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The semantic representation of social groups and its neural substrate

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Abstract

Neuropsychological studies described brain damaged patients with a deficit at recognizing exemplars from some semantic categories while being still able to recognize exemplars from other categories, and vice versa. This evidence suggested that categories such as animals, plants, artifacts and conspecifics might be independently organized in the brain. Several theories tried to explain the category specificity, and proposed that concepts are represented in the brain according to the modality of their features, on the relevance of a domain for survival or on the degree of inter-correlation between features.

Perhaps one limitation on investigation on how categories are represented in the brain has to do with the poor characterization of the concept about conspecifics often limited to famous and familiar persons as unique entities, and as such not very comparable with the other categories of stimuli. Recent findings suggested that even the knowledge about categories of conspecifics defined as social groups might well be represented independently of other categories.

In the current thesis I investigated whether social group knowledge is indeed represented independently of other categories, consistently with previous findings, and the eventual neural substrates of such knowledge. In two different studies, I tested the knowledge of patients with brain tumors and neurodegenerative diseases about social groups, animate and inanimate entities. Correlating patients' behavioural performance with structural MRI data, I found that the lesion of a left-lateralized set of areas was selectively associated with the impairment in naming social group pictures. Specifically, inferior frontal gyrus, insula and anterior temporal cortex were associated with social group processing in both the studies. Since these areas were reported to be involved in emotional processing, In a third study with healthy individuals, I tested whether one of the above brain regions, within the opercular part of inferior frontal gyrus, might be involved in processing social groups per se or in processing

the valence of stimuli. Results revealed that this area was involved in the processing of negative stimuli and suggested that the semantic impairment in processing social groups might be related to the intrinsic emotional value of this category of stimuli. This pattern of findings suggests that human conceptual knowledge is associated with modality-specific processing areas, and that social group representation might interacts with emotional features.

CHAPTER 1

Introduction

When we experience the world, we come across several types of entities, varying in their shape, colour, taste, smell and sound. In order to cope with this complexity, and to prevent the need to newly process the items each time, we automatically sort them into different *categories*. Thus, when we perceive an entity with a particular configuration of features, we are able to identify it effortlessly as an “apple” or a “lion”, and adapt our behaviour consistently with item perceived. For instance, in the former case we will move toward the fruit - in the event we wish to eat it, while in the latter case we will run away from it. Hence, to cope with the complexity of the world and to immediately react with the appropriate behaviour we rely on this information organized in different *concepts* in our *conceptual system* (or *semantic system*).

From an evolutionary perspective, the categorization process is likely to have played a critical role in human survival, allowing to rapidly escape from multiple type of hazardous entities - including animals and conspecifics - and conversely to recognise possible sources of food, as vegetables or animals, and reproduction (conspecifics). In the upcoming text I will use the term *domain* to indicate broad groups of entities, such as animate entities, inanimate entities or conspecifics, and the term category to indicate smaller groups of items, such as animals, plants, tools and conspecifics. The term animate entities will be used as a synonym of living entities, including both animals, plants, fruits and vegetables, while the term inanimate entities or non-living entities, or artifacts will reflect the category of non-living artificial objects (e.g. tools).

In my thesis I will focus on the conceptual representation of conspecifics, and specifically on categories of individuals sharing common features or social groups (Rumiati et al., 2014). The study of how social groups are represented in the brain is motivated by the fact that most of the literature explored conspecifics knowledge at a very specific level of representation (i.e., *unique-entity level*) and compared this knowledge with more general stimuli (i.e., each concept could be applied to many different exemplars) such as animals or artifacts. Moreover understanding how social groups are represented is particularly relevant for its relationship with social prejudice.

I will begin my dissertation by describing two important phenomena – global and category-specific semantic impairments – which have been very instrumental in promoting the formulation of several theories of how concepts are represented in the semantic system.

1.1 The emergence of semantic deficits in neurological patients

1.1.1 Global semantic impairment

The selective impairment of semantic memory, with spared (or relatively spared) visuo-perceptual abilities, executive functions, attention and episodic memory was firstly reported by Warrington (1975). She reported three patients with impaired recognition of both pictorial and verbal stimuli, particularly when tested at a subordinate level of specificity. Indeed these patients, if presented with pictures of flowers, were strongly impaired at recognizing and naming the specific flower type depicted, but not at identifying the item as a flower.

Warrington (1975) ascribed the deficit reported at the level of the semantic memory thus providing support to the distinction made by Tulving (1972) between semantic and episodic memory. The patients suffered from a form of degenerative disease, affecting primarily the semantic system, has been observed often afterwards (e.g., Hodges et al., 2007) and named semantic dementia (SD). More recently SD has been classified among the frontotemporal lobar degenerations, together with the behavioural variant of fronto-temporal dementia (bvFTD) and primary non-fluent progressive aphasia (PNFA) (see Neary et al., 1998). The pattern of brain atrophy is remarkably different among patients affected by these syndromes, with the bvFTD prominently affected at the level of frontal lobes (Frisoni et al., 1996), PNFA at peri-sylvian level (including both frontal and temporal lobes) (Nestor et al., 2003) and SD at the level of anterior temporal lobes (ATLs) (Mummery et al., 2000).

A distinction between left and right anterior temporal variants within the semantic dementia syndrome has been proposed. Indeed, some patients with a pattern of atrophy more located within the left ATL tend to be impaired more at naming tasks, with a better recognition performance; conversely, patients with a more atrophic right ATL than left ATL tend to be impaired at both naming and comprehension tasks (Lambon Ralph et al., 2001). Moreover, SD patients with more pronounced right temporal atrophy tend also to be impaired in face perception, to show delusions and to get lost (Chan et al., 2009).

1.1.2 The category-specificity effect

The term category-specificity effect indicates a condition, now described in many patients, characterized by the selective loss of semantic information for one or more categories of concepts. The deficit was first observed in a patient with a selective deficit in recognizing inanimate entities presented visually or by touch, and food (except by taste), than for animate entities (Neilsen, 1946). The opposite pattern was also reported, and referred to a patient with a deficit at recognizing living entities than inanimate entities but, unfortunately, the clinical description was not associated with quantitative measures (Neilsen, 1946). Years after, Warrington and Shallice (1984) first piece documented in a quantitative manner the presence of categorical semantic impairments in patients affected by herpes simplex virus encephalitis (HSVE), a rare brain disease affecting, especially at the beginning of the onset, the anterior-inferior temporal lobes (Gitelmann et al., 2001; Noppeney et al., 2007). Two of the patients reported (J.B.R. and S.B.Y.) were tested on their knowledge about different categories of entities (e.g., animate entities, foods and inanimate entities) using different modality of presentation (e.g., visual, auditory) and types of stimuli (e.g. line drawings, coloured pictures, words). Results showed that both patients had a selective loss of knowledge about living entities (animals and plants) and foods. It is worth noting for the theoretical implications which will be discussed in the following sections, the case of patient J.B.R, who not only failed at recognizing animals (insects, fish), plants (flowers, trees, fruits and vegetables) and foods (drinks) but also with inanimate categories such as precious stones and musical instruments.

The opposite pattern - that is impaired recognition of inanimate entities and spared recognition of animate entities - has been shown in two patients V.E.R. and Y.OT (Warrington and McCarthy, 1983; 1987). These two patients, after a vascular damage, became globally aphasic and showed impairments at recognizing inanimate entities than animate entities in a word-to-picture matching task.

Before discussing the different theoretical accounts of categorical effects I would like to mention that some neuropsychologists questioned that these deficits were true. First, it has been argued that these deficits arose from the lack of control on stimulus factors, such as frequency, familiarity or visual complexity, that are known to have an impact on patients' performance (Funnel and Sheridan, 1992; Gaffan and Heywood, 1993; Stewart, Parkin and Hunkin, 1992). For instance, Stewart et al. (1992) reported a patient H.O. with herpes simplex encephalitis who showed a categorical semantic impairment for the animate entities on picture naming task (accuracy: animate entities 65%, inanimate entities 86%). After the stimuli were matched for familiarity, frequency and visual complexity, the categorical effect disappeared (accuracy: animate entities 42%, inanimate entities 36%). These results suggest that these variables need to be controlled when selecting the stimuli used in neuropsychological studies to avoid that the categorical semantic deficits observed reflect differences in the relevant variables described above. However, categorical semantic deficits were observed very often after controlling stimuli for the relevant variables (see Capitani et al., 2003, for a review), suggesting that the categorical effects can be reliable.

Secondly, categorical semantic deficits have been suggested to reflect the pre-morbid knowledge about each category. More specifically, in a study on healthy participants Barbarotto et al. (2002) reported that males tended to have a better knowledge for artifacts, while females tended to know biological categories better. However, even after controlling for gender-specific familiarity, the categorical semantic deficits were still reported (Albanese et al., 2000; Samson and Pillon, 2003).

Further investigations showed the existence of finer-grained categorical deficits of patients, with selective impairment in the knowledge of plants (Hart et al., 1985; Farah and Wallace, 1992), animals (Hart and Gordon, 1992) and person-specific items (Lucchelli and De Renzi, 1992; McKenna and Warrington, 1980).

1.1.3 Category-specificity effect: neural substrates

The double dissociations between animate and inanimate entities knowledge in brain damaged patients, somewhat implies that two subsystems have discrete neural substrates. A critical review of single-case studies showing category-specific semantic impairments in patients (Gainotti et al., 2000) reported a bilateral anterior-mesial temporal damage associated with animate-entities knowledge deficit, and damage within the left dorso-lateral convexity associated with deficits affecting man-made artifacts. Moreover, Brambati et al. (2006) tested a big sample of patients (N=152) with different neurodegenerative diseases on a naming task including animate and inanimate entities as stimuli and correlated grey matter thickness volumes with naming performance using VBM. They found that the animate entities naming performance positively correlated with the right anterior-mesial temporal cortex, while performance on inanimate entities positively correlated with the left posterior middle temporal gyrus. These patterns of association between right ATL and left superior temporal gyrus/inferior parietal lobe corresponding to, respectively, living and non-living entities have been confirmed using other techniques such as functional magnetic resonance imaging (fMRI) (e.g., Anzellotti et al., 2011; Damasio et al., 1996; Devlin et al., 2002) and electroencephalography (EEG) (Chan et al., 2011).

1.2 Theoretical accounts of the semantic organization

Many theories have been proposed to explain how category-specific semantic deficits arise in patients and, importantly, these observations have been used to account for how the semantic system is organized in the brain. Here I will review three main groups of theories according to which concepts are represented in the brain depending on the modality of their features, on the relevance of a domain for survival or on the degree of inter-correlation between features.

1.2.1 Categories: the domain-specific hypothesis

According to the domain-specific hypothesis (DSH) (Caramazza and Shelton, 1998) evolution has shaped our semantic system into different, independent domains. According to the authors, to efficiently discriminate among animals (that might represent predators or sources of food), plants (representing source of food and medicine), conspecifics (as competitors or source of protection and reproduction) and artifacts is critical for human survival. A key aspect in the DSH is that innate constrains, evolved in human brain evolution, influence the acquisition of different members of each category of entities, and hence their recognition and categorization. This aspect was corroborated, according to the Caramazza and Shelton (1998), by developmental studies reporting that infants were able to distinguish animate-inanimate entities and their relevant features (Bertenthal, 1993; Bertenthal et al., 1984; Mandler, 1992; Baillargeon, 1993, Spelke, 1988; Spelke et al., 1995).

The distributed DSH (Mahon and Caramazza, 2009) is an updated version of the original theory emphasizing how categorical, sensory, motor and emotional properties shape conceptual knowledge organization. Moreover, categorical domains influence both conceptual representations and perception. According to their view, the functional connectivity between different regions of the brain shapes their domain-specific properties. Hence, the domain-specificity of a certain region is related to its connection with other brain areas, and to the types of computation they perform. The emergence of these domain-specific networks, in Mahon and Caramazza's view, has been induced by human evolution. One example might be that the need of integration of emotional and biological motion processing is higher for animals and conspecifics than tools and plants. And so the specialized function of fusiform face area (FFA) in visual processing arise from its pattern of connections, including amygdala, superior temporal sulcus (STS) and many other areas which are important in representing social relevant information (Mahon and Caramazza, 2011).

Both the versions of the DSH predict that patients' selective semantic impairment could affect not only the categories of animals, plants, conspecifics and artifacts, and not finer-grained deficits as for land animals or kitchen utensils, while only the distributed DSH also predicts that, within domain-specific semantic impairments, some modality-specific features might be spared and other impaired as in the case of patients with prosopagnosia and completely spared knowledge about conspecifics (Mahon and Caramazza, 2011)

1.2.2 Modality: the sensory/functional theory

In order to explain the categorical specific semantic impairments, Warrington, McCarthy and Shallice (Warrington and McCarthy, 1983; Warrington and Shallice, 1984) proposed the existence of distinct semantic subsystems, processing different types of attributes. On the one hand, a (visual) sensory semantic system involved in processing visual features and, on the other, a functional semantic system involved in processing functional features. The modality of the “core” attribute, which is the minimal information necessary to recognize a concept, is held to be different between animate and inanimate entity knowledge. Hence, animate entity knowledge tends to rely on sensory attributes, while inanimate/artifactual entity knowledge tends to rely on functional attributes. The SFT does not exclude that both animate and inanimate entities might be described also by, respectively, functional and sensory features, but according to the SFT, the key factor in defining each category of knowledge is the modality of their “core” attributes. Following this theory, damage to the perceptual semantic subsystem would selectively impair patients’ recognition of animate entities due to a degradation of the perceptual feature knowledge. Conversely, the selective deficit in recognizing inanimate entities would be caused by damage to the functional semantic subsystem, as a consequence of a degradation of the functional feature knowledge. This theory was corroborated by the observation that the patient J.B.R. was impaired not only in processing many different animate entities, including animals, plants and foods, but also inanimate entities such as musical instruments, metals and precious stones, implying that both musical instruments and precious stones “core” attributes might be sensory.

The basic tenets of the SFT have been tested and confirmed in a computational study (Farah and McClelland, 1991). In their model, the authors included different sets of units, corresponding to verbal inputs (or outputs), visual inputs (or outputs) and a semantic system (divided into two parts - sensory and functional semantic systems – as assumed by the SFT). The four sets of units were bi-directionally connected to each other, excluding the connection between visual and verbal inputs. The model was trained by presenting living and non-living items (which had been previously assessed for their sensory and functional features) and then damaged on either the sensory and functional semantic systems. Results showed that lesions of the visual semantic system led to a lower performance on the living entities, while damaging the functional semantic system led to a poorer performance on non-living entities, as predicted by the SFT.

In line with these predictions a number of studies investigated feature knowledge in patients showing category-specificity effect. Silveri and Gainotti (1988) reported a patient, L.A., with selective deficit in animate entities and food knowledge. The effect was consistent across repetitions of the stimuli and was equally present with both visual and verbal descriptive stimuli. Importantly, the patient was more impaired in recognizing animals from visual than functional descriptions. However, other studies (see Capitani et al. 2003 for a review), as the one by Borgo and Shallice (2003) found that in patients with the very same deficit as that shown by patient L.A. (Silveri and Gainotti, 1988), the feature knowledge was equally impaired for both functional and sensory features. In contrast to the prediction of the SFT and Farah and McClelland model, the investigation of feature knowledge in patients with categorical semantic deficits is not conclusive.

One of the most relevant arguments that has been moved against the SFT is the existence of patients with selective sub-categorical semantic impairment, as that for plants or animals. Indeed, since both animal and plant knowledge should rely on sensory features, damage to the sensorial subsystem should not affect neither animal nor plant knowledge. Three accounts have been proposed to clarify this point. First, according to the multiple processing channels account (MPCA) (Warrington and McCarthy, 1987; Crutch and Warrington, 2003), which might be considered a refinement of the SFT, within the sensory and functional distinction, different contributions from sub-sensory (e.g. visual, auditory, tactile) and sub-functional (e.g. kinematics, proprioception) modalities, might define each sub-category (i.e., fruit representation might rely on both visual (shape, colour) and gustatory featural knowledge). Hence, the impairment in fruit knowledge might arise from the selective lesion of the sub-modal semantic systems representing shape, colour and taste. Second, according to Sartori and colleagues (2007), pre-morbid individual differences in the degree of knowledge of each sub-category of concepts might be the cause of these phenomenon, leading patients with a poorer pre-morbid knowledge of plants, more prone to plant knowledge impairment following brain damage. Third explains the plant-animal double dissociations suggesting that the two categories represent two distinct domains of knowledge as suggested by the Domain specific Hypothesis (Caramazza and Shelton, 1998) that we will discuss in the next section.

1.2.2.1 Convergence zone theory

Damasio (1989) proposed that, when we perceive an entity, our modality-specific cortical areas activate and process its basic features (e.g., sensory or motor feature); in this respect, the specific pattern of activation represents the modality-specific experience of such entity. These modality-specific areas are connected to associative areas (Convergence zones) (CZ) that are involved in the storage of modality-specific states. According to the author, CZs are present at multiple levels of processing, leading to a hierarchical processing of each stimulus. High-order associative areas (which are placed within anterior frontal and temporal cortices) store the multi-modal information relative to each concept, while uni-modal associative areas encode specific patterns of modality-specific experiences. This does not mean that information is stored into different formats; rather, neurons (or sets of neurons) within a certain CZ encode the neural pathway necessary to activate other lower-level CZs, and hence modality-specific representations. According to the CZ theory perceiving some features of a given object (e.g. sound) will activate a convergent zone, triggering the activation of specific pattern of sensory cortices, representing other specific feature of the object. For example, hearing the bark of a dog will activate a population of neuron within a CZ, triggering the activation of visual and tactile features of the concept “dog” in somatosensory and visual cortices.

The domain representation, and hence categorical semantic deficits, will emerge as a consequence of reality constrains, such as feature similarity, spatial and temporal sequence and temporal placement of a given entity or group of entities, and neurobiological reasons, as the presence of neurons recording the temporal coincidence and the inter-relationship between different entities within the same categories.

1.2.2.2 Conceptual topography theory

After the formulation of Damasio's CZ theory (1989), other authors (Simmons and Barsalou, 2003) further developed Damasio's basic assumption, proposing the conceptual topography theory (CTT) that basically consists in adding two basic principles guiding semantic and perceptual representation in the brain: the similarity-in-topography principle (STP) and the variable dispersion principle (VDP). Their aim was to reconcile apparently mutually exclusive theories as the SFT and the conceptual structure account (CSA) (Tyler and Moss, 2001).

According to the STP, in associative areas (CZs) the topographical distance between two neurons is negatively correlated to the similarity of the features they are conjoining. In other words, the neurons conjoining very similar features will be very close topographically, while for less similar feature they will more dispersed. For example, when perceiving different faces of humans and monkeys, the activations of different neurons within an associative area will be very close to each other respectively for human faces and for monkey faces, while there will be a certain topographical distance between human and monkey faces. This should not be confused with the presence of categorical representation within each associative area (members of the same category tend to share many features), since it does not imply the absence of conjoining neurons for different categories of entities. Indeed, as the VDP claims, as members of the same category decrease in their similarity, conjoined neurons will tend to be more dispersed in associative areas topography.

Aside from these two principles, Simmons and Barsalou (2003) further differentiated distinct modules within each CZ. When we perceive and object, distinct sensory early-processing areas activate, irrespective of attention allocation, leading to modality-specific states, necessary for experiencing the basic features of that object (as also claimed by Damasio, 1989). For instance, feature maps will encode colour, line orientation, pitch and tactile sensations of a specific object. Neurons representing such features will be connected to two different module of a given modality-specific CZ: the analytic CZ and the holistic CZ. The function of these two modules is guided by attention, and is necessary for encoding conceptual properties of a given object, but while the first processes high frequency properties (i.e., colour, line direction for the visual modality), the second processes more global properties (i.e., shape and location for the visual modality). Both analytic and holistic CZs are connected to the modality CZ. This area extracts statistical regularities across the activity of analytic and holistic CZs in order to form modality-specific categorical representations. Modality-specific CZs are also connected to cross-modal CZs, which are responsible for cross-modal representation of categories of knowledge.

In Simmons and Barsalou's view, category specificity effect will arise from lesion of distinct units in the model, depending of the importance of feature representation for each category of entities. Single category semantic impairment might arise from both modality (in case one modality of representation is crucial for the knowledge of the category) and cross-modal CZs, while generalized semantic impairment should be observed only when the damage is localizes to cross-modal CZs.

1.2.3 Featural correlation

Several connectionist models have been developed in order to explain how semantic knowledge is represented in the brain, building on the categorical semantic deficits in patients. The common feature of these models is that categories emerge from patterns of featural similarity between semantic concepts. Two concepts of the same category tend to share more semantic features than those included in different categories (i.e., a cat and a cow both have four legs, eyes, and fur). One basic assumption common to these models is that distinct categories do not have discrete neural underpinnings. Accordingly, following brain damage, patients' categorical deficits tend to emerge as the degradation of certain semantic features, shared by many members of the same category. In this context, a very specific model that aims at explaining category-specific semantic impairments is the conceptual structure account (CSA) (Tyler and Moss, 2001; Tyler et al., 2004).

1.2.3.1 The conceptual structure account

Differently from other accounts, the CSA proposed that the patterns of specific semantic impairments could arise from differences in the internal structure of different categories of knowledge. In this account the feature structure defines high-level conceptual organization. Specifically, members of the animate entities, as dogs and lions, are defined by many inter-correlated, shared features (i.e. have four legs, eyes and fur) and also by a few distinctive features (specific for each concept), which are scarcely correlated with the other features. Conversely, artifacts tend to be represented with more distinctive and less shared features. Shared features in artifact knowledge are less correlated with other features. Shared features are important in order to accurately recognize the category of each entity, while distinctive properties are necessary to identify each distinct exemplar. Since the most represented features are the most resilient to damage, after brain lesion of the semantic processing areas, distinct patterns of impairments will emerge across categories/domains. Distinctive features of each concept, being less correlated with the other properties of the same concept, will be more vulnerable to damage for animate entities than shared features, leading to a deficit in distinguishing member of this category but recognizing their membership. Conversely, since there is a tight correlation between form and function in artifacts and shared properties are less correlated, shared and distinctive features will not dissociate for the artifacts category. According to Tyler and Moss (2001), distinct tasks will induce the findings of different patterns of dissociations, depending on the differential demand on distinct and shared features. Their prediction also explains some finer-grained dissociation, as the selective impairment for fruit and vegetables. Indeed, this particular category of items has fewer inter-correlated shared features than other entities in the animate domain (e.g., animals), leading to their particular vulnerability to damage. However this does not explain the dissociation reported by Caramazza and Shelton (1998), of a patient with a selective loss of knowledge about animals and spared knowledge for plants and artifacts.

1.3 Representing conspecifics

The ability to perceive and semantically represent other people is fundamental for human survival and is the basis for social cognition. Indeed, our ability to function in large groups is possible thanks to our ability to correctly perceive, store and retrieve information related to our conspecifics. Although the existence of a distinct cognitive domain involved in social processing is still a matter of debate, some evidence seems to suggest that many different brain areas could be specialized in processing conspecifics.

1.3.1 Perceiving other humans

The perception of other humans involves, as for other categories of concepts, distinct modality: visual (faces and body parts) and auditory (voices) stimuli. The evidence of a dedicated network in perceiving other humans, as well as the theoretical models developed to explain experimental findings will be reviewed in the following sections.

1.3.1.1 Face perception

Apperceptive prosopagnosia is a selective deficit at recognizing faces (Young & Ellis, 1989). Patients with this deficit tend to correctly perceive all the different details of a facial stimulus, but fail to integrate them in a unitary representation (Ramon et al., 2010; Van Belle et al., 2010). Thus they are impaired at forming the representation of faces from visual inputs following lesions in occipito-temporal areas (see Davies-Thompson, et al., 2014, for a recent review). On the other hand, patients with associative prosopagnosia, typically associated with lesions of the right anterior temporal lobe (ATL), after having formed a face representation successfully, may fail to associate an identity to a face structure (e.g., De Renzi, 1986; Farah et al., 1995). Within the occipital and temporal lobes, three regions have been consistently associated to face perception in functional neuroimaging: occipital face area (OFA), the lateral part of the fusiform gyrus (fusiform face area, FFA) and posterior aspects of the superior temporal sulcus (pSTS) (Haxby et al., 2000). While FFA has been shown to process the invariant aspects of each face, allowing to distinguish different faces (i.e. identity) (Hoffmann et al., 2000; George et al., 1999; Sergent et al., 1992), pSTS has been associated to the processing of changeable aspects of facial stimuli, as expression and mouth movement (Hoffmann et al., 2000; Puce et al., 1998). OFA is thought to selectively process details of facial stimuli, as mouth, eyes or nose (Pitcher et al., 2011), and, might have functional connections with FFA and pSTS, constituting their input of information (Haxby et al., 2000).

