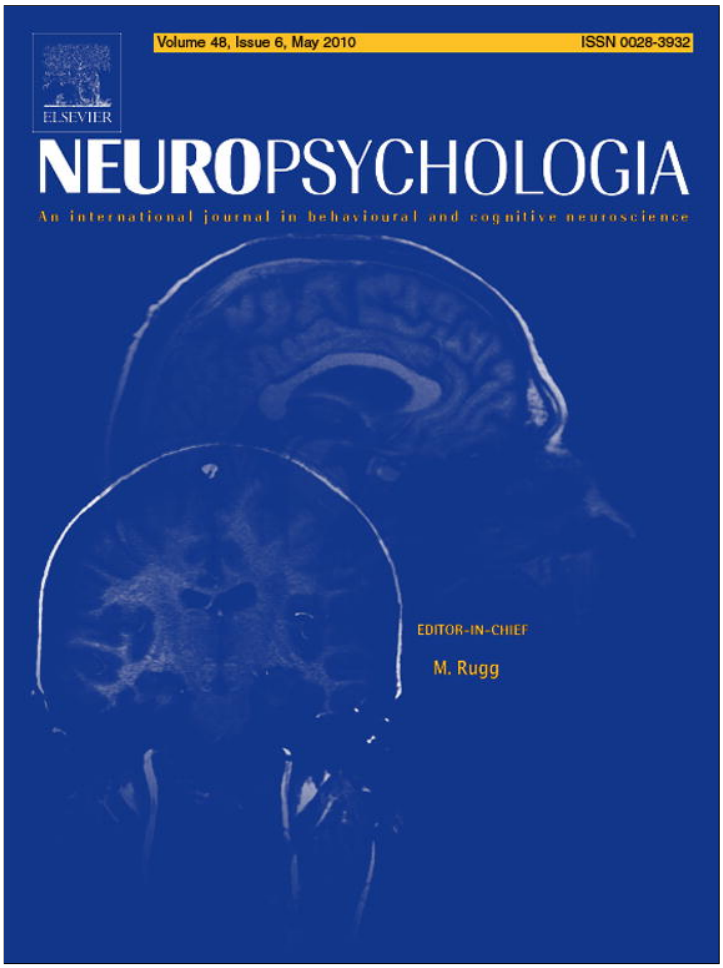

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Naming manipulable objects: Anatomy of a category specific effect in left temporal tumours

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ABSTRACT

Whether semantic knowledge is categorically organized or is based in an undifferentiated distributed network within the temporal lobes or it is at least partially organized in property-based networks is still an open issue. With a naming task involving living and nonliving entities, the latter divided according to degree of manipulability, we studied a group of 30 tumour patients with either right, left anterior or left posterior temporal lobes' lesions and a herpes simplex encephalitis patient (MU). Both cross-subject and cross-stimulus analyses were conducted. Left hemisphere patients were overall worse than both right hemisphere patients and controls in the naming task. They moreover named nonliving items worse than living. This effect was larger in left posterior temporal than both right temporal and also left anterior temporal patients and significant both at a cross-subject and cross-stimulus levels of analysis. In addition the left posterior temporal group had more difficulties with highly manipulable objects than left anterior temporal patients, but the effect was significant only on a cross-subject analysis. VLSM lesion analysis revealed that the area most critically associated with the larger naming deficit for manipulable objects was the posterior superior portion of the left temporal lobe, particularly the posterior middle temporal gyrus. These results support a 'property-based networks' account of semantic knowledge rather than an 'undifferentiated network' account. For manipulable objects, this would be a posterior-temporal/inferior-parietal left hemisphere "action/manipulation-property-based" network related to the dorsal pathways which is thought to be important in action control, as suggested by neuroimaging results.

1. Introduction

The debate in cognitive neuroscience on the organisation and anatomical underpinnings of the semantic memory is still open. Semantic memory impairments have been widely associated with damage to the temporal lobes bilaterally but more prominently with respect to the left hemisphere (see e.g. Gainotti, 2000; Mummery et al., 2000; Noppeney et al., 2007). Several aetiologies have moreover been found to be likely to produce semantic impairments (see Patterson, Nestor, & Rogers, 2007 for a review), ranging from degenerative syndromes such as semantic dementia (e.g. Hodges, Patterson, Oxbury, & Funnel, 1992; Snowden, Goulding, & Neary, 1989) or Alzheimer disease (e.g. Giffard et al., 2001; Grossman et al., 2003), to herpes simplex encephalitis (e.g. Noppeney et al., 2007; Warrington & Shallice, 1984), stroke (e.g. Jefferies & Lambon Ralph, 2006) or, as in this context, brain tumours (e.g. Campanella, Mondani, Skrap, & Shallice, 2009).

In a recent investigation on the semantic abilities of patients affected by temporal lobes tumours, it has been shown that tumours in the posterior portion of the left temporal lobe consistently produce difficulties in accessing concepts from verbal input (Campanella et al., 2009). These difficulties have been interpreted as resulting from the disconnection of the lexical input from the more inferior temporal semantic areas, caused by the presence of gliomas (tumours involving the subcortical white matter). Interestingly, the material used in the study by Campanella et al. (2009) comprised stimuli belonging only to the category of small manipulable objects.

A similar type of deficit and a similar anatomical localization are found in one of the first seminal investigations about category specific semantic memory impairments. Warrington and McCarthy (1987) described a patient (YOT) who suffered a left posterior temporal-parietal lesion following a left middle cerebral artery occlusion. As for the tumour patients described by Campanella and colleagues, this patient also had a semantic deficit of an access rather than degradation type. YOT was also one of the first patients

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described as having a selective semantic deficit affecting the category of nonliving things. A similar deficit had been previously reported in only one occasion but in a patient with a different aetiology: like YOT, patient VER (Warrington & McCarthy, 1983) suffered from a semantic access impairment which selectively affected nonliving things. Her lesion involved the left frontal ant parietal areas.

The selective loss of knowledge specific to one (or a few) categories of knowledge has been extensively investigated in the last 30 years but from a theoretical point of view this phenomenon still remains an open issue. The most investigated category specific effect involves the double dissociation between the selective loss of knowledge about living entities with respect to artefacts (Warrington & Shallice, 1984) and the complementary syndrome (Warrington & McCarthy, 1983; Warrington & McCarthy, 1987). From a clinical point of view, many more cases of deficit for living things than nonliving entities have been reported in the literature (see Capitani, Laiacona, Mahon, & Caramazza, 2003; Gainotti, 2000 for reviews), in a ratio of approximately 3:1. However, in a recent investigation on the naming ability of a very large sample of patients suffering from different neurodegenerative diseases, Brambati et al. (2006) found a brain area which was more clearly associated with a deficit in naming nonliving things. This area was restricted to a portion of the posterior and superior parts of the left temporal lobe which was close to that reported by Campanella et al. (2009).

From a theoretical point of view, the original account proposed to explain category specific deficits (later called the Sensory Functional Theory or SFT) was that knowledge could be stored in modality congruent 'channels', with the relative weight of information contained in these channels varying across different concepts. The knowledge which is crucial in order to distinguish between living entities is held to rely mainly on sensory quality features (mainly visual 'channels': shape, colour, texture) and therefore could be primarily retained in bilateral ventral temporal brain areas (Gainotti, 2000) which process visual aspects of percepts (Ungerleider & Mishkin, 1982). On the other hand, knowledge about artefacts was originally held to rely more on functional attributes (what it is for, how it is used) and more recently (e.g. Saffran & Schwartz, 1994) to rely more specifically upon a system controlling action, with a different anatomical substrate. This means that one's knowledge of a concrete entity would comprise both visual and functional/action attributes, but not in equal proportions for all categories of entities. Therefore the categorical dissociation effect would be a byproduct of this differential weighting of features.

In recent years, a considerable amount of evidence, coming mainly from fMRI studies, has been accumulated suggesting that there are brain areas that selectively respond to a variety of tasks in which the recognition or semantic processing of manipulable objects is required (Beauchamp, Lee, Haxby, & Martin, 2002; Beauchamp, Lee, Haxby, & Martin, 2003; Canessa et al., 2008; Chao & Martin, 2000; Kellenbach, Brett, & Patterson, 2003; Martin, 2007; Mahon et al., 2007; Weisberg, van Turennout, & Martin, 2007; see also Brambati et al., 2006; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Tranel, Kemmerer, Adolphs, Damasio, & Damasio, 2003 for evidence coming from neuropsychology). These areas constitute a complex left hemisphere lateralized network including the middle temporal areas, the inferior parietal lobe (IPL) and the intraparietal sulcus (IPS), as well as premotor areas. Many of these areas are indeed part of the cortical circuit which is responsible for the processing of action related information and for visuomotor interaction: the so called "dorsal" or "where" pathway (Culham & Valyear, 2006; Goodale & Milner, 1992; Goodale, Milner, Jakobson, & Carey, 1991). The dorsal pathway comprises several cortical areas, including the medial temporal area (MT or V5), the medial superior temporal area (MST), and the ventral and lateral intraparietal areas (VIP and LIP). It has, however, been suggested that the activation of at least some the areas involved in this 'manipulable object processing' complex left hemisphere circuit (in particular pre-motor areas) may also reflect a post-semantic activation more linked to explicit imagery processes, rather than reflecting access to stored knowledge about the concept (e.g. Harris, Clifford, & Miniussi, 2008; Papeo, Vallesi, Isaja, & Rumiati, 2009).

The main argument against the sensory/functional account has been that some patients exhibiting category specific losses of knowledge did not show a concomitant selective loss of perceptual or functional knowledge, the loss of the two types of knowledge being comparable (Caramazza & Shelton, 1998; Lambon Ralph, Howard, Nightingale, & Ellis, 1998). However, while there has been overall agreement on how to define "perceptual" features, the common definition of a "functional feature" has been much broader and less well defined. It has even ranged from strictly functional and motor related aspects (how it is manipulated) to more contextual aspects (where it is found). Indeed, Caramazza and Shelton (1998), when testing the semantic competence of their patient EW, just divided the features to be tested into Visual/Perceptual and Associative/Functional, conflating action and function-related information with more encyclopaedic information. Moreover they conflated all inanimate entities together as 'nonliving things'. This conflation in the criteria for functional features can lead to the use of a category of "nonliving things" which, from the perspective of the Sensory Functional Theory, encompasses too many heterogeneous categories of inanimate objects such as manipulable as well as non-manipulable objects as well as buildings, vehicles and so on.

