ON THE REPRESENTATION OF SEMANTIC AND MOTOR KNOWLEDGE

EVIDENCE FROM BRAIN DAMAGED PATIENTS

by

Gioia Anna Laura Negri

SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHYLOSOPHY
AT
SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI (S.I.S.S.A.)
TRIESTE, ITALY

A mio fratello.

Contents

IV A Neuropsychological investigation of the contention scheduling model

V General Discussion 154

References 165

Acknowledgments 177

Abstract

"The sight of the little madeleine had recalled nothing to my mind before I tasted it...."but"....as soon as I had recognized the taste of the piece of madeleine soaked in her decoction of lime-blossom which my aunt used to give me .... immediately the old grey house upon the street, where her room was, rose up like a stage set to attach itself to the little pavilion opening on to the garden which had been built out behind it for my parents."

Marcel Proust (1871-1922), Remembrance of Things Past

When we think of an apple, do we actually feel the same as when we eat it?

The central theme of this work is to understand whether the permanent representation of an object corresponds to a reactivation of sensations we perceived when we actually had it in our hands.

A recent debate in cognitive neuroscience, in fact, is concerned with the possibility that the neural systems that mediate overt action and sensory experience are causally involved in the neural representation of actions and real objects. On the other hand, more classical models postulate a relative separation between the *how* system and the *what* system, the former being more related to action, the latter more related to visual and semantic object representation. Such a classical view does not deny that the two streams normally have a close interaction but, based on neuropsychological and behavioral evidence, it holds that they can work separately in the case of selective brain damage or in particular experimental conditions.

In this thesis I will explore the possible role of the motor processes in understanding objects and actions by studying brain damaged patients performing a series of action- and object-related tasks. In Chapter I, I will briefly introduce the literature on the relationship between actions and concepts of both healthy and brain damaged subjects. Chapter II reports a study on a group of 37 stroke patients who have been tested for their ability to recognize and use objects, as well as to recognize and imitate actions. In this group I found double dissociations suggesting that these tasks depend on separable cognitive processes. In Chapter III, I will describe a double dissociation study in which we compared the performance of two patients with apraxia with that of two patients with semantic impairment, and I will show how the object knowledge of the latter patients decline in time although they maintained relatively good ability to use objects. Finally, in Chapter IV I will analyze the performance of a new series of apraxic patients on a set of tasks aimed at testing a computational model which accounts for the errors that apraxic patients make when using objects.

The results will not completely fit with the embodied theories of knowledge. Rather, they are compatible with "disembodied" models that postulate a separation between the object conceptual knowledge and the sensory-motor input and output systems.

Chapter I.
Literature Review

1.1. Embodied and disembodied theories of actions and objects representation

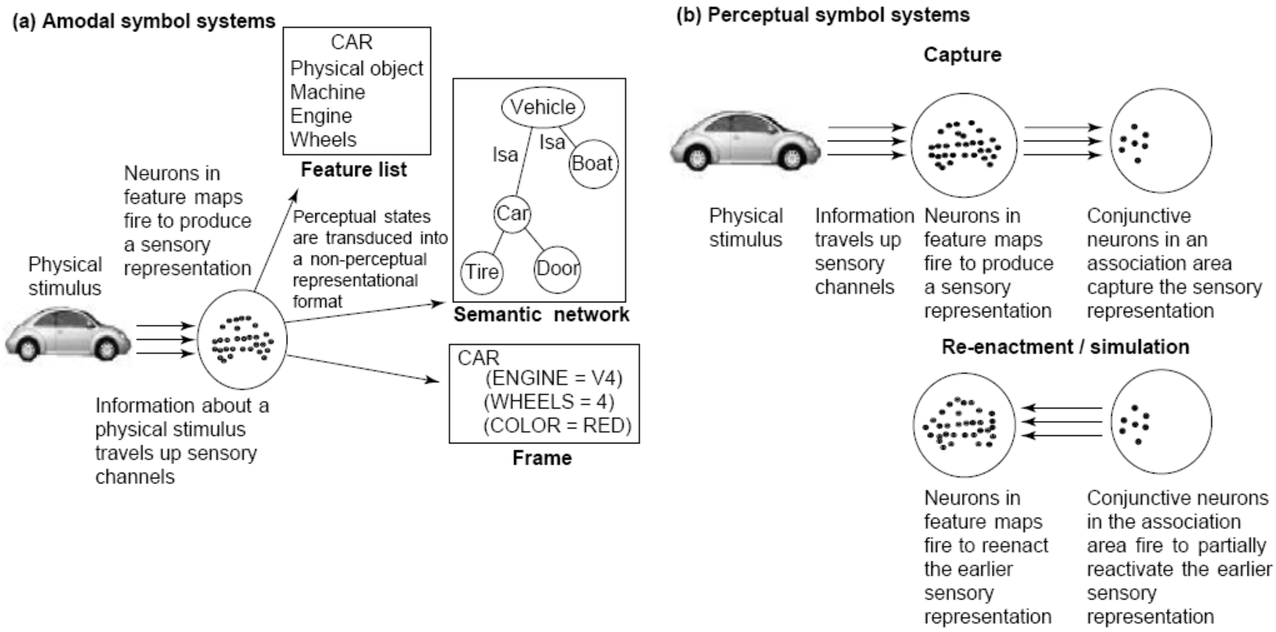
There are two main theoretical views on the role of the sensory-motor information in the representation of actions and concepts: the *embodied* (or modal) and the *disembodied* (or amodal) approaches (for a discussion, see Mahon and Caramazza, 2005).

According to the embodied approach, the sensory-motor content has a substantial role in the representation of actions and concepts. The boldest versions of this approach claim that the conceptual content is reducible to sensory-motor content (e.g. Gallese and Lakoff, 2005; Barsalou, Simmons, Barbey, and Wilson, 2003; Pulvermuller; 2001). These authors hold that the key role of the sensory-motor systems is not only linked to the perception of, and learning about, the real world, but it is also essential for permanent representation of concepts. During the processing of a word, an action, or a concept, the sensory-motor information is newly in use through a process of reactivation, also called *simulation* (Gallese and Lakoff, 2005) or *re-enactment* (Barsalou et al., 2003). Simulation is used during development in order to learn to understand others' mental states and produce congruent responses to the external stimuli. At the same time, similarly to Vygotsky's idea of *Zones of Proximal Development* (ZDL), the mechanism of simulation must allow the formation of the Self (Gallese, Migone and Eagle, 2006), and has to be different from the other's actions. For this reason, the simulation mechianisms develop inhibitory mechanisms, in order to avoid that the individual merely reproduces the action of the other. In children and adult subjects, the process of re-enactment tends to be unconscious, as opposed to the mental imagery that is considered to be a conscious process (Barsalou, 1999). Similarly, the "direct matching hypothesis" postulates that the actions performed by others are recognized by activating the same spatiomotor representations used for performing the actions themselves (e.g. Prinz, 1997).

In contrast, disembodied theories of knowledge hold that concepts are not totally grounded in the sensory-motor systems; rather, the sensorimotor processes are not sufficient to exhaust all we know about concepts (e.g., Caramazza, Hillis, Rapp, and Romani, 1990; Humphreys and Forde, 2001; Plaut, 2002; Tyler and Moss, 2001; Warrington and McCarthy, 1987). After a sensorimotor experience, information is stored in an "amodal" format: sensorimotor representations are transduced into a symbolic representation, such as a feature list, semantic network, or frame.

An example of embodied vs. disembodied concept is reported in Figure 1.1.

Figure 1.1 (adapted from Barsalou et al., 2003) (a) In amodal (*disembodied*) symbol systems, neural representations are established initially to represent objects in vision. Subsequently, however, these neural representations are transduced into another representation language that is amodal, such as a feature list, semantic network or frame. Once established, these amodal descriptions provide the knowledge used in cognitive processes, such as memory, language and thought. (b) In perceptual (*embodied*) symbol systems, neural representations similarly represent objects in vision. Rather than being transduced into amodal descriptions, however, visual representations are partially captured by conjunctive neurons in nearby association areas. Later, in the absence of sensory input, activating these conjunctive neurons partially re-enacts the earlier visual states. These re-enactments contribute to the knowledge that supports memory, language and thought. This figure illustrates knowledge acquired through vision, but analogous accounts exist for acquiring knowledge in the other modalities (e.g. audition, action, emotion).



1.2. Neurophysiological studies in monkeys: the Mirror Neuron System

In 1992, Di Pellegrino, Fadiga, Fogassi, Gallese and Rizzolatti performed the first study in which the Mirror Neurons (hereafter: MN) were described. While recording the brain activity from the monkey cortex *in vivo*, they found a percentage of neurons in the area F5 of the ventral premotor cortex, that fired not only when the monkey performed an action -like grasping a piece of food- but also when it saw the same action performed by the experimenter. This particular type of neurons was therefore named “mirror”, because the observed action seemed to be reflected in the motor representation of the same action of the observer.

In this circuit, the congruence between observed and performed action can be very strict (*strictly congruent MN*) or broad (*broadly congruent MN*), the latter being more diffused. Another class of neurons found in this circuit, called “canonical” neurons, fire when the monkey performs the action, but also when the monkey sees the object involved in that action alone (e.g. the piece of food).

In addition, MNs discharge only when the effector is biological, rather than mechanical, (e.g. a hand but not a mechanical arm, see Figure 1.2.) and only if the hand interacts with a real object: mimicked actions do not activate the MNs, and the presence of the object alone is not sufficient either (Rizzolatti and Luppino, 2001).

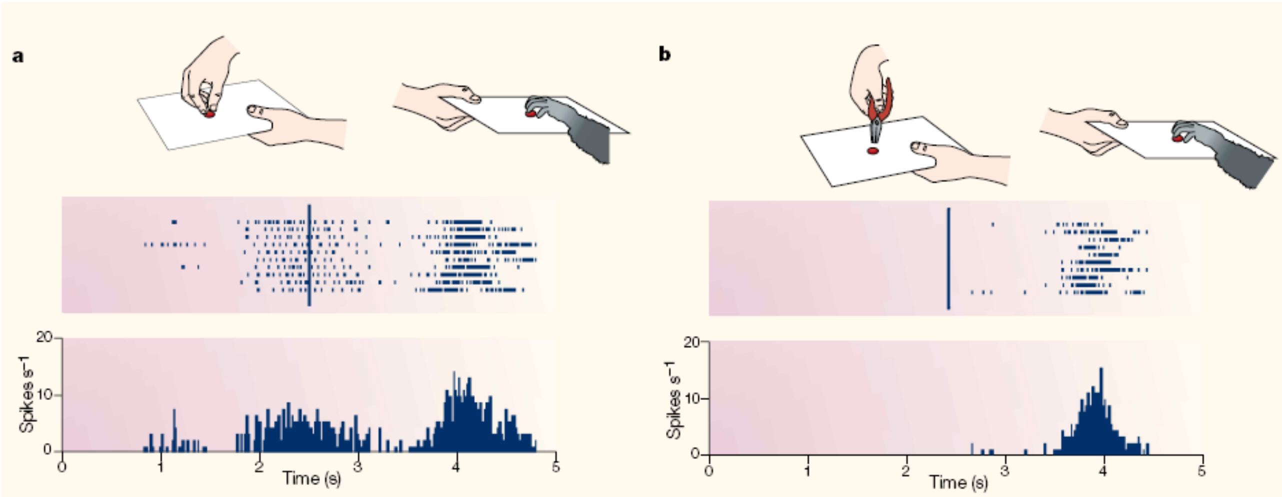
In a study by Umiltà et al. (2001), it was shown that the MN fire also when the experimenter grasps a hidden object behind an occluder, suggesting that the MNS is necessary, to some extent, to understand action goals. More recent experiments have demonstrated that there are also audio-visual MNs, that fire for example when the monkey cracks a nut and also when it hears the noise of a nut being cracked (Koehler et al., 2002).

Based on the reported findings, it has been claimed by Rizzolatti, Fogassi and Gallese (2001) that the Mirror Neuron System (MNS) is a circuit central not only for imitation, but also for understanding actions, goals and intentions of others. Moreover, the fact that the area F5 of the monkey can be considered as the homologue of the human Broca’s area (Binkofski and Buccino, 2004), led some authors to claim that the MNS is a possible precursor, as an anatomical base, for the evolution and understanding of language (Rizzolatti and Arbib, 1998). In fact, MN were described also for mouth actions, such as communicative or ingestive actions (Ferrari, Gallese, Rizzolatti and Fogassi, 2003).

The existence of the MNS has been considered strong evidence of the strong links between action performance and action perception in the brain, as well as for the embodied cognition hypothesis.

More evidence for embodied theories of knowledge comes from imaging and behavioral studies conducted on healthy humans.

Figure 1.2. Visual and motor responses of a mirror neuron in area F5. **a)** A piece of food is placed on a tray and presented to the monkey. The experimenter grasps the food, then moves the tray with the food towards the monkey. Strong activation is present in F5 during observation of the experimenter's grasping movements, and while the same action is performed by the monkey. Note that the neural discharge (lower panel) is absent when the food is presented and moved towards the monkey. **b)** A similar experimental condition, except that the experimenter grasps the food with pliers. Note the absence of a neural response when the observed action is performed with a tool. Rasters and histograms show activity before and after the point at which the experimenter touched the food (vertical bar). Source: Rizzolatti, Fogassi and Gallese, 2001.



1.3.Studies of healthy participants

1.3.1 Imaging studies

Object representation. Experiments conducted using neuroimaging techniques have shown that there is usually a co-occurring activation in the ventral premotor cortices when healthy subjects process information about manipulable objects relative to other categories of stimuli. This happens even in tasks that do not require the explicit use of motor information, such as for instance silent naming or passive watching. For example, Chao and Martin (2000) found an activation of the left ventral premotor and posterior parietal cortices for tools but not for faces, animals, or houses, both in passive viewing and in silent naming tasks. Martin et al. (1996) found similar activation for naming tools compared to naming animals (see also Grafton et al., 1997; Perani et al., 1995). Recently it was also demonstrated (Mahon et al., 2007) that visual information about manipulable objects is represented separately from that of arbitrarily manipulable objects in the ventral stream. In this study, the authors found that stimulus-specific repetition suppression (RS) in one region of the ventral stream is biased according to motor-relevant properties of objects, suggesting that neural specificity for 'tools' in the ventral stream is driven by similarity metrics computed using motor-relevant information represented in dorsal structures.

Action representation. A circuit homologous to the monkey MNS has been described in humans for action understanding and action observation tasks (Buccino, Lui, Canessa, Patteri, Lagravinese, Benuzzi, Porro, Rizzolatti, 2004). In general, there is an overlap in brain activation during action observation and action execution in premotor and parietal areas (Buccino et al., 2004; Buccino et al., 2001; Decety and Grezes, 1999). It has been found also that the circuits involved in action observation and execution are somatotopically organized: in fact, the pars opercularis of the IFG reflects the observation of distal hand and mouth actions, whereas the precentral cortex reflects proximal arm actions and neck movements (Buccino, Binkofski, Fink, Fadiga, Fogassi et al., 2001).

Using PET, Rumiati, Weiss, Shallice, Ottoboni, Noth, Zilles, and Fink (2004) found that the production of object-related pantomimes activated the left inferior parietal lobe and the ventrolateral prefrontal cortex, in a circuit partially overlapping with the MNS. However, subtraction analysis revealed that the pantomime-to-object task and the object naming task led to activation also in different brain areas. This result is at variance with predictions of embodied theories claiming that the object representation should overlap with the sensory-motor information stored in the motor and premotor areas.

1.3.2. Behavioral studies

Objects. Experiments using Stimulus-Response Compatibility paradigms (SRC) have brought evidence of a correspondence not only between seen and performed action, but also between object shape and motor response. The term *affordances* refers to action-relevant characteristics of the object or its surface (Michaels, 1988; Gibson, 1979): the shape of an object can, in fact, facilitate particular types of actions but not others. Tucker and Ellis (1998) demonstrated that simply viewing an object, in a task that does not require explicit processing of its motor-related features -e.g. judging if an object is upright or inverted- potentiates the response with the hand most suitable to reach and grasp the seen object. More recently, the same authors (Tucker and Ellis, 2001) have shown that, in a category judgment, the type of grasp (precision or power grip) is facilitated if the size of the object to judge is compatible with the grip used to perform the response. Taken together, these behavioral results seem to suggest that the visual representation of an object and its motor counterpart are anatomically and functionally embedded and, when the execution of an action is guided by a visual stimulus, the more the stimulus is compatible to the action, the more the execution of that action is facilitated.

However, other behavioral studies brought evidence for an independent representation at least at the cognitive level. For example, Rumiati and Humphreys (1998) asked participants to name or pantomime, under time deadline condition, the use of objects in response to pictures or written words. Based on the subjects' types of errors, the authors concluded that participants were using a direct visual route when gesturing to pictures (prevalence of "visual" errors); whereas they used an indirect, semantic route when they had to pantomime to written words ("semantic" errors only). The existence of a dual route also for imitation will be discussed in the paragraph about the neuropsychological literature.

