the abstract domain may be captured along a continuum ranging from low to high abstracteness. Some abstract concepts are rated as more abstract then others, consider for example words like idea and government (Della Rosa et al., 2010; Wiemer-Hastings et al., 2005), and the abstract end of the concreteness scale may not account for this variability. Della Rosa and co-workers (2010) documented that the abstractness dimension captures variations in the degree of abstractness better than the concreteness dimension. In addition they reported as the different levels of abstractness are predicted by the Modality of Acquisition (MoA, Della Rosa et al., 2010), a construct grounded in the assumption that the meaning of a word can be acquired perceptually, linguistically or by a combination of both (Wauters et al., 2003). The relationship between MoA and abstractness/concreteness becomes clear if MoA is considered a variable able to ‘weigh’ the amount of experience and language shaping the core meaning of a concept. The prevalence of one or the other type of information may give a more ‘concrete’ or more ‘abstract’ label to word content (Della Rosa et al., 2010; Gleitman, Cassidy, Nappa, Papafragou, & Trueswell, 2005). While Moa can account for differences in abstractness, variables as IMG and Ca are more suitable for differences between abstract and concrete domains, but not inside the domain. In the same manner abstract words may be labelled with different degrees of emotional valence and consequently perceived as less or more abstract.

In addition to studies with healthy subjects, important information concerning the differences between abstract and concrete domains of knowledge derive from patients with semantic memory impairments. A concreteness effect has been reported in several clinical studies (e.g., Coltheart et al, 1980; Franklin, Howard, & Patterson, 1995; Franklin, Howard, & Patterson, 1994; Howard & Franklin, 1988) whereas the opposite pattern has been only rarely observed (Bachoud-Lévy & Dupoux, 2003; Bonner et al., 2009; Breedin, Saffran, & Coslett, 1994; Cipolotti & Warrington, 1995; Macoir, 2009; Marshall, Pring, Chiat, & Robson, 1996; Papagno et al., 2007; 2009; Sirigu, Duhamel, & Poncet, 1991; Yi, Moore, & Grossman, 2007; Warrington, 1975, 1981; Warrington & Shallice, 1984). In particular patients with Alzheimer's disease (AD) seem to show a better performance for concrete concepts with respect to the abstract ones, even if very few evidences have been reported (Fung et al., 2000; Rissenberg et al., 1987). The inverse of concreteness effect is generally described in patients with semantic dementia (Bonner et al., 2009; Breedin et al., 1994; Papagno et al., 2007; 2009; Cipolotti & Warrington, 1995; Grossman & Ash, 2004; Macoir, 2009; Reilly et al., 2006, 2007a, 2007b; Vesely, Bonner, Reilly, & Grossman, 2007; Warrington, 1975; Yi et al., 2007), however some studies, reporting the opposite pattern, suggested as the inverse of concreteness effect could be just an exceptional finding in these patients (Jefferies et al., 2009).

However all these studies account only for the different pattern of degradation between abstract and concrete concepts in different pathologies, whereas no information concerning different pattern of deterioration into the abstract domain were available.

Nowadays only few tests are able to assess the abstract domain of knowledge (Novelli et al., 1986), in that the majority of tests actually uses only concrete concepts (Adlam et al., 2010; Hodges et al., 1992; Laiacona et al., 1993; Moreno et al., 2005). In Italy only one standardized test exists (Novelli et al., 1986) a naming on a verbal definition, that includes both concrete and abstract words. Moreover different studies assessing the abstract domain in patients have used tests created ad hoc and sometimes not controlling for all the variables that can influence performance (Jefferies et al. 2009; Yi et al., 2007). Thus none of them can make a significant contribution in order to clarify if different types of abstract knowledge impairments characterize different pathologies.

The aim of this study was to develop and standardize a new battery of semantic memory tests (DeCAbs), in order to overcome the lack of Italian tests and to assess the specific status of abstract knowledge in different neurological conditions through comprehension and production tasks and controlling for all the variables that can impact on subjects' performance.

2.3.1 Test construction

2.3.1.1 Norms for emotional valence and arousal

In order to control for the potential impact of emotional valence and of arousal (as we have stated above that this type of information may be crucial for the representation of abstract concepts), as no Italian norms are available, we collect norms for both variables for 428 words, the 417 words of Della Rosa database plus other 11 concrete words in order to be included all the 82 concepts used for the study on concrete concepts (see above).

22 subjects (mean age= 24,14 sd=2,12; 10 males) were asked to rate concepts on Emotional valence and arousal 9 points-scales. The set of 428 words were inserted into 4 different rating lists. The instructions were based largely on those of ANEW (Affective Norms for English Words, Bradley & Lang, 1999). Emotional valence ranges from pleasant (represented by a happy figure) to unpleasant (frowning figure); arousal ranges from excited (figure with wide open eyes) to calm (sleepy figure) (see appendix D.1).

We selected 40 items from Della Rosa database (2010) in order to obtain the values of the variables of interest (see appendix E.1 for the list of the stimuli). The stimuli are divided in 5 categories: Emotions (e.g. fear), Cognitions (e.g. ideal), Traits (e.g. weakness), Social Relations (e.g. friendship) and abstract concepts related to Human Actions (e.g. revenge); each category includes 8 Items. The selection of the categories is in accordance with two different criteria. We selected the categories on the basis of the classification made by Multi-wordnet (Miller, 2005), a database based on the lexico-semantic relationship between concepts. Moreover we carried out a norming task in which 30 subjects were asked to indicate the category or categories to which they believe the concept belonged. To classify the category of each concept, we selected from the norms the category produced by the majority of subjects for each concept.

The items were tightly balanced between categories for concreteness ($p=.732$), imageability ($p=.523$), context availability ($p=,502$), familiarity ($p=.848$), age of acquisition ($p=.883$), mode of acquisiton ($p= .453$), abstractness ($p= .614$), number of letters ($p=.941$), values taken from Della Rosa database and for arousal ($p=.371$), but not for emotional valence ($p<0,05$)

2.3.2 Test description

The battery based on the stimuli described above includes the following three subtests: a Sentence completion task, a Multiple-choice, naming-to-description Task and an association Task. For all tests the stimuli were presented both visually and orally. The sequence of presentation of the stimuli is randomized for each task.

The Sentence completion Task. Subjects are asked to complete 40 sentences in which the final word is missing and needs to be completed with the target (see appendix E.2 for instructions and an example). We created the sentences using definitions taken from two different Italian vocabularies: Garzanti (2006) and De Mauro (2000). One point is given for each correct response (range 0-40). However the other responses are classified on the basis of their relation with target as synonyms, semantically related, semantically related but contextually inappropriate, contextually suitable but not related with target, opposite, circumlocution, repetition of words or phrase just spoken, anomia or other. Reaction times are also collected from each subject.

Multiple-choice, naming-to-description Task. The subjects are asked to select the best of four words that matched a verbal definition (see appendix E.3). 40 definitions were created, and for each definition a target word and three foils were presented:
1 foil semantically related to the target word (SRTW); 1 with opposite meaning to target word (OMTW) and 1 semantically related to the opposite meaning (SROTW).
The description were adopted from two Italian dictionaries (Garzanti, 2006; De Mauro, 2000) and were modified into colloquial Italian. Definitions were kept as short as possible and in order to bias synonyms or related words they were included in the definition. The number of words in definitions is balanced between categories (p=0,214). We balanced the strength associations between target and the distracters across the categories taking the values from LSA (Latent Semantic Analysis; http://LSA.colorado.edu/, Landauer & Dumais, 1997). Finally we used the two Italian dictionaries, Garzanti (2006) and De Mauro (2000), to extrapolate the synonyms and the opposites of the target.

Association Test. In this task subjects are asked to choose the item more associated to the stimulus presented (see appendix E.4). This task requires the subject to match a target word (e.g. friendship) with to one out of three option responses which was more closely associated to target. The three options includes: an item with high association strength (e.g. bond), a distractor with low association strength (e.g. embrace) and a distractor that belongs to another category (e.g. colour).

In order to obtain the value of the association strength, we first collected the association norms. 30 participants were asked to write the first 3 words that come to mind that are meaningfully related or strongly associated to the presented word (see appendix D.2). From these norms we selected the stimuli for this task. We used as a target the word with higher association strength with the cue, the word reported from the higher number of participants in association to the cue. As a related distracter we selected a word reported by only one participant in association to the cue. The second distracter, not related to the cue, is a word with low association to another cue belonging to another category.

The position of targets and distracters is balanced within and between the categories. One point is given for each correct response (range 0-40).

2.3.3 Battery standardization

2.3.3.1 Methods

Subjects

108 healthy subjects took part in the study (54 females). Their mean age was 54,31 (SD = 17,31, range 25 - 84 years) and the years of education mean was 11,52 (SD = 4,23; range 5 - 20). The distribution of demographic data is shown in appendix F.1. Subjects with past or present neurological or psychiatric illnesses or a corrected score less than 24 at Mini Mental State Examination were excluded.

Procedures

The battery was presented to all participants in one session. The Sentence completion Task was administered as the first task, the order of the other two tests was randomised across the subjects.

Data analyses

All subtests were scored as described above. We carried out the same procedure of standardization adopted for CaGi battery (see above).

2.3.4 Results

Multiple linear regressions analysis revealed that while the association and the Sentence completion tasks resulted influenced only by education (respectively, F(1,107)=10,634, p<0,005, t=3,261, p<0,005; F(2,107)=35,037, p<0,001, t=6,515, p<0,001) with better scores for higher values of education, both education and age influenced Multiple-choice, naming-to-description task (F(2,107)=37,941, p<0,001, t=6,246, p<0,001; t=-2,370, p<0,05). On these tasks the performance resulted better for younger and higher educated subjects. Correction grids and equivalent scores for each task are shown in appendix F.

2.3.5 Discussion

Differing from the most part of studies focused on the dissociation between abstract and concrete concepts, in this study we have created and standardized a new battery of semantic memory tests in order to investigate the organization of abstract conceptual domain only, in that until now it remains almost neglected. Three different verbal tasks, a Sentence completion, association and Multiple-choice, naming-to-description tasks, have been developed and standardized. Education influenced performance in all three tasks, while age contributed to predict performance only in Multiple-choice, naming-to-description task. The availability of normative data allows the use of this battery in clinical assessment.

Differently form the majority of studies considering abstract knowledge as a unique block opposed to the concrete one, some studies tried to argue a possible internal organization .

Similarly to concrete domain, based on a categorical organization, some studies have focused on the identification of categories within the abstract domain (Altarriba et al., 1999; Setti & Caramelli, 2005). A number of studies suggest that emotion words can represent a category independently from the other abstract words (Altarriba & Bauer, 2004; Altarriba et al., 1999; Setti & Caramelli, 2005). Other categories have also been proposed, as cognitive processes, states of self and nominal kinds, but they are not still well supported by stringent evidences. In this study we traced a boundary between five different categories. The use of this battery could reveal if some categories of abstract concepts result more impaired than others in different pathologic conditions, in that all categories are tightly matched for all variables that can have a role in predicting performance.

However it is possible that there is not a clear cut-off between categories, other investigators in fact tried to infer differences among abstract concepts considering abstract domain as a continuum composed by concepts perceived as more and less abstract. Differences in this continuum may be captured by the different contribution of language and experience in the acquisition of the concept meaning (MoA), by different degrees of imageability, or emotional valence, or context availability or familiarity. Della Rosa et al. (2010) documented as different levels of abstractness could be predicted by the modality of acquisition of a concept. Kousta and co-workers (in press; 2009) documented the important role of the affective association in the representation of abstract concepts, and put forward that affective associations should be considered as a continuous variable encompassing words of all types and not a variable identifying only emotion words.

Thus, we control the stimuli for several variables, IMG, AOA, CNC, Arousal, Valence, CA, MoA. in order to investigate their possible role in predicting performance.

Interestingly studies deriving from both categorical and continuum framework suggested a privileged role of emotion words and/or emotional valence in the abstract conceptual domain. The assessment of abstract knowledge in patients with semantic memory impairments could aid to determinate the nature of these findings.

In addition Kousta et al. (in press; 2009) showed that valence has the largest effect in predicting subjects' performance, whereas arousal also a modest role; thus they considered valence and arousal together, as affective associations. However we prefer to consider them as two different factors. In fact as neuroanatomical and theoretical reasons distinguish between the two constructs (Lewis et al., 2007; Posner et al., 2009), there is a clear rationale to expect dissociations between them for abstract words in different neurological pathologies.

In the same manner we consider CNC and IMG as two different constructs. In clinical studies there is not a common accord in selecting stimuli on the basis of imageabilty or concretness dimensions. Many authors, using the two terms interchangeably (Jefferies et al., 2009), could raise the inconsistencies and variability of the data.

In conclusion this new battery of tests can be considered a new important tool in order to investigate the organization of the abstract knowledge.

2.4 General conclusion

In this study we introduced and standardized two new batteries of semantic memory test in order to evaluate respectively the concrete and the abstract domain of knowledge. These batteries may prove to be a useful and sensitive tool to investigate the presence of semantic deficits in brain damaged patients, investigating the organization of conceptual knowledge.

In fact as no theory of semantic or conceptual representation is complete without an explicit account of how abstract and concrete knowledge is acquired, represented, and processed, at the same time no neuropsychological assessment is comprehensive of semantic memory impairments without the evaluation of both abstract and concrete concepts disorders.

These new instruments will prove useful for research in both experimental and clinical areas.

Chapter 3: The loss of semantic memory in Alzheimer's disease: a neuropsychological study

3.1 General Introduction

Alzheimer's Disease (AD), the most common cause of dementia, affects many cognitive domains, leading patients to a dramatic disability. The earliest and most pervasive deficits concern episodic memory loss, in accordance with the earliest signs of disease, involving neuronal atrophy, synapse loss, and the abnormal accumulation of amyloid plaques and neurofibrillary tangles, in the medial temporal lobe structures (e.g., hippocampus, entorhinal cortex) (Braak & Braak, 1991). As the neuropathology of AD spreads to the association cortices of the temporal, frontal, and parietal lobes, different cognitive abilities are affected. In particular, the involvement of the inferior temporal lobe, temporo-occipital junction and temporo-parietal junction (Braak & Braak, 1991) generally lead to semantic memory impairments. Executive functions deficits are associated with extension of the degenerative process to the frontal lobe (Morris, 1996).

Semantic memory deficits cause severe functional impairments, due to the difficulty or inability, for example, to name objects. The nature of these deficits is largely debated. The question is whether they result from a loss of semantic information, that deteriorates progressively (Chertkow et al., 1989; 1994; Hodges et al., 1992a; Martin et al., 1992), or whether AD patients have a defective access and manipulation of semantic information that remains intact (Nebes et al., 1989, 1992, 1994; Ober & Shenaut, 1988). Recent reviews suggest that semantic memory is impaired early in AD, in particular in the case of effortful semantic tasks (Altmann at al., 2008; Chertkow et al., 2008).

Most studies examining semantic memory in AD concern only concrete concepts. They have shown that subordinate information is most vulnerable to the impairment, whereas superordinate concepts are generally more preserved (Martin & Fedio, 1983).

The most studied category effect in patients with AD concerns the dissociation between living and non living entities, documenting a better performance for non living things (Chertkow et al., 1990; Silveri et al., 1991). Extensive research on this topic has been reported, with contradictory results. Differences in stimuli selection as well as the heterogeneity of AD patients could in part explain the data (Whatmough & Chertkow, 2002). However, the genuineness of this phenomena remains debated. A limited number of studies have also addressed the abstract versus concrete dissociation, reporting a more severe impairment for abstract than for the concrete knowledge (Rissenberg & Glanzer, 1987).

In this study we try to shed further light on some aspects, more or less investigated, of the semantic memory impairment in AD, focusing on the following topics:

PART I - The semantic degradation at feature level and its relation with picture naming performance
PART II - The presence of category effect
PART III - The status of abstract knowledge

To this aim, we have applied the test batteries (CaGi and DeCAbs), described in the previous chapter.

PART I

3.2 The semantic degradation at feature level and its relation with picture naming performance

3.2.1 Semantic memory in AD: deficit of access or storage?

Difficulties with expressive language are among the earliest symptoms of AD. For many patients, a progressive difficulty in finding the name of people and things sets in from the onset of the disease. However, a controversy persists regarding the explanation for the anomia seen in AD, with two major positions proposed. The first, the degraded store account, explain deficits as a result of a progressive impoverishment of semantic information (Alathari, Trinh Ngo, & Dopkins, 2004; Chan, Salmon, Butters, & Johnson, 1995; Chan, Salmon, Nordin, Murphy, & Razani, 1998; Chertkow & Bub, 1990; Garrard, Lambon Ralph, Patterson, Pratt, & Hodges, 2005; Lambon Ralph, Patterson, & Hodges, 1997). The second, the degraded access account, posits that AD patients have a defective access and manipulation to semantic information that remains intact (Bonilla & Johnson, 1995; Nebes & Brady, 1988; Nebes et al., 1989, 1992, 1994; Ober & Shenaut, 1999). Several evidences are in accordance with the first view. A profound anomia in AD may be observed in several semantic tests, such as picture naming (Hodges et al., 1992a), verbal fluency (Martin & Fedio, 1983; Salmon et al., 1998) and naming to definition (Hodges et al., 1996; Lambon Ralph et al., 1997). In addition patients often produce semantic errors, such as a superordinate term (e.g. animal for tiger) or semantic paraphasias (a substitution with a related word), while phonological and perceptual errors are less evident. Hodges and colleagues documented that the deficits were related to the frequency of the items; less frequent items were more impaired than frequent items (Hodges, Salmon, & Butters, 1992a). In naming task, phonological and semantic cues are only minimally helpful for AD patients, suggesting a more “central” problem in respect to aphasic patients (Chertkow et al., 1990). However, Balthazar and co-workers (2008) found that, although AD performed worse than controls and amnesic mild cognitive impairment (aMCI) subjects on the Boston Naming Task, the three groups showed the same types of errors (coordinate, superordinate, and circumlocution) and were influenced by phonemic cues in the same manner. However, the authors included in their study AD patients with mild cognitive impairment (Mini Mental State Examination, Folstein et al., 1975; MMSE mean= 23,9) and it may be possible that in this stage of disease AD patients had only mild naming impairments. Chenery et al. (1996) showed that, while in the severe stages of disease the naming responses reflect a degraded semantic representation, in the early stage of the disease this is not necessarily the case. Inconsistencies in errors in the early stage of the disease could reflect minimal semantic damage. With disease progression the same items become progressively degraded and no more available (Chertkow et al., 1989). As Balthazar and co-workers suggested, the inclusion of patients with more severe deficits could show a different pattern of errors and of response to facilitations after a phonemic cue.

Although semantic fluency is considered a complex task involving different cognitive processes (including attention, working memory, retrieval strategies, and phonological processes), an imbalance between a better performance on semantic fluency in respect to phonemic fluency seems to be in favor of a semantic impairment in AD (Marczinski et al., 2006; for a longitudinal study see Salmon, 1999). In addition, semantic memory impairments have also been documented on probe questioning (Done & Gale, 1997); semantic association (Mauri, Daum, Sartori, Riesch & Birbaumer, 1994); and word to picture matching task (Garrard, Lambon Ralph, Watson, Powis, Patterson, & Hodges, 2001b). AD subjects failed or succeed on the same items in test-retest (Chertkow & Bub, 1990) and showed an item-by-item consistency between tests (Chertkow & Bub, 1990; Hodges et al., 1992a; Huff et al., 1986; Lambon Ralph et al., 1997), showing a correspondence on the same items between performance on naming and tasks probing properties of concept. Item consistency has been also documented using a battery of semantic tasks that allowed to assess semantic memory though different input and output modalities (Hodges et al., 1992a). The relationship between object naming and the status of underlying semantic representations have been documented in studies asking patients to define the concepts (Hodges et al., 1996). The quantity of information generated for resulted greater for named than for unnamed picture. A more striking demonstration of this relationship has been documented by Garrard and co-workers (2005). However, more recently, Joubert and co-workers (2010) showed that in aMCI and early AD patients there was no association between naming performance and the underlying semantic deficits. They analyzed performance for each item across each subject and found no significant association between naming and semantic knowledge for objects, with a preponderance of correct naming and incorrect semantic errors (by mean of semantic probes). They suggested that a mild semantic decline is not sufficient to compromise the access to the lexical representations of objects.

Chan et al. (1993, 1995, 1997, 2001) and Hornberge et al.(2009) used triadic comparison tasks to investigate semantic memory impairments in AD. In this task subjects were asked to make a relatedness judgment, indicating which two out of three animals were most similar in meaning. The first reports of Chan and co-workers documented, through a multidimensional scaling (MDS) assessment, that in AD patients some aspect of semantic memory are more spared than others (as for the concrete dimension versus abstract concepts). The authors interpreted the data as supporting a storage problem. However several methodological limitations have been highlighted, which could affect the plausibility of the results (Storms et al., 2003). In particular Storms and co-workers showed that AD judgments on MDS were indistinguishable from random responses. Hornberge and co-workers (2009) used the triadic comparison task contrasting the performance on two semantic dimensions of equal saliency to controls, but varying in their specificity (land/water versus bird/non-bird). The results showed that multidimensional scaling (MDS) methods fail to reveal important behaviours in semantic tasks, showing, as previously reported, that AD and controls responses were not discriminable from random choices. However trough an accuracy-based analysis they showed that while controls performed in similar way on both dimensions, AD performed worse on the more specific dimension. These data are consistent with degraded-store account.

Although all these evidences seem to support the presence of a semantic impairment, in particular in production tasks, there are also contrasting results. Some studies reported no semantic deficits in AD patients (Bonilla & Johnson, 1995; Ober & Shenaut, 1999), others reported an impairment only for some tasks. A relatively preserved performance on word-picture matching, category sorting and semantic priming has been documented, in contrast with an impaired performance on picture naming, naming fluency and naming on definition (Ober, 2002; for a review see Altmann et al., 2008). Aronoff and co-workers (2006) suggested that some of these inconsistencies may be due to differences in AD samples and in the number of items used (Aronoff et al., 2006). In addition AD patients could obtain a good performance on the “broad sorting task”, such as the one used by Ober and Shenaut (1999), which assesses general knowledge that is commonly preserved, at least in the first stages of disease. The performance in picture naming is in general more impaired, as this task demands specific knowledge that is degraded from the early stage of disease. Aronoff and co-workers used a picture naming and a broad sorting task (a similarity judgment task in which the patients were asked to put together similar concepts) to assess semantic memory impairment. AD patients tended to cluster stimuli more closely together than controls, in particular for categories in which AD produced more naming errors (Aronoff et al., 2006). Several investigators have suggested that task demands have a strong influence on AD performance. A poor performance on tasks such as picture naming and category fluency may reflect an inefficient access to an intact semantic representation, as these tasks are characterized by intentional and effortful processing (to search in semantic memory and discriminate between similar items). On the other hand, tasks like semantic priming and category verification, involving only automatic processes, are typically preserved in AD (for similar evidences see also Cuetos et al., 2003)[2]. In fact, the most striking evidences supporting the access hypothesis are based on findings of normal semantic priming for words in AD. Semantic priming tasks allow to assess semantic memory implicitly, minimizing the effects of non-semantic cognitive processes. However, also semantic priming studies have yielded contradictory results in AD, with authors reporting normal priming (Balota & Duchek, 1991), less-than-normal priming (Ober & Shenaut, 1988; Salmon et al., 1988; Silveri et al., 1996), or increased priming effects (hyperpriming; Balota & Duchek, 1991; Balota et al., 1999; Bell et al., 2001; Chertkow et al., 1989; Giffard et al., 2001, 2002; Nebes et al., 1989). These controversies could be in part due to methodological issues, or to different stages of semantic memory impairments. Some longitudinal studies reported both normal semantic priming and hyperpriming effect. The hyperpriming effect has been interpreted within the semantic memory deterioration framework (however, see Nebes et al. 1989 and Ober & Shenaut, 1995 for different interpretations), suggesting that a preserved effect cannot be considered a proof of the integrity of semantic memory (Whatmough & Chertkow, 2002). An interesting study has been reported by Duong and co-workers (2006). They investigated the performance on explicit tasks that required intentional processes (picture naming and semantic probes), tasks with automatic access to semantic memory (lexical decision and lexical semantic priming) and tasks assessing frontal executive functions (Stroop and Stroop-Picture naming) in controls, aMCI and AD. They showed that MCI patients were impaired on intentional tasks, but not on automatic tasks in respect to controls, while AD patients were impaired on both types of tasks. The authors suggested that intentional access to semantic memory is impaired earlier than automatic access.

3.2.2 The loss of distinctive features

According to feature-based theories of semantic memory, concepts are composed of subordinate elements, or features (McRae, de Sa, & Seidenberg, 1997; Rosch, 1973; Smith & Medin, 1981). Distinctive features are those that occur in only one or a very few concepts, allowing to differentiate between closely related concepts, typically members of the same semantic category. For example "it has a trunk" occurs only in one concept, *elephant*, and is considered a distinctive feature, while "has 4 legs" occurs in a very large number of concepts and is labelled as shared. Thus, a distinctive feature is important to identify the corresponding concept. In addition,

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[2] Some authors reported that tasks like property verification are more automatic than picture naming, requiring less controlled processes (Duarte et al., 2009; Garrard et al., 2005). However, even if the property verification task is easier , AD patients scored significant lower than controls (Garrard et al., 2005; Duarte et al., 2009).

distinctiveness can be considered as a continuum. This feature dimension has been named and measured in various ways, such as cue validity (Bourne & Restle, 1959), distinguishingness (Cree & McRae, 2003), distinctiveness (Garrard, Lambon Ralph, Hodges, & Patterson, 2001a), and informativeness (Devlin, Gonnerman, Andersen, & Seidenberg, 1998). The privileged role played by distinctive features in semantic processing has been reported in several studies involving connectionist models (Cree et al. 2006; Rogers et al., 2004; Mirman et al., 2009; Moss et al., 2000) in both healthy subjects (Marques, 2005; Mirman et al., 2009) and patients (Alathari et al., 2004; Duarte et al., 2009; Garrard et al. 2005; Laisney et al., 2009; Rogers et al., 2004). While in healthy subjects distinctive features have a privileged role, in that they are activated more strongly than the shared ones, in patients with semantic memory impairments they resulted more vulnerable to damage (because they lack reinforcing correlations with other features). Evidences supporting the idea that the difficulties with expressive language in AD are due to an underlying semantic deficits suggest that this featural representations can become partially disrupted. However, some authors suggest that the other cognitive functions involved in the naming process, such as working memory, attention, visuoperceptual skills, and lexical access, might also have an influence (Rogers, Ivanoiu, Patterson, & Hodges, 2006).

Early observations of the gradual loss of semantic memory in AD showed that the exemplar-level is the most vulnerable and the category-level the most preserved (Martin & Fedio, 1983). First explained within the traditional framework of hierarchical organization (Collins & Quillian, 1969), this pattern can be easily explained also by feature-based models, where the exemplar-level is supported by distinctive properties of objects that are lost at earlier stages of the dementia, and the category level is supported by shared properties that remains preserved for longer. Category is an emergent property of a distributed network of more fine-grained components (Masson, 1995).

Indirect evidences supporting this proposal derive from patients' performance in different semantic tests, such as picture naming and fluency (Martin & Fedio, 1983). Longitudinal studies investigating types of errors in picture naming showed progressively more generic response-types (Gonnermann et al. 2004, Paganelli et al., 2003), a pattern also evident in patients with semantic dementia (see chapter 1, Hodges, Graham & Patterson, 1995 and for connectionist implementation see Rogers et al., 2004; however see also Lambon Ralph, 2010). As the disease progressed, errors evolved from semantic paraphasias –coordinate error- (lion for tiger), to superordinate (animal for tiger), to an inability to name the item. It has been suggested that semantic errors can be due to an early loss of distinctive features and to the preservation of shared ones, leading to ambiguous semantic representations (when the tiger loses the stripes and the lion loses the mane, they remain both wild animal, that have 4 legs etc.). With a verbal fluency task, Martin and Fedio (1983) showed that AD patients are more impaired in reporting items at the specific level than at the superordinate level. It has been also showed that AD patients could sort picture at the category level (Hodges & Patterson, 1995) and similarly could correctly answer to question at the category level (is it an animal?) but they were not able to answer correctly to questions concerning specific features (Is it bigger than a cat or is it made of metal?).

The earlier loss of distinctive features following a semantic memory breakdown in the human brain has been suggested by many authors (Garrard et al., 2001a, 2001b; Laatu, Portin, Revonsuo, Tuisku, & Rinne, 1997; McRae et al., 1997; Moss, Tyler, Durrant-Peatfield, & Bunn, 1998; Warrington & Shallice, 1984). A direct proof of a selective impairment of distinctive features at the early stage of AD has been provided by a longitudinal study using a systematic approach at the feature level (Garrard et al., 2005; see also Alathari et al., 2004; Duarte et al., 2009). The values of parameters of semantic features, such as distinctiveness, were computed starting from the norms of features derived from a feature-listing task. In this study, AD patients showed a gradual loss of distinctive features, preceding the shared ones. The same pattern of deterioration has been demonstrated by Duarte et al. (2009).

Convergent results derive from a number of semantic priming studies, revealing an hyperpriming effect in AD patients (Alathari et al., 2004; Chertkow et al., 1989; Giffard et al., 2001; 2002). A longitudinal study (Giffard et al., 2002) revealed a different semantic priming effect for different levels of semantic memory impairment and for different semantic relationship between prime and target (attribute condition e.g. tiger – stripes; and coordinate condition tiger - lion). While in the attribute condition the semantic priming effect decreased with disease progression, in the coordinate condition there was an initial hyperpriming effect followed by a decrement. The hyperpriming effect has been interpreted as due to the specific loss of distinctive attributes that make it possible to distinguish between semantically close concepts, leading to a confusion due to the shared features that are preserved. Two wild animals, as tiger and lion, share several features, as "for legs" "has fur", and some distinctive features that enable people to identify the two concepts: "has mane" and "has stripes". When at first stage of semantic memory impairment the distinctive features are lost, the two animals are both wild. It has been suggested that the observed effect can be considered as a repetition priming (wild animal-wild animal) (Martin, 1992). In a more recent study, Laisney and co workers (2011) reported an impaired semantic priming effect for the attribute relationship involving distinctive features, but not for the shared ones (but see also Rogers et al., 2008).

However, as a number of authors have argued, not all the distinctive features have an identical salience for the concept (Cree et al., 2006). Some features, such as “uses tail to keep balance” are distinctive, in that they are listed only for *kangaroo,* but at the same time they are not highly salient as they are infrequently reported in feature-norming tasks, and presumably do not play a prominent role in the representation of concept. Ashcraft (1978) and McRae et al. (1997) found that production frequency (or dominance, referring to the number of participants who listed a feature) is a strong predictor of feature verification latency. Smith and co-workers (1995) showed that AD patients were more impaired in attributes with lower dominance, while no differences were detected between distinctive and shared features. However, they reported as example of distinctive feature “the apple is red”. Probably they did not use an appropriate measure of distinctiveness. Considering both distinctiveness and dominance Sartori and Lombardi (2004) introduced a new semantic variable, semantic relevance. “Semantic features with high relevance are those which are useful for distinguishing the target concept from similar concepts”. Features like *has trunk* is considered as a feature with high relevance, in that it is present for only one concept and many subjects use it to define an elephant. In contrast, has *legs has* a lower value of semantic relevance in that it is present in many concept and less subjects use it to define an elephant.

Differently from distinctiveness, considered as not concept dependent, semantic relevance is concept dependent, in that the same feature can have different values for different concepts (dependent from the number of subjects who listed that feature for different concepts). In order to better understand the difference between distinctiveness and semantic relevance, consider the two features “uses tail to keep balance” and “has pouch”. Both are distinctive features, in that they are reported only for kangaroo. However, the first is listed by 3 subjects, the second by 20 (example taken form features norms described in chapter 2). The different importance of the two features is captured by relevance, but not by distinctiveness. Sartori and co-workers (2005) showed that semantic relevance is the best predictor, among other concept (age of acquisition, familiarity, frequency) and features dimensions (distinctiveness, dominance), of a naming to description task both in healthy subjects and AD patients. Marques and co-workers (2010) showed that features with high semantic relevance and non sensory features were the most important in a naming to description task, both in healthy subjects and in AD. However the authors compared semantic relevance independent from distinctiveness, i.e., while high semantic relevance features were also distinctive as “has a concave part” for *spoon*, features with low semantic relevance were also shared, as “it is a tool” for *spoon*.

Finally, not all the studies reporting evidences on semantic impairments at the featural level are based on empirical norms. The importance of deriving these parameters from empirical norms is well explained by Duarte and co-workers (2009). They highlight as “irrelevant criteria of distinctiveness” have used in a number of studies, in which distinctiveness effect was not found. Features considered distinctive in other studies resulted in Duarte study (2004; as reported in Duarte te al., 2009) as shared features.

3.2.3 Picture naming and specific features loss

Several authors have proposed that the failure to name an object in AD patients reflects an underlying degradation of semantic knowledge (Chertkow & Bub 1990b, Hodges et al., 1996; Whatmough et al., 2003). Several studies highlight that not all features are equally important in picture naming (Hodges et al., 1996; Marques et al., 2002, Moss et al., 1998; Whatmough & Chertkow, 2002), and different types of features have been indicated as responsible for the naming failure in AD.

Chertkow and Bub (1990b; Wathmough & Chertkow, 2002) showed that a normal performance on picture naming task does not guarantee by itself that all or the most part of semantic representation remain intact, suggesting that only a subset of semantic knowledge is necessary for naming. In their study, AD patients who were able to name a picture of a zebra, correctly answered to questions that uniquely identified the animal (e.g. Is the zebra striped?). However at the same time these patients answered incorrectly to many basic questions concerning the animal (“Do zebras meat eat?”, “Do they live in Africa?”). In contrast, when patients could not correctly answer to identification questions concerning an animal, then they could not name the picture of the same animal. The authors (1990b) used the conceptual model proposed by Miller and Johnson-Laird (1976) to explain these dissociations. The model is constituted by two “semantics”: the identification and the associative semantic system. Identification semantics refer to both perceptual and functional features. However Chertkow et al. (1992) stressed the importance of the perceptual features for the correct identification of concrete objects. Associative semantics refer instead to additional information not immediately important for the identification of the object. Chertkow and Bub (1990b) suggested that associative knowledge is lost earlier in AD. In addition the authors highlighted that the preservation of identification semantics, with respect to the associative, shows a hierarchy in the strength of the different semantic information. In fact AD who were unable to name a picture of an animal, could identify it from an array of pictures belonging to different semantic categories (Chertkow et al., 1992; Daum et al., 1996, Hodges et al., 1992a). Summarizing, the specific features important for picture naming are the identification features, both perceptual and functional, that uniquely identify the object. In 1992 Chertkow and co-workers, analysing the performance of AD with questions about pictures and word concepts, indicated that the perceptual features were the most important for the naming process. Hodges and co-workers (1996) evaluated AD patients in picture naming and verbal definition tasks. The information produced by AD were labelled as Physical – "visually based pieces of information" and Associative – "features that one learns to associate with the object but cannot be directly perceived"; both were subdivided in -general- common to all members of a category- and specific -specific (though not necessarily unique) to the item. In addition, they considered also the superordinate category. They showed that object naming depends from physical (i.e., perceptual) features that are specific to the concept to be named. However, these results were interpreted as only in part consistent with the model proposed by Chertkow and co-workers (Chertkow & Bub, 1990b; Chertkow et al., 1992). They found that impaired naming correlated more with the loss of identification semantics ("largely comprising physical features") than with associative knowledge loss. However, both physical and associative information was impaired with respect to controls. In addition, they documented that knowing the general category of an object is not predictive of the success in naming it, in accordance with the general pattern of semantic memory degradation in AD, in which specific features are more vulnerable. In this case a patient is unable to name a picture of an item, because he is unable to discriminate it from similar members. However, he could still name a picture with a superordinate or sort the item in the right domain of knowledge (e.g. living vs non living, Hodges & Patterson, 1995).

All these studies controlled for different type of features (visual/perceptual or associative) but not for other features dimensions, such as distinctiveness. Hodges et al (1996) divided the features in general and specific, and identified among the latter the physical features more important for picture naming. Marques (2005) reported that distinctive features were more often selected than shared features to support naming to definition. The results could reveal an important role of distinctive features in picture naming, an effect sometimes confounded with feature type effect. In addition identification semantics, as reported above, includes features that uniquely identify the concept (Whatmough & Chertkow, 2002). Other authors (Moss, Tyler, & Devlin, 2002; Tyler, Moss, Durrant-Peatfield, & Levy, 2000) highlighted the peculiar role of distinctive features in comparison with shared features. They suggest that distinctive features are essential in order to discriminate between concepts belonging to the same semantic category (e.g. tiger and lion), and consequently crucial in tasks like picture naming.

Summarizing, independently of the feature types (perceptual, functional, etc.) distinctive features appear to be overall more important for naming than shared features, as they are more informative in distinguishing one category member from others (Marques, 2005; Moss et al., 2002; Tyler et al., 2000).