A second theoretical account which has been proposed to explain the phenomenon is that knowledge could actually be organized in the brain on a purely categorical base (Caramazza & Shelton, 1998): categories of knowledge developed under evolutionary pressure so as to represent animals, artifacts and plant life separately for adaptive reasons. A problem with this account is that very few patients have been reported showing animal-specific deficits and no clear anatomical localization of the deficit has been provided.

In more recent years, an alternative to the categorical and to the feature-related organization positions has become popular, namely that categories of knowledge can be conceived as an emergent property of the structure of semantic memory based on the distinctiveness and correlation between features. The features defining a concept are conceived as distributed in a semantic network which is undifferentiated from the point of view of different features within the temporal lobes (Tyler & Moss, 2001) rather than emerging from a semantic system organized architectonically in terms of categories or type of features. The only anatomical differentiation is held to occur following a postero-anterior gradient within the temporal lobes when processing objects at different levels of specificity (Tyler et al., 2004), with anterior regions responsible for the processing of basic-level exemplars and posterior regions devoted to process concepts at a more general categorical level. A key prediction from this account is that no anatomical difference should be related to the different types of category specific semantic deficits.

Another theoretical framework has been recently proposed by Rogers, Patterson and colleagues: the so-called "distributed-plus-hub" account (Patterson et al., 2007; Rogers et al., 2004). According to this approach which can be considered as a halfway-house between the sensory/functional and the categorical accounts, sensory-motor aspects of conceptual knowledge are a necessary aspect but not a sufficient one to explain the organization of semantic memory. Since an important role of semantic memory is that of categorizing and abstracting across concepts that have similar semantic significance (but not necessarily similar specific attributes), the authors argue that sensory-functional attributes alone are not a sufficient basis for these kind of operations and that a 'semantic hub' needs to be postulated. The role of this 'hub' is that

of connecting all the modality-specific sensory-motor representations into a general amodal semantic representation. To support their view, the authors take the example of semantic dementia, characterized by the selective bilateral atrophy of temporal poles, but more prominently on the left (Hodges et al., 1992; e.g. Mummery et al., 2000).

Taking into account also the more recent findings from neuropsychology and neuroimaging and the consideration that the stimuli used in the study of Campanella et al. (2009) in which semantic problems have been consistently found in posterior temporal tumour patients, were manipulable objects, we aimed to shed further light on the organization of the semantic system by testing the naming abilities of a group of patients affected by tumours in the left or right temporal lobes. A naming task was used, as naming tasks are relatively quick and easy to administer and more importantly they are sufficiently difficult to be sensitive to even small semantic difficulties and so are more likely to allow a proper comparison with a control group since this will be less prone to perform at ceiling.

The naming task we designed consisted of both living and nonliving things. However, we restricted the category of nonliving things to manipulable objects only and graded the stimuli according to their degree of manipulability. Our definition of manipulability combines two different aspects of the physical interaction with the object: the 'affordances' and the 'utilization movement' *associated with the proper use* of the object, which is something that has to be learned.

Affordances, in the original definition made by Gibson (1979) are all "action possibilities" latent in the environment, independent of the individual's ability to recognize them. In the following years the term shifted its meaning referring more specifically to just those action possibilities which are readily perceivable and made available to an actor (Norman, 1988). Gibson was later criticized for grounding his theory of affordances only on perception and neglecting the process of cognition. For instance, Lakoff (1987, p. 216) claims that "the Gibsonian environment is not the kind of world-as-experienced that is needed in order to account for the facts of categorization".

The concept of manipulability used in this paper is more linked to this later "experience-related" definition of affordances. Indeed, if it is true that an object automatically affords a certain number of actions on it, these action possibilities that are readily perceivable by the actor are not always necessarily linked to the *proper* use of the same object. An interesting work by Creem and Proffitt (2001) gives a good example of this difference. In a series of behavioural experiments, using a dual task paradigm to interfere with cognitive or visuomotor processing, the authors showed that a semantic task interferes with grasping objects by their handles in the appropriate way, showing that the visuomotor system alone can direct the effective grasping of an object, but this grasping is *inappropriate* for its use. This means that, while the concept of affordance grasps of course an important 'perceptual' aspect of the properties of an object, it is not sufficient to explain, alone, how we build the knowledge of the appropriate manipulation of an object. We think this difference is critically linked to the building of a *semantic* representation of manipulable objects.

From this perspective, the affordances would of course be important in building the representation of the object, however also (and maybe more) crucial is the role of the *movement associated with the proper use* of the object, and this latter aspect is not necessarily triggered by the affordances alone; it is rather more likely to be built with experience. A crucial example to explain the distinction between affordance and this '*utilisation movement*' is that of the *syringe*. A syringe affords a type of grasping movement that is similar to that of grasping a stick. However, the action which is most appropriate to use it (and which therefore has to be learned) is very different. This action appears to be unique, not being shared with any other similar object. The more distinctive the movement, the easier is the identification of the object will be, since fewer objects will be manipulated in the same way: these objects are, in our definition, *highly manipulable objects.* Hence, our definition of manipulability of an object comprises both aspects of the physical interaction with the object (perceptual affordances and utilization movement) with the latter, however, being more crucially linked to the building of a *semantic* representation of the object in that it is learned by experience. This definition of manipulability is similar to that given in a paper by Magnie and colleagues: 'the capacity of an object to evoke an action that *unambiguously allows it [the object] to be recognized*' (Magnie, Besson, Poncet, & Dolisi, 2003, p. 524).

It has indeed been proposed (Allport, 1985) that knowledge about concepts might be distributed across all the areas that are active at the time of encoding. In the case of manipulable objects, these areas should include the ones that are dedicated to encode the movement needed to interact with it in the appropriate way. In this perspective, the semantic representation of highly manipulable objects might rely more on features processed in action-related areas in the "dorsal pathway".

When the manipulability of the object is, on the contrary, *weak*, the object will not have a specific, distinctive way of being manipulated and may afford different grasping, none of them being distinctive. It is therefore possible that such weakly manipulable objects will rely more on perceptual properties for identification than highly manipulable objects do and be processed more in bilateral inferior temporal areas (following the ventral pathway) together with most of the living entities which heavily rely on these features.

If categories within the semantic system are an emergent property of the differential weighting of sensory and motor attributes, then we predict that possible category specific deficits for nonliving entities should be more likely to occur to patients with lesions involving action-related areas in the "dorsal pathway", such as the left posterior middle temporal as well as inferior parietal areas. Category specific deficits for living things would instead be linked to damage to bilateral inferior temporal areas. A second prediction is that patients showing selective difficulties with nonliving entities should experience particular difficulty with the more highly manipulable objects. In contrast, patients with category specific deficits for living things should also experience some difficulty with some nonliving objects, but *only* with weakly manipulable ones.

We tested these predictions in an unselected series of 30 patients suffering from brain tumours involving either the left or the right temporal (or temporo-parietal) areas. Since all the patients were tested in the days around the operation for the removal of the tumour, the time available for testing the patients was restricted. Patients were available for one testing session of two hours before the surgery and one such session after. Therefore, the assessment of their semantic skills was limited to the only naming task developed. Their performance was compared with that of a control group of 20 healthy subjects matched for age and education. In addition, the task was also administered to a patient with widespread bilateral inferior temporal cortical damage (MU) who suffered from herpes simplex encephalitis (HSE), and who in previous investigations (Borgo & Shallice, 2001; Borgo & Shallice, 2003) showed clear category specific semantic impairment for living entities. From our predictions, we expect MU also to show some difficulty in naming weakly manipulable objects.

To try to localize which areas of the brain might then be more likely to be linked to any possible category specific effect, a Voxel-Based Lesion-Symptom Mapping (VLSM) procedure (Bates et al., 2003; Rorden, Karnath, & Bonilha, 2007) was also adopted to relate the behavioural finding to a more specific lesion site. With this technique, it is possible to correlate the score obtained in a given

neuropsychological test to each voxel of the reconstructed lesion of a patient and, by means of a statistical voxel by voxel confrontation of the lesions of each patient, it is possible to test which voxels are correlated with a larger effect on the relevant cognitive dimension. The importance of the VLSM analysis lies in the fact that no a-priori anatomical assumption is made in grouping the patients.

2. Methods

2.1. Subjects

2.1.1. Tumour patients group

This study involved a consecutive series of 30 patients with a tumour located within the temporal lobes. Most of the tumours ($n = 24$) were either high ($n = 10$) or low ($n = 14$) grade gliomas. The selection of the patients followed a clinical criterion: regardless of their cognitive level or neuropsychological picture, patients were selected on the basis the presence of a tumour within the left or the right temporal lobe. The study was approved by the ethical committee of SISSA-ISAS (International School for Advanced Studies, Trieste). 20 patients had a left and 10 a right hemisphere lesion. Left hemisphere patients were further subdivided into an anterior and a posterior temporal group. Patients were assigned to the two groups according to the position of the centre of mass of their reconstructed lesions (see VLSM analysis section). The centres of mass of the lesions of left temporal lobe patients were clustered in two non-overlapping groups divided by a line separating regions near the temporal pole from more posterior temporal and temporo-parietal regions (see supplementary Fig. 1). This imaginary line was perpendicular to the long axis of the middle temporal gyrus and passed through a point placed halfway between the centres of mass of the most anterior of the posterior lesions (MNI coordinates: $x = -52$; $y = -16$; $z = -10$) and the most posterior of the anterior lesions (MNI coordinates: $x = -45$; $y = -25$; $z = -2$). There were 11 left anterior temporal and 9 left posterior temporal patients (see supplementary Fig. 2 for the overlap of lesion sites of the three groups).

Patients were available for testing in two sessions, one usually the day before the surgery and the second from 3 to 6 days after the operation. Due to the strict time constrains for testing patients only a brief neuropsychological assessment was administered in order to monitor the broad perceptual, linguistic and attentive skills. Some of the patients, especially after the operation, had limited availability and were able to sustain only brief testing sessions. Therefore, for a few of the patients only the experimental naming task was administered.