Actions. Several behavioral studies have shown that there is a strict link between perceived and executed actions. For example, using stimulus-response compatibility (SRC) paradigms, it has been demonstrated that the observed movement of a finger can influence a finger tapping task, as the response is faster in compatible trials than in incompatible trials (Brass, Bekkering, Wohlschlaeger and Prinz, 2000), even using a simple response task (Brass, Bekkering and Prinz, 2001). Similar results were found in a reaching-and-grasping task by Craighero, Bello, Fadiga and Rizzolatti (2002), in which subjects were shown a picture of a hand before grasping a bar oriented in different angles: reaction times were faster if the prime picture corresponded to the final hand posture required to grasp the bar.

1.4. Limb Apraxia: an overview

If action and object conceptual knowledge were based on motor simulation processes (which take place in the motor areas), then, damage to the sensory-motor system would significantly affect conceptual processing of actions and objects. The ideal way to test this hypothesis is to assess the fine-grained conceptual knowledge of tools and manipulable objects of patients that have lost the ability to use them correctly, like patients with limb apraxia. In this thesis I will present three studies on such a relation between action and object knowledge in patients with brain lesions, with particular focus on limb apraxia.

The term *apraxia* refers to a primary deficit in voluntary goal-directed movements, not due to a loss of perceptual input (like agnosia, anaesthesia, deafness or blindness) or motor output deficits (hemiplegia, tremor, ataxia). It is frequently characterized by *automatic-voluntary dissociation*, as patients cannot perform an action in the experimental or clinical setting, but they might be able to do it spontaneously in the everyday life. The word *apraxia* was used for the first time by Steinthal (1871) to describe particular errors made by aphasic patients that had lost their ability to use objects properly. In the following paragraphs I will describe two main forms of limb apraxia and a cognitive neuropsychological model of limb praxis put forward to explain both pathological and normal behavior.

1.4.1. Ideational Apraxia (IA) and Object Use

Ideational Apraxia has been characterized as an impairment of object use, manifested in incorrect selection and conceptually inappropriate use of tools (Morlaas, 1928; De Renzi, Pieczuro and Vignolo, 1968; De Renzi and Lucchelli, 1988; Ochipa, Rothi and Heilman, 1989, 1992), but also in erroneous sequencing of actions that require the consecutive use of several objects to achieve a certain goal (Pick, 1905; Liepmann, 1920; Lehmkuhl and Poeck, 1981; Poeck, 1983). IA is usually associated with lesions to the left posterior temporo-parietal regions (Liepmann, 1920; De Ajuriaguerra, Hecaen and Angelergues, 1960; De Renzi and Lucchelli, 1988). As patients affected by IA make errors that are not attributable to motor problems, even when the ipsilesional hand is used to perform the tasks, it was hypothesized that high motor control of both hands is lateralized in the left hemisphere.

According to Roy and Square (1985), IA is a result of the disruption of the *conceptual* praxis system that contains abstract information about a) knowledge of objects and tools functions, b) decontextualized knowledge of actions, c) knowledge of serial organization of actions. The conceptual praxis system is separate from the *production* system, which includes the knowledge of actions in their sensorimotor form, as well as the actions programs for skilled movements (including the mechanisms that translate such programs into a motor activity). Similarly, other neuropsychologists have proposed that IA derives from a conceptual disruption of the action program at a central (symbolic) level, as it is often associated with a loss of functional and manipulation knowledge about objects even in visual and verbal tasks that do not require their actual use (Lehmkuhl and Poeck, 1981; Roy, 1981; Ochipa, Rothi and Heilman, 1989, 1992). According to this view, IA patients should also fail in discriminating correct from incorrect actions when performed by others, because the motor representation is lost at the central level. Morlaas (1928) introduced the term "agnosia of usage" to describe IA patients as incapable of recognizing objects in order to use them.

Functional knowledge of objects however can be found intact in patients with IA, in fact they can still be able to classify erroneous actions and even sort pictures of action sequences in which they commit errors (Rumiati et al., 2001). The models that separate conceptual information from functional and manipulation knowledge are most suited to explain the deficits encountered in the literature. Finally, Zangwill (1960) hypothesized that IA is just a severe form of IMA (see next paragraph) but the existence of the double dissociation between the two deficits (e.g. De Renzi et al., 1968; De Renzi and Lucchelli, 1988) led this argument being ruled out.

1.4.2. Ideomotor Apraxia (IMA) and action imitation

According to the Roy and Square model (1985), IMA is the result of impairment to the *production* subcomponent of the action system. Patients with IMA are still able to plan a motor sequence correctly, but they fail in executing it. Moreover they should still be able to use objects, because their conceptual knowledge of an action is intact. The most sensitive task to investigate this deficit is asking the patient to imitate: in this task, he/she is not required to generate a motor plan but only to execute it after having seen it done. In IMA patients, it is possible to encounter conceptual errors (like lexicalizations[1], body-part-as-tool[2], bad hand configuration, clumsiness) or kinematic alterations, for example in speed, amplitude and frequency of the movement. IMA has been observed in association with lesions in the left inferior parietal cortex (Liepmann, 1920; De Renzi et al., 1968), although it has been documented also after damage to the basal ganglia and thalamus.

Finkelburg (1870) proposed that IMA is due to a more general disturbance of the representation of symbols, including gestures and verbal languages (“asymbolia”), as it is usually associated to language impairments. However, Liepmann (1905) noted that one of his patients with IMA did not show signs of aphasia, and that the patients were not able to reproduce the gestures even by imitation, discarding the “asymbolia” hypothesis. He instead proposed that, in right-handers, the mechanism responsible for skilled movements of both hands is situated in the left hemisphere. In 1965, Geschwind proposed a disconnection model similar to Wernicke's (1874) model of language, in which IMA is caused by lesions to the arcuate fasciculus or the supramarginal gyrus, so as to interrupt

[1]Lexicalization: a meaningless action is tranformed in a meaningful actions existing in the patient's repertoire

[2]Body part as tool: e.g.: using the index finger as a toothbrush when imitating the action of brushing teeth

the flow of information from the language areas to the anterior motor associative areas. More recently, it was proposed that IMA is caused by damage to the visuo-kinestesic engrams for skilled movements, or to the connections between these and the motor associative areas (Heilman, 1979; Heilman and Rothi, 1985). According to Goldenberg and colleagues (1996) IMA is the result of an inability to encode movements on body-based coordinates, involving the body schema representation: the patients affected by IMA cannot encode the end-state of limb posture relative to the body, so the kinematic errors that they produce result from attempts to imitate the posture of the examiner. A recent study by Tessari and colleagues (2007) offered an alternative model of imitation, which I will describe in detail in the next paragraph.

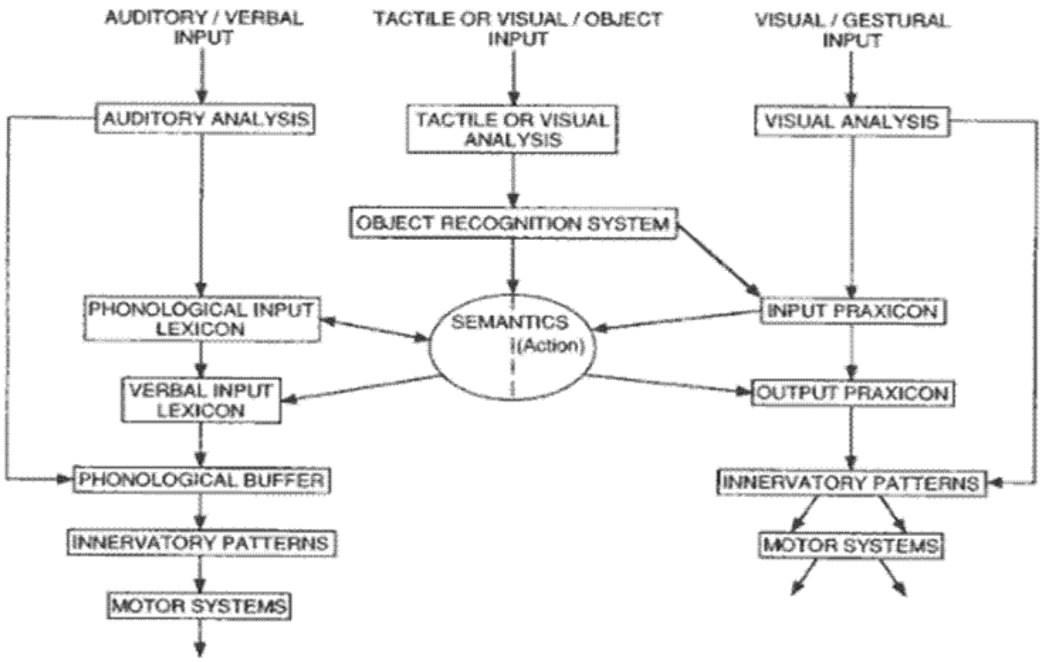
1.4.3. A Cognitive Neuropsychological model of limb praxis

Rothi, Ochipa and Heilman (1991) proposed a composite model of praxis based on dissociations reported in the literature. A model, represented in Figure 1.3., was originally developed to account for the different subtypes of IMA but it is also suitable to interpret normal behaviour. It postulates a separation between units that store the meaning of the actions (*semantics*) and units that store the motor features of an action (*Action lexicons,* or *praxicons*). The authors believe that *movement formulae* are represented and stored permanently in the brain (specifically, in the left parietal lobe) so that they can be recalled from memory in case of need, without reconstructing them *de novo* at each request. This is consistent with the fact that patient with apraxia due to parietal lesions were also impaired at recognizing pantomimes, whereas apraxic patients with anterior lesions were good at this task (Heilman et al., 1982). Observations of patients who perform worse at imitation of pantomimes than production of pantomimes on verbal command, and patients who show the reverse pattern, suggest that there is a separation between input and output action praxicons. Evidence of input modality-specific apraxias (Rothi, Mack and Heilman,

1986) led the authors to hypothesize that three different types of inputs (auditory, visual/gestural and visual/object) can reach the input praxicon.

Another important feature of this model is the existence of a non-semantic route for imitation, which allows imitation of unfamiliar actions through a visuo-motor conversion mechanism.

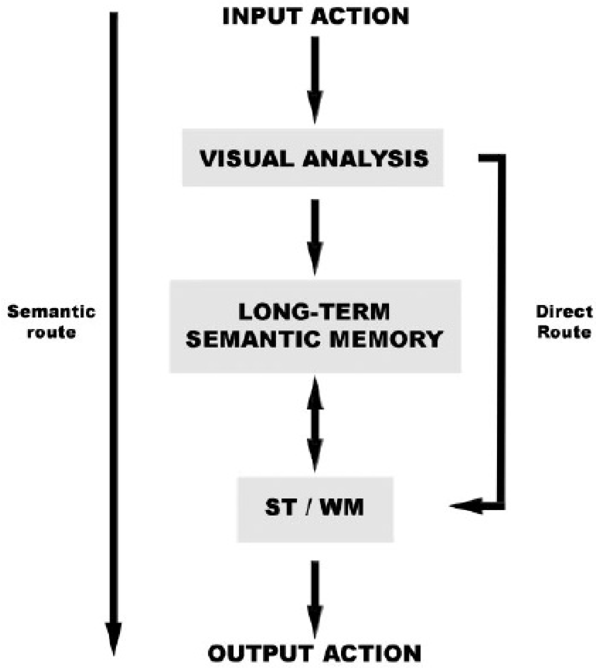
Figure 1.3.. Rothi et al. (1991) modelof praxis processing , as revised in Heilman and Rothi (2003) and its relation to semantics, naming, and word and object recognition.



Tessari and colleagues (2007) tested the dual-route model for imitation using a sample of 32 brain-damaged subjects. They found a double dissociation between patients who could not imitate novel meaningless gestures but were preserved at the imitation of meaningful gestures, *versus* patients who showed the opposite pattern. The authors interpreted the first deficit as a result of damage to the semantic route for action, whereas the opposite pattern should result from a breakdown of the direct route. These data, together with other studies that found selective impairments in the imitation of meaningful (Bartolo, Cubelli and Della Sala, 2001) or meaningless actions (Goldenberg and Hagmann, 1997) support the view that the two types of actions are imitated via different cognitive mechanisms (see Figure 1.4.).

Based on the neuropsychological literature, models that propose a fractionation within the praxis system are most suitable to explain the dissociation found in patients, compared with models that postulate the existence of a unique mechanism underlying praxis and semantics.

Figure 1.4. The two route model for explaining imitation of actions. Following visual analysis, known, meaningful actions automatically activate the selection of the semantic long-term memory route. The direct route is selected to imitate novel, meaningless actions, but it is also used to reproduce both meaningful and meaningless actions when these are presented intermingled. ST/WM = short term/ working memory. (Taken from Tessari et al., 2007)



1.5. Neuropsychological studies of the relationship between actions and objects representation

1.5.1. Actions.

The neuropsychological evidence in favor of the embodied cognition theory is, so far, very scarce. This is probably because the double dissociation methodology (Shallice, 1988), is most suited for investigating the independence of two cognitive functions rather than associations of deficits. Embodied theories of cognition assume that sensory motor information is necessary for the semantic knowledge of actions and objects (e.g. Gallese and Lakoff, 2005). The following prediction is that a patient who has lost his/her motor ability, should also retain impoverished knowledge about the objects or the actions that he/she is no longer able to produce. In particular, patients with IMA would be unable to recognize the gestures that they are not able to perform, and patients with IA would loose their fine conceptual knowledge about objects. A recent study by Buxbaum, Kyle and Menon (2005) addressed this issue by asking 44 patients with left hemisphere stroke to perform a series of object-related tasks. Analyzing the results at the group level, there was a significant correlation between the ability to imitate object-related pantomimes and the pantomime recognition task. In addition, because the maximum overlap of lesions was in the left inferior parietal lobe, the authors attributed a central role to this structure in the recognition and production of actions.

These associations seem to support the view that motor processes play a central role in the processing and recognition of actions. However, such correlations were not found in a similar study of imitation conducted by Tessari, Canessa, Ukmar and Rumiati (2007). The study failed to find significant correlation between performance of a pantomime imitation task and a pantomime recognition task ($r = .32$, $p = .07$). A more detailed discussion about this issue will be presented in chapter III, in which a similar group study is described.

Existing single case studies do not seem to go in the same direction either. In fact, double dissociations between object use and object recognition have been described, as well as between action imitation and action recognition. For example, the selective impairment in recognizing pantomimes (i.e. pantomime agnosia) has been first reported by Rothi, Mack, and Heilman (1986) and by Bell (1994) for patients who were no longer able to name and recognize pantomimes, despite their relatively preserved ability to produce object-related actions. On the opposite side there are patients who, despite severe IMA, can still recognize object-associated pantomimes. Patient GW for instance, described by Rapcsak, Ochipa, Anderson, and Poizner (1995), was unable to produce any correct pantomimes of object use either on visual presentation of objects (on a total of 15 stimuli), verbal command, or using imitation. However, he could name all 15 object-associated pantomimes presented, and he could discriminate correct from incorrect pantomimes of object use (14/15). Rumiati, Zanini, Vorano and Shallice (2001) described patients DR and FG, with severe ideomotor and ideational apraxia, who were able to recognize object-associated actions (DR: 15/15; FG: 14/15). FG and DR were also tested on multiple object tasks (such as making coffee or preparing a letter to post), which test the ability of sequencing a series of steps and subgoals: they made significantly more errors than controls, however they were good at sequencing cards depicting the different steps of the same activities (9/10 in both patients). Moreover, FG could discriminate correct from incorrect pantomimes of actions (19/20) even when the experimenter reproduced the same errors that he had made in a previous session.

1.5.2. Objects.

fMRI studies seem to suggest a strong association between visual-semantic processing of manipulable tools and involvement of premotor and parietal areas. If these areas were necessary for semantic processing of objects (as claimed, for example, by Gallese and Lakoff, 2005), then IA patients would be impaired at recognizing objects or, at some level, they would retain impoverished knowledge of the objects' details.

Neuropsychological results do not support the idea of embodiment of objects concepts. For example, patients with IA with no semantic impairments have been repeatedly described (Buxbaum and Saffran, 2002; Buxbaum, Sirigu, Schwartz, and Klatzky, 2003; Buxbaum, Veramonti, and Schwartz, 2000; Cubelli et al., 2000; Halsband et al., 2001; Hodges, Spatt, and Patterson, 1999; Montomura and Yamadori, 1994; Moreaud, Charnallet, and Pellat, 1998; Ochipa et al., 1989; Rapcsak et al., 1995; Rosci, Chiesa, Laiacona, and Capitani, 2003). IA patients have been also described as having completely preserved performance on tests tapping semantic knowledge of the same objects they failed to use (patients DR and FG in Rumiati et al., 2001; patient HB in Buxbaum, Schwartz and Carew, 1997). Several patients with spared semantic knowledge in the presence of an object-use impairment have been reported (Ochipa, Rothi and Heilman, 1989; case 3 in Hodges, Spatt and Patterson, 1999; Buxbaum, Veramonti and Schwartz, 2000).