Garrard and co-workers analyzed the role of distinctiveness on the picture naming performance. AD patients were administered a picture naming task and a probed test of semantic attribute knowledge. They asked patients to produce all the information available in relation to a concept. In a second time, based on a set of semantic attributes previous collected in a group of healthy subjects, patients were assessed with questions on semantic features that were not spontaneously generated. All the features dimensions, as well as the production frequency (dominance) and distinctiveness, were derived from a previous database. They documented a closer relationship of better performance in picture naming of visual than of functional features, suggesting a greater importance of visual knowledge to naming object. In addition, differently from their expectations, they showed no clear evidence that distinctive feature are significantly more associated with correct naming responses than shared information. They attributed these results to an insufficient statistical power, and to a numerical superiority of shared attributes. In addition, it is important to note here that not all the distinctive features have the same importance for identifying an object. Considering semantic relevance, we can argue that distinctive features with high values of relevance are the distinctive features that play the most important role in naming (see Sartori et al., 2005). Semantic features with high relevance are those which are useful for distinguishing the target concept from similar concepts. Garrard and collegues (2005) used all the distinctive features of their database, and even if they considered the weight of the dominance, they did not discriminate between distinctive features with high and low dominance (namely, for different values of semantic relevance). This could be the true motivation of the lack of the relationship between naming and distinctive features reported in their study.

Finally, Duarte and co-workers (2009) showed that distinctive features progressively declined in the course of AD. Even if they subdivided the patients on the basis of MMSE scores, they could document a progressively lower performance in a picture-naming task and in the distinctive property verification task.

3.2.4 Experimental study

The aim of the study

In this study we investigated the performance of AD patients in a picture naming task and in a sentence verification task, in which different types of features are involved. The general purpose of this study is to investigate the degradation of distinctive and shared features at different levels of naming performance in AD. We hypothesize that impaired performance in picture naming is associated with a greater loss of distinctive than shared features. In particular, we propose that not all distinctive features have the same importance. Distinctive feature with high values of semantic relevance (with high values of dominance) may result more important than distinctive features with lower values of semantic relevance in picture naming. In order to verify this hypothesis, we subdivided a group of AD patients in three different subgroups on the basis of their picture naming performance, and for each group we analysed the performance on distinctive and shared features.

As distinctive features are essential in discriminating similar member of a category, allowing to identify a concept, we suppose that these features begin to get lost in the same period in which the naming impairment becomes evident. In particular, as features with high semantic relevance capture the importance of a feature for the core of a concept, we propose that these features are crucial for the naming process.

Subjects

Fifteen patients suffering from AD (6 males) were enrolled in this study. The diagnosis of probable AD was made according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) (McKhan et al., 1984). The AD group was constituted by subjects with mild to moderate levels of dementia (Mini mental state examination, Folstein et al., 1975; MMSE range 16–25). AD participants were recruited from Ville Turro San Raffaele Hospital. All patients were submitted to an extensive neuropsychological assessment.

A group of 15 normally elderly individuals (6 males) took part in this study. None had a history of neurological illness or mental decline, and all had an adjusted score on the MMSE of > 24 (range of not adjusted score 24-29). The two groups were matched for age and education (see table 1).

	Controls mean (sd)	**AD mean (sd)**	**P**
Age	74,3 (7,66)	75,6 (7,02)	.64
Education	8,3 (4,1)	8,4 (3,44)	.96
MMSE	27,3 (1,63)	21 (2,67)	<.0001

Table 1: Demographic characteristics of AD and control group participants, Means and, in parentheses, standard deviations (sd).

All subjects were submitted to CaGi, the full semantic memory battery for concrete concepts described in the previous chapter.

Written consent was obtained from all participants and/or caregivers.

Tests

Two semantic tasks of CaGi battery were used in the following order:

1) naming of coloured photographs task: participants were requested to name the 48 pictures
2) sentence verification of 480 semantic features: This task is divided in two sessions, in the first the subject is asked to say everything he\she knows about each concept; in the second session she\he is asked to answer questions related to the features he\she has not generated. Ten features were selected for each concept from the collected norms:
    - 4 features with higher semantic relevance, of which 2 shared (1 sensorial and 1 non sensorial) and 2 distinctive (1 sensorial and 1 non sensorial)
    - 4 features with lower semantic relevance, of which 2 shared (1 sensorial and 1 non sensorial) and 2 distinctive (1 sensorial and 1 non sensorial)
    - 1 with higher and 1 with lower value of semantic relevance (different from those described above) independently of sensoriality or distinctiveness.

Each question includes a correct and an incorrect choice (see chapter 2 for further details).

We analysed the scores obtained in picture naming and in the sentence verification task.

Results

A T-Test revealed a significant lower performance of AD patients with respect to control subjects in both tests (naming: AD mean =0,89; sd=0,64; controls mean = 0,97, sd=0,3; t=-4,286, p<0,001; features verification: AD mean =0,93; sd=0,04; controls mean = 0,99, sd=0,1; t=-5,438, p<0,001; see Figure 1).

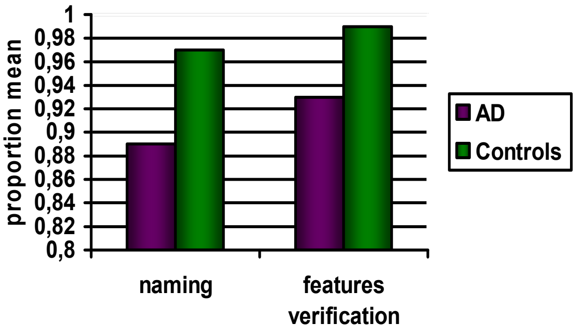

Figure 1: Performance of patients with Alzheimer's disease and controls at picture naming and features verification task

Comment

AD patients showed a significantly lower performance in both semantic tasks: naming and sentence verification. These results are in line with study showing a semantic memory impairment in AD patients.

3.2.4.1 The progressive deterioration of semantic memory

Subdivision of AD patients on the basis of naming performance

In order to investigate the loss of semantic memory at feature level within the progressive deterioration of semantic memory, AD patients were divided into three groups on the basis of the performance obtained on naming task.

The three groups were divided on the bases of naming performance as follow:

- MINIMAL AD (n=6): in this group we included patients with an equivalent scores of >1 (based on the validation obtained in chapter 2) and a performance within 2 SD of mean of the controls
- MILD AD (n=5): patients with an equivalent scores of 1 and 2-3,5 SD below controls mean
- MODERATE AD (n=4): patients with an equivalent scores of 0 and more than 3,5 SD below mean of controls mean.

The four groups were matched for age (p=,324) education (p=,201) and MMSE (p=,342).

In Table 2 are shown the performances obtained from each patient in naming and feature verification and the relative equivalent scores, obtained from the standardization described in chapter 2.

	pt1	pt15	pt3	pt8	pt6	pt10	pt4	pt5	pt9	pt13	pt14	pt11	Pt18	pt12	pt2
Naming (48)	47	46	45	45	45	45	43	43	43	42	42	41	40	38	36
ES naming	3	3	2	3	3	3	1	1	1	1	1	0	0	0	0
Feature v (480)	461	465	475	443	443	451	433	456	451	442	447	458	450	430	396
ES features v	2	2	4	0	0	0	0	0	0	0	0	1	0	0	0
Group	min	min	min	min	min	min	mild	mild	mild	mild	mild	mod	mod	mod	mod

Table 2: scores of each AD patient at picture naming and at feature verification task and respective equivalent scores. For each patient is indicated the group: min= minimal AD; mild= mild AD; mod=moderate AD; ES=Equivalent Score, feature v.=feature verification

Whereas the mild and moderate groups obtained an equivalent score of 0 in the feature verification task and, respectively, 1 and 0 in the naming task (except for pt 11 with an equivalent score of 1 at features verification), the minimal group was more heterogeneous. In fact, whereas three of six patients showed a normal performance in both tasks, the other three showed an impaired performance in the feature verification task.

In order to have a more homogeneous group of patients, with a normal performance in naming, feature verification task and MMSE, we enrolled 4 amnestic MCI patients (aMCI, range age: 72-77; range education= 8-18; range MMSE: 24-30). They obtained an equivalent scores of ≥1 in both tasks (see table 3). All the 5 groups, controls, minimal AD, mild AD, moderate AD and aMCI are matched for age (p=,496) and education (p=,182).

	aMCI 1	aMCI 2	aMCI 3	aMCI 4
Naming (48)	46	47	47	46
ES naming	3	3	3	3
Feature v (480)	472	470	461	466
ES feature v	3	3	1	2

Table 3: score of each aMCI patient at picture naming and at feature verification task, ES=Equivalent Score, Features v.=feature verification

Comment

The heterogeneity between patients in the minimal group are in accordance with the variability of naming deficits documented in AD patients, specially in the early stage of the disease, in which to a normal performance obtained in a naming task can correspond a semantic impairment as assessed with other tasks (Joubert et al., 2010). However, we can see that an equivalent number of features was scored both by a patient with normal naming and by one with an impaired performance. If the number of features is not so important to predict the naming performance, is the type of features maybe more important?

3.2.4.2 The degradation of distinctive features

In order to investigate if the different levels of semantic memory loss, and in particular the different levels of performance in the naming task, are characterised by a different pattern of distinctive feature deterioration in comparison to shared ones, we compare performance of the five groups for:

1) distinctive (n=245) versus shared features (n=235)
2) distinctive features with high values of semantic relevance (n=137) vs distinctive features with low semantic relevance (n=108) vs shared features (n=235, 107 with high semantic relevance and 128 with low values of semantic relevance)[3].

Statistical methods

Accuracy was calculated as the proportion of correct responses for each item and for each feature, and calculated for each group separately. Analyses were carried out with performance (accuracy, mean proportion of correct responses) as a dependent variable. ANOVAs were performed with type of features (distinctive and shared features) as factors, group (control group, aMCI, minimal, mild and moderate AD) as a repeated measure. ANOVAs were carried out for the item performance and two different analysis were performed, one at the concept level (Fc, n=48), the other at the feature level (Ff, n=480).

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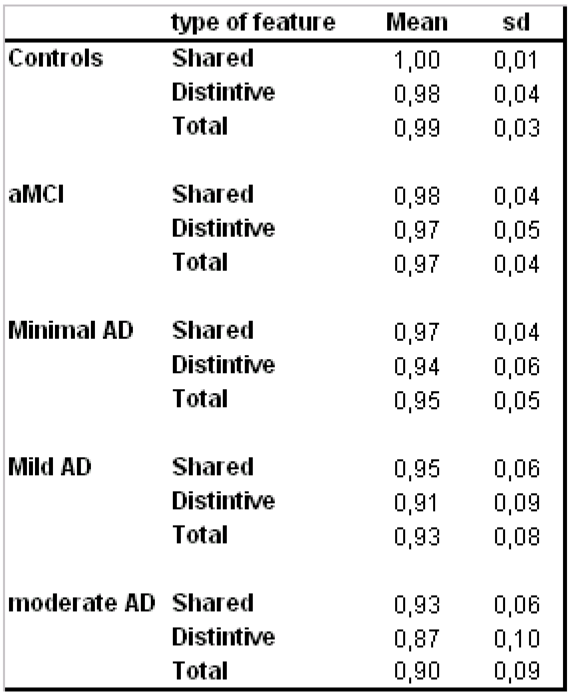
[3] The aim of the study is to investigate the difference between distinctive and shared features, thus we maintain all the shared features clustered together. In feature norms , subjects generally tend to list more distinguishing features than features that are true of large number of entities (McRae et al, 2005). Features with low values of dominance obtain low values of semantic relevance, in addition, the more common are the features, the lower value of semantic relevance they obtain.

Results

Two ANOVAs were performed with the type of feature (distinctive vs shared) as a factor, group (five levels: controls, aMCI, minimal AD, mild AD, moderate AD) as a repeated measure. There was a significant main effect of distinctiveness [Fc(1,94)=16,59, p<0,001; Ff(1,478)=21,102, p<0,001], as distinctive features generated more errors than shared features. A major effect of group (Fc(4,376)=46,806, p<0,001; Ff(4,1912)=57,258) was also observed, with response accuracy gradually decreasing. The distinctiveness and group interaction was significant [Fc(4,376)=4,485, p<0,01; Ff (4,1912)=4,976, p<0,005] (see Table 4 and Figure 2).



	type of feature	Mean	sd
Controls	Shared	1,00	0,01
	Distintive	0,98	0,04
	Total	0,99	0,03
aMCI	Shared	0,98	0,04
	Distintive	0,97	0,05
	Total	0,97	0,04
Minimal AD	Shared	0,97	0,04
	Distintive	0,94	0,06
	Total	0,95	0,05
Mild AD	Shared	0,95	0,06
	Distintive	0,91	0,09
	Total	0,93	0,08
moderate AD	Shared	0,93	0,06
	Distintive	0,87	0,10
	Total	0,90	0,09

Table 4: Mean accuracy and standard deviation for each group on shared and distinctive features at feature verification task.

Post-hoc analyses revealed that distinctive features are more vulnerable than the shared ones for all pathological groups, except for aMCI (p=,129). The difference between shared and distinctive features became marked from minimal group (see interaction between group and distinctiveness) and progressively increased in mild and moderate groups (all p<0,01).

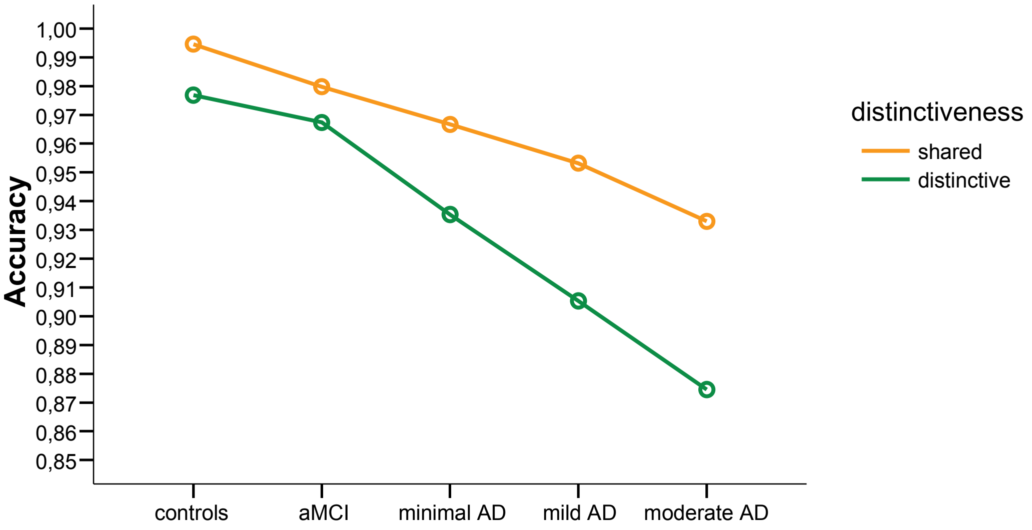


Figure 2: Mean performance of each subgroups on shared and distinctive features at features verification task.

Comment

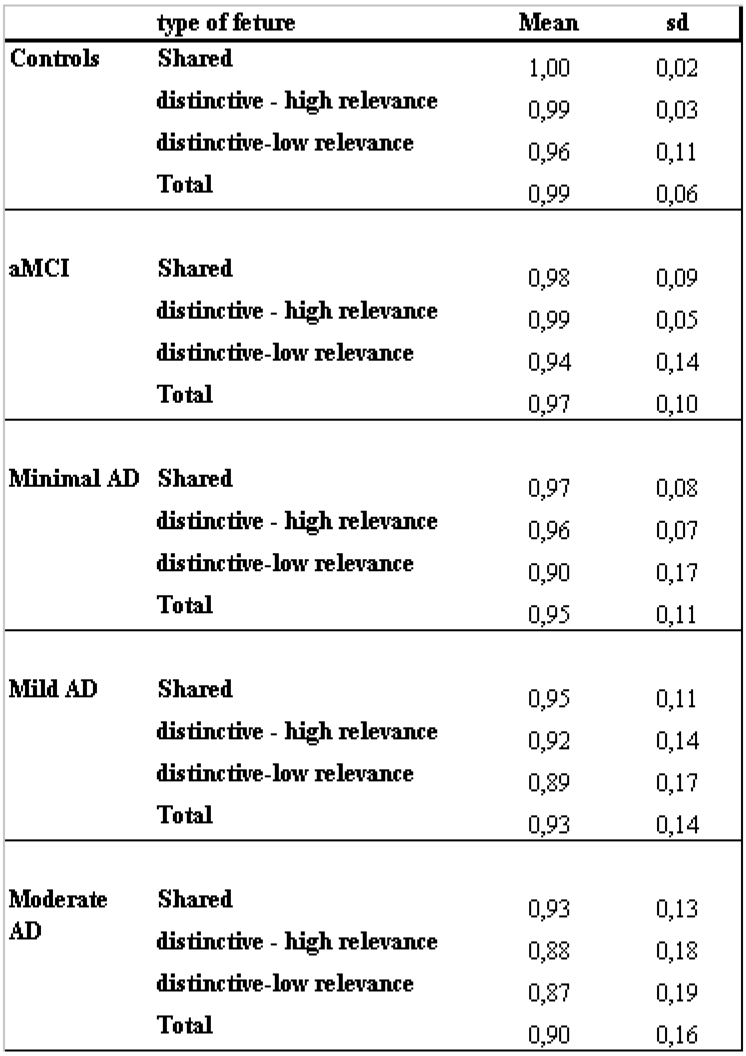
In AD patients distinctive features are more vulnerable than shared ones. The difference between the two types of feature is present also in the minimal group, in which naming was unaffected.

3.2.4.3 The role of semantic relevance for distinctive features

The question that still remains open is whether all the distinctive features are vulnerable to the same degree and have the same importance in maintaining the core of a concept meaning. In particular, we want to investigate whether the three AD groups show a pattern of degradation compatible with their naming deficit, and if distinctive features with high values of semantic relevance are more robust than the distinctive features with low relevance

In the following analysis we kept all shared features together (a t-test revealed no significant difference between high relevance and low relevance shared features for all groups, except for aMCI and mild AD $p<0,05$).

To better investigate the different role of high relevant distinctive features versus low relevant distinctive features, an ANOVA was performed with type of features (shared, high relevant distinctive, low relevant distinctive) as factor, and group (five levels: controls, aMCI, minimal AD, mild AD, moderate AD) as a repeated measure. Both main effects [(group: Ff(4,1908)=60,642, p=0,001; distinctiveness: Ff(1,477)= 11,523, p<0,001] and interaction were significant (Ff(8,1908)=5,822; p<0,005) (see Table 5 and Figure 3).



	type of feture	Mean	sd
Controls	**Shared**	1,00	0,02
	distinctive - high relevance	0,99	0,03
	distinctive-low relevance	0,96	0,11
	Total	0,99	0,06
aMCI	**Shared**	0,98	0,09
	distinctive - high relevance	0,99	0,05
	distinctive-low relevance	0,94	0,14
	Total	0,97	0,10
Minimal AD	**Shared**	0,97	0,08
	distinctive - high relevance	0,96	0,07
	distinctive-low relevance	0,90	0,17
	Total	0,95	0,11
Mild AD	**Shared**	0,95	0,11
	distinctive - high relevance	0,92	0,14
	distinctive-low relevance	0,89	0,17
	Total	0,93	0,14
Moderate AD	**Shared**	0,93	0,13
	distinctive - high relevance	0,88	0,18
	distinctive-low relevance	0,87	0,19
	Total	0,90	0,16

Table 5: Mean accuracy and standard deviation for each group on shared, distinctive features with high values of semantic relevance and distinctive features with low values of semantic relevance at feature verification task.

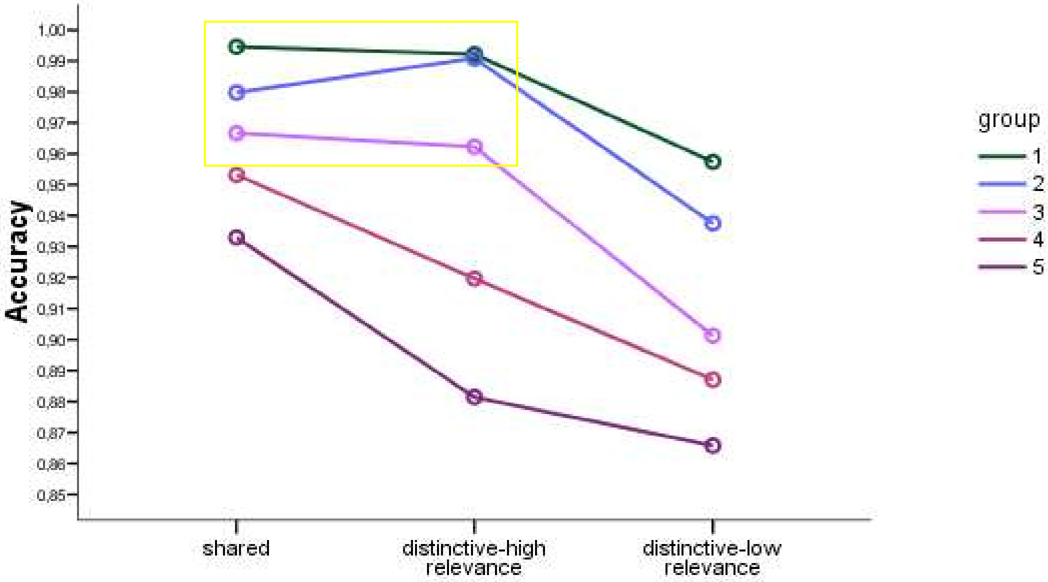


Figure 3: Mean performance of each subgroup on features: shared, distinctive with high values of semantic relevance and distinctive with low values of semantic relevance. Group: 1= controls, 2=aMCI, 3=Minimal AD, 4=Mild AD, 5= Moderate AD.

Tukey post-hoc analyses showed that shared features were as accurate as distinctive with high values of semantic relevance, and both were better than distinctive features with low values of semantic relevance. A One-way ANOVA for each group was carried out in order to investigated the differences between the three types of features (shared, distinctive with high relevance and distinctive with low relevance). All five ANOVAs resulted significant (p<0,001). Tukey post hoc analysis showed that for controls (p=0,918), aMCI (p=0,512) and Minimal AD (p=0,921) there was no difference between shared and distinctive features with high relevance, whereas a significant difference was present for Mild (p=0,057) and Moderate AD (p<0,005). The distinctive features with low relevance were different from shared and distinctive with high relevance for controls, aMCI and minimal AD (all p<0,001). In the mild and moderate group the distinctive features with low values of semantic relevance were less accurately verified than shared features (all p<0,001), but no differences were detected with respect to distinctive with high values of semantic relevance (p>0,149). In addition further comparisons between groups showed a progressive decline in processing features, but different for the different kinds of features (shared: controls > aMCI ≥ minimal ≥ mild ≥ moderate, aMCI>mild, aMCI>moderate, minimal>moderate, ≥ indicates differences approached statistical significance with a p value from 0,054 to 0,058; distinctive with high relevance: controls = aMCI > minimal > mild > moderate, p<0,05; distinctive with low relevance controls = aMCI > minimal = mild = moderate, minimal > moderate, p<0,05).

Finally, in order to verify whether the loss of distinctive features with respect to shared is not merely due to different values of dominance between shared and distinctive features or to the greater number of shared features, we selected 137 shared features (at least two for each concept) matched for dominance with distinctive features with high semantic relevance (p=0,97; see table 6).

Type of feature	Number	Dominance Mean (sd)	semantic relevance Mean
Shared	137	11,35 (5,3)	33,37
Distinctive with high relevance	137	11,65 (4,9)	63,65
Distinctive with low relevance	108	3,56 (1,02)	15,29

Table 6: number, mean values of dominance and semantic relevance for the three different types of features, considering a subset of shared features (see text).

An ANOVA was performed with type of features (shared, high relevant distinctive, low relevant distinctive) as factor and group (five levels: controls, aMCI, minimal AD, mild AD, moderate AD) as a repeated measure. Both main effects [(group: Ff(4,1516)=46,736, p=0,001; distinctiveness: Ff(1,379)= 16,097, p<0,001] and the interaction were significant (Ff(8,1516)=4,022; p<0,005) (see table 7 and figure 4).

Tukey post-hoc analyses showed that shared features were as accurate as distinctive with high values of semantic relevance and both were better than distinctive features with low values of semantic relevance. A One-way ANOVA for each group was carried out in order to investigated the differences between the three types of features (shared, distinctive with high relevance and distinctive with low relevance). All five ANOVAs resulted significant (p<0,001). Tukey post hoc analysis revealed the same results reported in the previous analysis, with the exception that in this case the difference between shared and distinctive features with high relevance in the mild AD group was more marked (p<0,05). Considering only minimal and mild AD, they differed in the distinctive features with high relevance (p<0,05), but not for shared and distinctive features with low relevance.

	type of features	Mean	Std. Dev.
Controls	Shared	0,99	0,02
	distinctive-high relevance	0,99	0,03
	distinctive- low relevance	0,96	0,11
	Total	0,98	0,06
aMCI	Shared	0,98	0,10
	distinctive-high relevance	0,99	0,05
	distinctive- low relevance	0,94	0,14
	Total	0,97	0,10
Minimal AD	Shared	0,97	0,08
	distinctive-high relevance	0,96	0,07
	distinctive- low relevance	0,90	0,17
	Total	0,95	0,11
Mild AD	Shared	0,96	0,10
	distinctive-high relevance	0,92	0,14
	distinctive- low relevance	0,89	0,17
	Total	0,93	0,14
Moderate AD	Shared	0,95	0,12
	distinctive-high relevance	0,88	0,18
	distinctive- low relevance	0,87	0,19
	Total	0,90	0,17

Table 7: Mean accuracy and standard deviation for each group on distinctive features with high values of semantic relevance, distinctive features with low values of semantic relevance and a subset of shared features (see text).

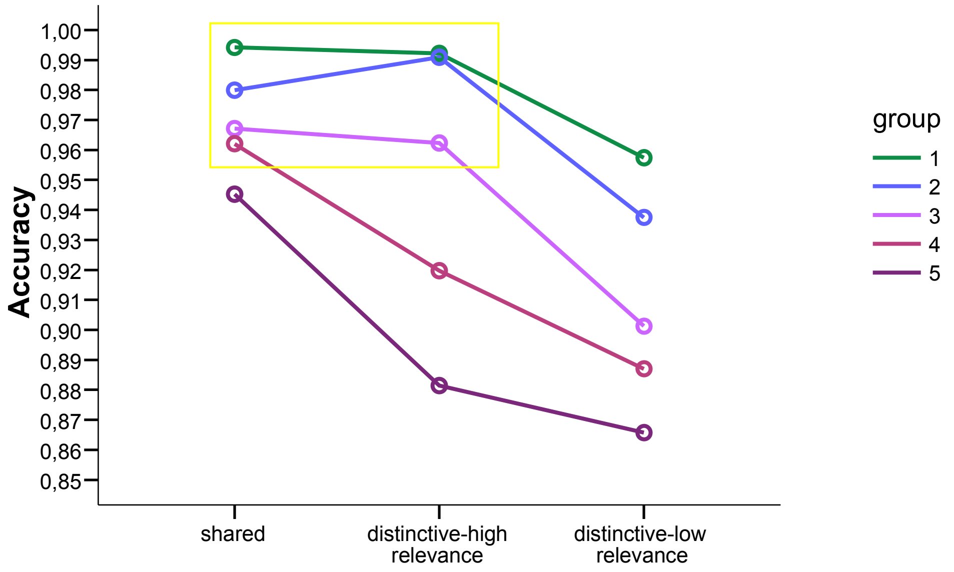


Figure 4: Mean performance of each subgroup on features: distinctive with high values of semantic relevance and distinctive with low values of semantic relevance and on a subset of shared features. Group: 1= controls, 2=aMCI, 3=Minimal AD,4=Mild AD, 5= Moderate AD.

Comment

Also in this case we reported a greater impairment for distinctive features in comparison to the shared ones. The differences between shared and distinctive features was present in the mild group, associated with mild naming impairments, and progressively increased in the moderate groups. This result contrasts with the results of the previous analysis regarding distinctiveness independent from relevance. In that analysis the difference between shared and distinctive feature was present also in the minimal group, with no naming impairment. We can suppose that the differences found in the minimal stage are due to the impairment of distinctive features with low semantic relevance.

3.2.4.4 Semantic impairment in the MINIMAL AD group

Finally, in order to investigate the pattern of semantic features degradation in the three patients of the minimal group, who had a normal performance in naming task but an impaired performance in sentence verification, we conducted a further analysis. We subdivided the minimal group separating these three patients (MINIMAL2) from the others 3 who obtained a normal performance in both tasks (MINIMAL1). We carried out two one-way ANOVAs, one for each MINIMAL group, in order to investigate the differences between the three types of features (shared, distinctive with high relevance and distinctive with low relevance). The two ANOVAs resulted significant ($p<0,001$). Tukey post-hoc analysis showed that for both Minimal groups there was no difference between shared and distinctive features with high relevance (MINIMAL1, mean shared=0,985, mean distinctive high relevance=0,992, $p=0,840$; MINIMAL2, mean shared=0,949, mean distinctive high relevance=0,932, $p=.652$), while the distinctive features with low relevance (MINIMAL1, mean=0,926; MINIMAL2, mean=0,877) were less accurately verified than both shared and distinctive features with high relevance ($p<0,05$). The same results were found considering all the shared features.

Comment

Although three patients of the minimal group (in which no naming impairment was detected) had an impaired performance in the sentence verification task, we found that distinctive features with high values of semantic relevance were not less accurately verified than the shared ones, as it was the case in the Mild and Moderate groups.

3.2.5 Discussion

In this study we assessed semantic memory in patients with AD using two tasks of the CaGi battery: picture naming and sentence verification. The latter task allows to investigate the status of the semantic system at the feature level. AD patients performed worse than controls in both tasks.

In order to include a pathological group without evident semantic memory impairment, we recruited also a group of aMCI patients.

AD patients were subdivided on the basis of picture naming performance and all groups of subjects (controls, aMCI, Minimal AD: without naming impairment, Mild AD: with mild naming impairment, Moderate AD with moderate naming impairment) were assessed for shared and distinctive semantic features. In all AD groups, including patients without naming impairments, but not in aMCI patients, distinctive features (independently from semantic relevance values) were more impaired than shared features. Further investigations allowed to investigate the different progression of deterioration of two different types of distinctive features, distinctive with high semantic relevance and features with low semantic relevance. Whereas in the minimal group there was a significant difference between shared and distinctive features with low relevance, no differences were detected between shared and distinctive features with high values of semantic relevance, a pattern shown also by aMCI and controls. In contrast, a significant difference between shared and distinctive features with high values of semantic relevance was observed in AD groups with Mild and Moderate semantic memory impairments, as assessed with the picture naming task. In addition, we verified that these results were not due to the greater number of shared features or to a dominance effect.

Picture naming is generally considered to reflect the degree of semantic memory loss in patients with AD (Whatmough et al., 2003). In particular, some authors suggested that distinctive features may play an essential role in picture naming (Duarte et al., 2009). Distinctive features characterize a small number of concepts, permitting to differentiate between similar concept belonging to the same category (tiger and lion). Generally, they are evaluated indirectly through picture naming tasks, or directly through property verification tasks. Shared features characterise several concepts (both lion and tiger have legs), without a contribution in differentiating similar concepts. Generally, they are assessed indirectly with a sorting task or more directly through property verification tasks. According to several studies, in neurodegenerative disorders, as in AD, shared features are more resistant than distinctive features (Garrard et al., 2005; Hodges et al. 1996). The loss of distinctive features and the sparing of shared ones lead to a confusion between similar concepts. This pattern of deterioration has been used to explain semantic errors in picture naming, such as *lion* for *tiger* or *animal* for *tiger*. However, although some authors suggested the different importance of different distinctive features, no one has verified this hypothesis in AD patients. In this study, we found that patients with an impairment in picture naming showed a greater loss of distinctive features with high values of semantic relevance in comparison to shared ones. These findings support the idea that features with high semantic relevance allow us to distinguish between similar concepts and to identify them (Sartori & Lombardi, 2004). These features may be those of the identification semantics, necessary for the correct identification of concrete objects and that uniquely identify the concept (Chertkow & Bub, 1990b; Whatmough & Chertkow, 2002). On the other hand associative semantics may be constituted of distinctive features with low semantic relevance. Similarly to Garrard and co-workers (2005), we confirm the greater loss of distinctive features with respect to the shared ones in AD. Concerning the results obtained in the first analysis, in which we consider the distinctiveness independent of semantic relevance, we documented a greater loss of distinctive features in comparison with the shared, without an association with picture naming performance in AD. In fact, the loss was evident in a stage of disease in which no naming impairments were found. In the same manner, Garrard and co-workers (2005), who used distinctive features, failed to demonstrate a relationship between naming performance and quantity of correctly verified distinctive features. The discrimination of distinctive features on the basis of semantic relevance allowed us to show a greater loss of distinctive with high semantic relevance in respect to the shared ones only in patients with naming impairment. No differences were in fact detected in patients without naming impairment. However, it is important to note that we discriminate the role of semantic relevance only for distinctive features, in order to capture the different importance between distinctive features. Generally, studies concerning semantic relevance compare features with high and low values of this dimension, including shared features, that commonly have lower values of relevance (in that they are common to many concepts). Summarizing, the difference considered in this study is between distinctive features with high and low dominance.

In this study the underlying semantic impairment does not fully account for the naming performance. This is particularly true in patients with a normal performance in the naming task, labelled as MINIMAL AD. Some of these patients showed an impaired performance in the sentence verification task. A similar pattern has already been reported in the early stage of AD (Joubert et al., 2010).

We can suppose that, even if the number of features correctly verified is under the normal cut off, patients maintain the same proportion of shared and distinctive features, a pattern which probably does not lead to a confusion between similar concepts. It is necessary to study a larger number of patients with normal performance in naming and a pathological score in feature verification task to verify this hypothesis. Although naming performance does not always reflect the integrity of semantic memory there is evidence that in AD this is usually the case (Whatmough et al., 2003). A general measure of dementia, such as MMSE, does not account for differences in semantic memory impairment, in that patients with equivalent level of disease severity can show a different level of semantic impairment (Whatmough et al., 2003).

In this study we showed as the progressive deterioration of the semantic representation of objects could be detected only in part with the performance in picture naming. However, patients with the same performance on MMSE showed different levels of semantic memory impairment. Thus, even if picture naming cannot be considered as an exhaustive measure of semantic memory, it seems more accurate than the MMSE. The different levels of question difficulty in sentence verification task could in part explain why some features were more impaired then others. However, the three AD groups, different in naming performance, had comparable MMSE scores. In addition, the three groups performed differently on feature verification, on the basis of their naming performance. If difficulty was the predictive variable, all AD groups could be expected to perform in the same way.

In conclusion, this study suggests that lower performance in picture naming is associated with a greater impairment of distinctive features with high values of semantic relevance than of the shared ones. Even if the study has been conducted on the same items, we did not look for a item by items correspondence. Thus, we can only argue that AD patients with impaired picture naming performance showed a greater loss of distinctive than of shared features. We have shown that not all the distinctive features are lost in respect to the shared ones with the same progression in AD. Distinctive features high values of semantic relevance, in fact, are maintained at the same level as the shared ones in patients without naming impairments. These results are not divergent from those showing a greater importance of visual features in picture naming, in that the type of features and distinctiveness are different, but not mutually exclusive dimensions. It is likely that visual features are often distinctive features with high relevance (see Mechelli et al., 2006). These results must be however verified with a larger number of patients and with a longitudinal study.

PART II

3.3 The presence of category effect

The differential deterioration of semantic memory within the living (L) and non living domains (NL) in AD is a complex research issue.

Differently from some of the reported cases of focal brain damage, in which the difference in accuracy between the two domains could reach 50%, with the preserved category intact, in AD all the categories are degraded. The category difference is rarely more than 20% (Whatmough et al., 2003) or 25% (Whatmough & Chertkow, 2002), and is generally called a category effect (Whatmough et al., 2003). Chertkow & Bub (1990a) were the first to notice a worse performance for living things in comparison to non living things in patients with AD. The patients were administered probe questions requiring yes-no answers for both living entities (including animal, fruit and vegetables) and non-living things (vehicles, furniture and clothing). One of the first studies that systematically compared the two domains has been carried out by Silveri and co-workers (1991). They used a picture naming and an associative task. Living and non living items were matched for word frequency and category typicality. AD were more impaired for living things than for non living items. A subsequent study using the same stimuli verified this effect (Tippet et al., 1996). However, the effect disappeared using a set of stimuli matched for familiarity, frequency, visual complexity and prototypicality (Tippet et al., 1996). Previous studies had in fact documented the important role of familiarity, visual complexity and age-of acquisition (Funnell & Sheridan, 1992; Stewart, Parkin, & Hunkin, 1992) in the explanation of living – non living dissociation. However, even indicating an important role of intrinsic variables, the results of Tippet and co-workers (1996) could be, at least in part, due to the familiarity of the stimuli. In fact AD patients were more accurate in the set of accurately matched stimuli than in that used to document the category effect (Whatmough & Chertkow, 2002). In addition, using the same set of well-matched stimuli in a subsequent study, Tippet et al. (2007) showed a deficit for non living things. They assumed that this pattern was not evident in the 1996 study because of the small number of patients. In addition the authors explained this category effect as a bias in the stimuli used, undetected because controls scored at ceiling. Several subsequent studies reported divergent results. Most studies have documented a greater impairment for living things (Chertkow & Bub, 1990a; Garrard et al., 1998; Gonnerman et al., 1997; Silveri et al., 1991; Zannino et al., 2002). Also the opposite dissociation and or combinations of both deficit types have been reported, although more rarely (Garrard et al., 1998; Gonnerman et al., 1997; Laws et al., 2003). In addition, other studies reported no category effect (Hodges et al., 1992; Perri et al., 2003; Tippett et al., 1996, 2007). Inconsistent results have been reported for groups (Silveri et al., 1991; Tippett et al., 1996), subgroups (Laiacona et al., 1998; Montanes et al., 1995) and for individual patients (Garrard et al., 1998; Gonnerman et al., 1997; Mauri et al., 1994).