Demographic as well as baseline neuropsychological information is summarized in Table 1. All the patients (with the exception of patient LA5) were tested prior to the surgical removal of the mass, 26 of them being also available for retesting after surgery (except patients LA4, RH3, RH4, RH5).

2.1.2. Control patient MU

To check whether the naming tasks developed could potentially provide evidence also on the presence of category specific deficits in naming living entities, we also administered the naming task to a patient who in previous investigations found a stable category specific semantic deficit for living things. Patient MU suffered from Herpes Simplex Encephalitis. His semantic memory skills were gravely degraded after his illness. For further details on his neuropsychological profile see Borgo and Shallice (2001, 2003).

2.1.3. Healthy control sample

The performance of the patients in the experimental tasks was compared with that of a group of 20 control subjects divided into two age groups (below and above 50 years of age) and two education groups (below and above 12 years of schooling). Age and education cutoffs were determined on the basis of the demographic characteristics of a group of similar patients (Campanella et al., 2009). Thus, the performance of four subgroups of five subjects each could be compared with that of each tumour patient matched for age and education at the single case level of analysis. At the group level however, all control subjects were collapsed into a group of 20 subjects.

The mean age for the patient group was 46.42 (+/− 12.1 SD) and for the control group it was 45.65 (+/− 19.40 SD). The mean age for the right temporal group was 51.20 (+/− 10.56 SD), for the left anterior temporal group it was 42.55 (+/− 11.76 SD) and for the left posterior temporal group was 50 (+/− 14.35 SD).No significant age difference was found between the three groups of patients and the controls (Kruskal-Wallis ANOVA$_{(H=3,\ N=50)} = 2.22$; $p = 0.53$). The mean years of education for the patient groups was 10.9 years (+/− 4.11 SD); for control group it was 12.94 (+/− 4.52 SD). The mean education for the right temporal group was 11.20 (+/− 4.32 SD), for the left anterior temporal group it was 11.73 (+/− 3.98 SD) and for the left posterior temporal group was 8.78 (+/− 3.80 SD). No significant education difference was found between the three groups of patients and the controls (Kruskal-Wallis ANOVA $_{(H=3,\ N=50)} = 3.92$; $p = 0.27$).

The distribution of accuracy scores distribution for the control group did not differ significantly from normal (Shapiro-Wilks Test: $W = 0.974$; $p = 0.836$). The average naming level of the control sample was 92.62% with a standard deviation of +/− 3.60%. Scores were considered to be pathological when below 1.96 SD from the mean ($\alpha = 0.05$, 2-tailed). Cutoff accuracy score was therefore set at 85.56%.

3. Experimental procedure

The task used was a computer presented naming task. The stimuli consisted of a set of 120 digital coloured pictures of real objects and animals. 60 pictures represented living things and 60 represented manipulable objects. The living things were further divided into 30 animals (both mammals and birds) and 30 vegetables (both fruit and vegetables). The nonliving things (all artefacts) were divided into 30 highly manipulable objects and 30 weakly manipulable objects.

The procedure was as following: a cross was presented in the centre of the screen for 500 ms immediately followed by the picture of the stimulus to name. The picture remained on the screen until an answer was provided or until the patient claimed he/she could not name the target stimulus. The subsequent stimulus was then presented by the experimenter (FC) pressing the spacebar on the keyboard. The same pseudo-random order of administration was used across subjects. The whole procedure was divided into two sub-sessions separated by a pause.

Picture stimuli were collected from the web. All pictures were processed with Adobe Photoshop 7.0 in order to eliminate all the background and contextual information, and were therefore presented on a white background. Pictures were sized to a dimension of 500×400 pixels and presented in the centre of the screen. Experimental stimuli were selected from a larger corpus of 219 pictures that later underwent selection to obtain the best balancing possible for the most common semantic confounding dimensions.

3.1. Balancing of the experimental material

In order to exclude the possibility that any effect found could be explainable in terms of spurious nonsemantic variables, experimental material was balanced for the standard nonsemantic lexical and perceptual variables that can influence the naming of a stimulus (Albanese, Capitani, Barbarotto, & Laiacona, 2000; Funnell &

Table 1
Baseline assessment and neurological data of the group of tumour patients.

	Patient	Age	Edu	Tumour type	Tumour location	Semantic fluencies (1 min)						Borb[a]						Visual search[b]	
						Animals		Objects		Proper names		Size match (*n*/30)		Foreshorten. views (*n*/25)		Object decision easy (*n*/32)			
						Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	RH1	33	13	Meningioma	Right Ant. Tempor	21	–	13[d]	–	22[d]	–	NA	–	24	–	NA	–	49	–
2	RH2	48	17	Grd II Astrocyt	Right Frontal-Temp	32	36	26	30	29	20	26	NA	24	NA	30	NA	47	NA
3	RH3	44	8	Glioblastoma	Right Ant. Tempor	24	–	14	–	18	–	28	–	24	–	31	–	58	–
4	RH4	65	5	Glioblastoma	Right Ant. Tempor	12	–	12	–	21	–	27	–	22	–	NA	–	46	–
5	RH5	53	8	Grd II Astrocyt	Right Frontal-Temp	16	NA	13	NA	19	NA	27	27	24	23	24[c]	20[c]	51	42
6	RH6	65	8	Glioblastoma	Right Ant. Tempor	12	17	16	6[d]	13	13	23	24	24	25	27[c]	27[c]	NA	45
7	RH7	41	17	Grd II Astrocyt	Right Frontal-Temp	23	29	35	19	37	26	24	22	25	23	28	29	41	40
8	RH8	52	13	Grd II Astrocyt	Right Inf-Post Temp	17	17	16	23	10[d]	15[d]	27	25	23	23	21	21	50	NA
9	RH9	49	15	Glioblastoma	Right Post Med Tmp	24	24	17	17	24	20	22	NA	24	24	31	32	43	NA
10	RH10	62	8	Glioblastoma	Right Post Tmp-Par	29	26	21	13	22	14	26	25	25	23	25[c]	30	42	NA
11	LA1	38	9	Grd II Astrocyt	Left Frontal-Temp	18	14[d]	21	14[d]	27	15[d]	NA	NA	24	25	NA	NA	40	NA
12	LA2	25	17	Grd II Astrocyt	Left Frontal-Temp	26	21	21[d]	23	12[d]	17	20	NA	17	NA	25	NA	46	NA
13	LA3	46	17	Grd II Astrocyt	Left Ant Med Temp	23	21	21	16[d]	25	22	NA	NA	25	25	NA	NA	42	48
14	LA4	48	13	Metastasys	Left Temp-Polar	19	–	21	–	28	–	29	–	23	–	29	–	NA	
15	LA5	36	17	Glioblastoma	Left Ant Med Temp	19	23	18	24	21	23	26	23	24	24	30	31	46	48
16	LA6	42	8	Dysembryogen	Left Hippocampus	24	31	20	18	33	29	27	27	24	24	30	29	46	NA
17	LA7	62	12	Grd II Astrocyt	Left Temp-Polar	22	15	32	16	45	31	28	26	21	23	31	29	53	NA
18	LA8	29	13	Grd II Astrocyt	Left Sup-Ant Temp	30	18	25	25	26	22[d]	28	28	25	24	30	32	43	44
19	LA9	34	8	Grd II Astrocyt	Left Temp-Polar	25	17	18	15	24	20	29	28	23	22	29	31	50	51
20	LA10	60	8	Gliosarcoma	Left Frontal-Temp	12	5	9	2	19	10	28	30	25	24	30	28	NA	29[c]
21	LA11	48	7	Glioblastoma	Left Temp-Polar	11[d]	4[d]	12[d]	5[d]	18	13[d]	28	28	25	24	32	27[c]	48	53
22	LP1	51	12	Glioblastoma	Left Sup-Post Tmp	7[d]	10[d]	7[d]	11[d]	13[d]	14[d]	30	27	25	25	29	NA	54	51
23	LP2	44	15	Meningioma	Left Post. Tempor	–	–	–	–	–	–	–	–	–	–	–	–	–	–
24	LP3	55	2	Metastasys	Left Tmp-Par + Front	–	–	–	–	–	–	–	–	–	–	–	–	–	–
25	LP4	18	12	Ependymoma	Left Occip-Temp	14[d]	–	14	–	23	–	25	–	24	–	31	–	59	57
26	LP5	64	8	Metastasys	Left Post Temp-Par	–	–	–	–	–	–	–	–	–	–	–	–	–	–
27	LP6	41	8	Grd II Astrocyt	Left Parieto-Temp	28	8[d]	23	6[d]	28	7[d]	25	26	22	25	28	31	50	40
28	LP7	58	8	Glioblastoma	Left Parieto-Temp	19	17	16	15	26	24	28	27	24	23	30	30	54	56
29	LP8	55	8	Glioblastoma	Left Sup-Post Temp	18	4[d]	NA	8	NA	12	NA	NA	23	NA	NA	NA	NA	NA
30	LP9	64	6	Grd II Astrocyt	Left Post-Tmp Insul	4[d]	4[d]	9	2[d]	14	7[d]	21[c]	22[c]	20	21	18[c]	16[c]	NA	NA

NA = not administered.

[a] BORB = Birmingham Object Recognition Battery (Riddoch & Humphreys, 1993).

[b] Spinnler and Tognoni (1987).

[c] Below normal range.

[d] Below age/education matched sample (5 subjects) range.

Table 2
Experimental material balancing: Average values for the main extra-semantic variables for each of the categories involved in the experimental task.

	Word Freq.			Familiarity			Visual Compl.			No. of Syllables			Manipulability		
	Average[a]	SD	p[b]	Average[a]	SD	p[b]	Average[a]	SD	p[b]	Average[a]	SD	p[b]	Average[a]	SD	p[b]
Living	2.53	1.18	0.39	1.58	0.22	0.42	1.31	0.27	0.10	1.03	0.25	0.30	–	–	–
Nonliving	2.83	1.62		1.60	0.24		1.25	0.25		1.03	0.36		–	–	
Hi Manip	2.87	1.59	0.67	1.58	0.26	0.49	1.24	0.22	0.50	1.07	0.38	0.96	1.43	0.09	<0.001
Lo Manip	2.79	1.68		1.63	0.23		1.25	0.29		0.98	0.33		0.70	0.24	

[a] All the values reported refer to the NatLog of the original raw values obtained from control subjects. NatLog transformation was performed in order to make the values more homogeneous across variables and the distributions closer to normal.
[b] Mann–Whitney U-test.