On the other hand, there are patients with semantic disorders who are still able to use objects correctly. For example, Lauro-Grotto, Piccini and Shallice (1997) reported that patient RM, who was impaired in naming, recognizing and semantic tasks concerning objects, was still able to use objects in everyday life. Patient DM described by Buxbaum et al. (1997) showed a similar pattern. It has been proposed that the spared ability to use objects correctly depends on objects' affordances and preserved mechanical problem solving skills (Hodges, Bozeat, Lambon Ralph, Patterson and Spatt, 2000).

A double dissociation between the ability to perform tasks tapping semantic information about objects and the movements necessary to use them appropriately suggest that these two abilities may be independent and have different neural substrates (see Rumiati et al., 2004). However, the fact that not all of the aforementioned studies used the same materials across patients (or even across tasks), may give rise to some objections about the nature of the dissociations found (see for example Hillis and Caramazza, 1991). In the studies that I present, the double dissociations that we detected are always based on the same items presented in different conditions.

Vision for action and vision for perception

The most represented sensory modality in the brain of nonhuman primates is certainly vision. In fact, anatomical and physiological studies have revealed that there are at least thirty separable visual areas occupying almost half the total volume of the monkey brain (Von Der Heydt, Peterhans and Baumgartner, 1984; Desimone and Schein, 1987). In primates, the visual areas are classically subdivided into two main functionally specialized processing pathways: a “ventral stream” for object vision, and a “dorsal stream” for spatial vision (Ungerleider and Miskhin, 1982). Lesion studies in monkeys have indeed shown that lesion of inferior temporal cartex causes severe deficits in performance on a wide variety of visual discrimination tasks (e.g. pattern, object, color), but not on visuospatial tasks like visually guided reaching (Gaffan, Harrison and Gaffan, 1986). On the other hand, posterior parietal lesions do not affect visual object discrimination performance; but instead cause severe deficits in visuospatial performance (for a review, see Ungerleider and Miskin, 1982).

As for humans, it has been shown that appropriate reaching and grasping can still be possible even if an adequate three-dimensional representation of the object to be grasped is lost. Goodale, Milner, Jokobson, and Carey (1991) described patient DF, affected by visual form agnosia due to bilateral occipital lesion. DF was severely impaired in perceptually judging the orientation of a line and could not indicate with her fingers the size of visually presented objects (Milner, Pereett, Johnston, Benson, Jordan, Heeley, Bettucci, Mortara, Mutani, Terazzi and Davidson, 1991). Despite her agnosic deficits, DF could orient her hand correctly in a posting task and her reaching-grasping movements were characterized by a normal correlation between the grip and the size of the objects. In contrast, Goodale, Meenan, Bulthoff, Nicolle and Racicot (1994) have shown that accurate, conscious visual information about an object may not be satisfactorily used by an intact motor system. RV, the patient they studied with bilateral occipital lesion, failed to grasp objects that he was almost perfectly able to recognize. Taken together, this double dissociation has been used to support the position that the "what" system is involved in the identification of objects and is impaired in DF but spared in RV. The "what" system is separate from the "how" system (damaged in DF bu spared in RV) guiding the action of the agent toward the stimuli. (Milner and Goodale, 1993, 1995). According to the authors, the "vision-for-perception" and the "vision for action" systems, that normally cooperate in an intact brain, can be selectively damaged by brain lesions and give rise to such patterns of behaviour. More recently, the dichotomy between dorsal and ventral streams has been further articulated to include the function of a "how" system in the dorsal stream. This may contain the representation of affordances, namely the learned associations between the objects and the basic motor components necessary for their use, such as the orientation and the shape of the hand grip (Grèzes et al., 2003; Tucker and Ellis, 1998; 2001; Ellis and Tucker, 2000). Such a "how" system of the dorsal pathway would also involve higher-level action representations acquired by past experience, which are lost in patients with Ideational Apraxia (Rumiati etal., 2001).

The functional separation between the two visual pathways has also been shown by means of experimental manipulations in healthy subjects. Visual illusions can be used to show a discrepancy between what we perceive and what our motor system actually does. Kroliczak, Heard, Goodale and Gregory (2006), employed the "hollow face illusion" to show that what subjects had reported to perceive (i.e. a three-dimensional protruding face, even if the surface of the face was the concave inside of a mask) was in fact different from their actual behavior. Although they were fooled by this illusion, the actions that they directed at the face were not influenced by perception. In fact, if they were asked to touch a 'bug-like' target stuck on the face, they actually reached out to the correct point in space (see 1.5.). Similar results with visual illusions have been observed with perception of orientation (Dyde and Milner, 2002) and with the Ebbinghaus illusion (Aglioti, Goodale and De Souza, 1995).

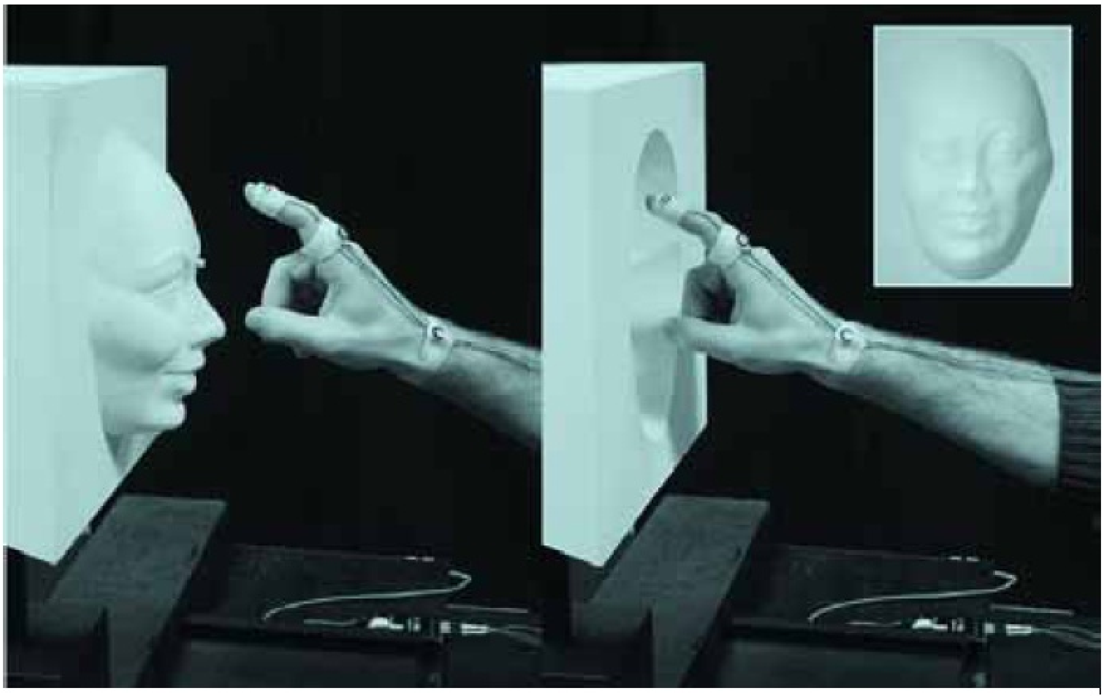


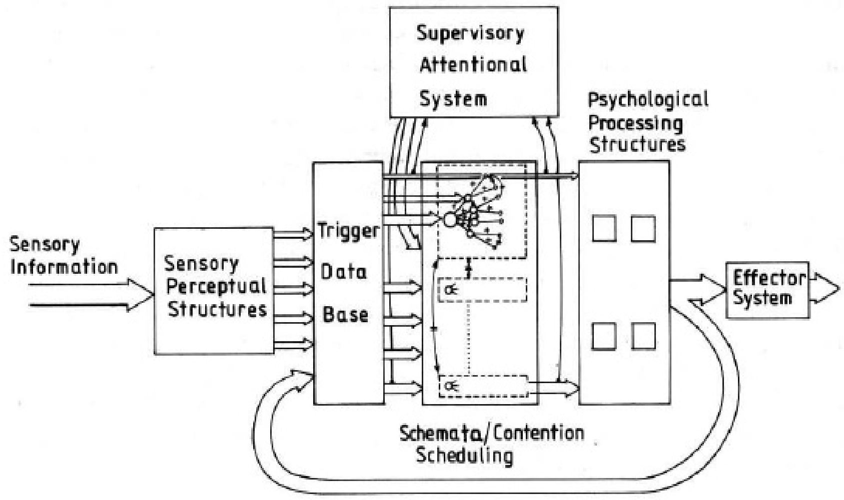
Figure 1.5. The “hollow-face” illusion used in the experiment of Kroliczak et al., 2006.

1.6. A computational account: the contention scheduling model

1.6.1. Description of the model

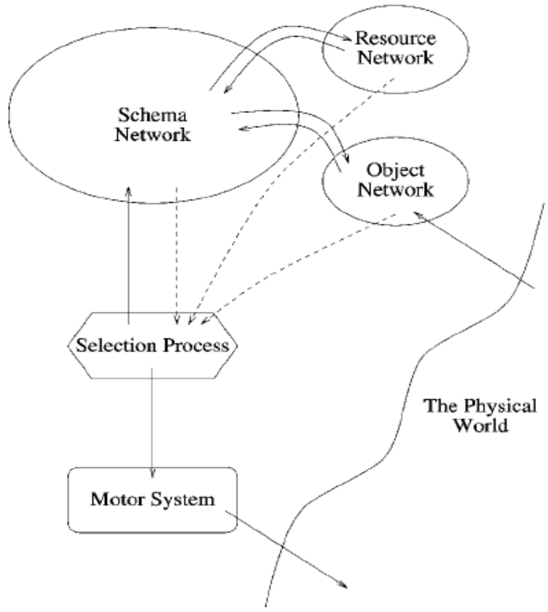
In 1986, Norman and Shallice proposed a computational model suited to explain both action slips of normal subjects and the types of errors made by brain damaged patients. Norman and Shallice's model was composed of two main units: a supervisory attentional system (SAS) and a contention scheduling system (CS); the model is represented in Figure 1.6. According to the authors, the SAS acts when conscious attentional control is required and it provides excitatory or inhibitory inputs to the contention scheduling system, which is engaged in the control of routine behaviour. Damage to the SAS would cause a form of apraxia defined as “frontal” by Luria (1966), described for example by Schwartz, Reed, Montgomery, Palmer, and Mayer (1991). Frontal apraxic patients in fact commit specific errors, such as step omissions, anticipations, argument errors, and perseverations affecting the correct planning of an action sequence. These errors are due to the weakened top-down influence from the SAS to the other component of the system.

Figure 1.6. The Norman and Shallice's model of action control (1986)



Complementary to the SAS is the CS system, that, in contrast, is involved in the control of routine activities and comes into play after a familiar sequence of actions is selected by the SAS. According to the authors, CS is composed of three main networks: the schema network, the resource network and the object network (see Figure 1.7.). The role of CS is to select the appropriate subgoals of well-learned sequences: for example, when preparing Italian coffee, pouring water in the base of the moka should be done before adding coffee in the filter. The specific subcomponents of routine tasks are labeled with the term *action schemas*. Action schemas can exist for low-level actions (e.g. to grasp, to pick up, to put down) or higher level goals (e.g. spreading marmalade). Action schemas are closely dependent on object affordances and have specific action goals. The activation of a schema unit is influenced by five factors: top-down influence, environmental influence, self influence and random noise.

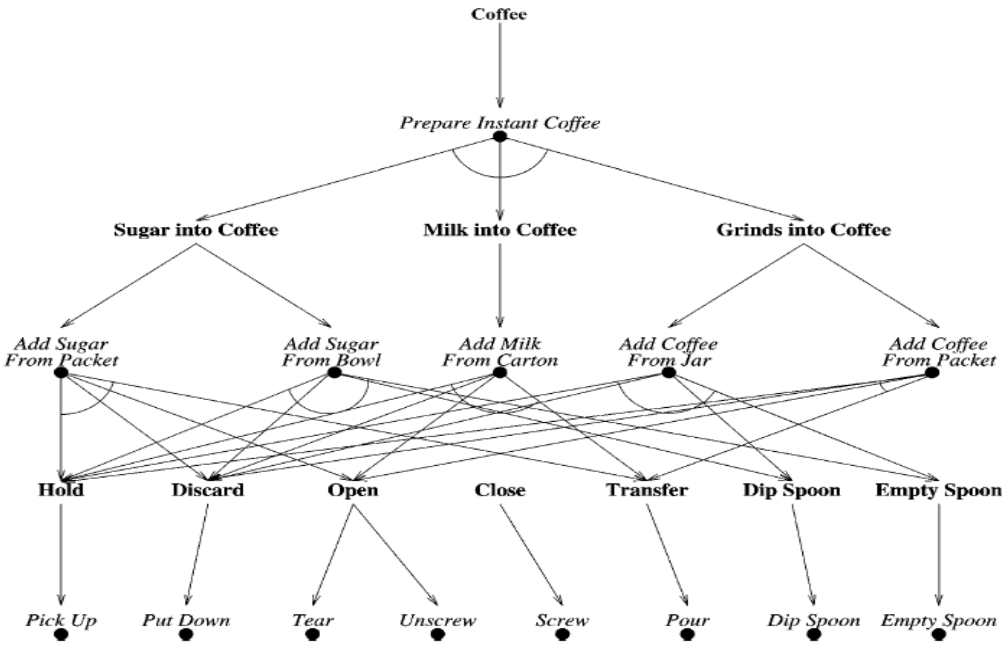
Figure 1.7. The principal components of the contention scheduling implementation by Cooper and Shallice (2000).



Within the schema network, activations interact through a variety of excitatory and inhibitory mechanisms. A selection process coordinates the schema network, interfacing with the object representation, resource, and motor systems. The selection of a given schema occurs when the activation of its unit exceeds a threshold (Figure 1.8.). Selection of a high-level schema modifies the flow of activation in the schema network such that component schemas of the selected schema receive additional excitation (thus increasing their likelihood of selection). Low level schemas correspond to discrete actions (such as pick-up, put-down). Selection at this level leads first to the assignment of object representations and resources to the corresponding action and then to the execution of that action. Furthermore, distinct from other studies which propose that routine tasks are sequentially organized (Botvinick and Plaut, 2004), Cooper and Shallice (2000)'s model considers the architecture of the task hierarchical: higher levels represent progressively larger scale aspects of the tasks (see Figure 1.8)

In the next paragraph I will discuss how, distinct from frontal apraxia, which can be interpreted as a deficit of the SAS, Ideational Apraxia (IA) could be caused by a malfunctioning of CS (Rumiati et al., 2001).

Figure 1.8. Schema/goal organisation in the coffee preparation domain. Schemas are indicated by italic type and goals by bold type (taken from Cooper and Shallice, 2000).



1.6.2. The simulation of apraxic errors

According to Rumiati et al. (2001), Ideational apraxia (IA) can be the result of a deficit in the contention scheduling system, bringing evidence against theories that explain IA as a general deficit of action sequencing (Lehmkuhl and Poeck, 1981; Poeck and Lehmkuhl, 1980). The authors were able to show that there are qualitative differences among the errors of a frontal patient with disexecutive syndrome (WH2) and the two apraxic patients mentioned above, FG and DR. In particular, the frontal patient was not able to sequence pictures depicting everyday multi-step actions, whereas FG and DR performed the task normally (see also Zanini, Rumiati and Shallice, 2002). On the other hand, FG and DR failed in a Multiple-Object-Task (MOT) in which they were required to perform sequences of actions, (such as preparing coffee or preparing a letter to post) whereas WH2 performed well in the MOT.

More recently, Cooper (2007) reproduced the pattern of error for the two IA patients described by Rumiati and colleagues (2001), by lesioning the connections among units inside the CS system. The author considered the qualitative differences between the errors of FG and DR, and concluded that both patients have a general action selection deficit that may be modelled by the addition of noise to the schema and object representation networks. DR's deficit is best accounted for by assuming, in addition, the complete lesion of the object representation to schema links, but keeping intact schema to object representation links. Whereas FG's errors are best accounted for by assuming, in addition, a partial lesion of the schema to object representation links with intact object representation to schema links. The simulations thus support the view that DR and FG have related but distinct deficits, and may account for the different error profiles that one could find in IA patients. In chapter IV we will explore the Cooper and Shallice's (2000) model in a multiple single case study.

IPM and SAS/CS: a unifying perspective

Both Rothi (1991)'s model and the SAS/CS model of Cooper of Shallice (2000) have so far successfully accounted for dissociations found in patients. While the first one takes in account all aspects of praxis production and understanding, the second is focused on routine activities that involve objects and tools, and their control from higher cognitive functions. However, the two models are not mutually exclusive: rather, the SAS/CS model integrates and expands the IPM considering higher cognitive functions such as attention and planning. Indeed, the two models have several similarities:

a) both models consider the object recognition module/object representation network as separate from the actual "semantics";

b) the notion of *praxeme* can be considered almost analogous to that of *action schema;*

c) both models can predict the behavior of patients based on the damage to modules or disconnections between them.

In this thesis I will try to bring evidence for the validity of both models, which will be contrasted with the strong embodied views of conceptual knowledge.