Nuisance variables and methodological problems have an important role in accounting for these contrasting results. In addition the heterogeneity of the semantic deficits in AD has also been proposed as a factor accounting for these discrepancies. Category effects in AD have been assessed with a variety of semantic tasks (Daum et al., 1996; Mauri et al., 2004), with picture naming as the most used, and sometimes the only one (e.g. Moreno Martinez & Laws, 2007; Whatmoughet al., 2003; Tippet et al., 2007). A recent meta-analysis of 21 studies using picture naming task in AD patients, revealed no a significant difference in the effect sizes for living and nonliving things, although more studies revealed deficits for living things (Laws et al., 2007). Some authors suggested that using picture naming as a critical test of category effects would miss some patients who show consistent category deficits in other tasks. In addition it could mask the lack of consistency across tasks. Laws and Sartori (2005) showed category inconsistencies across different semantic tasks. A paradoxical dissociation has also been reported in a patient scoring better in picture naming for living things and showing the opposite dissociation in a feature verification task. In contrast, in a group study, Moreno Martinez and Laws (2008) showed the same performance in picture naming task, naming to definition and word-picture matching. In some semantic tasks, like category fluency, member dominance and ranking, no category effect has been documented (Cronin-Golomb et al., 1992; Hodges et al., 1992). A better performance on living things has been observed in a sorting task by Montanes et al. (1996). It has been supposed that some of these tasks, as category fluency, involved additional non-semantic processes that could obscure category effect in AD (Whatmough et al., 2003). Furthermore, it may be possible that category effects are evident only in tasks requiring specific information about objects.

In conclusion, as suggested by Moreno-Martinez and Laws (2008) it is recommendable to use different tasks, in order to assess the consistency across tasks and the presence of category effects in tasks other than picture naming.

3.3.1 The role of nuisance variables

Several investigators suggested that category effects may be an artefact of uncontrolled item variables (Funnell & Sheridan, 1992; Stewart, Parkin, & Hunkin, 1992). Living things may result more vulnerable than non living things, because they are associated to lower values of concept familiarity (Funnel & Sheridan, 1992), word frequency, and higher values of visual complexity (Stewart et al., 1992). This account can explain deficits for living things, while it cannot be reconciled with studies showing the opposite dissociation. Some authors supported the idea that items selection may casually result in a between category imbalance, penalizing nonliving items (Sartori & Lombardi, 2004; Zannino et al., 2006a). However, opposite dissociations have been observed with the same test material (Gonnermann et al., 1997). Zannino et al. (2006a) suggested that individual premorbid differences can explain these cases.

Several studies reported no category effect or an attenuation of the category effect in AD when stimuli were matched for nuisance variables (Moreno-Martinez & Laws, 2008; Tippet et al., 1996; 2007), A surprising result derives from a study of Albanese (2007), who showed a category effect only after having taken into account the role of concomitant variables. This effect was observed only for AD, with a better performance on non living things, but not for controls. Other studies have also shown that category effects persist even when the effects of nuisance variables are controlled (Gale et al, 2009; Zannino et al., 2002).

All these studies varied for the number and the type of variables matched. It is difficult to match multiple stimulus variables simultaneously, and in addition it is not clear which are the most important variables (Tippet et., 2007). In fact new variables have recently been identified, which have an important role in predicting naming accuracy and category dissociation in AD, such as age of acquisition, name agreement (Silveri et al., 2002), imageability and number of target alternatives (Albanese, 2007). Zannino et al. (2006a) demonstrated that the disadvantage on living items observed in patients with Alzheimer's disease was attenuated when semantic distance was taken into account. In addition, Sartori and Lombardi (2004) demonstrated that the impairment for L items disappeared when stimuli were matched for semantic relevance. Nevertheless, a recent meta-analytic review documented as the number of matching variables controlled had no impact on effect sizes for either L or NL naming in AD (Laws et al., 2007). Tippet and co-workers (2007) showed in the same group of AD patients three different patterns of deterioration (a better performance on L items than on NL, the opposite pattern and no difference between the two domains) on the basis of different stimulus selection. Similar evidences were reported by Sartori and Lombardi (2004), who, matching or not matching stimuli for semantic relevance, showed the three different patterns in AD patients. In addition Tippet and co-workers documented that patient with AD showed a deficit for L when items were loosely matched for familiarity (with a p value from 0,5 to 0,15). When tightly matched stimuli were used, the effect disappeared (Tippet et al., 2007). However in this study they used a very small set of stimuli, 14 living and 14 nonliving items. Some studies reported a category effect for living even after a stringent control of the variables (Albanese, 2007; Martinaud, 2009; Zannino et al., 2002). Because of the difficulty in the matching of the stimuli, these studies adopted regression analyses. This method permit to examine category effects partialling out the possible influence of multiple intrinsic stimulus variables (Laiacona et al., 1993; Perri et al., 2003; Silveri et al., 2002; Zannino et al., 2002). However, contrasting results derived from studies using this approach, with Silveri et al. (2002) Zannino et al. (2002), Albanese (2007) and Martinoud (2009) finding a L impairment, and Perri et al. (2003) and Tippet et al. (2007) finding no evidence for a category effect.

More recently, some investigators put forward the hypothesis that the impact of concept-level variables on picture naming is similar for both AD patients and healthy controls (Gale et al., 2009; Moreno-Martinez et al., 2007; 2008). The differences between the two groups are proposed to be only quantitative, with AD performing worse, but not qualitatively different, with the same size and direction of the category effect. Moreno-Martinez & Laws (2007) used control performance as a difficulty index. Covarying for the level of difficulty, category effects in AD disappeared in all tasks adopted, i.e. picture naming, naming to description and word-picture matching. Similar results have been reported in another study in which the category effect persisted even after controlling for nuisance variables, but not after covarying for control performance (Moreno Martinez & Laws, 2008). More recently Gale et al. (2009) carried out a hierarchical regression analysis, including as predictors nuisance variables (i.e. concept familiarity, visual complexity, word frequency, and age of acquisition), category (living/nonliving), and elderly control group performance. The results suggested that, while an independent effect of category may be present, the effects of intrinsic item variables, and especially of the normal tendencies can be much more substantial.

The majority of semantic memory studies used, as previous mentioned, picture naming tasks. The black and white drawings taken from the Snodgrass and Vandervent set (1980) were the most used. A number of authors reported that category effects for living things may be an artefact due to the removal of colour from images. Montanes and co-workers (1996) showed a disadvantage for living things using line drawings as stimuli. The category effect disappeared when coloured stimuli were used. However, different items were used for the different displays. A meta-analytic review suggested that coloured stimuli increase the impairment of naming L in AD, although few studies were considered (Laws et al. 2007). More recently Zannino et al. (2007), using the same items for both displays, showed how colored photographs with respect to line drawings improve the controls and AD performance on L items. Adlington et al. (2009) showed that naming improved for colour images only for controls; AD patients showed no improvement. In addition Laws et al.

(2007) reported that the number of stimuli did not predict the effect sizes for either L or NL, although the studies varied in the number of the stimuli used (range 20-120).

3.3.2 Methodological issues concerning category effect

The criteria adopted to define the presence of the category effect are not well-defined. Different methods have been in fact adopted to quantify performance in L and NL categories, diverging among studies. Some authors put forward the necessity of common guidelines and the importance of some minimal criteria in documenting category effect in patients (Laws, 2005). Laws reported that the most part of studies assessing category effect has used within subject analysis without a group of controls, assessing the living–nonliving naming difference only in patients. Excluding controls from studies prevents to know the "normal" performance and its direction. In fact if it could be supposed that the category effect in patients is an exaggeration of the controls performance, in that living things are more demanding than non living things. Although several studies documented that healthy subjects showed a better performance on non living things, others reported the opposite pattern (Laws, 2000, Laws & Gale, 2002; Laws & Neve, 1999). Thus, it results extremely important to explicitly examine the controls performance, as its lack may distort the interpretation of patient data. Clear hypothetical examples of how the lack of controls data could lead to a distort interpretations of patient pattern have been reported in the study of Laws (2005). For example, deficit for L in patients could simply be an exaggeration, if also controls find more difficult to name L. Otherwise, a hypothetical deficits for L in patients when compared with controls could appear as a NL deficit, if controls perform better on non-living things, and have the same performance as patients on L. In a study with AD patients Laws and co-workers (2005) compared the impact of using and not using controls data and showed very similar patterns to the hypothetical ones. Several studies reported other methodological problems. Sometimes healthy subjects were not matched for age, gender or background with AD patients (Caramazza & Shelton, 1998; Laiacona et al., 1997; Turnbull and Laws, 2000; but see Capitani & Laiacona, 2005). Capitani & Laiacona (2005) proposed that the inclusion of the name agreement in the analysis could be considered a good index of the difficulty of the stimuli, in that it measures the percentage of controls providing a correct name for the stimulus. In addition, controls should be sex matched with patients, as some studies reported an important impact of sex on category effect (Laiacona et al., 1998). Furthermore a ceiling effect in healthy subjects could distort the results, as it may mask any category effect exhibited by controls. Laws (2005) reported high level of controls performance in most studies using the Snodgrass and Vanderwart (1980) corpus of pictures. In a study with AD patients, Laws and co-workers (2005) compared the impact of using and not using stimuli producing ceiling effect in controls. They documented an exaggeration for living deficits when controls performed at ceiling. Some studies manipulated the difficulty of the stimuli in order to avoid the ceiling effect limit (Fung et al., 2001; Laws et al., 2005; Whatmough et al., 2003). Whatmough and co-workers (2003) showed a category effect, with a better performance on NL even using a set of low frequency items, not producing a ceiling effect in controls. However, the use of uncommon and difficult stimuli could lead to the inverse problem, a floor effect in patients (Capitani & Laiacona, 2005). These stimuli would be less representative of the common experience or “more subject to any peculiar habits of the subjects” (Capitani & Laiacona, 2005). In addition, some authors suggested to use degraded stimuli, but their use could introduce unknown variables in the experiment (Laws, 2005). Disagreeing with Laws and co-workers, Capitani and Laiacona (2005) concluded that several studies adopted an accurate methodology, specifically referring to the use of logistic regression analysis in which the difficulty of the stimuli, obtained from controls, was included in the model. Other investigators suggested the use of bootstrap multiple regression analysis in order to overcome the problems deriving from ceiling effects in control subjects, e.g. non normal data distributions (e.g., Gale et al., 2010; Moreno-Martínez & Laws, 2007).

3.3.3 Heterogeneity of AD patients

Some investigators suggested that the heterogeneity of AD subjects could account for category effect, in terms of its consistency and direction. It has been proposed that a changing pattern of categorical impairment could occur with the increasing disease severity and semantic deficits (Gonnermann et al., 2007; Whatmough et al., 2003). As the nature of the deficits is not consistent across AD, a typical group analysis could obscure the category effects. As the disease progresses, semantic impairments increase, but AD patients can show different pattern of semantic, verbal and visuospatial deficits. Considering all these differences, it could be possible that a small number of patients could not be sufficient to detect a category effect (Whatmough & Chertkow, 2002).

Some studies have actually shown category effect only in subgroup of patients. Montanes et al. (1995) described a subgroup of patients more impaired on verbal than on visuo-constructional tasks in which a category effect (with a lower performance for living things) was more probably to be evident. Furthermore some studies that did not reveal a category effect at group level, showed category effect with opposite directions in individual patients (Laiacona et al., 1998). Gonnerman et al. (1997) investigated in a longitudinal study the progression of semantic impairments in two AD patients. One patient consistently showed a progressively worsening performance on artefacts. The other patient showed no category effect at first assessment, a worse performance on artefacts at second assessment and finally a greater difficulty with L. Gonnermann et al.(1997) wanted to demonstrate that, at different semantic deficit levels, AD could show a different direction in the category effect. They subdivided AD in two groups on the basis of picture naming performance on L. They proposed that at mild impairment level AD were more impaired in naming artefact, while in a more severe stage, they resulted more impaired on L. The authors suggested that studies showing no category deficits, have generally failed to identify the differential effects of early and late stages of the disease. However, Garrard and co-workers (1998) did not confirm these results, in that they showed a better performance on artefacts at all different level of semantic impairment. Finally Whatmough et al. (2003) documented the category effect in large number of AD patients (72). They stratified patients in 5 groups, on the basis of picture naming performance. AD with scores within the normal range showed no category effect. With the increasing impairment in naming, a category effect was documented, with a better performance on artefacts. The authors suggested that in order to observe in AD a category effect on picture naming task the patients must be at least moderately anomic. In addition, if deficits in picture naming are mild, stimuli must be less familiar in order to obtain a defective performance in AD and a performance not at ceiling in controls.

These evidences suggest that some results reporting no category effects could be due to the fact that AD patients have been considered independently of their naming impairments. Collapsing AD patients with different naming deficits together could mask the effect. However Tipped and co-workers (2007) reported that in Whatmough et al. study (2003) the stimuli were only loosely matched for familiarity. As reported above, a stringent criteria in stimulus matching is required in order to neutralize the influences of nuisance variables. Finally the meta-analytic review (Laws et al., 2007) revealed that category effects are not associated with the severity of the dementia, when it is measured with MMSE.

3.3.4 Theoretical accounts for category effects in AD

Some explanations for category effects have been provided especially to account for their presence in AD. Several authors have proposed a functional-anatomical explanation to account for cases showing a deficit for L. Silveri et al. (1991), comparing their results in AD with those of earlier studies of Herpes Simplex Encephalitis patients, suggested that disproportionately more severe impairment for L can be associated to the early neuropathological changes predominantly affecting temporo-limbic regions in AD. Silveri et al. proposed that L may have a greater biological importance for humans in respect to artifact, and for this they may rely on the hippocampus and amygdala. The Warrington and Shallice explanation (1984) was adopted by Daum et al (1996) and Garrard et al (1998). Visual features are essential or more important for L and are vulnerable to temporal lobe damage. In contrast, functional features are more important for NL. A deficit for NL could be observed when pathology in AD may affect parietal and frontal cortex, as these regions are specialised for the representation of functional knowledge (Garrard et al., 1998).

Others suggested that concepts are represented as distributed patterns of activation over semantic features in a common unitary semantic space (see also chapter 1). Category effects result as an emergent property of the different conceptual organization, in that they differ in the number and type of properties and in the extent to which these properties are correlated with each other. Two opposite proposal have been put forward. Gonnermann et al. (1997; Devlin et al., 1998) proposed that correlated features (those that are frequently activated together, such as 'has-wings' and 'has-beak') are more common for living than for nonliving items, and are more resistant to damage because they are supported by multiple correlations. In contrast, distinctive features (those that uniquely identify an item from other similar items) are more vulnerable because they lack multiple correlations. At an early stage of disease, NL items were more affected than L, because their features are not maintained by collateral support from other correlated features. However, as damage progresses, also correlated features are lost, resulting in a greater degradation of L, resulting in a crossover pattern. With this model the authors tried to explain the double dissociation documented in AD in relation to the severity of damage. Devlin et al (1998) verified these hypothesis in a connectionist model (see chapter 1). However a number of studies failed to confirm the crossover effect in relation to the severity of damage (measured with MMSE in Zannino et al., 2002; with naming performance in Whatmough et al., 2003; Garrard et al., 1998;). In addition, evidences deriving from others computational models showed opposite results. Tyler et al (2000) in fact proposed an opposite longitudinally pattern of degradation for the two domains of knowledge. In this model, L are more vulnerable at an early stage of the disease, NL only at moderate stages. As Gonnermann et al (1997), they proposed that L are characterized by a greater number of correlated features than NL. In addition, they proposed an important role for the correlation between functional and perceptual features, that differs between L and NL. In L shared perceptual features co-occurs (are correlated) with biological functional information (e.g. has eyes-can see), while distinctive perceptual features are not correlated with functional ones (e.g. has stripes for zebra). In the artefact category, in contrast, distinctive perceptual features co-occur with distinctive functional information (e.g. has sew-cut). More correlated features are more resilient to damage than less correlated ones, as shared features (as they occur more frequently) than distinctive ones. At a mild degree of semantic memory impairment, L were more degraded because their distinctive features are only weakly correlated with others features. A deficit for NL occurs only for severe damage. Tyler et al (2000) verified these assumptions in a connectionist model. However, recent evidences failed to support this model in AD. Duarte et al. (2009) investigated the progressive loss of distinctive and shared features in both domains of knowledge. AD subjects were divided in 3 different levels of severity on the basis of their MMSE scores. Patients at an early stage of the disease did not show a prevalent loss of distinctive features for L, ,while this pattern was found in patients with mild and moderate deficits. Contrary to Tyler et al. assumptions (2000), the degradation of distinctive features of L was not found at an earlier stage of disease, but only in later stages. Distinctive features were more vulnerable than the shared ones.

Dixon and co-workers (1999) suggested that category effects may result from a different semantic similarity between concepts belonging to different categories. A greater structural and semantic similarity has been documented for L than for NL. Consequently, L are more confusable. NL are more resilient to semantic memory erosion because of their greater distinctiveness. Very similar conclusions have been reported by Zannino et al (2006a). They in fact reported that a preponderant deficit for L in AD could be due in part to the greater processing demands due to higher degree of semantic similarity between L.

3.3.5 The experimental study

The aim of the study

The aim of this study is to investigate the presence of category effect in AD and controls subjects, trying to overcome some of the limitations of the previous studies.

First, the majority of studies used picture naming task to assess category effects. Several studies, adopting different semantic tests, reported inconsistencies across tests and the presence of category effects in tests other than picture naming (Laws & Sartori, 2005). In this study we used two different naming tasks, involved different modalities of input, i.e. a picture naming task and a naming to verbal definition task.

Second, it is now well known that in order to verify the presence of category effects confounding variables must be taken into account (e.g. Law, 2005; Sartori & Lombardi, 2004, see also chapter 2). In addition, spurious category effect could be reported using stimuli loosely matched for confounding variables (Tippet et al., 2007). Previous studies varied largely in the number and in the type of variables considered. As some variables have been only recently introduced as possible predictors of category effects, they were not largely investigated. In this study we consider the majority of variables proposed as possible confounding variables in category dissociation, as emotional valence, semantic relevance, semantic distance, arousal, number of feature, functional and volumetric manipulability, together with the more widely used ones, i.e. age of acquisition, familiarity, visual familiarity, tipycality, (but see chapter 2 for further details).

Third, another import methodological problem concern the performance of controls, generally at ceiling. As discussed above, ceiling affect in controls could mask the direction of the normal performance, creating a bias in the interpretation of AD data. In this study we adopt two different tasks, and only in one of these, the picture naming tasks, controls scored at ceiling.

Fourth, some authors suggested that a group analysis could mask specific category effect due to the different severity of semantic memory impairment of patients. In this study we analyzed individual subjects' performances in order to overcome this problem.

Finally, some authors have suggested that the effects observed in the naming performance of AD patients are an exaggeration of those that can be observed also in the controls' performance. When controls performance was included in regression analysis the category effect in AD disappeared (Moreno-Martinez & Laws, 2007). In order to verify this hypothesis we included in the regression analysis, both at group level and at individual level, the controls' performance as a possible predictor, in addition to those mentioned above.

Subjects

For this study we enrolled 14 AD patients and 14 controls. The subjects are the same enrolled in the first study, with the exception of one patient and one control (see above for inclusion criteria and further details). We excluded pt18 because he was unable to complete the naming to description task. Consequently, we excluded a control male, in order to match controls for gender (5 males in each group). No differences were found between the two groups for age (p=0,69) and education (p=0,96).

Tests

We analysed the performances in the picture naming task and in naming to definition of the CaGi battery (see chapter 2 for details), focusing on the differences between L and NL. Both tasks required a naming processes, through different modalities of input. Controls performed at ceiling in picture naming (96%), but not in naming to definition (89%). The stimuli were matched across the two domains for visual complexity (p=0,2), Visual Familiarity (p=0,08), Name Agreement (p=0,18) Word Frequency (p=0,1), Age of Acquisition (p=0,25), number of letters (p=0,14), Semantic Distance between concepts and centroids (p=0,61) Semantic Relevance sum (p=0,16), arousal (p=0,76), emotional valence (p=0,1), volumetric manipulability (p=0,14) and, for naming to description only, for summed relevance of features (p=0,85, see chapter 2 for further details).

Results

Naming accuracy, as percentage of correct responses for each item, were calculated for each group and for each task separately. Table 8 reports the mean of correct responses for each tasks, for each group and for each patient. As anticipated, controls performed at ceiling only in the picture naming task. All the patients showed the same trend in both tasks, i.e. a better performance on NL. The largest difference was of 5 items for picture naming (pt13, pt14) and of 12 for naming to description task (pt4). Pt3 and pt8 are the only patients that in picture naming showed the inverse trend, but the difference is of 1 item only. Both patients revealed the opposite pattern in naming to verbal description task.

	pt1	pt2	pt3	pt4	Pt5	pt6	pt8	Pt9	pt10	pt11	pt12	pt13	pt14	Pt15	AD Mean (sd)	Controls Mean (sd)
Picture naming																
Living	0,96	0,71	0,96	0,83	0,83	0,92	0,96	0,79	0,92	0,75	0,71	0,79	0,79	0,92	0,85(0,22)	0,96(0,13)
Non living	1	0,79	0,92	0,96	0,96	0,96	0,92	1	0,96	0,96	0,88	0,96	0,96	1	0,94(0,13)	0,97(0,76)
Tot	0,98	0,75	0,94	0,90	0,90	0,94	0,94	0,90	0,94	0,85	0,79	0,88	0,88	0,96	0,89(0,19)	0,967(0,11)
ES	**3**	**0**	**2**	**1**	**1**	**3**	**3**	**1**	**3**	**0**	**0**	**1**	**1**	**3**		
naming to definition																
Living	0,75	0,42	0,71	0,38	0,58	0,54	0,79	0,58	0,58	0,67	0,54	0,54	0,63	0,79	0,61(0,34)	0,85 (0,22)
Non living	0,96	0,63	1	0,88	0,79	0,92	0,88	0,83	0,83	0,79	0,83	0,75	0,92	0,92	0,85(0,18)	0,94 (0,15)
Tot	0,85	0,52	0,85	0,63	0,69	0,73	0,83	0,71	0,71	0,73	0,69	0,65	0,77	0,85	0,73(0,3)	0,89(0,19)
ES	**3**	**0**	**3**	**0**	**0**	**1**	**3**	**0**	**0**	**0**	**0**	**0**	**1**	**3**		

Table 8: Proportion mean of correct responses for each tasks, for each patient and for each group.

In order to compare the naming performances of AD and controls with regard to the effect of category, we carried out two two-way ANOVAs (two groups: AD, controls; by two domains: L and NL), one for each task.

For picture naming, the ANOVA showed a significant main effect of Group (F (1,46)=20,016, p=0,005), with controls better than AD. Domain (F (1,46)= 1,698, p=,199) had no significant impact. However, the interaction between group and domain was significant (F (1,46)=8,011, p<0,01).

For naming to verbal description, both main effects, Group (F (1,46)= 43,685, p<0,001) and domain (F (1,46)= 7,301, p<0,05), and the interaction (F (1,46)= 8,513, p<0,001) were significant (see Figure 5).

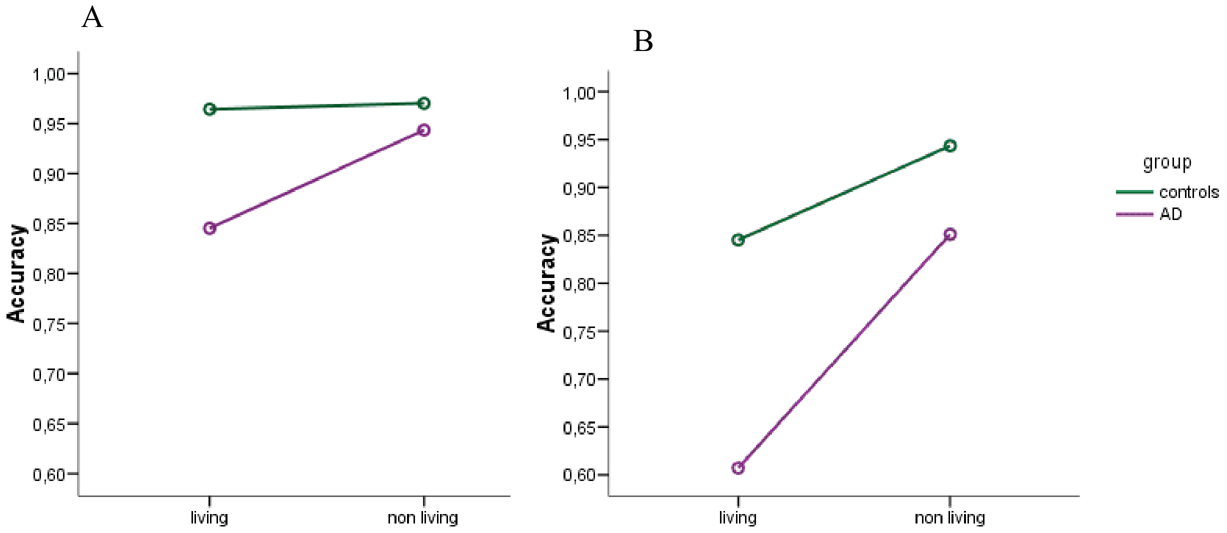


Figure 5: Mean accuracy of controls and AD on (A) picture naming task and (B) naming to description task.

Comment

Category effect has been reported in AD patients for both naming tasks. However, items were only loosely balanced across domains for many confounding variables. It has been demonstrated that a category effect could detected only for loosely matched items, but not for those tightly matched (Tippet et al., 2007). In addition an exaggeration of living deficits when controls scored at ceiling has also been reported. This is possible in the case of picture naming task, but not for naming to description task.

3.3.5.1 Stringent control of nuisance variables

Four stepwise regression analyses were carried out (see Zannino et al., 2002 for the same method), in order to investigate whether the category influenced AD and controls naming performances (on both tasks), once the confounding influence of intrinsic properties was taken in account. The dependent variable was the naming performance, the independent variables were domain and all the intrinsic variables available for the pictures and words (for pictures only: Visual Complexity, Visual Familiarity, Name Agreement; for both pictures and words: Word Frequency, Familiarity, Age of Acquisition, number of letters, Semantic Distance between concepts and centroids, Semantic Relevance sum, arousal, emotional valence, volumetric and functional manipulability, number of features and typicality, and for words only the sum relevance of features). In respect to previous studies, we added three others variables never considered before, i.e. functional manipulability, typicality and familiarity. The forward stepwise method enters the variables into the model one at a time, in an order determined by the strength of their correlation with the dependent variable. Considering previous findings, we had reasons to believe that some variables were likely to be more important than others, suggesting the use a hierarchical method. However, as in this model we introduced new variables, like emotional valence, manipulabity, arousal, semantic relevance etc., that were not considered in the previous models, we opted for the forward method (see Martinaud et al., 2009; Zannino et al., 2002 for the same methodology). In addition, as some independent variables are high correlated, we adopted the stepwise forward method in that multicollinearity could be a problem. The variance inflation factors (VIF) did not indicate multicollinearity.

For the controls' performance in the picture naming task, the only variable that entered in the equation was frequency($R^2 = 0.093$; $F(1,47) = 4{,}729$; $p= 0.035$), with more frequent items more accurately named. No other independent variable showed a significant influence on the dependent variable.

For AD, the first variable that entered in the model was frequency ($R^2 = 0.319$; $F(1,46) = 21{,}584$; $P < 0.001$), and also in this case more frequent items were named better. In a second step , age of acquisition showed a significant contribution in predicting the dependent variable (R^2change $= 0.099$; $F(1,45) =7{,}682$; $P = 0.008$).

For the controls' performance in the naming to verbal definition task, the only variable that predicted the performance was age of acquisition ($R^2 = 0.199$; $F(1,47) = 11{,}399$; $P = 0.002$), with earlier acquired words more accurately named.

For AD performance, the first variable that entered in the model was age of acquisition ($R^2 = 0.370$; $F(1,46) = 27{,}070$; $P < 0.001$), with earlier acquired items more accurately named. In the second step, domain entered into the equation (R^2 change = 0.098; F(1,45) = 8,258; P = 0.006), with NL more accurately named than L. In addition, also semantic relevance (sum) showed a significant contribution in predicting performance (R^2 change = 0.081; F(1,44) = 7,961; P = 0.007), with items with higher values of semantic relevance named better. No other independent variable made a significant contribution to the regression equation.

Some authors suggested that the naming performance of AD mirrors controls performance, and that category effect can be considered as an exaggeration of a normal behaviour. Gale et al (2009) introduced the controls' performance as a difficulty index in order to verify this hypothesis. Similarly, we conducted a hierarchical regression analysis, considering in addition to the other confounding variables the controls' performance (as difficulty index), in order to verify if category effect survived performance. These analysis were performed only for naming to description task, as we found a category effect only for this task. We conducted a hierarchical regression analysis using the same order of blocks as in Gale et al. (2009). In block 1 we entered only those nuisance variables with a significant correlation with the dependent variable (familiarity r=0,547, p<0,0005, word frequency r=,423, p<0,005, age of acquisition r=-,609, p=0,0005, semantic relevance r=,343, p<0,005 and semantic distance r=298, p<0,05), followed by domain (r=, 412, p<0,005) in Block 2, and controls' performance (r=,798, p<0,005) in Block 3. The regression model for block 1 was significant [R^2 = .499, F (5, 42) = 8,377, p = <0,0005]. The addition of domain to the model in the second block produced a significant R^2change = .061, F (1, 41) = 5,659, p = 0,022]. Also the third block resulted in a significant R^2change = .218, F (1, 40) = 39,129, p < 0,0005. Finally, we conducted another hierarchical regression analysis inverting the order of bock 2 and 3 (using the same order for blocks Gale et al., 2009). In block 1 we entered the nuisance variables, as before, followed by control performance in Block 2, and domain in Block 3. The regression model for block 1 was significant [R^2 = .499, F (5, 42) = 8,377, p = <0,0005]. The addition of difficulty index (controls' performance) to the model in the second block produced a significant R^2change = ,245, F (1, 41) = 39,163, p <0,0005. The addition of the domain resulted in a small but significant R^2change = ,034, F (1, 40) = 6,052, p =0,018.

Comment

Regression analysis showed a significant impact of domain only on AD performance in the naming to definition task, after partialling out the influence of nuisance variables. Considering also the controls performance in the analysis as a difficulty index the influence of domain diminished. In fact, after controlling for all nuisance variables, domain accounted for 6% of patients' naming variance. After controlling for all nuisance variables and the difficulty index, domain accounted only for 3% of the variance. In contrast, the controls' performance accounted for 24% of the variance after controlling for all nuisance variables and for 21% after controlling for both nuisance variables and domain. These results are similar to those of Gale et al. (2009).

3.3.5.2 Category effect at individual level

In order to confirm the results obtained at the group level, we performed for each individual subject a multiple logistic regression with a forward likelihood-ratio method (see Martinaud, 2009 for the same method). The dependent variable was the subject's performance in picture naming or naming to verbal description. All the intrinsic properties of the words and pictures and the domain were entered as independent variables.

For picture naming, no AD and no control showed a significant contribution of category to the prediction of performance. Age of acquisition predicted performance for 2 controls. The results for AD were heterogeneous. Frequency resulted an explanatory variable for 6 AD (but for 4 it only approached significance), age of acquisition for 4, familiarity for 2, volumetric manipulability for 2, visual complexity for 1, number of letters for 1, sum of semantic relevance for 1 and arousal for 1 (but only approaching to significance).

For naming to verbal definition (Model I in table 10) domain was significant only in 2 AD subjects, pt1 and pt4 (but in pt1 it only approached significance p=0,083, see table 10). No control showed a significant contribution of domain to the prediction of the performance. Age of acquisition was an explanatory variable for 4 controls, familiarity for 3 (1 only approached significance), number of letter for 1.

Age of acquisition was an explanatory variable for 7 AD, familiarity for 4, semantic distance for 3 (see table 10).

In order to verify the influence of difficulty index (controls performance) on the performance of each patient in the naming to description task, and to confirm whether it results in a reduction of category effects (in this case only in pt4) we carried other 14 logistic regression analysis, one for each patient. The dependent variable was subject performance in naming to verbal description. All the intrinsic properties of the words, domain and difficulty index were entered as independent variables (Model II, see table 9). In 9/14 cases the difficulty index entered as predictor, and in 6\9 as the only predictor. Only in four cases the difficulty index did not enter as predictor. In these case the pattern remained the same as in the previous analysis, and only in one case no variable entered in the model (pt1, see table 9). Particularly interesting is the case of pt4, who showed a category effect in the previous analysis. In this case the difficulty index had not influence.

	Logistic regressions naming to description task			
	Model I		Model II	
	Predictor	P	Predictor	P
pt1	Aoa	0,012	Difficulty index	0,032
	Domain	0,083		
pt2	Aoa	0,029	Aoa	0,029
	Vol. manipulability	0,013	Vol. manipulability	0,013
	Number of features	0,003	Number of features	0,003
pt3	Familiarity	0,013	Difficulty index	0,015
pt4	**Domain**	**0,001**	**Domain**	**0,001**
	Sum relevance f.	**0,032**	**Sum relevance f.**	**0,032**
pt5	Aoa	0,003	Difficulty index	0,004
	Semantic distance	0,022		
pt6	Semantic distance	0,017	Difficulty index	0,01
	Tipycality	0,015		
	Familiarity	0,001	Domain	0,034
	Arousal	0,030		
pt8	Frequency	0,02	Difficulty index	0,002
pt9	Frequency	0,015	Difficulty index	0,006
pt10	Aoa	0,015	Difficulty index	0,005
pt11	Aoa	0,001	Difficulty index	0,041
			Aoa	0,032
pt12	Familiarity	0,005	Familiarity	0,005
pt13	Semantic distance	0,08	Difficulty index	0,025
	Aoa	0,01	Sum. relevance f.	0,031
pt14	Familiarity	0,003	Difficulty index	0,019
			Familiarity	0,023
pt15	Aoa	0,042	Difficulty index	0,003

Table 9: significant predictors of naming to description task in logistic regression analysis for each patient. Model I: all the nuisance variables and domain were considered in the model; Model II: all the nuisance variables, difficulty index and domain were considered in the model; Vol. manipulability= volumetric manipulability, Sum relevance f.= sum semantic relevance of features.

Comment

Different variables influenced the naming processes in AD patients. Only 1 patient showed a category effect in naming to description task, after considering all confounding variables and the difficulty index.

3.3.6 Discussion

In this study we have looked for category effects in a group of AD patients and in a group of control subjects, using two tasks involving two different modalities of input, a picture naming task and a naming to word definition task.

When items were only loosely matched, category effects emerged in both tasks for AD patients. However, the regression analysis showed a category effect with a better performance on NL only in the naming to definition task. These results are in line with studies showing the presence of category effect with items only loosely matched. In addition, controls performed at ceiling in the picture naming task, masking the direction of the normal pattern. A category effects not detected in picture naming task was evident in the naming to verbal definition, in accordance with previous studies showing inconsistencies across different semantic tasks (Laws et al., 2005). These results suggest that the use of different semantic tasks in assessing category effect is important.

The lack of category effect in the picture naming task in this study could be due to the fact that AD patients had relatively high scores, although in the pathological range. As proposed by Whatmough et al (2003), category effect have been generally described in patients who were moderately anomic. AD with mild anomia or with scores not significantly different from controls did not show category effect. In particular, in their study patients showing category effects scored less than 59%. In our study the poorest performance was at 75%. 9 of 14 patients scored ≥ 90%. In respect to Whatmough et al study (2003) we used a different picture naming task, with more familiar items. It could then be possible that the degree of naming impairment was not sufficient to detect category effect. A category effect was in fact detected in naming to description task, in which the impairment was more severe (see the case of pt4). Frequency and age of acquisition were predictors of picture naming performance in AD, in line with previous studies (Cuetos et al., 2008; Martinaud et al., 2009; Tippet et., 2007). Names with higher frequency and acquired early are more resistant to deterioration (Hodges, Salmon, & Butters, 1992; Silveri, et al., 2002). Age of acquisition, domain and semantic relevance predicted performance in the naming to description task in AD. The role of age of acquisition and semantic relevance in naming to description task has been also reported by other studies (Marques et al., 2010; Sartori et al., 2005). In contrast to the study reported by Sartori and Lombardi (2004), even considering the impact of semantic relevance, we showed a significant category effect. This is the first evidence reporting a category effect after controlling for semantic relevance .

The analysis conducted for each patient allowed us to explore the role of different variables in predicting naming accuracy. For each task different parameters influenced the performance of different patients. The most frequently observed were age of acquisition, frequency, familiarity and semantic distance. Cuetos et al. (2008) investigated the influence of semantic categories, psycholinguistic and visual–perceptual characteristics of the stimuli, such as lexical frequency, age of acquisition, familiarity, imageability, word length, and visual complexity on naming accuracy in two AD patients. They showed that different variables could predict naming accuracy in each patient, and also at different stages of disease. For the first case, only age of acquisition was the predictor for both stages of examination; for the second patient age of acquisition was the predictor at the time of the first evaluation, but in the second assessment it was replaced by familiarity.