Sheridan, 1992; Stewart, Parkin, & Hunkin, 1992). The variables considered were word frequency, number of syllables, familiarity and visual complexity. A summary of the average values for these variables in each of the categories of interest s given in Table 2.

3.1.1. Word frequency

Norms for word frequency were obtained from the CoLFIS Italian corpus of word frequency (CNR, Unpublished). No significant difference was found either between Living and Nonliving things (Mann–Whitney U test: $U = 1635.5$, $p = 0.39$) or between highly and weakly manipulable objects (Mann–Whitney U test: $U = 421$, $p = 0.67$) (see Table 2).

3.1.2. Number of syllables

No significant difference was found either between living and nonliving things (Mann–Whitney U test: $U = 1708$, $p = 0.63$) or between highly and weakly manipulable objects (Mann–Whitney U test: $U = 405$, $p = 0.66$).

3.1.3. Familiarity and visual complexity

Norms for familiarity and visual complexity were obtained from a group of 20 control subjects. Stimuli were presented on a computer screen one at the time and subjects were asked to rate them on both dimensions on a 7 point scale using the keys from 1 to 7 on the keyboard.

Regarding the familiarity, no significant difference was found either between living and nonliving things (Mann–Whitney U test: $U = 1647.5$; $p = 0.42$) or between highly and weakly manipulable objects (Mann–Whitney U test: $U = 403$; $p = 0.49$). Also for visual complexity, no significant difference was found either between Living and Nonliving things (Mann–Whitney U test: $U = 1484.5$; $p = 0.10$) or between Highly and Weakly manipulable objects (Mann–Whitney U test: $U = 404.5$; $p = 0.50$).

Since differences have been found between male and female subjects in judging the familiarity of different categories of semantic material (Albanese et al., 2000), a further control was performed in order to assess the possible presence of such biases. For each comparison (male vs. female in living vs. nonliving) a Bonferroni corrected threshold p-value of $0.05/4 = 0.0125$ was adopted. Neither male (Mann–Whitney U test: $U = 1570$; $p = 0.23$) nor female subjects (Mann–Whitney U test: $U = 1632$; $p = 0.38$) found living things more familiar than nonliving. Moreover male or female subjects did not rate living (Mann–Whitney U test: $U = 1355$, $p = 0.019$) or nonliving (Mann–Whitney U test: $U = 1460$, $p = 0.07$) differently with respect to familiarity. As far as the nonliving things category is concerned, no statistical difference of any kind was found across sex in rating high vs. low manipulability items. This was probably due to the fact that the manipulable objects we chose were not only tools in general, which are more prone to gender biases (e.g. microphone, tennis racket, ashtray, basket, hourglass).

3.2. Manipulability ratings

A group of 20 subjects was asked to rate the level of manipulability of each object picture from al large set of 147 manipulable object pictures. The rating procedure was similar to that adopted in the study by Magnie and colleagues (2003) (see introduction). Subjects were asked to judge how easy it was for them to mime the action commonly associated to the presented object so that anyone seeing that action could understand which object is associated to that action. The scale ranged from 1 to 5, with '5′ meaning that the action was easily 'mimeable' and was unique for that object, and '1′ meaning that there is not a specific action that could identify the object. Manipulability ratings were significantly higher for highly than for weakly manipulable objects (Mann–Whitney U Test: $z = 6.652$ $p < 0.0001$). Highly manipulable objects ratings ranged from 3.50 to 4.88 (mean rating = 4.20 ± 0.37 SD); weakly manipulable objects' ratings ranged from 1.30 to 2.90 (mean rating= 2.06 ± 0.46 SD).

4. General procedures for behavioural data analysis

4.1. Accuracy scoring

All responses from each subject were tape-recorded in order to allow a more adequate analysis of the answers of the patients in the case of ambiguous responses. For an answer to be considered as correct, the lexical form had to be either clearly correct or the word had to be entirely pronounced, with the first phoneme and 2/3 of the word being correctly pronounced. Since what was important was not the word per se, but rather the concept behind the word, 'conduit d'approche' were allowed if the target word (or an appropriate synonym) was produced in the end. Dialect forms of the target word were also treated as correct.

4.2. Cross-subject analysis

In analyzing the behavioural data a twofold statistical approach was adopted. Accuracy data from the patients were indeed analysed both at a single case and at a group level of analysis. Since not all the patients could be tested both before and after surgery, for the patients that were tested twice the main analyses were performed on the average score obtained in both testing sessions for each of the variables considered. For the patients that were tested only once the tests were performed on the actual score obtained in the testing session they performed. The scores for each session were however kept separated at the group level of analysis when assessing the effects of surgery.

4.3. Single case level

The naming performance of each patient in the task was compared, at a single case level of analysis, with that of an appropriate age and education matched subgroup of control subjects. Statistical analysis was performed by means of Crawford t-test (Crawford &

Garthwaite, 2002) in order to assess the abnormality of possible test scores differences when compared with small size control samples. In addition to the scores obtained by the patient in the two conditions of interest, this statistic takes into account the mean scores and standard deviation obtained by the control sample in the same two conditions as well as the correlation between the scores of the controls in the two conditions.

For each patient two statistical tests were performed: the first one assessed the presence of category specific deficits in naming living or nonliving things in general. The second one assessed the presence of possible selective naming difficulties for high or low manipulability objects within the category of nonliving entities.

4.4. Group level

Since the data obtained from the performance of the patients (especially for left hemisphere) was not normally distributed, only nonparametric tests were used to assess the presence of any effect at a group level of analysis. A series of nonparametric tests were used to compare the performance of the group of patients with respect to that of the controls. The presence of within-group significant category specific effects was also directly assessed by means of series of Wilcoxon Matched-Pairs Tests.

The size of any possible effect of category or manipulability was then computed by subtracting the accuracy score obtained by each patient (and control subject) with the first category of interest (Nonliving things and highly manipulable objects respectively) from that obtained with the other category (Living things and weakly manipulable objects respectively). The presence of any significant difference in these effects between groups was thus directly assessed by means of Kruskal Wallis ANOVA with the attendant post-hoc corrected comparisons (Siegel & Castellan, 1988).

4.5. Cross-stimulus analysis

In addition to a 'cross-subject' analysis, a 'cross-stimulus' analysis was also conducted in order to double-check the generalizability of the results (see Clark, 1973). A series of ANCOVAs was conducted on the average accuracy obtained by each group of subjects for each stimulus, co-varying it with the average level of each of the variables (familiarity, visual complexity, frequency, number of syllables) for each stimulus. The category of interest (Living/Nonliving or High/Low manipulability) was used as a categorical predictor, to check whether possible categorical effect would survive.

5. Behavioural results

5.1. Cross-subject analysis

5.1.1. General naming skills

8/20 left hemisphere patients performed below the accuracy cutoff score of 85.56% obtained from control subjects, while only 1/10 of the right hemisphere patients did. A series of chi-square tests were used to assess whether these proportions were significant when compared with control subjects. As two groups were being compared with contrasts, Bonferroni correction for multiple comparisons was set to a threshold of 0.05/2 = 0.025.

A significant number of left hemisphere patients (Fisher Exact χ^2: $p = 0.002$) scored below the cutoff value. The proportion of right hemisphere patients scoring below the cutoff value was not significant (Fisher Exact χ^2: $p = 0.310$). Within the left hemisphere group itself however, only 1/11 of the left anterior temporal patients performed below the cutoff naming score, while 7/9 of the left posterior temporal patients did. This difference was again highly significant (Fisher Exact χ^2: $p = 0.003$) indicating that not only are left hemisphere patients the only ones to show naming problems but that in our sample these difficulties were restricted almost exclusively to left posterior temporal patients, as left anterior temporal patients did not differ significantly from controls (Fisher Exact χ^2: $p = 0.355$).

5.1.2. Group level analysis

5.1.2.1. Categories × hemisphere interactions. A first assessment of the possible presence of category specificity or manipulability effects was conducted by separating the group of patients on the basis of the hemisphere of interest. A series of Wilcoxon Matched Pairs Test was conducted on the performance of (i) controls, (ii) left hemisphere and (iii) right hemisphere patients to test whether significant within-group differences could be detected in naming living and nonliving items. For both series of comparisons, Bonferroni threshold for multiple comparisons was set to 0.05/3 = 0.017. To look for possible interactions in the size of the potential effects detected between the groups, a series of Kruskal–Wallis nonparametric ANOVAs was then conducted, with the attendant post-hoc corrected comparisons (Siegel & Castellan, 1988).

The within-group comparison revealed that left hemisphere patients showed a significant category specific naming difficulty for nonliving things compared with living things (Wilcoxon Matched Pairs Test: $z = 3.808$; $p < 0.001$) (see Fig. 1). No category specificity effect was found either in the control subjects (Wilcoxon Matched Pairs Test: $z = 0.491$; $p = 0.623$) or the right hemisphere patients (Wilcoxon Matched Pairs Test: $z = 1.481$; $p = 0.139$).

Since, however, the size of this left hemisphere effect (though significant) might not be larger than that of right hemisphere patients or that of control subjects, the presence of possible interactions was assessed by comparing the size of the category effect (nonliving-living) between controls, right and left hemisphere patients. A significant main effect of group was found (Kruskal–Wallis ANOVA: $H_{(2,\ N=50)} = 16.650$; $p < 0.001$). Post hoc analysis revealed that the category effect was larger in left hemisphere patients than in either controls ($z = 3.812$; $p < 0.001$) or right hemisphere patients ($z = 2.873$; $p = 0.012$).

5.1.2.2. Manipulability × hemisphere interactions. No significant effect of manipulability was found at the group level of analysis. The lack of effect, however, may be due to the heterogeneity of behaviour within subgroups of left hemisphere patients, as will be seen in the next section.