1.3.1.2 Voice perception

The selective deficit at recognizing human voices (phonagnosia) has been reported in a few case reports (Peretz et al., 1994; Van Lancker et al., 1988). Patients' lesions were distributed bilaterally within frontal, temporal and occipital lobes, and hence they were insufficient, in order to localize brain areas associated to this deficit. In addition, group studies (Lang et al., 2009; Van Lancker and Canter, 1982; Van Lancker et al., 1989), reporting deficits in recognizing voices for right or bilateral brain damaged patients, were not conclusive in identifying the brain areas that might be involved in voice processing. Conversely, functional neuroimaging studies suggested that activations in the middle and anterior portions of the superior temporal gyrus (STG) and STS (mainly in the right hemisphere) could to be involved in voice-identity recognition (Andics et al., 2010; Belin and Zatorre, 2003; von Kriegstein et al., 2003; von Kriegstein and Giraud, 2004), while the posterior part of STG and STS is thought to process acoustic properties of voices (von Kriegstein and Giraud, 2004; von Kriegstein et al., 2007).

1.3.2 Conceptual knowledge about conspecifics

The semantic knowledge about conspecifics, as for the other categories of knowledge, might be retrieved at different levels of specificity, ranging from general (i.e., humans) to unique entities (i.e., person-specific knowledge). General concepts might be applied to many different individuals (i.e., categories of individuals or social groups), while very specific concepts (i.e., unique entities) only describe one single individual. Thus far, conceptual knowledge about conspecifics has been widely investigated at the unique-entity level of specificity. Indeed the stimuli most frequently used in testing both patients and healthy participants were pictures or written names of familiar and famous persons (Blank et al., 2014), as we will discuss in the next section.

1.3.2.1 Person-specific knowledge

The impairment in recognition of other individuals is surprisingly common in neurosurgical and neurological population. A study investigating person-specific knowledge through different modalities (pictures, voices, names) (Neuner and Schweinberger, 2000), in a sample of patients (N = 37) with many different types of brain damage, recruited in a neuropsychological rehabilitation unit, found that the 58% were impaired in person-specific knowledge, and moreover, 28% were selectively impaired in this particular type of knowledge.

Evidence obtained with different methods including neuropsychological and functional neuroimaging studies seems to suggest that person-specific knowledge might be represented independently of other categories of knowledge. A first piece of evidence is provided by a double dissociation between patients with herpes simplex encephalitis, neurodegenerative diseases and traumatic brain injury with a person-specific knowledge deficit (i.e., loss of biographical information about famous people) but spared knowledge about other categories (Hanley et al., 1989; Evans et al., 1995, Miceli et al., 2000), and patients with the opposite and less frequent pattern, that is spared knowledge about conspecifics but a loss of knowledge about other categories such as animals, vegetables, and tools (Kay and Hanley, 2002; Lyons et al., 2006; Thompson et al., 2004). The loss of person-specific knowledge has been associated with lesion of the ATL (Gainotti, 2015) and, in particular, lesions of the right ATL seems to be associated with problems in person-specific knowledge retrieval from visual and auditory modalities, while lesions of the left ATL seem to lead to impaired production or recognition of verbal person-specific items. Imaging studies showed also an involvement of both ATL in person-specific processing, when contrasting person vs. non-person (tools or buildings) stimuli, in addition to the involvement of posterior cingulate (PCC), inferior frontal gyrus (IFG) and medial prefrontal cortex (mPFC) (Gorno-Tempini and Price, 2001; Simmons et al., 2009).

Overall, this neuropsychological and neuroimaging evidence seems to suggest that person-specific knowledge and knowledge about living and non-living things might be supported, at least in part, by different neuro-mechanisms. Importantly, some authors (Tyler et al., 2004; Rogers et al., 2006) claimed that, since person-specific knowledge has a higher degree of specificity (i.e., describes only one individual) than the stimuli used for testing animate and inanimate knowledge (i.e., describing categories of entities), this double dissociations might simply reflect a different level of specificity if the stimuli (i.e., subordinate vs. basic level stimuli). A study that considered a less specific form of person knowledge, as the social group knowledge would be useful in disambiguating this issue.

1.3.2.2 Models of conspecific representation

Several models have been developed to explain the emergence of specific deficits in face perception (and more recently in voice perception) and in person-specific knowledge. One of the first models was proposed by Bruce and Young (1986) and later revised by Burton et al. (1990, 1999). They proposed that face perception and person-specific knowledge were represented independently, in parallel, of other forms of knowledge. According to their model, a set of processing units were specialized in recognizing human features in distinct modalities, as faces (face recognition units, FRUs), voices (voice recognition units, VRUs) and names (name recognition units, NRUs). Each of these perceptual units encodes information specific for a single individual, which are invariant. All perceptual units converged to person identity nodes (PINs), storing amodal semantic representations of each person. Then each PIN, corresponding to a specific person, is connected to semantic information units (SIUs), important in order to recollect biographical knowledge of each individual, and to lexical output units, which are relevant for associating a face and a voice to the corresponding name of the person. This model assumes that modality-specific processing areas are encapsulated, hence converging only at the level of PINs and not allowing any possible link between perceptual processing areas. This model has been revised based on more detailed neuroanatomical studies on brain-damaged patients and experiments on healthy individuals with functional imaging, by associating each unit to specific brain areas (Belin et al., 2004; Gainotti, 2007; Gainotti et al., 2010; Gainotti and Marra, 2011; Hailstone et al., 2011; Haxby et al., 2000, Blank et al., 2014). Thus facial identity is recognized at the level of FFA (FRUs), while voice identity is recognized at the level of STS and STG (VRUs). Both FFA and STS (and STG) should be connected to the ATL in which the identity of each individual (PINs) is represented. Moreover, recently, ATL has also been linked to inappropriate social behaviours (Thompson et al., 2003; Chan et al., 2009), and to social concepts impairment (Zahn et al., 2009). Based on this evidence, some authors suggested that the ATL may play a critical role in representing social knowledge (social knowledge hypothesis of ATL, Skipper, Ross & Olson, 2011; Olson et al., 2012). However other authors proposed a different view on the role of ATL. Indeed, based on the evidence of patients with semantic dementia, in which ATL atrophy is typically associated with a multi-modal semantic impairment, it has been proposed that ATL might represent a semantic 'hub', integrating inputs from modality-specific areas (the hub-and-spoke theory, Rogers et al., 2004; Patterson et al., 2007) and thus representing multi-modal concepts. Conversely, it is worth noting that semantic dementia patients tend to be impaired, even at the early stages of the disease, in the knowledge of specific-concepts (e.g., dog, cat), with a preserved knowledge of more general concepts (e.g., mammal, animal) (Patterson et al., 2007). Therefore ATL might be involved in processing specific entities (e.g., unique entities) (Tyler et al., 2004; Rogers et al., 2006; Martin 2007). However, both fMRI and TMS studies revealed that ATL is involved in both subordinate and basic-level semantic processing (Pobric et al., 2007; Visser and Lambon-Ralph, 2011)

These models on the role of ATL did not make any clear distinction between distinctive roles of left and right ATL. Since it has been shown that distinct patterns of performance between patients with right or left temporal lobe lesions in recognizing and naming persons might arise, some authors suggested distinct roles of processing in the two hemispheres, at the level of ATL. Indeed patients with semantic dementia tend to show different types of impairment depending on the predominant laterality of the atrophy, with patients with more pronounced left atrophy showing disproportionate production impairment compared to comprehension, and patients with a more pronounced right atrophy showing a similar impairment in production and comprehension (Lambon Ralph et al., 2001). Patients with unilateral left brain damage have been reported with impaired performance on tasks involving verbal production as in picture naming, but spared recognition abilities (Lambon

Ralph et al., 2010; Lambon Ralph, et al., 2012; Drane et al., 2013). The explanation of these findings is still a matter of debate. In fact, according to Thompson et al. (2004), person knowledge is cross-modal and likely to be represented as a category within the right ATL, while general semantic processing may rely on left ATL. However, in Snowden et al.'s view (2004; 2012), person knowledge, as general semantic knowledge, is expected to be represented in modality-specific areas, with the right ATL being important for visual processing, and the left ATL for verbal processing. Conversely, Lambon Ralph et al. (2001) proposed a model in which semantic knowledge is stored in bilateral areas and includes partially redundant information. Damage to the left semantic storage, which provides the main inputs to a left-sided phonological area, will impair verbal production, while damage to the right ATL will not lead to any impairment, since semantic information is redundant in the two hemispheres. The critical aspect is that, according to Thompson's theory (2004) conspecifics might be represented as category, converging on DSH (Caramazza and Shelton, 1998; Caramazza and Mahon, 2009), while in Snowden's (Snowden et al., 2004, 2012) and Lambon Ralph's (Lambon Ralph et al., 2001) view conspecifics knowledge is not independent of the other semantic domains.

1.3.2.3 Social group knowledge

What we know about other individuals includes not only their physical appearance, their psychological or internal states and their biographical information, but also the social group they belong to (i.e., categories of persons, sharing category-specific features, Rumiati et al., 2014). Thus when we meet an individual we automatically realize that, for example, she is a woman, she is Chinese and she is a lawyer. Thanks to this categorization, as for non-social items, we can readily access to a pre-existing knowledge about these social groups (i.e., stereotypes), predict this person's behaviour and consequently modify our actions accordingly (Gilmour, 2015).

The knowledge about social groups has been investigated only in a few studies to date. In a neuropsychological study, Rumiati et al. (2014) tested patients with primary dementias on the knowledge about three semantic categories (i.e., animate entities, inanimate entities and social groups) on word sorting tasks. They reported double dissociations in participants' performance on the three categories, providing a first piece of evidence that social groups might be represented independently of the other categories of knowledge. Moreover, a study using functional imaging on healthy subjects tested knowledge about social groups and non-social knowledge (i.e., artifacts, animals) (Contreras et al., 2011). These authors found different sites of activations when contrasting the social vs. non-social knowledge: specifically the medial prefrontal cortex (MPFC), posterior cingulate (PCC) and bilateral TPJ. From a slightly different perspective, the featural representation of social groups has also been investigated (Mitchell et al., 2002; Zahn et al., 2007; 2009). In their experiments, instead of using social groups as stimuli, the authors focused on the representation of psychological and internal human attributes (e.g., anxious, envy) and contrasted this knowledge to animal function attributes. While both patients (Zahn et al., 2009) and healthy participants (Mitchell et al., 2002; Zahn et al., 2007) studies highlighted the role of ATL in processing social concepts, only the imaging studies with healthy participants found the activation of dorso-medial prefrontal cortex (DMPFC) and left temporo-parietal junction (TPJ) (Mitchell et al., 2002; Zahn et al., 2007), regions that were found to be activated also in the study by Contreras et al. (2011) on social group knowledge.

Taken together, even though these results seem to suggest that social group knowledge might be represented independently of the other categories of knowledge, however, it is still unclear which are the brain areas that when lesioned may give rise to a deficit in processing social groups, as the study by Rumiati et al. (2014) lacks of neural anatomical correlates.

1.4 A meta-analysis on conspecifics representation

In order to investigate the neural correlates of conspecifics neural representation I performed a meta-analysis of functional neuroimaging studies in which human stimuli at different level of specificity (famous faces, unfamiliar faces and voices, social concepts and social groups) were included. The aim of the meta-analysis is to highlight the areas that might be associated to the processing of conspecifics, *irrespective* of modality and level of specificity.

1.4.1 Methods

I performed a systematic review of the literature of the functional neuroimaging studies in which knowledge about humans was investigated using fMRI and positron emission tomography (PET) on healthy individuals. I included only the studies that directly compared human vs. non-human stimuli (i.e., animals, tools, buildings, scenes), irrespective of modality (e.g., visual, auditory) or stimulus type (e.g., pictures, words, vignettes, vocal and non-vocal stimuli), in order to capture category selective activations, while I discarded the results associated with general semantic processing. Specifically, in PubMed (http://www.ncbi.nlm.nih.gov/pubmed) I typed: ((“social groups” OR “conspecifics” OR “social concepts” OR “social knowledge” OR “person knowledge” OR “person-specific knowledge” OR “social semantic” OR “stereotype” OR “unique entities”) AND (“neuroimaging” OR “fMRI” OR “functional magnetic resonance” OR “PET” OR “positron emission tomography”)). I first found a total of 289 studies and, after the selection, I ended up with 12 studies; to this sample I added papers chosen from the relevant literature on this topic, thus reaching as sample of 30 papers and 36 relevant contrasts (total of 290 foci) (see Table 1).

1.4.2 Statistical analysis

Activation-likelihood-estimation was performed using GINGER-ALE software (version 2.3.6) (Eickhoff et al., 2009; https://www.brainmap.org). Statistical significance was assessed using a cluster-level analysis (corrected through family wise error with $p < .05$), setting 1000 permutation and using as input uncorrected (*p* = .01) results. The analysis was performed using the Turkelthaub non-additive method (Turkelthaub et al., 2012) and subject-based smoothing (Eickhoff et al., 2009).

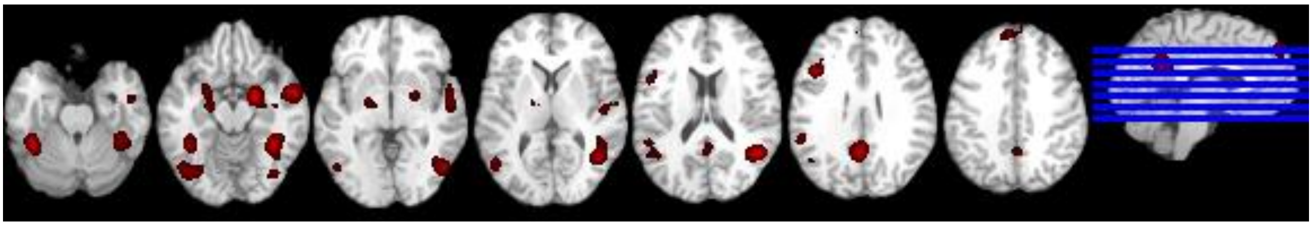
Table1

Authors	Date	Title	Contrast	Familiarity	Stimulus type
Beauchamp et al.	2003	fMRI responses to video and point light displays of moving humans	humans > tools	unfamiliar	dots
Belin et al.	2000	Voice-selective areas in human auditory cortex	humans > tools, animals, places	unfamiliar	voices
Bobes et al.	2013	Timing and tuning for familiarity of cortical responses to faces	humans > places	unfamiliar	faces
Chiao et al.	2009	Neural representations of social status hierarchy in human inferior parietal cortex	humans > cars	familiar	faces
Contreras et al.	2011	Dissociable neural correlates of stereotypes and other forms of semantic knowledge	humans > objects	unfamiliar	words
			humans > fruit, clothing	unfamiliar	words
Contreras-Rodrıguez et al.	2014	Disrupted neural processing of emotional faces in psychopathy	humans > shapes	unfamiliar	faces
Damasio et al.	1996	A neural basis for lexical retrieval	humans > animals, tools	familiar	faces
Fairhall and Caramazza	2013	Category-selective neural substrates for person- and place-related concepts	humans > places	familiar	words
Fairhall et al.	2014	Person- and place-selective neural substrates for entity-specific semantic access	humans > places	familiar, unfamiliar	faces
			humans > places	familiar	faces
			humans > places	familiar	words
Filippi et al.	2010	The brain functional networks associated to human and animal suffering differ among omnivores, vegetarians and vegans	humans > animals	unfamiliar	faces
			humans > animals	unfamiliar	faces
			humans > animals	unfamiliar	faces
Filippi et al.	2013	The "vegetarian brain": chatting with monkeys and pigs?	humans > monkeys	unfamiliar	faces
			humans > monkeys	unfamiliar	faces
			humans > monkeys	unfamiliar	faces
			humans > pigs	unfamiliar	faces
			humans > pigs	unfamiliar	faces
			humans > pigs	unfamiliar	faces
Gervais et al.	2004	Abnormal cortical voice processing in autism	humans > tools, animals	unfamiliar	voices
Gorno Tempini and Price	2001	Identification of famous faces and buildings. A functional neuroimaging study of semantically unique items	humans > places	familiar, unfamiliar	faces

Authors	Date	Title	Contrast	Familiarity	Stimulus type
Grabowski et al.	2001	A role for left temporal pole in the retrieval of words for unique entities	humans > places	familiar, unfamiliar	faces
			humans > places	familiar	faces
			humans > places	unfamiliar	faces
			humans > places	familiar, unfamiliar	faces
Harvey et al.	2007	Modulation of memory formation by stimulus content: specific role of the medial prefrontal cortex in the successful encoding of social pictures	humans > objects	unfamiliar	faces
Hasson et al.	2002	Eccentricity bias as an organizing principle for human high-order object areas	humans > letter, buildings	unfamiliar	faces
Haxby et al.	1999	The effect of face inversion on activity in human neural systems for face and object perception	humans > places	unfamiliar	faces
Ishai et al.	1999	Distributed representation of objects in the human ventral visual pathway	humans > places	unfamiliar	faces
Ishai et al.	2000	The representation of objects in the human occipital and temporal cortex	humans > places	unfamiliar	faces
Ishai et al.	2000	Distributed neural systems for the generation of visual images	humans > places	unfamiliar	faces
Kujala et al.	2012	Dog experts' brains distinguish socially relevant body postures similarly in dogs and humans	humans > dogs	unfamiliar	faces, body
			humans > dogs	unfamiliar	faces, body
Nakamura et al.	2000	Functional delineation of the human occipito-temporal areas related to face and scene processing	humans > places	familiar	faces
Pourtois et al.	2005	View-independent coding of face identity in frontal and temporal cortices is modulated by familiarity: an event-related fMRI study	humans > places	familiar, unfamiliar	faces
Ross and Olson	2010	Social cognition and the anterior temporal lobes	humans > animals	unfamiliar	words
Scherf et al.	2007	Visual category-selectivity for faces, places and objects emerges along different developmental trajectories	humans > places, objects	unfamiliar	faces
Simmons et al.	2010	The selectivity and functional connectivity of the anterior temporal lobes	humans > places	unfamiliar	words
			humans > tools	unfamiliar	words
Skipper et al.	2011	Sensory and semantic category subdivisions within the anterior temporal lobes	humans > animals	unfamiliar	words
Straube et al.	2010	Social cues, mentalizing and the neural processing of speech accompanied by gestures	humans > places	unfamiliar	faces
Zahn et al.	2007	Social concepts are represented in the superior anterior temporal cortex	humans > animals	unfamiliar	words

Note. The table shows all the studies included in the meta-analysis

Figure 1



Note. The figure shows the results of the meta-analysis

Table 2

Cluster	Volume (mm^3)	Coordinates X	Y	Z	ALE value (*10^3)	Hemisphere	AAL Label
1	12616	42	-56	-4	35.8	Right	Inferior fusiform gyrus Inferior temporal gyrus Middle temporal gyrus Inferior occipital gyrus
2	11640	40	-7	-11	33.37	Right	Amygdala Hippocampus Parahippocampal gyrus Superior temporal gyrus Middle temporal gyrus
3	4304	-1	-55	25	27.62	Left	Posterior cingulate
4	4272	-41	-71	-10	17.68	Left	Fusiform gyrus Inferior occipital gyrus
5	4016	-38	-49	-21	30.46	Left	Fusiform gyrus
6	2864	-19	-10	-9	16.51	Left	Inferior temporal gyrus Parahippocampal gyrus Hippocampus Amygdala Thalamus
7	2704	-49	-53	19	14.57	Left	Superior temporal gyrus Inferior parietal lobule
8	2488	-4	48	38	16.55	Left	Medial frontal gyrus Superior frontal gyrus
						Right	Medial frontal gyrus
9	2344	-42	15	23	24.27	Left	Inferior frontal gyrus

Note. The table shows the results of the meta-analysis. Coordinates are reported in the Talaraich space

1.4.3 Results

I obtained a total of 9 clusters (see Figure 1 and Table 2) including: bilateral occipital lobes (inferior occipital gyri), bilateral temporal lobes (fusiform gyri, superior temporal gyri, middle temporal gyrus, parahippocampal gyri and amygdala), left frontal lobe (inferior frontal gyrus and superior medial frontal gyrus), left posterior cingulate and left inferior parietal lobe.

1.4.5 Discussion

The aim of the current meta-analysis was to document whether previous studies identified areas that were selectively associated with knowledge about conspecifics, regardless of the modality of presentation of the stimuli. The selected studies included both verbal and non-verbal stimuli, presented in the visual or auditory modality. Results highlighted several areas that are thought to be involved in processing conspecifics at different levels; these areas range from perceptual areas, such as the inferior occipital and temporal cortices or superior temporal cortex, to affective processing areas such as the amygdala, medial prefrontal cortex and posterior inferior frontal gyrus, to high-order cognitive areas, as posterior cingulate and temporo-parietal junction.

The emergence of perceptual areas, including bilateral visual processing cortices (clusters 1, 4, and 5), such as the inferior occipital and fusiform gyri, (OFA and the FFA) and an auditory processing area located at the level of right superior temporal gyrus (cluster 2), confirmed the evidence of specialized human processing areas within the visual and auditory systems (see Gainotti et al., 2015, for a recent review). It is worth noting that, while activations of the visual system were bilateral, activations of auditory system were only located within the right hemisphere.

Results also showed the involvement of bilateral amygdala (clusters 2 and 6) and medial prefrontal cortex (MPFC) (cluster 8), areas that are widely inter-connected with each other and very often associated to emotional and social stimuli processing (see Fossati, 2012, for review). The role of the amygdala in emotional processing has been widely investigated in both human brain imaging and animal studies. Specifically, amygdala function has been found to be associated with fear conditioning, an experimental paradigm in which a neutral stimulus might induce defensive behaviour as effect of emotional learning (Phelps and LeDoux, 2005; Bückel and Dolan, 2000). Moreover, as a consequence of a lesion of the amygdala, individuals tend to show impaired fear processing, perceiving a reduced experience of fear (Feinstein et al., 2011). More recently other evidence challenged the notion of amygdala as an area dedicated to processing aversive stimuli (Öhman and Mineka, 2001). In fact, the amygdala was found to be active even in presence of positive stimuli (Sergerie et al., 2008), thus suggesting that it might well be involved in processing self-relevant stimuli (Fossati, 2012).

Conversely, MPFC that is part of the default mode network (DMN) has been associated with several different functions (Roy et al., 2012). Indeed, it was found to be relevant in emotion (Wager et al., 2008), economic evaluation (Rangel and Hare, 2010), theory of mind (Amodio and Frith, 2006), semantic memory (Buckner and Carroll, 2007; Binder et al., 2009) and endocrine/autonomic regulation (Fellows and Farah, 2003). Taken together, these findings led some authors to suggest that MPFC might work as a hub, integrating many different inputs, and representing conceptual knowledge useful for survival and translating this knowledge into affective behavioural and physiological responses (Roy et al., 2012).

Another important area which lighted up in my meta-analysis was the left inferior frontal gyrus (IFG) (cluster 9), which is quite often found to be active in many fMRI studies and its function has been associated to semantic processing, phonological processing and working memory (Liakakis et al., 2011). In the current meta-analysis, I found a significant cluster located within the posterior part of IFG, which is held to process facial emotions as both neuroimaging on healthy participant and patients' studies showed (Blakemore, 2008; Shamay-Tsoory et al., 2009).

We also found bilateral activations within the temporo-parietal junctions (clusters 1 and 7). This area has commonly been found activated in social and attentional (i.e., re-orienting of attention) tasks (Carter and Huettel, 2013; Krall et al., 2016). Specifically, TPJ activation is particularly consistent in experiments on theory of mind, in which participants are required to infer other person's mental states (Saxe, 2010).

The role of PCC (cluster 3) is more controversial. If on the one hand it is acknowledged that it is part of the DMN (Raichle et al., 2001), and particularly active during autobiographical retrieval and planning future events (Buckner et al., 2007), suggesting that it might support internally driven cognition, on the other different studies highlighted the role of the PCC in regulating the focus of attention (Gusnard and Raichle, 2001; Hampson et al., 2006; Hahn et al., 2007).

Taken together our results showed a network of areas involved in the selective processing of conspecifics, including perceptual, emotional and high-order processing areas. This meta-analysis while it offers a picture of the relevant network involved in processing conspecifics, however it does not allow disentangling different theories. While the existence of a dedicated network for processing conspecifics supports the DSH, the activation of modality-specific areas (including emotions) speaks in favour of sustain the CZT or the CTT. This issue required to be tested with ad-hoc studies that will be presented in the following chapters.

CHAPTER 2

The neural network associated with lexical-semantic knowledge about social groups

This chapter is a modified version of the following paper: Piretti, L., Carnaghi, A., Campanella, F., Ambron, E., Skrap, M., & Rumiati, R. I. (2015). The neural network associated with lexical-semantic knowledge about social groups. *Cortex*, *70*, 155-168.