Chapter II

The Role of Motor Simulation in Action and Object Recognition: Studies on Brain Damaged Patients

Abstract. As discussed in the introduction an important issue in contemporary cognitive neuroscience concerns the role of motor production processes in perceptual and conceptual analysis. To address this issue, in this study we analysed the performance of a large group of unilateral stroke patients across a range of tasks using the same set of common manipulable objects. All patients[3] (n = 37) were tested for their ability to demonstrate the use of objects, recognize objects, recognize corresponding object associated pantomimes, and imitate those same pantomimes. Results will show that damage to the motor processes does not significantly affect the ability to recognize actions and objects, and vice versa.

[3]Behavioral data of the 37 patients are published in Negri et al. (2007b).

INTRODUCTION

In this study I will examine the role of those motor processes that subserve object use in recognizing visually presented object-associated actions, and in recognizing visually presented objects. I will focus on this particular topic for the following reason. Studying action recognition and object recognition offers a stringent test of the hypothesis that motor production processes play a critical role in perceptual and conceptual analysis. Cognitive neuropsychological analyses of apraxic patients provide a direct means for testing the degree to which motor systems are involved in the recognition of actions and objects. Thus, if motor production systems are necessary in order to recognize actions and/or manipulable objects, then patients with Ideational Apraxia (defined as impairments in using objects that cannot be attributed to aphasia, sensory impairment, or an impairment to basic motor responses; Pick, 1905; Liepmann 1920; De Renzi and Lucchelli, 1988) will necessarily be impaired for recognizing actions associated with the use of those objects, and/or recognizing the objects themselves.

Neurophysiological and Imaging studies (see Chapter I for a review) indeed indicate that the observation of actions and manipulable objects results in activation of neural structures in the observer that mediate overt action. We will refer to such automatic activation of motor production processes in the course of observing actions and manipulable objects as '*motor simulation*.' A number of authors have argued, on the basis of such activation evidence, that motor simulation, as defined herein, is constitutively involved in perceptual and conceptual processing of actions and/or manipulable objects (e.g., Buxbaum, Kyle, and Menon, 2005; Gallese and Lakoff, 2005; Gallese, 2005; Helbig, Graf, and Kiefer, 2006; Martin, Ungerleider, and Haxby, 2000; Pulvermüller, 2005; for an earlier proposal of this idea, see Allport, 1985). We refer to the hypotheses that the motor system is necessarily involved in action and object recognition as the Motor Theory of Action Recognition and the Motor Theory of Object Recognition, respectively. Two versions of the Motor Theories of Action and Object Representation can be distinguished (for discussion, see Mahon and Caramazza, 2005). In one version, there is an overlap in the processes subserving action production and action (and object) recognition. On a second version, while the processes subserving action production are functionally separable from those subserving the recognition of actions and objects, the activation of such motor processes is necessary in order for successful recognition to proceed. Critically, in both formulations of the Motor Theories of Action/Object Recognition, activation of motor information is necessary in order to successfully recognize and understand actions and objects.

Neuropsychological investigations of apraxic patients suggest that the ability to use objects is not necessary in order to either recognize those objects or to recognize actions associated with their use. For example, authors have reported patients demonstrating impairments for using objects but relatively spared ability to recognize object associated gestures (see Chapter I for a discussion). On the basis of such dissociations, it has been proposed that there are separate input and output 'praxicons' (e.g., Heilman and Rothi, 2003, see Figure 1.3.). In this study, we will refer to such input and output representations, as input and output '*praxemes*'. The term '*praxeme'* is intended to evoke an analogy that has been drawn between models of apraxia and models of language processing, without reference to the analogous term used in linguistics. By analogy to models of language processing, input praxemes refer to representations that are tied to perceptual analysis of actions, while output praxemes are those representations that are tied to processes subserving innervation of effectors. We can refer to the model that assumes separate input and output praxemes as the *Independent Praxemes Model* (IPM). The prediction of the IPM (see Cubelli et al., 2000; Rothi et al., 1991) is that an impairment for using objects will not necessarily be associated with an impairment for recognizing the corresponding object-associated movements.

Recently however, a strong form the Motor Theory of Action Recognition has been advocated on the basis of neuropsychological data. Buxbaum and colleagues (2005) analyzed patterns of association of impairments across a group of patients on action imitation and action recognition tasks. A significant correlation was observed between the performance of patients in recognizing pantomimes and their performance in imitating pantomimes. On the basis of the correlation observed between pantomime recognition and pantomime imitation, Buxbaum and colleagues argued that the same representations are used for both the production and perception of object directed (i.e., transitive) hand actions. Those authors proposed that such shared representations are located, neuroanatomically, in the left inferior parietal lobule. However, studies with similar tasks and sbjects failed to find significant correlations between pantomime imitation and recognition (Tessari, Canessa, Ukmar, and Rumiati, 2007)

In general, studies based on analyses of a large number of patients who are tested on the same materials and evaluated with the same methods and error criteria have an advantage of providing a relatively broad view of the relation between cognitive processes. At the same time however, focusing only on correlations in performance across tasks at the group level, we run the risk of overlooking single cases that present dissociations that are not in line with group level trends. Moreover, part of the contrasting results reported in literature may be due to the type of analysis done on the patients' scores. For example, the use of chi-square can be misleading, as this measure is highly prone to type I and type II errors. The use of chi-square might be problematic also if controls show advantage for one of the two analysed tasks. In this case, even the lack of absolute difference in the score of the patients can be important (Laws and Sartori, 2005, Crawford and Garthwaite, 2005).

For the above mentioned reasons, the present study adopts both approaches. First, we study a large group of unselected patients in order to document group level correlations in performance across praxis tasks. We then provide analyses of the behavioral profiles at the single case level using a reliable test to detect dissociations (Crawford and Garthwaite,

2005) to study potential exceptions to the group level pattern. This methods assesses whether the discrepancy observed in the patient is significantly different from that present in controls. Previous studies that have analyzed praxis performance of multiple patients within the same study, and across the same materials, have focused either only on group level trends (Buxbaum et al., 2005), single case analyses (Cubelli et al., 2000), or have not observed both the group level trends and the dissociations at the single case level (Rosci et al., 2003; Tessari et al., 2007).

The substantive issues at stake in the present study are as follows. First, are output praxemes functionally separable from: input praxemes and the processes subserving visual object recognition? Second, in the measure to which output praxemes are functionally separable from input praxemes and from processes subserving visual object recognition, is motor simulation (i.e., the activation of output praxemes) necessary in order for successful recognition of actions and manipulable objects to occur?

METHODS

Participants

Patients. Thirty-seven consecutively admitted patients (mean age 63.9 $\pm$ 10.4 years; education 9.3 $\pm$ 3.9 years) took part in the study. Patients were recruited from the rehabilitation ward of the Ospedali Riuniti in Trieste. Only patients with focal unilateral brain lesions and no previous neurological history were included. CT- or MRI-scans were available for 35 patients. The lesions for those 35 patients were mapped using MRIcro software (www.mricro.com) onto a standard MRIcro template by a neuroradiologist (M.U.) who was unaware of the aims of the study. The Brodmann areas (see Appendix 2.1.) involved in the lesions have been identified using MRIcro software[4].

Controls. Twenty-five neurologically healthy individuals matched for age and education (mean age 66 $\pm$ 11; education 8.96 $\pm$ 4.1) with the patient group were recruited from

[4] see Chapter III for a detailed description of this procedure

patients' and staff's relatives, as well as from the rehabilitation ward of the Ospedali Riuniti in Trieste, where they were treated following orthopedic surgery. They were administered the Edinburgh Handedness questionnaire (Oldfield, 1971) and took part in the experimental session only if they were right-handed. They performed the object-related tasks described below with their dominant hand. A second group of control subjects recruited on the basis of the same criteria (N = 11; right-handed, age 69.9 ± 6.85; education 10.4 ± 4.2) were tested on the action imitation task described below using their non-dominant (i.e., left) hand. This was in order to have a suitable baseline with which to compare the performance of patients, who due to hemiparesis, were not able to complete the tasks with their dominant hand. There were no differences (all t's < 1, independent samples) between the controls groups, or the control groups and the patient groups, for either age or education.

The Revised Standardized Difference Test (RSDT) was computed to detect classical and strong dissociations, as suggested by Crawford and Garthwaite (2006), using the software released with the article by Crawford and Garthwaite (2005). Classical dissociations, in which a patient was impaired compared to controls on task A, but within the normal range on task B, were determined based on the significance values of the t scores, taking into account the correlation within controls across the two tasks. Strong dissociations, in which a patient was impaired on both tasks A and B compared to controls, but relatively more impaired on task A were also determined with the RSDT method. Because a number of patients with apraxic deficits were not able to perform praxis tests with their dominant hand, we computed separate t scores for pantomime imitation based on the performance of the group of 11 controls who performed those tasks with their non-dominant left hand. The pattern of findings for the pantomime imitation task remained the same regardless of which control group was used as the baseline (see Table 2.1. for all data).

Neuropsychological assessment

All 37 patients were administered a neuropsychological assessment evaluating language, praxis, visuo-spatial abilities, executive functions and memory. They were tested in a quiet room in the hospital or at home. The neuropsychological results for all 37 patients are summarized in Appendix 2.1.

Experimental study

In all experimental tasks, no feedback was provided to participants (patients or controls) about their performance, either verbally or in any other way. The order of tasks was counterbalanced across participants, whereas the order of presentation of the items was fixed for the imitation tasks and randomized for the object use task. All patients and the group of twenty-five controls completed the following tasks, over the same set of 29 objects of common use (the complete set of stimuli is listed in Appendix 2.2.).

• *Object recognition.* Patients and controls (n = 25) were asked to name the 29 objects, presented as colored photographs. For each item, a participant's response was scored '0' if they were not able to name the object and '1' if they named the object correctly. Dialectal names were considered acceptable (i.e., scored as '1'). The maximum possible score was 29/29. Because the objective of the object naming task was to determine whether the patients were able to recognize the object at a basic level, patients were allowed to self-correct after making phonological errors or dysfluencies. If the patient produced the correct name after having made a phonological error, the response was scored as correct. However, semantic paraphasias, even at the first attempt, were scored as errors. In place of the naming task, patients with severe language impairments were administered a multiple choice task in which three color photographs were presented simultaneously, and the experimenter said aloud the name of the target photograph. Distractors were semantically related to the target (e.g., target: pen; distractors: eraser, scissors). The list of distractors for the multiple choice test for object recognition and pantomime recognition (see below) is reported in Appendix 2.3.

- *Pantomime recognition*. Patients and controls (n = 25) were asked to name 29 pantomimes of object use (with the object absent), performed by the experimenter. Responses were scored as correct (1 point) either if the patient named the action (e.g. "hammering", "you are driving a nail") or the object involved in the action (e.g. "you are using a hammer"). Responses were scored as incorrect (0 points) if the participant did not correctly recognize the action. The maximum possible score was 29/29. Patients with severe language impairments completed a multiple choice task in which they were asked to indicate the picture (out of three) depicting the action pantomimed by the experimenter. Distractors were semantically related photographs and, when possible, depicted an action visually similar to the target (e.g., target: brushing teeth: distractors: washing hands; shaving). The materials for the multiple choice version of the pantomime recognition test are listed in Appendix 2.3.

- *Imitation of Pantomimes*. All participants were asked to imitate the pantomimes corresponding to the same 29 objects demonstrated by the experimenter. The objects were not visible during this task. Performance was videotaped and subsequently scored as follows: 2 points were given if the action was correctly imitated, 1 point if the action was imitated with errors but still recognizable, and 0 points if the action was not recognizable. The maximum possible score was 58/58. One group of controls (n = 25) performed this task with the dominant right hand, while the other group of controls (n = 11) performed this task with their non-dominant left hand.

- *Object use*. Patients and controls (n = 25) were asked to demonstrate, with the object in hand, the use of the 29 objects. The same videotaping and scoring criteria were applied as were used in the Imitation of Pantomimes Task (2 points were given if the object was used correctly, 1 point if the action was performed with errors but still recognizable, and 0 points if the action was not recognizable). The maximum possible score was 58/58.

- *Imitation of Intransitive actions.* All participants were asked to perform a separate imitation task, similar to that devised by De Renzi et al. (1980). This task involves the imitation of 20 intransitive actions (i.e., in which objects are not involved), including 10 meaningless (e.g. raising thumb and little finger) and 10 meaningful gestures (e.g. moving the index finger back and forward to signal for someone to come closer). Performance was videotaped and then scored as described above: 2 points were given if the action was correctly imitated, 1 point if the action was imitated with errors but still recognizable, and 0 points if the action was impossible to recognize. The maximum possible score was 40/40. One group of controls (n = 25) performed this task with the dominant right hand, while the other group of controls (n = 11) performed this task with their non-dominant left hand.

Table 2.1. Summary of performance[5] of all patients across all experimental tasks. Patients are sorted alphabetically by their initials. ctrls= controls, M=controls' mean; SD=controls' standard deviation

	Object recognition		Pantomime Recognition		Object Use		Pantomime Imitation			Imitation of Intransitive actions		
Patient	**% correct**	**t score**	**% correct**	**t score**	**% correct**	**t score**	**% correct**	**t score (25 controls)**	**t score (11 controls)**	**% correct**	**t score (25 controls)**	**t score (11 controls)**
AN	100	0.49	100	1.04	100	0.83	80	0.23	0.58	90	0.77	0.33
BA	97	-1.97	100	1.04	89.5	-1.35	82.5	0.4	0.76	65	-1.2	-3.72
BE	90	-7.71	100	1.04	78.5	-3.65	72.5	-0.28	0.04	50	-2.39	-6.16
BL	100	0.49	83	-2.36	80.5	-3.22	10	-4.52	-4.46	35	-3.57	-8.59
BO	100	0.49	86	-1.76	100	0.83	87.5	0.77	1.12	88.6	0.68	0.13
BR	93	-5.24	93	-0.36	81	-3.13	70	-0.45	-0.14	65	-1.2	-3.72
CA	100	0.49	100	1.04	100	0.83	87	0.74	1.08	85	0.38	-0.48
CE	90	-7.71	97	0.44	93.5	-0.52	50	-1.89	-1.58	40	-3.18	-7.78
CI	100	0.49	90	-0.96	87	-1.88	60	-1.13	-0.86	77.5	-0.21	-1.67
CS	97	-1.97	97	0.44	86	-2.08	62.5	-1	-0.68	55	-1.99	-5.35
DM	93	-5.24	100	1.04	93	-0.62	77.5	0.06	0.4	70	-0.81	-2.91
DP	100	0.49	100	1.04	100	0.83	90	0.91	1.3	72.5	-0.61	-2.51
DR	96	-2.79	93	-0.36	80	-3.33	40	-2.48	-2.29	55	-1.99	-5.35
DU	100	0.49	96	0.24	96.5	0.1	87.5	0.77	1.12	67.5	-1	-3.32
FG	100	0.49	100	1.04	93	-0.62	70	-0.45	-0.14	72.5	-0.61	-2.51
FL	100	0.49	96	0.24	88	-1.67	60.5	-1.09	-0.82	63.3	-1.34	-4.01
FS	100	0.49	86	-1.76	50	-9.58	17.5	-4.01	-3.92	42.5	-2.98	-7.38
FU	100	0.49	100	1.04	100	0.83	100	1.59	2.02	100	1.56	1.96
GO	93	-5.25	86	-1.76	86.5	-1.88	67.5	-0.65	-0.32	72.5	-0.61	-2.51
MA	100	0.49	100	1.04	98.5	0.52	90	0.91	1.3	100	1.56	1.96
ME	100	0.49	100	1.04	95.5	-0.1	85	0.57	0.94	90	0.77	0.33
MZ	100	0.49	90	-0.96	90	-1.25	52.5	-1.64	-1.4	75	-0.41	-2.1
PE	100	0.49	93	-0.36	89.5	-1.35	70	-0.47	-0.14	80	-0.02	-1.29
PI	83	-13.44	79	-3.16	98.5	0.52	92.5	1.08	1.48	87.5	0.58	-0.07
PN	97	-1.97	100	1.04	94	-0.41	50	-1.89	-1.58	52.5	-2.19	-5.75
PO	100	0.49	100	1.04	98.5	0.52	87.5	0.77	1.12	95	1.17	1.14
PT	97	-1.97	93	-0.36	91	-1.04	27.5	-3.33	-3.2	35.6	-3.51	-8.47
RO	100	0.49	69	-5.16	58.5	-7.81	10	-4.52	-4.46	42.5	-2.98	-7.38
SC	90	-7.71	97	0.44	65	-6.46	50	-1.89	-1.58	45	-2.78	-6.97
SO	100	0.49	93	-0.36	100	0.83	70	-0.45	-0.14	95	1.17	1.14
SR	97	-1.97	72	-4.56	81.5	-3.02	52.5	-1.64	-1.4	65	-1.2	-3.72
ST	90	-7.71	72	-4.56	47.5	-10.1	27.5	-3.33	-3.2	45	-2.78	-6.97
SV	93	-5.25	90	-0.96	48	-10	30	-3.16	-3.02	40	-3.18	-7.78
TO	97	-1.97	100	1.04	98.5	0.52	85	0.6	0.94	82.5	0.18	-0.88
TS	100	0.49	100	1.04	100	0.83	82.5	0.42	0.76	85	0.38	-0.48
ZA	86	-10.98	86	-1.76	63	-6.88	42.5	-2.32	-2.12	42.5	-2.98	-7.38
ZE	100	0.49	100	1.04	96	0	85	0.6	0.72	70	-0.81	-2.91
ctrls	M=99,4 SD=1,22		M=94,76 SD=5,01		M=96,04 SD=4,1		M=76,6 SD=14,1			M=80,2 SD=12,4		

[5] We have chosen the RSDT method because it is reliably less prone to type I and type II errors respect to a nonparametric test. Moreover, since controls show effect of difficulty in the imitation tasks, we chose a test that takes in account such discrepancy in the normal population.