In this study, in addition to age of acquisition, frequency and familiarity, and differently from controls, AD patients naming performance resulted influenced by variables like arousal, volumetric manipulability, semantic distance and semantic relevance. It has been already reported that the manipulability of objects may influence the identification of stimuli (e.g. Filliter et al., 2005). Even if manipulability has always been considered as a fundamental characteristic of artefacts, and particularly of tools, the definition of manipulability in literature is still unclear In particular, a distinction can be made between two different kinds of manipulation: the first one (functional manipulability) is related to using an object for its intended purpose, while the second one (volumetric manipulability) is related to picking up an object (Bub et al., 2008). A recent study showed that manipulable objects (defined as any object that you could pick you up with one hand, i.e. volumetric manipulability), were identified more quickly than non manipulable ones if stimuli are not matched for familiarity (Filliter et al., 2005). The authors suggested that these findings may indicate that the selection of items may generally favour NLT, as tools and animals are among the most frequently used categories. In this study we have shown that volumetric manipulability is a significant predictor of naming performance for some AD patients, with items with higher values of volumetric manipulability named better then those that are not manipulable.

The role of semantic distance has been well documented in AD patients in tasks as picture naming and word to picture naming (Zannino et al., 2006a). In this study we show its role also in naming to description, with items with more overlapping features named worse.

These data are not conclusive in identifying which are the most important variables in predicting naming performance, but suggest that other dimensions in addition to the most studied ones could be have a role.

Finally, we have found that only 1 of 14 patients showed category effect in naming to description task, with better performance for NL. Other studies reported similar evidences on picture naming task (9/50 in Martinaud, 2009; 8/26 and 3/26 with inverse pattern in Laiacona et al., 1998;18/58 and 3/58 with inverse pattern in Garrard et al., 1998; 6/68 and 3/68 in Tippet et al., 2007; 6/53 Zanninno et al., 2002). In addition, we demonstrate that AD performance is not a merely exaggeration of the controls' performance. In fact, even if the results at the group level are in accordance with Gale et al data (2009), showing a strong effect of index difficulty on AD performance and in diminishing the predictive power of domain, at the single subject level this is not the case. The difficulty index influenced the performance of most subjects, in general exclusively. However, this was not the case of the patient who showed a category effect. In this patient the difficulty index did not enter in the model explaining the naming variance. This finding indicates that category effects could be a peculiar features of some AD patients.

In conclusion, no a single account can explain the heterogeneity of evidences concerning category effects in AD. Certainly several methodological issues, such as ceiling effects in controls, the effects of confounding variables, the degree of semantic impairments may account for part of this variability. However, genuine category effects may be (infrequently) observed in individual patients.

PART III

3.4 The status of abstract knowledge

Many studies concerning semantic memory impairments in Alzheimer's disease focused on concrete concepts. Very few studies investigated the abstract domain of knowledge in these patients. They commonly report a greater impairment of this domain with respect to the concrete one (Rissenberg & Glanzer, 1987). Abstract reasoning deficits constitute an important symptom of dementia. Particularly, a loss of "verbal abstracting ability" can be detected with the increase of concreteness in speech and thought processes (Hall et al., 1981; Miller, 1977). Rissenberg and Glanzer (1987) reported a concreteness effect in a group of AD in a free recall task, in WAIS vocabulary (where however the abstract words were more difficult then the concrete ones) and in a naming to verbal definition task. In another study, AD patients and control subjects underwent a semantic association judgment task, modeled on the basis of Pyramids and Palm Trees Test (Howard & Patterson, 1992), but in a verbal written modality. Subjects were asked to indicate which of two words was associated with a target (e.g.: sheep: goat, lamb; Fung et al., 2000). Six semantic categories were tested: animals, fruit and vegetables, tools, clothing and furniture, action verbs and abstract nouns. AD showed greater impairment for living things and abstract words than for non living things and action verbs. Accuracy measures for abstract nouns did not differ from those on living things. In a study in which AD were compared with patients with subcortical vascular dementia and controls, the concrete and abstract word synonym test (which requires the subject to choose one of two words that is similar in meaning to the target word- Warrington et al., 1998) was used, in addition to a very comprehensive neuropsychological battery of tests, in order to identify an overall profile of cognitive impairment of the two groups of patients. The concrete and abstract word synonym test results showed no significant concreteness difference (Graham, Emery, and Hodges, 2004). In addition, some data are presented in a study in which the main aim was to investigate semantic memory impairments in MCI and early AD patients (Adlam et al., 2006a). The assessment included a comprehensive battery of semantic memory tests, including the aforementioned concrete and abstract word synonym test (Warrington et al., 1998). AD were significantly impaired compared to control group for both concrete and abstract items. Although no explicit analyses were carried out in order to address the abstract-concrete dissociation, the authors reported scores for each type of word for both patients and controls. For concrete items (maximum score 25) they reported a mean of 20,71 (sd: 2,43) and for abstract ones (maximum score 25) a mean of 20,71 (sd: 2,56) for AD patients (pag.679). Controls' mean was 23,80 (sd:1,24) for concrete words and 23,35 (sd:1,66) for abstract words. These data do not provide any evidence for a concreteness effect, at least in early AD.

The limited number of studies concerning abstract knowledge could in part be explained by the fact that abstract knowledge is generally regarded as a dimension to be contrasted with the concrete domain of knowledge. As abstract domain resulted impaired in AD (at least in those studies in which this domain has been explicitly investigated, e.g. Fung et al., 2000; Rissenberg et al., 1987) studies have tried to infer important insight from pathologies in which a reversal of the concreteness effect has been reported, as in semantic dementia (SD; e.g. Papagno et al., 2007; 2009). A number of studies, investigating abstract knowledge, enrolled both types of patients, AD and SD, in order to assess differences in their performance. Yi et al (2007) using a multiple choice, naming to description task investigated the concreteness effect for verbs (cognition verbs versus motion verbs) and nouns (abstract versus concrete nouns) in AD, SD and control subjects. Both AD and SD were more impaired in verbs than in nouns. AD showed a better performance on concrete versus abstract nouns but no difference between motion and cognition verbs. Analysis of individual performances showed a less marked concreteness effect for nouns (showed by 13/28 participants) and a better performance for motion than cognition verbs for 17/28 subjects. SD instead showed a reversal of the concreteness effect for verbs, as they were more impaired for motion than cognition verbs, but not for nouns, where a marginally greater difficulty for abstract than concrete nouns was detected. Analysis of individual performances showed a better performance on cognition versus motion verbs in 9/11 patients, but only 3/11 had a reversal of the concreteness effect for nouns, while the frequency of concreteness effect for noun did not differ from that observed in AD. In conclusion, at the group level, while the concreteness effect was reported for nouns but not for verbs in AD, the reversal of the concreteness effect was reported for verbs but not for nouns in SD.

A small number of studies were focused on the abstract domain of knowledge, showing a similar pattern of degradation both in AD and in semantic dementia patients (Crutch & Warrington, 2006). As reported above and in chapter 1, a gradual degradation of semantic memory, characterized by a relative sparing of superordinate information in respect to the more specific one, has been largely documented both in semantic dementia and in AD patients. However, the vast majority of these works focused on the concrete concepts. Crutch and Warrington (2006) investigated the existence of comparable effects for abstract concepts. Three groups of subjects, AD, SD and controls subjects, underwent a synonymy task, in which they were asked to identify which of two alternatives was most related in meaning to a target word. 3 different levels of synonymy comprehension were assessed (Crutch & Warrington, 2006): in the first the distractor was the antonym of the target, in the second a semantically distant word and in the third a semantically close word. The target was a synonym of the stimulus. All subjects showed lower performance in the condition in which more specific information was required, however this pattern was more pronounced in the pathological groups. They concluded suggesting that this partial degradation could be considered a general characteristic of a degraded knowledge base, not restricted to concrete concepts only. The partial degradation has been explained both within the traditional framework of hierarchical organization (Collins & Quillian, 1969), and by feature-based models (Rogers et., 2004). Crutch and Warrington (2004; 2005; Crutch et al., 2006) recently suggested that abstract and concrete concepts are supported by two qualitatively different representational frameworks, associative for abstract concepts and hierarchical for concrete ones. They provided evidence for this view in patients with semantic refractory access dysphasia. Using a spoken word–written word matching procedure, the authors demonstrated that patient A.Z. showed semantic relatedness effects among synonymous for concrete word stimuli but not for the abstract ones. On the hand A.Z. showed an effect of semantic associations for abstract words but not for concrete words. Thus, they concluded that the partial degradation of abstract concepts observed in patients with neurodegenerative diseases can be reframed as a damage to an associative network which is tighter for abstract words with respect to concrete ones.

As discussed in chapter 1 and 2, different psycholinguistic variables have been defined to quantify and measure the differences between concrete and abstract concepts. The most important ones are: Concreteness (CNC), Imageability (IMG), Context availability (CA), Familiarity (FAM) and Age of Acquisition (AoA). Concrete concepts are, respectively, more concrete, more imageable, more easy to contextualize, more familiar and acquired earlier than abstract words (Altarriba et al., 1999; Paivio, 1986; Schwanenflugel, 1991). Contrary to the Crutch and Warrington's theory, some authors suggested the existence of categories within the abstract domain, similarly to concrete domain, (Altarriba et al., 1999; Setti & Caramelli, 2005). In particular, it has been proposed that emotions represent a category quite different from the other abstract words. In addition, Setti and Caramelli (2005) tried to provide evidence for the existence of other categories in the abstract domain, such as cognitive processes, states of self and nominal kinds. On the other hand, other investigators tried to infer differences among abstract concepts considering the abstract domain as a continuum composed by concepts perceived as more and less abstract (Wiemer-Hastings et al., 2001; Della Rosa et al., 2010). Wiemer-Hastings et al. (2001) proposed that contextual constraints could account for the differences in the perceived abstractness. In addition other variables, such as the mode of acquisition (Della Rosa et al., 2010; Wauters et al.,

2003) and emotional valence and arousal (Kousta et al., in press; 2009; see also chapter 1 and 2) have been proposed to have a role.

It is noteworthy how rarely the status of abstract knowledge has been investigated in AD patients. The concreteness effect seems more a commonplace than an empirically investigated effect (Chertkow et al., 2008; Fung et al., 2000; Yi et al., 2007). No investigations have been carried out in order to document if abstract knowledge results impaired from the early stage of the disease or also in its prodromal stage. In addition this pathology could represent a model to investigate the internal organization of the abstract domain. A number of evidences deriving from recent studies suggest that abstract concepts are not all the same, and a certain degree of variability is recognized in their internal organization, both in terms of categories or of a continuum.

3.4.1 The experimental study

The aim of the study

The aim of this study was to specifically address the status of abstract knowledge in AD patients, in which semantic memory is generally reported to be affected (see above). In particular we wanted to investigate if specific impairments of abstracts entities can be paralleled by different degrees of semantic memory impairments at different stages of severity in AD . In addition, in this study we wanted to verify if a categorical organization underlies the abstract domain or /and if it is possible to find a different way in which these concepts are organized. For this purpose, we used the DeCAbs battery, where both categories of stimuli and variables that could account for subjects' performance were included. We consider both the variables specifically proposed to have a role in the abstract domain, such as abstractness, mode of acquisition (Della Rosa et al., 2010), emotional valence, arousal (Kousta et al., in press), and the variables proposed to account for differences between concrete and abstract concepts, such as concreteness, imageability, context availability, familiarity and age of acquisition (Altarriba et al., 1999; Paivio, 1986; Schwanenflugel et al., 1992).

Subjects

For this study we enrolled 10 AD patients (6 females and 4 males) and 10 control subjects (6 females and 4 males). The subjects are the same enrolled in the first study, with the exception of those who were not able to complete the DeCAbs battery (see above for inclusion criteria and further details of patients). The two groups were matched for age and education (see table 11). The performance at MMSE (Mini Mental State Examination) between patients (range: 16-24) and controls was different (p<0,0001; see table 10).

	Controls mean (sd)	AD mean (sd)	p
Age	74,1 (8,12)	74,7 (7,54)	.87
Education	8,1 (3,08)	7,9 (2,6)	.88
MMSE	26,9 (2,21)	20,01 (2,47)	<.0001

Table 10: Demographic characteristics of AD and control group participants, Means and, in parentheses, standard deviations (sd).

Tests

The three semantic tests of DeCAbs battery, described in chapter 2, were used:

1. Sentence completion task: Subjects were asked to complete 40 sentences in which the final word is missing and needs to be completed with the target.
2. Multiple-choice, naming-to-description task: subjects were asked to select the best of four words that matched a verbal definition. The four options included target, 1 foil semantically related to the target word; 1 with opposite meaning to target word and 1 semantically related to the opposite meaning.

5) association task: subjects were asked to match a target word with one out of three option responses, which was more closely associated to target. The three options included: an item with high association strength with target, a distractor with low association strength and a distractor that belongs to another category.

One point was given for each correct response (range 0-40).

The tasks include the same 40 stimuli divided into five different categories: Emotions, Cognitions, Traits, Social Relations and Human Actions; each category includes 8 items. The items were tightly balanced between categories for concreteness (p=.732), imageability (p=.523), context availability (p=,502), familiarity (p=.848), age of acquisition (p=.883), mode of acquisition (p= .453), abstractness (p= .614), number of letters (p=.941) and for arousal (p=.371), but not for emotional valence (p<0,05). In addition, all the subjects were administered the CaGi battery.

Statistical analysis

Naming accuracies, as proportions of correct responses for each item, were calculated for each group and for each task separately. Differences between AD and controls' performances at each task were analysed using a paired T-test.

Results

Table 11 shows patients' scores at the DeCAbs tests and at three tests of the CaGi battery. Most of patients showed a similar performance on concrete and abstract tests, as indicated by equivalent scores. Pt1 showed a normal performance at both types of tests, however pt11 showed a reversal of the concreteness effect.

Battery	**Test**	**pt1**	**pt2**	**pt3**	**pt4**	**pt5**	**pt6**	**pt8**	**pt9**	**pt10**	**pt11**
	SCT (40)	16	6	15	6	17	14	15	8	13	14
	SCT ES	**3**	**0**	**1**	**0**	**2**	**1**	**2**	**0**	**2**	**2**
	MCND (40)	22	13	13	11	14	27	34	24	13	31
	MCND ES	**1**	**0**	**0**	**0**	**0**	**2**	**4**	**1**	**0**	**3**
	Association (40)	34	21	34	18	27	34	39	23	25	35
DeCAbs	**Association ES**	**3**	**0**	**3**	**0**	**0**	**3**	**4**	**0**	**1**	**3**
	picture naming (48)	47	36	45	43	43	45	45	43	45	41
	picture naming ES	**3**	**0**	**2**	**1**	**1**	**3**	**3**	**1**	**3**	**0**
	naming to description (48)	41	25	41	30	33	35	40	34	34	35
	naming to description ES	**3**	**0**	**3**	**0**	**0**	**1**	**3**	**0**	**0**	**0**
	sentence verification (480)	461	396	475	433	456	443	443	451	451	458
CaGi	**sentence verification ES**	**2**	**0**	**4**	**0**	**0**	**0**	**0**	**0**	**0**	**1**

Table 11: raw scores and equivalent scores for each patient at Decabs tests and at three CaGi tests; SCT=Sentence completion Task; MCND=Multiple-Choice Naming to Description Task; ES=Equivalent Scores.

Table 12 reports the mean proportions of correct responses for each tasks and for each group. A by item analysis revealed a significant lower performance of AD patients with respect to control subjects at all three tests (see also figure 6, paired t-test, Sentence completion Task = SCT, t=-5,619, p<0,0005, Multiple-choice, naming-to-description Task = MCND, t=-9,133, p<0,0005 and the association task =ass, t=-5,213, p<0,0005).

TEST	GROUP	Mean	Std. Dev.
SCT	**AD**	0,31	0,32
	Controls	0,51	0,32
MCND	**AD**	0,51	0,20
	Controls	0,77	0,17
ASS	**AD**	0,73	0,17
	Controls	0,86	0,14

Table 12: mean accuracy proportions and standard deviations for AD and controls at three tasks, SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description; ASS= association task.

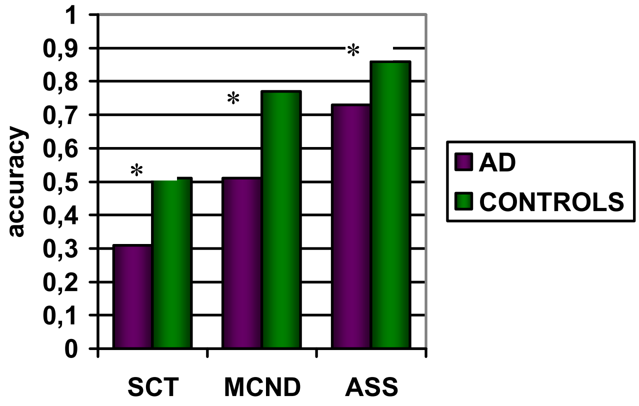


Figure 6: Performance of patients with Alzheimer's disease and controls at SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task. *= significant difference, see text.

Comment

AD patients performed significantly worse than controls in all three DeCAbs tasks. Furthermore in all three tasks healthy subjects did not show a ceiling effect, overcoming those limits generally found in semantic memory tasks.

3.4.1.1 Category effect?

In order to assess the existence of different semantic categories in the abstract domain we carried out three different ANOVAs, one for each task, with category (Emotions, Cognitions, Traits, Social Relations and Human Actions) as factors and group (control group and AD) as a repeated measure. Further analyses were performed using Wilcoxon signed-rank test in order to compare performances of the two groups separately for each of the 5 categories.

Results

Sentence Completion Task- for this task, ANOVA showed a significant main effect of group [F(1,35)=30,464, p<0,0001], with controls performing better than AD. The main effect of category [F(4,35)=0,616, p=,654] and the interaction between group and category [F(4,35)=0,658, p=,625] were not significant. As showed in figure 6 in the Sentence completion Task (SCT), the only category in which the performance between AD and controls did not differ was the category of emotions (p=0,138).

Multiple-choice, naming-to-description Task- Also in this case ANOVA showed a significant major effect of group [F(1,35)=78,224, p<0,0001] and category [F(4,35)=2,686, p<0,05], but no significant interaction [F(4,35)=0,394, p=,812]. Further analysis showed in fact that in all categories patients' performance differed significantly from the controls (see table 14 and figure 7).

Association Task- ANOVA showed a significant main effect of group [F(1,35)=30,676, p<0,0001], but not a main effect of category [F(4,35)=0,924, p=,461]. The interaction between category and group approached significance [F(4,35)=2,255, p=0,083]. As showed table 14 and figure 7, in the association task the only category in which the performance between AD and controls did not differ was the category of emotions (p=1).

Cat	**Attribute**			**Human action**			**Emotion**			**Social relation**			**Cognition**		
Test	**AD** Mean (sd)	**Control** Mean (sd)	**p**	**AD** Mean (sd)	**Control** Mean (sd)	**p**	**AD** Mean (sd)	**Control** Mean (sd)	**p**	**AD** Mean (sd)	**Control** Mean (sd)	**p**	**AD** Mean (sd)	**Control** Mean (sd)	**p**
SCT	0,19 (0,21)	0,44 (0,21)	,018	0,29 (0,26)	0,50 (0,35)	,017	0,36 (0,33)	0,46 (0,35)	**,113**	0,46 (0,35)	0,63 (0,33)	,048	0,25 (0,41)	0,50 (0,39)	,033
MCND	0,39 (0,16)	0,70 (1,18)	,016	0,45 (0,41)	0,66 (0,17)	,017	0,56 (0,23)	0,82 (0,13)	,028	0,61 (0,23)	0,85 (0,15)	,027	0,51 (0,16)	0,81 (0,15)	,017
ASS	0,69 (1,14)	0,86 (0,74)	,01	0,69 (0,1)	0,88 (0,1)	,023	0,85 (0,16)	0,85 (0,18)	**1**	0,76 (0,15)	0,88 (0,16)	,024	0,64 (0,21)	0,83 (0,2)	,034

Table 13: Accuracy mean, standard deviations and statistics for each category at three tasks for controls and AD; p values based on Wilcoxon Signed Ranks Test; Cat= Category; SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task.

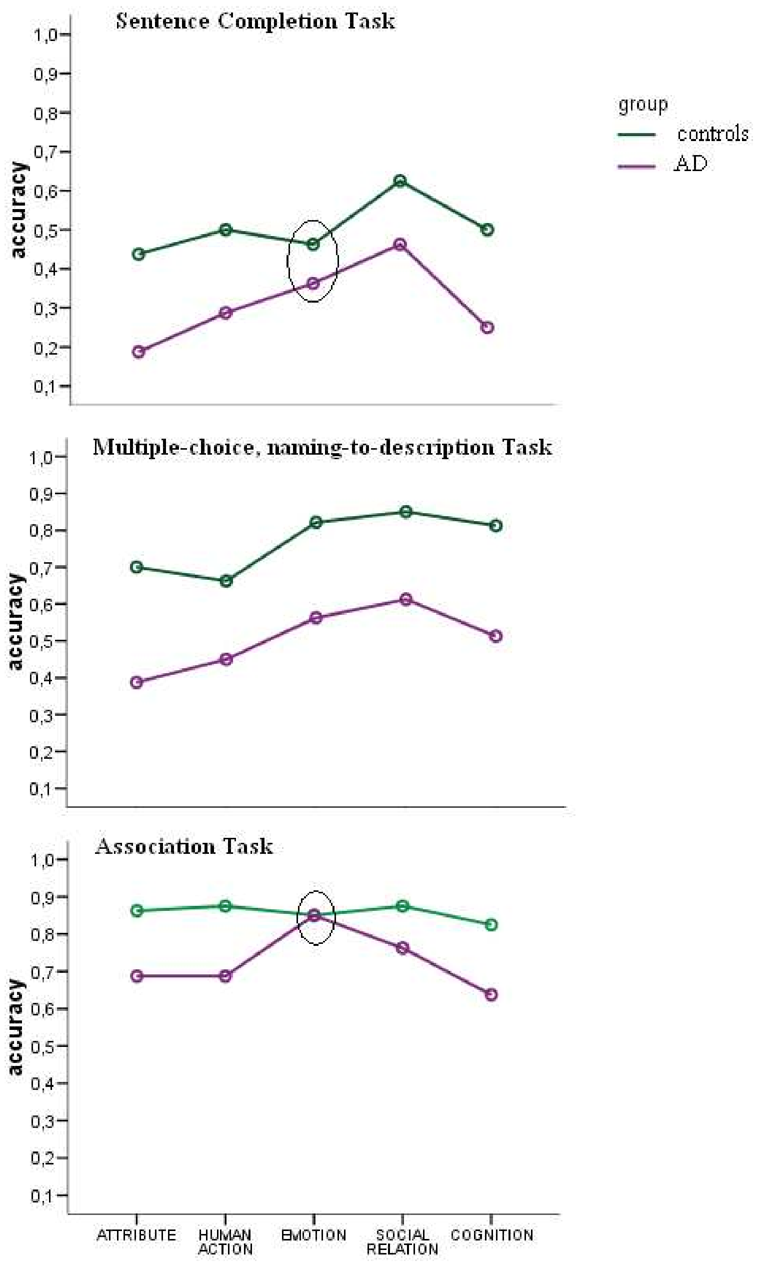


Figure 7: performances of controls and AD in the three tests

Comment

Emotion words were the only category in which AD performance did not differ form the controls in two of the three tasks. For all the other categories and for all three tasks, AD and controls performances were significantly different.

3.4.1.2 A different principle of organization?

In order to investigate the presence of a different way in which abstract concepts could be organized, namely which variable influence the performance of controls and AD, six different stepwise regression analysis were carried out, one for each group's performance in each semantic task (SCT, MCDT, ASS). The dependent variable was the group performance. We introduced imageability, context availability, familiarity, age of acquisition, mode of acquisition, abstractness, arousal, emotional valence and number of letters as possible predictors. The forward stepwise method enters the variables into the model one at a time in an order determined by the strength of their correlation with the dependent variable. As some independent variables are high correlated, we adopted the stepwise forward method in that multicollinearity could be a problem. The variance inflation factors (VIF) did not indicate multicollinearity.

Results

Sentence Completion Task- For the controls' performance, only context availability resulted significant (R^2=.271; p=.001), with better performance for words with higher values of context availability. AD performance was also predicted only by context availability (R^2=.345; p<.0005), in the same direction.

Multiple-choice, naming-to-description Task- Controls performance was predicted only by age of acquisition (R^2=.108; p=.038), with better performance for acquired words earlier. AD performance was predicted only by context availability (R^2=.120; p=.029), with better performance for words with higher values of context availability.

Association Task- Controls performance was predicted only by familiarity (R^2=.216; p=.002), However, it should be noted that this variable exerted its predictive power in the opposite direction to what could be expected. Indeed, performance accuracy was higher for the less familiar words. Arousal was the only predictor of AD performance (R^2=.144; p=.016), with better performance for words with higher values of arousal.

Subsequently, we added a categorical independent variable, labeled as "emotion-not emotion words", classifying emotion words (coded as 1) and non emotion words (coded as 0). All the regressions were carried out again, in order to investigate whether the category "emotion-not emotion words" influenced AD and controls naming performances (on the three tasks), once the confounding influence of intrinsic properties was taken in account. All the results remained the same, with the only exception for AD performance on association task. In this task in fact AD performance was predicted first by the "emotion-not emotion words" category (R^2=.145; p=.015), with a better performance for emotions in respect to non emotion words, and only subsequently by arousal (R^2=.236; p=.043), with a predictive power in the same direction as in the previous analysis.

Comment

Context availability resulted the predictor of controls and AD performance in Sentence Completion, and Multiple-choice, naming-to-description tasks (with the exception of controls' performance in the last task, in which age of acquisition predicted accuracy). The Association task was influenced by familiarity for controls and by arousal for AD. When the categorical variable (emotion vs. not emotion words) was added, it predicted, together with arousal, AD performance on the association task.

3.4.1.3 Category effect at different degrees of abstract semantic impairments

As suggested for the category effect for living and non living things, combining participants at different stages of AD progression may confound patterns of categorical deficits. In order to asses this possibility, we divided AD patients in two sub groups with a different degree of semantic memory impairment, on the basis of their performance on the three DeCAbs tests. A hierarchical cluster analysis using squared Euclidean distance was carried out in order to classify patients in different groups. As shown in figure 8, the patients are divided in two groups: a group with a mild semantic deficit on abstract concepts and a group with moderate deficits. The two AD subgroups were balanced for age (p=,914), education (p=,610) and MMSE (p=,114).

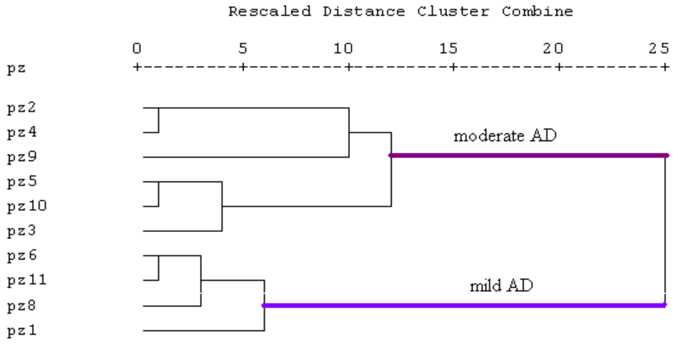


Figure 8: hierarchical clustering dendrogram constructed with the performances obtained at DeCAbs tests using squared Euclidean distance. AD patients are clearly divided into two groups.

Statistical analysis

In order to compare the performance of the three group separately for the three tasks, three ANOVAs were carried out, one for each task. In order to compare performances of the three groups on each category, Friedmann non parametric test was performed, and further analysis were carried out, using Wilcoxon signed-rank test, to compare each pair of groups on each single category in each task.

Results

The overall performance at three tasks of the three groups is showed in Table 14 and figure 9.

Sentence Completion Task- ANOVA showed that the three groups performed differently [F(2,78)=19,650, p<0,0001]. Least Significant Difference test showed that controls performed better than mild AD and both groups better than moderate AD (all p<0,001).

Multiple-choice, naming-to-description Task- ANOVA showed a significant effect of group [F(2,78)=58,879, p<0,0001], however controls and mild AD performed similarly (p=,103) and both groups performed better than moderate AD (both p<0,001).

Association Task- ANOVA showed a significant effect of group [F(2,78)=46,418, p<0,0001], with controls and mild AD performing similarly (p=0,136) and both groups performing better than moderate AD (both p<0,05).

		Mean	**sd**
SCT	**Controls**	0,51	0,32
	Mild AD	0,37	0,40
	Moderate AD	0,27	0,29
MCND	**Controls**	0,77	0,17
	Mild AD	0,71	0,24
	Moderate AD	0,37	0,24
ASS	**Controls**	0,86	0,14
	Mild AD	0,89	0,14
	Moderate AD	0,62	0,23

Table 14: Accuracy mean and standard deviations (sd) for controls, Mild AD and Moderate AD (classified on the basis of the performance obtained at DeCAbs tests) at three tasks; SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task.

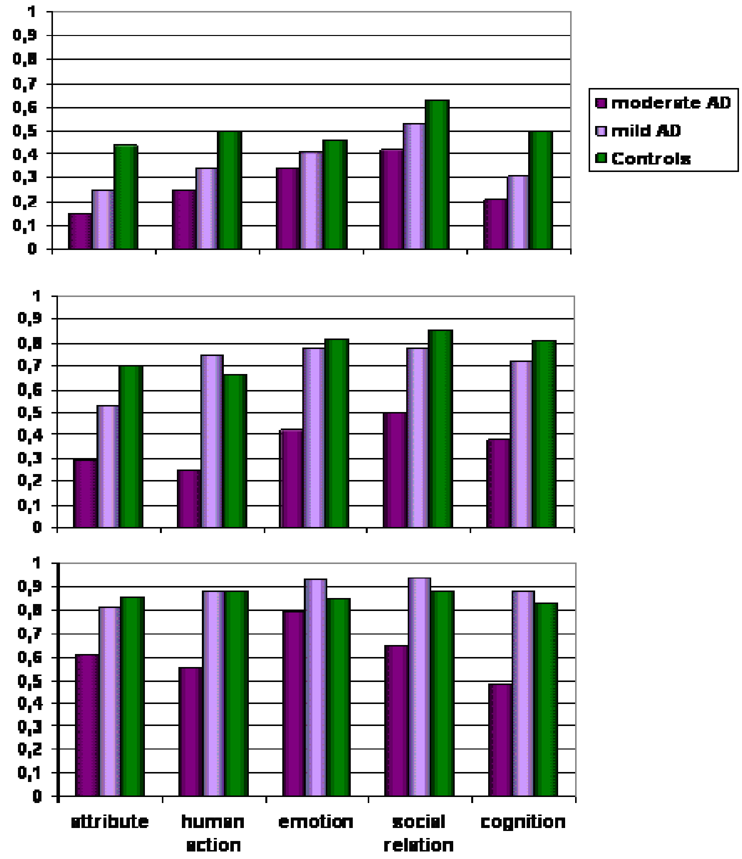


Figure 9: Performance of Moderate AD, Mild AD (classified on the basis of performance obtained at DeCAbs tests) and controls at SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task.

Friedman non-parametric test allowed us to assess the performance of the three different groups (Mild AD, Moderate AD, controls) separately for each category and for each task. Emotion words resulted the only category in which the performance of the three groups did not differ in all three tasks (see table 15; for Sentence completion Task p=0,17; Multiple-choice, naming-to-description Task p= 0,054; associations p=0,075). Further analysis performed using Wilcoxon signed-rank test on the single categories showed no differences between the three groups in the sentence completion task (Controls = mild= moderate) only in the case of emotion words (see table 16). Concerning this last category, in the Multiple-choice, naming-to-description Task Mild AD had a normal performance (controls = Mild AD), significantly different from the Moderate AD performance (controls = Mild AD > moderate AD). An interesting pattern was observed in the association task. Specifically, Mild AD showed a significantly better performance with respect to the Moderate AD, but not to the controls, while Moderate AD had a similar performance as controls (Mild AD = controls p=0,136; Mild AD > Moderate AD p= 0,042; Moderate AD = controls p=0,461).

		SCT			MCND			ASS		
CATEGORY		**Mean**	**SD**	**P**	**Mean**	**SD**	**P**	**Mean**	**SD**	**P**
ATTRIBUTE	**Controls**	0,44	0,21	0,02	0,44	0,21	0,053	0,86	0,074	0,011
	mild AD	0,25	0,3		0,25	0,30		0,81	0,116	
	moderate AD	0,15	0,19		0,15	0,19		0,61	0,216	
HUMAN ACTION	**Controls**	0,5	0,35	**0,06**	0,50	0,35	0,002	0,88	0,104	0,027
	mild AD	0,34	0,38		0,34	0,38		0,88	0,134	
	moderate AD	0,25	0,22		0,25	0,22		0,56	0,178	
EMOTION	**Controls**	0,46	0,35	**0,17**	0,46	0,35	0,054	0,85	0,177	**0,075**
	mild AD	0,41	0,44		0,41	0,44		0,94	0,116	
	moderate AD	0,34	0,28		0,34	0,28		0,79	0,213	
SOCIAL RELATION	**Controls**	0,63	0,33	**0,1**	0,63	0,33	0,03	0,88	0,158	0,002
	mild AD	0,53	0,45		0,53	0,45		0,94	0,116	
	moderate AD	0,42	0,3		0,42	0,30		0,65	0,208	
COGNITION	**Controls**	0,5	0,39	0,03	0,50	0,39	0,021	0,83	0,198	0,006
	mild AD	0,31	0,44		0,31	0,44		0,88	0,189	
	moderate AD	0,21	0,4		0,21	0,40		0,48	0,243	

Table 15: Accuracy mean, standard deviations and statistics for each category at three tasks for controls, Mild AD and Moderate AD (classified on the basis of performance obtained at DeCAbs tests); p values based on Friedman non parametric test; SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task

		SCT			MCND			ASS		
CATEGORY		controls vs. mild AD	controls vs. moderate AD	moderate AD vs. mild AD	controls vs. mild AD	controls vs. moderate AD	Moderate AD vs. mild AD	controls vs. mild AD	controls vs. modera te AD	moderate AD vs. mild AD
ATTRIBUTE	**Z**	-1,873	-2,524	-1,382	-1,68	-2,38	-1,703	-0,986	-2,527	-1,843
	P	**0,061**	0,012	**0,167**	**0,093**	0,017	**0,089**	0,324	0,012	**0,065**
HUMAN ACTION	**Z**	-2,033	-2,313	-1,063	-1,263	-2,521	-2,555	0	-2,313	-2,254
	P	0,042	0,021	**0,288**	**0,206**	0,012	0,011	**1**	0,021	0,024
EMOTION	**Z**	-0,734	-1,612	-0,848	-0,736	-2,197	-2,197	-1,483	-0,738	-2,032
	P	**0,463**	**0,107**	**0,396**	**0,462**	0,028	0,028	**0,138**	**0,461**	0,042
SOCIAL RELATION	**Z**	-0,632	-2,392	-1,529	-0,511	-2,524	-2,106	-1,461	-2,371	-2,388
	P	**0,528**	0,017	**0,126**	**0,61**	0,012	0,035	**0,144**	0,018	0,017
COGNITION	**Z**	-1,185	-2,207	-1,633	-1,265	-2,38	-2,243	-0,738	-2,328	-2,552
	P	**0,236**	0,027	**0,102**	**0,206**	0,017	0,025	**0,461**	0,02	0,011

Table 16: comparisons between each pair of the three groups of subjects (controls, Mild AD, Moderate AD) on each single category in each task. Statistics (Z and p values) based on Wilcoxon signed-rank test. SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task

Comment

Patients with mild semantic impairment on abstract concepts showed a similar performance as controls in two of the three semantic tests: Multiple choice, naming to description task and in the association task. moderate AD had a lower performance on all three tasks with respect to mild AD and to controls. In addition, emotion words were the only category in which both mild and moderate AD performed similarly to controls in two of the two of the three tasks. Even if moderate AD showed a lower accuracy in sentence completion and association tasks with respect to controls and mild AD, they performed similarly to these two groups only in the case of emotion words.

3.4.1.4 Category effect at different levels of general impairment

In order to confirm the pattern described above, we classified patients in the AD group according to a more general criterion by using the MMSE score. A hierarchical cluster analysis was carried out in order to divide patients in different groups: the group with mild general cognitive impairment and the group with moderate general cognitive impairment (see Figure 10). The two groups of patients were balanced for age (p=,690) and education (p=,421).

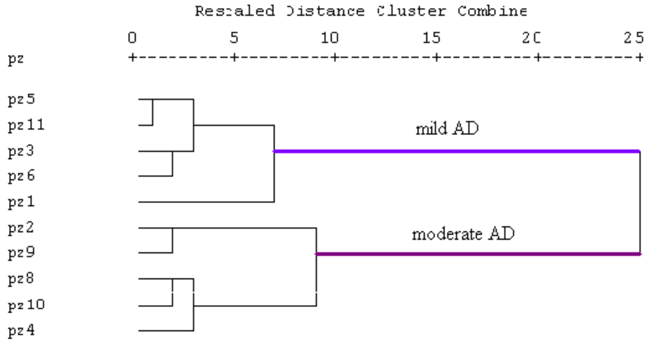


Figure 10: hierarchical clustering dendrogram constructed with the performances obtained at MMSE using squared Euclidean distance. AD patients are clearly divided into two groups.

Statistical analysis

In order to compare the performance of the three groups separately at the three tasks, we performed the same analysis as in the previous section. Three ANOVAs were carried out, one for each task. In order to compare performances of the three groups on each category, Friedmann non-parametric test was performed, and further analysis were carried out, using Wilcoxon signed-rank test, to compare each pair of groups on a single category for each task.