Abstract

A person can be appraised as an individual or as a member of a social group. In the present study we tested whether the knowledge about social groups is represented independently of the living and non-living things. Patients with frontal and temporal lobe tumors involving either the left or the right hemisphere performed three tasks - picture naming, word-to-picture matching and picture sorting - tapping the lexical semantic knowledge of living things, non-living things and social groups. Both behavioural and voxel-based lesion-symptom mapping (VLSM) analyses suggested that social groups might be represented differently from other categories. VLSM analysis carried out on naming errors revealed that left–lateralized lesions in the inferior frontal gyrus, amygdala, insula and basal ganglia were associated with the lexical-semantic processing of social groups. These findings indicate that the social group representation may rely on areas associated with affective processing.

2.1 Introduction

Humans can be appraised as individuals or as members of social groups. When encountering Hillary Clinton, for instance, we might recognize her as an individual, characterized by idiosyncratic features (e.g., her name, her psychological states or characteristics, such as extroversion), or as a member of a broader group (e.g., woman, politician, American). Based on neuropsychological evidence, and corroborated by neuroimaging studies (Haxby et al., 2002; Tsukiura et al., 2006), it has been suggested that the appraisal of our conspecifics involves distinct stages, including the person perception (their face, voice, gait and mannerisms), the semantic knowledge about other persons and the lexical retrieval of their names (Bruce & Young, 1986; Campanella et al., 2013). The evidence supporting the organization of the person related information in three different processing levels will be discussed in the following.

First, patients suffering from apperceptive prosopagnosia are impaired at forming the representation of faces from visual inputs such as age, ethnicity and gender (Young and Ellis, 1989; Kracke, 1994; de Haan and Campbell, 1991) following lesions in occipito-temporal areas (see Davies-Thompson et a., 2014, for a recent review). On the other hand, patients with associative prosopagnosia and lesions of the right anterior temporal lobe (ATL), after having formed a face representation successfully, may fail to associate an identity to a face structure (e.g., De Renzi, 1986; Farah et al., 1995).

Second, what we know about the identity of other people, in addition to the person-specific knowledge, also includes their psychological or internal states (social concepts, e.g., loyal; Zahn et al., 2007) and the knowledge about the social group an individual primarily belongs to (i.e., social groups). Thus, while recognizing Hillary Clinton as an individual implies to link some specific perceptual features to unique semantic and lexical features (Gorno Tempini and Price, 2001), including knowledge about social concepts (Zahn et al., 2007), identifying her as a woman relies on a more general knowledge that can be applied to many other individuals who have in common the characteristic of being a woman.

Third, even if the face structure and semantic and social identity have been correctly built, there might be patients who are unable to retrieve specific names of people they are supposed to know, despite showing intact person-specific knowledge and being still able to name living and non-living things (McKenna and Warrington, 1980; Lucchelli and De Renzi, 1992). This deficit, called proper name anomia, is caused by lesions in the left temporal pole that often affects also famous landmark naming (Gainotti, 2007).

In the current study we set out to investigate visual, semantic and lexical processes involving social groups, living things and non-living things in patients with brain tumors and neurologically intact individuals. As suggested by several strands of evidence that we will briefly review in the following sections, people's lexical-semantic knowledge about both the individual and social group level is likely to be represented independently of what they know about living and non-living things.

A first piece of evidence is provided by a double dissociation between patients with encephalitis, neurodegenerative diseases and traumatic brain injury with a person-specific knowledge deficit (i.e., loss of biographical information about famous people) but spared knowledge about other categories (Hanley et al., 1989; Evans et al., 1995, Miceli et al., 2000), and patients with the opposite and less frequent pattern, that is spared knowledge about conspecifics but a loss of knowledge about other categories such as animals, vegetables, and tools (Kay and Hanley, 2002; Lyons et al., 2006; Thompson et al., 2004). A similar dissociation between social concepts and animal concepts (animal behaviours and properties) has been observed in patients with fronto-temporal dementia, especially those with a more pronounced hypometabolism in the anterior temporal lobe (Zahn et al., 2009). This is the same region that lighted up when, in an fMRI study with healthy individuals, social concepts were compared with concepts about animal functions (Zahn et al., 2007), or with clothes and fruit (Mitchell et al., 2002). In addition, processing social concepts also led to the activation of the dorso-medial prefrontal cortex (DMPFC) and left parieto-temporal junction (TPJ) (Mitchell et al., 2002; Zahn et al., 2007).

Overall, this neuropsychological and neuroimaging evidence seems to suggest that person-specific knowledge (including social concepts) and knowledge about living and non-living things might be supported, at least in part, by different neuromechanisms. By contrast, only a few studies have addressed the issue of whether the knowledge about social groups - defined as categories of individuals that share common category-relevant characteristics and/or features (Contreras et al., 2011; Rumiati et al., 2014) - is represented independently of the knowledge about other categories and has brain correlates of its own. In a neuropsychological study, Rumiati et al. (2014) found that patients with a presumptive diagnosis of dementia double dissociated in performing word sorting tasks of living things, non-living things and social groups. Likewise, using fMRI, Contreras et al. (2011) found an activation of the medial prefrontal cortex (MPFC), posterior cingulate (PCC) and bilateral TPJ when contrasting social groups versus non-social objects (artifacts and animals) in a feature verification task, and an activation of left inferior frontal gyrus (lIFG) and infero-temporal cortex when contrasting non-social versus social stimuli. The double dissociations between the different categories (social groups, living things and non-living things) observed in patients with dementia (Rumiati et al., 2014), and the different sites of activation for social and non-social stimuli (Contreras et al., 2011), indicate that social groups may constitute a category independent of other living or non-living categories. However, although these two studies have the general common goal of assessing the status of the representations about social groups, they are not directly comparable as they differed for the stimuli, tasks and methods used. In the former study (Rumiati et al., 2014), patients sorted names of different entities into categories including social groups, while in the latter (Contreras et al., 2011) they had to decide which of two groups was related to a specific stereotype-congruent behaviour or attitude. Moreover, it remains unclear which are the brain areas that when lesioned may give rise to a deficit in processing social groups, as in Rumiati et al. (2014) the behavioural deficit could not be correlated with brain volumes in the patients with dementia. This lack of information does not allow us to argue that the knowledge about social groups recruits a neural network distinct from those recruited by living and non-living things, as tentatively suggested by Contreras et al. (2011).

That the knowledge about conspecifics might be independent of other types of knowledge (i.e., living and non-living things) is still a matter of debate. Indeed, the severe multi-modal semantic impairments observed in patients with semantic dementia - a neurodegenerative disease associated to ATLs atrophy - led to suggest that ATL serves as an amodal semantic "hub" in which inputs from different modality-specific brain areas converge and are integrated (the hub-and-spoke theory, Rogers et al., 2004; Patterson et al., 2007). Hence multi-modal representations of concepts are held to be housed in the ATL. More recently damage to the ATL has also been linked to inappropriate social behaviours (Chan et al., 2009), to social concepts impairment (Zahn et al., 2009) and to person-specific knowledge (Olson et al., 2012). Based on this evidence, some authors suggested that the ATL may play a critical role in representing social (social knowledge hypothesis of ATL, Skipper et al., 2011; Olson et al., 2012).

One critical aspect that should be taken into account is the specificity of the stimuli. Evidence in support of the hub-and-spoke theory is by and large provided by cases of semantic dementia, a condition that is characterized, even at early stages, by the loss of specific knowledge, with patients naming for instance a chicken "bird" or "animal", while the superordinate knowledge remains available for a longer time (e.g., Patterson et al., 2007). In contrast, evidence in support of the social knowledge hypothesis mostly relies on studies in which the person knowledge has been investigated only at a very specific level of representation (i.e., famous or familiar persons). It is worth noting that specific level entities are also more demanding for the semantic system, and that some recent fMRI (Visser and Lambon Ralph, 2011) and TMS (Pobric et al., 2007) studies showed that the ATL is also implicated in processing subordinate or basic level concepts. Thus, there are three possible hypotheses about the role played by ATL: it might only deal with the specific-level of processing (irrespective of the category), as suggested by Martin (2007), it might selectively process social knowledge (Skipper et al., 2011) or it might represent multimodal semantic concepts (Rogers et al., 2004).

Moreover, the relative contribution of left and right ATL in processing person knowledge remains undecided. In fact, according to Thompson et al. (2004), person knowledge is cross-modal and likely to be represented as a category within the right ATL, while general semantic processing may rely on left ATL. However, in Snowden et al.'s view (2004; 2012), person knowledge, as general semantic knowledge, is expected to be represented in modality-specific areas, with the right ATL being important for visual processing, and the left ATL for verbal processing.

Patients with unilateral brain damage have been reported with impaired performance on tasks involving verbal production as in picture naming, but spared recognition abilities (Lambon Ralph et al., 2010; Lambon Ralph et al., 2012; Drane et al., 2008). Moreover, patients with semantic dementia tend to show different types of impairment depending on the predominant laterality of the atrophy, with patients with more pronounced left atrophy showing disproportionate production impairment compared to comprehension, and patients with a more pronounced right atrophy showing a similar impairment in production and comprehension (Lambon Ralph et al., 2001). The explanation of these findings is still a matter of debate. On the one hand, Snowden et al. (2004) proposed that the right ATL is involved in processing visual stimuli, and the left ATL in processing verbal stimuli, while on the other, Rogers et al. (2004) proposed a model in which semantic knowledge is stored in bilateral areas and includes partially redundant information. Damage to the left semantic storage, which provides the main inputs to a left-sided phonological area, will impair verbal production, while damage to the right ATL will not lead to any impairment, since semantic information is redundant in the two hemispheres.

We used social groups as stimuli to test a level of specificity different from the one normally investigated with familiar and famous people (e.g., Gainotti, 2007). More in general, this study evaluated whether, relative to healthy controls, the performance of patients with a unilateral left or right hemisphere tumor in the temporal or frontal lobe on three different tasks differed across categories depending on the side and site of the lesion. As expected on the basis on previous studies (Rumiati et al., 2014; Contreras et al., 2011), we hypothesized that, if the knowledge about social groups is independent of other categories (living and non-living things), the patients' impaired performance on social groups should be caused by lesions in brain areas that are different from those affecting the performance with the other categories.

More specifically, if the knowledge about other humans, including social groups, is represented in distinct modality-dependent areas as proposed by Snowden et al. (2004), left-brain damaged patients (LBD) should be more impaired than both right-brain damaged patients (RBD) and healthy controls with verbal tasks involving social groups. On the other hand, RBD patients were expected to be more impaired when performing visual tasks than both LBD and healthy controls. Conversely, if the knowledge about conspecifics is represented categorically within the right ATL (as suggested by Thompson et al., 2004), RBD patients should have impaired knowledge about social groups, and LBD patients should have impaired knowledge about living and non-living things. The hub-and-spokes theory and the social knowledge hypothesis do not seem to make any clear prediction as to the lateralization of the deficit. Only we can say is that the former predicts that the impairment on all the three categories should be associated to overlapping lesioned areas within the ATL, and the latter that the impairment in processing social groups should be associated with lesions to specific areas. As mentioned earlier, imaging studies reported frontal areas also implicated in the evaluation of social groups and in representing mental states of social groups. Thus, if the evaluation and the mental state attribution were an epiphenomenon of social group processing, lesions of the medial prefrontal cortex should not affect patients' performance with social groups. However if the evaluation and/or mental state attribution are necessary to fully access the knowledge about social groups, the lesion in this region of the cortex should damage the mental state processing or group evaluation resulting in a reduced performance on social groups (for a similar rationale, see Zahn et al., 2007). We also expected that a deficit in processing non-living things correlated with the left posterior middle temporal gyrus and, the deficit in processing living things with the lateral part of the fusiform gyrus and superior temporal sulcus (Martin, 2007, for a review).

The same set of stimuli was used in the three different tasks that tapped the lexical-semantic processes in order to identify at which processing level the deficit occurred. While, picture naming requires intact visual recognition and verbal production, word-to-picture matching taps both visual and verbal recognition of the item, bypassing verbal production. Moreover, the analysis of participants' error types in the naming task were also analysed to further characterize the locus of the deficit, with circumlocutions and anomias indicating a faulty lexical-semantic processing, and visual errors tapping a perceptual deficit. The picture sorting task, that aims at establishing the integrity of the knowledge about the category the stimulus belongs to, does not require participants to access to the specific knowledge about a stimulus (e.g., dog) but only to its superordinate (e.g., living). We included in the study patients with different tumor histologic types (i.e., high grade gliomas, low grade gliomas, meningiomas, and metastasis). Although their growing rate is quite heterogeneous across patients and, as such, it consequently may give rise to compensation effects (i.e., patients with LGG show cognitive deficits only in 10-20% of cases, see DeAngelis, 2001), testing both HGG and LGG patients after surgery might reveal impaired cognitive functions (Campanella et al., 2015).

2.2 Methods

2.2.1 Participants

Thirty-five patients (10 females, age = 49.2±15.2, education = 12.1±4.1) with unilateral brain tumors either in the left or right hemisphere, and twenty-five healthy participants (14 females, age = 54.8±13.7, education = 11.6±4.0) took part in the study (see, Table 3). Patients' lesions were located either in the left frontal lobe (LF, N = 10), left temporal lobe (LT, NN = 10), right frontal lobe (RF, N = 7), or right temporal lobe (RT, N = 8). If the lesion involved both the frontal and the temporal lobes, the patient was assigned to either one or the other group depending on which lobe was more affected by the tumor (and decided after detecting the center of the lesion after normalization). Unfortunately our sample does not include patients with right temporal pole lesions. According to the histology, our sample included 18 high grade gliomas (HGG), 11 low grade gliomas (LGG), 5 meningiomas and one metastasis. Chi-square analysis showed that tumor type did not differ across patient groups (χ^2 (3) = 3.05, p = .38). The exclusion criteria were the presence of neurological or psychiatric disease, previous brain surgery and diffuse lesions (e.g., gliomatosis cerebri). Healthy controls were selected to match patients for age and education.

Table 3: Participants' demographic information.

Group	Side	Site	N	Age (SD)	Education (SD)	Days after surgery (SD)
LF	Left	Frontal	10	53.5 (16.7)	11.9 (3.7)	7.7 (2.1)
LT		Temporal	10	47.3 (15.4)	10.7 (3.9)	6.4 (0.8)
RF	Right	Frontal	7	42.7 (16.6)	13.1 (5.1)	8.3 (3.0)
RT		Temporal	8	51.8 (11.5)	13.0 (4.4)	6.9 (4.0)
Controls			25	54.8 (13.7)	11.6 (4.0)	-

Note. Mean age, education and delay between surgery and experimental examination (days after surgery).

Table 4: Neuropsychological assessment

Group	Token	Flu	FAB	Rey-fig copy	Benton	Vis search	Star	Span-f	Span-b	Corsi	Prose	Rey-fig del
LF	27.3	17.6	14.4	29.8	22.3	41.4	53.8	4.7	3.3	4.0	15.9	15.1
	(8.6)	(15.8)	(1.0)	(5.5)	(3.0)	(15.7)	(0.4)	(1.3)	(0.9)	(0.5)	(2.8)	(4.1)
LT	26.6	30.5	14.5	31.8	24.2	42.9	53.8	4.2	4.2	4.5	12.4	19.0
	(6.0)	(21.0)	(2.8)	(3.3)	(2.1)	(11.3)	(0.6)	(1.1)	(1.4)	(1.0)	(3.9)	(5.0)
RF	32.2	35.1	15.7	27.3	22.0	44.5	53.1	5.1	4.1	4.3	18.1	17.0
	(1.1)	(9.4)	(1.2)	(5.1)	(2.3)	(5.3)	(1.9)	(1.6)	(1.1)	(1.0)	(4.3)	(6.0)
RT	32.5	45.6	15.6	28.6	21.4	40.9	53.3	6.0	5.1	5.3	20.4	15.4
	(0.9)	(16.6)	(1.7)	(6.1)	(2.4)	(14.5)	(1.0)	(1.2)	(1.6)	(0.8)	(2.3)	(4.7)

Note. Patients' mean scores and standard deviations on the neuropsychological battery: Token + Token test, Spinnler and Tognoni, 1987; Flu = Verbal fluency, Carlesimo et al., 1995; FAB = Frontal Assessment Battery, Apollonio et al., 2005; Rey-fig copy = Rey Figure immediate copy, Caffarra et al., 2002; Benton = Benton facial recognition test, Benton et al., 1990; Vis search = Visual search, Spinnler and Tognoni, 1987; Star = Star Cancellation, Wilson et al., 1987; Span-f = Digit span forward, Orsini et al., 1987; Span-b = Digit span backward – qualitative score, Orsini et al., 1987; Corsi = Corsi spatial span, Orsini et al., 1987; Prose = Memory of Prose, Novelli et al., 1987; Rey-fig del = Rey Figure delayed copy, Caffarra et al., 2002.

2.2.2 Neuropsychological assessment

After surgery to remove the tumor, patients underwent a neuropsychological assessment (Table 4) of language (Token test), executive functions (Frontal Assessment Battery, FAB, verbal fluency), attention (visual search, stars cancellation), face recognition (Benton Facial Recognition), visuo-spatial ability (Rey figure copy) short- (digit span forward and backwards, Corsi spatial span) and long-term memory (Memory of Prose, Rey figure delayed copy).

2.2.3 Experimental tasks

The experiment was approved by the SISSA ethics committee, and all patients gave their informed consent to participate to the study. The experimental tasks were administered 7 days after surgery (± 3) in a different session from the neuropsychological assessment, and lasted nearly one hour. Stimuli included 45 coloured pictures divided into three categories: living things (N = 15; animals, plants), non-living things (N = 15; tools, clothes, means of transport) and social groups (N = 15; a subset of stimuli used by Rumiati et al., 2014, e.g., Asians, clerks, obese) (see Table 5 for the complete list of items). Since our aim was to test the knowledge about social groups, which is a basic/superordinate type of knowledge, and not person-specific knowledge, we did not include pictures of famous people.

In order to choose the experimental stimuli two pilot studies were performed. In the first study we selected the social groups. A sample of 44 Italian native speakers was asked to generate names with which people tend to categorize other people. We then selected the 20 most frequent names from those indicated by the participants. Then pictures of 20 socials groups, 20 pictures of living things, and 20 of non-living things were presented to 19 healthy participants. The final 45 pictures (15 for each category) were chosen among those that reached the highest name agreement. The stimuli belonging to the three categories were matched for letter length and written frequency (all *ps* $> .05$), and were used in three different

Table 5

Category	Item	Translation
Living	albero	tree
	farfalla	butterfly
	cane	dog
	tartaruga	tortoise
	castagna	chestnut
	peperone	pepper
	serpente	snake
	gatto	cat
	coccodrillo	crocodile
	coniglio	rabbit
	elefante	elephant
	fiore	flower
	cavallo	horse
	pappagallo	parrot
	mela	apple
Non-Living	cappello	hat
	bicchiere	glass
	Borsa	bag
	cacciavite	screwdriver
	Finestra	window
	occhiali	glasses, spectacles
	schiaccianoci	nutcracker
	chiave	key
	cucchiaio	spoon
	bottiglia	bottle
	posacenere	ashtray
	automobile	car
	piatto	plate
	forchetta	fork
	elicottero	helicopter
Social groups	musulmani	Muslims
	immigrati	Immigrants
	giovani	Youth
	anziani	Elderly
	cinesi	Chineese people
	europei	Europeans
	donne	Women
	laureati	Graduate
	obesi	Obese people
	studenti	Students
	omosessuali	Homosexuals
	impiegati	Employee
	politici	Politicians
	africani	Africans
	disabili	Disabled

tasks: picture naming, word-to-picture matching and picture sorting. In addition, we collected age-of-acquisition (AoA) and familiarity scores for all 45 stimuli. AoA has been found to influence picture naming performance (Brown and Watson, 1987; Papeo et al., 2010), with items acquired earlier tending to be more resilient to damage compared to items learnt later in development (Morrison et al., 2003; see also Papeo et al., 2010). A total number of 18 healthy individuals rated at which age they acquired the knowledge for each word presented (45 items presented in random order), using a 1 to 7 Likert scale, with 1 indicating up to three years, 2 between four and five years, and so on, up to 7 that indicated more than 13 years. Then the same participants also rated how familiar they were with the same words, using a 1 to 7 Likert scale (1 totally unfamiliar, 7 completely familiar). The AoA ratings differed across semantic categories (all *p*s < .01); in particular, living things were reported as being acquired earlier (less than three years) than social groups later (between 8 and 9 years) and non-living things (between the four and five years). Familiarity ratings significantly differed only between non-living things and social groups (*p* < .05), with social groups being less familiar than non-living things. Moreover, Spearman's correlations between the mean accuracy across patients were calculated for each item belonging to the three categories and the corresponding AoA and familiarity ratings. Results showed that living things and non-living things (but not social groups) significantly correlated with each variable. We performed a multiple backward regression analysis, using as dependent variable the average patients' scores for each item and as independent variable the stimuli's AoA, the familiarity and category. The analysis revealed that AoA was the only significant predictor (B = -.068, Beta = -.721, p < .05), accounting for the 37 % of naming variance. We also explored the relative contribution of AoA to the performance on each category. We carried out the same analysis (except for category, that was not used as predictor), for each of the three categories. The analyses revealed that the model was not significant for both living things and social groups, while for non-living things AoA significantly accounted for the 48% of variance (B = -.056, Beta = -.691, p < .001). The order of the stimuli and of the tasks was the same across participants.

2.2.3.1. Picture naming task

Participants were presented with 45 consecutive coloured photographs (each sized 13x21 cm), each printed on the center of an A4 sheet in a landscape orientation, and asked to name them as accurately as possible. These stimuli belonging to the three categories (living things, non-living things, social groups) were presented in pseudorandom order. This task required participants to accurately perceive the stimuli, associate them with the corresponding meanings, and retrieve their nouns. To prevent participants from naming pictures too specifically or too generally, we excluded pictures of famous people and selected photographs depicting groups of people with salient group-specific features. Participants' accuracy and type of errors were recorded and categorized into different types. Participants' errors were categorized as follows: good circumlocutions (when patients provide a relatively good description of the target word, e.g., "The man's best friend", following the presentation of the picture of a dog), poor circumlocutions (when patients provide a rather impoverished description of the target word, e.g., "The animal with fur"), anomias (when patients do not produce any word), semantic paraphasias (the patients' response is semantically related to the target word, e.g., "kennel" for 'dog'), verbal paraphasias (the patients' response is not related to the target word, e.g., ceiling instead of 'dog'), phonological paraphasias (the patients' response differs from the target word for one phoneme, e.g., "dob" instead of 'dog'), visual errors (the patients' response denote an item that is perceptually similar to the one denoted by the target word, e.g., table), and visual-semantic errors (this is the case of a response that can shares both visual and semantic characteristics with the target e.g., "fox" instead of "dog". The error analysis can contribute to identify the locus of the eventual breakdown (e.g., degraded storage, impaired access to the semantic store, impaired lexical access).

2.2.3.2 Word-to-picture matching task

In this task, patients were asked to indicate among four alternatives, which photograph corresponded to the target named by the examiner. Participants were presented with 4 coloured photographs, (each sized 8x12 cm), randomly arranged in a 2x2 matrix on an A4 paper sheet in a landscape orientation. In addition to the target (e.g., African-Americans), the remaining three photographs used a distractors belonged to the same category as the target (e.g., students, homosexuals and disables). On each trial, the participants were asked to point to the picture that matched the noun uttered by the experimenter, for a total of 45 trials. Target stimuli were the same as in the picture naming.

2.2.3.3 Picture sorting tasks

The participants performed three consecutive picture-sorting tasks (30 trials for each sorting task, including 15 related to one category and 15 related to another one). On each sorting, the participants were presented with a block of coloured cards (each sized 10.5 x15 cm) randomly shuffled, depicted each an experimental stimulus. Stimuli belonged to two categories and participants were asked to place each of them under two labels: living things and non-living things (sorting 1), living things and social groups (sorting 2), and non-living things and social groups (sorting 3). To perform this task participants must access to the knowledge of the category the item belongs to. As such, the task does not necessarily require to access to the specific knowledge about a particular exemplar, but only to the information about its superordinate.

2.2.4 Statistical analyses

A series of univariate analyses of variance (ANOVA) with side (left, right) and site (frontal, temporal) as a between subject factors, and the patients' scores on the neuropsychological tests as the dependent variables (Token test, Verbal fluency, Frontal Assessment Battery, Visual Search, Stars Cancellation, Benton Facial Recognition, Rey Figure immediate and delayed copy, Digit span forward, Corsi spatial span and Memory of Prose) was performed in order to highlight possible cognitive differences between the patient groups on the different tests.

A repeated-measures ANOVA was performed on the naming accuracy scores of each category of stimuli as dependent variable, with category (living things, non-living things and social groups) as within-subject factor, and side (left, right) and site of lesion (frontal, temporal) as between-subject factors. Moreover to compare patients and controls, we performed a series of independent sample t-tests between each group performance on the three categories and healthy controls'.