RESULTS

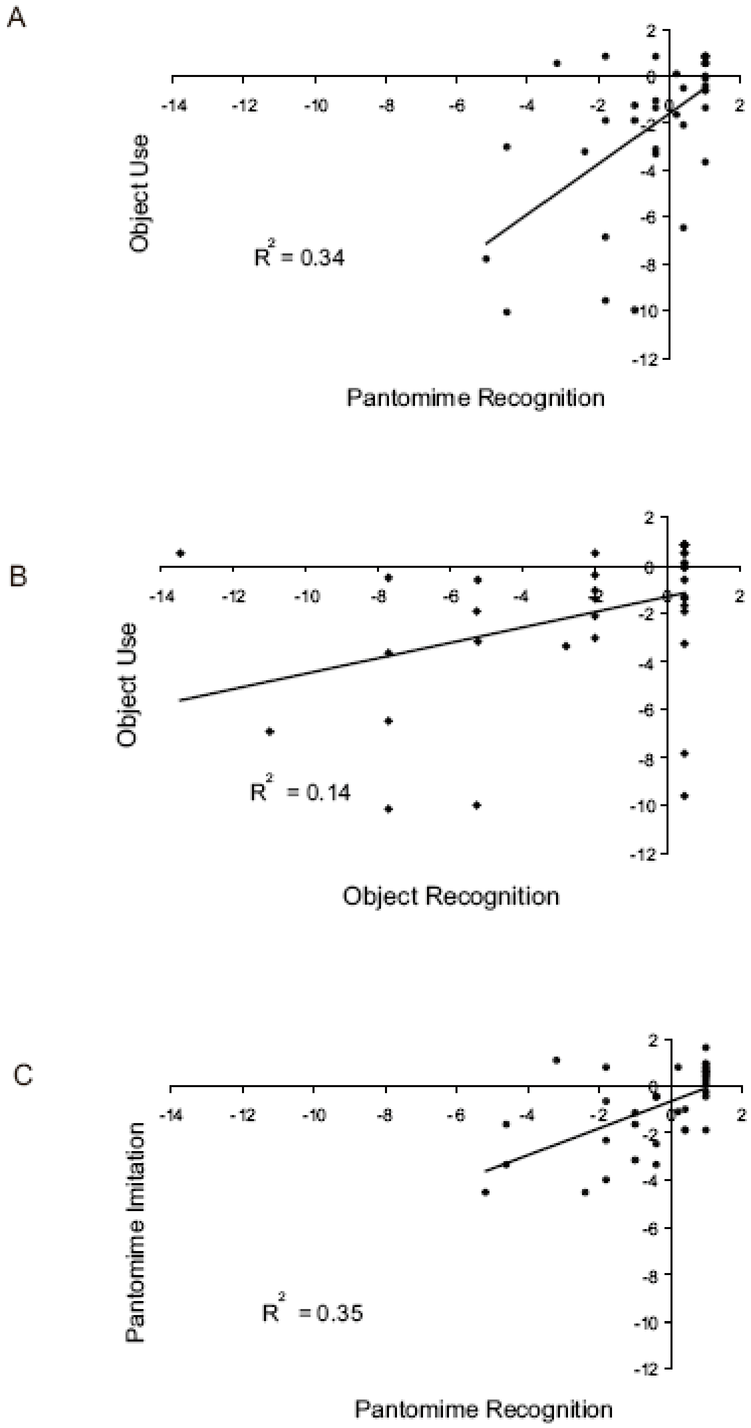
The performance of all patients on the praxis and recognition tasks using the same set of 29 objects is summarized in Table 2.1. Results of the neuropsychological assessment are reported in Appendix 2.1.

Correlational analyses

As noted in the introduction, recent research (e.g., Buxbaum et al., 2005) has based inferences regarding the role of motor processes in action recognition on group level correlations observed in large numbers of patients. The logic of the present study is to consider whether in our group of unselected unilateral stroke patients, it is possible to reproduce the correlations that have previously been observed between the different praxis related tasks that were administered. To that end, we computed Pearson's correlations between the four praxis tasks that were performed with the same set of 29 objects. These correlations were carried out over both t-scores and raw data, and were essentially the same with both data sets.

There were significant and positive correlations between Object Use and Pantomime Recognition ($r = .58$, $p < .001$; see Figure 2.1.a), Object Use and Object Recognition ($r = .37$, $p < .05$; see Figure 2.1.b), and Object Use and Pantomime Imitation ($r = ..78$, $p < .001$). There was a significant and positive correlation between Pantomime Recognition and Pantomime Imitation ($r = .59$, $p < .001$; see Figure 2.1.c) but no significant correlation between Pantomime Recognition and Object Recognition ($r = .27$, $p > .05$). There was also no significant correlation between Object Recognition and Pantomime Imitation ($r = .154$, $p > .05$).

Figure 2.1. Group level correlations in performance across tasks. **A.** The ability of patients to use a set of 29 objects was correlated (p < .001; Spearman's Rho) with their ability to recognize the same object associated actions when performed by the experimenter. **B.** The ability of the patients to use the same set of objects was correlated (p < .003) with their ability to recognize those objects. **C.** The ability of the patients to imitate the same set of object associated actions was correlated (p < .001) with their ability to imitate the same actions.



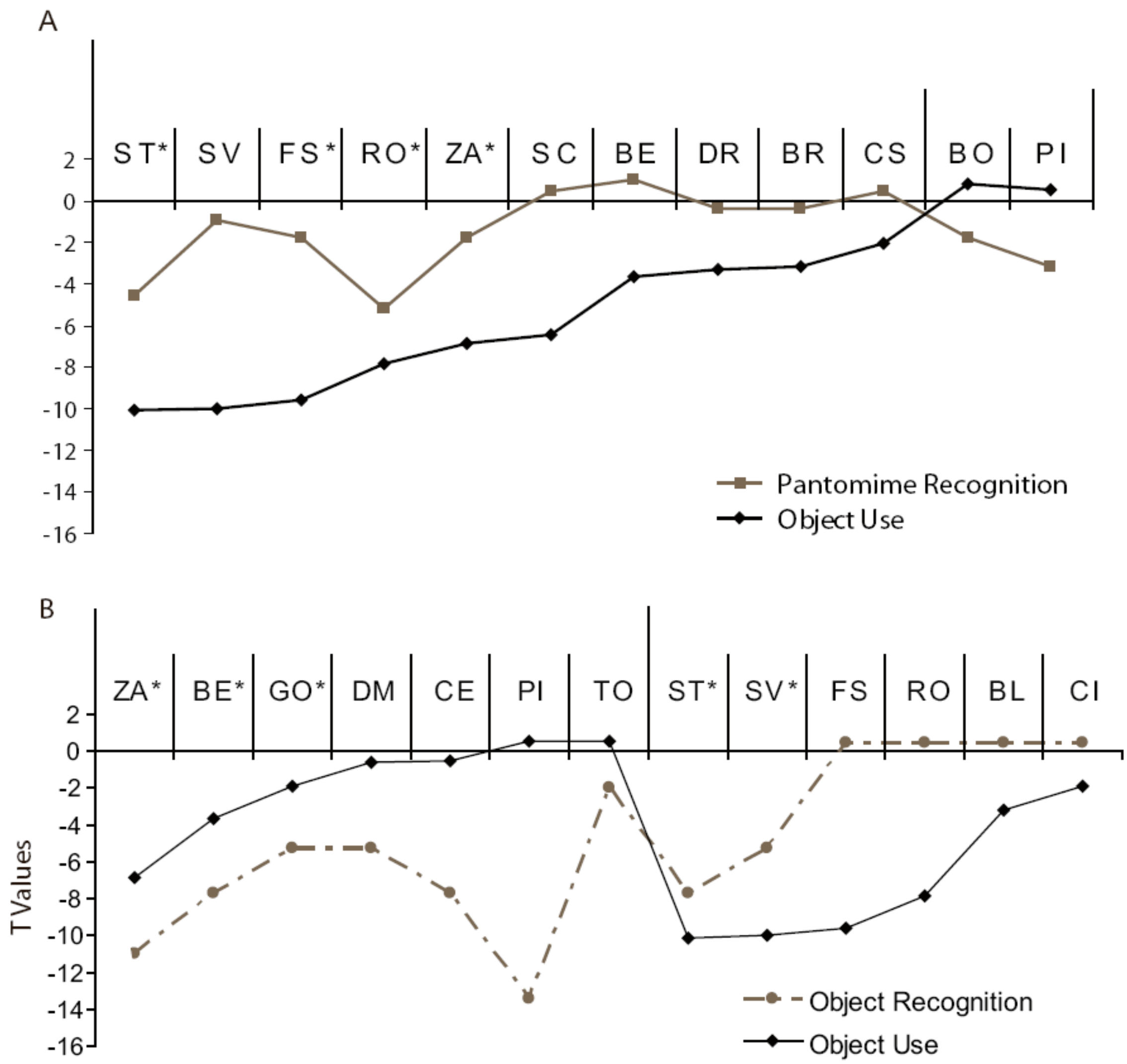
As described in Chapter I, the presence of correlations across tasks within a group of patients has served as the empirical basis for the inference that representations/processes involved in action production are required in order to recognize actions and objects. For instance, such inferences have been argued to follow from the observations (reported above) that performance in using objects is correlated with performance in recognizing objects, recognizing pantomimes, and imitating pantomimes. In the same vein, the correlation between pantomime recognition and pantomime imitation (reported above) reproduces the pattern observed by Buxbaum et al. (2005).

The mere presence of statistically significant correlations between performance across the group of patients on the different tasks does not, in itself, indicate that there is a relation between the abilities required to perform the tasks. However, the logic of demonstrating that such correlations can be obtained within the present group of patients is to show that this group of patients is comparable to those previously discussed (e.g., Buxbaum et al., 2005). In the next section we show, that even though there are demonstrated correlations, at the single case level the 'abilities' that are correlated between tasks in fact clearly dissociate. In this sense, the multiple single case approach described below cannot be criticized as being drawn from an 'atypical' group of patients.

Single case dissociations

As discussed in the Introduction, a number of previous case studies have reported that impaired production of object associated actions can be observed despite unimpaired 1) pantomime recognition, and/or 2) object recognition. There have also been cases reported who are impaired at pantomime imitation, but spared at pantomime recognition. Here we describe patients from this group who demonstrated these three dissociations. Table 2.2. provides a summary of those cases that are discussed in this dissociations analysis.

Figure 2.2. Double dissociations between object use and pantomime recognition (A) and object use and object recognition (B) (* indicates strong (i.e., disproportionate) dissociations).



• *Impaired object use compared to pantomime recognition.* As depicted in Figure 2.2a (see also Table 2.2.), six patients (SV, SC, BE, BR, DR and CS) were impaired at using objects but within the normal range for recognizing object-associated pantomimes. This pattern was observed both in patients who were administered the naming version of the pantomime recognition test (BE, CS) as well as in those who performed the multiple choice version of the pantomime recognition task (SC, SV, DR, BR). Of these six patients, five of them were impaired at recognizing objects (SV, BE, SC, BR and DR) while CS was in the normal range for object recognition. Two of the six patients were impaired for pantomime imitation (SV and DR) while the others were in the normal range. The imitation of intransitive actions was impaired in SV, SC and BE, but within normal limits for BR, DR and CS.

Another four patients (FS, RO, ST and ZA) presented with disproportionate deficits (i.e., strong dissociations) for using objects compared to recognizing pantomimes (see Appendix 2.4a and Table 2.2.). For these four patients, performance on both object use as well as recognizing pantomimes was outside of the control range. All four of these patients were impaired at imitating pantomimes as well as imitating intransitive actions. Patients FS and RO performed normally on the object recognition task, whereas ST and ZA were impaired in recognizing objects.

• *Impaired pantomime recognition compared to object use*. Two patients (BO and PI) were able to use objects despite being impaired at recognizing the associated pantomimes. Both patients BO and PI were unimpaired for imitating pantomimes. PI's deficit for pantomime recognition was associated with a deficit in recognizing objects (both recognition tasks performed with the multiple choice versions of the tasks).[6] Interestingly, BO was in the normal range for object recognition. The observation of a selective impairment for recognizing pantomimes, termed *pantomime agnosia* (Rothi, Mack, and Heilman, 1986), suggests functionally dissociable processes for action and object recognition.

• *Impaired Object Use compared to Object Recognition*. As depicted in Figure 2.2b, four patients BL, RO, CI and FS were impaired in using objects but were within the normal range for recognizing objects. Patients BL, RO, and FS were impaired for pantomime recognition, pantomime imitation, and imitation of intransitive actions, whereas CI was in the normal range for these tasks.

[6] It is unlikely that PI's impairment for recognizing the pantomimes can be explained by a general visual impairment, because the patient was within the normal range on the VOSP and object decision screening tests, ruling out at least some types of a general visual impairment (see Appendices 3.1 and 3.3).

Two patients (ST and SV) presented with disproportionate impairments (i.e., strong dissociations) in using objects compared to Object Recognition. Both patients were also impaired for imitating pantomimes and intransitive actions. ST was impaired for recognizing pantomimes while SV was in the normal range.

• *Impaired object recognition compared to object use.* In contrast, four patients CE, TO, DM and PI were impaired for object recognition but were within the normal range for using the same objects. Patient CE, TO and DM were unimpaired for recognizing pantomimes, whereas PI was impaired in this task (using the multiple choice version). These four patients performed within the normal range for imitating pantomimes, while only patient CE was impaired for imitating intransitive actions.

Three patients (ZA, BE, GO) presented with disproportionate deficits (i.e., strong dissociations) for Object Recognition compared to Object Use. Patient BE was within the normal range for pantomime recognition while GO and ZA were impaired on this task. Patients BE and GO were within the normal range for imitating pantomimes, while ZA was impaired on this task. Patients ZA and BE were impaired for imitating intransitive actions, while patient GO was in the normal range.

• *Impaired pantomime imitation compared to pantomime recognition.* As discussed above (see Figure 2.1; see also Buxbaum et al., 2005) we observed a significant correlation between the ability of patients to imitate pantomimes and their ability to recognize object associated pantomimes. However, contrary to this group level pattern, patient PT was impaired at imitating both object associated actions and intransitive actions. Within the category of 'intransitive' gestures, PT was equivalently impaired for meaningful and meaningless gestures (36.5% and 35 % correct, respectively). However, PT was able to recognize object associated pantomimes and was within the normal range in using and naming objects.

The pattern of performance of patient PT represents an important exception to the group level pattern. The performance of PT indicates that even if input praxemes are 'disconnected' from output praxemes, it is still possible to successfully recognize pantomimes. Other studies have reported patients who are impaired at imitating meaningless gestures but still able to recognize gestures (LK and EN; Goldenberg and Hagmann, 1997; cases 12 and 23 in Tessari et al., 2007; BS, Bartolo et al., 2001; FG, Rumiati et al., 2001).

• *Analysis of lesions*. Since the lesions results were not straightforward, we cannot draw strong conclusions about the anatomical bases of the different abilities. A higher number of dissociating cases would have allowed to make statistical analyses, in order to compare between the dissociating groups and to identify the lesions most probably associated with a given deficit (e.g. using a Chi-square analysis with MRIcro). However, the dissociations at the behavioural level are important to stress out the fact that two processes can be independently damaged by brain lesions, and the main goal of the study, was to address the predictions of embodied theories using a dissociation logic rather than a localization one. For the interested reader we have included the brain lesions of the dissociating patients in Appendix 2.4.

Table 2.2. The table presents a simplified profile of those patients discussed in the text. "√" indicates performance within the normal range; "X" indicates impaired performance compared to control subjects (n = 25). The subscript "MC" indicates that the multiple choice version of the task was completed by the patient. "*" indicates patients with disproportionate impairments (i.e. strong dissociations).