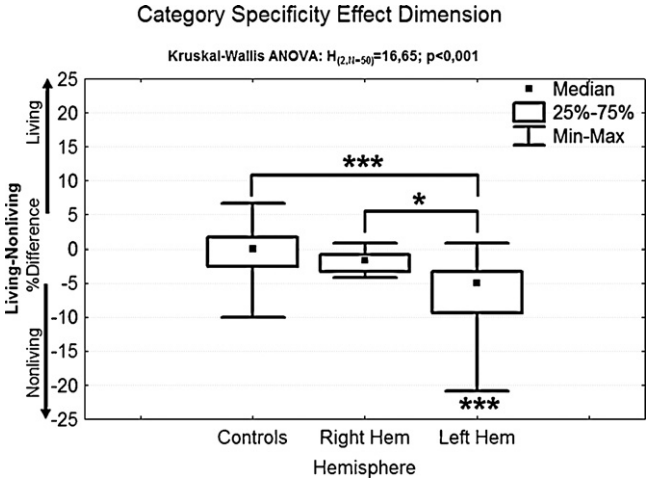

Fig. 1. Category specific effect dimension between controls, left and right hemisphere patients. Left hemisphere patients show a clear category specific naming difficulty for nonliving items. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

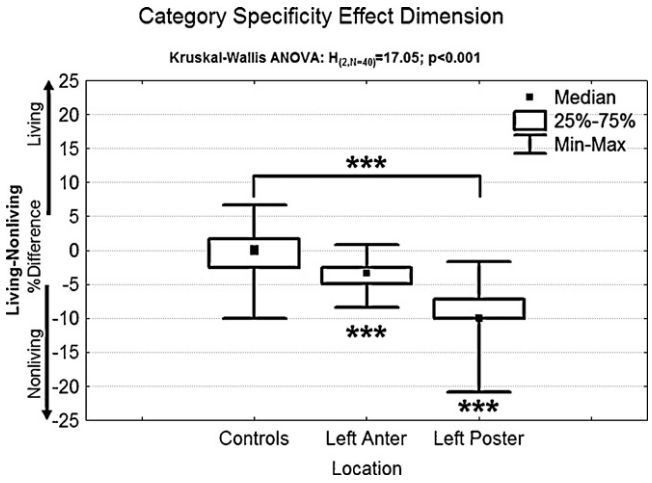

Fig. 2. Within the left hemisphere, left posterior temporal patients showed a larger category specificity effect with respect to controls. Left anterior temporal did not. $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$.

5.1.3. Left Hemisphere patients

5.1.3.1. Category effects. Since right hemisphere patients did not show any apparent naming deficit at all, a further analysis compared possible category or manipulability effects in left hemisphere patients with respect to controls. The analyses was performed on controls, left anterior temporal and left posterior temporal patients: therefore a Bonferroni correction threshold was set at: 0.05/3 = 0.017. At a within group level of analysis, both left posterior and anterior temporal patients showed a significant category specific naming deficit for nonliving things compared to living things (Wilcoxon Matched Pairs Test: $z = 2.666$; $p = 0.008$ for both groups). In addition, when comparing the size of the effect between the controls, the left anterior and the left posterior temporal patients, a significant main effect of group was found (Kruskal–Wallis ANOVA: $H_{(2,\ N=40)} = 17.045$; $p = 0.002$) (Fig. 2). Subsequent post hoc analysis revealed that only the category effect of left posterior temporal patients was larger than that of controls ($z = 4.068$; $p < 0.001$), the performance of left anterior temporal patients being no different from that of the controls (Kruskal–Wallis ANOVA post hoc test: $z = 1.992$; $p = 0.138$).

5.1.4. Left hemisphere patients

5.1.4.1. Manipulability effects. To assess for possible manipulability effects, the performance of the left hemisphere patients (anterior and posterior temporal) and that of controls subjects within the category of nonliving things only were directly compared (Fig. 3). The within-group analysis, comparing directly controls, left anterior temporal and left posterior temporal patients (Bonferroni correction threshold: 0.05/3 = 0.017) revealed that the manipulability influenced the patient groups in opposite ways: thus left posterior temporal patients had significantly greater difficulties in naming highly than weakly manipulable objects (Wilcoxon Matched Pairs Test: $z = 2.521$; $p = 0.012$). By contrast left anterior temporal patients tended to perform worse, but not significantly (Wilcoxon Matched Pairs Test: $z = 2.191$; $p = 0.028$) with weakly than highly manipulable objects. The between-group analysis of the effects of manipulability comparing controls, left anterior and left posterior temporal patients, gave a main effect of group (Kruskal-Wallis ANOVA: $H_{(2,\ N=40)} = 14.362$; $p = 0.008$). Post hoc analysis revealed that the manipulability effect was significantly greater for left posterior patients than it was for both controls ($z = 2.878$; $p = 0.012$) and left anterior temporal patients ($z = 3.669$; $p < 0.001$).

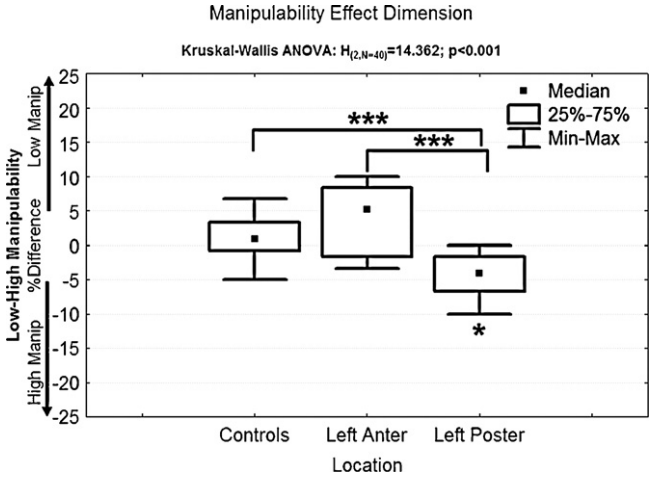

Fig. 3. Manipulability effect dimension: Left posterior temporal patients performed worse with highly manipulable objects. $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$.

5.2. Effects of surgery

A final group analysis was performed in order to assess possible effects of the surgery on the naming skills of the patients. Only patients who were tested both before and after the surgery (25/30) were included. Considering the effects of surgery on both left and right hemisphere patients (Fig. 4a) it was evident that left hemisphere patients were more impaired by surgery than were right hemisphere patients (Mann–Whitney U Test: $U = 26$; $p = 0.025$). Thus, left hemisphere patients showed a significant decline in their post-operative performance (Wilcoxon Matched Pairs Test: $z = 2.887$; $p = 0.003$), but right hemisphere patients did not do so (Wilcoxon Matched Pairs Test: $z = 0.929$; $p = 0.352$). Again, when comparing the left anterior and the left posterior temporal patients (Fig. 4b), it was only the left posterior temporal patients who showed a significant reduction in performance after surgery (Wilcoxon Matched Pairs Test: $z = 2.310$; $p = 0.021$). However the effect of surgery was only marginally greater for these patients than for the left anterior temporal patients (Mann–Whitney U Test: $U = 21.5$; $p = 0.093$).

5.3. Cross-stimulus analysis

The effects of category and especially of manipulability, while significant, were small. It was therefore thought appropriate to examine the robustness of the effects by assessing their generalizability across stimulus items as well as across subjects (Clark, 1973). The performance of all subjects in a group was averaged for each stimulus item, and this average performance was used as the dependent variable. The performance of left anterior and posterior temporal patients was separately analyzed with this method.

Analyzing the results obtained by left posterior temporal patients, category membership (living-nonliving) still exerted a highly significant effect on the naming performance of this group (ANCOVA: effect of category: $F_{(1,114)} = 27.75$, $p < 0.0001$). Many of the baseline lexical variables also had a significant influence on the naming abilities of the patients: familiarity ($F_{(1,114)} = 25.50$, $p < 0.0001$); word frequency ($F_{(1,114)} = 23.12$, $p < 0.0001$); number of syllables ($F_{(1,114)} = 15.85$, $p = 0.0001$). Visual complexity did not influence performance ($F_{(1,114)} = 0.68$, $p = 0.41$). Somewhat similar results were obtained for the left anterior temporal patients. Category membership had still a significant (even if smaller) effect: $F_{(1,114)} = 6.68$, $p = 0.011$). Frequency ($F_{(1,114)} = 22.89$, $p < 0.0001$) and number of syllables ($F_{(1,114)} = 4.19$, $p = 0.042$) also had a significant effect. Familiarity and visual complexity did not influence the performance (visual complexity: $F_{(1,114)} = 0.121$, $p = 0.728$; familiarity: $F_{(1,114)} = 0.842$, $p = 0.361$).

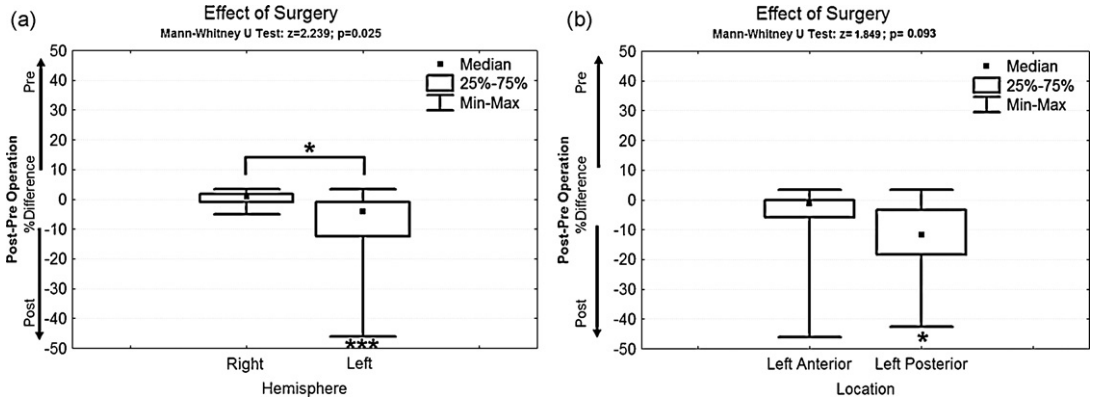

Fig. 4. (a) The naming abilities of left hemisphere patients were impaired following the surgery. Right hemisphere patients did not show any impairment. (b) Left anterior temporal patients did not suffer significantly from surgery, while left posterior temporal patients did. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

However, when the same type of analysis was performed on the manipulability effect within the category of nonliving things, a more complex pattern of results was obtained. For the left posterior temporal patients a significant effect of many of the extra-semantic variables was found (familiarity: $F_{(1,114)} = 33.73$, $p < 0.0001$; frequency: $F_{(1,114)} = 10.92$, $p = 0.002$; number of syllables: $F_{(1,114)} = 8.46$, $p = 0.005$), while visual complexity did not influence performance ($F_{(1,114)} = 0.00$, $p = 0.97$). However the effect of manipulability in this case was far from significant ($F_{(1,114)} = 0.00$, $p = 0.92$). By contrast, a significant effect of manipulability was found for the performance of left anterior temporal patients; patients in this group had more difficulty in naming weakly manipulable than highly manipulable objects. Thus, in addition to familiarity ($F_{(1,114)} = 5.25$, $p = 0.025$) and frequency ($F_{(1,114)} = 8.66$, $p = 0.005$), manipulability *also* influenced naming performance ($F_{(1,114)} = 4.75$, $p = 0.033$).