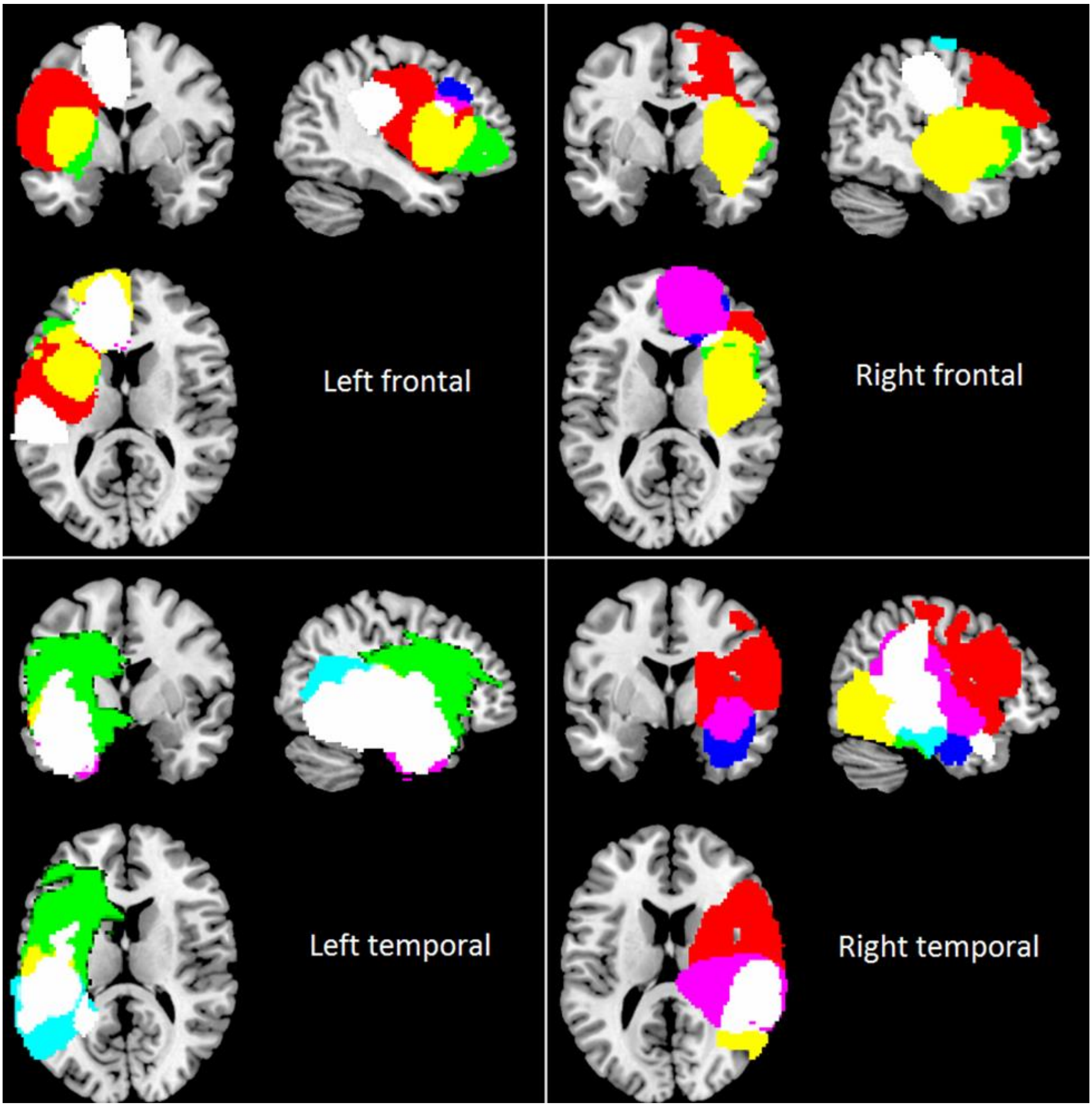
Since the histology of the tumor is thought to influence the growing rate of the tumor mass, and consequently lead to compensation effects, we performed again the same ANOVA, adding the tumor type as between-subject factor. It is worth noting that we considered two main tumor types, based on the histological grading of the tumor: high grade included fast growing tumors that tend to infiltrate adjacent tissues (HGG and metastasis) and lead to more severe deficits, whereas low grade tumors (LGG, meningiomas) tend to increase their volume slowly and compress neighbouring tissues.

Mann-Whitney U tests were performed on each error type using the percentage of errors as a dependent variable and patient sub-groups as independent variable. Moreover two series of Spearman's correlations (one on RBD patients and the other on LDB patients) were performed between patients' raw naming scores on each semantic category, and scores on the neuropsychological tests; the magnitude of the correlations between LBD and RBD patients was also tested. Finally, to confirm that the level of specificity (i.e., the extent to which a concept can be applied to different entities) of the items was similar for the three categories, we had 12 participants rate the level of specificity of each word on a Likert scale ranging from 1 (general) to 7 (specific). A few examples were provided to be sure that participants understood the task (e.g., a list of words ranging from general to specific: "animal, mammal, elephant, white elephant, Dumbo").

2.2.5 Lesion Analysis

In order to compare the patients' performance on the experimental tasks with brain lesions we performed a first voxel-based lesion-symptom mapping (VLSM, Bates et al., 2003). This analysis sorts for every voxel two distinct groups of patients (lesioned, not lesioned), and then compares the behavioural performance of the two groups, returning maps of areas associated with behavioural deficits. On each patient' structural MRI (T1 or T2-weighted), a region of interest (ROI) was traced on each horizontal slice using MRIcron software (http://www.mccauslandcenter.sc.edu/mricro/mricron). Lesions were mapped using patients' preoperative MRI scans, as in post-operative MRI scans parenchymal dislocations may lead to biases in the lesion mapping (see Campanella et al., 2014, for similar procedure and argument). Both the patients' scans and ROIs were then normalized using spm8 software, in order to be comparable (see Figure 2, for lesion overlap maps).

Figure 2



Note: The figure shows the extension of the lesions in the four subgroups of patients.

Then the NPM (non-parametric mapping, (http://www.mccauslandcenter.sc.edu/mricro/mricron) software was used to perform the VLSM, setting the Brunner-Munzel test and 1000 permutations, and ignoring voxels lesioned in less than three patients. A first VLSM was performed using as dependent variable a score obtained by subtracting the average accuracy score on the picture naming task from the picture naming scores for each of the three categories. This computation allows us to show the specific contribution of each of the three categories, ignoring general naming deficits. A second VLSM analysis was performed using the patients' errors on the picture naming task as continuous behavioural variable. To perform such analysis we computed the error ratio between the absolute error rate on each error type (divided by category), and the naming accuracy for each patient. Then, for each error type, we subtracted the average error rate for each category from the error rate (divided by category) and we used this score as dependent variable for the VLSM. This computation is important because it allows correcting the error rate for the total amount of errors and it highlights possible categorical differences in the error production. Additionally, we have run the same analysis using the average between anomia and good circumlocutions scores, in order to find areas associated with word-finding problems.

Since the patients performed at ceiling level on the word-to-picture matching and picture sorting tasks, we did not perform the VLSM analyses on the scores on those tasks.

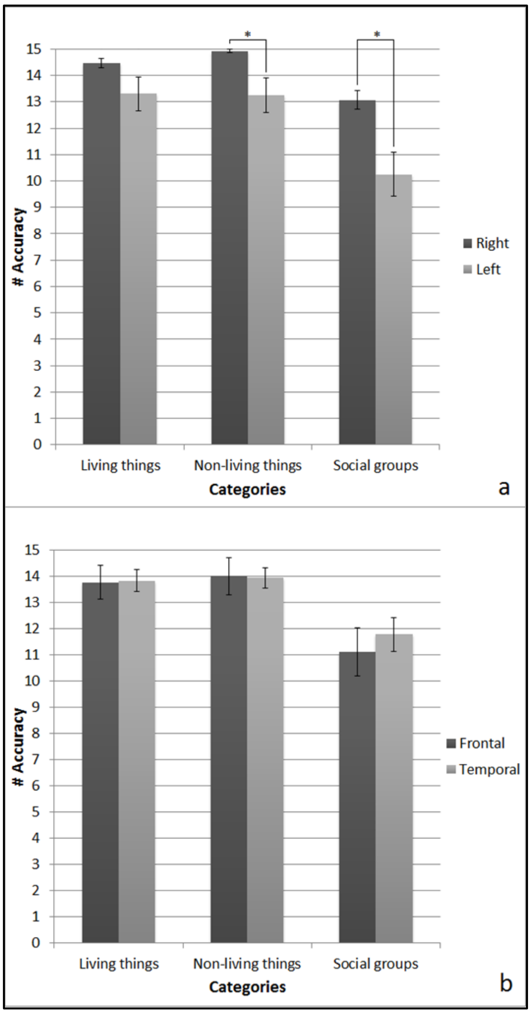
2.3 Results

2.3.1 Neuropsychological assessment

The univariate ANOVAs on the neuropsychological tests (Table 2) revealed significant main effects of side for the Token test ($F(1,30) = 6.43, p < .05$), Verbal Fluency ($F(1,30) = 4.84, p < .05$), Digit Span forward ($F(1,30) = 8.00, p < .01$), Digit Span backward ($F(1,30) = 5.25, p < .05$) and Memory of Prose ($F(1,28) = 26.09, p < .000$), and significant main effects of site for

Verbal Fluency (F(1,30) = 4.53, p < .05), Rey figure immediate copy (F(1,29) = 5.22, p < .05), Digit Span backward (F(1,30) = 10.83, p < .005), and Corsi spatial span (F(1,30) = 7.35, p = .001), but no significant interactions between side and site. More specifically LBD patients performed worse than RBD patients on the Token test, Verbal fluency, Memory of Prose, Digit Span Forward and Backwards. Moreover, patients with lesions in the frontal lobes were worse than those with lesions within the temporal lobes on the Rey figure immediate copy, Digit span backwards and Corsi's spatial span, whereas lesions within the temporal lobes gave rise to lower performance on Verbal fluency task, than frontal lesions.

Figure 3



Note: Mean accuracy (Z-scores) on Picture Naming task for each side (Left, Right) (panel a) and site (Frontal, Temporal) (panel b) divided by category (living things, non-living things, social groups). * p < .05, ** p < .005

2.3.2 Picture naming task

The repeated measure ANOVA on naming raw scores showed significant main effects of category ($F(1.3,40) = 46.37$, $p < .001$), side ($F(1,31) = 5.46$, $p < .05$), and a significant interaction of category x Side ($F(1.3) = 4.35$, $p < .05$). To better understand the category x side interaction, pairwise comparisons with Bonferroni corrections were carried out and revealed that LBD patients performed significantly worse than RBD patients on non-living things ($p < .05$) and social groups ($p < .05$), but not on living things ($p = .13$) (see Figure 3a). Moreover both LBD and RBD were more impaired in naming social groups than living things (LBD: $p < .001$; RBD: $p < .05$) and non-living things (LBD: $p < .001$; RBD $p < .05$)), while no difference between living and non-living things occurred (LBD and RBD: $p > .05$). LBD patients performed significantly more poorly than healthy controls on all the categories of stimuli (living things: $t(19.7) = 2.29$, $p < .05$; non-living things: $t(19.15) =-2.63$, $p < .05$; social groups: $t(22.24) = -3.54$, $p < .01$), whereas RBD patients did not perform differently from healthy controls (all ps > .05). Both patients' and controls' naming scores as a function of the category are reported in the Table 6.

Although the category x site interaction was not significant, for exploratory sake, the participants' raw accuracy score was compared with healthy controls' as a function of category and site (see Figure 3b). These analyses revealed that frontal tumor patients' scores were significantly lower than those of healthy controls only in naming social groups ($t(18.28)= -2.33$, $p < .05$), (living non-living things were not significant: ps > .05) whereas temporal tumor patients' performance was worse than that of healthy controls on all the categories (living things: $t(18.46)= 2.15$, $p < .05$; non-living things: $t(17.3) = 2.64$, $p < .05$; social groups: $t(21.87) = 2.24$, $p < .05$). The same ANOVA as above was carried out using the tumor type as independent factor. Results showed that the tumor type did not interact with any other factors (i.e., side, $p = .31$, site, $p = .54$, category, $p = .20$), neither did it moderate the first order or the second order interactions (p = .19). The type of tumor did not show a significant main effect (p = .23), Hence, the variable can be discarded from the analyses.

Table 6: Picture naming: raw data.

Side	Site	Living		Non-Living		Social	
		Mean	SD	Mean	SD	Mean	SD
Controls	Controls	14.76	0.44	14.96	0.20	13.32	1.22
Right	Frontal	14.71	0.49	15.00	0.00	12.86	0.90
	Temporal	14.25	0.71	14.88	0.35	13.25	1.75
	Total	14.47	0.64	14.93	0.26	13.07	1.39
Left	Frontal	13.10	3.38	13.30	3.77	9.90	4.56
	Temporal	13.50	2.32	13.20	1.87	10.60	2.88
	Total	13.30	2.83	13.25	2.90	10.25	3.73

Note. Mean and Standard Deviations of patients' raw accuracy scores as a function of side (right vs. left), site (frontal vs. temporal) and category (living, non-living, and social).

2.3.2.1 Picture naming task: correlation analyses

The results of the correlation analyses are summarized in Table 7 for RBD and in Table 8 for LBD. RBD patients' naming social groups and living things positively correlated only with performance on an attentional task (Star Cancellation), whereas naming non-living things did not correlate with any neuropsychological test. LBD patients' overall naming (all categories) positively correlated with language comprehension (Token test), and executive functions (verbal fluency). More specifically, LBD patients' naming social groups correlated with another executive test (FAB), with an attentional test (Star Cancellation) and tasks tapping visuo-spatial short-term memory (Corsi's spatial span), naming living things positively correlated with short-term memory (Digit Span Forward), while naming non-living things correlated with performance on tasks tapping long-term memory (memory of prose). Moreover naming both non-living things and social groups positively correlated with performance on an attentional task (Visual Search). Importantly naming social groups did not correlate with facial recognition (Benton's test)

The analysis of the correlations' magnitude between LBD and RBD patients (see Table 9) revealed that correlations between a comprehension task (Token test) and the naming task were significantly higher in LBD than in RBD patients for each category. The same pattern of results was obtained when correlations between long-term memory (memory of prose) and non-living things, and working memory (Digit Span Backwards) and social groups were performed. Importantly there was no difference between LBD and RBD patients when correlations of executive functions (Verbal Fluency, FAB) with face recognition (Benton's test).

2.3.2.2. Picture naming task: error analyses

LT made significantly more good circumlocutions than LF patients in naming social groups (*p*s < .05), and more anomias than RF patients (*p* = .05) in naming both social groups and living things (see Table 10).

2.3.3 Word-to-picture matching task and picture sorting tasks

The results of the other two experimental tasks (word-to picture matching and picture sorting) were not analysed, as participants performed at ceiling level (word-to-picture matching task - mean accuracy > 98.5%; sorting task – mean accuracy > 98.5) and healthy control groups (word-to-picture matching – mean accuracy > 99.5%; picture sorting task – mean accuracy: all categories = 100%).

2.3.4 Level of specificity

Results showed that healthy controls named the items belonging to living and non-living things at the same level of specificity (*p* = .69), while social groups were named at a lower level of specificity than the other two categories (*p*s < .000).

Table 7: Correlations between picture naming accuracy and performance on neuropsychological tests of RBD.

Category	Token	Fluency	FAB	Rey-fig copy	Benton	Vis Search	Star	Span-f	Span-b	Corsi	Prose	Rey-fig delayed
Living things	-0.09	0.25	0.38	-0.03	0.24	-0.01	0.57*	-0.16	-0.14	-0.01	-0.30	0.18
Non-living things	0.03	0.17	0.43	0.25	0.35	-0.06	0.37	-0.06	-0.20	-0.06	-0.34	0.06
Social groups	0.05	0.50	0.17	-0.13	0.36	0.28	0.68**	0.07	-0.25	0.25	-0.11	-0.20

Note. Spearman's rho correlations of RBD patients between the raw accuracy scores on each category of the picture naming task and neuropsychological tests. * = *p* < .05 ** = *p* < .005 *** = *p* < .001.

Table 8: Correlations between picture naming accuracy and performance on neuropsychological tests of LBD.

Category	Token	Fluency	FAB	Rey-fig copy	Benton	Vis Search	Star	Span-f	Span-b	Corsi	Prose	Rey-fig delayed
Living things	0.70**	0.63**	0.25	0.43	-0.11	0.40	-0.03	0.47*	0.33	0.31	-0.12	0.17
Non-living things	0.86**	0.58**	0.35	0.23	-0.33	0.55*	0.19	0.55*	0.24	0.17	0.62**	0.07
Social groups	0.69**	0.73**	0.65**	0.22	-0.17	0.49*	0.15	0.41	0.33	0.46*	0.46	0.13

Note. Spearman's rho correlations of LBD patients between the raw accuracy scores on each category of the picture naming task and neuropsychological tests. * = *p* < .05 ** = *p* < .005 *** = *p* < .001.

Table 9: Magnitude of correlations between LBD and RBD performance on naming and neuropsychological tests.

Category	Token	Fluency	FAB	Rey-fig copy	Benton	Vis Search	Star	Span-f	Span-b	Corsi	Prose	Rey-fig delayed
Living things	-2.55*	-1.23	0.38	-1.28	0.86	-1.17	1.81	-1.77	-1.29	-0.88	-0.5	0.04
Non-living things	-3.36***	-1.24	0.27	0.06	1.77	-1.82	0.53	-1.79	-1.19	-1.4	-2.76**	-0.01
Social groups	-2.09*	-0.96	-1.54	-0.92	1.39	-0.66	1.82	-0.97	-2.01*	-0.65	-1.54	-0.83

Note. Fisher's z-transformation. * = $p < .05$ ** = $p < .005$ *** = $p < .001$.

Table 10: Picture naming: error types.

Group	Poor circ			Good circ			Anomia			Semantic par			Phonemic par			Verbal par			Visual error			Visual-semantic		
	L	NL	S	L	NL	S	L	NL	S	L	NL	S	L	NL	S	L	NL	S	L	NL	S	L	NL	S
LF	0	0	4	0	0	8	6	9	15	0	1	3	3	3	3	6	2	8	2	0	5	1	0	1
LT	0	3	6	0	4	19	4	3	7	1	0	1	1	1	1	0	0	0	1	0	1	0	0	1
RF	0	0	3	0	0	3	0	0	0	0	0	3	0	0	1	0	0	1	2	0	2	0	0	2
RT	0	0	3	0	0	4	1	0	1	2	1	1	0	0	0	0	0	0	3	0	3	0	0	2

Note. Total amount of errors made by each patient subgroup, divided by type of error (Poor circ = poor circumlocutions, Good circ = good circumlocutions, Semantic par = semantic paraphasia, Phonemic par = phonemic paraphasia, Verbal par = verbal paraphasia, Visual-semantic = visual semantic error) and category (L = living things, NL = non-living things, S= social groups).

2.3.5 Lesion Analysis

2.3.5.1 Picture Naming

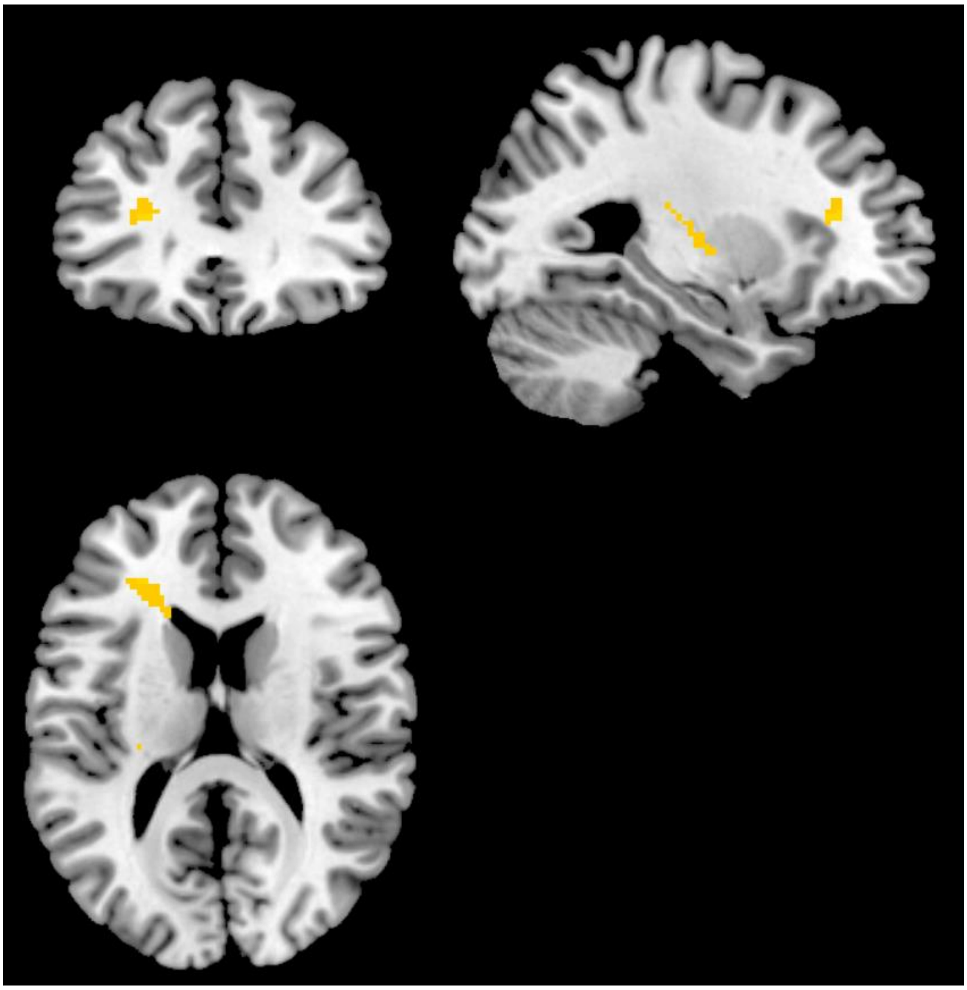
The VLSM analyses on picture naming task revealed a set of areas whose selective damage was associated with social group naming impairments, while no area was selectively associated with the remaining categories (see Table 11 and Figure 4). Specifically the analyses showed significant clusters within the left hemisphere involving the putamen, and minor cluster including insula, pallidum and inferior temporal lobe.

Table 11: Areas resulting from the VLSM analyses on naming social groups.

AAL label	N of voxels	% of total	Max Z-score	Max X	Max Y	Max Z
Putamen	172	2.17	3.48	-28	-10	1
Insula	29	0.19	3.89	-27	30	12
Pallidum	28	1.23	3.48	-27	-10	1
Inferior temporal gyrus	12	0.05	3.39	-39	-26	-23
Fusiform gyrus	10	0.05	3.39	-37	-26	-23
Middle frontal gyrus	8	0.02	3.29	-32	34	15
Caudate	6	0.08	3.29	-19	22	16
Subcortical	638	0.01	3.89	-25	30	12

Note. All the areas are located in the left hemisphere. AAL = automated anatomical labeling

Figure 4



Note: VLSM analysis on picture naming accuracy. Areas significantly associated to social groups naming deficits (p < .05)

2.3.5.2 Error Analyses

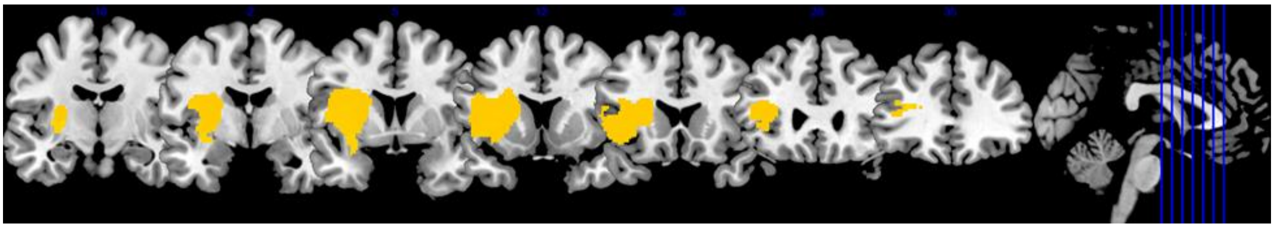
The second VLSM on picture naming errors (Figure 5) revealed that patients with higher rates of good circumlocutions with the social groups had lesions located within the left insula, inferior frontal gyrus, frontal operculum, superior temporal pole and basal ganglia (putamen, caudate and pallidum) and amygdala (see Table 12 for details). Moreover the same analysis on word-finding errors (performed considering anomia and good circumlocution as the same error) revealed the same areas. No particular area reached the threshold when errors in naming living and non-living things were considered.

Table 12: Areas resulting from the VLSM analyses on picture naming errors for the social group category.