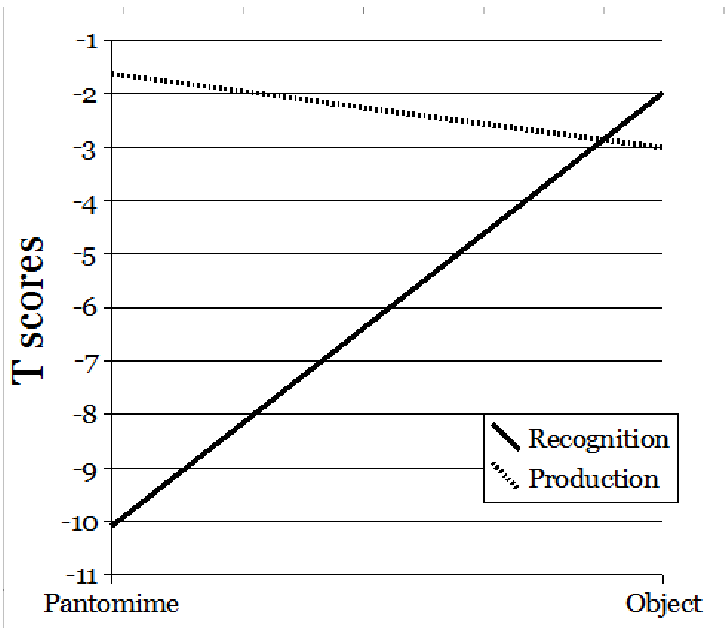
Patient Initials	**Object Recognition**	**Pantomime Recognition**	**Object Use**	**Pantomime Imitation**	**Imitation of Intransitive Actions**
Impaired Object Use compared to Pantomime Recognition					
SV	X $_{MC}$	√ $_{MC}$	X	X	X
SC	X $_{MC}$	√ $_{MC}$	X	√	X
BE	X	√	X	√	X
BR	X $_{MC}$	√ $_{MC}$	X	√	√
DR	X $_{MC}$	√ $_{MC}$	X	X	X
CS	√	√	X	√	X
FS*	√	X	X	X	X
RO*	√ $_{MC}$	X $_{MC}$	X	X	X
ST*	X $_{MC}$	X $_{MC}$	X	X	X
ZA*	X $_{MC}$	X $_{MC}$	X	X	X
Impaired Pantomime Recognition compared to Object Use					
BO	√	X	√	√	√
PI	X $_{MC}$	X $_{MC}$	√	√	√
Impaired Object Use Compared to Object Recognition					
BL	√ $_{MC}$	X $_{MC}$	X	X	X
RO	√ $_{MC}$	X $_{MC}$	X	X	X
CI	√	√	X	√	√
FS	√	X	X	X	X
ST*	X $_{MC}$	X $_{MC}$	X	X	X
SV*	X $_{MC}$	√ $_{MC}$	X	X	X
Impaired Object Recognition Compared to Object Use					
CE	X	√	√	√	X
TO	X	√	√	√	√
DM	X	√	√	√	√
PI	X $_{MC}$	X $_{MC}$	√	√	√
ZA*	X $_{MC}$	X $_{MC}$	X	X	X
BE*	X	√	X	√	X
GO*	X	X	X	√	√
Selectively Impaired Pantomime and Action Imitation					
PT	√	√	√	X	X

Paradoxical dissociations: the case of Patient SR

According to Laws and Sartori (2005), double dissociations can occur not only between patients, but also *within* patients. Such double dissociations across tasks, within a single patient, are called *paradoxical*. According to the authors, the existence of paradoxical dissociations is theoretically problematic when two tasks are believed to share common processes.

We searched for paradoxical dissociations in our patients sample, considering two factors: task (recognition vs. production) and type of stimulus (objects vs. pantomimes). Only one patient showed a paradoxical dissociation: patient SR (see Figure 2.3.), who was impaired in recognition of pantomimes (t=-4.56) despite being normal at imitating them (t=-1.64), and was normal in recognizing objects (t=-1.97) but impaired at using them (t=-3.02). The RSDT test for dissociations was significant across tasks ($p < .05$).

Figure 2.3. Paradoxical dissociation in patient SR.



Discussion. Laws and Sartori (2005) tested Alzheimer and HSE[7] patients in naming and feature verification tasks, using two types of stimuli: living and nonliving items. In both patients samples they found cases of classical double dissociations across tasks (i.e.

[7] Herpes Simplex Encephalitis

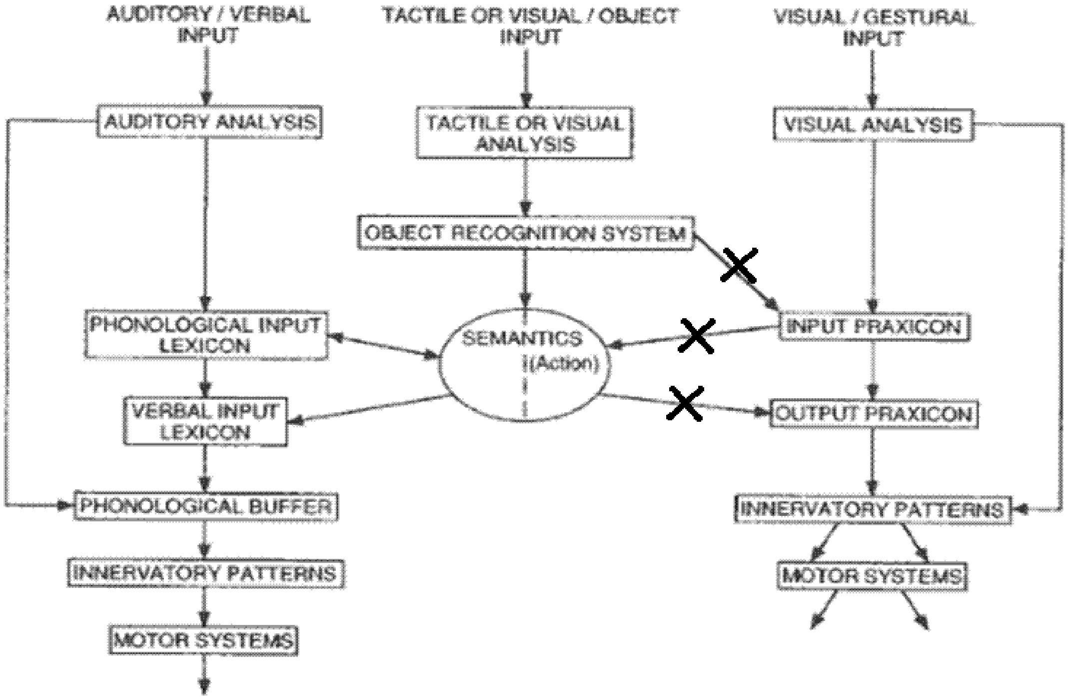
paradoxical). Such a finding is problematic in the framework of category specificity, because it raises theoretical issues about the most suitable task to individuate the semantic deficit. Indeed, a semantic impairment specific for a category of stimuli should affect all tasks tapping that category. One possible explanation that the authors propose for the phenomenon of paradoxical dissociations is that they might originate from confounds -such as fluctuation of attention- or they are chance findings emerging from noisy patient data. However, the use of RSDT test should provide excellent control over type I error rate, whereas nonparametric statistics like Chi-square give rise to several false negatives and false positives.

Also in the case of the paradoxical dissociation found in SR, one could hypothesize that the two visual tasks (recognition of objects and pantomimes) depend on a common mechanism, as well as the two praxic tasks (imitation and object use). Instead, it might be the case that this result confirms the idea of fractionation within the system controlling object-directed actions. Indeed, the double dissociation across tasks showed by patient SR is compatible with the model by Rothi et al. (1991) presented in the Introduction (see Figure 2.4.)[8]. In the case of patient SR, we can hypothesize that the input and output praxicons are disconnected from the semantic route. Such a damage prevents the access to action meaning when a pantomime is presented (pantomime recognition impairment) and to retrieve the correct motor pattern starting from the presentation of an object (object use impairment). We can hypothesize that the direct route for imitation is preserved in SR because the patient can imitate meaningless pantomimes (t= -1.2).

The dissociation pattern of patient SR, as well as data from patients reported above, are better explained by modular models of praxis, such as the SAS/CS or the IPM. It is difficult to conciliate embodied theories with the results found.

[8] However, we agree with Laws and Sartori (2005) that the best way to control for spurious findings would have been to test the consistency of deficit over time, but this was not possible due to time constraints (our battery lasted about three hours including the neuropsychological assessment).

Figure 2.4. Hypothesized disconnections in Patient SR (modified by Heilman and Rothi, 2003)



DISCUSSION

In this chapter, I have considered the performance of brain damaged patients on tasks involving the use and the recognition of objects, as well as the imitation and the recognition of the corresponding pantomimes. The results show that, at the single case level, recognition and production processes can be dissociable for objects, although these functions significantly correlate at the group level. We observed individual cases whose performance profiles are problematic for the Motor Theories of Action and Object Recognition. First, patients were observed who were impaired for object use, but relatively unimpaired for action recognition, as well as the reverse. Second, patients were observed who were impaired for object use but were relatively unimpaired for object recognition, as well as the reverse. Third, one patient was observed who was impaired for imitating pantomimes, but was relatively unimpaired for recognizing pantomimes and using objects.

There is an asymmetry, within neuropsychological evidence, between specific theoretical proposals and observations of associations versus dissociations of abilities. In the introduction we described the IPM (Independent Praxeme Model) in which input and output praxemes are functionally separable (see Rothi et al., 1991). This model can be contrasted with the Motor Theory of Action Recognition. Both the IPM and the Motor Theory of Action Recognition are consistent with the group level correlations that we and others (Buxbaum et al., 2005) have reported. On the other hand, the dissociations observed within single cases indicate that both object use and pantomime imitation can be impaired despite normal performance in pantomime and object recognition (for a similar discussion in the context of agrammatism, see Caramazza, Capasso, Capitani, and Miceli, 2005). The dissociations reported in this study indicate that: 1) the ability to use objects is not necessary in order to be able to recognize object associated pantomimes; 2) the ability to imitate pantomimes is not necessary in order to be able to recognize object associated pantomimes; and 3) the ability to use objects is not necessary in order to be able to recognize objects. This means that: a) output praxemes and input praxemes are functionally dissociable, and b) that the integrity of output praxemes is not necessary in order for the successful functioning of input praxemes and object recognition processes. This conclusion means that we must reject the strong forms of the Motor Theories of Action and Object Recognition. It is important to note that this conclusion does not mean that motor production processes may not serve as important inputs to help object and action recognition processes. Sensorimotor experience is probably indispensable in the acquisitional phase of conceptual knowledge, but once the knowledge is acquired and stored in the ventral stream, the two pathways become specialized for their specific functions (for discussion on object recognition processes, see Mahon, Milleville, Negri, Rumiati, Caramazza, and Martin, 2007).

The fact that brain structures subserving motor production are automatically activated when participants observe manipulable objects (for review, see Martin, 2007) would seem to be at variance with the claim that motor production processes are not necessary in order to recognize objects and actions. In the General Discussion (Chapter V), we will consider more closely some possible roles of motor simulation in action and object recognition.

However, results from imaging and behavioral studies showing that the motor and conceptual systems strongly interact cannot be ignored, and they are not completely in contrast with the present findings. Indeed, we believe that in a healthy brain the ventral and dorsal streams interact, however selective damage to one of the two circuits does not significantly affect the functioning of the other. The dorsal/ventral stream dychotomy will be discussed more in detail in Chapter III.

Appendix 2.1. Results of the neuropsychological evaluation for all patients.

Patient Initials	Sex	Age	Educ (years)	Months post onset	Oldfield	IMA	IA	AAT token	AAT rep	AAT write	AAT read	AAT nam	AAT oc	AAT wc	Raven's CPM	VOSP screen.	VOSP o.d.	Span fwd	Span bwd	Corsi
AN	f	48	11	2	100	70	14	0	148	90	-	120	60	60	33	18	19	6	6	5
BA	m	70	13	2	42	61	14	27	114	25	-	60	33	0	12	15	8	4	2	4
BL	m	68	3	6	100	46	14	23	130	n.a.	24	108	49	47	14	20	17	3	p.u.	3
BE	m	65	8	2	83	58	12	15	134	78	-	109	51	48	19	20	12	3	3	4
BO	m	78	13	3	100	71	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	21	19	18	8	5	5
BR	m	58	11	3	100	53	14	48	39	12	-	0	41	0	36	20	16	n.a.	n.a.	5
CA	m	58	8	2	100	68	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	21	20	16	4	3	4
CS	m	76	12	1	83	65	13	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	22	19	13	4	4	5
CE	m	61	5	2	100	51	13	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	11	10	6	6	3	3
CI	m	70	8	1	-83	63	14	4	140	85	-	108	51	54	24	20	13	4	3	3
DM	f	68	5	1	100	68	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	18	20	13	5	2	3
DP	f	73	5	1	100	62	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	20	20	15	5	3	4
DU	m	72	5	2	100	53	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	25	18	17	4	2	4
DR	m	55	15	72	100	54	8	1	94	15	-	69	60	35	34	20	19	4	n.a.	5
FL	f	61	8	1	100	62	12	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	33	20	19	7	5	5
FG	m	50	13	60	100	60	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	29	20	19	4	4	5
FU	m	62	18	2	67	60	14	3	142	88	-	120	58	59	24	20	15	6	4	4
FS	f	55	9	2	100	52	14	13	133	82	-	109	60	57	29	19	16	5	3	4
GO	f	78	4	1	92	59	13	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	15	20	18	4	2	4
MA	m	60	13	2	100	67	14	4	131	84	-	119	58	60	34	20	15	5	4	5
MZ	m	81	13	2	100	65	12	1	125	85	-	110	55	56	27	20	20	6	4	4
ME	m	55	14	1	100	66	14	15	123	75	-	110	51	51	28	18	18	4	3	5
PE	f	43	8	2	83	63	14	1	131	88	-	115	49	52	23	19	17	4	3	4
PT	f	66	8	1	100	51	12	20	141	57	-	102	50	39	21	20	18	5	2	3
PI	f	65	8	2	100	58	14	31	96	55	-	29	44	43	26	18	16	2	3	4
PO	f	50	8	2	100	68	13	n.a.	148	n.a.	30	n.a.	59	n.a.	30	20	19	5	4	5
PN	f	63	5	2	83	65	13	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	21	20	18	4	3	2
RO	f	80	5	3	100	43	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	22	18	16	4	2	4
SR	f	69	8	1	100	54	11	39	147	29	-	67	47	40	24	20	13	4	2	3
SC	f	82	5	1	100	55	11	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	16	17	13	5	2	4
SO	m	70	11	1	100	69	14	2	149	89	-	114	58	60	32	20	18	5	4	5
SV	f	50	10	2	100	50	11	37	97	18	-	10	45	27	17	19	17	3	n.a.	4
ST	m	63	5	2	100	53	14	21	73	25	-	0	48	16	29	19	16	n.a.	n.a.	5
TO	m	67	13	6	100	51	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	n.a.	18	8	5	4	3
TS	m	66	15	2	100	70	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	25	18	19	6	4	3
ZA	m	40	18	2	83	49	10	47	1	0	-	0	37	31	26	20	17	p.u.	p.u.	4
ZE	f	65	5	2	100	62	14	n.a.	n.a.	n.a.	-	n.a.	n.a.	n.a.	20	20	20	4	4	4

Appendix 2.1. (continued) Results of the neuropsychological evaluation for all patients.