Results

Sentence Completion Task- for this task, ANOVA showed that the three groups performed differently [F(2,78)=24,256, p<0,0001]. Least Significant Difference test showed that controls performed better than mild AD and both groups better than moderate AD (all p<0,005).

Multiple-choice, naming-to-description Task- Also in this case ANOVA showed a significant effect of group [F(2,78)=42,890, p<0,0001], with controls performed better than mild and moderate AD (both p<0,001), while mild AD performed similarly to moderate AD (p=0,083).

Association Task- ANOVA showed a significant effect of group [F(2,78)=25,367, p<0,0001], with controls and mild AD performing similarly (p=0,190), and both groups performing better than moderate AD (both p<0,001).

As in the previous analysis, performances on the Sentence Completion and association tasks for the three groups did not differ only for emotion words (respectively p=0,130 and p= 0,075; see Table 17 and 18). However in this case in the Sentence Completion task the difference between moderate AD and controls approached significance (p=0,056). In the association task, instead, Mild AD showed a significant better performance with respect to the Moderate AD, but not to the controls, while Moderate AD had a similar performance as controls (Mild AD = controls p=0,102; Mild AD > Moderate AD p= 0,039; Moderate AD = controls p=0,246).

		SCT			MCND			ASS		
CATEGORY		Mean	SD	p	Mean	SD	P	Mean	SD	P
ATTRIBUTE	Controls	0,44	0,21		0,70	0,18		0,86	0,07	
	mild AD (MMSE)	0,23	0,20		0,40	0,21		0,75	0,18	
	Moderate AD (MMSE)	0,15	0,23	0,004	0,38	0,17	0,013	0,63	0,13	0,005
HUMAN ACTION	Controls	0,50	0,35		0,66	0,17		0,88	0,10	
	mild AD (MMSE)	0,35	0,40		0,50	0,19		0,80	0,15	
	Moderate AD (MMSE)	0,23	0,23	0,054	0,40	0,15	0,022	0,58	0,20	0,045
EMOTION	Controls	0,46	0,35		0,82	0,13		0,85	0,18	
	mild AD (MMSE)	0,45	0,42		0,60	0,30		0,95	0,09	
	Moderate AD (MMSE)	0,28	0,24	**0,130**	0,53	0,21	0,013	0,75	0,26	**0,075**
SOCIAL RELATION	Controls	0,63	0,33		0,85	0,15		0,88	0,16	
	mild AD (MMSE)	0,58	0,43		0,68	0,26		0,85	0,21	
	Moderate AD (MMSE)	0,35	0,30	0,026	0,55	0,23	0,008	0,68	0,24	**0,135**
COGNITION	Controls	0,50	0,39		0,81	0,15		0,83	0,20	
	mild AD (MMSE)	0,30	0,44		0,50	0,15		0,75	0,26	
	Moderate AD (MMSE)	0,20	0,39	0,030	0,53	0,24	0,010	0,53	0,24	0,022

Table 17: Accuracy mean, standard deviations and statistics for each category at three tasks for controls, Mild AD and Moderate AD (classified on the basis of performance obtained at MMSE); p values based on Friedman non parametric test; SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task

		SCT			MCND			ASS		
CATEGORY		controls vs. mild AD	controls vs. moderate AD	moderate AD vs. mild AD	controls vs. mild AD	controls vs. moderate AD	moderate AD vs. mild AD	controls vs. mildAD	controls vs. moderate AD	moderate AD vs. mild AD
ATTRIBUTE	**Z**	-2,060	-2,388	-1,732	-2,388	-2,322	-0,333	-1,633	-2,585	-1,890
	P	0,039	0,017	**0,083**	0,017	0,020	**0,739**	**0,102**	0,010	**0,059**
HUMAN ACTION	**Z**	-2,058	-2,043	-1,089	-2,032	-2,413	-1,414	-1,511	-2,201	-1,930
	P	0,040	0,041	0,276	0,042	0,016	0,157	0,131	0,028	0,054
EMOTION	**Z**	-0,136	-1,913	-1,823	-2,032	-2,375	-0,966	-1,633	-1,160	-2,060
	P	**0,892**	**0,056**	**0,068**	0,042	0,018	0,334	**0,102**	**0,246**	0,039
SOCIAL RELATION	**Z**	-0,284	-2,375	-2,081	-1,491	-2,536	-1,667	-0,272	-2,041	-1,536
	P	0,776	0,018	0,037	0,136	0,011	0,096	0,785	0,041	0,125
COGNITION	**Z**	-1,450	-2,214	-1,633	-2,379	-2,111	-0,276	-1,057	-2,176	-1,983
	P	**0,147**	0,027	0,102	0,017	0,035	**0,783**	**0,290**	0,030	0,047

Table 18: comparisons between each pair of the three groups of subjects (controls, Mild AD, Moderate AD) on each single category in each task. Statistics (Z and p values) based on Wilcoxon signed-rank test. SCT= Sentence completion Task, MCND=Multiple Choice, Naming to Description and ASS= association task

Comment

Patients with mild general cognitive impairment (based on MMSE score) showed a similar performance to controls only in the association task. Moderate AD showed a lower performance in all three tasks with respect to controls. In addition, emotion words were the only category in which both mild and moderate AD performed similarly to controls, in this case only in the association task. Moderate AD showed a lower accuracy in sentence completion with respect to controls for emotion words. Even if moderate AD showed a lower accuracy in the association task with respect to controls and mild AD, they performed similarly to these two groups only for emotion words.

3.5 Discussion

In this study we have investigated the abstract knowledge in AD patients, using the DeCAbs battery, formed by one production task, the Sentence Completion, and two comprehension tasks: the Multiple Choice Naming to Description and the association task. The three tasks differ also for level of difficulty (see table 13 in which the controls' scores are reported for each task). The Sentence Completion task was the most difficult, the association task the easiest.

The aim of this study was twofold. First, we aimed at investigating impairments in the domain of abstract knowledge in AD. Second, we focused on the definition of an internal organization of abstract knowledge, using a battery where both categories of stimuli and variables that could account for subjects' performance were included.

Concerning the first point, we can conclude that AD patients have an lower performance with respect to controls in all three tasks (see also table 12). However, the degree of impairment is different at different stages of the disease. When we divided the patients on the basis of their performance in all three tasks, we observed that AD with mild semantic deficits performed similarly to controls in two of three tasks. In particular, they showed a significant different performance from controls (but not pathological, see equivalent scores in table 11) only in the production task, in which word finding ability is required. This task was the most difficult for controls as well (see table 12). Moderate AD showed instead an impaired performance in all three tasks. When dividing the patients on the basis of MMSE scores, Mild AD performed at similar levels as controls only in the association task. Again, the performance of moderate AD was pathological in all three tasks. These results suggest that, even if abstract knowledge is affected in AD, this pattern cannot be confirmed for all AD subjects, at least at the first stage of disease. In addition, the impairment was more marked in tasks requiring more effortful processes, that are impaired in AD. Patients with mild cognitive impairment (as detected by MMSE) performed well in the association task, the most automatic of the three tasks, requiring less controlled processes.

Considering the second point, namely the investigation of the internal organization of abstract knowledge, several interesting conclusions can be derived from this study. In particular, five different categories of stimuli (Emotions, Cognitions, Traits, Social Relations and abstract concepts related to Human Actions) were included in the battery. AD showed a similar performance to controls only for emotion words in two of the three tasks, the Sentence Completion Task and the Association task. Differently form the living – non living dissociation, in which all the categories are usually impaired in AD with respect to controls (Whatmough & Chertkow, 2002), in this case emotion words were spared in AD. In addition, no methodological or artefactual accounts can explain this pattern, because the categories were tightly matched for all variables that can account for subjects ‘ performance, and the controls did not perform at ceiling.

Different variables predicted performances in the three tasks, suggesting that the influence of different types of variables can be driven by the specific task employed. Context availability predicted AD performance in the Sentence Completion Task and Multiple Choice Naming to Description task, as well as the controls performance in the Sentence Completion Task. AD and controls performed better for items for which it is easier to generate possible contexts. Traditionally, context availability has been proposed as an appealing explanation for concreteness effects, in that abstract words are more difficult to process because of less available context (Schwanenflugel & Shoben 1983; Schwanenflugel et al., 1988). It is generally more difficult to retrieve situations for abstract concepts, because of the greater quantity of situations to which they are associated. Wiemer-Hastings et al. (2001) suggested that if context information must be accessed to comprehend the concept (e.g., Schwanenflugel, 1991; Schwanenflugel & Shoben, 1983), “constraints can be used to guide the mental construction of a context example”. Constraints include concrete situation elements, object attributes, agent characteristics, situation elements, relations, and information about temporal characteristics and sequences. The nature of contextual constraints involved (more concrete or more abstract) results to be the most critical type of information for abstract concepts. The influence of CA on AD and controls performances suggest that the notion of a dichotomy between abstract and concrete entities is poorly supported. Concepts in the abstract domain are not all abstract in the same manner, as indicated by the fact that differences between concepts could be detected, also in terms of context availability. Furthermore, Altarriba et al. (1999) found that the correlation of CA with concreteness differed for abstract, concrete, and emotional terms. As reported in the previous chapter, emotion words were higher in CA than other abstract words. Interestingly, we found in Sentence Completion Task that AD performed similarly to controls only for emotion words. However, when in the regression analysis we consider both emotion category and CA, in addition to the other variables, only CA predicted AD performance. The better accuracy evidenced for emotions could be in part explained in terms of CA, because emotions have high values of CA.

The performance of patients and controls in the Association task was influenced by other variables. Controls performance was predicted only by familiarity, with accuracy higher for the less familiar words. The association task is more automatic, requiring less controlled processes, with respect to the other two. Interestingly, in automatic tasks low frequency words typically yield larger priming effects than high frequency words (e.g., Balota & Spieler, 1999).

Arousal was the best predictor of AD performance, with higher performance for words with higher values of arousal. When in the regression analysis we consider both emotion category and arousal, in addition to the other variables, both variables influenced the performance. In this task, AD patients showed a similar performance to controls only for the emotions category, also when they were divided on the basis of both DeCAbs score or MMSE score.

The peculiar role of emotional words has been highlighted by a number of investigators. Altarriba et al. (1999) suggested to consider emotions as special category independent from other concrete and abstract concepts. Kousta and co-workers (in press) suggested that affective information plays a crucial role in the processing and representation of abstract concepts, considering affective information as a continuous variable not specific for emotional words only. Emotional affect has been generally conceptualized along two different dimensions, arousal and valence. As these two dimensions are highly correlated, they are generally difficult to dissociate. However, functional imaging studies reported that the two dimensions involve different brain areas, with subregions of orbitofrontal cortex preferentially processing valence, whereas amygdala processes arousal (Lewis et al., 2007; but see also Posner et al., 2009). The results of this study support the importance to keep separate the two dimensions, with an important role of arousal in predicting AD performance. Alzheimer's disease is characterized by a severe atrophy of the amygdala. A pronounced reduction in the amygdala volume has been detected in very early stage of the disease (Mizuno et al., 2000). However, it has been suggested that emotional processes are relatively preserved at the beginning of the disease, compared with other cognitive domains (Albert, Cohen, & Koff, 1991; Bucks & Radford, 2004). In addition, Kensinger, Anderson, Growdon, and Corkin (2004) showed that the ratings of emotional valence and arousal provided by AD patients were similar to those of young and older adults. Giffard and co-workers (2009) documented, in a lexical decision task with concrete concepts, that in AD the emotional connotations of concepts modulates semantic deficits. They showed a preservation of emotional processes that led to a pathological hyperpriming (due also to the loss of distinctive features), larger for negative emotional concepts with respect to neutral ones. Their data could be explained by the stimuli’s degree of emotional arousal. Negative concepts were significantly higher in arousal with respect to positive ones, which showed the same priming effect as the neutral concepts. Giffard et al. (2009) suggested that these results could reflect a facilitation effect of the emotional component on semantic processing, as emotional processes are preserved at least at the stage of AD assessed in their study. At that stage, lesions of the amygdala, leading to deficits in the recognition and processing of emotional content, especially for negative stimuli (Adolphs, Tranel, Damasio, & Damasio, 1994; LeDoux, 1992), could be mild and not sufficient to impair the emotional processing of words.

Two interpretations may be put forward in this context. On one hand we may assume that arousal modulates semantic processing, and that this modulation can play a major role in a more automatic task as Association. Patients with semantic memory impairments may benefit from the modulation of the emotional content of an abstract word in order to retrieve its meaning. On the other hand, it could be possible that the emotional information captured by arousal at early stages of the acquisition of concept meaning (see Della Rosa et al, 2010) may 'consolidate' as part of the semantic representation of an abstract concept. It may occur that, just like a distinctive feature of a concrete concept as zebra may be represented by its stripes, for an abstract concept as 'rage', arousal may shape the distinctive feature of this “introspective state” (Barsalou & Wiemer-Hastings, 2005). Some theories retain that affective information and semantic representations are processed by two different systems (LeDoux, 1992; Murphy & Zajonc, 1993), probably interconnected (Ferrand, Ric, & Augustinova, 2006). Others claim instead that affective information is stored within the semantic system (De Houwer, Hermans, Rothermund, & Wentura, 2002; Fazio, Sanbonmatsu, Powell, & Kardes, 1986; Hermans, De Houwer, & Eelen, 1994).

Although far to give a solution to this important question, the results of this study demonstrate that arousal has a role in the processing of abstract concepts. The role of arousal seems in part independent from emotional valence and not specific for the emotion words only. Altarriba et al. (1999) suggested that emotions are characterized by higher values of CA and IMG than the other abstract words. Similarly, Kousta et al. (in press) reported that the more emotionally valenced words are characterized by higher values of imageability. Thus, we suggest that a single variable cannot account for the specific effects reported for emotion words in this context.

3. 6 General conclusion

In this chapter we have investigated semantic memory impairments in patients with Alzheimer’s disease using two new batteries of tests for concrete and abstract concepts, described in the previous chapter. The use of these tests permitted us to investigate with more detail a field rich of scientific contribution, in which however some aspects remain almost neglected.

We have shown that not all the distinctive features are lost in respect to the shared ones with the same progression in AD. Distinctive features with high values of semantic relevance seem more robust to damage with respect to distinctive features with low values of semantic relevance. In particular, in patients without naming impairment features with high values of semantic relevance are maintained at the same level as shared ones. A significant loss of distinctive feature with high level of semantic relevance with respect to shared ones has been shown in AD patients with picture naming deficits. Probably this pattern of deterioration leads to a confusion between close member of the same category, preventing the identification of the objects. In addition, category effects, with a worse performance on living items compared to non living ones has been also documented in a naming to verbal definition task, even considering all the possible methodological confounds. More strikingly, we found a category effect in the abstract domain of knowledge. Emotion words are the only category spared in AD, while the other abstract concepts are all affected.

The data of these studies suggest that concrete and abstract concepts are less different than what it is generally assumed. Both domains seem to share the subdivision in categories (for example, living and non living for concrete words and emotion for abstract words). In addition, the same variables seem to affect performance in both domains. Context availability has been traditionally considered as a dimension accounting for concreteness effects and for differences in the domain of concrete words. In this study, we have shown its important role also in the abstract domain. In fact, CA predicted the performance of controls and AD in semantic tests. In addition, we also found that arousal could predict picture naming and association for abstract concepts performance by AD patients. A recent study has shown a role of arousal in modulating semantic processing of concrete concepts (Giffard et al., 2009). However if a hierarchical or a continuum framework supports the organization of the semantic representations of abstract concepts remains an open question.

Chapter 4: Neural basis of semantic memory: an fMRI study

4.1 Introduction

Important insights concerning the organisation and the neural basis of the semantic memory derived from studies of neurological patients and, more recently, from functional brain imaging studies. In the last decades, advances in brain imaging technology (functional Magnetic Resonance Imaging, fMRI, and Positron Emission Tomography, PET) have increased our understanding of the functional organization of the semantic memory. Functional neuroimaging techniques have been largely used to investigate the neuronal basis of category specificity, and have been inspired by the clinical dissociations between Living (L) and Non Living (NL) entities. The existence of category-specific deficits (e.g. Caramazza & Shelton, 1998; Warrington & Shallice, 1984) suggests that knowledge may be categorically organized in the brain, or that the different categories are processed in different ways. Neuropsychological research has investigated the underlying neuronal basis by individuating which brain regions tend to be damaged in association with category-specific deficits. For example, anterior temporal lesions have been generally associated with a deficit for L, while fronto-parietal damage has been related to deficits for NL (Gainotti et al., 2005, see chapter 1). It is sometimes problematic to compare the results of functional studies with those of lesion studies. The advantage of using functional neuroimaging techniques, such as PET and fMRI, is that they may provide greater spatial resolution than lesion studies for identifying the neural substrates, because the lesions responsible for semantic memory deficits are often very extensive. In addition, in the last case the study is obviously limited to region of the brain that is damaged (Capitani et al, 2010).

As reported in Chapter 1, several different hypotheses have been proposed in order to explain category-specific deficits, but none seems to be able to account for all the available data. All these accounts have very different implications concerning the neural substrates of conceptual knowledge for different domains. Both the Sensory- Functional/Sensory Motor Theory and the Domain Specific Hypothesis share the assumption that separable neural substrates are crucially involved in L and NL impairments. The Sensory- Functional/Sensory Motor Theory posits that L are distinguished primarily on the basis of their visual semantic properties, while NL are differentiated on the basis of their functional/motor attributes. Because our representations of L are more dependent on perceptual properties, they are expected to cause more activations in areas subserving perceptual information. In contrast, man-made objects should engage areas processing functional properties or action knowledge, e.g. what is the use of an object, or how it is manipulated

(Martin et al., 2000; Warrington & McCarthy, 1983; Warrington & Shallice, 1984). Caramazza and Shelton's hypothesis (1998) postulates the existence of dissociable neural circuits dedicated to processing individual semantic categories, such as animals, fruits and vegetables, conspecifics, and tools, as a result of evolutionary pressures (Caramazza & Mahon, 2003). This theory predicts that these neural circuits should not overlap. Finally, correlated features accounts arguing for a unitary distributed semantic system (i.e. a semantic system not organized according to feature types or domains) propose no specialised activation for different categories in the normal brain, as long as the materials are carefully matched for confounding variables. Nevertheless, the conceptual-structure theory (Moss & Tyler, 2000; Tyler et al., 2000) predicts that, as L are more difficult to differentiate (in that they share more common features than artefacts), they, may be associated with greater activations compared to NL in tasks requiring fine-grained differentiation between stimuli.

4.2 Evidence from functional neuroimaging

Functional studies concerning category specificity have generally used the "subtraction" approach, in which experimental conditions have to be as closely matched as possible, in order to differ only in the process of interest (Price & Friston, 2002). The findings form by imaging studies are as divergent and inconsistent as those reported in the neuropsychological studies (Price & Friston, 2002). Different factors, such as the sensitivity of the scanner, the type of analysis, the threshold of the selected significance level and the variable matching of the possible confounding factors (familiarity, visual complexity etc.) could account for this inconsistency.

Differences between L and NL have been reported both in the ventral occipito-temporal pathway dedicated to object recognition, and in the dorsal occipito-parietal pathway responsible for object localization (Ungerleider & Mishkin, 1982). In the ventral stream, specific activations were found for both L and NL in different portions of the fusiform gyrus that processes visual properties of objects, such as color and form. In addition a greater activation for L has been reported in the left medial anterior temporal cortex. In the dorsal stream, a network of regions (left middle temporal gyrus, posterior parietal cortex, inferior parietal lobule) associated with visual motor knowledge, seems to be more associated with NL. In addition tools selectively active frontal regions, such as the ventral premotor cortex. These evidences are however not univocal. Below we summarise the often conflicting results.

The first published study concerning category specificity has been carried out by Perani and co-workers using PET (1995). Subjects performed a same-different matching task on pairs of L and NL line drawings. Differences between the two domains were detected, with a greater activation for L in respect to NL in the left fusiform and in the lingual gyri; NL relative to L items had enhanced activation in the left inferior frontal gyrus. The authors interpreted these results as supporting a neural fractionation of semantic memory.

Many functional studies have been subsequently reported (both PET and fMRI), showing different neural specialization for domain or type of feature. Only a few studies failed to document any kind of specialization (Devlin et al., 2002; Tyler et. 2003).

The lingual gyrus has been associated both with L (Martin et al., 1996) and NL (Moore & Price, 1999; Perani et al., 1999). Moore and Price (1999) showed a greater activation of this region for vehicles in respect to animals and fruits, and for animals in respect to fruits, suggesting that the activation of the lingual gyrus could depend from the complexity of the visual configuration rather than from the domain. Similarly, Gerlach et al. (2007) suggested that most of the activations reported in the posterior and ventral regions of the brain (the lateral occipital cortex, the medial occipital cortex, the calcarine sulcus, and the lateral fusiform cortex) reflected structural, rather than semantic or lexical differences between categories. In fact, they showed that the majority of these activations were present in studies in which animals were compared with tools. It is noted that animals are generally rated as more visual complex than tools. Tyler et al. (2003) showed only one category-specific effect for animals in the right occipital cortex, which they interpreted as due to the "extra visual processing demands required in order to differentiate one animal from another". It has been in fact suggested that it is especially difficult to discriminate among animals because of structural similarity within the category, in that the members share many visual features (Humphreys, Riddoch, & Quinlan, 1988).

In agreement with theories proposing that the properties of an object are stored into sensory - motor systems, several functional imaging studies have shown evidence of category-specific neural responses in the ventral and lateral regions of the posterior temporal lobe. A peculiar role has been proposed for the fusiform gyrus, which processes visual properties of objects, such as colour and form (Martin et al., 1995; Miceli et al., 2001). Some studies reported that animals elicit more activation than tools in the lateral portion, while tools involve the medial regions (e.g., Chao et al., 1999). Moreover, it has been documented that the involvement of fusiform gyrus is independent of stimulus modality (auditory, visual) and format (picture, word). Mechelli et al. (2006) suggested that the activations in the right and left medial fusiform gyrus are modulated by semantic relevance (in this specific case-picture naming - related to the high-order visual features) rather then to category per se). Indeed, the category effect was greatly reduced when the two categories (animals and tools) were matched for semantic relevance. Contrary to these findings, Mahon et al. (2007) reported a neural specificity in the left medial fusiform gyrus for tools. This neural specificity is based on the similarity metrics computed over motor information represented in dorsal regions, such as in the middle temporal gyrus and in the left inferior parietal lobule. According to their interpretation this neural circuit is “domain specific” and not due to the different types of information processed (form, motion etc.). More recently, Mahon et al. (2009), using an auditory size-judgment task, found that adults who were blind since birth showed the same category preference in the ventral stream, i.e. they had differential activation in the medial fusiform gyrus for NL stimuli compared to animals, as well as differential activation in the lateral occipital cortex for animal stimuli compared to NL. Their conclusion is that visual experience is not necessary for some aspects of the organization of object knowledge. However, this does not imply that visually-based dimensions do not contribute to this organization.

Category specific patterns have been also observed in the posterior lateral temporal cortex. Chao et al. (1999) showed that L differentially activated the superior temporal sulcus, while tools activated regions of the left middle temporal gyrus (see also Cappa et al., 1998b; Damasio et al., 1996; Martin et al., 1996; Moore and Price, 1999; Mummery et al., 1996, 1998; Perani et al., 1999). These regions are involved in the processing of object-associated motion. Beauchamp and co-workers (2002) found that, while the superior temporal sulcus is involved in the biological motion processing, the middle temporal gyrus is related to tool-associated motion. In particular, the left middle temporal gyrus have been linked to object use and identification in many studies (e.g. Devlin et al., 2002b; Lewis, 2006) and it has been directly linked to tool naming (e.g. Chao et al., 1999). However, Whatmough et al. (2002) in a PET study showed increased cerebral blood flow during a picture naming task in the left posterior middle temporal gyrus[4] when the stimuli were less familiar. This pattern was observed for both tools and animals. The authors concluded that this region stores semantic information for both biological and non-biological categories of objects. As previous mentioned, this area is associated with action knowledge or features concerning the motion of objects. Motion represents a more salient feature for tools than for animals, and this could be the reason why tools cause increased activation in this area. In addition, the influence of familiarity suggest that the posterior middle temporal gyrus also responds to less specific differences between

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[4] Although they reported a peak of activation 12 mm more anterior to that reported by other studies (Chao et al., 1999), they demonstrated that that region was functionally the same.

categories (Whatmough et al., 2002). The activation of the left posterior middle temporal gyrus was not observed when tools were mixed with other man-made items (Gerlach et al, 2000). Downing, Chan, Peelen, Dodds, and Kanwisher (2005) reported similar activations for tools and fruit and vegetables in this area and Phillips et al (2002) showed that the posterior middle temporal gyrus is not specific for tools only (see below).

In addition to the left posterior middle temporal gyrus, several studies showed that tools selectively active regions in frontal and parietal cortices, that store information about motor/manipulation-based properties. A distinction within the parietal cortex has been proposed. Regions in the posterior parietal cortex along the intraparietal sulcus process visual information for reaching and grasping objects (e.g., Binkofski et al., 1998; Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005; Goodale & Milner, 1992; Pisella, Binkofski, Lasek Toni, & Rossetti, 2006; Rizzolatti & Matelli, 2003), while the left inferior parietal lobule processes complex actions required for tool use (e.g., Boronat et al., 2005; Canessa et al., 2008; Goldenberg, 2009; Heilman, Rothi, & Valenstein, 1982; Hermsdörfer, Terlinden, Mühlau, Goldenberg, & Wohlschläger, 2007; Johnson-Frey, 2004; Kellenbach, Brett, & Patterson, 2003; Rumiati et al., 2004). Chao & Martin (2000; Chao et al., 2002; for a review see Martin, 2007) have reported that naming tools or simply viewing tools compared to naming or viewing animals activated the left ventral premotor cortex and the left intraparietal sulcus. Tyler et al. (2003) failed to replicate these data, finding no evidence of any differential activation for specific categories. In particular, they did not find cortical regions more active for tools. Phillips et al (2002) tried to explore "the extension to which the neural substrates for action/motor knowledge and tools process are equivalent". They required subjects to answer questions about action and size information for tools and fruit and vegetables. A greater activation of the left posterior middle temporal lobe was found for the retrieval of action versus size information, regardless of the category, and when tools were compared with fruits, also for size retrieval. These results suggest that the activity in the left posterior middle temporal lobe was not specific for tools. However, they showed a greater activation for tools than for fruits and vegetables in the left posterior middle temporal cortex and in the right Supplementar motor area (SMA), but not in the left premotor cortex. They proposed that in tasks in which the response is not manual (as in naming or viewing), tools may elicit manual responses that are incidental with respect to task requirements. Devlin et al (2002) suggested that left premotor cortex is generally more active for tools, when they are compared with animals, but not when compared with fruits and vegetables, because in this last case both stimuli (tools and fruit and vegetables) are manipulable. Interestingly, Gerlach an co-workers reported that the activation of the premotor cortex is not specifically activated by artefacts, but rather by manipulable objects in general (Gerlach, Law & Paulson; 2002). They showed no differences in activation in this area comparing manipulable NL (articles of clothing) with manipulable natural objects (vegetables/fruit).

Mahon et al. (2007) showed within the left inferior parietal lobule a significant repetition suppression for tools but not for animals and arbitrary manipulable objects. Saccuman et al.(2006) found a greater activation for the production of nouns denoting manipulable objects, compared to nouns denoting non manipulable objects, in the ventral premotor cortex and inferior parietal cortex. A recent study reports that manipulation, but not functional knowledge, modulates neural responses in the inferior parietal lobule (Canessa et al., 2008). This suggests that he specific way in which an object is manipulated is reflected in the neural representation of object words.

Even if several studies have accounted for manipulability, this is not a well-defined concept in literature. Recently, some authors (Bub, Masson, & Cree, 2008; Masson, Bub, & Newton-Taylor, 2008) have demonstrated that a distinction may be made between different types of manipulability. Functional manipulability is defined as the knowledge about how objects are used for their intended purpose, whereas volumetric manipulation is defined as the knowledge about how objects are moved. As Salmon et al. (2010) suggested, it is easy to pick up an apple, but impossible to do the same with a bicycle; whereas it is easy to pantomime riding a bicycle, it is hard to pantomime the use of an apple. So both concepts are manipulable, but with a different connotation. If an apple can be rated as having a high volumetric manipulability and a low functional manipulability, a bicycle can rated exactly in the reverse pattern (low volumetric manipulability and high functional manipulability). In addition, some objects (tools) are both easy to pick up and to pantomime. Studies that take into consideration just one kind of manipulability cannot be able to highlight these differences, and this may play a role in explaining the divergences between the results of different studies. Bub et al. (2008) discussed the premotor activations reported for fruits and vegetables by Gerlach et al. (2002), suggesting that “a substantial component of premotor activation must include gestural knowledge associated with the shape of objects in addition to their function”. In previous neuroimaging studies examining brain activation patterns associated with manipulable objects, the stimuli were both volumetrically and functional manipulable (as in the case of tools). Furthemore, these items have generally been contrasted with items neither functionally nor volumetrically manipulable, because they were too large or too heavy to be held in the hand (e.g., house, traffic lights). Rueschemeyer et al. (2010) were the first to investigate the differences between words denoting volumetrically manipulable objects, such as clock or bookend, and functionally and volumetric manipulable objects, such as pen, cup, hammer. They found a large overlap between the activations associated to the two conditions. However, functionally manipulable words showed a greater activation in the fronto-parietal sensorimotor areas compared to volumetrically manipulable words. In particular, greater activations for functionally manipulable words were seen in the ventral premotor cortex, in the inferior parietal cortex and in the pre-SMA.

Finally, several studies reported a greater activation for L in the left medial anterior temporal cortex (Bright et al., 2005; Mummery et al., 1996; Phillips et al., 2002). Although these evidences are supported by clinical studies (Gainotti et al., 2005), some authors have suggested that those activations depend from demands in differentiating or integrating semantic features. L items, such as fruits, generally require the integration of multiple features, i.e. a more fine-grained discrimination for their identification, while tools are identified on the basis of individual distinctive features, and thus result less confusable (Bright et al., 2005; Devlin et al., 1998; McRae & Cree, 2002). Devlin et al. (2002) showed in fact that this region was active for both tools and fruits during a semantic categorization task, in which a within-category semantic differentiation was required. Moreover, Tyler et al. (2004) documented activation on the medial surface of the left ATL when subjects silently named common objects at the basic level (e.g., monkey), relative to a more general identification (L) or to baseline. Zannino et al. (2009) showed a robust semantic distance (SemD) effect in the anterolateral temporal cortex bilaterally, in which activity increased linearly with increasing semantic distance between target and foil (for example, during a word-picture matching task, the stimuli *fox-giraffe*, with high SemD, would increase anterolateral cortex activity more than the stimuli *squirrel-mouse*, with low SemD). No differential category-specific activation was found in the anterior temporal lobes. Zannino et al. (2009) and Whatmough et al. (2002) reported greater activity in the lateral temporal cortex for the less demanding semantic condition (i.e., respectively, for stimuli with high SemD between target and foil and for more familiar items). This stands in contrast studies reporting greater activation of the anterior lateral temporal lobe (for both L and NL) for more specific, relative to more general classification tasks. However, even if the conditions were matched for difficulty, specific classification elicited significantly longer RTs than did intermediate or general classification (Rogers et al., 2006). Zannino et al. (2009) suggested that the activation of the anterior temporal lobe is proportional to the number of recruited features.

It is difficult to accommodate these heterogeneous evidences on the basis of one theory. Studies showing specific activations for different categories seem to agree with more than one organizational principle, reconciling a sensory motor organization with an organization by domain of knowledge. Some studies failed to find category-specific activations in the brain (Tyler at al., 2003). This result is problematic for theories assuming category-specific neural correlates, but is readily accounted for by theories that assume a distributed conceptual system without no specialization for different semantic categories. Several factors can account for these contrasting results. First of all, the numerous published neuroimaging studies concerning semantic processing employed a wide range of tasks and task comparisons (Devlin et al., 2002; Noppeney & Price, 2002). For example, Joseph et al. (2001) in their meta-analysis found a greater inferior occipital activation during matching tasks compared to naming or viewing tasks, and a greater activation in anterior ventral temporal regions during naming tasks compared to matching or viewing tasks. A second problem concerns contrasts in which the conditions differ in difficulty. Functional neuroimaging measurements are very sensitive to differences in accuracy, response time and level of effort between tasks. Moreover, differences in the stimuli used to elicit semantic processes might also contribute to the variable findings. In fact, the differential activations may be related to uncontrolled differences in object processing that are not directly related to category-specific effects.

4.3 Evidences from meta-analysis

Differently from previous reviews (Devlin, Russell, et al., 2002; Joseph, 2001; Price & Friston, 2002), which included studies involving both words and pictures as stimuli, Gerlach et al in their meta analysis (2007) considered only tasks involving pictures. They included picture naming task at basic level (12/20), object decision, passive viewing, matching to sample, superordinate classification, global shape matching, picture matching and semantic categorization. The authors found no specific area consistently active for a specific category across all the studies considered, even when they considered only studies involving basic level naming. In addition, the studies differed for the subcategories of stimuli considered. Even considering only animals in comparison with tools, little evidence for category specific activations was found.

A more stringent criterion has been adopted in a more recent review. Chouinard and Goodale (2010) included only studies using picture naming as task and animals and tools as stimuli. They reported greater activations for animals in visual areas and in ventral prefrontal structures. Concerning the occipital activations, the authors suggested that they could be due to the greater structural complexity of the animals in respect to tools. Concerning the activation in the left ventral prefrontal cortex (BA 47/12), the authors suggested that it could be explained by an emotional response associated with animals, as suggested by Caramazza and Shelton (1998). In fact, this region is strongly connected to limbic structures. These results are in agreement with behavioural data, described in chapter 2, showing that L items are typically rated as having more emotional content than NL items (Brousseau et al., 2004). All these evidences suggest that, in order to avoid spurious category activations, the stimuli (L and NL) have to be matched for emotional valence and/or arousal. In contrast, tools, in comparison with animals, recruited regions in the ventral stream (different from those more active for animals) and in the parieto-frontal regions (the left ventral premotor area, the left post-central gyrus, and the left anterior superior parietal lobule). The authors underline that it was not always possible to assess if and how well the different studies were controlled for the confounding variables (such as familiarity, etc.).

4.4 The experimental study

4.4.1 The aim of the study

In parallel with the aim of the neuropsychological study described in chapter 2, here we investigate the category-specificity issue using fMRI in healthy subjects. The aim of this study is to investigate the presence of category effects, trying to overcome some of the limitations of the previous studies. As mentioned for the neuropsychological study, and as described above, it is now well known that, that in order to verify the presence of category effects, confounding variables must be taken into adequate account. fMRI studies varied largely in the number and the type of variables considered, and this may have led to inconsistence in the results. Indeed, some authors consider several category effects as spurious activations due to a lack of balance in the stimuli used. In addition, as some variables, such as volumetric manipulability, semantic relevance, emotional valence, distinctiveness etc have been only recently introduced as possible predictors of category effects, they have up to now not been controlled for, unless they were the core of the study. The majority of studies considered only the most widely used variables, such as familiarity although with a high degree of variation from a study to another. An important aspect of the study presented in this section is that the stimuli were carefully matched on a large number of variables in order to avoid spurious activation differences between domains.

4.4.2 Materials and Methods

4.4.2.1 Participants

Fourteen right-handed healthy monolingual native speakers of Italian (7 females; mean age 63.21, age range= 56-76 years; education mean=13,21; range education 8-18) with normal or corrected-to-normal vision took part in the experiment. Handedness was verified by means of the Edinburgh Inventory (Oldfield, 1971). None of them had a history of neurological or psychiatric disorders and MMSE score less than 24. Subjects gave informed written consent to the experimental procedure, which was approved by the local Ethics Committee.

4.4.2.2 Stimuli creation and matching procedure

Subjects were required to overtly name visually presented coloured photographs depicting real objects. Thirty-two items, sixteen L and sixteen NL things, were selected from the database of 82 concepts described in chapter 2. Photographs were obtained from the Viggiano et al. database (2004), and the respective non pictures were specifically created. L items belonged to three distinct semantic categories (i.e., animals, fruits and vegetables), and NL items belonged to four distinct semantic categories (i.e., vehicles, tools, kitchen utensils, furniture; see Appendix G.1 for a complete list). In each category there were 4 items, with the exception of the animal category where we selected 8 items. In addition, the 32 stimuli included 16 manipulable (fruits and vegetables for the L items and tools e kitchen tools for the NL things) and 16 non manipulable items (animals for the L and furniture e vehicles for the NL). In order to distinguish between manipulable and non manipulable items, we used the volumetric manipulability values of the norms described in chapter 2. In particular, items with manipulability values between the lower value of the manipulability distribution and the 40th percentile were considered as non manipulable, whereas items with values ranging from the 60th percentile to the highest value of the distribution were considered as manipulable.

The same 32 stimuli were used to build homogeneous and heterogeneous blocks. In the homogeneous subset, each block consisted of 4 items belonging to the same category. Based the normative study on semantic features described in chapter 2, we chose stimuli belonging to the same category with at least five features in common, in order to maximize the semantic similarity. In this way, 4 homogeneous blocks were composed for L items (of which two were also manipulable and two were not manipulable), while the other 4 blocks were composed of NL things (of which two were manipulable and two were not manipulable). In the heterogeneous condition, even if the same items were used, each block consisted of 4 pictures belonging to different categories: one L manipulable (e.g. *pineapple*), one L non manipulable (e.g. *giraffe*), one NL manipulable (e.g. *drill*) and one NL and non manipulable item (e.g. *helicopter*).