AAL label	N of voxels	% of total	Max Z-score	Max X	Max Y	Max Z
Insula	6928	46.11	3.89	-28	30	12
Putamen	4832	60.84	3.89	-28	-10	1
Inferior frontal gyrus, pars triangularis	3867	19.23	3.89	-32	35	12
Inferior frontal gyrus, pars opercularis	3066	37.07	3.43	-50	5	6
Inferior frontal gyrus, pars orbitalis	943	6.94	3.43	-42	17	-12
Rolandic operculum	875	11.02	3.43	-51	4	4
Caudate	505	6.57	3.29	-17	17	5
Precentral	260	0.92	3.29	-51	7	15
Superior temporal pole	216	2.11	3.62	-32	4	-20
Pallidum	215	9.41	3.89	-27	-10	1
Amygdala	118	6.81	3.62	-31	0	-19
Middle frontal gyrus	23	0.06	3.89	-32	34	15
Subcortical	7114	0.13	3.89	-31	32	12

Note. All the areas are located in the left hemisphere. AAL = automated anatomical labelling

Figure 5



Note: VLSM analysis on good circumlocutions. Areas significantly associated to a higher amount of good circumlocutions for the social group category (*p* < .05)

2.4 Discussion

In the present study, we tested whether in patients with brain tumors the lexical-semantic knowledge about social groups and the knowledge about other categories such as living and non-living things are independently represented in the brain, and whether they can result as being differentially impaired, depending on the specific site of the lesion.

The first main result is that the patients performed pathologically only on the picture naming task, while their performance on the word-to-picture-matching and picture sorting showed no sign of being affected by brain damage. Moreover, there was an effect of side of the lesion on picture naming, with left-brain damaged patients (both temporal and frontal) being more impaired than both right-brain damaged patients and healthy controls, while no difference was observed between the latter two groups. To explain this pattern of results it is necessary to consider two aspects: the aetiology of patients' lesions (HGG, LGG, meningioma, and metastasis) and the focal nature of such lesions. Fast growing tumors (HGG, metastasis) may give rise to more severe deficits than slow growing lesions (LGG, meningiomas), since the latter tend to recruit ipsi- and contralateral areas more efficiently than the former (Desmurget et al., 2007). On the other hand, LGG patients' deficits, although milder than HGG patients', are more pronounced immediately after surgical resection (Campanella et al., 2015), and some specific lesion locations tend to compensate minimally (Ius et al., 2011). Moreover, previous studies testing semantic memory in patients with unilateral lesions (Campanella et al.,2010, Lambon Ralph et al., 2010; 2012) or bilateral lesions but more pronounced within one hemisphere (Lambon Ralph et al., 2001), reported prominent verbal output deficits and mild or normal receptive performance. In a computation model proposed to account for this phenomenon (Lambon Ralph et al., 2001), semantic knowledge is hypothesised to rely on a bilateral, distributed semantic system, with the left hemisphere semantic areas having privileged connections to the left-lateralized phonology. Hence, the left-sided damage of the semantic store is predicted to lead to a deficit in production sparing comprehension.

Second, VLSM analyses on picture naming accuracy revealed that lesions of specific areas were associated to deficits in naming social groups while no specific area reached the threshold for living and non-living things. Specifically, social group naming impairment was associated with the lesion of left putamen and a minor cluster within left insula. Left putamen has been found to be highly activated during picture naming (Kiyosawa et al., 1996) and has been suggested to be involved in computing both syntactic and lexical processes (Teichmann et al., 2008). Importantly, since putamen was not associated with patients' performance on other categories, this result cannot be ascribed to a general language disorder.

Since the patients' naming impairment could occur at different processing levels (Kreisler et al., 2000), we also performed a VLSM analysis on the different error types made by the patients, discarding effects due to general language impairments. The types of error made in naming can help us to identify the level at which the lexical-semantic processing breaks down, while correlating the main error types with the brain lesions pinpoints the sub-regions responsible for the emergence of those particular errors. The rate of word-finding errors (anomia and circumlocutions) with the social groups was significantly associated with lesions involving left insula, left inferior frontal gyrus, left amygdala and left basal ganglia (putamen, caudate, pallidum), while no error was associated with specific areas for the living and non-living things. Verbal production impairments (especially word-finding impairments) without associated receptive deficits have been typically observed in patients with left sided unilateral temporal damage. In the present study the involvement of ATL was only marginal: indeed we found a more prominent involvement of left inferior frontal gyrus (IFG), left insula, left amygdala and basal ganglia. Left IFG damage tends to lead to non-fluent aphasia (Damasio, 1992), which in turn is associated with a higher rate of anomia, while in fMRI studies it has been found to be implicated in the selection among semantic information and in recollecting information from long-term memory (Thompson-Schill et al., 1997; Moss et al., 2005). In our study, as the errors selectively involved the social stimuli, we cannot explain the results as being due to a general language impairment.

Many of the areas (amygdala, insula and striatum) associated with higher rate of word-finding errors with social groups have often been found implicated in emotional processing. Indeed, amygdala has been associated with social evaluation and perception (Adolphs, 2009), its activation has been found to be modulated by racial stereotype (Phelps et al., 2000, Cunningham et al., 2004) and its lesion seems to lead to the impairment in perceiving facial expressions of fear (Adolphs et al., 1994). Insula seems to be involved in interoception, in processing stimuli with emotional content, and in empathy (Singer et al., 2009). A recent review (Bickart et al., 2014) on converging evidence from studies involving animals (rodents and monkeys) and humans (both healthy and patients), showed that insula, amygdala and striatum are part of a network processing aversive stimuli. Interestingly the same set of areas (insula, amygdala and putamen) and left inferior frontal gyrus have been associated to implicit emotion processing (Critchley et al., 2000). Finally, left inferior frontal gyrus was found to be activated in studies contrasting social vs. animal concepts (Zahn et al., 2007) and person vs. object knowledge (Contreras et al., 2011), and might play a role in processing conspecifics. It is plausible that social knowledge includes also an evaluative component (also referred in literature as *prejudice*), in addition to a classical semantic component (see, Carnaghi et al., 2015). Indeed social groups (i.e., immigrants) might be intrinsically defined by attributes with high emotional content (i.e., dangerous, dirty, untrustworthy), and the lesion of emotion processing areas could impoverish their representation.

The selective impairment in naming non-living things, with spared knowledge about living things has previously been observed in brain tumor patients with lesions located within the left temporal lobe (Campanella et al., 2010). In the current study, patients' performance was predicted by AoA and the VLSM showed no specific area associated with non-living naming impairment. Importantly, patients' naming performance cannot be explained by social groups and living things differing in familiarity, as they were rated alike in our pilot study. On the other hand, even though the AoA significantly explained the 37% of variance in patients' performance, when splitting the items according to category, we found that it significantly explained only the performance on non-living items (48% of variance explained). Moreover, since naming social groups did not correlate neither with AoA nor with familiarity, one can hypothesize that, in addition to lexical-semantic knowledge, affective/evaluative processes might contribute to naming (Barsalou et al., 2003).

Moreover, relative to naming other categories, social group naming is unlikely to have been influenced by higher level of specificity of the stimuli and, consequently, by higher demand on cognitive abilities. However the level of specificity was not constant across categories, being the social groups named at a more superordinate level than living and non-living things.

In our study, the ATL is only marginally associated with patients' performance on social groups; thus, neither the social knowledge hypothesis, which highlights the importance of ATL in social knowledge representation, neither the Thompson et al.'s (2004) position, whereby person knowledge is represented within the right ATL, seem to explain our results.

In conclusion, our results indicate that the lexical-semantic knowledge about social groups may be independent of living and non-living things, consistently with previous neuropsychological (Rumiati et al., 2014) and neuroimaging studies (Contreras et al., 2011). We suggest that the knowledge about conspecifics differs from the other types of knowledge, since it includes also an affective component, as suggested by the association of the naming deficits with amygdala, insula and putamen lesions and the higher rates of word-finding errors.

The extent to which social group knowledge is independent of other categories and whether the nature of social group attributes might influence categorization should need further investigation. In the next chapter I will report a study investigating social group knowledge in patients with primary dementia that aimed at addressing these questions.

CHAPTER 3

Is social group representation explained by the sensory/functional theory?

Abstract

Recent findings revealed that social group representation might be independent of the other categories of knowledge (e.g., living and non-living entities), and that might be associated to emotion-processing areas. Current models on semantic knowledge proposed that concepts might be represented according to the modality of their attributes (Sensory/Functional Theory (SFT), Conceptual-Topography Theory (CTT)) or segregated into independent domains shaped by evolution (DSH). In order to better characterize social group representation, we tested patients with primary dementia on their knowledge about social groups as well as living (natural things) and non-living (artificial things) things. Moreover, social groups could belong to one of two different sub-categories, defined one by sensory features (natural groups), such as the ethnic groups, the other by functional features, such as professions. The results on voxel-based morphometry showed that both social group categories were associated with emotion-processing areas, natural groups and natural things were associated with inferior temporal areas and artificial things and groups were associated with motor- processing areas (DLPFC). Taken together, our results showed a tight association between category-specific semantic deficits and unimodal-processing areas, and are more easily explained by the SFT or the CTT.

3.1 Introduction

Double dissociations in neurological and neurosurgical patients (for review see Capitani et al., 2003) between the ability to process different categories, such as animals, plants, artifacts and conspecifics greatly helped in explaining how semantic knowledge might be represented in the brain. To account for these observations, three main groups of theories were formulated. According to a first group of theories, our semantic system stores each concept in modality-specific semantic areas (SFT, Warrington & Shallice, 1984; hub-and-spokes theory, Patterson et al., 2007) or in low level perceptual cortices (CTT, Simmons & Barsalou, 2003) depending on the attributes defining each concept. Thus, if on the one hand, the concept of a “dog” might be defined by its perceptual features as its physical aspect or its bark, on the other, a “hammer” might be defined by its function, as it is useful to hit a nail. It follows that damage to a perceptual- or motor-related areas will lead to a specific deficit, in recognizing animate or inanimate entities knowledge, respectively. It is worth noting that, while some theories (i.e., SFT, hub-and-spokes theory) highlight the need for recoding perceptual representations into abstract and symbolic formats (and hence the need for an amodal symbolic semantic system which interface with perceptual areas) in order to achieve conceptual representations, others (i.e., CTT) proposed that perceptual areas and the re-enactment of previous experience is sufficient for allowing semantic cognition.

A second group of theories (e.g., Tyler and Moss. 2001) holds that the inter-correlation and the degree of distinctiveness of concept features would shape the categorization in the brain: since animate entities tend to share many inter-correlated features and a few distinctive features, while artifacts tend to share many distinctive features, strongly correlated with their perceptual features and a few inter-correlated features. These theories highlighted the importance of the task and of the level of specificity of the stimuli used in the emergence of semantic deficits in patients. Hence damage to areas processing more general inter-correlated features are expected to impair recognition of animate entities, while damage to areas processing more distinctive features are expected to impair recognition of artefacts.

The third group of theories (DSH, Mahon and Caramazza, 2009; 2011) proposed that evolution has shaped our conceptual system into distinct domains, which are thought to be relevant for human survival: animals, plants, artifacts and conspecifics. The type of process performed within a certain region, as well as its pattern of connection with other regions has induced the development of specialized, category-specific networks through evolutionary pressure.

One type of knowledge that has received little attention is that about conspecifics; this has been investigated at a very general level of specificity, in contrast with the unique entity level which has been extensively studied (see Blank et al., 2011 for review), in both in neuropsychological (Zahn et al., 2009; Rumiati et al., 2014; Piretti et al.. 2015) and neuroimaging (Contreras et al., 2012; Zahn et al.. 2007, Chedid et al., 2016) studies. Rumiati et al. (2014) found that patients with primary dementia could be either selectively impaired in sorting social group nouns, while being still able to sort animate and inanimate items – but also other patients showing the opposite pattern of behaviour. These double dissociations led to suggest that conspecifics might be represented in the brain independently of the other categories. Both neuroimaging and neuropsychological findings converge on the evidence of associating ATLs with famous and familiar person knowledge (Gainotti, 2007; Blank et al., 2011), with social concepts (Zahn et al., 2007, 2009) and social groups (Chedid, 2016; Piretti et al., 2015) and led some authors to suggest that ATLs might play a role in representing social knowledge (social knowledge hypothesis, Ross and Olson, 2010; Skipper et al., 2011). Aside the ATL, a set of areas - frequently associated with emotional processing - insula, the opercular part of IFG, amygdala, medial prefrontal cortex, ACC and orbitofrontal cortex - have been also found (Zahn et al., 2007; Chedid et al., 2016, Skipper et al., 2011).

The importance of emotional processing is not new in the social group cognitive research field, and especially in the study of inter-group relations. Indeed the race bias is thought to include both stereotypes, which are representations of culturally held beliefs about social groups members, (or the knowledge about social groups, including personal traits or circumstantial attributes) (Hamilton, 1981) and prejudice, which is the affective response toward social group members (typically negative toward out-groups) (McConahay and Hough, 1976), reflecting, respectively, cognitive and affective aspects. It has been proposed that these two aspects might rely on different brain networks, with stereotypes more associated to anterior temporal cortices, IFG and medial PFC and prejudice more associated to amygdala, insula, striatum and orbital frontal cortex (for review, see Amodio, 2014).

Together these findings converging on both DSH and social knowledge hypothesis, but might also reflect the affective nature of social features, and hence confirming the assumption that modality-processing areas are involved in conceptual representation as proposed by the SFT or the CTT.

In order to disentangle the role of modality-specific processing we tested patients with primary dementia and healthy controls on semantic knowledge about animals, artifacts and social groups, and modulating the latter category along the sensory-functional dimension. Specifically, social groups as stimuli were characterized by either perceptual features (natural groups) (e.g. ethnic groups. social groups defined by physical appearance) or by functional features (artificial groups) (e.g. professions). If modality-specific information is relevant for representing social groups, patients with atrophy involving motor areas and visual areas would be impaired in the knowledge about artificial and natural groups, respectively. Conversely, if modality-specific processing is not necessary for social group representation, the atrophy of those areas should not affect semantic knowledge. Moreover if the distinction between stereotype and prejudice is genuine, the deficit on social group knowledge should be associated to the atrophy of the stereotype network (ATLs, IFG, medial PFC)

3.2 Materials and methods

3.2.1 Participants

The study includes patients with a diagnosis of dementia (N = 26) recruited from the neurology wards of "Santa Maria della Misericordia" hospital (Udine, Italy) or from "Ospedali Riuniti di Trieste" (Trieste, Italy). The study also included 19 healthy controls (Ctrls). Inclusion criteria for healthy controls were the absence of any neurological, psychiatric or neurosurgical condition, to be Italian native-language speakers and to obtain at least an uncorrected score of 28 at the MMSE. Patients' group included 10 patients with the behavioural variant of frontotemporal dementia (bvFTD) (Raskovsky et al., 2007; 2011), 10 patients with Alzheimer's disease (AD) (McKahn et al., 2011) and 6 patients with primary progressive aphasia (PPA) (Gorno-Tempini et al., 2011), diagnosed according to the international criteria. PPA group comprises three patients with semantic dementia (SD), one patient with non-fluent progressive aphasia (NFPA) and two patients with logopenic progressive aphasia (LPA). Participant groups differed significantly for education, but not for age. Specifically, AD patients had significantly more years of education than Ctrls ($p < .01$) (See Table 13).

All participants were tested on neuropsychological and experimental tasks and underwent a MRI scanning session. The experiment was approved by independent regional ethic committee and participants signed an informed consent before taking part to the experiment.

Table 13

Group	Age (SD)	Education (SD)	N (F)
Ctrls	69.9 (5.3)	13.0 (4.5)	19 (13)
bvFTD	71.7 (5.4)	10.3 (4.5)	10 (6)
AD	75.1 (7.1)	7.5 (3.2)	10 (8)
PPA	71.5 (6.8)	9.8 (6.4)	6 (2)

Note: The table shows age, years of education, sample size and number of female (F), for each of the four groups of participants

3.2.2 Stimuli

All stimuli used in the study proper belonged to four categories: natural things (i.e. animals), artifical things (i.e., artifacts), natural groups (i.e., social groups defined by their sensory features; e.g., obese people, Africans-Americans) and artifical groups (i.e., professions). The selection of the stimuli was performed through four successive steps: rating of a large set of words, selection of 8 words for each category, rating of a large set of photographs depicting the words selected, selection of three photographs for each word.

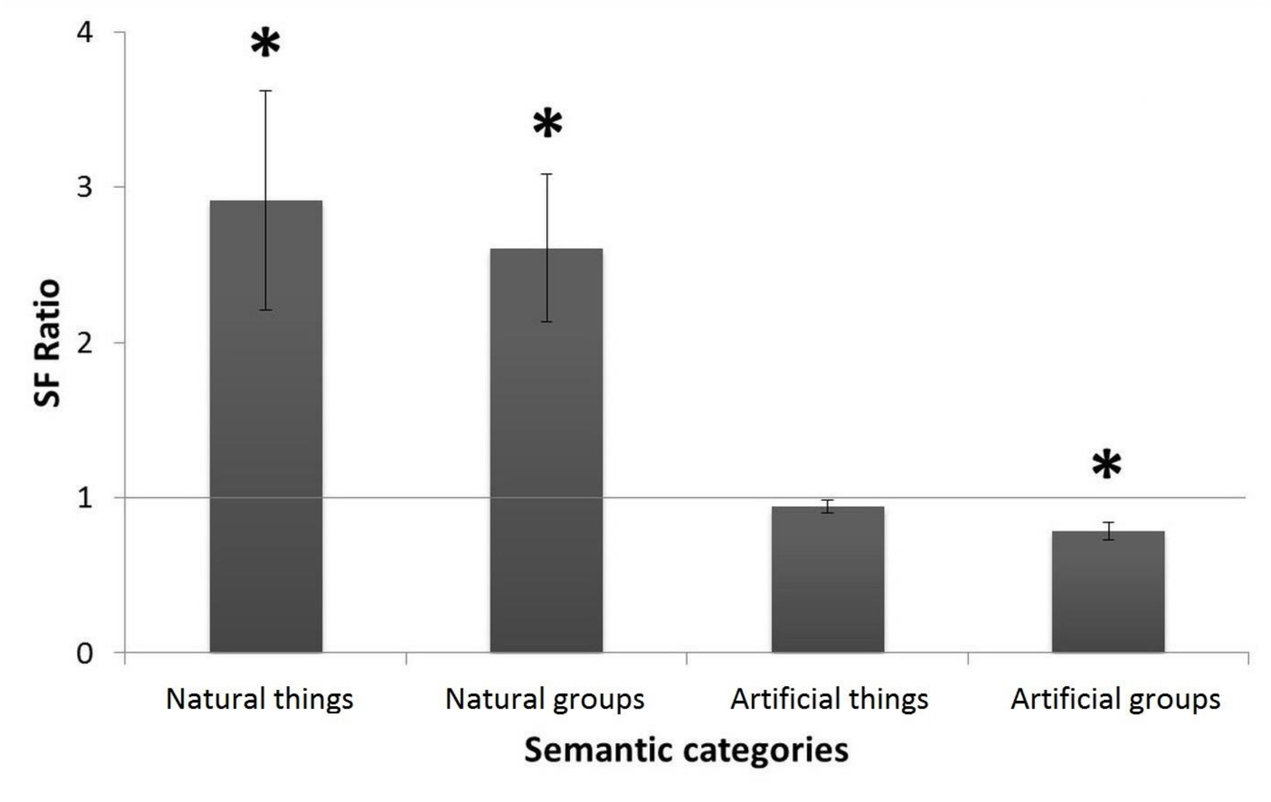
First, a total set of 167 words, including animals, artificial objects and social groups (i.e., Chinese people, doctors, obese people), were rated by 14 healthy Italian-native speaking healthy participants on three different dimensions (positive and negative attitude of the society towards the items and frequency of exposition to the items) on a scale from 1 to 7. Positive and negative society attitudes were used, instead of an explicit measure of the valence, in order to avoid possible effects due to social conformity. A valence index was then computed subtracting the negative to the positive attitude. Familiarity ratings were averaged into a single frequency index.

We selected 8 words for each category and stimuli belonging to all categories were matched for letter length, valence and familiarity (it was not possible to match natural and artificial groups according to valence, since professions were globally high in valence, while natural groups were associated to low valence ratings).

In the next step, for each item we selected ten different coloured photographs (640x480 pixels) and asked 12 different healthy participants to name and rate all photographs for the ambiguity, typicality and valence (scale 1-9). Then, we selected three photographs for each item (among those which were named more accurately and with the least ambiguity) matching each category of pictures for ambiguity, valence and typicality. Hence we selected three different exemplars for each of the 8 items of the four categories. The same set of pictures was used in both the picture naming and the word-to-picture matching tasks.

To make sure that the items selected were truly modulated by the nature of their attributes (sensory, functional), in two different ratings further 24 participants rated how much each item was defined by sensory (i.e., How much '*lawyers*' can be defined by their physical appearance?) or functional (i.e., How much '*lawyers*' can be defined by their function?) features. A ratio between sensory and functional attributes for each semantic category was obtained by dividing the average sensory scores by the average functional scores (SF-ratio). A repeated-measure analysis of variance (ANOVA) was performed on the SF ratios, with humankind (things, groups) and naturality (natural, artificial) as within-participant factors. The ANOVA showed a significant main effect of naturality ($F(1, 23) = 11.98$, $p = .002$) with SF-ratio being higher for natural than for artificial stimuli (Figure 6). One-sample t-tests versus 1 showed that the SF-ratio was above 1 for natural things and natural groups ($t > 2.6$), but below 1 for artificial groups ($t(23) = -3.81$, $p = .001$), and equal to 1 for artificial things ($t(23) = -1.31$, $p = .21$). Neither the main effect of humankind ($F(1, 23) = .68$, $p = .4$), nor the humankind x naturality interaction ($F(1. 23) = .07$, $p = .79$) were significant.

Figure 6



Note: The graph shows the SF Ratio across the four different conditions. * indicates *p* < .05 for the one-sample t-test versus 1.

3.2.3 Neuropsychological assessment

All participants' global cognitive functions were assessed using the Addenbrooke's Cognitive Examination – revised (ACE-R) (Pigliautile et al., 2012). This test provides two global indexes (ACE-R and MMSE) and five subscales for different cognitive domains: attention and orientation (ACEao), memory (ACEm), language (ACEl), fluency (ACEf) and visuo-spatial abilities (ACEvs). They were also tested on executive functions through the Frontal Assessment Battery (FAB) (Apollonio, 2005). Two patients (one from the bvFTD and the other from AD group) and one participant from the Ctrls were not tested using the FAB.

3.2.4 Experimental tasks

Participants were asked to perform two tasks, tapping the semantic system: a picture naming task and a word-to-picture matching task. Both tasks were presented on a 17-inches laptop using E-prime 2.0 (www.pstnet.com). Each participant performed first the picture naming task, in which they had to provide a name for each photograph at a time, providing a single word, and then the word-to-picture matching task (except for one patient with LPA who did want to perform the word-to-picture matching task). In the latter task, they were asked to associate the name of each item (e.g. Chinese people) presented auditorily, through computer headphones, to one of the four pictures (all of the same category) presented on the computer screen. Using this set of tasks we were able to evaluate both receptive and productive semantic abilities.

To obtain a more reliable measure of the lexical/semantic abilities of our participants, we recoded patients' accuracy scores in both picture naming and word-to-picture matching into consistency scores (range: 0-8). Consistency scores were calculated considering one point if the participant responded correctly at least in one on three trials for each item and zero points if the participant could not name any of the trials for each item. This consistency index is useful for two reasons: i) the score is less biased by visual/perceptual errors, since each item is presented with three different exemplars, and ii) it sheds light on the lexical/semantic storage degradation. It has been proposed that semantic memory impairments might be associated with two distinct patterns of deficits: the degradation of the semantic storage or semantic access impairment. Warrington and Shallice (1979) described four main criteria to distinguish between the two conditions: consistency of the responses for each item, the effect of word frequency, susceptibility to cueing from a semantically related word and depth of processing (the type of word produced in case the right word is not retrieved).

3.2.5 Neuroimaging acquisition

Each participant T1-weighted MRI was acquired using a Philips Achieva 3.0 T MRI scanner at the hospital “Santa Maria della Misericordia” in Udine, Italy. Imaging parameters for structural T1-weighted images were: 170 slices, voxel size (mm) = 1.0 x1.0 x 1.0. TR/TE = 8.1/3.7, flip angle = 12°, slice orientation = sagittal, scan duration = 7.59 mins.

3.2.6 Statistical analyses

3.2.6.1 Behavioural analyses

All the behavioural analyses were conducted using SPSS (version 21.0.0.0) (http://www.ibm.com/analytics/us/en/technology/spss).

Neuropsychological assessment scores on MMSE, FAB, ACER_tot and its subscales were analysed using a series of One-way ANOVAs, with the group (Ctrls, bvFTD, AD, PPA) between-subject factor. Post-hoc analyses were performed using Bonferroni correction. The same analysis was performed on the total accuracy scores on picture naming and word-to picture matching tasks, in order to highlight differences in the global patients’ performance. Moreover, to show possible pattern of categorical deficits in our sample of participant we performed two repeated-measure ANOVAs on both picture naming and word-to-picture matching tasks, using Humankind (non-human, human) and Naturality (Natural, Artificial) as within-subject factors, and Group (Ctrls, bvFTD, AD, PPA) as between-subject factor. Pairwise comparisons were corrected for Bonferroni.