INITIALS	P&P words	P&P pictures	TMT A	TMT B	TMT B-A	WEIGL	WCST N.cat	WCST pers	REY imm.	REY del.	REY rec.	WARR. faces	naming	Hemisph	Description of Lesion (Numbers indicate Brodmann Areas)
AN	n.a.	50	33	63	30	n.a.	5	6	35	6	26/32	n.a.	30/30	L	11
BA	n.a.	50	p.u.	p.u.	p.u.	n.a.	6	4	p.u.	p.u.	p.u.	15	7/30	L	17,18,19,21,22,23,37,39,40,41
BL	n.a.	49	113	407	294	3	n.a.	n.a.	27	8	29/32	n.a.	28/30	L	43,48
BE	n.a.	48	203	p.u.	p.u.	7	n.a.	n.a.	18	2	38/46	n.a.	29/30	L	48
BO	n.a.	52	197	p.u.	p.u.	13	6	2	29	4	27/32	n.a.	26/30	R	11,38,39,44,45,47,48
BR	n.a.	48	50	p.u.	p.u.	p.u.	p.u.	p.u.	n.a.	n.a.	n.a.	n.a.	0/30	L	20,21,22,37,38,39,42,48
CA	n.a.	51	70	388	318	9	3	1	37	8	43/46	n.a.	27/30	R	6,44,48
CS	n.a.	51	300	460	160	n.a.	6	2	35	6	30/32	n.a.	27/30	R	2,3,20,21,22,36,37,38,39,40,41,42,43,47,48
CE	49	n.a.	p.u.	p.u.	p.u.	n.a.	4	5	25	7	27/32	n.a.	21/30	R	48
CI	n.a.	44	90	p.u.	p.u.	6	p.u.	p.u.	17	2	26/32	n.a.	29/30	L	7,18,19,21,22,37,39,40,41
DM	n.a.	50	142	530	388	n.a.	6	3	25	4	28/32	n.a.	26/30	R	48
DP	n.a.	n.a.	51	360	309	10	n.a.	n.a.	22	4	45/46	24	27/30	L	48
DU	n.a.	50	72	525	453	9	1	10	25	3	34/46	n.a.	27/30	R	42,48
DR	n.a.	51	n.a.	n.a.	n.a.	n.a.	6	1	p.u.	p.u.	p.u.	19	21/30	L	2,3,4,6,8,9,10,11,20,21,22,37,38,39,40, 41,42,43,44,45,46,47,48
FL	n.a.	52	41	142	101	n.a.	4	10	45	5	44/46	n.a.	20/20	L	inferior parietal lobe (no scan available)
FG	n.a.	52	125	p.u.	p.u.	n.a.	2	3	25	1	40/46	n.a.	19/20	L	2,3,4,5,6,7,17,18,19,20,21,23,37,39,40,41
FU	n.a.	50	46	129	83	12	n.a.	n.a.	45	10	31/32	n.a.	29/30	L	10,45,46,47,48
FS	n.a.	51	78	324	246	n.a.	4	15	15	0	25/32	n.a.	25/30	L	Basal ganglia
GO	n.a.	49	79	371	292	n.a.	3	4	30	6	27/32	n.a.	27/30	R	6,44,45,46,48
MA	n.a.	52	32	142	110	10	n.a.	n.a.	38	8	29/32	n.a.	30/30	L	48
MZ	n.a.	51	152	238	86	n.a.	2	11	n.a.	n.a.	n.a.	20	30/30	L	nucleus lenticularis (no scan available)
ME	n.a.	51	35	217	182	4	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	29/30	L	22,43,48
PE	n.a.	n.a.	166	235	69	10	3	7	50	14	45/46	n.a.	28/30	R	Subcortical
PT	n.a.	50	211	p.u.	p.u.	6	n.a.	n.a.	21	1	28/32	n.a.	27/30	L	7,19,39,40
PI	n.a.	48	n.a.	n.a.	n.a.	9	5	2	n.a.	n.a.	n.a.	n.a.	2/30	L	20,21,22,37,38
PO	n.a.	51	30	80	50	n.a.	3	12	37	11	44/46	n.a.	29/30	R	20,21,22,37,39,41,42
PN	n.a.	51	198	p.u.	p.u.	n.a.	6	3	40	9	30	n.a.	26/30	R	3,6,7,40
RO	n.a.	n.a.	76	p.u.	p.u.	n.a.	n.a.	n.a.	30	5	41/46	n.a.	n.a.	L	21,22,41,42
SR	n.a.	46	n.a.	n.a.	n.a.	3	3	9	n.a.	n.a.	n.a.	23	17/30	L	Subcortical
SC	n.a.	52	197	p.u.	p.u.	5	p.u.	p.u.	38	8	29/32	n.a.	28/30	R	2,40,41,42
SO	n.a.	52	42	215	173	8	2	5	24	1	18/32	n.a.	29/30	L	20,41
SV	n.a.	47	n.a.	n.a.	n.a.	n.a.	6	3	n.a.	n.a.	n.a.	24	3/30	L	21,22,37,38,39,41,48
ST	n.a.	49	n.a.	n.a.	n.a.	10	2	5	n.a.	n.a.	n.a.	n.a.	0/30	L	2,3,4,38,47,48
TO	50	47	197	p.u.	p.u.	11	3	7	43	6	n.a.	n.a.	30/30	R	6,20,21,22,37,38,39,41,42,43,44,45,48
TS	n.a.	51	62	300	238	10	6	0	33	7	44/46	n.a.	29/30	R	47,48
ZA	n.a.	50	56	410	354	n.a.	5	7	p.u.	p.u.	p.u.	13	p.u.	L	6,22,40,41,42,44,45,47,48
ZE	n.a.	52	62	213	151	5	3	2	43	8	30/32	n.a.	29/30	R	Subcortical

Caption for Appendix 2.1.

Abbreviations used in the neuropsychological assessment: **Oldfield** = Oldfield (1971); **IMA** = Ideomotor Apraxia (De Renzi, Motti, and Nichelli, 1980); **IA** = Ideational Apraxia (De Renzi and Lucchelli, 1988); **AAT** = Aaachener Aphasie Test, Italian norms (Luzzatti, Willmes, De Bleser. Firenze, Organizzazioni Speciali, 1996); **AAT token** = token subtest; **AAT rep** = repetition; **AAT writ** = written language; **AAT read** = shortened version of the reading task with 30 items; **AAT name** = naming; **AAT oc** = oral comprehension; **AAT wc** = written comprehension; Raven's CPM: Raven Coloured Progressive Matrices (Carlesimo, G.A.; Caltagirone, C.; Gainotti, 1996); **VOSP** = Visual Object and Space Perception battery (Warrington and James, 1991). **VOSP screen** = screening task; **VOSP o.d.=** object decision task; **Span fwd** = digit span forward; **Span bwd** = backward digit span; **Corsi** = Corsi test, spatial short-term memory (Spinnler and Tognoni, 1987); **P&P words** = The Pyramids and Palm Trees test, version with words (Howard & Patterson, 1992); **P&P pictures** = The Pyramids and Palm Trees test, version with pictures; **TMT A**= Trail Making Test Version A, with letters only (italian norms from Giovagnoli, Del Pesce, Mascheroni, Simoncelli, Laiacona, and Capitani, 1996); **TMT B** = Trail Making Test Version B, alternating numbers and letters; **TMT B-A** = difference in score between TMT A and B; **WEIGL** = Weigl's Sorting Test (Spinnler and Tognoni, 1987). **WCST** = Wisconsin Card Sorting Test (normative data: Caffarra, Vezzadini, Dieci, Zonato, Venneri, 2004); **N.cat** = Number of correct categories chosen by the patient; **N pers** = Number of perseverations; **REY** = REY Auditory Verbal Learning test; **REY imm**=Immediate Recall; **REY del.=** delayed recall; **REY rec.=** recognition (Rey, 1964); **WARR. Faces** = Recognition Memory Test for faces (Warrington, 1996). **Naming** = Trieste screening battery, unpublished norms; **Hemisph** = side of the lesion.

n.a. = task not administered

p.u. = patient unable to perform the task

Appendix 2.2. List of the experimental stimuli in alphabetical order.

Bottle
Cigarette
Coffee mug
Comb
Duster
Eraser
Fork
Glass
Gun
Hammer
Iron
Jug
Key
Knife
Ladle
Lemon squeezer
Light bulb
Lipstick
Match
Paintbrush
Pen
Razor
Saw
Scissors
Screwdriver
Spanner
Spoon
Tennis racket
Toothbrush

Appendix 2.3. List of distractors in the multiple choice tasks. Target items are in capital letters.

OBJECT RECOGNITION		
PEN	Eraser	Scissors
LIPSTICK	Razor	Comb
Pen	SCISSORS	Eraser
screwdriver	saw	PAINTBRUSH
Spoon	carafe	COFFEE MUG
Spanner	Screwdriver	KEY
coffee mug	Spoon	CARAFE
Hammer	light bulb	CIGARETTE
Eraser	Pen	Scissors
Saw	Hammer	GUN
Spanner	SCREWDRIVER	Hammer
SAW	Scissors	Paintbrush
Spanner	HAMMER	Screwdriver
Coffee mug	LEMON SQUEEZER	Carafe
IRON	Light bulb	Carafe
Comb	Lipstick	RAZOR
Pen	LIGHT BULB	Scissors
Hammer	SPANNER	Screwdriver
SPOON	Coffee mug	Carafe
Razor	COMB	Lipstick
Spoon	LADLE	Whisk
Carafe	Glass	BOTTLE
TOOTHBRUSH	Razor	Hairbrush
Spoon	Carafe	GLASS
MATCHSTICK	Lighter	Candle
Baseball bat	Table tennis bat	TENNIS RACKET
FORK	Coffee mug	Spoon
Scissors	Saw	KNIFE
Vacuum cleaner	sponge	CLOTH

Appendix 2.3. (continued). List of distractors in the multiple choice tasks. Target items are in capital letters.

PANTOMIME RECOGNITION		
WRITING WITH PEN	Writing with keyboard	Cutting with scissors
Applying nail polish	Using a nail file	APPLYING LIPSTICK
Knitting	Sewing	CUTTING WITH SCISSORS
Turning a spanner	PAINTING A WALL	Turning a screwdriver
DRINKING FROM COFFEE MUG	Pouring from a carafe	Eating with a spoon
Turning a tap	Opening a door handle	TURNING A KEY
POURING FROM A CARAFE	Beating a pestle in the mortar	Squeezing an orange
Applying eyeshadow	SMOKING A CIGARETTE	Shaving with a razor
Drawing with pencil	RUBBING WITH ERASER	Cutting with scissors
Using hairdryer	Using a spray	SHOOTING WITH A GUN
TURNING A SCREWDRIVER	Hammering	Using a chisel
Turning a spanner	SAWING	Using a chisel
Planing wood	HAMMERING	Cutting with an axe
SQUEEZING AN ORANGE	Eating pasta	Opening a bottle with a corkscrew
Vacuuming	IRONING	Knitting
Washing hands	Brushing Teeth	SHAVING WITH A RAZOR
Turning a screwdriver	Using pliers	TURNING A LIGHT BULB
TURNING A SPANNER	Drilling	Sawing
Using a whisk	EATING WITH A SPOON	Drinking a cup of coffee
Applying makeup	COMBING HAIR	Drying hair
Vacuuming	Cleaning dishes with a sponge	CLEANING WINDOW WITH A CLOTH
Playing table tennis	Playing baseball	PLAYING TENNIS
Sawing	CUTTING WITH A KNIFE	Cutting with scissors
BRUSHING TEETH	Shaving with a razor	Combing hair
STIRRING WITH A LADLE	Stirring with a whisk	Eating with a spoon
Pouring from a carafe	DRINKING FROM A GLASS	Drinking from a coffee mug
Using a lighter	Lighting a candle	STRIKING A MATCH
Drinking from a glass	Pouring from a carafe	POURING FROM A BOTTLE
Eating with a spoon	Drinking from a coffee mug	EATING WITH A FORK

Appendix 2.4. Lesion analysis

Here, I report the lesions of patients who showed the classical dissociations reported in Chapter II, as computed with the RSDT test (Crawford and Garthwaite, 2006). The lesions, reconstructed with MRIcro software, are showed below.

The lesion analysis of the five patients with impaired object use but spared pantomime recognition is reported in Figure 2.3.A. The top panel row in A shows the lesion overlap analysis for patients CS and SC, who had right hemisphere lesions, whereas the bottom panel row shows the overlap of DR, BR and BE, who had left hemisphere lesions. There was overlap across the two right-hemisphere lesioned patients in the supramarginal gyrus and the superior temporal gyrus, and across the three left hemisphere lesioned patients in a small portion of the putamen.

Figure B. shows the lesion overlap for patients BO and PI, who were impaired at recognizing pantomimes despite intact pantomime recognition. The lesions of the two patients did not overlap.

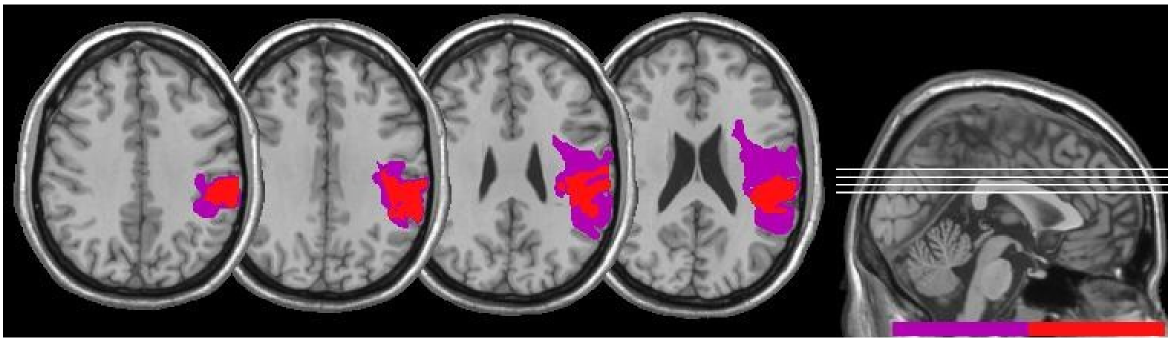
Figure C. depicts the lesions of patients CE, TO, and DM, who had right hemisphere lesions and were impaired for recognizing objects, but unimpaired for recognizing object associated pantomimes, imitating pantomimes, and using objects. The lesions of these three patients overlapped in the right putamen. PI's lesion is shown in panel B.

Figure D. reports the right hemisphere lesions overlap of patients FS, RO, BL and CI, which had spared object recognition despite impaired object use. There was no common region lesioned in all four patients.

Figure E. depicts PT's brain, who has a selective deficit for imitating transitive and intransitive gestures. Her brain lesion is restricted to a small portion of the left hemisphere, in the left inferior parietal lobe and angular gyrus.

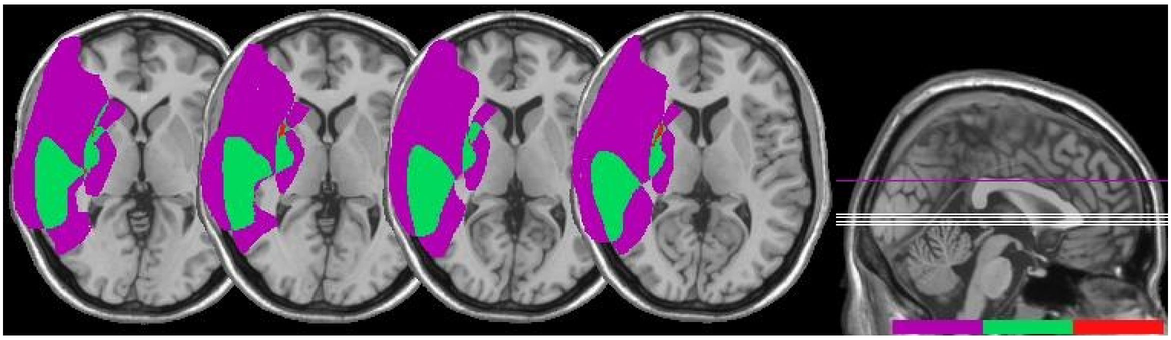
Appendix 2.4. (continued) Color bars indicate (from purple=1 to red=all) the number of patients showing lesion overlap in a given region. Left and right hemispheres are not inverted. In single cases, the lesion is colored in red.

A.



Patient CS: frontal inferior operculum, rolandic operculum, insula, postcentral g., inferior parietal g., supramarginal g., angular g., Heschl g., superior temporal. g., sup. temporal pole, mid. temporal g., inf. temporal g.

Patient SC: inf. parietal g., supramarginal g., sup. temporal g.

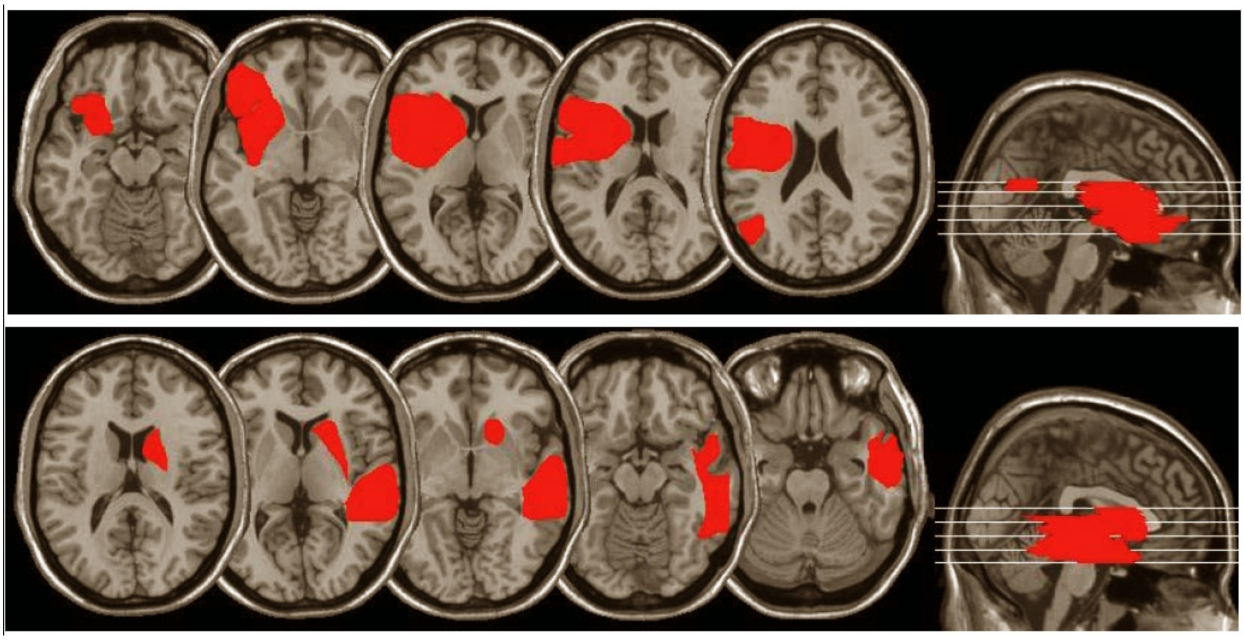


Patient DR: putamen, precentral g., middle frontal g., frontal inf. operculum, frontal inf. g., rolandic operculum, insula, postcentral g., inf. parietal g., supramarginal g., angular g., Heschl g., sup. temporal g., sup. temporal pole, middle temporal g., middle temporal pole.