Thirty two non pictures were generated in order to create a baseline condition. The 32 previously selected images were manipulated using Photoshop. A 64 x 64 pixels matrix mosaic was created for each image. Margins were vanished with a gaussian filter. We used these stimuli to create 16 non pictures blocks corresponding to the homogeneous and heterogeneous ones (see appendix G.2).

Thus, we created the following experimental conditions:

- 8 homogeneous pictures blocks:
  - 2 L manipulable (fruits and vegetables)
  - 2 L non manipulable (animals)
  - 2 NL manipulable (tools, kitchen tools)
  - 2 NL non manipulable (vehicles and furniture)
- 8 heterogeneous pictures blocks
- 8 homogeneous non pictures blocks
- 8 heterogeneous non pictures blocks

The two different types of blocks were created in order to minimize the visual similarity in the homogeneous blocks, while in the heterogeneous blocks the items had high visual similarity. In order to control the visual similarity of blocks, as this variable could cause spurious category activation (L are generally more visual similar than NL), a rating task was administered to 16 subjects (8 males), who did not participate in the subsequent fMRI experiment. The age of the subjects ranged from 55 and 85 years (age 64,43 ± 9,10). The aim was to obtain quantitative judgements about how similar in appearance the four stimuli of each block were. We used the same homogenous and heterogeneous blocks described above. 2 different blocks were used as examples, the first block composed of items with high visual similarity but belonging to different semantic categories; the latter was characterized by items with low visual similarity, but sharing the same semantic category (see appendix G.3). Pictures were displayed on the monitor of the computer; we presented each block at a time with a Powerpoint presentation. The subject had to say how similar the 4 images were . The scale of similarity ranged from 1 to 7, in which 1 indicated *not at all similar* and 7 indicated *very similar.* The participants were instructed to ignore semantic similarity (the category to which the 4 pictures belonged) and to judge similarity on the basis of visual appearance (shape, colour and size). The instructions for similarity were based largely on those used by Damian et al. (2001), but with a different range (see appendix G.3). The order of the items in each block was randomized (4 different list version were created) as the order of the blocks, with a randomization between homogeneous and heterogeneous blocks.

A very strict matching between L and NL was achieved. Values of visual, psycholinguistic and semantic variables were taken from Viggiano et al. (2004), Dell'Acqua et al. (2000), Della Rosa et al. (2010), LEXVAR database (Barca, Burani, Arduino, 2002) and from norms obtained in chapter 2.

Considering the **Homogeneous condition** (on which the analysis of interest are based), **L versus NL** were matched for bigrams frequency (p=0,250), number of letters (p=0,116), number of syllables (p=0,566), number of letters for block (p=0,285), letters frequency (p=0,992), visual familiarity (p=0,862), visual complexity (p=0,993), name agreement (p=0,901), frequency of word use (p=0,08), concreteness (p=0,159), imageability (p=0,811), age of acquisition (p=0,831), familiarity (p=0,622), context availability (p=0,614), arousal (p=0,07), emotional valence (p=0,127), volumetric manipulability (p=0,960), visual similarity (0,179), visual relevance[5] (p<0,06), number of distinctive features (p=0,609), Garrard's distinctiveness (p=0,375) and for number of distinctive features for each word over the total number of distinctive features for each block (RfD) (p=1). However, L and NL concepts could not be matched for functional manipulability (p<0,001) and typicality (p=0,044), with higher values for NL. **.**

4.4.2.3 Experimental paradigm

The experiment consisted of two runs. Each run was composed by:

·4 homogeneous blocks and 4 heterogeneous blocks of pictures. The subjects were asked to name each picture.

·4 homogeneous blocks of non pictures (the non pictures were obtained from the pictures of the respective homogeneous block) and 4 heterogeneous blocks of non pictures (the non pictures were obtained from the pictures of the respective heterogeneous block). The subjects were asked to say "ok" after each non picture.

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[5] Note that visual semantic relevance is different from semantic relevance described in chapter 2. In this case the subjects were asked to generate all the visual features that they detected in the pictures. The procedure of computation is the same described in chapter 2 for semantic relevance. The values used in this study are based on pervious norms obtained on the same coloured pictures used in this experiment (using the procedure described in Mechelli et al. 2006).

Thus, for each run a total of 16 blocks were presented, leading to a total of 64 trials per run (16 blocks x 4 items in each block). Each homogeneous and heterogeneous block was followed or preceded by its corresponding non picture block; items were not repeated more than twice in each run. Moreover, for each run the order of blocks were randomized, in order to avoid that blocks of the same experimental condition was presented in succession (e.g. homogeneous picture - homogeneous picture, or heterogeneous non picture - heterogeneous non picture, or homogeneous L manipulable pictures - homogeneous L manipulable pictures, etc.). For each run, two different randomizations were created, containing the same items, but with a different order between and within blocks. Each subject performed both runs (1 and 2), and the order of presentation of the two runs and the randomizations were counterbalanced between subjects.

The block presentation was as follows:

(i) at first the instructions " fix the cross" appeared for 2000 msec, than a fixation cross (+) was presented at the centre of a computer screen for 12000 msec

(ii) instructions specific for the block appeared and stayed on the screen for 2000 msec,

(iii) the fixation cross appeared again and stayed on the screen for 12000 msec.

(iv) four visual stimuli, belonging to each block, were presented on a black background for 2200 msec, replaced immediately by a centrally positioned fixation cross (see figure 11).

An alternation of stimulus and fixation cross presentation was repeated for a total of 4 times. The ISI (interstimulus interval) between pictures lasted or 1750 or 2250 or 3000 msec and different ISI were randomized within blocks. Each run lasted 11 minutes, so the experiment lasted approximately 22 minutes. The same design and procedure were adopted for fMRI acquisitions, however the answers were not collected. Subjects were asked to respond as quickly but as accurately as possible, but they were instructed to mouth the name silently to eliminate movement artefacts in resonance.

Even if each part of the experimental paradigm has been described in detail, the focus of this study concerns exclusively the homogeneous condition: As a block design was employed, this is the only condition in which we could discriminate between blocks of L, manipulable and not, and NL, manipulable and not. Thus, all the subsequent analyses, both behavioural and functional, are based only on the homogenous experimental conditions (both pictures and non pictures).

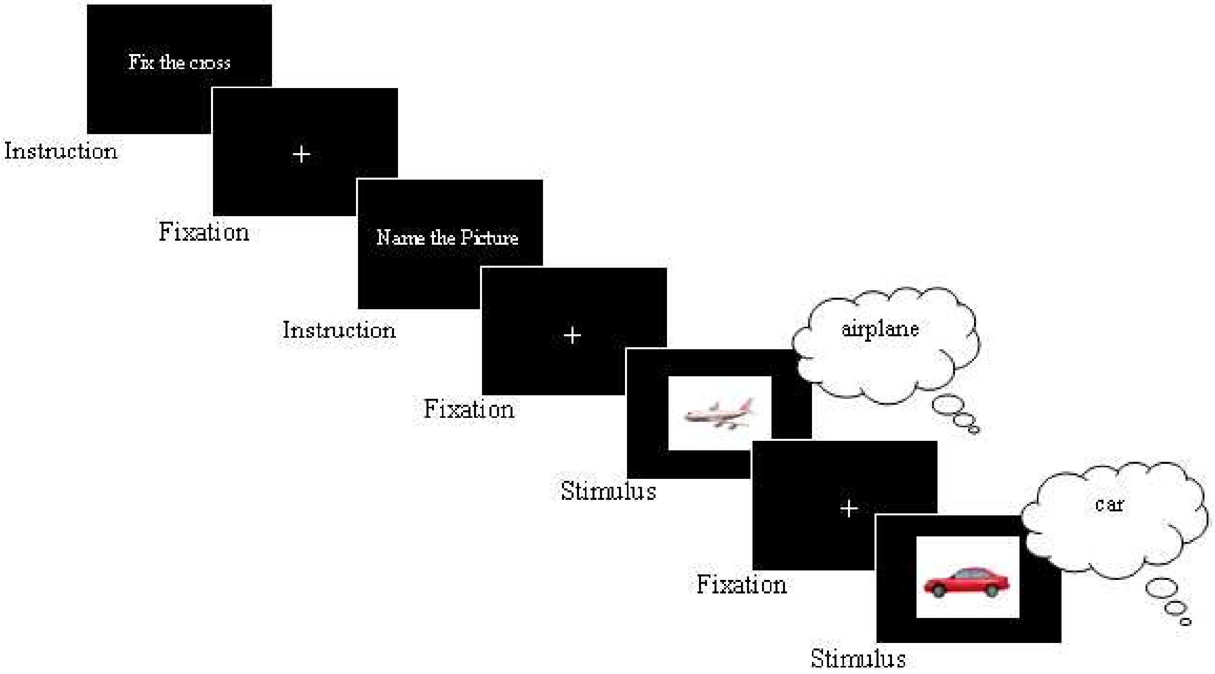

Figure 11: Schematic representation of the picture naming task in the homogeneous condition (vehicles category).

4.4.2.4 Procedure

Prior to scanning, in order to familiarize with the task, subjects were asked to perform the picture naming task by viewing experimental stimuli on a laptop screen. The stimuli were presented with the stimulus delivery program, Presentation software V10.3 (NeuroBehavioral Systems Inc., Albany, CA). All the subjects were instructed to overtly name the presented objects as quickly and as accurately as possible. Vocal responses were recorded via a microphone in order to measure naming accuracy and reaction times.

4.4.2.5 fMRI Data Acquisition

An fMRI-blocked technique was used (3T Intera Philips body scanner, Philips Medical Systems, Best, NL, 8 channels-sense head coil, sense reduction factor = 2, TE = 30 ms, TR = 3000 ms, FOV = 240 x 240, matrix size = 96 x 96, 51 contiguous axial slices per volume, 234 volumes for each run, slice thickness = 2.5 mm, gap = 0.2 mm).

Furthermore, optimal EPI parameters at 3T were defined in order to gain BOLD sensitivity in the temporal poles and anterior temporal lobes (Weiskopt et al., 2006). Specifically, in order to minimize susceptibility induced artefacts and signal dropouts in the anterior temporal lobes and the temporal poles the slice tilt was set to +30 degrees, denoting a tilt of the anterior edge of the slice towards the feet. The phase encoding (PE) gradient polarity was chosen to be negative with the phase encoding direction going form the anterior part to the posterior part of the brain. Five dummy scans preceded each run, all of which were then discarded prior to data analysis to optimize EPI image signal. For each subject a high-resolution structural image was acquired for means of coregistration, segmentation and spatial normalisation of the epi scans (MPRAGE, 150 slice T1-weighted image, TR = 8.03 ms, TE = 4.1 ms; flip angle = 8°, TA = 4.8 min, resolution = 1mm x 1mm x 1mm) in the axial plane.

4.4.2.6 fMRI Data Analysis

Data were preprocessed and analyzed using SPM8 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK). Prior to analysis, all images for two sessions underwent a series of preprocessing steps. Time series diagnostics using tsdiffana (Matthew Brett, MRC CBU: http://imaging.mricbu.cam.ac.uk/imaging/DataDiagnostics) were run to verify the quality of the functional data. Image volumes, slices, and voxels with significant artifact were identified using the ArtRepair toolbox (http://cibsr.stanford.edu/tools/ArtRepair/ArtRepair.htm) based on scan-toscan motion (1 SD change in head position) and outliers relative to the global mean signal (3 SD from the global mean). A field-map sequence was acquired for each subject for distortion correction, and all images were motion corrected using realign and unwarp procedure. For each scanning session, all functional volumes were then realigned to the first one in the time series. BOLD images were then coregistered to MP-RAGE anatomic image sequence for each subject.

To integrate the functional and structural data and to ensure normalization to the same coordinate space across the group of older subjects diffeomorphic image registration (DARTEL) in SPM8 (Ashburner, 2007; Ashburner & Friston, 2005) was used. Unified segmentation was performed to iteratively bias field correct and segment the images into their native space tissue components. This procedure also generated normalization parameters thatwere used during the DARTEL procedure to coregister the segmented gray matter images (Ashburner, 2007). The recursive DARTEL procrustes procedure involves diffeomorphic registration to preserve cortical topology using a membrane bending energy or Laplacian model. This procedure creates invertible and smooth deformations for each subject’s native space gray matter image to a common coordinate space, thereby producing a template that is representative of the brain size and shape of all the participants. The flow fields that describe the spatial deformations were applied to each subject's EPI data to normalize the images into a common coordinate space.The EPI dataset for each subject was first coregistered to the T1-weighted image using the mutual information algorithm in SPM8 (Collignon et al., 1995). The T1 and EPI images were then visually inspected to ensure that they were properly coregistered. With the EPI datasets in the same space as the T1 image for each subject, the DARTEL flow fields were used to normalize the EPI data into the study specific normalized space of the gray matter template. The images were then smoothed using an 6 mm Gaussian kernel to ensure that the data were normally distributed and appropriate for parametric testing. The data were analyzed adopting a two-stage random-effects approach to ensure generalizability of the results at the population level. At the individual level, the set of 8 homogeneous blocks was modeled taking in consideration two factors: category (living/non-living) and manipulability (manipulable/non-manipulable) for a total of 4 regressors. The heterogeneous blocks, the homogeneous non-picture blocks and heterogeneous non-picture blocks were then modeled as separate regressors. The conditions were modeled by convolving a box-car function of each block with a 'canonical' hemodynamic response as the basis function to create regressors of interest. Data were highpass-filtered at 1/128 Hz to remove low-frequency signal components and were then analyzed with a general linear model as implemented in SPM8. Temporal autocorrelation was modeled using a first order autoregressive process. The contrast images of interest from individual subjects were then entered in a one sample t-test to treat subjects as a random effect and account for inter-subject variability in order to assess the significance of the effects at the group level (n=14 participants).

For the purpose of this study we took in account the following contrasts for second level analysis: Living Pictures vs Non Pictures and Non Living Picture vs Non Pictures (L–baseline and NL–baseline), in order to assess the main effects of domain (L and NL); and the direct comparison between Living vs Non Living and viceversa (Non Living vs Living) in order to assess domain-specific effects. SpmT-maps were finally overlaid on the mean normalized skullstrip images for visual inspection

4.4.3 Behavioural results

The mean percentage of correct responses was high, 99% of correct responses. No differences were found between L and NL. Concerning the reaction times, 12% of data were discarded (9% for registrations problems and 3% were outliers). The mean correct reaction times (RTs) to the 32 pictures presented in the naming task were compared with a paired T-test. No significant differences were detected between the two domains (L mean= 9445,33 , sd=1092,82; NL mean=9353,67, sd=1311,22; t=0,663, p=0,517).

4.4.4 Nuroimaging results

Table H.1 in appendix reports significant activations for the two contrasts L–baseline and NL–baseline. The contrast L–baseline revealed larger activations than the NL–baseline contrast. In the L- baseline contrast, the main peak activations were observed in the left inferior occipital gyrus and bilaterally in the middle occipital gyrus and in the fusiform gyrus. In addition, further activations were detected in the left inferior parietal lobule and in the left inferior frontal gyrus (p. Triangularis). NL– baseline contrast revealed activations in the inferior occipital gyrus bilaterally, in the left fusiform gyrus and in the inferior parietal lobule (see also figure H.2 in appendix).

The direct contrast showed that compared with L, NL activated the left inferior parietal lobule, the right superior parietal lobule and the right inferior frontal gyrus (p. Triangularis) (see figure 12 below and table H.3 in appendix). No activations were found for the opposite comparison.

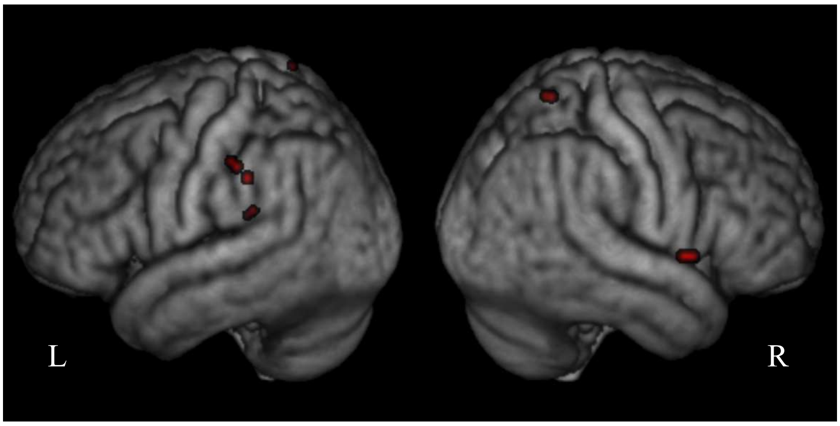

Figure 12: Differences in BOLD response for pictures representing Non Living (NL) versus Living (L) (NL > L) objects (p < .005, k > 2). Lateral view, L=left; R=right.

Comment

The direct contrasts revealed no significant activations when L were compared with NL. The opposite comparison revealed activations in the left inferior parietal lobule and the right superior parietal lobule. The stimuli were balanced pairwise for several confounding variables, with the exception of functional manipulability. NL were more functionally manipulable than L.

4.5 Discussion

To summarize, we used a picture naming task in which the two domains, L and NL, have been carefully matched for several confounding variables, such as bigrams frequency, number of letters, number of syllables, number of letters for block, letters frequency, visual familiarity, visual complexity, name agreement, frequency of word use, concreteness, imageability, age of acquisition, familiarity, context availability, arousal, emotional valence, volumetric manipulability, visual similarity, visual relevance, number of distinctive features, Garrard's distinctiveness and for RfD. However, the stimuli were not balanced for functional manipulability, with NL resulting higher than L.

The behavioural results showed no significant differences in reaction times between L and NL items. Turning to imaging results, we showed that when the materials are carefully matched for confounding variables, no or only minimal category effects are detected. In particular, L, when compared with NL, showed no significant activations. In contrast, when NL were compared with L, significant, although modest, activations were found in the left inferior parietal lobule (IPL) and in the right superior parietal lobule (SPL).

In this study we carefully matched L and NL for several confounding variables, in order to avoid spurious activations. Indeed, several differential activations usually observed for L or NL stimuli have not been observed here, probably for the careful matching adopted. Natural objects are generally more visually complex and similar than artefacts, and tend to cause greater activations in posterior and ventral parts of the brain (e.g., the calcarine sulcus, the inferior occipital cortex, the medial occipital cortex, and the lateral parts of the fusiform gyri; see Gerlach et al., 2007). When the categories are matched for visual complexity and similarity, as in our case, these activations are not reproduced. In addition, semantic relevance could modulate the activations in the right and left medial fusiform gyrus (Mechelli et al., 2006). These activations were shown to reflect semantic relevance rather than category per se. Confirming this hypothesis, in our study in which we matched stimuli for visual semantic relevance, no category specific activation were found in the fusiform area. The differential role of medial anterior temporal cortex in the processing of L has been proposed to reflect the fact that L have more shared properties than NL, so that more fine-grained discriminations are required to name them (Bright et al. 2005, Damasio et al. 2004, Simmons & Barsalou 2003; see also Humphreys & Forde 2001). In order to avoid this confound, we matched stimuli for the number of shared and distinctive features. Furthermore, some studies reported a greater activation of the left ventral premotor cortex for tools (Chao & Martin, 2000; Chao et al., 2002), while others suggested that these activations are due to the manipulability of the stimuli (Devlin et al., 2002; Gerlach et al., 2002). Our results are in accordance with the second view, in that, matching stimuli for volumetric manipulability, we did not find such activations. A recent meta-analysis (Chouinard & Goodale, 2010) showed a greater activation in the left ventral prefrontal cortex (BA 47/12) for animals, suggesting that it could be explained by an emotional component associated with animals. In this study we matched for emotional valence, and this activation was not found.

The failure to show differences in activation provided supports for the correlated features accounts that postulate that when items are balanced for relevant variables the category-effect studies are absent or reduced. However, in order to match for all these confounding variables it was not possible to use only one category for each domain (we in fact collapsed together, for example, animals and fruit and vegetables). A recent meta analysis (Chouinard & Goodale, 2010) considered only studies including animals and tools as stimuli, showing different category specific activations. Nevertheless, animals and tools generally differed for several confounding variables, such as visual complexity and similarity, manipulability, emotional valence, that could account for some of the specific activations reported.

The only specific activations that we detected in the contrast NL-L were in parietal regions, i.e. the right SPL and the left IPL. Both areas are part of the neural systems supporting tool use (see Lewis 2006). SPL is postulated to code the location of the limbs relative to other body parts during for example grasping and manipulating objects or during meaningful hand gestures (Binkofski et al., 1999; Chao & Martin 2000; Culham et al., 1998; Emmorey et al., 2004; Wolpert et al., 1998). In particular, the right SPL has been associated with visuospatial analysis of gesture (Lewis et al., 2006). The left inferior parietal lobule (IPL) is involved in several aspects of planning of motor skills and imagery of object use (for a review see Lewis, 2006). As reported above, it is associated with the processing of complex actions required for tool use. Several authors showed the activation of left IPL in tasks requiring judgments on the object manipulability (Boronat et al., 2005; Rumiati et al., 2004). It has been proposed that this area stores engrams of known hand movement gestures, as the IPL is involved in planning and preparation of movements (Buxbaum et al., 2003; Buxbaum et al., 2005). Patients with a damage in this area can show deficits in tools use and pantomime. These patients, however, may be able to handle objects in simple way (Sirigu et al., 1995), to retain the function of the object and to name it (Buxbaum & Saffran 2002). In addition, in a recent study with a group of unilateral stroke patients, Mahon et al. (2007) showed a relationship between performance in object identification and object use only in patients with lesions involving the inferior parietal cortex but not in patients without parietal involvement. Canessa et al. (2008) showed that the inferior parietal lobule (x=-50, y=-30, z=42) increased activation for action relative to function knowledge. Okada et al. (2000) reported a greater activation in the left IPL (x=-48, y=-36, z=56) comparing naming tools versus naming animals. A recent TMS study (Pobric et al., 2010) showed that the stimulation of the left IPL (x=−49, y=−44, z=48) induced a category-specific deficit for manipulable man-made objects but not for non manipulable man-made objects and L entities. Mahon et al. (2007) found a neural specificity (in addition to the medial fusiform gyrus, the left meddle temporal gyrus) in the left IPL (x=-51, y=-34, z=36) for tools (hammer, scissors, wrench), but not for arbitrarily manipulated objects (e.g., book, wallet, envelope), non manipulated objects (anchor, desk) and animals. Mahon et al. (2007) distinguished tools from arbitrarily manipulated objects in that for tools “the motor movements associated with their use are instrumental in determining their function”. Otherwise, arbitrarily manipulated objects have a “variable relationships between their physical form and their manner of manipulation/function”. In addition, tools and arbitrarily manipulated objects did not differ with respect to participants’ experience in physically manipulating the objects. Rueschemeyer et al. (2010) reported the first study that systematically compared objects with high values of both volumetric and functional manipulbility with volumetric manipulable objects (see above). Interestingly, they showed a greater levels of activation in the fronto-parietal sensorimotor areas, involving the ventral premotor cortex, the inferior parietal cortex and the pre-SMA, for functionally manipulable stimuli compared to volumetrically manipulable ones. These evidence are in line with our results, in that the differences between NL-L reported in the inferior parietal regions could be due to the unmatched functional manipulability, higher for NL than for L. In fact, both tools and vehicles (although tools>vehicles and furniture) have higher values of functional manipulability compared to L (both fruits and animals).

The results of this study are in line with the sensory motor theory. In fact, if on one hand we did not find specific activations for L, on the other hand we found specific activations for NL in regions subserving visual motor knowledge. Further analysis could investigate directly the neural basis of manipulability effects not only for NL but also for L.

In conclusion we suggest that both types of knowledge (visual, functional, action, etc) and other distributional factors, like features distinctiveness, semantic similarity, visual complexity, familiarity, name frequency and so on can account for the present results, as all these "factors influence the way in which these concepts are structured and computed" (Cree & McRae, 2003).

Chapter 5: General conclusions

We return to the patients reported at beginning of this work:

When the patient described by Patterson and co-workers (2007) was asked to name a picture of a zebra, she replied: "It's a horse, ain't it?" Then, pointing to the stripes, she added, "But what are these funny things for?". This patient was affected by semantic dementia and showed a dramatic and selective loss of semantic memory.

Laisney et al (2011) showed, using a semantic priming task, that semantic memory impairment follows the same course in both AD and SD patients. As in several other studies (for AD see Duarte et al., 2009; Garrard et al., 2005; Alathari et al., 2004), they documented that distinctive attributes are lost first, shared ones later. In agreement with feature-based models of semantic memory, the loss of distinctive attributes leads to a confusion between close concepts, causing, in the case of Laisney et al study (2011), an hyperpriming phenomenon (a larger semantic priming effect than in controls).

In this study, using a battery of test (CaGi) specifically created and standardized in order to assess concrete knowledge, we confirmed that distinctive features are lost earlier than shared ones in patients with Alzheimer's disease. In addition, we showed that not all the distinctive features are lost with the same progression in respect to the shared ones, and that not all the distinctive features have the same importance in leading to a confusion between close concepts, leading, in our case, to a picture naming deficit. Distinctive features with high values of semantic relevance, like "*has stripes"* for zebra, are maintained longer at the same level as shared ones and seem more important (more salient) for identifying and discriminating between close concepts, in comparison to distinctive features like, for example, "*has rounded ears*". In fact, a significant loss of distinctive features with high values of semantic relevance in comparison to shared ones was observed only in patients with deficits in picture naming task.

Consider now the patient described by Chertkow et al. (1990):

who was able to name a picture of a zebra and correctly answer to questions that uniquely identified the animal (e.g. Is the zebra striped?), however at the same time the patient incorrectly answered to many basic questions concerning the animal ("Do zebras meat eat?", "Do they live in Africa?"). When the patient could not answer to identification questions concerning an animal then he could not name the picture of the same animal.

This patient showed a loss of semantic memory, and was affected by Alzheimer's disease. In this case, the associative features reported here are similar to those that in our study are called

”distinctive features with low values of semantic relevance”. These are features not immediately important for the identification of the concept, but they are not specifically distinctive. In contrast, identificative features are closely similar to our “distinctive features with high values of semantic relevance”, and they are less vulnerable and essential for the identification and consequently naming of the concepts. The patients’ behaviour is similar, as they lost the knowledge of distinctive features with high value of semantic relevance only for the items that they could not name.

In conclusion, this study reconciles evidences supporting the idea that distinctive features may play an essential role in picture naming (Moss et al., 1998; Duarte, 2009), with those studies that failed to demonstrate an association between the status of distinctive features and picture naming performance (Garrard et al., 2005). Not all the distinctive features have the same importance for the identification of a concept (Cree et al., 2006; Sartori & Mechelli, 2004). However the demonstration that distinctive features with high values of semantic relevance are lost, in respect to the shared ones, in AD patients with deficits in picture naming require further investigations considering also the feature type (modality, such as visual etc.) As the two dimensions are not mutually exclusive, further investigations should address the role of different types of features and of their distinctiveness in picture naming.

Patients with Alzheimer’s disease, other then a generalized impairment of semantic memory, may show a selective deficit for living entities. This is the case of HELGA, the patient reported by Mauri et al (1994) with a *“disorder relating to processing of knowledge about animate objects in the presence of spared knowledge of inanimate objects”* .

HELGA was a patient with Alzheimer’s disease who showed a category effect, with a poorer performance on living entities (both animals and fruits and vegetables) than on non living entities. Mauri et al. (1994) compared her performance with that of Michelangelo, a post encephalic patient, who manifested a well-documented category-specific deficit for animate objects. Nowadays, it is well known that several methodological issues must be taken in account when studying category specific impairments. In fact, in order to verify the presence of category effects several confounding variables must to be considered. Previous studies varied largely in the number and in the type of variables considered. As some variables have been only recently introduced as possible predictors of category effects, they have not been frequently investigated. This is particularly true for the role of semantic relevance, a semantic variable introduced recently as possible factor explaining category-specific deficits. Interestingly, the patient Michelangelo, reassessed ten years later (Sartori & Lombardi, 2004) still showed a specific deficits for living entities when assessed with traditional tests, in which the stimuli were not matched for semantic relevance. When the stimuli were balanced for semantic relevance, the category effect disappeared. The same effect has been shown in a group of AD patients (Sartori & Lombardi, 2004). Who knows if HELGA, after controlling for semantic relevance, would still show a category effect?.

In this study, using the CaGi battery, we investigated category effects in AD considering the majority of the methodological concerns, including the variables proposed as possible confounds in category dissociation, such as emotional valence, semantic relevance, semantic distance, arousal, number of feature, functional and volumetric manipulability, together with the more widely used ones, i.e. age of acquisition, familiarity, visual familiarity, typicality. Similarly to the conclusion reported in Mauri et al study (see also Cherkow & Bub, 1990b), we showed that the presence of category effects is a reliable phenomenon present in a few AD patients, also after controlling for semantic relevance. Category-effects in AD are probably dependent from stages of disease progression, associated to specific location and extent of brain damage.

Further investigations should address if patients showing category effects present also a disproportionate loss of distinctive features with high values of semantic relevance in respect to the shared ones for the more impaired category. The structural conceptual account (CSA, Tyler et al., 2000; 2001) does not consider the possibility of a different pattern of degradation of the two type of distinctive features, that could not be due to their different strength of correlation. In fact, *has stripes* is not correlated with functional features in the same manner as *has rounded ears* has no correlation with functional features. Thus, according to the CSA, both kinds of features are expected to be lost at the same stage of the disease. However, in this study we have demonstrated that it is not the case, and that, while *has rounded ears* is lost first, *has stripes* is maintained for a longer period of time at the same levels as shared features.

The neural basis of category specific effects has been also intensively investigated using the fMRI technique in healthy subjects. Similarly to neuropsychological studies, several confounding variables could account also in this case for spurious activation differences. In this study, we showed that, after matching stimuli for several confounding variables, only a modest, but significant category effect could be detected, when non living entities were compared with living, involving the left inferior parietal lobule. This area has been generally associated with the manipulabilty of the objects. The results presented in this study suggest, in line with others (Rueschemeyer et al., 2010), an important role of functional manipulability, i.e. the knowledge about how objects are used for their intended purpose (Bub et al., 2008). This interpretation is supported by the fact that stimuli were balanced pairwise for several confounding variables, but not for functional manipulability, and that non living entities were more functional manipulable than living entities.

All these findings, concerning concrete knowledge, suggest that both the type of knowledge (visual, functional, manipulability etc) and other factors, such as features distinctiveness, semantic similarity, visual complexity, familiarity and name frequency influence the way in which concepts are structured and processed (see also Cree & McRae, 2003) .

Finally, Martin & Fedio (1983) describing the performance in several tasks of a group of AD patients, reported that "*single-word comprehension was impaired, except when judgments of affective meaning were required*".

In one of the first reports concerning semantic memory impairments in AD, Martin & Fedio showed preserved word comprehension for emotion words. Word comprehension was assessed at superordinate and subordinate levels. In the former case subjects were asked to rate words for degree of pleasantness. At the subordinate level, using a Symbol Referent Test, subjects were asked to match "abstract pictorial representations with printed words denoting objects, actions, emotion, and modifiers". AD performed normally in a pleasantness rating, but they were impaired in the comprehension of single words related to objects (table), actions (to sit), modifiers (strong), but not for emotion words (happy, sad, hungry, love). Although this test is not similar to those generally used to asses comprehension, and it is not well clear for which variables the stimuli were controlled, Martin & Fedio showed an interesting effect that has been neglected for many years. The authors, referring to the preservation of emotion words, suggested that "(the fact) that such judgments were unimpaired may be related to emotional meaning per se, or possibly to the fact that such evaluative judgments require knowledge only on a global, superordinate level; especially in relation to judgments assumed to require knowledge of specific attributes of objects, actions and modifiers".

In this study, using a battery of semantic tests (DeCAbs) specifically created and standardized to asses abstract concepts, we confirm that AD patients show a preserved comprehensions of emotion words with respect to other abstract words when assessed with an association task. In addition, we found that this impairment is related to emotional meaning per se. In fact, the stimuli were closely matched for several confounding variables, and we have no reason to suppose that emotion words rely more on superordinate information than the others abstract concepts used in our study (as ideal, weakness, friendship, revenge). Crutch and Warrington (2006) showed the same progression of the deterioration of semantic memory, characterized by a relative sparing of superordinate information for both abstract and concrete concepts, including abstract concepts with high value of emotional valence.

In conclusion, even if the results presented here need to be confirmed with further analyses and investigations, we believe that they provide some important insights. In the first place, it in necessary to increase the number the patients, and to extend the study to other pathological conditions, such as semantic dementia. Second, extending the two batteries of semantic tests (CaGi and DeCAbs) with tasks including both abstract and concrete items could be an important way to further understand semantic memory impairments. This would make possible to investigate if the same variable influence the subjects' performance on abstract and concrete concepts in the same task. We believe that in order to improve our understanding of the semantic memory organization, future studies must to take in account both concrete and abstract concepts. It is unlikely that one principle/theory will be able to explain all the results presented in this study. In fact, theories concerning only concrete concepts are not explicit in their predictions about the representation of abstract concepts. New proposals, which attempt to integrate different framework, such as those focusing on both experiential (visual, motor, affective) and linguistic information, rather than contrasting them as mutually exclusive, may represent a promising approach.

References

Adlam, A.L., Patterson, K., Bozeat, S., Hodges, J.R. (2010). The Cambridge Semantic Memory Test Battery: detection of semantic deficits in semantic dementia and Alzheimer's disease. *Neurocase*, *16*, 193-207.

Adlam, A.-L.R., Bozeat, S., Arnold, R., Watson, P., Hodges, JH. (2006a). Semantic knowledge in Mild Cognitive Impairment and Mild Alzheimer's disease. *Cortex*, 42, 675-684.

Adlam, A.-L.R., Patterson, K., Rogers, T.T., Nestor, P.J., Salmond, C.H., Acosta-Cabronero J., Hodges, J.R. (2006b). Semantic dementia and fluent primary progressive aphasia: two sides of the same coin?. *Brain*, 129, 3066-3080.

Adlington, R.L., Laws, K.R., Gale, T.M. (2009). Visual processing in Alzheimer's disease: surface detail and colour fail to aid object identification. *Neuropsychologia*, 47, 2574-83.

Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature,* 372(6507), 669-672.

Alathari, L., Trinh Ngo, C., Dopkins, S. (2004). Loss of distinctive features and a broader pattern of priming in Alzheimer's disease. *Neuropsychology*, 18, 603-612.

Albanese, E. (2007). The "hidden" semantic category dissociation in mild-moderate Alzheimer's disease patients. *Neuropsychologia*, 45, 639-643.

Albert, M. S., Cohen, C., & Koff, E. (1991). Perception of affect in patients with dementia of the Alzheimer type. *Archives of Neurology,* 48(8), 791-795.

Allport, P. (1985). Distributed memory, modular subsystems and dysphasia. In Current perspectives in dysphasia. S. K. N. R. Epstein (Ed.). Edinburgh, Churchill Livingstone: 32-60.

Altarriba, J. & Bauer, L.M. (2004). The distinctiveness of emotion concepts: a comparison between emotion, abstract and concrete words. *American journal of psychology*, 117 (3), 389-410.

Altarriba, J., Bauer, L.M., Benvenuto, C. (1999). Concreteness, context availability and imageability ratings and words associations for abstract, concrete and emotion words. *Behavior Research Methods, Instruments and Computers,* 31 (4), 578-602.

Altmann, L.J.P., McClung, J.S. (2008). Effects of semantic impairment on language use in Alzheimer's disease. *Seminars in Speech and Language*, 29, 18-31.

Andrews, M., Vigliocco, G., & Vinson, D. (2009). Integrating experiential and distributional data to learn semantic representations. *Psychological Review, 116*(3), 463-498.

Aronoff, J. M., Gonnerman, L. M., Almor, A., Arunachalam, S., Kempler, D., & Andersen, E. S. (2006). Information content versus relational knowledge: semantic deficits in patients with Alzheimer's disease. *Neuropsychologia,* 44(1), 21-35.

Ashburner, J. (2007). A Fast Diffeomorphic Image Registration Algorithm. *NeuroImage*, 38(1), 95-113.

Ashburner, J., & Friston, K.J. (2005). Unified segmentation. *NeuroImage*, 26, 839-851.

Ashcraft, M. H. (1978). Property norms for typical and atypical items from 17 categories: a description and discussion. *Memory & Cognition*, *6*, 227-232.

Bachoud-Lévi, A. C., & Dupoux, E. (2003). An influence of syntactic and semantic variables on word form retrieval. *Cognitive Neuropsychology*, 20(2), 163–188.

Balota, D. A., & Duchek, J. M. (1991). Semantic priming effects, lexical repetition effects, and contextual disambiguation effects in healthy aged individuals and individuals with senile dementia of the Alzheimer type. *Brain and Language,* 40(2), 181-201.

Balota, D. A., & Spieler, D. H. (1999). Word frequency, repetition, and lexicality effects in word recognition tasks: beyond measures of central tendency. *Journal of Experimental Psychology: General*, 128(1), 32-55.

Balota, D. A., Watson, J. M., Duchek, J. M., & Ferraro, F. R. (1999). Cross-modal semantic and homograph priming in healthy young, healthy old, and in Alzheimer's disease individuals. *Journal of the International Neuropsychological Society,* 5(7), 626-640.