5.3.1. Single case level analysis

The analysis of the results at a single case level provides further support for the group level results. Table 3 shows that significant category specificity naming deficits were only present in left posterior temporal patients. While none of the right hemisphere or even left anterior temporal patients showed significant category effects, 6/9 of the left posterior temporal patients had a category specific naming deficit for nonliving entities, using the Crawford procedure. Moreover, 4 of those 6 patients *also* showed a category specific naming deficit for highly manipulable objects.

6. VLSM analysis

Using the VLSM approach to lesion analysis (Bates et al., 2003) we aimed to localize which areas of the temporal lobes were involved with respect to the category specific naming difficulty. Original T1 and (when available) T2 weighted scans of each patients were obtained for all the patients (except for patient RH6) in 'analyze' digital format to determine the preoperative location of the tumour. Only preoperative MRI scans were used for reconstruction purposes, as in postoperative scans, the region of the surgical lesion is usually at least partially replaced by healthy neighbouring tissue. The 3D reconstruction of lesions were drawn as Regions Of Interest (ROI) by one of the researchers (FC) using each slice of the MRI scan of each patient on the horizontal plane, using MRIcro software (Rorden & Brett, 2000). ROIs included both the lesion boundaries and oedema (since oedema is found to commonly cause cognitive deficits).

All the ROIs were then double-checked and, if necessary, corrected by an expert neuroradiologist (SDA) who was blind to the aims of the study and to the performance of each patient on the task. Each patient's MRI scan underwent spatial normalization using SPM2 software, in order to match and align images on a common Talairach (Talairach & Tournoux, 1988) space.

Initially, whether the severity of any deficit observed in naming could merely be linked to lesion volume was checked. The volume of the reconstructed lesions of three subgroups of patients (right vs. left anterior vs. left posterior temporal) was therefore compared. No significant differences were found between groups (Kruskal–Wallis ANOVA: $H_{(2,\ N=29)} = 1.051$; $p = 0.591$).

Voxel by voxel statistical analyses were performed by means of NPM software (www.MRIcro.com). Since manipulability results were considered as not being completely reliable after cross-stimulus analysis, only data coming from the general category contrast (living vs. nonliving) underwent VLSM analysis. The behavioural measure used to compute the statistic was obtained by subtracting the scores obtained in naming living things from the score obtained in naming nonliving objects for each patient. The statistical test used to compute for the presence of any effect was a *T*-test. A threshold of $p < 0.001$ (with False Discovery Rate correction applied) was used to consider a result as significant. To minimize the effects of observation of possible outliers the analyses were conducted only on those voxels that were damaged in at least 3 patients.

Fig. 5 shows the areas associated with a significant naming deficit for nonliving things ($p < 0.001$). These areas involve a large part of the posterior temporal lobe. The cortical area associated with the largest category specific deficit in naming artefacts is the posterior portion of the left middle temporal gyrus (centre of mass: $x = -55$; $y = -30$; $z = 8$) (Fig. 5: panels b and c). In addition, posterior portions of the left superior and inferior temporal gyri were involved as well as a small portion of the inferior parietal cortical areas and part of the hippocampus. However, the largest number of voxels involved in category specific naming deficit was found in the subcortical white matter underlying the left posterior temporal lobe. Of particular interest is that a part of this white matter lesion disconnects large portions of the left inferior parietal lobe from the temporal lobe (see Fig. 6, panels b and d).

7. Patient MU

Patient MU, who had previously been found to have a stable category specific loss of knowledge for living entities (Borgo & Shallice, 2001; Borgo & Shallice, 2003), was also tested on the same task. The pattern of performance was as would be predicted (see Fig. 6): he named living things worse than nonliving things (40% and 58.33% respectively; Crawford *t*-test: $t = -2.63$, $p = 0.029$) and low manipulability objects worse than high manipulability ones (43.33% and 73.33% respectively; Crawford *t*-test: $t = -2.99$, $p = 0.020$). The per-

Table 3
Single case level results. The only group showing category specific naming deficits for artefacts is that of left posterior temporal patients.

Pat.	Lesion type	Category							Manipulability						
		Before surg.		After surg.		*Average cat.*		Crawford *t*-test	Before surg.		After surg		*Average manip.*		Crawford *t*-test
		LIV.	NLIV.	LIV.	NLIV.	*LIV.*	*NLIV.*		HI-MAN	LO-MAN	HI-MAN	LO-MAN	*HI-MAN*	*LO-MAN*	
RA1	Meningioma	100,00	93,33	100,00	98,33	100,00	95,83	$p = 0.190$	86,67	90,00	93,33	100,00	90,00	95,00	$p = 0.111$
RA2	Grd II Astrocyt	98,33	95,00	100,00	96,67	99,17	95,84	$p = 0.250$	100,00	90,00	100,00	93,33	100,00	91,67	$p = 0.136$
RA3	Glioblastoma	96,67	95,00	95,46	93,80	96,07	94,40	$p = 0.400$	96,67	93,33	94,27	93,29	95,47	93,31	$p = 0.490$
RA4	Glioblastoma	83,33	80,00	81,50	82,16	82,42	81,08	$p = 0.470$	83,33	76,67	82,87	81,41	83,10	79,04	$p = 0.419$
RA5	Grd II Astrocyt	93,33	95,00	98,68	92,95	96,01	93,98	$p = 0.370$	93,33	96,67	92,65	93,24	92,99	94,96	$p = 0.243$
RA6	Glioblastoma	98,33	100,00	100,00	100,00	99,17	100,00	$p = 0.370$	100,00	100,00	100,00	100,00	100,00	100,00	$p = 0.386$
RP1	Grd II Astrocyt	98,33	95,00	93,33	90,00	95,83	92,50	$p = 0.260$	96,67	93,33	90,00	90,00	93,34	91,67	$p = 0.467$
RP2	Grd II Astrocyt	96,67	96,67	100,00	100,00	98,34	98,34	$p = 0.440$	96,67	96,67	100,00	100,00	98,34	98,34	$p = 0.379$
RP3	Glioblastoma	96,67	100,00	100,00	95,00	98,34	97,50	$p = 0.470$	100,00	100,00	93,33	96,67	96,67	98,34	$p = 0.272$
	MEAN	95,74	94,44	96,55	94,32	96,15	94,38		94,82	92,96	94,05	94,22	94,43	93,59	
	SD	5,01	5,89	6,15	5,65	5,38	5,50		6,04	7,16	5,60	6,03	5,42	6,22	
LA1	Grd II Astrocyt	98,33	93,33	95,00	86,67	96,67	90,00	$p = 0.080$	96,67	90,00	93,33	80,00	95,00	85,00	$p = 0.095$
LA2	Grd II Astrocyt	100,00	96,67	100,00	96,67	100,00	96,67	$p = 0.253$	96,67	96,67	93,33	100,00	95,00	98,34	$p = 0.180$
LA3	Grd II Astrocyt	96,67	93,33	95,00	93,33	95,84	93,33	$p = 0.061$	96,67	90,00	96,67	90,00	96,67	90,00	$p = 0.210$
LA4	Metastasys	96,67	90,00	84,65	82,09	90,66	86,05	$p = 0.330$	93,33	86,67	83,86	80,31	88,60	83,49	$p = 0.320$
LA5	Glioblastoma	96,21	94,63	98,33	90,00	97,27	92,32	$p = 0.153$	94,57	94,47	90,00	90,00	92,29	92,24	$p = 0.357$
LA6	Dysembryogen	95,00	90,00	96,67	95,00	95,84	92,50	$p = 0.262$	96,67	83,33	96,67	93,33	96,67	88,33	$p = 0.140$
LA7	Grd II Astrocyt	91,67	93,33	93,33	85,00	92,50	89,17	$p = 0.271$	96,67	90,00	90,00	80,00	93,34	85,00	$p = 0.150$
LA8	Grd II Astrocyt	95,00	98,33	98,33	96,67	96,67	97,50	$p = 0.363$	96,67	100,00	96,67	96,67	96,67	98,34	$p = 0.272$
LA9	Grd II Astrocyt	95,00	93,33	91,67	95,00	93,34	94,17	$p = 0.354$	93,33	93,33	93,33	96,67	93,33	95,00	$p = 0.250$
LA10	Gliosarcoma	91,67	95,00	93,33	81,67	92,50	88,34	$p = 0.211$	93,33	96,67	90,00	73,33	91,67	85,00	$p = 0.230$
LA11	Glioblastoma	85,00	64,41	26,67	30,51	55,84	47,46	$p = 0.067$	63,33	65,52	36,67	24,14	50,00	44,83	$p = 0.494$
	MEAN	94,66	91,12	88,45	84,78	91,55	87,95		92,54	89,70	87,32	82,22	89,93	85,96	
	SD	4,05	9,20	20,91	18,86	12,14	13,87		9,81	9,35	17,23	21,08	13,47	14,66	
LP1	Glioblastoma	85,00	71,67	83,33	55,00	84,17	63,34	***p < 0.001***	60,00	83,33	60,00	50,00	60,00	66,67	***p = 0.037***
LP2	Meningioma	96,67	96,67	95,00	91,67	95,84	94,17	$p = 0.405$	96,67	96,67	90,00	93,33	93,34	95,00	$p = 0.261$
LP3	Metastasys	70,00	43,33	18,33	10,00	44,17	26,67	***p = 0.001***	33,33	53,33	10,00	10,00	21,67	31,67	***p = 0.005***
LP4	Ependymoma	75,00	66,10	76,67	71,19	75,84	68,65	$p = 0.084$	63,33	68,97	70,00	72,41	66,67	70,69	$p = 0.094$
LP5	Metastasys	56,67	43,33	40,00	33,33	48,34	38,33	***p = 0.036***	43,33	43,33	33,33	33,33	38,33	38,33	$p = 0.164$
LP6	Grd II Astrocyt	98,33	98,31	70,00	52,54	84,17	75,43	***p = 0.039***	96,67	100,00	46,67	58,62	71,67	79,31	***p = 0.034***
LP7	Glioblastoma	100,00	94,92	98,33	91,53	99,17	93,23	$p = 0.104$	96,67	93,10	90,00	93,10	93,34	93,10	$p = 0.373$
LP8	Glioblastoma	95,00	85,00	83,33	73,33	89,17	79,17	***p = 0.020***	83,33	86,67	73,33	73,33	78,33	80,00	$p = 0.209$
LP9	Low Grade	56,67	53,33	45,00	28,33	50,83	40,83	***p = 0.035***	50,00	56,67	26,67	30,00	38,33	43,33	***p = 0.039***
	MEAN	81,48	72,52	67,78	56,32	74,63	64,42		69,26	75,79	55,56	57,12	62,41	66,45	
	SD	17,53	22,42	27,34	28,45	21,31	24,33		24,77	20,82	28,28	28,89	25,24	23,53	