3.2.6.2 Voxel-based morphometry

Participants’ structural T1 images and fMRI scans were pre-processed using spm12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/), a software running on Matlab (versions R2012b) (www.mathworks.com). Each T1-weighted image was segmented into grey matter, white matter and CSF images. Then a study-specific template was created using the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL)

(Ashburner. 2007), implemented in spm12, using as inputs the scans of the entire sample of participants. All participants' grey matter DARTEL templates were then affine registered to tissue probability maps in MNI space. For each participant, a non-linear warping of grey matter DARTEL image to MNI space was created, and then used to modulate the normalization of grey matter images. Following this procedure, the final images had a voxel size of 1.5x1.5x1.5 mm and were smoothed using a 8mm Gaussian kernel.

VBMs (Ashburner and Friston, 2000), were performed using a general linear model (multiple regression), putting as factors the consistency scores of the picture naming task of each of the category investigated and as covariates of no interest age, education and sex. We also used a proportional global normalization, using the total intracranial volume for each subject. To increase the power of the analysis and to highlight the neural substrates associated to poor performances on natural and artificial categories, and on social and non-social categories, we performed other two analyses on Naturality, using as factors the sum of the consistency scores natural (things and groups) items and of artificial (things and groups) items and on Humankind, using as factors the sum of the consistency scores on non-human items (natural and artificial things) and the ones on human items (natural and artificial groups). The consistency scores on word-to-picture naming task was not analysed because participants performed almost at ceiling.

3.3 Results

3.3.1 Neuropsychological assessment

One-way ANOVAs on score of the neuropsychological assessment battery revealed significant effects of MMSE ($F(3, 41) = 15.65$, $p <.001$), ACEtot ($F(3, 41) = 36.18$, $p < .001$), ACEao ($F(3, 41) = 11.79$, $p < .001$), ACEm ($F(3, 41) = 24.36$, $p < .001$), ACEf ($F(3, 41) = 28.55$, $p < .001$), ACEl ($F(3, 41) = 23.61$, $p < .001$), ACEvs ($F(3, 41) = 8.90$, $p < .001$) and FAB ($F(3, 41) = 15.61$, $p < .001$). Pairwise comparisons (see Table 14) showed that Ctrls performed significantly better than all the other groups on global cognitive functions (ACEtot) (all *p*s <. 001), memory (ACEm) (bvFTD *p* < .01; AD *p* < .001; PPA *p* < .001) and executive functions (ACEf, FAB) (all *p*s <. 001), while they performed better than AD and PPA patients on attention and orientation (ACEao) (Ctrls vs AD: *p* < .01; Ctrls vs. PPA: *p* < .001), linguistic abilities (ACEl) (Ctrls vs AD: *p* < .01; Ctrls vs. PPA: *p* < .001) and the MMSE (all *p*s < .001). bvFTD patients showed a better performance than PPA patients on global cognition (ACEtot p < .001; MMSE p < .01), attention and orientation (ACEao) (*p* < .01), fluency(ACEf) (*p* < . 01) and linguistic abilities (ACEl) (*p* < .001), and a better performance on memory (ACEm) (p < .05) than AD patients. PPA patients' scores were also lower than all the other groups on visuo-spatial abilities (ACEvs) (Ctrl vs PPA: *p* < .001; bvFTDvs PPA: *p* < .05; AD vs PPA: *p* < .001), language (ACEl) (all *p*s < .001) and ACEtot (AD vs PPA *p* < .05).

Table 14

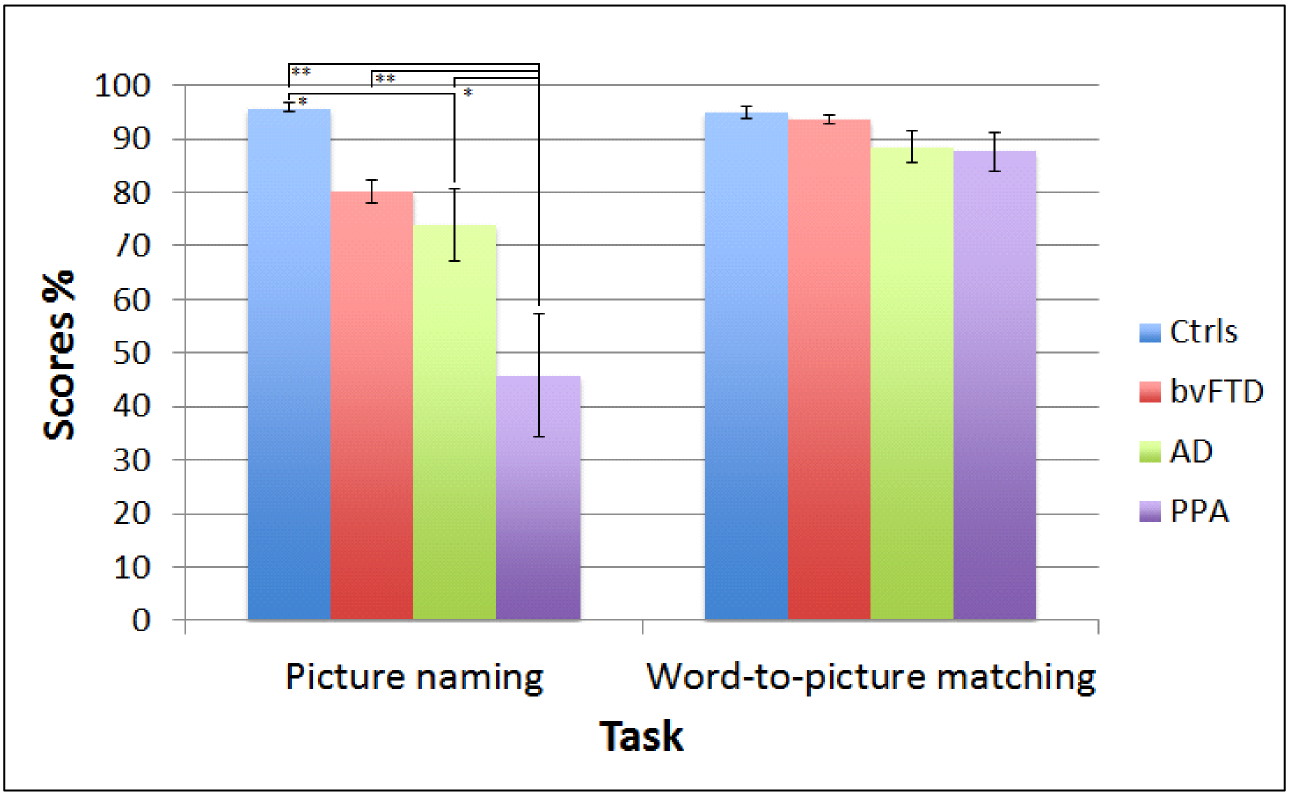
Group	MMSE (0-30)		ACE_tot (0-100)		ACE_ao (0-18)		ACE_m (0-26)		ACE_f (0-14)		ACE_l (0-26)		ACE_vs (0-16)		FAB (0-18)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ctrls	29.5	0.6	94.3	4.7	17.9	0.2	23.3	2.8	11.4	2.4	25.7	0.5	16.0	0.0	16.4	1.7
bvFTD	26.3	2.9	76.0	8.2	15.8	2.4	15.8	6.0	6.8	1.8	23.7	2.2	13.9	1.3	11.6	2.8
AD	23.3	3.6	63.2	13.8	14.0	2.4	8.9	4.8	4.9	3.3	21.7	4.3	14.7	4.5	11.4	3.0
PPA	19.0	8.2	43.7	23.4	10.8	6.4	8.5	8.5	2.2	1.9	13.0	6.8	9.2	5.0	8.7	4.2

Note: the table shows the average uncorrected scores for MMSE, ACE-R total score, ACE-R subscales and FAB in the different groups of participants.

3.3.2 Experimental tasks: Behaviour

Univariate ANOVA on total naming accuracy revealed a significant effect of Group (*F*(3, 41) = 18.78, *p* < .001). Pairwise comparisons (see Figure 7) revealed that Ctrls' total accuracy score was higher than both AD and PPA groups (AD *p* < .01; PPA *p* < .001), while the difference between Ctrls and bvFTD was only marginally significant (p = .056). Moreover, both bvFTD and AD groups performed significantly better than PPA (bvFTD *p* < .001; AD *p* < .01).

Figure 7



Note: The graph shows the mean of the total accuracy scores across the different groups of participants on the picture naming (a) and word-to-picture matching (b) tasks. * indicates *p* < .01 and ** indicates *p* < .001.

Table 15

Task	Group	Accuracy Scores								Consistency Scores							
		Natural				Artificial				Natural				Artificial			
		Things		Group		Things		Group		Things		Group		Things		Group	
Picture naming	Ctrls	21,8	2,0	22,8	1,3	23,5	1,0	23,8	0,5	7,8	0,4	7,9	0,3	7,9	0,3	8,0	0,0
	bvFTD	16,2	3,3	19,1	1,6	21,3	2,3	20,4	3,5	6,5	1,1	7,6	0,5	7,8	0,4	7,7	0,7
	AD	16,5	5,6	16,4	5,0	20,3	4,6	17,9	6,1	6,9	1,4	6,7	1,3	7,4	1,0	7,0	1,3
	PPA	8,8	6,5	12,8	6,8	11,8	7,0	10,5	8,9	4,0	2,3	5,3	2,5	4,7	2,7	4,0	2,9
Word-to-picture matching	Ctrls	23,1	1,3	22,6	2,6	23,5	0,9	22,0	1,1	8,0	0,0	7,9	0,5	8,0	0,0	8,0	0,2
	bvFTD	22,8	1,1	22,1	1,5	23,6	0,5	21,4	1,4	8,0	0,0	8,0	0,0	8,0	0,0	8,0	0,0
	AD	22,0	1,6	20,2	3,5	22,7	2,3	20,1	2,4	8,0	0,0	7,9	0,3	8,0	0,0	8,0	0,0
	PPA	21,0	1,9	20,4	3,2	22,6	2,1	20,2	2,4	8,0	0,0	8,0	0,0	8,0	0,0	7,8	0,5

Note: Mean and standard deviations of the Accuracy scores and Consistency scores on both Picture Naming and Word-to-picture matching tasks

The repeated-measure ANOVA on the naming consistency revealed a significant main effect of group ($F(3,40) = 16.28$, $p < .001$) and significant interactions of Naturality * Group, ($F(3, 40) = 3.40$, $p < .05$), Humanking * Naturality * Group ($F(3, 40) = 5.53$, $p < .01$), Humankind * Education ($F(1,40) = 5.51$, $p < .05$) and a trend for Humankind * Group ($F(3,40) = 2.78$, $p = .053$). Pairwise comparisons (see Table 15) revealed that PPA patients performed overall worse than all the other groups (all *p*s < .001), that bvFTD patients performed worse on natural entities than artificial entities ($p < .01$) and more specifically they named worse natural things than artificial things ($p = .001$). Moreover, PPA patients' consistency scores on natural groups were higher than their scores on natural things ($p < .01$) and artificial groups ($p < .001$), and their performance on artificial things were higher than the one on artificial groups ($p < .05$).

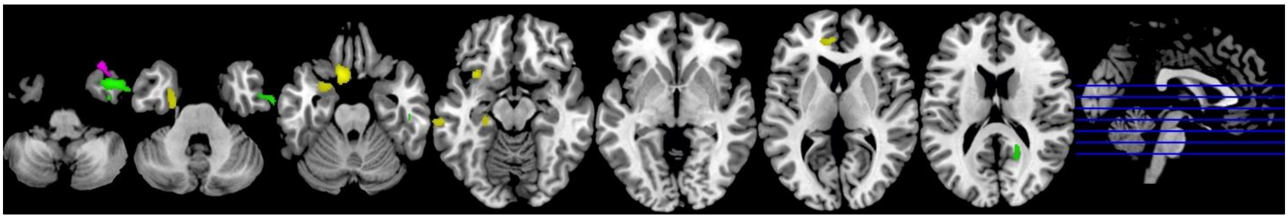
Univariate ANOVA on total accuracy score of word-to-picture matching revealed a significant main effect of Group ($F(3, 40) = 3.47$, $p < .05$), with AD patients performing marginally worse than Ctrls ($p = .067$) (see Figure 7). The repeated-measure ANOVA on word-to-picture matching consistency scores did not reveal any significant result (see Table 15).

3.3.3 VBM

VBM analyses revealed significant clusters of results only in two conditions (VBM on Humankind and Naturality), when corrected for family-wise error (FWE) at the cluster-level (see Table 16 and 17), and hence the results will be reported uncorrected, with $p < .001$.

The VBM analysis on each semantic category (see Figure 8 and Table 15) showed that naming performance on natural things was associated to the atrophy of right inferior temporal cortex (fusiform gyrus and middle temporal gyrus) and right occipito-parietal cortex (precuneus, cuneus), while artificial things did not revealed any significant area.

Figure 8



Note: VBM results showing the areas associated to the deficit in naming pictures of natural things (green), natural groups (yellow) and artificial groups (violet).

Table 16

Category	Anatomical label	Cluster size	T	x	y	z
Natural things	Right temporal pole	734	4.26	47	8	-45
			4.06	38	-9	-50
			3.78	54	2	-41
	Right precuneus	181	4.10	18	-56	14
			3.76	18	-48	17
	Right middle temporal gyrus	243	3.87	65	-8	-32
			3.65	48	-8	-30
			3.55	57	-5	-32
Natural groups	Left medial orbital gyrus	492	4.49	-12	18	-26
	Left temporal pole	546	4.23	-24	8	-27
			3.72	-23	-9	-35
	Left cerebellum (Crus II)	76	4.12	27	-74	-20
	Left anterior insula	197	3.90	-33	17	-12
	Left anterior cingulate	217	3.79	-15	45	3
			3.78	-6	47	8
	Left middle temporal gyrus	77	3.66	-65	-26	-14
	Left hippocampus	71	3.60	-26	-24	-15
Artificial groups	Right temporal pole	203	3.96	39	18	-48
			3.91	33	24	-45

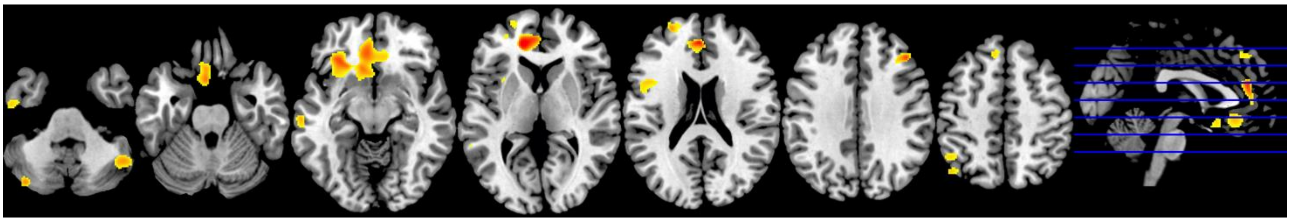
Note: The table shows the significant clusters of VBM analysis on the picture naming consistency scores. Results are reported uncorrected with $p < .001$

Moreover naming artificial groups was associated with the atrophy of right anterior temporal cortex (fusiform gyrus and middle temporal gyrus), anteriorly to the area associated to natural things, while natural groups were associated to left temporal cortex (hippocampus, parahippocampal gyrus, superior and middle temporal gyri, fusiform gyrus and amygdala), left insula, left prefrontal cortex (ACC, medial and orbital prefrontal cortex) and right cerebellum.

A second VBM on Humankind (see Table 16 and Figure 9) revealed that naming human stimuli (social groups) was associated with the atrophy of left frontal cortex (mainly left medial and orbital prefrontal cortices, ACC and left posterior inferior frontal gyrus), left temporal cortex, left parietal cortex, left insula and cerebellum (mainly in the right hemisphere). No specific area was associated with picture naming tapping non-social knowledge.

The third VBM on Naturality (see Table 18 and Figure 10) showed two distinct sets of areas. While the deficit at naming artificial entities was associated with the atrophy of left prefrontal cortex (middle and superior frontal gyri), the deficit at naming natural entities was associated with bilateral inferior temporal cortices, occipito-temporal areas and right precuneus.

Figure 9



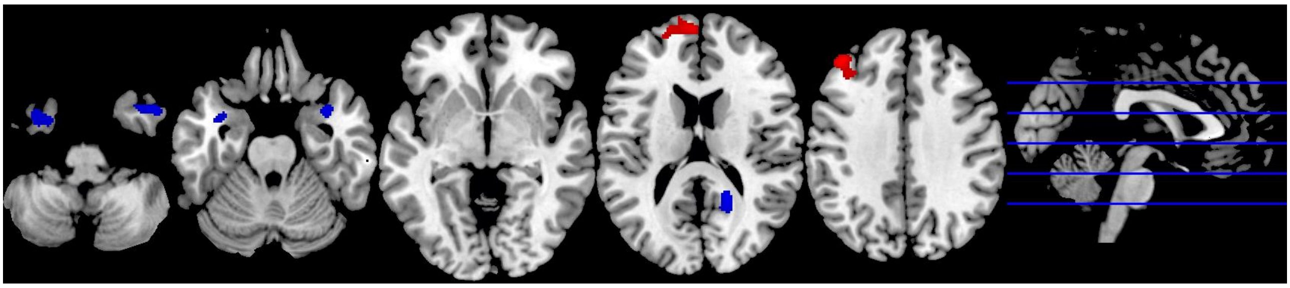
Note: VBM results showing the areas associated to the deficit in naming pictures of social groups

Table 17

Category	Anatomical label	Cluster size	T	x	y	z
Social groups	Left anterior cingulate*	6309	5.47	-15	42	2
			5.20	-29	33	-6
			5.11	-2	45	20
	Right cerebellum (Crus II)	816	4.82	45	-63	-45
			4.49	51	-65	-35
	Left superior frontal gyrus	526	4.16	-5	41	44
			3.96	-8	33	57
	Right middle frontal gyrus	497	4.67	42	32	35
	Left angular gyrus	337	4.28	-45	-66	45
			3.62	-47	-54	50
	Left middle temporal gyrus	286	4.06	-63	-24	-14
	Left inferior frontal gyrus	172	3.73	-47	11	20
			3.57	-51	3	20
	Left inferior temporal gyrus	122	3.66	-50	-9	-41
	Left middle temporal gyrus	84	4.18	-62	-48	8
	Left cerebellum (Crus II)	64	4.14	-38	-77	-41
	Left middle frontal gyrus	56	3.63	-29	63	8

Note: The table shows the significant clusters of VBM analysis on the picture naming consistency scores. * indicates that the cluster survives the correction for the family-wise error ($p < .05$). All the other results are reported uncorrected with $p < .001$

Figure 10



Note: VBM results showing the areas associated to the deficit in naming pictures of natural entities (blue) and artificial entities (red).

Table 17

Category	Anatomical label	Cluster size	T	x	y	z
Natural	Left fusiform gyrus*	1040	4.34	-26	-8	-39
			3.76	-23	5	-50
			3.71	-33	-9	-29
	Right precuneus	242	4.22	20	-56	14
			4.16	18	-48	17
	Right temporal pole	666	4.05	47	9	-47
			3.89	35	8	-26
			3.71	36	8	-35
	Right middle temporal gyrus	295	4.05	65	-6	-33
			3.76	62	-18	-30
	Left superior temporal gyrus	145	3.90	-38	5	-20
	Left temporal pole	54	3.89	-48	15	-41
	Right supramarginal gyrus	87	3.68	54	-39	56
			3.66	47	-42	56
Artificial	Left middle frontal gyrus	317	4.43	-42	41	36
			4.42	-42	29	42
			3.63	-38	32	36
	Left superior frontal gyrus	332	4.17	-5	62	18
			3.71	-18	60	15
			3.64	-14	68	15
	Left frontal pole	61	3.98	-27	63	5
			3.55	-29	59	12

Note: The table shows the significant clusters of VBM analysis on the picture naming consistency scores. * indicates that the cluster survives the correction for the family-wise error ($p < .05$). All the other results are reported uncorrected with $p < .001$

3.4 Discussion

In the current study we investigated whether the conceptual knowledge about social groups might be organized into sensory and functional components. To achieve this aim, in addition to the categories of animals (natural things) and artifacts (artificial things), we tested the semantic knowledge of social groups defined by their perceptual features (natural groups) and defined by their functional features (artificial groups) in patients with different neurodegenerative diseases (bvFTD, AD, PPA) and in healthy controls.

Results showed that each patient group performed worse than Ctrls on picture naming, and that PPA patients performed worse than bvFTD and AD patients. Conversely, patients were only mildly impaired at recognizing the items in the word-to-picture matching task. This asymmetry might be explained at least by two factors: one related to patients' cognitive deficits and the other to task-specific features. Indeed one possibility is that patients in the study have impaired lexical production, but spared recognition abilities. The other factor to take into account is that in this task patients are required to choose between four possible options in the word-to-picture matching, in contrast with the number of possible choices in the picture naming task, leading this latter task to be much more sensitive than the former to semantic deficits.

The first VBM analysis revealed that the naming performance with natural things (animals) was associated with the atrophy of right anterior inferior temporal cortex and precuneus, confirming the findings of previous studies (Brambati et al., 2006, Damasio et al., 1996, Devlin et al., 2002), while no areas was found to be selectively associated with knowledge about artificial things. Moreover, the same analysis revealed the association between left orbito-frontal and anterior temporal cortices and naming natural groups, and between right anterior temporal cortex and artificial groups. This dissociation might reflect a difference in the stimuli valence. Indeed, it was not possible to match the valence of the two stimuli categories, with natural groups being more negative than artificial groups ($p > .05$).

The VBM analysis on humankind revealed a set of areas, whose atrophy is associated to social group (natural and artificial groups) naming deficit, while no area was associated to non-human entities (natural and artificial things) deficit. Differently from deficits affecting other semantic categories, those affecting the social group semantics were associated with a set of areas frequently associated with affective processing: left medial (including ACC) and orbital prefrontal cortex, insula and left posterior inferior frontal gyrus. Indeed, in neuroimaging studies on emotions, the activation of insula is quite often associated with that of ACC and the pars opercularis of IFG (Craig, 2009). Their concurrent activation of ACC and insula/IFG is thought to represent, respectively, complementary limbic motor and sensory areas, and their coupled activity could be relevant in emotional processing in the same fashion as somatosensory and motor cortices are for manual dexterity (Craig, 2009; 2011). While insula/IFG are relevant to integrate interoceptive and environmental inputs in order to form emotional representations, the ACC might be relevant in the engendering motivation and initiation of behaviour (Craig, 2009; 2011; Holroyd and Yeung, 2012). The association of emotion-processing areas and social group naming impairment is in contrast with the assumption proposing a distinction between stereotype and prejudice (Amodio, 2014). Indeed the lexical-semantic knowledge impairment should only involve the lesion of the stereotype network and not the prejudice network (insula, orbitofrontal PFC).

Our results converge on the findings from both neuropsychological (Piretti et al., 2015) and functional neuroimaging (Chedid et al., 2016) studies. In the study reported in the previous chapter (Piretti et al., 2015), we found that lexical-semantic deficits in naming social groups were associated to the lesion of a left-lateralized set of areas (IFG, insula, amygdala and superior anterior temporal cortex), while Chedid et al. (2016) reported the activation of bilateral areas (IFG, MFG, medial prefrontal cortex, middle temporal gyrus and occipital areas) when participants judge the profession of both names and pictures of famous people (and hence categorizing individuals according to the social group they belong to). *Taken together, these findings suggest that social groups, or more broadly, conspecifics knowledge, differently from other categories, relies on affective processing.*

A further VBM analysis on naturality revealed two distinct patterns of atrophy, associated to deficits in naming natural and artificial entities. If on the one hand, the deficit affecting natural entity knowledge was associated with the bilateral atrophy of anterior inferior temporal cortices, on the other, deficit affecting artificial entity knowledge was associated with the atrophy of left dorso-lateral prefrontal cortex. This distinction might mirror two different processing modalities depending on the content of the concept: the former is associated with visual processing and the latter with motor processing. Indeed, after the perception of a visual stimulus, its processing might follow two distinct pathways starting from the striate occipital cortex: a ventral stream through the occipito-temporal cortex, up to the inferior anterior temporal lobe, which is involved in encoding objects' identities, and a dorsal stream, going through occipito-parietal cortex to the inferior parietal lobule but with probably further extensions to the DLPFC, encoding spatial information, necessary for visually guided actions (for reviews see Kravitz et al., 2011; 2013). Furthermore DLPFC was associated with planning, preparation and execution of motor actions (Hoshi and Tanji, 2007) and is very frequently associated to the activation of premotor cortex and supplementary motor area during fMRI experiments on motor imagery (Hetù et al., 2013). Taken together, this findings seem to suggest that entities which are highly defined by their perceptual/visual features, as natural things (animals) and groups (e.g., ethnic groups) might be represented at the anterior part of the ventral visual pathway, whereas entities defined more by their functional features, as artificial things (objects) and groups (professions) might be represented at the level of the most anterior part of the dorsal visual stream, which is thought to be relevant for motor representation.