Balota, D.A., Yap, M.J., Cortese, M.J., Hutchison, K.I., Kessler, B., Loftis, B., et al (2007). The English Lexicon Project. *Behavior Research Methods*, 39, 445-459.

Balthazar, M. L., Cendes, F., & Damasceno, B. P. (2008). Semantic error patterns on the Boston Naming Test in normal aging, amnestic mild cognitive impairment, and mild Alzheimer's disease: is there semantic disruption?. *Neuropsychology,* 22(6), 703-709.

Barbarotto, R., Capitani E., Jori T., Laiacona, M., Molinari, S. (1998). Picture naming and progression of Alzheimer's disease: an analysis of error types. *Neuropsychologia*, 36, 397-405.

Barbarotto, R., Capitani, E., Spinnler, H., & Trivelli, C. (1995). Slowly progressive semantic impairment with category specificity. *Neurocase*, 1, 107–119.

Barca, L., Burani, C., Arduino, L.S. (2002). Word naming times and psycholinguistic norms for Italian nouns. *Behavior Research Methods, Instruments & Computers*, 34(3), 424-34.

Barry, C., Morrison, C. M., & Ellis, A. W. (1997). Naming the Snodgrass and Vanderwart pictures: Effects of Age-of-Acquisition, frequency, and name agreement. *Quarterly Journal of Experimental Psychology*, 50A, 560–585.

Barsalou, L. W. (1999). Perceptual symbol systems. *Behavioral and Brain Sciences* , 22(4), 577-609; discussion 610-560.

Barsalou, L. W. (2008). Grounded cognition. *Annual Review of Psychology, 59*, 617-645.

Barsalou, L. W. (2010). Grounded cognition: Past, present and future. *Topics in Cognitive Science*, 2(3), 322– 327.

Barsalou, L. W., Santos, A., Simmons, W. K., & Wilson, C. D. (2008). Language and simulation in conceptual processing. In M. De Vega, A. M. Glenberg, & A. C. A. Graesser (Eds.), Symbols, embodiment, and meaning (pp. 245–283). Oxford, England: Oxford University Press.

Barsalou, L.W. (1999b). Language comprehension: Archival memory or preparation for situated action? *Discourse Processes, 28*, 61-80.

Barsalou, L.W., & Wiemer-Hastings, K. (2005). Situating abstract concepts. In D. Pecher and R. Zwaan (Eds.), *Grounding cognition: the role of perception and action in memory, language and thought* (pp: 129-163). New York: Cambridge University Press.

Barsalou, L.W., Simmons, W.K., Barbey, A.K., and Wilson, C.D. (2003). Grounding conceptual knowledge in the modality-specific systems. *Trends in Cognitive Sciences*, 7, 84-91.

Basso, A., Capitani, E.,& Laiacona, M. (1988). Progressive language impairment without dementia: A case with isolated category specific semantic defect. *Journal of Neurology, Neurosurgery and Psychiatry*, *5*, 1201– 1207.

Battig, W.F., & Montague, W.E. (1969). Category norms for verbal items in 56 categories, a replication and extension of the Connecticut category norms. *Journal of Experimental Psychology Monographs,* 80, 3 part 2.

Beauchamp, M.S., Lee, K.E., Haxby, J.V., Martin, A. (2002). Parallel visual motion processing streams for manipulable objects and human movements. *Neuron*, 34, 149–159.

Bell, E. E., Chenery, H. J., & Ingram, J. C. (2001). Semantic priming in Alzheimer's dementia: evidence for dissociation of automatic and attentional processes. *Brain Lang,* 76(2), 130-144.

Bier, N., & Macoir, J. (2010) How to make a spaghetti sauce with a dozen small things I cannot name: a review of the impact of semantic-memory deficits on everyday actions. *Journal of Clinical and Experimental Neuropsychology,* 32(2), 201-211.

Binkofski, F., Buccino, G., Posse, S., Seitz, R.J., Rizzolatti, G., Freund, H-J. (1999). A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *European Journal of Neuroscience,* 11, 3276–3286.

Binkofski, F., Dohle, C., Posse, S., Stephan, K.M., Hefter, H., Seitz, R.J., Freund, H.J. (1998). Human anterior intraparietal area subserves prehension: A combined lesion and functional MRI activation study. *Neurology*, 50, 1253–1259.

Bleasdale, F. A. (1987). Concreteness-dependent associative priming: Separate lexical organization for concrete and abstract words. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 13(4), 582–594.

Blundo, C., Ricci, M., & Miller, L. (2006). Category-specific knowledge deficit for animals in a patient with herpes simplex encephalitis. *Cognitive Neuropsychology, 23*(8), 1248-1268.

Bonilla, J. L., & Johnson, M. K. (1995). Semantic space in Alzheimer's disease patients. *Neuropsychology*, 9(3), 345–353.

Bonner, M. F., Vesely, L., Price, C., Anderson, C., Richmond, L., Farag., G., Avants, B., Grossman, M. (2009). Reversal of the concreteness effect in semantic dementia. *Cognitive Neuropsychology*, 26(6), 568-79.

Borgo, F., & Shallice, T. (2001). When living things and other 'sensory quality' categories behave in the same fashion: a novel category specificity effect. *Neurocase, 7*(3), 201-220.

Boronat, C.B., Buxbaum, L.J., Coslett, H.B., Tang, K., Saffran, E.M., Kimberg, D.Y., Detre, J.A. (2005). Distinctions between manipulation and function knowledge of objects: Evidence from functional magnetic resonance imaging. *Cognitive Brain Research*, 23, 361–373.

Bourne, L.E. , Jr., & Restle, F.(1959). Mathematical theory of concept identification. *Psychological Review,* 66*,* 278–296.

Bozeat, S., Lambon Ralph, M. A., Patterson, K., Garrard, P., & Hodges, J. R. (2000). Non-verbal semantic impairment in semantic dementia. *Neuropsychologia*, 38, 1207-1215.

Braak, H. & Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta neurophatologica*, 82, 239-259.

Bradley, M.M., & Lang, P.J. (1999). Affective norms for English words (ANEW): Stimuli, instruction manual and affective ratings. Technical report C-1, Gainesville, FL. The Center for Research in Psychophysiology, University of Florida.

Brambati, S. M., Myers, D., Wilson, A., Rankin, K. P., Allison, S. C., Rosen, H. J., et al. (2006). The anatomy of category-specific object naming in neurodegenerative diseases. *Journal of Cognitive Neuroscience*, 18, 1644–1653.

Breedin, S.D., Saffran, E.M., Coslett, H.B. (1994). Reversal of the concreteness effect in a patient with semantic dementia. *Cognitive neuropsychology*, 11 (6), 617- 660.

Bright, P., Moss, H. E., Stamatakis, E. A., & Tyler, L. K. (2005). The anatomy of object processing: the role of anteromedial temporal cortex. *Quarterly Journal of Experimental Psychology B,* 58(3-4), 361-377.

Brousseau, G., Buchanan, L. (2004). Semantic category effect and emotional valence in female university students. *Brain and Language*, 90, 241-248.

Bub, D., Masson, M.E.J., Cree, G.S. (2008). Evocation of functional and volumetric gestural knowledge by objects and words. *Cognition*, 106, 27-58.

Bucks, R. S., & Radford, S. A. (2004). Emotion processing in Alzheimer's disease. *Aging & Mental Health,* 8(3), 222-232.

Burgess, C., & Lund, K. (1997). Modeling parsing constraints with high dimensional context space. *Language and Cognitive Processes,* 12, 177–210.

Buxbaum, L.J., Johnson-Frey, S.H., Bartlett-Williams, M. (2005). Deficient internal models for planning hand-object interactions in apraxia. *Neuropsychologia* 43, 917–929.

Buxbaum, L.J., Saffran, E.M. (2002). Knowledge of object manipulation and object function: dissociations in apraxic and nonapraxic subjects. *Brain Lang*, 82, 179–199.

Buxbaum, L.J., Sirigu, A., Schwartz, M.F., Klatzky, R. (2003). Cognitive representations of hand posture in ideomotor apraxia. *Neuropsychologia,* 41, 1091–1113.

Canessa, N., Borgo, F., Cappa, S.F., Perani, D., Falini, A., Buccino, G., et al. (2008). The different neural correlates of action and functional knowledge in semantic memory: An fMRI study. *Cerebral Cortex*, 18,740–751.

Capitani, E. (1987). Statistical methods. In H. Spinnler & G. Tognoni (Eds.), standardizzazione e taratura italiana di test neuropsicolpogici. *Italian journal of neurological sciences*, 6 (Suppl.8).

Capitani, E., & Laiacona, M. (2005). An illusory illusion?. *Cortex,* 41(6), 854-855; discussion 869-872.

Capitani, E., & Laiacona, M. (2010). Facts and hypotheses relevant for contrasting animal and plant life semantics. A comment to Gainotti. *Cortex*.

Capitani, E., Laiacona, M., Mahon, B.Z., Caramazza, A. (2003). What are the facts of semantic category-specific deficits?. A critical review of the clinical evidence. *Cognitive Neuropsychology*, 20, 213-261.

Capitani, E., Laiacona, M., Pagani, R., Capasso, R., Zampetti, P., & Miceli, G. (2009). Posterior cerebral artery infarcts and semantic category dissociations: a study of 28 patients. *Brain,* 132(Pt 4), 965-981.

Cappa, S. F., Frugoni, M., Pasquali, P., Perani, D., & Zorat, F. (1998a). Category-specific naming impairment for artifacts: A new case. *Neurocase,* 4, 391–397.

Cappa, S. F., Perani, D., Schnur, T., Tettamanti, M., & Fazio, F. (1998b). The effects of semantic category and knowledge type on lexical–semantic access: A PET study. *NeuroImage,* 8, 350–359.

Caramazza A, Hillis AE, Rapp BC, Romani C. (1990). The multiple semantics hypothesis: multiple confusions? *Cognitive Neuropsychology*, 7: 161-189.

Caramazza, A., & Mahon, B. Z. (2003). The organization of conceptual knowledge: the evidence from category-specific semantic deficits. *Trends in Cognitive Sciences,* 7(8), 354-361.

Chan, A. S., Salmon, D. P., & De La Pena, J. (2001). Abnormal semantic network for “animals” but not “tools” in patients with Alzheimer’s disease. *Cortex*, 37(2), 197–217.

Chan, A. S., Salmon, D. P., Butters, N.,& Johnson, S.A. (1995). Semantic network abnormality predicts rate of cognitive decline in patients with probable Alzheimer’s disease. *Journal of the International Neuropsychological Society*, 1(3), 297–303.

Chan, A., S., Butters, N., Salmon, D. P., & McGuire, K.A. (1993). Dimensionality and clustering in the semantic network of patients with Alzheimer’s disease. *Psychology and Aging*, 8(3), 411–419.

Chan, A., Salmon, D., Nordin, S., Murphy, C., & Razani, J. (1998). Abnormality of semantic network in patients with Alzheimer’s disease. Evidence from verbal, perceptual, and olfactory domains. *Annals of New York Academy of Science*, 855, 681–685.

Chao L. L, Haxby JV, Martin A. (1999). Attribute-based neural substrates in temporal cortex for perceiving and knowing about objects. *Nature Neuroscience*, 2, 913-919.

Chao, L. L., & Martin, A. (1999). Cortical regions associated with perceiving, naming, and knowing about colors. *Journal of Cognitive Neuroscience*, 11, 25–35.
Chao, L. L., Weisberg, J., & Martin, A. (2002). Experience-dependent modulation of category-related cortical activity. *Cerebral Cortex,* 12(5), 545-551.

Chao, L.L., Martin, A. (2000). Representation of manipulable manmade objects in the dorsal stream. *NeuroImage*, 12, 478–484.

Chenery, H. J., Murdoch, B. E., & Ingram, J. C. L. (1996). An investigation of confrontation naming performance in Alzheimer's dementia as a function of disease severity. *Aphasiology,* 10, 423–441.

Chertkow, H., & Bub, D. (1990a). Semantic memory loss in dementia of Alzheimer's type. What do various measures measure?. *Brain,* 113 (Pt2*)*, 397-417.

Chertkow, H., & Bub, D., Schwartz, M. (1990b) Semantic memory loss in Alzheimer-type dementia. in M.F. Schwartz (ed), *Modular deficits in Alzheimer-type dementia* (pp. 207-244). Cambridge, MA, MIT Press.

Chertkow, H., Bub, D., & Caplan, D. (1992). Constraining theories of semantic memory processing: Evidence from dementia. *Cognitive Neuropsychology*, 9, 327–365.

Chertkow, H., Bub, D., & Seidemberg, M. (1989). Priming and semantic memory loss in Alzheimer's disease. *Brain and Language,* 36*,* 420–446.

Chertkow, H., Bub, D., Bergman, H., Bruemmer, A., Merling, A., & Rothfleisch, J. (1994). Increased semantic priming in patients with dementia of the Alzheimer's type. *Journal of Clinical and Experimental Neuropsychology,* 16(4), 608-622.

Chertkow, H., Whatmough, C., Saumier, D., Duong, A. (2008). Cognitive neuroscience studies of semantic memory in Alzheimer's disease. *Progress in Brain Research*, 169, 393-407.

Chouinard, P. A., & Goodale, M. A. (2010). Category-specific neural processing for naming pictures of animals and naming pictures of tools: an ALE meta-analysis. *Neuropsychologia,* 48(2), 409-418.

Cipolotti, L., & Warrington, E. K. (1995). Semantic memory and reading abilities: A case report. *Journal of the International Neuropsychological Society*, 1, 104–110.

Collignon, A., Maes, F., Delaere, D., Vandermeulen, D., Suetens, P., & Marchal, G., (1995). "Automated multimodality image registration based on information theory," In Y. Bizais, C. Barillot, and R. Di Paola, (Eds.). *Information Processing in Medical Imaging*, Netherlands, Kluwer, (pp. 263-274).

Collins, A. M., & Quillian, M. R.. (1972). Experiments on semantic memory and language comprehension. In L. W. Gregg (Ed.), *Cognition in learning and memory* (pp. 117-137). NY: Wiley.

Collins, A.M., & Loftus, E.F. (1975). A spreading-activation theory of semantic processing. *Psychological Review,* 82, 407-428.

Collins, A.M., & Quillian, M.R. (1969). Retrieval time from semantic memory. *Journal of Learning and Verbal Behavior*, 8, 240-247.

Coltheart, M., Patterson, K., & Marshall, J. C. (1980). *Deep dyslexia.* London: Routledge and Kegan Paul.

Cree, G. S., McNorgan, C., & McRae, K. (2006). Distinctive features hold a privileged status in the computation of word meaning: Implications for theories of semantic memory. *Journal of Experimental Psychology Learning Memory and Cognition,* 32(4), 643-658.

Cree, G.S., McRae, K. (2003). Analyzing the Factors Underlying the Structure and Computation of the Meaning of Chipmunk, Cherry, Chisel, Cheese, and Cello (and Many Other Such Concrete Nouns). *Journal of Experimental Psychology*, 132(2), 163-201.

Cronin-Golomb, A., Keane, M. M., Kokodis, A., Corkin, S., & Growdon, J. H. (1992). Category knowledge in Alzheimer's disease: normal organization and a general retrieval deficit. *Psychology and Aging,* 7(3), 359-366.

Crutch, S.J. & Warrington, E.K. (2003). Preservation of propositional speech in a pure anomic: the importance of an abstract vocabulary. *Neurocase,* 9, 465-481.

Crutch, S.J. & Warrington, E.K. (2006). Partial knowledge of abstract words in patients with cortical degenerative conditions. *Neuropsychology*, 20 (4), 482-489.

Crutch, S.J. & Warrington, E.K. (2007). Semantic priming in deep-phonological dyslexia: contrasting effects of association and similarity upon abstract and concrete word reading. *Cognitive neuropsychology*, 24 (6), 1-20.

Crutch, S.J., & Warrington, E.K. (2004). Abstract words are represented in an associative network whilst concrete words are represented in a categorical network. *Brain and language,* 91, 13-14.

Crutch, S.J., & Warrington, E.K. (2005). Abstract and concrete concepts have structurally different representational frameworks. *Brain,* 128, 615-627.

Crutch, S.J., Ridha, B.H., Warrington, E.K. (2006). The different frameworks underlying abstract and concrete knowledge: evidence from a bilingual patient with a semantic refractory access dysphasia. *Neurocase*, 12 (3), 151-163.

Crystal, D. (1995). *The Cambridge encyclopedia of the English language*. Cambridge: Cambridge University Press.

Cuetos, F., Gonzalez-Nosti, M., &Martinez, C. (2005). The picture-naming task in the analysis of cognitive deterioration in Alzheimer's disease. *Aphasiology*, 19, 545–557.

Cuetos, F., Martinez, T., Martinez, C., Izura, C., & Ellis, A. W. (2003). Lexical processing in Spanish patients with probable Alzheimer's disease. *Cognitive Brain Research,* 17(3), 549-561.

Cuetos, F., Rosci, C., Laiacona, M., & Capitani, E. (2008). Different variables predict anomia in different subjects: A longitudinal study of two Alzheimer's patients. *Neuropsychologia*, 46, 249–260.

Culham, J.C., Brandt, S.A., Cavanagh, P., Kanwisher, N.G., Dale, A.M., Tootell, R.B. (1998). Cortical fMRI activation produced by attentive tracking of moving targets. *Journal of Neurophysiology,* 80, 2657–2670.

Culham, J.C., Danckert, S.L., DeSouza, J.F., Gati, J.S., Menon, R.S., Goodale, M.A. (2003). Visually guided grasping produces fMRI activation in dorsal but not ventral stream brain areas. *Experimental Brain Research*, 153, 180–189.

Damasio, A. R. (1989).The brain binds entities and events by multiregional activation from convergence zones. *Neural Computation*, 1, 123–132.

Damasio, H., Grabowski, T., Tranel, D., Hichwa, R., and Damasio, A. (1996). A neural basis for lexical retrieval. *Nature,* 380, 499–505.

Damasio, H., Tranel, D., Grabowski, T., Adolphs, R., Damasio, A. (2004). Neural systems behind word and concept retrieval. *Cognition,* 92, 179–229.

Damian M.F., Vigliocco G. , Levelt W.J.M. (2001). Effects of semantic context in the naming of pictures and words. *Cognition*, 81: B77- B86.

Daum, I., Riesch, G., Sartori, G., & Birbaumer, N. (1996). Semantic memory impairment in Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology,* 18(5), 648-665.

de Groot, A.M.B. (1989). Representational aspects of word imageability and word frequency as assessed trough word association. *Journal of experimentalpsychology: learning, memory and cognition*, 15, 824-845.

De Houwer, J., Hermans, D., Rothermund, K., &Wentura, D. (2002). Affective primingof semantic categorization responses. *Cognition and Emotion*, 16, 643–666.

De Mauro, T. *Il dizionario della lingua italiana* (2000), Torino, Paravia

Dell'Acqua, R., Lotto, L., Job, R. (2000). Naming times and standardized norms for the Italian PD/DPSS set of 266 pictures: direct comparisons with American, English, French and Spanish published databases. *Behavior Research Methods, Instruments & Computers*, 32, 588-615.

Della Rosa, P.A., Catricalà E., Vigliocco G., Cappa S.F., (2010). Beyond the abstract-concrete dichotomy: Mode of Acquisition, Concreteness, Imageability, Familiarity, Age of Acquistion, Context Availability and Abstractness norms for a set of 417 Italian words. *Behaviour Research Methods*, 42(4), 1042-10488.

Devlin JT, Russel RP, Davis MH, Price CJ, Wilson J, Moss HE, Matthews PM, Tyler LK. (2000). Susceptibility-induced loss of signal : comparing PET an fMRI on a semantic task. *Neuroimage*, 11: 589-600.

Devlin, J. T., Russell, R. P., Davis, M. H., Price, C. J., Moss, H. E., Fadili, M. J., & Tyler, L. K. (2002b). Is there an anatomical basis for category-specificity?. Semantic memory studies in pet and fMRI. *Neuropsychologia,* 40*,* 54–75.

Devlin, J.T., Gonnerman, L.M., Anderson, E.S., Seidenberg, M.S. (1998). Category-specific semantic deficits in focal and widespread brain damage: a computational account. *Journal of Cognitive Neuroscience*, 10, 77-94.

Devlin, J.T., Russell, R.P., Davis, M.H., Price, C.J., Moss, H.E., Fadili, M.J. (2002a). Is there an anatomical basis for category-specificity?. Semantic memory studies in PET and fMRI. *Neuropsychologia,* 40, 54–75.

Dixon, M. J., Bub, D. N., Chertkow, H., & Arguin, M. (1999). Object identification deficits in dementia of the Alzheimer type: combined effects of semantic and visual proximity. *Journal of the International Neuropsychological Society,* 5(4), 330-345.

Done, D.J., & Gale, T.M. (1997). Attribute verification in dementia of Alzheimer type: evidence for the preservation of distributed concept knowledge. *Cognitive Neuropsychology*, 14(4), 547-571.

Downing, P. E., Chan, A. W., Peelen, M. V., Dodds, C. M., & Kanwisher, N. (2006). Domain specificity in visual cortex. *Cerebral Cortex,* 16(10), 1453-1461.

Duarte, L.R., Marquié, L., Marquié, J.C., Terrier, P., Ousset, P.J. (2009). Analyzing feature distinctiveness in the processing of living and non-living concepts in Alzheimer's disease. *Brain and Cognition*, 71, 108-117.

Duong, A., Whitehead, V., Hanratty, K. and Chertkow, H. (2006) The nature of lexico-semantic processing deficits in mild cognitive impairment. *Neuropsychologia*, 44(10), 1928–1935.

Emmorey, K., Grabowski, T., McCullough, S., Damasio, H., Ponto, L., Hichwa, R., et al. (2004). Motor-iconicity of sign language does not alter the neural systems underlying tool and action naming. *Brain Lang*, 89, 27–37.

Farah, M. J., & McClelland, J. L. (1991). A computational model of semantic memory impairment: modality specificity and emergent category specificity. *Journal of Experimental Psychology: General, 120*(4), 339-357.

Fazio, R. H., Sanbonmatsu, D. M., Powell, M. C., & Kardes, F. R. (1986). On the automatic activation of attitudes. *Journal of Personality and Social Psychology*, 50, 229–238.

Ferrand, L., Ric, F., & Augustinova, M. (2006). Quand "Amour" amorce "Soleil" (ou pourquoi l'amorc¸ age affectif n'est pas un (simple) cas d'amorc¸ age sémantique) [Affective priming: A case of semantic priming?]. *L'Année Psychologique*, 106, 79–104.

Filliter, J.H., McMullen, P.A., Westwood D. (2005). Manipulability and living/non-living category effects on object identification. *Brain and Cognition*, 57, 61-65.

Fodor, J. A., Garrett, M.F., Walker, E.C.T. & Parkes, C.H. (1980). Against definitions. *Cognition*, 8, 263-367.

Folstein, M., Folstein S., Mchugh P.R. (1975). Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, 12, 189–198.

Forbes-McKay, K. E., Ellis, A. W., Shanks, M. F., & Venneri, A. (2005). The age of acquisition of words produced in a semantic fluency task is highly predictive of early Alzheimer's disease. *Neuropsychologia*, 43, 1625–1632.

Franklin, S., Howard, D., & Patterson, K. (1994). Abstract word meaning deafness. *Cognitive Neuropsychology*, 11, 1–34.

Franklin, S., Howard, D., & Patterson, K. (1995). Abstract word anomia. *Cognitive Neuropsychology*, 12, 549–566.

Frey, S.H., Vinton, D., Norlund, R., Grafton, S.T. (2005). Cortical topography of human anterior intraparietal cortex active during visually guided grasping. *Cognitive Brain Research*; 23, 397–405.

Fung, T. D., Chertkow, H., & Templeman, F. D. (2000). Pattern of semantic memory impairment in dementia of Alzheimer's type. *Brain and Cognition*, 43(1–3), 200–205.

Fung, T.D., Chertkow, H., Murtha, S., Whatmough, C., Peloquin, L., Whitehead, V., et al. (2001). The spectrum of category effects in object and action knowledge in Alzheimer's disease. *Neuropsychology*, 15, 371-379.

Funnel, E., & Sheridan, J. (1992). Categories of knowledge? Unfamiliar aspects of living and non living things. *Cognitive Neuropsychology*, 9, 135-153.

Funnell, E., & De Mornay Davies, P. (1996). JBR: A reassessment of concept familiarity and a category-specific disorder for living things. *Neurocase*, 2, 461–474.

Gainotti, G. (2000). What the locus of brain lesion tells us about the nature of the cognitive defect underlying category-specific disorders: a review. *Cortex,* 36(4), 539-559.

Gainotti, G. (2004). A metanalysis of impaired and spared naming for different categories of knowledge in patients with a visuo-verbal disconnection. *Neuropsychologia*, 42, 299–319.

Gainotti, G. (2005). The influence of gender and lesion location on naming disorders for animals, plants and artefacts. *Neuropsychologia,* 43(11), 1633-1644.

Gale, T. M., Irvine, K., Laws, K. R., & Ferrissey, S. (2009). The naming profile in Alzheimer patients parallels that of elderly controls. *Journal of Clinical and Experimental Neuropsychology,* 31(5), 565-574.

Gallese, V., & Lakoff, G. (2005). The brain's concept: the role of the sensorimotor system in conceptual knowledge. *Cognitive Neuropsychology, 21*, 455-479.

Gamboz, N., Cosuccia, E., Iavarone, A., Brandimonte, M. A., (2009). Normative data for the Pyramids and Palm Trees Test in the elderly Italian population. *Neurological Science*, 30, 453–458.

Garrard, P., Lambon Ralph, M. A., Watson, P., Powis, J., Patterson, K., & Hodges, J. R. (2001b). Longitudinal profiles of semantic impairment for living and nonliving concepts in dementia of Alzheimer's type. *Journal of Cognitive Neuroscience*, 13, 892–909.

Garrard, P., Lambon Ralph, M.A., Hodges, J.R., Patterson, K. (2001a). Prototypicality, distinctiveness and intercorrelation: analyses of the semantic attributes of living and nonliving concepts. *Cognitive Neuropsychology*, 18, 125-174.

Garrard, P., Lambon Ralph, M.A., Patterson, K., Pratt, K.H., Hodges, J.H. (2005). Semantic feature knowledge and picture naming in dementia of Alzheimer's type: a new approach. *Brain and Language*, 93, 79-94.

Garrard, P., Patterson, K., Watson, P. C., & Hodges, J. R. (1998). Category specific semantic loss in dementia of Alzheimer's type. Functional-anatomical correlations from cross-sectional analyses. *Brain,* 121(Pt 4), 633-646.

Garrard, P., R. Perry, & Hodges, J. R. (1997). Disorders of semantic memory. *Journal of Neurology, Neurosurgery, and Psychiatry,* 62(5), 431-435.

Garzanti, *Garzanti Italiano*, Varese, Garzanti (con CD-ROM), 2006.

Gerlach, C. (2007). A review of functional imaging studies on category specificity. *Journal of Cognitive Neuroscience,* 19(2), 296-314.

Gerlach, C., Law, I., & Paulson, O.B. (2002). When action turns into words. Activation of motor-based knowledge during categorization of manipulable objects. *Journal of Cognitive Neuroscience*, 14, 1230–1239.

Gerlach, C., Law, I., Gade, A., and Paulson, O. B. (2000). Categorization and category effects in normal object recognition—A PETstudy. *Neuropsychologia,* 38, 1693–1703.

Gibbs R. W. (2006). Embodiment and Cognitive Science. New York: Cambridge Univ. Press.

Gibbs, R. W. (1994). *The poetics of mind: Figurative thought, language, and understanding*. New York: Cambridge University Press.

Giffard, B., Desgranges, B., Nore-Mary, F., Lalevee, C., Beaunieux, H., de la Sayette, V., Pasquier, F., & Eustache F. (2002). The dynamic time course of semantic memory impairment in Alzheimer's disease: clues from hyperpriming and hypopriming effects. *Brain*, 125, 2044–2057.

Giffard, B., Desgranges, B., Nore-Mary, F., Lalevée, C., da la Sayette, V., Pasquier, F., Eustache, F. (2001). The nature of semantic memory deficits in Alzheimer's disease. New insights from hyperpriming effects. *Brain*, 124, 1522-1532.

Giffard, B., Laisney, M., Eustache, F., & Desgranges, B. (2009). Can the emotional connotation of concepts modulate the lexico-semantic deficits in Alzheimer's disease?. *Neuropsychologia,* 47(1), 258-267.

Gleitman, L.R., Cassidy, K., Nappa, R., Papafragou, A., & Trueswell, J.C. (2005). Hard words. *Language Learning and Development*, 1, 23–64.

Goldenberg, G. (2009). Apraxia and the parietal lobes. *Neuropsychologia*, 47, 1449–1459.

Gonnerman, L. M., Andersen, E. S., Devlin, J. T., Kempler, D., & Seidenberg, M. S. (1997). Double dissociation of semantic categories in Alzheimer's disease. *Brain Lang,* 57(2), 254-279.

Gonnerman, L. M., Aronoff, J. M., Almor, A., Kempler, D., & Andersen, E. S. (2004). From Beetle to bug: Progression of error types in naming in Alzheimer's disease. In K. Forbus, D. Gentner, & T. Regier (Eds.), *Proceedings of the 26th Annual Conference of the Cognitive Science Society* (p. 1563).

Gonzalez, J., Barros-Loscertales, A., Pulvermueller, F., Meseguer, V., Sanjuan, A., Belloch, V., et al. (2006). Reading cinnamon activates olfactory brain regions. *Neuroimage*, 32, 906–912.

Goodale, M.A., Milner, D. (1992). Separate visual pathways for perception and action. Trends in *Neurosciences*, 15, 20–25.

Goodglass, H., Hyde, M. R., & Blumstein, S. (1969). Frequency, picturability and availability of nouns in aphasia. *Cortex, 5,* 104–119.

Graham, N. L., Emery, T., & Hodges, J. R. (2004). Distinctive cognitive profiles in Alzheimer's disease and subcortical vascular dementia. *Journal of Neurology, Neurosurgery & Psychiatry,* 75(1), 61-71.

Grossman, M., & Ash, S. (2004). Primary progressive aphasia: a review. *Neurocase,* 10(1), 3-18.

Hall, R.C.W., Levenson, A.J., LeCann, A.F. (1981). Evaluation and assessment of non-functional psychiatric illness in the elderly. In: Levenson AJ, Hall RCW, eds. *Neuropsychiatric Manifestations of Physical Disease in the Elderly*. New York: Raven Press, 133-149.

Hart J Jr, Berndt RS, Caramazza A. (1985). Category-specific naming deficit following cerebral infarction. *Nature,* 316:439–40.

Hauk O., Johnsrude I., Pulvermuller F. (2004). Somatotopic representation of action words in human motor and premotor cortex. *Neuron*, 41, p.301–7.

Heilman, K.M., Rothi, L.J., Valenstein, E. (1982). Two forms of ideomotor apraxia. *Neurology*, 32, 342–346.

Hermans, D., De Houwer, J., & Eelen, P. (1994). The affective priming effect: Automatic activation of evaluative information in memory. *Cognition and Emotion*, 8, 515–533.

Hermsdörfer, J., Terlinden, G., Mühlau, M., Goldenberg, G., Wohlschläger, A.M. (2007). Neural representations of pantomimed and actual tool use: Evidence from an event-related fMRI study. *NeuroImage*, 36, T109–T118.

Hillis, A.E., Caramazza, A. (1991). Category-specific naming and comprehension impairment: a double dissociation. *Brain*, 114, 2081-2094.

Hirsch, K. W., & Funnell, E. (1995). Those old, familiar things: Age of acquisition, familiarity and lexical frequency in progressive aphasia. *Journal of Neurolinguistics*, 9, 23–32.

Hodges, J. R. & Patterson, K. (2007). Semantic dementia: a unique clinicopathological syndrome. *The Lancet Neurology,* 6(11), 1004-14.

Hodges, J. R., & Patterson, K. (1995). Is semantic memory consistently impaired early in the course of Alzheimer's disease?. Neuroanatomical and diagnostic implications. *Neuropsychologia*, 33, 441-459.

Hodges, J. R., Patterson, K., Graham, N., & Dawson, K. (1996). Naming and knowing in dementia of Alzheimer's type. *Brain and Language,* 54(2), 302-325.

Hodges, J. R., Patterson, K., Ward, R., Garrard, P., Bak, T., Perry, R., & Gregory, C. (1999). The differentiation dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: A comparative neuropsychological study. *Neuropsychology*, 13, 31–40.

Hodges, J.R., Graham, N., Patterson, K. (1995). Charting the progression in semantic dementia: Implications for the organization of semantic memory. *Memory*, 3, 463-495.

Hodges, J.R., Salmon, D.P., Butters, N. (1992a). Semantic memory impairment in Alzheimer's disease: failure of access or degraded knowledge?. *Neuropsychologia*, 30, 301-314.

Hodges, JR., Patterson, K., Oxbury, S., Funnell, E. (1992b). Semantic dementia: Progressive fluent aphasia with temporal lobe atrophy. *Brain*, 115, 1783-1806.

Hornberger, M., Bell, B., Graham, K. S., & Rogers, T. T. (2009). Are judgments of semantic relatedness systematically impaired in Alzheimer's disease?. *Neuropsychologia,* 47(14), 3084-3094.

Howard, D., & Franklin, S. (1988). Missing the meaning?. Cambridge: MIT Press.

Howard, D., & Patterson, K. (1992). Pyramids and palm trees: A test of semantic access from pictures and words. Bury St. Edmunds, UK: Thames Valley Publishing.

Huff, F. J., Corkin, S., & Growdon, J. H. (1986). Semantic impairment and anomia in Alzheimer's disease. *Brain and Language,* 28(2), 235-249.

Humphreys, G. W., & Forde, E. M. E. (2001). Hierarchies, similarity, and interactivity in object recognition: "Category-specific" neuropsychological deficits. *Behavioural and Brain Sciences*, *24*, 453–509.

Humphreys, G. W., Riddoch, M. J., & Quinlan, P. T. (1988). Cascade processes in picture identification. *Cognitive Neuropsychology*, 5, 67–104.

James, C.T. (1975). The role of semantic information in lexical decisions. *Journal of experimental psychology*, 104, 130-136.

Jefferies, E., Baker, S. S., Doran, M., & Lambon Ralph, M. A. (2007). Refractory effects in stroke aphasia: A consequence of poor semantic control. *Neuropsychologia,* 45*,* 1065–1079.

Jefferies, E., Patterson, K., Jones, W.R., Lambon Ralph, M.A. (2009). Comprehension of concrete and abstract words in semantic dementia. *Neuropsychology*, 23 (4), 492-499.

Johnson-Frey, S.H. (2004).The neural basis of complex tool use in humans. *Trends in Cognitive Sciences*, 8, 71–78.

Joseph, JE. (2001). Functional neuroimaging studies of category specificity in object recognition: a critical review and meta-analysis. *Cognitive, Affective, & Behavioral Neuroscience,* 1(2), 119-136.

Joubert, S., Brambati, S. M., Ansado, J., Barbeau, E. J., Felician, O., Didic, M., et al. (2010). The cognitive and neural expression of semantic memory impairment in mild cognitive impairment and early Alzheimer's disease. *Neuropsychologia,* 48(4), 978-988.

Kaplan, E., Gooidglass, H., & Weintraub, S. (1983). *Boston Naming Test.* Philadelphia: Lea and Febiger.

Kellenbach, M.L., Brett, M., Patterson, K. (2003). Actions speak louder than functions: The importance of manipulability and action in tool representation. *Journal of Cognitive Neuroscience*, 15, 20–46.

Kensinger, E. A., Anderson, A., Growdon, J. H., & Corkin, S. (2004). Effects of Alzheimer disease on memory for verbal emotional information. *Neuropsychologia,* 42(6), 791-800.

Kieras, D. (1978). Beyond pictures and words: Alternative information processing models for imagery effects in verbal memory. *Psychological Bulletin*, 85, 532–55.

Kounios, J., & Holcomb, P. J. (1994). Concreteness effects in semantic processing: ERP evidence supporting dual-coding theory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 20(4), 804–823.

Kousta, S., Vigliocco,G., Vinson,D., Andrews, M. (2009). Happiness is… an abstract word: The role of affect in abstract knowledge representation. *Proceedings of the 31st Meeting of the Cognitive Science Society.*

Kousta, S-T., Vigliocco, G., Vinson, D.P., Andrews, M., & Del Campo, E. (in press). The represenation of abstract words: Why emotion matters.

Kroll, J. F., & Merves, J. S. (1986). Lexical access for concrete and abstract words. *Journal of Experimental Psychology: Learning, Memory and Cognition*, 12(1), 92–107.

Kunisue, K., Fukushima, K., Kawasaki, A., Maeda, Y., Nagayasu, R., Kataoka, Y., Kariya, S., Fukutomi, Y., Takami, H., Nishizaki, K. (2007). Comprehension of abstract words among hearing impaired children. *International journal of pediatric otorhinolaryngol*, 71(11), 1671-1679.

Laatu, S., Portin, R., Revonsuo, A., Tuisku, S., & Rinne, J. (1997). Knowledge of concept meanings in Alzheimer's disease. *Cortex*, 33, 27–45.

Laiacona M., Capitani E. (2001). A case of prevailing deficit of nonliving categories or a case of prevailing sparing of living categories? *Cognitive Neuropsychology*,; 18: 39-70.