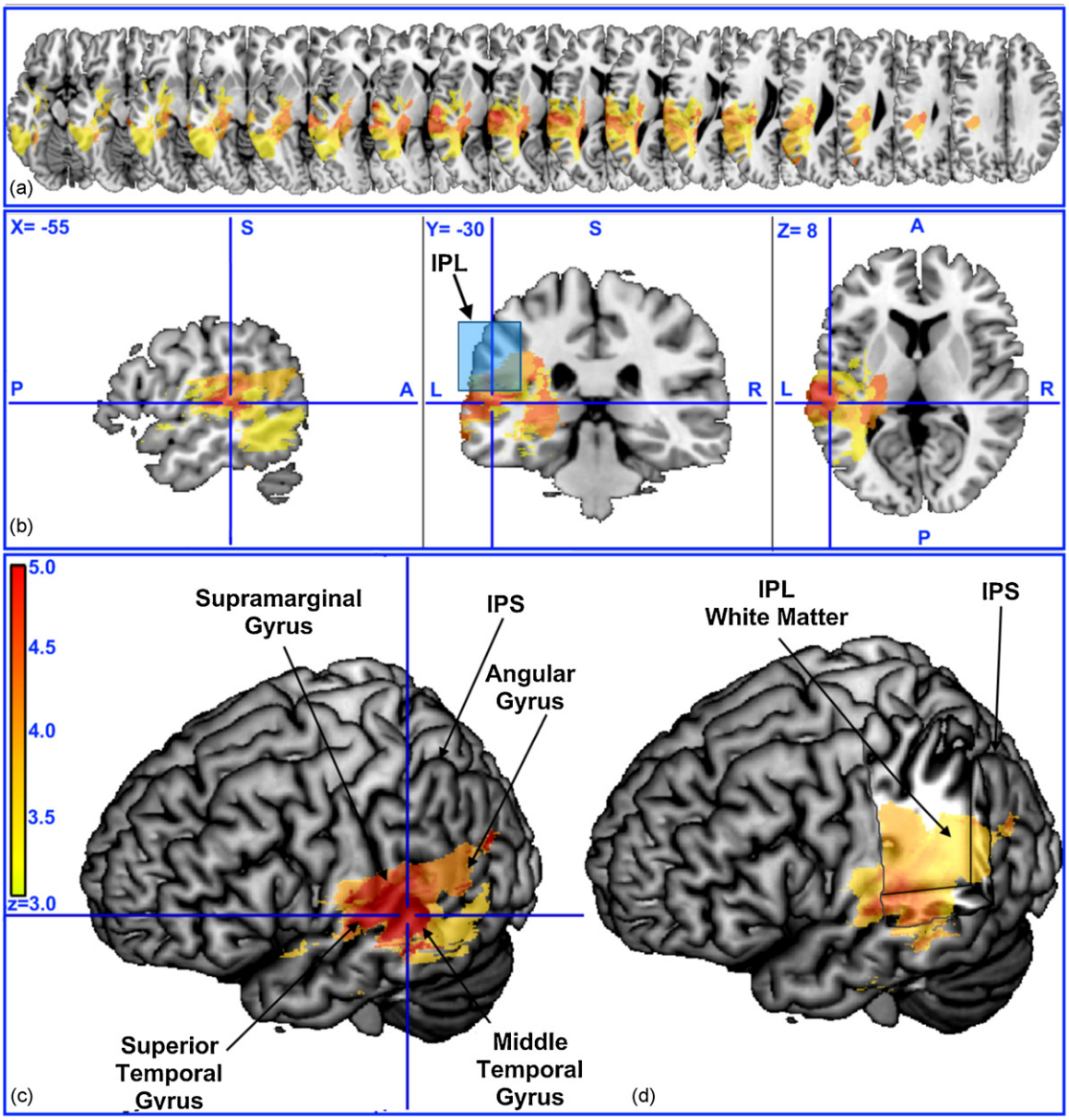

Fig. 5. VLSM analysis. The areas associated with a significant naming deficit for nonliving things ($p < 0.001$) involve a large part of the posterior temporal lobe. The cortical area associated with the largest category specific deficit in naming artefacts is the posterior portion of the left middle temporal gyrus. (a) Multi-slice coronal view, (b) anatomical centre of mass ($x = -55$; $y = -30$; $z = -8$) and (c) 3-D anatomical reconstruction of the areas involved.

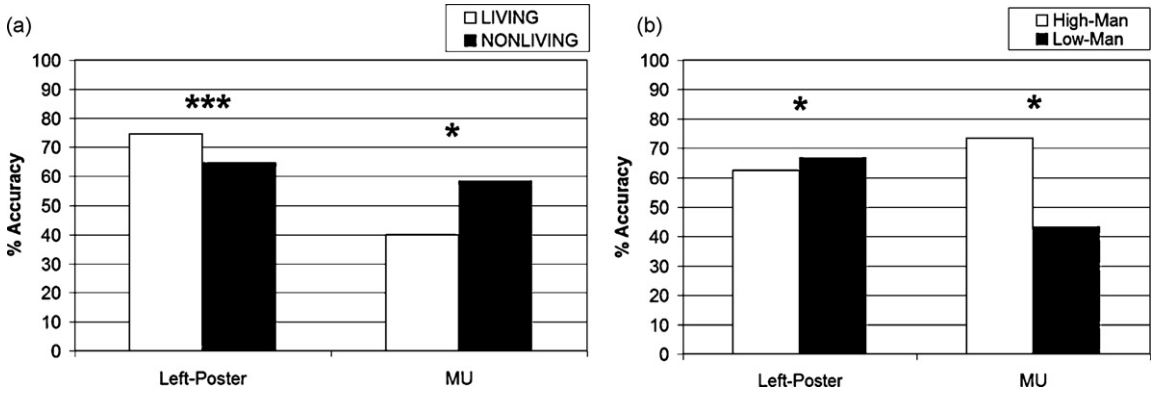

Fig. 6. Performance of patient MU compared with that of left posterior patients. MU shows the complementary pattern of naming, experiencing difficulties in naming living things (panel a) and also weakly manipulable objects (panel b). $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

formance of patient MU thus provides a double dissociation with respect to the performance of posterior temporal patients.

Cross-stimulus analysis confirmed the robustness of these results. as the analysis involved the results of a single subject only with just dichotomic (0 or 1) responses, a logistic regression was used. Category per se had a significant influence on the performance (Wald Statistic $_{(df=1)} = 3.99$, $p = 0.045$); there was also an influence of visual complexity and word frequency of the target item (Wald Statistic $_{(df=1)} = 4.34$, $p = 0.037$ and Wald Statistic $_{(df=1)} = 7.72$, $p = 0.005$ respectively). In addition, regarding manipulable objects only, the manipulability of the stimulus (high or low) significantly influenced the probability of MU finding the correct name (Wald Statistic $_{(df=1)} = 7.54$, $p = 0.006$). Among the extra-semantic variables, only familiarity was found to exert an influence on his naming ability ($F_{(1,114)} = 7.74$, $p = 0.007$) at this level of analysis.

8. Discussion

The aim of this study was to shed further light on the organization of concepts within the semantic memory. More specifically, we wanted to assess whether semantic information about concrete concepts is stored in more than one brain region. This could be according to the dominant type of feature necessary for their identification (sensory rather than motor/function related) on the one hand (Farah & McClelland, 1991; Saffran & Schwartz, 1994Warrington & McCarthy, 1983; Warrington & McCarthy, 1987; Warrington & Shallice, 1984), or by category (Caramazza & Shelton, 1998), or could involve a hub and spoke structure (Patterson et al., 2007; Rogers et al., 2004). The alternative possibility, on the other hand, is that it is stored in an undifferentiated semantic network within the temporal lobes with preservation of categories arising from underlying differences in distinctiveness and correlation structure (Tyler & Moss, 2001). These different accounts have been developed to explain the puzzling neuropsychological phenomenon of the selective loss of semantic information for one or more categories of knowledge shown by some brain-damaged patients. Of particular interest is the well known dissociation between the category specific loss of knowledge about living with respect to nonliving entities.

This study focused on the reverse pattern of loss (about nonliving things) which has been less frequently reported. By restricting this category only to manipulable objects, we tested two predictions. First, we investigated if there was a specific cortical region which is involved in the storing of information relevant specifically to nonliving things, as the literature about living things suggests. Second, if manipulability information (held to be a dimension related to motor knowledge) is a crucial feature in characterizing manipulable objects semantically, then patients showing a category specific deficit for nonliving things should experience more problems with highly manipulable objects, while patients with specific deficit for living things should have more difficulties with weakly manipulable objects (more defined in terms of their perceptual properties).