From a theoretical point of view, our findings seem to confirm the importance of modality-specific processing areas in category-specific conceptual representations.

Although they are not sufficient to reject the DSH (Mahon and Caramazza, 2009), our findings seem more easily explained by different theories proposing that unimodal-processing areas are relevant for the emergence of category-specific deficits, including the SFT (Warrington and Shallice, 1984), and CTT (Simmons and Barsalou, 2003) and the Hub-and-Spokes theory (Patterson et al., 2007). Further studies are necessary to establish whether low-level modality-processing areas are necessary for semantic representation or if concepts are recoded into modality specific semantic representations.

CHAPTER 4

Is left inferior frontal gyrus involved in social group processing?

Abstract

The posterior part (*pars opercularis*) of inferior frontal gyrus (IFGop) has recently been suggested to be associated with the semantic processing of social groups. However, the specific contribution of IFGop in this type of processing remains unclear. It has been suggested first, that the IFGop might be involved in categorical semantic knowledge about human stimuli and second that it might constitute an emotional component, involved in the processing of social groups. In the current study, I applied double-pulse transcranial magnetic stimulation on inferior frontal gyrus, inferior parietal lobe and vertex on 18 healthy participants while they were performing a priming task. The task included three categories of stimuli: living entities, non-living entities and social groups. I found that the stimulation of IFGop did not influence participants' performances on the three categories of items. Conversely, the same stimulation significantly slowed responses on negative stimuli, regardless of the category. Together, these results suggested that the involvement of the IFGop in social group processing is implicated in the processing of emotional features.

4.1 Introduction

From more than a century, starting with the classical studies of Paul Broca, the left inferior frontal gyrus (IFG) has primarily been associated with language production (Broca, 1861; Dejerine, 1914). This area is located within the lateral surface of frontal cortex, between Rolandic, Sylvian and inferior frontal sulci. Anatomically, IFG is composed by three distinct sub-regions: the anterior orbital part (*pars orbitalis*), the central triangular part (*pars triangularis*, IFGtr) and the posterior opercular part (*pars opercularis*, IFGop). While the importance of IFG in language processing has been confirmed (Price, 2010), a huge amount of literature suggests that it might play a role even in other cognitive domains. Indeed IFG has been associated to motor processing (Molnar-Szacacs et al., 2005), executive functions (Aron et al., 2003) and emotion processing (Shamay-Tsoory, 2011; Yamasaki et al., 2002). A large body of literature, including electroencephalography, functional neuroimaging, TMS, and a few neuropsychological studies, linked IFGop to action observation and imitation (Pazzaglia et al., 2008, Fazio et al., 2009; for review, see: Iacoboni, 2009; Cattaneo & Rizzolatti, 2009) and motor imagery (Hetù et al., 2013). IFGop shows activity when participants observe and perform (imitate) other people's actions (especially involving hands), and it is thought to be the neural substrate, together with the inferior parietal lobe (IPL), of imitation, as part of the 'mirror neuron system' (MNS). Neurons in F5 (which is thought to be the homologous of IFGop in humans) have been found to fire when the monkey observe or execute goal directed actions (Di Pellegrino et al., 1992), and this region has first been proposed to be the neural precursor of human imitation (Cattaneo and Rizzolatti, 2009). According to some authors (Wilson, 2005; Gallese, 2004), the MNS, allows the simulation of other people's actions, and it is necessary in order to understand and imitate them, as well as other people's intentions, emotions or mental states.

In addition to the linguistic and motor functions attributed to the IFGop, another function that has recently been associated with the IFGop is the emotional processing. Indeed this region has frequently found to be activated in fMRI studies, when emotionally salient stimuli are presented (Yamasaki et al., 2002; Koelsch et al., 2006; Jabbi and Keysers, 2008), and facial emotion recognition (Rosen et al., 2006; Adolphs et al., 2000) and empathy (Shamay-Tsoory et al., 2009) deficits were reported following lesions of the IFG. However, many studies in the field of affective neuroscience found that emotional stimuli tend to elicit the activity of both anterior insula and IFGop (for review see Craig, 2009). It has been proposed that insula and IFGop represent limbic sensory areas that are involved in the integration of interoceptive and environmental information, in order to achieve emotional perceptions (Critchley et al., 2004; Craig, 2011). Specifically, the involvement of IFGop in the voluntary control and perception of emotional facial expressions, its role in processing affective stimuli and empathy, suggest that the IFGop, together with the insula, constitute a hub that connects the affective and motor networks, as also suggested by animal studies (Jezzini et al., 2015; Gerbella et al., 2016; Morecraft et al., 2012).

More recently, a handful of neuroimaging and neuropsychological studies found the implication of the opercular part of the IFG in processing semantic information about conspecifics (Piretti et al., 2015; Chedid et al., 2016; Zahn et al., 2007; Skipper et al., 2011). However the role of the IFGop in this particular type of processing needs to be better specified. Different hypothesis have been put forward. According to the motor simulation theories, conspecifics knowledge might be associated with IFGop because, differently from other categories (e.g., artificial things, plants and animals), human stimuli are *imitable* (Wilson, 2005). In this context, the automatic and unconscious simulation of actions would be relevant in order to infer others' intentions and hence, for mentalization (Gallese et al., 2003; 2004). While action-related mentalizing might easily explain some findings concerning the knowledge about professions (implying actions and tool use) (Chedid et al., 2016), it does not appear to explain the association in patients of the IFGop with the lexical-semantic impairment in recognizing other social groups (e.g., ethnic groups, see Piretti et al., 2015), because these latter concepts are less obviously linked to action related features.

An alternative view holds that the association between IFGop and conspecifics knowledge might be due to the intrinsic emotional value of social stimuli. Many studies showed that social cognition (including theory of mind, empathy, social decision making, and moral judgment) and emotional processing tend to elicit the same neural network, including IFGop (for review, see Olsson and Ochsner, 2008). Although this overlap in brain areas of emotional and social processes is far from being understood, it has been proposed that the re-enactment of emotional states might be involved in the representation of social knowledge and in high-order social processes (Niedenthal et al., 2005).

Based on the above reviewed evidence, in the present study I tested the hypothesis that IFGop might be a key region in the categorical processing of conspecifics. In order to answer this question I tested participants on a classical priming paradigm, using three categories of stimuli (i.e., living entities, non-living entities and social groups), in which they were asked to judge whether the target was a real word or a pseudo-word (lexical decision task). Moreover transcranial magnetic stimulation (TMS) was applied between prime and target presentation, just before the participants responded, on three sites IFGop, IPL and vertex (VTX). My hypothesis was that, if IFGop is selectively involved in processing conspecifics (regardless of the valence), its stimulation would disrupt the priming effect only for the social groups, while IPL stimulation (which is thought to be involved in non-living entities processing, see e.g., Brambati et al., 2006) would interfere with the priming effect of the non-living entities. However, if the two areas are involved in categorical processing, their stimulation would also induce slower lexical decisions for targets belonging, respectively, to the category of social groups and non-living entities. Conversely, if the involvement of IFGop in conspecifics processing is triggered only by the processing of emotional features, I expect that, when this region is stimulated (compared to the other two), participants' lexical decisions reaction times (RT) to the target words would be biased by the valence of the stimuli (i.e., positive, negative). Specifically, RT are expected to be slower when IFGop was stimulated than in the control condition, consistently with the fMRI studies in which IFGop has been found to be associated with the processing of negative emotions (Kotz et al., 2002; Murphy et al., 2003; Kuchinke et al., 2005; Blair et al., 207; Goldin et al., 2008).

4.2 Methods

4.2.1 Participants

Eighteen participants (female = 14, age = 25.11 ± 3.55, years of education = 17.33 ± 2.72) took part to the study. Inclusion criteria were: to be Italian-native speaker, right-handed and to fulfil safety criteria for TMS (absence of neurological, psychiatric or cardiological conditions, acoustic prosthesis or pacemakers implantation, pregnancy). Each participant signed an informed consent, approved by SISSA Ethics Committee (Trieste, Italy), before taking part to the experiment, but was not informed about the purpose of the study until the end of it.

4.2.2 Stimuli

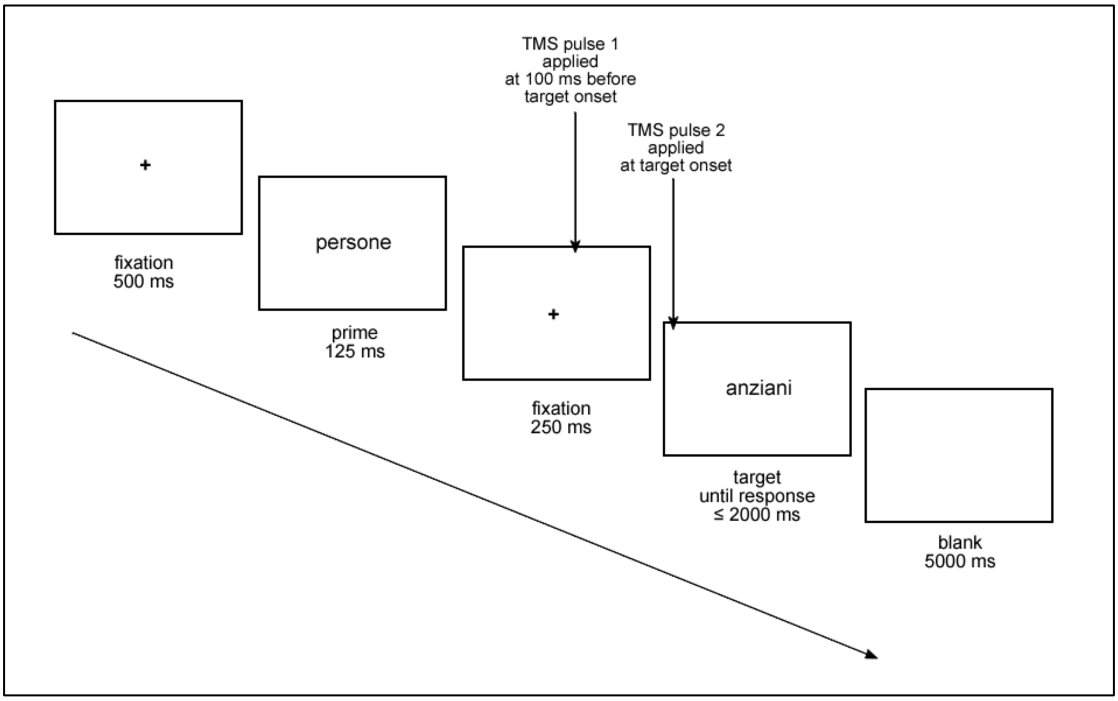
In order to select the target stimuli 14 participants were asked to rate the same words of the database used for the stimuli selection in chapter three, along four variables - age of acquisition (AoA), familiarity (Fam), imagenability (Ima) and valence (Val) - on a 1 to 9 point scale (except for AoA which was rated on a 1 to 7 point scale). For each category (living things, non-living things and social groups), 10 words were selected, matched for letter length, AoA, Fam, Ima and Val. Then, from this original sample of target words, words were sorted into two different subsets (N =10 and N =10) according to their valence (positive, negative) and independently of the category they belonged to. A χ^2 analysis revealed that overall positive and negative items did not differ (positive: χ^2 (1) = .33, p = .56; negative: χ^2 (2) = .00, p = 1.0). All pseudo-words were generated by Wuggy 0.2.0b2 Italian pseudo-word generator (http://crr.ugent.be/programs-data/wuggy), changing one-to-three consonants to the real target words. Pseudo-words were pronounceable according to the Italian phonological rules and their length was the same as that of the legal target words. Prime words were superordinate category nouns: *animali* (animals), *cose* (objects), *persone* (persons).

4.2.3 Experimental procedure

A PC running E-Prime 2.1 allowed the presentation of the stimuli and the recording of responses. Stimuli were projected via 19-inches CRT monitor with resolution of 1280*1024 pixels and a screen frame rate of 60Hz. Figure 11 depicts the sequence of events in a trial of the priming experiment: first the prime (i.e., animals, objects, persons) was presented, followed by a target word which could be real (e.g., 'cani' which means 'dogs') or a pseudo-word (e.g., 'bami'). More specifically, after a fixation cross (duration: 500 ms), the prime word was displayed for 125 ms and was followed by a second fixation cross (duration: 250 ms). During this latter fixation cross, 100 ms before target onset, a double-pulse stimulation was delivered (two stimulations with 100 ms of interval). Hence the last TMS pulse was temporally synchronized with the onset of the target word. Target words, which were presented in random order (avoiding the repetition of the same target in two consecutive trials), stayed on the screen until participant's response, with a deadline of 2000 ms. In order to avoid possible confounds associated to the stimulation of the previous trial, a 5000 ms interval was inserted between trials, and then the maximum duration for each trial was 7875 ms. Participants were asked to judge whether the word displayed was a real word or a pseudo-word, by pressing one of two keys (e.g., pressing either the left button if the word 'exists' and the right button if it 'does not exist'), the side of which was counterbalanced across participants. Since the TMS was mainly targeted to left-lateralized areas, participant responded using the task execution only their left index and middle fingers. Before the experiment proper, participants were given 25 practice trials with different stimuli.

The experimental task was presented three times, in three different blocks. In each block, which included 180 trials (30 words and 30 non-words applied to three priming conditions) participants were stimulated in different sites (IFGop, IPL, VTX), and the order of stimulation was counterbalanced across participants. In order to avoid discomfort or tiredness, that can be experienced when TMS is applied, a short break were inserted every 60 trials. Each participant performed the tasks in two different days (range: 1-4 days), with two blocks in the first day and one block in the second day, in order to avoid possible effects associated to tiredness. The average time for completing one block was around 25 minutes.

Figure 11



Note. The figure shows a schematic illustration of the task performed in the experiment.

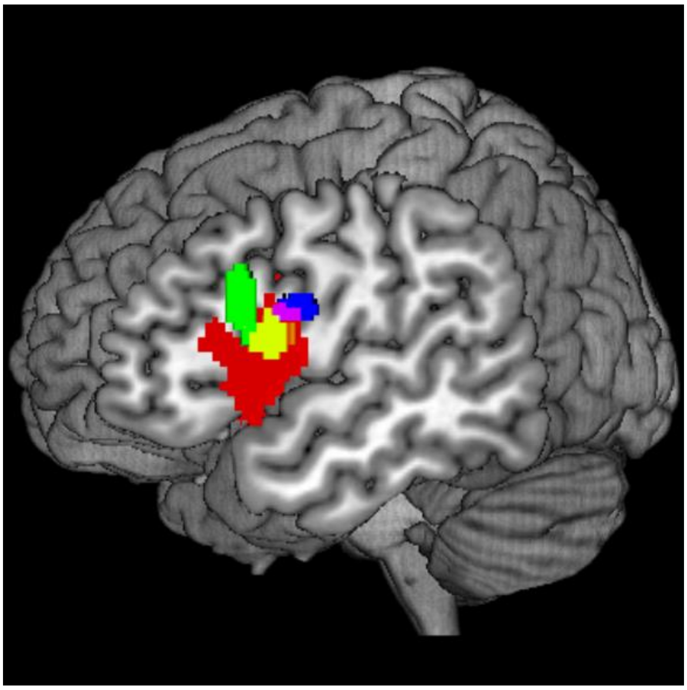
4.2.4 Transcranial Magnetic Stimulation

4.2.4.1 MR image co-registration and stimulation sites

Prior to the experiment, a high-resolution anatomical T1-weighted magnetic resonance images was acquired for each participant. In order to precisely position the TMS coil on the stimulation sites, individual brains were normalized into Montreal Neurological Institute (MNI) space manually by setting anterior commissure and posterior commissure in

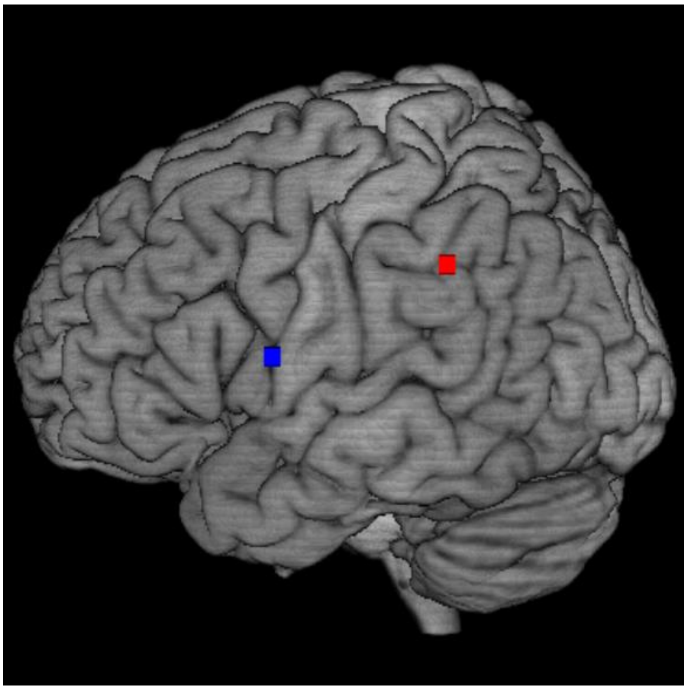
Brainsight 2.1.5 software (www.rogue-resolutions.com). TMS coil and the of participants' head were recognized and tracked using a Polaris Vicra Optical Tracking Systems (Polaris, Northern Digital, Ontario, Canada), so that the position of TMS coil could be positioned to the selected target site level. Stimulation sites were identified on each reconstruction brain on the basis of macro-anatomical landmarks (nasion, tip of nose, left and right lateral canthi, and left and right tragi). The sites of stimulation were left IFGop, left IPL and VTX. Left IFG was chosen based on previous findings, since lesion to this region has been associated with naming impairment for social groups (as reported in the studies included in Chapters 2 and 3 of this thesis) or retrieval of general person knowledge (Simmons, et al., 2010; Chedid et al., 2016) (see Figure 12); whereas left IPL was found involved in processing artefacts in previous TMS study (Pobric, et al., 2010; Brambati et al., 2006). VTX session was used as a control condition and was set manually in T1-weighted structural image for each participant. MNI coordinates for the stimulation sites in current experiment were l-IFG (x = -48, y = 1, z = 15), l-IPL (x = -49, y = -44, z = 48) (see Figure 13).

Figure 12



Note. Figure summarizes the findings reported in the previous chapters of the thesis, associating IFGop and conspecifics processing: in *blue* the results from the meta-analysis in Chapter 1), in *red*, from the neuropsychological study on brain tumor patients (Chapter 2) and, in *green*, from the study on patients with dementia (chapter 3). *Yellow* indicates an overlapping between the findings of the studies on patients with brain tumors and dementia, while *purple* indicates the overlapping of results from the meta-analysis and the study on brain tumor patients.

Figure 13



Note. Figure shows the location of the specific sites of stimulation: IFGop (blue) and IPL (red)

4.2.4.2 TMS parameters

Paired-pulse TMS was performed by two 200^2 units connected to a $BiStim^2$ module (Magstim Company, Whitland, UK). A 70 mm figure-of-eight coil was used to delivered TMS pulse. The interval between two pulses was set to 100 msec in order to better inhibit the activity of the target sites (Chen, et al., 1997; Oshio, et al., 2010). During the experiment, the coil was held by mechanical arm and maintained tangential to the skull with the handle pointing towards the midline.

The stimulation intensity used in the experiment was set at 90% of the individual resting motor threshold (mean = 30.66%, SD = 3.77% of maximum stimulator output intensity), which was defined as the intensity of single-pulse stimulation that evoked 5 out of 10 visible finger/hand motor responses for the participant. For every participant, the motor threshold was measured before the stimulation procedure, in both days of experiment.

4.2.5 Data Analysis

All the analyses were performed using SPSS (version 21.0.0.0, https://www.ibm.com/analytics/us/en/technology/spss/). Only trials with corrected responses and with real-word target were included. After a logarithmic transformation of the RT (necessary to normalize RT distribution), I filtered trials with logRT exceeding more than two standard deviations from the mean of each subject and each block. In order to reduce the influence of different testing session, we performed a z-transformation of the logRT, using means and standard deviations of each participant and block, and used this score (ZRT) for all the analyses. After the filtering procedure the 8.0% of trials were excluded from the analysis. In order to evaluate the priming effect we calculated the Priming size, subtracting from the ZRT of each congruent trial (e.g., prime = 'animals'; target = 'dogs') the average ZRT of incongruent trials (e.g., prime = 'objects', 'persons'; target = 'dogs') for each category of items in each of the three stimulation sites. A priming effect should lead to negative values of the priming size. Since a the priming effect was present for all the categories of all participants, I selected for each category, only the participants with a Priming size lower than zero at the level of the VTX, that served as a control condition (N = 10 for living entities; N = 12 for non-living entities, N = 8 for social groups). Then, for each category, I performed repeated-measure ANOVA, using the Priming size as dependent variable and the different stimulation sites as between-subject factor. However, since TMS might interfere also with the semantic access to the target word, regardless of the prime, I performed a repeated-measure analysis of variance (ANOVA) on the mean ZRT for each category of targets, using as within-subject factors the site of stimulation (IFG, IPL, VTX) and the target category (living things, non-living things, social groups). Moreover, a second ANOVA using the site of stimulation and the target valence (positive, negative) as factors was performed. Pairwise comparisons were performed using Bonferroni correction.

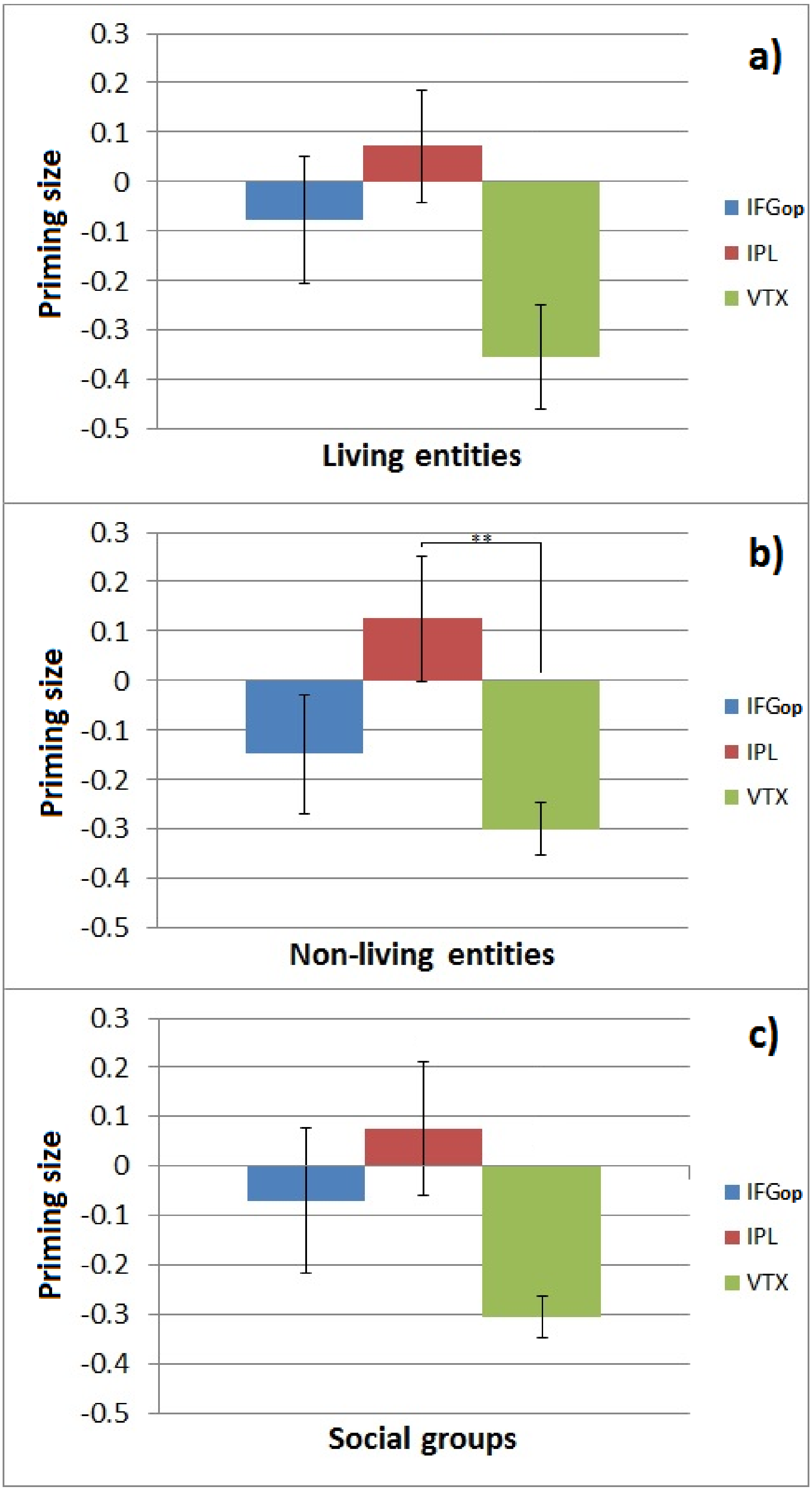
4.3 Results

The total accuracy was 97.7% (SD = 0.02%) for pseudo-words and 98.4% (SD = 0.013%) for words.