Laiacona, M., Barbarotto, R., & Capitani, E. (1993a). Perceptual and associative knowledge in category specific impairment of semantic memory: a study of two cases. *Cortex, 29*(4), 727-740.

Laiacona, M., Barbarotto, R., & Capitani, E. (1998). Semantic category dissociations in naming: is there a gender effect in Alzheimer's disease?. *Neuropsychologia,* 36(5), 407-419.

Laiacona, M., Barbarotto, R., Trivelli C., Capitani, E. (1993b). Dissociazioni semantiche intercategoriali: descrizione di una batteria standardizzata e dati normativi. *Archivio di Psicologia, Neurologia e Psichiatria*, 2, 209-248.

Laiacona, M., Capitani, E., Barbarotto, R. (1997). Semantic category dissociations: a longitudinal study of two cases. *Cortex*, 33, 441-461.

Laisney, M., Giffard, B., Belliard, S., de la Sayette, V., Desgranges, B., Eustache F. (2011). When the zebra loses its stripes: Semantic priming in early Alzheimer's disease and semantic dementia. *Cortex*, 47(1):35-46.

Lakoff G. & Johnson M. (1980). *Metaphors we live by*. University of Chicago Press.

Lakoff, G., & Johnson, M. (1999). *Philosophy in the flesh: the Embodied mind and its challenge to western thought*. New York: Basic Books.

Lambon Ralph MA, Howard D, Nightingale G, Ellis AW. (1998). Are living and nonliving category-specific deficits causally linked to impaired perceptual or associative knowledge? Evidence from a category-specific double dissociation. *Neurocase*, 4: 311-338.

Lambon Ralph, M. A., Graham, K. S., Ellis, A. W., & Hodges, J. R. (1998). Naming in semantic dementia: What matters?. *Neuropsychologia*, 36, 775–784.

Lambon Ralph, M. A., Patterson, K., & Hodges, J. R. (1997). The relationship between naming and semantic knowledge for different categories in dementia of Alzheimer's type. *Neuropsychologia*, 35(9), 1251–1260.

Lambon Ralph, M.A., Sage, K., Jones, R.W., Mayberry, E.J. (2010). Coherent concepts are computed in the anterior temporal lobes. *Proceedings of the National Academy of Sciences of the United States of America*, 107, 2717–2722.

Landauer, T., & Dumais, S. (1997). A solution to Plato's problem: The latent semantic analysis theory of acquisition, induction, and representation of knowledge. *Psychological Review*, 104, 211–240.

Laws, K. R. (2005). Illusions of normality: A methodological critique of category-specific naming. *Cortex*, 41, 842–851.

Laws, K. R. and G. Sartori (2005). Category deficits and paradoxical dissociations in Alzheimer's disease and Herpes Simplex Encephalitis. *Journal Cognitive Neuroscience,* 17(9), 1453-1459.

Laws, K. R., Adlington, R. L., Gale, T. M., Moreno-Martinez, F. J., & Sartori, G. (2007). A meta-analytic review of category naming in Alzheimer's disease. *Neuropsychologia,* 45(12), 2674-2682.

Laws, K. R., Gale, T. M., Leeson, V. C., & Crawford, J. R. (2005). When is category specific in Alzheimer's disease?. *Cortex,* 41(4), 452-463.

Laws, K.R. (2000).Category-specific naming errors in normal subjects: The influence of evolution and experience. *Brain and Language*, 75*,* 123-133,

Laws, K.R., & Gale, T.M. (2002).Category-specific naming and the 'visual' characteristics of line drawn stimuli. *Cortex*, 38, 7-21.

Laws, K.R., & Neve, C. (1999). A 'normal' category-specific advantage for naming living things. *Neuropsychologia,* 37, 1263-1269.

Laws,K.R., Leeson, V.C., Gale, T.M. (2003). Inflated and contradictory category naming deficits in Alzheimer's disease? *Brain and Cognition*, 5, 232-234.

LeDoux, J. (1992). *The Emotional Brain*. New York: Simon & Schuster.

Lewis, J.W. (2006). Cortical Networks Related to Human Use of Tools. *Neuroscientist*,12, 211–231.

Lewis, P.A., Critchley, H.D., Rotshtein, P. & Dolan, R.J. (2007). Neural correlates of processing valence and arousal in affective words. *Cerebral Cortex*, 17, 742-748.

Loiselle M., Macoir J., Felician O., Poncet M., Ceccaldi M., Joubert S. (2007). La compréhension des concepts abstraits est-elle mieux préservée que celle des concepts concrets dans la démence sémantique? *Paper presented at the XXIXe Symposium international du Groupe de recherche sur le système nerveux central.* L'essence de la mémoire, Montréal.

Macoir, J. (2009). Is a plum a memory problem? Longitudinal study of the reversal of concreteness effect in a patient with semantic dementia. *Neuropsychologia*, 47, 518-535.

Mahon, B. Z., & Caramazza, A. (2005). The orchestration of the sensory-motor systems: Clues from Neuropsychology. *Cognitive Neuropsychology, 22*(3), 480-494.

Mahon, B. Z., & Caramazza, A. (2008). A critical look at the embodied cognition hypothesis and a new proposal for grounding conceptual content. *J Physiol Paris, 102*(1-3), 59-70.

Mahon, B. Z., & Caramazza, A. (2009). Concepts and categories: a cognitive neuropsychological perspective. *Annual Review of Psychology,* 60, 27-51.

Mahon, B. Z., Anzellotti, S., Schwarzbach, J., Zampini, M., & Caramazza, A. (2009). Category-specific organization in the human brain does not require visual experience. *Neuron,* 63(3), 397-405.

Mahon, B. Z., Milleville, S. C., Negri, G. A., Rumiati, R. I., Caramazza, A., & Martin, A. (2007). Action-related properties shape object representations in the ventral stream. *Neuron,* 55(3), 507-520.

Mandler, J. M. (1992). How to build a baby: II. Conceptual primitives. *Psychological Review, 99*(4), 587-604.

Marczinski, C. A., & Kertesz, A. (2006). Category and letter fluency in semantic dementia, primary progressive aphasia, and Alzheimer's disease. *Brain Lang,* 97(3), 258-265.

Marques, J. F., Canessa, N., Siri, S., Catricala, E., & Cappa, S. (2008). Conceptual knowledge in the brain: fMRI evidence for a featural organization. *Brain Research, 1194*, 90-99.

Marques, J. F., Cappa, S. F., & Sartori, G.(2010) Naming from definition, semantic relevance and feature type: The effects of aging and alzheimer's disease. *Neuropsychology*, Oct 4.

Marques, J.,F. (2005). Naming from definition: The role of feature type and feature distinctiveness. Quarterly. *Journal of Experimental Psychology*, 58A, 603–611.

Marshall, J., Pring, T., Chiat, S., & Robson, J. (1996). Calling a salad a federation: An investigation of semantic jargon. Part 1. Nouns. *Journal of Neurolinguistics*, 9, 237–250.

Marshall, J., Pring, T., Chiat, S.,& Robson, J. (2001).Whenottomanis easier than chair: An inverse frequency effect in jargon aphasia. *Cortex*, 37(1), 33–53.

Martin A. Ungerleider LG, Haxby JV. (2000). Category specificity and the brain: the sensory/motor model of semantic representations of objects. In *Higher Cognitive Functions: The New Cognitive Neurosciences*, ed. MS Gazzaniga, pp. 1023–36. Cambridge, MA: MIT Press.

Martin, A. (1992). Semantic knowledge in patients with Alzheimer's disease: evidence for degraded representations. In: L. Backman (Ed.), *Memory functioning in dementia*. Amsterdam: Elsevier Science.

Martin, A. (2007). The representation of object concepts in the brain. *Annual Review of Psychology,* 58, 25-45.

Martin, A., & Fedio, P. (1983). Word production and comprehension in Alzheimer's disease: the breakdown of semantic knowledge. *Brain and Language*, 19, 124-141.

Martin, A., Haxby, J.V., Lalonde, F., Wiggs, C.L., Ungerleider, L.G. (1995). Discrete cortical regions associated with knowledge of color and knowledge of action. *Science*, 270, 102–105.

Martin, A., Wiggs, C.L., Ungerleider, L.G., Haxby, J.V. (1996). Neural correlates of categoryspecific knowledge. *Nature*, 379(6566), 649-6452.

Martinaud, O., Opolczynski, G., Gaillard, M. J., & Hannequin, D. (2009). Relevant category-specific effect on naming in Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders,* 28(5), 413-418.

Masson, M.E., Bub, D.N., Newton-Taylor, M. (2008). Language-based access to gestural components of conceptual knowledge. *Quarterly Journal of Experimental Psychology*, 61(6), 869-882.

Masson, M.E.J. (1995). A distributed memory model of semantic priming. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, 21, 3–23.

Mauri, A., Daum, I., Sartori, G., Riesch, G., & Birbaumer, N. (1994). Category-specific semantic impairment in Alzheimer's disease and temporal lobe dysfunction: a comparative study. *Journal of Clinical and Experimental Neuropsychology,* 16(5), 689-701.

McCarthy, R.A., Warrington, E.K., (1991). Cognitive Neuropsychology: A Clinical Introduction. *Academic Press*, New York.

McKenna, P., Warrington, E.K. Graded naming test Manual, *NFER-Nelson*, (1983).

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan EM. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of department of health and human services task force on Alzheimer's disease. *Neurology*; 34, 939–944.

McRae, K., & Cree, G.S. (2002). Factors underlying category-specific semantic deficits. In E. M. E. Forde and G. W. Humphreys (Eds.), *Category-Specificity in Brain and Mind*. (pp. 211-249). East Sussex, UK: Psychology Press.

McRae, K., Cree, G. S., Seidenberg, M. S., & McNorgan, C. (2005). Semantic feature production norms for a large set of living and nonliving things. *Behavior Research Methods,* 37(4), 547-559.

McRae, K., de Sa, V. R., & Seidenberg, M. S. (1993). Modeling property intercorrelations in conceptual memory. *In Proceedings of the 15th Annual Meeting of the Cognitive Science Society* (pp. 729–734). Hillsdale, New York: Erlbaum.

McRae, K., de Sa, V.R., Seidenberg, M.S. (1997). On the nature and scope of featural representations of word meaning. *Journal of Experimental Psycholology: General*, 126, 99-130.

McRae, K., Jared, D., & Seidenberg, M. S. (1990). On the roles of frequency and lexical access in word naming. *Journal of Memory and Language*, 29, 43-65.

Mechelli, A., Sartori, G., Orlandi, P., & Price, C. J. (2006). Semantic relevance explains category effects in medial fusiform gyri. *Neuroimage,* 30(3), 992-1002.

Miceli, G., Benvenista, M., Zannino, G.D., Capasso, R., (2000). Valori normativi di astrattezze/concretezza di 500 parole italiane. *Nuova Rivista di Neurologia*, 10(4), 143-158.

Miceli, G., Fouch, E., Capasso, R., Shelton, J. R., Tomaiuolo, F., & Caramazza, A. (2001). The dissociation of color from form and function knowledge. *Nature Neuroscience,* 4(6), 662-667.

Miller, E., Abnormal Aging, (1977*). John Wiley and Sons,* London.

Miller, G. A., & Johnson-Laird, P. N., (1976). *Language and Perception*. Cambridge, Mass. : Belknap Press of Harvard University Press.

Miller, G.A. (1995). WordNet: A Lexical Database for English. *Communications of the ACM*, 38(11), 39-41. Available at: http://wordnet.princeton.edu

Miller*,* G.A., & Johnson-Laird*,* P. N. (1976). In G.A. Miller, P.N. Johnson-Laird (Eds). *Language and perception*. Belknap Press of Harvard University Press

Mirman, D., & Magnuson, J. S. (2009). The effect of frequency of shared features on judgments of semantic similarity. *Psychonomic Bulletin & Review,* 16(4), 671-677.

Mizuno, K., Wakai, M., Takeda, A., & Sobue, G. (2000). Medial temporal atrophy and memory impairment in early stage of Alzheimer's disease: an MRI volumetric and memory assessment study. *Journal of the Neurological Sciences,* 173(1), 18-24.

Montanes, P., Goldblum, M. C., & Boller, F. (1995). The naming impairment of living and nonliving items in Alzheimer's disease. *Journal of the International Neuropsychological Society,* 1(1), 39-48.

Montanes, P., Goldblum, M. C., & Boller, F. (1996). Classification deficits in Alzheimer's disease with special reference to living and nonliving things. *Brain Lang*, 54(2), 335-358.

Moore ,C.J., & Price, C.J. (1999). A functional neuroimaging study of the variables that generate category-specific object processing differences. *Brain*, 122, 943-962.

Moreno, F.J., Peraita, H. (2005). A new set of items for evaluation of living/non living dissociation with norms collected from healthy elderly Spanish. *Journal of the International Neuropsychological Society*.

Moreno-Martinez, F. J., & Laws, K. R. (2007). An attenuation of the ‘normal’ category effect in patients with Alzheimer’s disease: A review and bootstrap analysis. *Brain and Cognition*, 63, 136–142.

Moreno-Martinez, F. J., & Laws, K. R. (2008). No category specificity in Alzheimer's disease: a normal aging effect. *Neuropsychology,* 22(4), 485-490.

Morris, R. G. (1996). *The Cognitive Neuropsychology of Alzheimer-type dementia.* Oxford University Press.

Moss, H. E., & Tyler, L. K. (2000). A progressive category-specific semantic deficit for non-living things. *Neuropsychologia,* 38(1), 60-82.

Moss, H. E., Rodd, J. M., Stamatakis, E. A., Bright, P., & Tyler, L. K. (2005). Anteromedial temporal cortex supports fine-grained differentiation among objects. *Cerebral Cortex,* 15(5), 616-627.

Moss, H. E., Tyler, L. K., & Devlin, J. T. (2002) The emergence of category-specific deficits in a distributed semantic system. In Forde & Humphreys (Eds.). *Category-specificity in mind and brain.* East Sussex, UK: Psychology Press.

Moss, H. E., Tyler, L. K., Durrant-Peatfield, M., & Bunn, E. M. (1998). Two eyes of a see-through: Impaired and intact semantic knowledge in a case of selective deficit for living things. *Neurocase*, 4, 339–352.

Mummery, C. J., Patterson, K., Hodges, J. R., and Price, C. J. (1998). Functional neuroanatomy of the semantic system: Divisible by what?. *Journal of Cognitive Neuroscience.* 10, 766–777.

Mummery, C. J., Patterson, K., Hodges, J., and Wise, R. J. (1996). Generating 'tiger' as an animal name or a word beginning with T: Differences in brain activation. *Proceedings of the Royal Society B: Biological Sciences,* 263, 989–995.

Murphy, S. T., & Zajonc, R. B. (1993). Affect, cognition, and awareness: affective priming with optimal and suboptimal stimulus exposures. *Journal of personality and social psychology,* 64(5), 723-739.

Nebes, R. D. (1992). Semantic memory dysfunction in Alzheimer's disease: Disruption of semantic knowledge or information-processing limitation?. In L.R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (2nd ed., pp. 233-240). New York: The Guilford Press.

Nebes, R. D., & Brady, C. B. (1988). Integrity of semantic fields in Alzheimer's disease. *Cortex*, 24(2), 291–299.

Nebes, R. D., Brady, C. B., & Huff, F. J. (1989). Automatic and attentional mechanisms of semantic priming in Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology,* 11, 219-230.

Nebes, R.D. (1989). Semantic memory in Alzheimer's disease. *Psychological Bulletin*, 106, 377 394.

Novelli, G., Papagno, C., Capitani, E., Laiacona, M., Vallar, G., Cappa, S.F. (1986a). Tre test clinici di ricerca e produzione lessicale: taratura su soggetti normali. *Archivio italiano di Neurologia, Psicologia e Psichiatria*, 47, 477-503.

Ober, B. A. (2002). RT and non-RT methodology for semantic priming research with Alzheimer's disease patients: a critical review. *Journal of Clinical and Experimental Neuropsychology,* 24(7), 883-911.

Ober, B. A., & Shenaut, G. K. (1988). Lexical decision and priming in Alzheimer's disease. *Neuropsychologia,* 26(2), 273-286.

Ober, B. A., & Shenaut, G. K. (1995). Semantic priming in Alzheimer's disease: Meta-analysis and theoretical evaluation. In E Allen & T. R. Bashore (Eds.), *Age differences in word and language processing* (pp. 247-271). Amsterdam: Elsevier.

Ober, B. A., & Shenaut, G. K. (1999). Well-organized conceptual domains in Alzheimer's disease. *Journal of the International Neuropsychological Society*, 5(7), 676–684.

Okada, T., Tanaka, S., Nakai, T., Nishizawa, S., Inui, T., Sadato, N., et al. (2000). Naming of animals and tools: a functional magnetic resonance imaging study of categorical differences in the human brain areas commonly used for naming visually presented objects. *Neuroscience Letters,* 296(1), 33-36.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia,* 9(1), 97-113.

Paganelli, F., Vigliocco, G., Vinson, D., Siri, S., & Cappa, S. (2003). An investigation of semantic errors in unimpaired and Alzheimer's speakers of Italian. *Cortex*, 39, 419–439.

Paivio ,A. U., Yuille J.C., Madigan, S.A. (1968). Concreteness, imagery and meanigfulness values for 925 nouns. *Journal of experimental psychology monographs,* 76, (1, pt. 2).

Paivio, A. (1971). Imagery and verbal processes. New York: Holt, Rinehart & Winston.

Paivio, A. (1986). Mental representation: a dual coding approach. New York: Oxford University Press.

Paivio, A. (1991). Dual coding theory: retrospect and current status. *Canadian journal of psychology*, 45, 255-287.

Papagno ,C., Capasso, R., Zerboni, H., Miceli, G. (2007). A reverse concreteness effect in a subject with semantic dementia. *Brain and language*, 103, 90-91.

Papagno, C., Capasso, R., Miceli, G. (2009). Reversed of the concreteness effect for nouns in a subject with semantic dementia. *Neuropsychologia*, 47, 1138-1148.

Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature Reviews Neuroscience,* 8(12), 976-987.

Perani, D., Cappa, S. F., Bettinardi, V., Bressi, S., Gorno-Tempini, M., Matarrese, M., et al. (1995). Different neural systems for the recognition of animals and man-made tools. *Neuroreport,* 6(12), 1637-1641.

Perani, D., Schnur, T., Tettamanti, M., Gorno-Tempini, M., Cappa, S. F., & Fazio, F. (1999). Word and picture matching: a PET study of semantic category effects. *Neuropsychologia,* 37(3), 293-306.

Perri, R., Carlesimo, G.A., Zannino, G.D., Mauri, M., Muolo, B., Pettenati, C., Caltagirone, C. (2003). Intentional and automatic measures of specific-category effect in the semantic impairment of patients with Alzheimer's disease. *Neuropsychologia*, 41, 1509-1522.

Pexman, PM, Lupker, SJ, Hino, Y. (2002). The impact of feedback semantics in visual word recognition: Number-of-features effects in lexical decision and naming tasks. *Psychonomic Bulletin & Review*, 9, 542–549.

Phillips, J.A., Noppeney, U., Humphreys, G.W., Price, C.J. (2002). Can segregation within the semantic system account for category-specific deficits?. *Brain*, 125, 2067--2080.

Pisella. L., Binkofski, F., Lasek, K., Toni, I., Rossetti, Y. (2006). No double-dissociation between optic ataxia and visual agnosia: Multiple sub-streams for multiple visuo-manual integrations. *Neuropsychologia*, 44, 2734–2748.

Plaut, D. C. & Shallice, T. (1993). Deep dyslexia: A case study of connectionist neuropsychology. *Cognitive Neuropsychology*, 10: 377-500.

Pobric, G., Jefferies, E., & Ralph, M. A. (2007). Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. *Proc Natl Acad Sci U S A,* 104(50), 20137-20141.

Pobric, G., Jefferies, E., Lambon Ralph, M.A. (2010). Category-specific versus category-general semantic impairment induced by transcranial magnetic stimulation. *Current Biology*, 20, 964-968.

Pobric, G., Lambon Ralph, M. A., & Jefferies, E. (2009). The role of the anterior temporal lobes in the comprehension of concrete and abstract words: rTMS evidence. *Cortex,* 45(9), 1104-1110.

Posner, J., Russell, J. A., Gerber, A., Gorman, D., Colibazzi, T., Yu, S., et al. (2009). The neurophysiological bases of emotion: An fMRI study of the affective circumplex using emotion-denoting words. *Human Brain Mapping*. 30(3):883-95.

Price, C. J., & Friston, K. J. (2002). Functional imaging studies of category specificity. In G. W. Humphreys & E. M. E. Forde (Eds.), *Category specificity in brain and mind* (pp. 427–447). Hove: Psychology Press.

Ratcliffe, G., & Newcombe, F. (1982). Object recognition: Some deductions from the clinical evidence. In *Normality and Pathology in Cognitive Functions,* A. W. Ellis (Ed.), (pp. 147-171). London: Academic Press, London.

Reilly, J., Cross, K., Troiani, V., & Grossman, M. (2007a). Single-word semantic judgements in semantic dementia: Do phonology and grammatical class count? *Aphasiology,* 21, 558–569.

Reilly, J., Grossman, M., McCawley, M.C. (2006). Concreteness effects in lexical processing of semantic dementia. *Brain and language*, 99: 157-158.

Reilly, J., Peelle, J.E., Grossman, M. (2007b). A unitary semantics account of reverse concreteness effects in semantic dementia. *Brain and language*, 103, 86-87.

Rico Duarte, L. (2004). Analyse de la mémoire sémantique dans le vieillissement normal et dans la maladie d'Alzheimer: Mise à l'épreuve du modèle de la structure conceptuelle (Devlin et al. et Tyler et al. 1997–2002). Thèse de Doctorat*,* Université Paul Valéry, Montpellier III.

Rissenberg, M., & Glanzer, M. (1987). Free recall and word finding ability in normal aging and senile dementia of Alzheimer's type: the effect of item concreteness. *Journal of gerontology*, 42, 318-322.

Rizzolatti, G., Matelli, M. (2003). Two different streams for the dorsal visual system: Anatomy and functions. *Experimental Brain Research,* 153, 146–157.

Rogers SL and Friedman RB. (2008). The underlying mechanisms of semantic memory loss in Alzheimer's disease and semantic dementia. *Neuropsychologia*, 46, 12–21.

Rogers, T. T., Hocking, J., Noppeney, U., Mechelli, A., Gorno-Tempini, M. L., Patterson, K., et al. (2006). Anterior temporal cortex and semantic memory: reconciling findings from neuropsychology and functional imaging. *Cognitive, Affective, & Behavioral Neuroscience,* 6(3), 201-213.

Rogers, T. T., Ivanoiu, A., Patterson, K., & Hodges, J. R. (2006). Semantic memory in Alzheimer's disease and the frontotemporal dementias: a longitudinal study of 236 patients. *Neuropsychology,* 20(3), 319-335.

Rogers, T. T., Lambon Ralph, M. A., Garrard, P., Bozeat, S., McClelland, J. L., Hodges, J. R., et al. (2004). Structure and deterioration of semantic memory: a neuropsychological and computational investigation. *Psychological Review,* 111(1), 205-235.

Rosazza, C., Imbornone, E., Zorzi, M., Farina, E., Chiavari, L., & Cappa, S. F. (2003). The heterogeneity of category-specific semantic disorders: evidence from a new case. *Neurocase,* 9(3), 189-202.

Rosch, E., H. (1973). On the internal structure of perceptual and semantic categories. In T. E. Moore (Ed.), *Cognitive developmentand the acquisition of language*. New York: Academic Press.

Rueschemeyer, S.A., Rooij, D., Lindemann, O., Willems, R., Bekkering, H. (2010). The function of Words. Distinct Neural Correlates for Words Denoting Differently Manipulable Objects. *Journal of Cognitive Neuroscience*, 22(8):1844-51.

Rumiati, R.I., Weiss, P.H., Shallice, T., Ottoboni, G., Noth, J., Zilles, K., Fink, G.R. (2004). Neural basis of pantomiming the use of visually presented objects. *NeuroImage*, 21, 1224–1231.

Sacchett, C., Humphreys, G.W. (1992). Calling a squirrel a squirrel but a canoe a wigwam: A category specific deficit for artefactual objects and body parts. *Cognitive Neuropsychology*, 9, 73-86.

Saccuman, M. C., Cappa, S. F., Bates, E. A., Arevalo, A., Della Rosa, P., Danna, M., et al. (2006). The impact of semantic reference on word class: an fMRI study of action and object naming. *Neuroimage,* 32(4), 1865-1878.

Saffran EM. The organization of semantic memory: in support of a distributed model (2000). Brain and Language, 71:204–12.

Salmon, D. P., Shimamura, A. P., Butters, N., & Smith, S. (1988). Lexical and semantic priming deficits in patients with Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology,* 10(4), 477-494.

Salmon, D.P., Heindel, W.C., Lange, K.L. (1999). Differential decline in word generation from phonemic and semantic categories during the course of Alzheimer's disease: Implications for the integrity of semantic memory. *Journal of the International Neuropsychological Society*; 5, 692-703.

Salmon, J.P., McMullen, P.A., Filliter, J.H.(2010). Norms for two types of manipulability (graspability and functional usage), familiarity, and age of acquisition for 320 pictures of objects. *Behavior Research Methods*, 42(1), 82-95.

Samson D, Pillon A. (2003). A case of impaired knowledge for fruit and vegetables. *Cognitive Neuropsychology*, 20: 373-400.

Santos, A., Chaigneau, S.E., Simmons, W.K., & Barsalou, L.W. (in press). Property generation reflects word association and situated simulation. *Language and Cognition*.

Sartori, G., & Lombardi, L. (2004). Semantic relevance and semantic disorders. *Journal of Cognitive Neuroscience*, 16, 439-452.

Sartori, G., Lombardi, L., Mattiuzzi, L. (2005). Semantic relevance best predicts normal and abnormal name retrival. *Neuropsychologia*, 43, 754-770.

Saumier, D. and H. Chertkow (2002). Semantic memory. *Current Neurology and Neuroscience Reports,* 2(6), 516-522.

Schwanenflugel, P. J., Akin, C., Luh, W. (1992). Context availability and the recall of abstract and concrete words. *Memory & Cognition*, 20(1), 96-104.

Schwanenflugel, P.J., & Shoben, E.J. (1983). Differential context effects in the comprehension of abstract and concrete verbal materials. *Journal of experimental psychology: Learning, Memory and Cognition,* 9, 82-102.

Schwanenflugel, P.J., Harnishfeger, K.K., Stowe, R.W. (1988). Context availability and lexical decisions for abstract and concrete words. *Journal of memory and language*, 27, 499-520.

Setti, A. & Caramelli, N. (2005). Different domains in abstract concepts. In *Proceedings of the 27th annual conference of the cognitive science society*, (pp:1997-2002).

Shallice, T. (1988). Specialization within the semantic system. *Cognitive Neuropsychology,* 5, 133-142.

Shallice, T., & Coughlan, A.K. (1980). Modality specific word comprehension deficits in deep dyslexia. *Journal of neurology, neurosurgery and psychiatry*, 43(10), 866-872.

Sheridan, J., & Humphreys, G. W. (1993). A verbalsemantic, category-specific recognition impairment. *Cognitive Neuropsychology*, *10*, 143–184.

Silveri, M. C., Monteleone, D., Burani, C., & Tabossi, P. (1996). Automatic semantic facilitation in Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology,* 18(3), 371-382.

Silveri, M.C., Cappa, A., Mariotti, P., Puopolo, M. (2002). Naming in patients with Alzheimer's disease: influence of age of acquisition and categorical effects. *Journal of Clinical and Experimental Neuropsychology*, 24, 755-764.

Silveri, M.C., Daniele, A., Giustolisi, L., & Gainotti, G.(1991). Dissociation between knowledge of living and nonliving things in dementia of the Alzheimer type. *Neurology*, 41(4), 545–546.

Simmons W.K., Hamann S.B., Harenski C.L., Hu X.P, Barsalou L.W. (2008). fMRI evidence for word association and situated simulation in conceptual processing. *Journal of Physiology – Paris*, 102: 106–119.

Simmons WK, Reddish M, Bellgowan SF, Martin A. (2009). The selectivity and functional connectivity of the anterior temporal lobes. *Cerebral Cortex*, 20(4) 813-25.

Simmons, W. K., Martin, A., & Barsalou, L. W. (2005). Pictures of appetizing foods activate gustatory cortices for taste and reward. *Cerebral Cortex*, 15, 1602–1608.

Siri, S., Kensinger, E. A., Cappa, S. F., Hood, K. L., & Corkin, S. (2003). Questioning the living/nonliving dichotomy: evidence from a patient with an unusual semantic dissociation. *Neuropsychology, 17*(4), 630-645.

Sirigu, A., Cohen, L., Duhamel, J.R., Pillon, B., Dubois, B., Agid, Y. (1995). A selective impairment of hand posture for object utilization in apraxia. *Cortex,* 31, 41–55.

Sirigu, A., Duhamel, J.-R., & Poncet, M. (1991). The role of sensorimotor experience in object recognition. *Brain*, 114, 2555–2573.

Smith, E. E., & Medin, D. L. (1981). *Categories and concepts*. Cambridge, MA: Harvard University Press.

Smith, E. E., Shoben, E.J. & Rips, L.J. (1974). Structure and process in semantic memory: Featural model for semantic decisions. *Psychological Review*, 81, 214-241.

Smith, S., Faust, M., Beeman, M., Kennedy, L., & Perry, D. (1995). A property level analysis of lexical semantic representation in Alzheimer's disease. *Brain Lang,* 49(3), 263-279.

Snodgrass, J.G., Vanderwart, M. (1980). A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. *Journal of Experimental Psychology and Human Learning*, 6, 74-215.

Snowden, J.S., Goulding, P.J., Neary, D. (1989). Semantic dementia: a form of circumscribed cerebral atrophy. *Behavioural neurology,* 2, 167–182.

Solomon, K.O., Barsalou, L.W., 2004. Perceptual simulation in property verification. *Memory and Cognition,* 32, 244–259.

Stewart, F., Parkin, A.J., Hunkin, N.M. (1992). Naming impairments following recovery from herpes simplex encephalitis: category-specific?. *Quarterly Journal of Experimental Psychology*, 44, 261-284.

Storms, G., Dirikx, T., Saerens, J., Verstraeten, S., & De Deyn, P. P. (2003). On the use of scaling and clustering in the study of semantic deficits. *Neuropsychology*, 17(2), 289–301.

Tettamanti, M., Buccino, G., Saccuman, M. C., Gallese, V., Danna, M., Scifo, P., et al. (2005). Listening to action-related sentences activates fronto-parietal motor circuits. *Journal of Cognitive Neuroscience,* 17(2), 273-281.

Tippett, L.J., Grossman M., Farah, M.J. (1996). The semantic memory impairment of Alzheimer's disease: Category-specific? *Cortex*, *32*, 143-153.

Tippett, L.J., Meier, S.L., Blackwood, K., Diaz-Asper, C. (2007). Category specific deficits in Alzheimer's disease: fact or artefact?. *Cortex*, 43, 907-920.

Tulving E. (1972). Organization of memory. In E. Tulving & W. Donaldson (Eds.), New York: Academic Press.

Turnbull, O. H. t., & Laws, K. R. (2000). Loss of stored knowledge of object structure: implications for "category-specific" deficits. *Cognitive Neuropsychology,* 17(4), 365-389.

Tyler L.K., Bright P, Dick P, Tavares P, Pilgrim L, Fletcher P. (2003). Do semantic categories activate distinct cortical regions?. Evidence for a distributed neural semantic system. *Cognitive Neuropsychology*, 20, 541–559.

Tyler, L. K., & Moss, H. E. (2001). Towards a distributed account of conceptual knowledge. *Trends in Cognitive Scencesi*, 5(6), 244-252

Tyler, L.K., Moss, H.E., Durrant-Peatfield, M.R., Levy, J.P. (2000). Conceptual structure and the structure of concepts: a distributed account of category-specific deficits. *Brain and Language*, 75, 195-231.

Tyler, L.K., Stamatakis, E. A., Bright, P., Acres, K., Abdallah, S., Rodd, J. M., et al. (2004). Processing objects at different levels of specificity. *Journal of Cognitive Neuroscience,* 16(3), 351-362.

Ungerleider, L.G., & Mishkin, M. (1982). Two cortical visual systems. In *Analysis of Visual Behavior*, M.A.G.D.J. Ingle and R.J.W. Mansfield, eds. (Cambridge, MA: The MIT Press),(pp. 549–586).

Uno, A., Haruhara, N., Kaneko, M. (2003). The standardized comprehension test for abstract words. *Interuna Publishing*, Tokyo.

Vesely, L., Bonner, M.F., Reilly, J., Grossman, M. (2007). Free association in semantic dementia: the importance of being abstract. *Brain and language*, 103, 154-155.

Viggiano, M.P., Vannucci, M., Righi, S. (2004). A new standardized set of ecological pictures for experimental and clinical research on visual object processing. *Cortex*, 40, 491-509.

Vigliocco, G., Meteyard, L., Andrews, M., & Kousta, S. (2009). Toward a theory of semantic representation. *Language and Cognition*, 1, 215-244.

Vigliocco, G., Vinson, D.P, Lewis, W. & Garrett, M.F. (2004). The meanings of object and action words. *Cognitive Psychology*, 48, 422-488.

Vinson, D. P., & Vigliocco, G.(2002). A semantic analysis of grammatical class impairments. *Journal of Neurolinguistics*, 15, 317-351.

Vinson, D. P., Vigliocco, G., Cappa, S., & Siri, S. (2003). The breakdown of semantic knowledge: insights from a statistical model of meaning representation. *Brain and Language, 86*(3), 347-365.

Visser M, Jefferies E, Lambon Ralph MA. (2009). Semantic processing in the anterior temporal lobes: a meta-analysis of the functional neuroimaging literature. *Journal of Cognitive Neuroscience*, 1-12.

Warrington, E. (1975). The selective impairment of semantic memory. *Quarterly Journal of Experimental Psychology*, 27, 635-657.

Warrington, E.K., (1981). Neuropsychological studies of verbal semantic systems. *Philosophical Transactions of the Royal Society B*, 295, 411–423.

Warrington, E.K., McCarthy, R., (1983). Category-specific access dysphasia. *Brain* 106, 859–878.
Warrington, E.K., McCarthy, R., (1987). Categories of knowledge: further fractionations and an attempted integration. *Brain* 110, 1465–1473.

Warrington, E.K., Shallice, T. (1984). Category specific semantic impairments. *Brain*, 107(3), 829-853.

Wauters, L.N., Tellings, A.E.J.M, Van Bon, W.H.J, Wouter Van Haaften, A. (2003). Mode of acquisition of word meanings: the viability of a theoretical construct. *Applied psycholinguistics,* 24, 385-406.

Weiskopf, N., Hutton, C., Josephs, O., Deichmann, R. (2006). Optimal EPI parameters for reduction of susceptibility-induced BOLD sensitivity losses: A whole-brain analysis at 3 T and 1.5 T. *NeuroImage*. 33, 493-504.

Whatmough C, Chertkow H, Murtha S, Hanratty K. (2002). Dissociable brain regions process object meaning and object structure during picture naming. *Neuropsychologia*, 40:174–86.

Whatmough, C., & Chertkow, H. (2002). Category-specific recognition impairments in Alzheimer's disease. In: E.M.E. Forde & G. Humphreys (Eds.), *Category specificity in mind and brain*. East Sussex, UK: Psychology Press.

Whatmough, C., Chertkow, H., Murtha, S., Templeman, D., Babins, L., & Kelner, N. (2003). The semantic category effect increases with worsening anomia in Alzheimer's type dementia. *Brain Lang,* 84(1), 134-147.

Wiemer-Hastings, K., Krug, J., Xu, X. (2001). Imagery, context availability, contextual constraint and abstractness. In *Proceedings of the 23rd annual conference of the cognitive science society* (pp: 1106- 1111).

Wolpert, D.M., Goodbody, S.J., Husain, M. (1998). Maintaining internal representations: the role of the human superior parietal lobe. *Nature Neuroscience,* 1, 529–533.

Yi, H.A., Moore, P., Grossman, M. (2007). Reversal of the concreteness effect for verbs in patients with semantic dementia. *Neuropsychology*, 21, 9-19.

Zannino, G. D., Buccione, I., Perri, R., Macaluso, E., Lo Gerfo, E., Caltagirone, C., et al. (2010).Visual and semantic processing of living things and artifacts: an FMRI study. *Journal of Cognitive Neuroscience,* 22(3), 554-570.

Zannino, G.D., Perri, R., Caltagirone, C., Carlesimo, G.A. (2007). Category-specific naming deficit in Alzheimer's disease: the effect of a display by domain interaction. *Neuropsychologia*, 45, 1832-1939.

Zannino, G.D., Perri, R., Carlesimo, G.A., Pasqualetti, P., Caltagirone, C. (2002). Category-specific impairment in patients with Alzheimer's disease as a function of disease severity: a cross-sectional investigation. *Neuropsychologia*, 40, 2268-2279.

Zannino, G.D., Perri, R., Pasqualetti, P., Caltagirone, C., Carlesimo, G.A. (2006a). (Category-specific) semantic deficits in Alzheimer's patients: the role of semantic distance. *Neuropsychologia*, 44, 52-61.

Zannino, G.D., Perri, R., Pasqualetti, P., Di Paola, M., Caltagirone, C., Carlesimo, G.A. (2006b). The role of semantic distance in category-specific impairments for living things: evidence from a case of semantic dementia. *Neuropsychologia*, 44, 1017-10