We tested these predictions in a consecutive series of 30 patients affected by brain tumours located in either the right or left temporal lobes using a naming task involving both living and nonliving items with nonliving things divided into high and low manipulability objects. The performance of the patients was compared with that of a patient showing a stable category specific semantic deficit for living things and with that of a group of 20 control subjects. We analyzed the findings at a behavioural level both at a single case and group level of analysis, and also by means of Voxel-based Lesion Symptom Mapping (VLSM) technique in order to localise the brain areas in which category or manipulability effects occurred.

Only left hemisphere patients had any naming deficit on our task. This effect was however entirely attributable to left posterior temporal patients, since the performance of left anterior temporal patients was generally similar to controls (with the one exception of patient LA11). Moreover left hemisphere patients in general showed a category specific deficit for nonliving things, but only for left posterior temporal patients was the category effect larger than that shown by controls.

The left posterior temporal patients *also* showed difficulties in naming highly manipulable objects more than weakly manipulable ones. These results were not just the outcome of a group effect as they were also present in many of the patients at a single case level of analysis. However, while the category specific deficit in naming manipulable objects in general was very robust, being confirmed both at a cross-subject level and also at a cross-stimulus level of analysis, the effect of manipulability was not consistent across the two types of analysis. Indeed, for left posterior temporal patients it was significant only at a cross-subject level of analysis, while at a cross-stimulus level of analysis left anterior temporal patients only showed an effect of manipulability being worse in naming weakly manipulable objects.

Giving however further support for a role of manipulability in influencing the naming of artefacts, patient MU who consistently showed in past investigations a category specific semantic deficit for living entities (Borgo & Shallice, 2001; Borgo & Shallice, 2003), on the same task named living things worse than manipulable objects and consistently with our predictions *also* had more difficulties in naming weakly than highly manipulable objects. This effect was also significant at a cross-stimulus level of analysis.

From an anatomical point of view, VLSM analysis showed that category specific naming deficit for manipulable objects was associated with lesions in the left posterior middle and superior temporal gyri. Interestingly, a large portion of the subcortical white matter underlying the inferior parietal cortex was also significantly involved in those patients showing the larger category specific naming deficit for manipulable objects, supporting the possibility of a disconnection between the inferior parietal cortex and the left temporal lobe.

The lack of category specificity deficits for living things found in the sample of tumour patients we tested may appear surprising. However it has been suggested (Gainotti, 2000) that knowledge about living things may be distributed more bilaterally in the temporal lobes than that of nonliving entities. Brain tumours only sporadically produce bilateral lesions and none of our patients showed bilateral temporal involvement. However, the performance of patient MU in this task supports the idea that patients affected by a selective loss of knowledge of living things, name the living stimuli used in this task more poorly than they do nonliving items. In addition, he experienced more difficulties with weakly manipulable objects, which lack a clearly unique manipulation.

Taken together, these data shed further light on the organization of content within semantic memory. It is difficult to account for these results in terms of any non-semantic explanation. The material we used was completely balanced to control for all the usual extra-semantic interfering variables. The cross-stimulus control analysis shows that the effect persists across stimuli indicating that the result cannot be explained by the possibility of a failure to balance the stimuli in a particular part of the range in one or the other stimulus dimension.

More problematic is the more fine-grained effect of the level of manipulability on the naming abilities of the patients. On one hand, the performance of MU gives support to the prediction that patients showing a category specific semantic deficit for living things will also have difficulties in dealing with weakly manipulable objects. However, the performance of the tumour patients was less clear-cut, since the selective difficulty of left posterior tempo-

ral tumour patients in naming highly manipulable objects found in the between-subject analysis was not confirmed in a between-stimulus analysis. However the possibility that manipulability does have a real effect in these patients is suggested by the performance of left anterior temporal patients who showed a significant difficulty in naming weakly manipulable objects, an effect that fits with the prediction that more ventral areas might process more perceptual kinds of information. That this effect, in left anterior temporal patients, was not coupled with a deficit in naming living entities too, might be explained by the fact that this latter deficit is usually associated with bilateral temporal lesions (as in the case of MU) (e.g. Capitani et al., 2003; Gainotti, 2000).

An important result of this experiment was that by carefully controlling the material used and the definition of what counts as a nonliving item (i.e. in this case an artefact), we were able to find a high density of patients with category specific naming difficulties for nonliving items. The adoption of the case series methodology (Woollams, Ralph, Plaut, & Patterson, 2007) gives further strength to the findings since the results of the group analyses were deriving from effects that were largely present and significant already at the single case level of analysis.

The VLSM analysis we performed showed that the cortical areas mostly involved also included areas that are situated within the Wernicke territory (especially the posterior portion of left superior temporal sulcus and the temporo-parietal junction) which have been linked to both speech comprehension and production (Blank, Scott, Murphy, Warburton, & Wise, 2002; Wise et al., 2001). This could explain the presence of a general naming deficit in this group of patients. However together with these regions, the left middle temporal gyrus and the white matter underlying the inferior parietal cortex (see Fig. 6) were also specifically involved. These areas have been extensively linked to object use and identification in many studies (Devlin et al., 2002; Lewis, 2006; Spatt, Bak, Bozeat, Patterson, & Hodges, 2002; Tranel et al., 2003; Weisberg et al., 2007) in recent years and have been moreover directly linked to tool naming (Chao, Haxby, & Martin, 1999; Martin, Wiggs, Ungerleider, & Haxby, 1996). These results are in agreement with the recent claims, coming from fMRI studies (Beauchamp et al., 2002; Beauchamp et al., 2003; Canessa et al., 2008; Chao & Martin, 2000; Kellenbach et al., 2003; Mahon et al., 2007; Martin, 2007) but also from neuropsychological investigations (Goodale et al., 1991; Hodges, Spatt, & Patterson, 1999; Spatt et al., 2002), about the important role of left parietal areas in the sensorimotor transformations underlying action organization and object use, with perception of a manipulable object affording the action towards it (Grezes & Decety, 2002; Johnson-Frey, Newman-Norlund, & Grafton, 2005; Rumiati et al., 2004).

9. Category specificity following temporal lobes tumours

As previously outlined, a category specific deficit for nonliving things has been more rarely reported than that for living entities (Capitani et al., 2003; Gainotti, 2000) and more importantly such evidence has come almost exclusively from single case investigations. Such studies are rarely able to assess individual differences in the relative strength of living things and artefacts deficits premorbidly, which could potentially produce selection biases (see e.g. Laws, 2005). Evidence for segregated cortical regions associated with naming deficits for artefacts have however been reported in some group studies. For example Damasio and colleagues (Damasio et al., 1996) found, in a large sample of patients with different etiologies (but mainly stroke), that naming deficits for artefacts were especially associated with damage to left posterior inferolateral temporal cortex damage, particularly to the posterior portion of the left middle temporal and angular gyri. More recently, in a voxel-based morphometry study, conducted by Brambati and colleagues (Brambati et al., 2006), the cortical volume preserved in the left posterior middle temporal gyrus was positively correlated with the ability to name familiarity-matched nonliving items. The study was conducted on a large sample of patients suffering from different types of neurodegenerative diseases (see also Garrard, Patterson, Watson, & Hodges, 1998, for related findings).

The results we report constitute a further confirmation that left posterior middle temporal regions are associated with a deficit in naming artefacts. This is especially important because our results come from a completely different population of brain-damaged patients, i.e. brain tumours, who consistently showed greater naming deficits for artefacts when the lesion involved left posterior middle temporal regions. Particularly striking, moreover, is the overlap between the sites of the lesions found in the study by Brambati and colleagues (Brambati et al., 2006), and the lesion site found in the sample of patients we investigated. The region of maximum overlap we found is clearly included and perfectly matches the region included in the peaks of maximum cortical volume reduction found by Brambati and colleagues.

From a theoretical point of view, the data from this study provide strong evidence to relate to current models of organization of semantic memory. The idea of a semantic system organized in a (both anatomically and functionally) undifferentiated network (Tyler & Moss, 2001) would seem to have great difficulty in accounting for these results. No anatomical specificity with respect to a selective deficit in naming nonliving entities would be predicted from this account.

Moreover, the findings do not completely support a 'categorical' organization of semantic memory. Indeed, we have shown that MU, a patient suffering from a selective loss of knowledge for living entities, was also found to have difficulties in naming a sub-set of the items belonging to the nonliving category, namely weakly manipulable objects.

The results from this study also appear to be somewhat problematic for the "distributed-plus-hub" account. Indeed, one of the key predictions of this approach is that damage to the temporal poles should produce generalized semantic problems (one of the most prominent symptoms of semantic dementia being indeed anomia). So, left anterior patients would be expected to be the most impaired in the naming task (regardless of any categorical selectivity). However, only 1 of the 11 left anterior temporal patients tested, had a significant naming deficit. It might, however, be argued that the 'hub' could be assumed to be distributed bilaterally in the temporal poles, and so a semantic deficit would only occur for bilateral lesions rather than for unilateral ones (as in our case). From these data then, the existence of a more general 'amodal hub' is not ruled out, but its anatomical underpinnings need to be clarified.

Even if the specific prediction on the role of manipulability gradients in the knowledge of manipulable objects was only partially confirmed, the findings support the idea that semantic system may be at least partially organized in modality congruent 'channels', with the relative weight of information contained in these channels varying across different concepts (Warrington & McCarthy, 1983; Warrington & Shallice, 1984) which can be viewed within a generally sensory-to-motor contrast (Chao et al., 1999). It may be useful to think of the semantic system as a "a giant distributed net in which regions tend to be more specialized for different types of processes (see also Shallice, 1988, 1993). This specialization could arise because of the pattern of connections -outside the semantic system itself-, used by each particular process. The basis on which differentiation between processing regions within the semantic system would develop would include *the most favoured modality of input* for that process" (cfr. Shallice, 1993, p. 254). It is reasonable to think that the most favoured modality of input would be the one that most easily (or critically) allows the most frequent type of opera-

tion to be carried out with the concept and that, because of this, becomes *favoured.* Processing related to the principal type of operation undertaken, would "support" the retrieval of other aspects of the representation. If processing within these 'specialized regions' became impaired, then the activation of other aspects of the target concept, or even its identification, would become defective.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuropsychologia.2010.02.002.

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