4.3.1 Categories

Repeated-measure ANOVAs on priming size (see Figure 14) on the non-living entity category revealed a significant main effect of site ($F(2, 22) = 6.01$, $p < .01$), with higher priming size score when the stimulation occurred at the level of IPL than of the VTX. The same analysis on the other categories did not reveal any significant main effect of site (ps > .05).

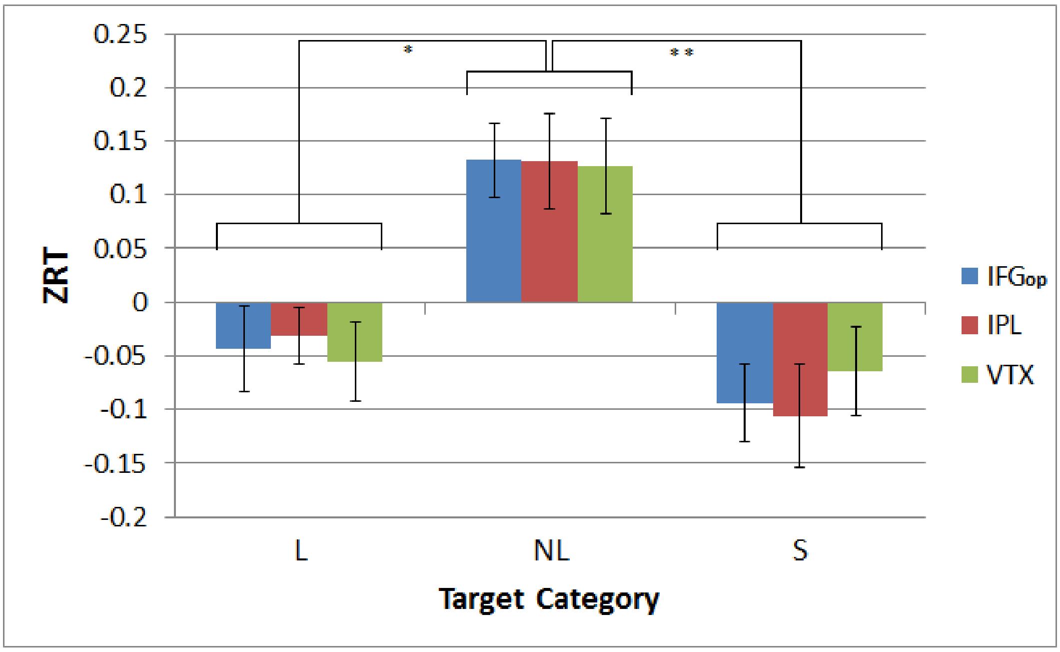
Figure 14



Note. The graph shows the priming size on the three different categories of targets, for the three sites of stimulation. ** $p < .01$

The repeated-measure ANOVA on target category (see Figure 15 and Table 19) revealed only a significant main effect of Category (*F*(2, 34) = 14.10, *p* < .001). Indeed non-living things were associated with slower ZRT than both living things (*p* < .01) and social groups (*p* < .001).

Figure15



Note. The graph shows ZRT of the three categories of targets for the three stimulation sites. * *p* < .05, ** *p* < .01.

Table 19

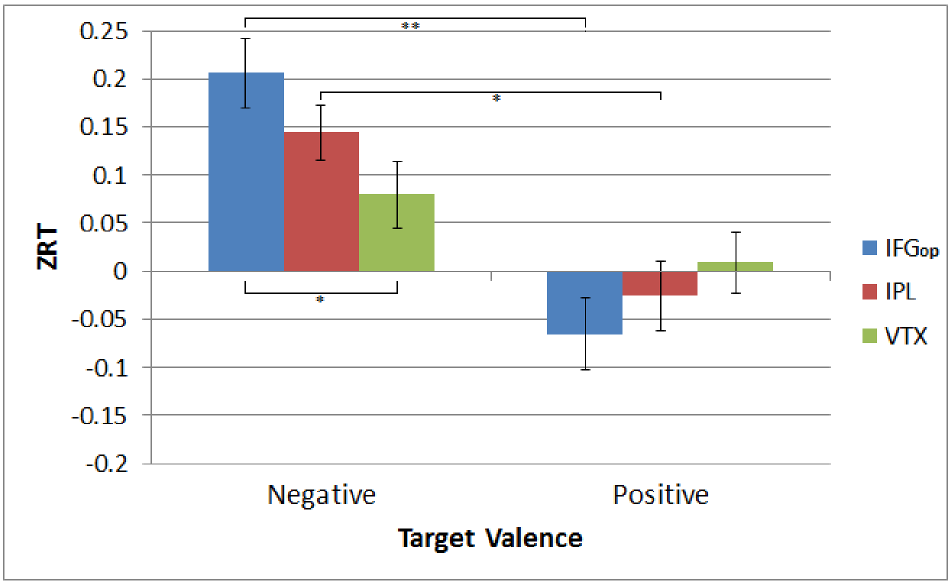
	Target category		
Site	Living things	Non-living things	Social groups
IFG	-0,04 ± 0,17	0,13 ± 0,15	-0,09 ± 0,15
IPL	-0,03 ± 0,11	0,13 ± 0,19	-0,11 ± 0,2
VTX	-0,06 ± 0,16	0,13 ± 0,19	-0,06 ± 0,18

Note. The table shows the means and standard deviations of ZRT of the three categories of targets, on the three stimulation sites.

4.3.2 Valence

The repeated-measure ANOVA on target valence (see Figure 16 and Table 20) revealed a significant main effect of valence ($F(1, 17) = 13.82$, $p < .001$) and a significant interaction of valence x site ($F(2, 34) = 4.20$, $p < .05$). Negative stimuli were overall recognized slower than positive ($p < .01$) and, more specifically, negative stimuli were associated to slower RT than positive during the stimulation of both IFG ($p = .01$) and IPL ($p < .05$). Moreover, negative stimuli were processed more slowly in the stimulation of IFG than the VTX ($p < .05$) but not the IPL ($p = .21$).

Figure 16



Note. The graph shows ZRT on the target valence, for the three stimulation sites. * $p < .05$, ** $p < .01$.

Table 20

	Target Valence	
Site	Negative	Positive
IFG	0,21 ± 0,15	-0,07 ± 0,16
IPL	0,14 ± 0,12	-0,03 ± 0,15
VTX	0,08 ± 0,15	0,01 ± 0,13

Note. The table shows the means and standard deviations of ZRT of the stimuli modulated by target valence, on the three stimulation sites.

4.4 Discussion

The aim of the study was to test whether IFGop was selectively implicated in processing conspecifics. To test this hypothesis I had participants perform a priming study with three semantic categories – animate entities, inanimate entities and social groups - while I applied the TMS on participants' IFGop. As control conditions we also stimulated IPL and VTX. Results revealed that only for the non-living category, the priming size was significantly higher when the IPL was stimulated relative to the VTX. IFGop did not show any significant difference with both IPL and VTX. These results confirmed what reported previously by both TMS (Pobric et al., 2010), neuropsychological (Brambati et al., 2006) and functional neuroimaging (Vitali et al., 2005) studies in which IPL was found to be implicated in semantic processing of non-living entities. Importantly, the main effect of category did not reach the significance threshold for either living entities or social groups. Moreover, the lack of association between IFGop and social group processing was confirmed by the results on the ZRT of the different target categories (from the lexical decision task) for the different sites of stimulation. Social groups did not show slower ZRT during the IFGop stimulation compared to when the other brain sites were stimulated. Indeed, only a main effect of category emerged, with non-living entities showing slower ZRT compared with the other categories, as also reported in other studies (e.g., Cattaneo et al., 2010). These results, together with the finding of the studies associating conspecifics processing and IFGop (Piretti et al., 2015; Chedid et al., 2016; Zahn et al., 2007; Skipper et al., 2011), suggests that IFGop could be involved in processing emotional stimuli, regardless of the semantic category.

The analysis of reaction times of the valence revealed that negative stimuli were recognized more slowly than positive stimuli, consistently with previous evidence (Estes and Verges, 2008). This effect has been assimilated to a freezing response (i.e., general suppression of motor activity) to threatening stimuli (Fox et al., 2001), which might be adapting in reducing the likelihood of being detected by dangerous entities. However this phenomenon has frequently been found only when stimulus valence was irrelevant for the accurate response (i.e., lexical decision task), as in the present study. Indeed, when participants pay attention to the valence (i.e., valence judgment), negative stimuli tend to elicit faster responses than positive items (Estes and Vargas, 2008; Grecucci et al., 2011). This phenomenon is thought to occur because attention tend to be disengaged more slowly from negative stimuli than other stimuli (Fox et al., 2001; Yend and Mathews, 2001), but when the access to the valence is relevant for the correct response of the task, the attentional disengagement from the valence of the stimulus is not required and the motor system might be prepared for immediate action (Estes and Vargas, 2008).

However, the analysis of target valence also revealed that the stimulation on IFGop was associated to slower ZRT than the one on the VTX. This finding is consistent with the role of IFGop in processing emotional stimuli (Baird et al., 2011). Specifically, this region appears to be selectively involved in processing negative emotions, thus confirming previous findings (Kotz et al., 2002; Murphy et al., 2003; Kuchinke et al., 2005; Blair et al., 207; Goldin et al., 2008).

Together these results suggest that IFGop is not relevant in the categorical processing of conspecifics and, apparently, seem to be in contrast with the studies reported about social group, and, more broadly, on conspecifics knowledge (Zahn et al., 2007; Piretti et al, 2015; Chedid et al., 2016). Indeed, the accurate matching of valence did not show any association between IFGop and knowledge about social groups. However, the stimulation of IFGop was associated with slower RT for the judgment of negative stimuli, and this is consistent with the hypothesis that, in the context of semantically processing social groups, IFGop might be involved in processing their emotional content. Further research is necessary, in order to confirm the role of IFGop in the processing of social emotional features.

CHAPTER 5

General discussion

In the current thesis, I investigated how the knowledge of conspecifics, living and non-living entities is represented in the brain. Results showed that, naming pictures of social groups was selectively impaired in patients both with focal lesions (brain tumors) and diffuse brain atrophy (neurodegenerative diseases) in the left hemisphere. Overall, this set of areas includes insula, inferior frontal gyrus (IFG), amygdala (only in Chapter 2 in tumor patients), and medial prefrontal cortex (MPFC) (only Chapter 3 in dementia patients), areas often found to be associated with affective processing (for review, see Pessoa, 2008). Moreover, a further investigation on healthy participants revealed that the stimulation of a specific area within the opercular part of IFG (IFGop), which was found associated with conspecifics knowledge in the meta-analysis and in both the neuropsychological studies in this thesis, led to slower response time when the valence of the stimuli was negative. In this section I will discuss how these findings, including the anatomical lateralization, can be accommodated within current models on person-specific recognition and general semantic knowledge.

The investigation of conspecific knowledge has for long coincided with the study of semantic memory for familiar and famous persons. In the light of these studies, Bruce and Young (1986) proposed a model, revised by Burton et al. (1990, 1999) and, more recently, by Blank et al. (2014), to explain how we recognize individuals from faces, voices and names. The model proposed that distinct recognition units would encode specific-persons' face, voice and name representations, and that each recognition unit would be connected to a person identity node (PIN), involved in the multimodal representation of each individual. The different versions of the model do not agree on how person-related information (e.g., the social group they belong to) is recollected. On the one hand, each PIN is relevant in forming a multi-modal semantic representation of the other individuals, including person-related semantic information (Bruce and Young, 1986), while on the other, they would be connected to the semantic information unit, representing only a merging zone between the different perceptual representation (Burton et al., 1990; 1999).

The meta-analysis I reported in Chapter 1 of my thesis revealed that the brain network was selectively associated with conspecific representation that included several areas in both hemispheres. More specifically the network included visual areas (bilateral occipital cortices, bilateral fusiform gyri, bilateral posterior STS) possibly corresponding to face recognition units (FRUs), auditory areas as the right STS possibly corresponding to voice recognition units (VRUs) and areas often found to be associated with emotional processing such as the amygdala bilaterally, medial prefrontal cortex, and left inferior frontal gyrus. Interestingly, no specific area within the anterior temporal lobes (ATLs) (PINs) has been found to be associated with the processing of conspecifics. The lack of an involvement of areas within the anterior temporal lobes can be explained in two ways. First, this might be due to the deformation of the magnetic field induced by air-filled structures close to ATLs, that, without distortion-corrected fMRI protocols, would induce a loss of signal in those areas (Murphy et al., 2007). Second, the studies included in the meta-analysis I performed might have used tasks and stimuli (e.g., unfamiliar faces) that failed to tap the identity of each individual.

The finding of unimodal processing areas (i.e., visual, auditory and emotion) associated with conspecific knowledge can be interpreted within the context of the model by Bruce and Young (1986) on person-specific recognition at least in two different ways. First, this functional neuroimaging evidence of emotion-related areas associated with conspecifics processing could be interpreted as recognition unit coded in a different modality (i.e., a putative emotion recognition unit), possibly involved in representing the attitude towards each individual, and second, it might represent the outcome of the recollection of person-related knowledge. Hence, the two explanations entangle two different roles of affective processing in conspecifics knowledge: According to the former account, affective processing is part of the conspecifics conceptual knowledge, while according to the latter it would merely be an epiphenomenon of conspecific knowledge recollection. Moreover, the prediction stemming from the two accounts is that, for the former, the lesion of emotional processing area would lead to the impoverishment of the conceptual knowledge about conspecifics, with spared abilities of recognizing people from faces, voices and names, while for the latter it would lead to no conceptual deficit of conspecifics knowledge.

The findings reported on patients with brain tumors and on patients with dementia reported respectively in Chapter 2 and Chapter 3,in which I investigated semantic knowledge about social groups and other entities (i.e., living things and non-living things), showed that the lesion of areas often associated with affective processing led to a selective impairment in naming that can be attributed to a degradation of lexical-semantic knowledge about social groups (i.e., basic level knowledge about conspecifics). Moreover, in Chapter 4 healthy participants performed a lexical decision task with nouns of social groups and exemplars from other categories and I observed that participants were slower RT when transcranial magnetic stimulation (TMS) was applied on one of these areas, i.e. IFGop, than in the control condition (i.e., vertex) specifically when the valence of the presented word was negative. This latter finding suggests that IFGop is sensitive to the valence of the stimuli. Taken together the findings reported in my thesis strongly suggest that affective features are relevant in building up a conceptual representation of our conspecifics. They also lead me to reject the hypothesis that the activation of emotion-related areas might be an epiphenomenon of the conspecifics perception as suggested by the meta-analysis on neuroimaging studies about conspecifics (Chapter 1).

The model of person recognition by Bruce and Young (1986) does not directly take into account the different levels of specificity of the human stimuli that might contribute towards their representation. A human stimulus might be recognized as a specific individual, say a person we personally know (unique entities), but also as belonging to a category of individuals, that is a social group (supra-ordinate level). Unique entities and supra-ordinate human stimuli might differ in several respects: unique entities are usually associated with specific semantic knowledge, they are usually associated also with episodic memory, they are denoted by a proper name, they might be associated with richer perceptual knowledge than supra-ordinate knowledge (which tends to be prototypical) (Ross and Olson, 2012; Wang et al., 2016) and the distinction among unique entity elements might be based on more subtle features than for supra-ordinate (Gorno Tempini and Price, 2001). The investigation on unique entities revealed that, although different categories of entities (e.g., famous persons and famous buildings) tend to be associated with distinct sites of activations, all unique entities were associated with the function of the temporal poles (Gorno Tempini and Price, 2001; Ross and Olson, 2012). Coherent with these findings some fMRI experiments showed that ATL tend to be activated when the task requires a semantic discrimination between sub-ordinate entities, but not between supra-ordinate entities (Tyler et al., 2004; Rogers et al., 2006). Moreover, patients with semantic dementia - a neurodegenerative disease associated with the atrophy of ATL - tend to show semantic impairments, which are more severe for subordinate knowledge than for supra-ordinate concepts (Patterson et al., 2006; Rogers et al., 2015). This pattern of findings suggests that along the temporal lobes, there might be a gradient of representation, from posterior to anterior, processing, respectively, from general to specific concepts (Martin, 2007). However, other studies made the picture more complex.

Indeed, ATL was found to be involved also in basic/supra-ordinate level of processing in TMS (Pobric et al., 2010) and FMRI (Visser et al., 2011) studies. Moreover, results from neuropsychological studies in Chapter 3, and to a smaller extent, in Chapter 2 of my thesis, showed that also social group knowledge, which codes information about individuals at a supra-ordinate level, was associated with temporal polar damage. Together my findings, strongly suggest that ATL might also be involved in the processing of basic-level concepts.

However, a critical aspect that must be considered when discussing about the representation of conspecifics, as well as about other categories of entities, is the functional lateralization. Although the meta-analysis (Chapter 1 of this thesis) highlighted a pattern of activations associated with conspecifics processing (except for the left IFG) mostly bilaterally, patients' results (reported in Chapters 2 and 3 of this thesis) highlighted the involvement of a left-lateralized network of areas. This pattern of findings might be explained, at least, in two ways. The lateralization might be explained by the type of task I used in the experiments, but it could also be specific for the representation of this category of knowledge. The relative contribution of left and right hemispheres to semantic representation is still a matter of debate. Indeed patients with a left-lateralized damage tend to have more impaired production abilities compared with their receptive abilities, while patients with right lateralized (or predominantly right–lateralized) damage tend to lead to both productive and receptive abilities or to very mild impairments (in case of unilateral brain damage) (Lambon Ralph et al., 2001; Rice et al., 2015). To explain these findings, two main theories were proposed. First, it has been proposed that semantic knowledge might be differently specialized into the two hemispheres, with the left ATL involved in representing verbal knowledge and right ATL representing non-verbal (e.g., visual, auditory) knowledge (Snowden et al., 2004; 2012). Second, another model proposed that semantic knowledge is represented bilaterally, but left-lateralized semantic storage would have a privileged access to phonological areas, leading left-lateralized semantic deficits to be expressed mainly as lexical impairments. Both the neuropsychological studies reported in this thesis (Chapters 2 and 3) demonstrate that patients with unilateral and diffuse brain damage showed impaired productive abilities (picture naming task) but spared recognition abilities (word-to-picture matching task). Moreover patients' picture naming deficits were mainly associated with lesions of a left-lateralized network. Hence, according to the model by Snowden (2004, 2012) the social group deficits we measured were basically at the lexical level, while according to the model by Lambon Ralph et al. (2001) they were at the level of the semantic representation. Although this pattern of findings is consistent with both theories on semantic deficits lateralization, right lateralized damage to the very same areas in patients with brain tumors did not give rise to any semantic deficit (on either production or recognition), thus the model by Snowden et al. (2004; 2012) cannot accommodate my results.

A critical issue about the person recognition model is how the specific processing of conspecifics relates to other categories of knowledge. For instance, several studies suggested that animate and inanimate entities tend to be processed in discrete neural areas, such as the inferior part of the ATL for animate entities, and the inferior parietal lobe (IPL)/posterior temporal lobe for inanimate entities (Gainotti, 2000). This pattern of findings was consistently found using different methodologies (neuropsychology, fMRI, TMS, electrophysiology) and led to propose that these two categories might be processed by different neural systems (see also Brambati et al., 2006; Anzellotti et al., 2011; Damasio et al., 1996; Devlin et al., 2002, Chan et al., 2011) and that, while animate entity processing might rely on areas within the ventral visual pathway (inferior temporal cortex) (Kravitz et al., 2013), inanimate entities might rely on areas within the dorsal visual pathway (IPL) (Kravitz et al., 2011). In this context the double dissociations in patients between the knowledge about conspecifics at both unique-entity (Hanley et al., 1989; Evans et al., 1995; Miceli et al., 2000;

Kay and Hanley, 2002; Lyons et al., 2006; Thompson et al., 2004) and social group (Rumiati et al., 2014) level of specificity, and living or non-living entities, suggest that conspecifics are processed independently of the exemplars from the other two categories.

My thesis adds a further piece of information about the way in which conspecifics are represented in the brain. In fact I have found evidence that the processing of conspecifics at a basic level of specificity is associated with areas typically involved in processing emotions. This might be interpreted in different ways depending on the model. For instance, according to the domain-specific hypothesis (DSH, Caramazza and Shelton, 1998; Mahon and Caramazza, 2011) distinct domains of entities such as animals, plants, artifacts and conspecifics, are processed by different neural networks as a result of the evolutionary pressure. Thus, the network of areas that I found to be selectively associated with social group processing, seems to support the view of a domain-specific representation for conspecifics. This interpretation is confirmed by the findings of the meta-analysis reported in Chapter 1 in which the same areas (except for insula) were found to be activated in studies which directly contrasted social vs. non-social (e.g., animals, places, objects) stimuli. However, the TMS study reported in Chapter 4 of the current thesis clarified that one if these areas, the left IFGop rather than being involved in the categorical processing of social groups, it might more likely be involved in processing emotional stimuli.

Conversely, other theories highlighted the role of modality-processing areas in representing concepts. According to the sensory-functional theory (SFT) (Warrington and Shallice, 1984), for instance, our cognitive system processes the distinct conceptual features into parallel modality-dependent semantic systems (i.e., sensory, motor/functional). Thus, categorical deficits may emerge as a consequence of damage to one of these subsystems, since the representation of distinct categories relies on different semantic features.

My findings can be better accounted for if, beyond the classical formulation of the theory, holding a distinction between sensory (mainly visual) and functional features, we also consider the emotional modality dedicated to process the emotional features of conspecifics. Indeed, in my study involving patients with neurodegenerative diseases (Chapter 3), the deficit in picture naming was associated with the atrophy at the level of bilateral inferior temporal cortices for natural categories (the ending point of the ventral visual pathway (Kravitz et al., 2013)), with dorso-lateral prefrontal cortex for artificial categories (relevant in motor processing (Hetù et al., 2013)), and emotion-related areas for social groups.

Moreover, Simmons and Barsalou (2003) proposed a hierarchical model, the conceptual topography theory (CTT), in which exemplars' features are represented within modality-specific areas that are integrated, through the sequential processing within distinct convergence zones (CZs), in order to assemble categorical representations. While analytic and holistic CZs are relevant in order to integrate features sharing similar properties, modality and cross-modal CZs are relevant for integrating conceptual properties in order to implicitly form categorical knowledge. Moreover, they proposed that, within convergence zones, neurons representing similar features are located topographically close. This complex model has the potential for explaining many different patterns of patients' deficits, ranging from isolated categorical deficits, to multi-categorical deficits (i.e., deficits in the knowledge of more than one category, with some categories preserved), to global semantic impairments. Categorical semantic deficits might emerge as a consequence of the damage modality and cross-modal CZs (respectively on uni-modal and multi-modal concepts), or in the case of analytic and holistic CZs lesion, only if the category relies on the damaged property. Thus the association between left insula, left anterior cingulate/medial PFC and left IFG lesion with the lexical-semantic impairment in patients' naming social groups is not easy to be explained in the light of the CTT. The model easily explains the categorical knowledge deficits reported in the study, but we are not able to say whether these areas are involved in the representation of some specific properties of social stimuli (which could be associated with the lesion of analytic or holistic CZs) or of their uni-modal categorical knowledge (modality CZs for the emotional modality). However, the posterior part of the IFG (pars opercularis) has been proposed as a hub connecting affective and motor networks (Jezzini et al., 2015; Gerbella et al., 2016; Morecraft et al., 2012), and might be interpreted, in the light of CTT, as a cross-modal CZ. Moreover, the pattern of findings on natural and artificial stimuli, which coincided with the ending points of, respectively the ventral and the dorsal visual pathways, could also be interpreted according to the CTT, as modality CZs (or alternatively, cross-modal CZs). Hence, the CTT, differently from the SFT, is able to explain why, the deficit in naming a certain category of stimuli might be associated with the atrophy within different modality processing areas, when is associated with other categories.

To sum up, the findings of the current thesis, suggest that conceptual knowledge is associated with modality-specific processing areas, and specifically that social group representation might interact with emotional features. From a theoretical point of view this is more easily explainable by the CTT, although is not possible to exclude the role of domain-specific networks explaining my findings, as suggested by the DSH. However, further research is necessary, in order to better understand how we represent our conspecifics and the specific role of each emotion-related area associated with social group lexical-semantic knowledge.

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