Patient BR: putamen, sup. temporal g., sup. temporal pole, middle temporal g., inferior temporal g.

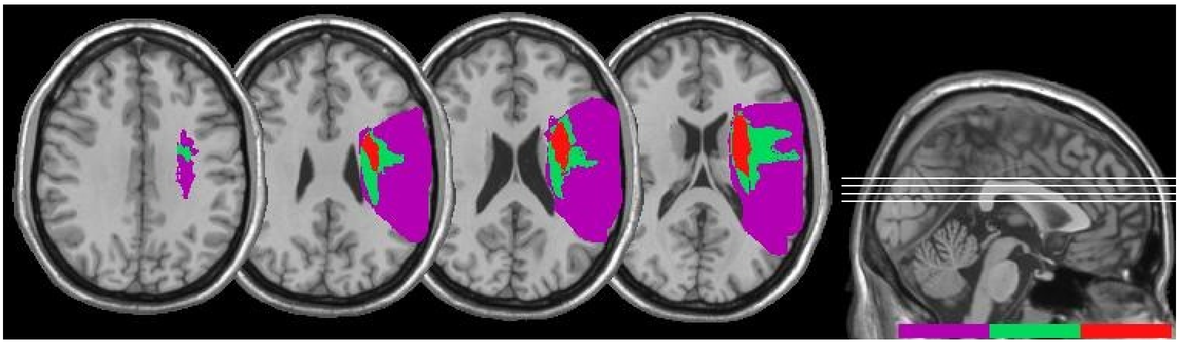
Patient BE: putamen, globus pallidum

B.



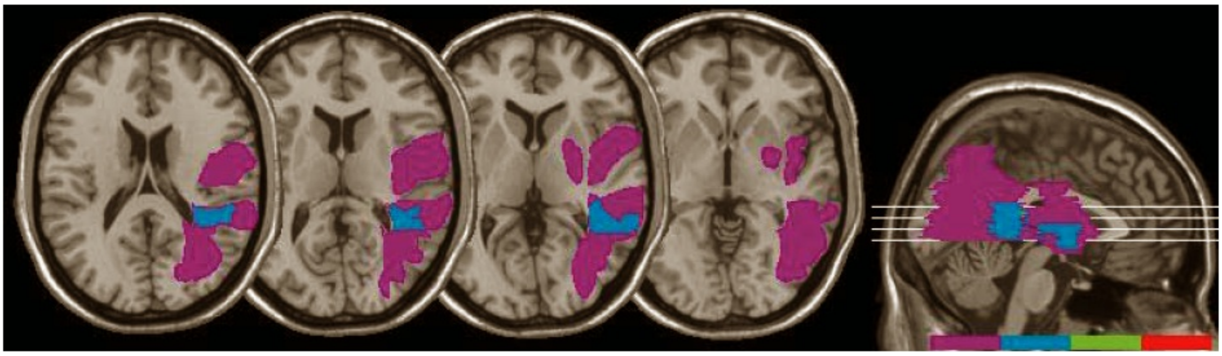
Patient BO: frontal inf. operculum, frontal inf. orbital, rolandic operculum, insula, postcentral g., caudate, putamen, Heschl g., sup. temporal g., middle temporal g.
Patient PI: caudate, putamen, sup. temporal g., middle temporal g., inf. temporal g.

C.



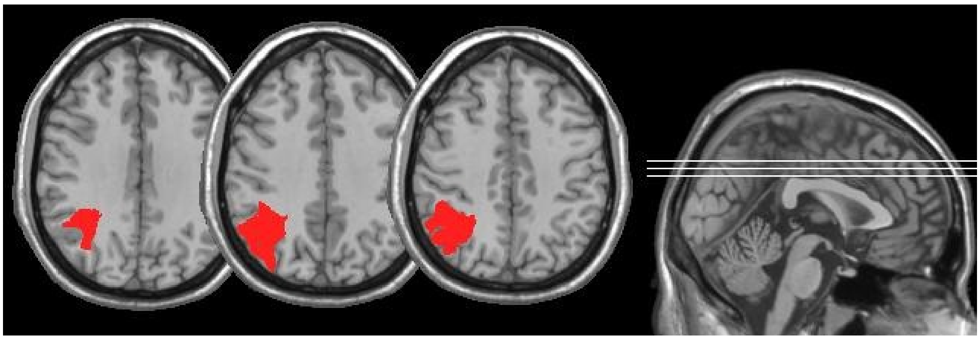
Patient CE: putamen, pallidum
Patient TO: precentral g., frontal inf. operculum, rolandic operculum, insula, postcentral g., supramarginal g., putamen, sup. temporal g., middle temporal g.
Patient DM: insula, putamen, pallidum

D.



Patient FS: putamen. pallidum
Patient RO: sup. temporal g., middle temporal g.
Patient BL: rolandic operculum, insula, postcentral g., sup. temporal g.
Patient CI: middle temporal g., sup. temporal g., sup. occipital g., middle occipital g., angular g., precuneus.

E.



Patient PT: angular g., inf. parietal g.

Chapter III.
The Separation of Semantic and Motor Knowledge of Tools In Humans

Abstract. In chapter II, we have shown that recognition and production processes for action and objects can be dissociable in a group of unselected patients. In this Chapter, I will describe in detail two single case studies that may provide insightful information about the relation between conceptual and motor knowledge in the mind. In study 3A[9], I will describe a double dissociation between the ability to carry out tasks tapping semantic knowledge, and the ability to use objects in two patients with Ideational Apraxia (F.G. and D.R., studied also in Rumiati et al., 2001) and two patients with semantic impairments (A.M. and D.L.). Study 3A proved that the two IA patients had intact semantic knowledge about the objects that they failed to use, whereas the two patients with semantic impairment showed the reverse pattern. In study 3B, patients AM's and DL's performance on object use and on semantic tasks has been assessed two years later, in order to see whether the patients' ability to use objects degraded as a function of their semantic knowledge about them. Results from the assessments in 2002 and in 2004 confirmed that patients A.M. and D.L. had a selective loss of lexical-semantic knowledge, despite relative preservation of other cognitive abilities including object use.

Since I have already described the literature on IA in the Introduction, here I will start by briefly introducing some studies on semantic dementia.

[9] Study 3A reports data from a manuscript in preparation (Rumiati et al., in prep.), whereas data of study 2B are published in Negri et al. (2007a).

Semantic Dementia

In 1975, Elizabeth Warrington described three patients with progressive anomia and impaired word comprehension. This syndrome has been successively considered as the temporal variant of the frontotemporal dementia or the fluent form of primary progressive aphasia (Luzzatti, 1999; Hodges et al., 1992; Snowden et al., 1989). Since it impacts primarily on the semantic memory of patients, the term Semantic Dementia (hereafter SD) has been proposed (Hodges et al., 1992, Snowden et al., 1989). Others called the same neuropsychological pattern *slowly progressive aphasia*, as conceptual loss is usually accompanied by a lexical deficit (see Poeck and Luzzatti, 1988). Whereas SD patients' naming and spontaneous speech are interspersed with anomias and semantic paraphasias, perceptual skills, non-verbal intelligence, syntactic skills and repetition. Day-to-day memory may be relatively spared at least at an earlier stage of the disease (Bozeat et al., 2000; Lambon Ralph and Howard, 2000). SD is generally associated with circumscribed temporal lobe atrophy, affecting the temporal pole, the antero-medial and infero-lateral temporal lobe, bilaterally but asymmetrically. In addition, the ventromedial frontal cortex and the amygdaloid complex have been found affected too (Mummery et al. 2000; Mummery et al., 1999). As shown in post-mortem examinations, in some instances the symptoms of progressive aphasia and semantic-lexical impairment may also be symptoms of an atypical focal dementia of Alzheimer type (see Galton et al., 2000; Greene et al., 1996).

Based on the behaviour of patients with impaired semantics, conceptual knowledge has been suggested to be modality-specific, as it was found to be affected either in its verbal (Lauro-Grotto et al., 1997; McCarthy and Warrington, 1988; Coughlan and Warrington, 1981) or visual components (Warrington and McCarthy, 1994). These findings have been taken as evidence that the semantic system is indeed multimodal (Shallice, 1988). The fact, however, that patients with degraded knowledge for verbal and non-verbal stimuli have also been reported (Hodges et al., 1992; Snowden et al., 1989; Bozeat et al., 2000), supported the opposite view that the semantic system is amodal (Caramazza et al., 1990; Riddoch et al., 1988).

Interestingly, at least two SD patients have been reported with spared object use in presence of semantic memory impairments. For instance, patients R.M. and D.M., described by Lauro-Grotto et al. (1997) and Buxbaum et al. (1997) respectively, were still able to use objects in everyday activities despite having a deficit in object naming and identification. Hodges et al. (2000) also described patients who, in some instances, were better at using objects than it would be predicted based on their semantic knowledge about those objects.

According to some authors (Coccia et al., 2004; Bozeat et al., 2002a, 2002b; Hodges et al., 2000), as SD progresses, patients would also become apraxic. Hodges et al. (2000) and Bozeat et al. (2000) reported SD patients who were still able to use highly familiar but not less common items, and therefore concluded that object familiarity is the best predictor of proper use. Because of the strong correlation between performance on object use and preservation of semantic knowledge about objects, Hodges et al. (2000) argued that in SD patients spared praxic skills seem to rely strictly upon object-specific conceptual knowledge, in addition to mechanical problem solving abilities and visual affordances. Furthermore, object use performance also seems to be strongly influenced also by the context in which objects are presented. Indeed Bozeat et al. (2002b) observed that patients' performance improved significantly when they were assessed at home using objects that belonged to them, as opposed to when they were tested in the laboratory using objects perceptually dissimilar to those of their own. However, the theoretical inferences based on some of these studies cannot be conclusive, as the patients who showed a dissociation were not tested on the same stimuli for object knowledge and object use (e.g. Buxbaum et al., 1997; Lauro-Grotto et al., 1997). Therefore the dissociations reported could have been due to items presenting different degrees of difficulty in either one or the other task.

The aim of the two studies presented in this Chapter was to verify whether semantic information is necessary to correctly use objects, and, *vice versa*, if an impairment in motor skills would compromise also the knowledge of objects and tools. To answer the first question, we have identified two patients with semantic impairments and we tested them on their ability to use objects. On the other hand, evidence that the semantic system is not sufficient to support tool use comes from the observation of FG and DR, two patients with Ideational Apraxia that have lost the ability to use objects properly (Rumiati et al., 2001; Buxbaum et al., 2000; Hodges et al., 1999; Ochipa et al., 1989).

Study 3A

A Comparison Between Two Apraxic Patients and Two Patients with Semantic Impairment

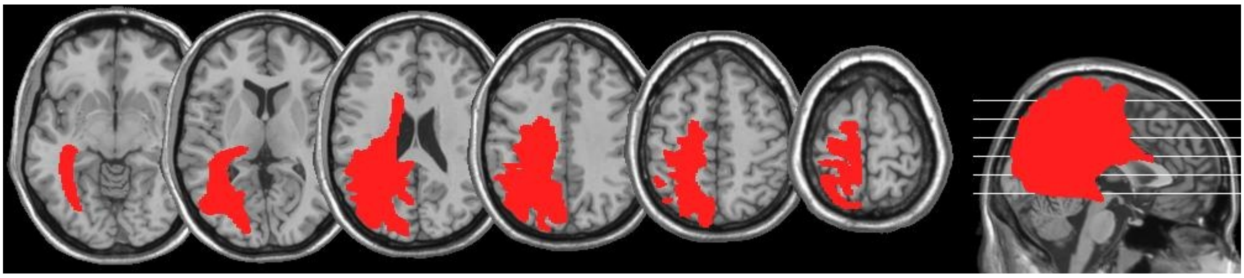
METHODS

Participants

Patients with the tool use deficit

Patient FG, a right-handed man, was born in 1953 and had 13 years of schooling. Before his illness (October 1998), he was employed in a local brewery company. In October 1998 he was admitted to hospital with aphasia and right hemiplegia. The first CT-scan (October 1998) showed left cortical-subcortical haemorrhage affecting the left posterior parietal lobe, involving Brodmann Areas 7, 39 and 40. A more recent MR scan performed in 2004 confirmed the previous findings (see Figure 3.1.). The results reported in this study were obtained between February and September 2002.

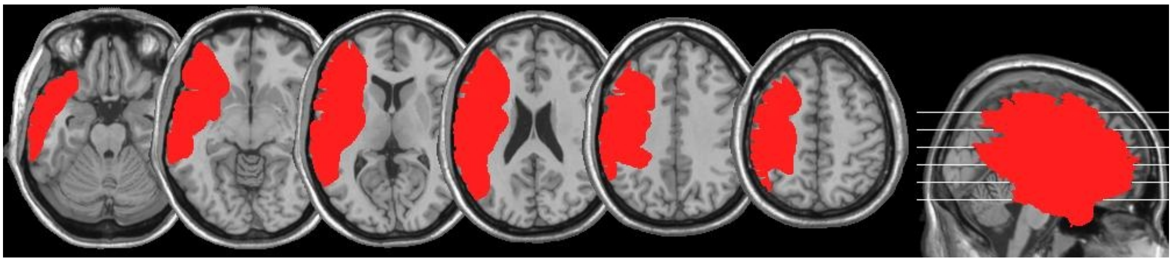
Figure 3.1. lesion reconstruction performed using MRIcro software, of patient FG's lesion.



Patient DR, a right-handed male, was born in 1949 and had 13 years of schooling. Before his illness (December 1997), he worked as a teacher at the elementary school and as an administrative staff member. He was admitted to hospital with a right hemiplegia and aphasia due to an infarct of the left medial cerebral artery. A series of CT scans revealed a large fronto-temporo-parietal ischemic lesion in the left hemisphere including BA 44 and 45, primary motor and sensory cortices and BA 40, while the prefrontal cortex was spared.

In 2004, a new MR scan of DR was collected and then used by an expert neuroradiologist to perform the lesion reconstruction using MRIcro software. The new analysis confirmed the involvement of BA 40, 44 and 45 (see figure 3.2.).

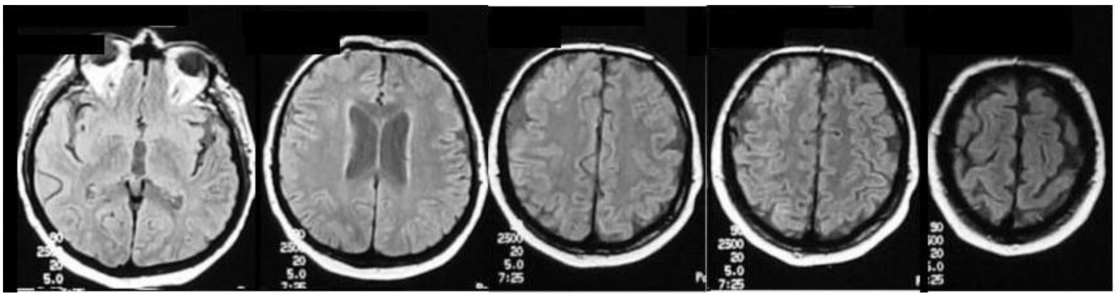
Figure 3.2. reconstruction performed using MRIcro software of patient DR's lesion.



Patients with semantic impairment

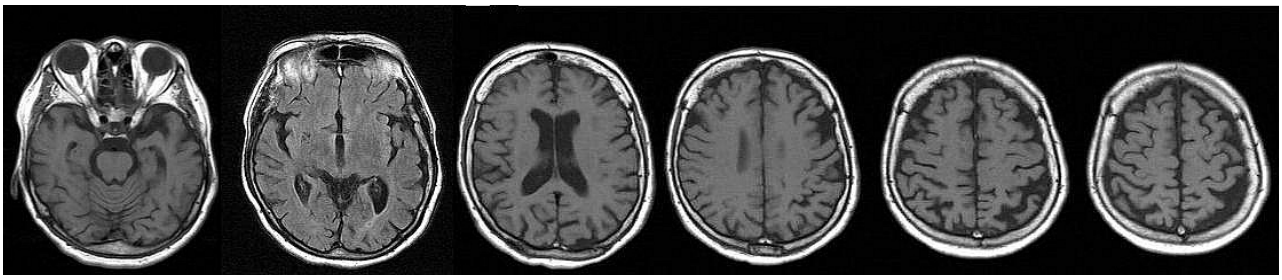
Patient DL, a right-handed man, born in 1933, had 5 years of education and worked as a baker and lorry-driver before retirement. He came to medical attention in October 2000 because of word finding problems, particularly for names of people, streets, but also of common objects. Since then, he was periodically assessed to monitor the progressing of the disease. Data reported in Study 3A were collected in spring of 2002. A NMR scan in September 2000 revealed bilateral temporal lobe atrophy, greater in the left temporal pole and Sylvian areas (see Figure 3.3.).

Figure 3.3. Selected images from the MR scan performed on patient DL in September 2000. in 2004, DL refused to perform a new neuroradiological exam.



Patient AM, a right-handed woman, was born in 1928. She had 5 years of education and had worked as an agricultural labourer. She came to the attention of the neuropsychologists in March 2002 complaining of memory loss and word finding impairments. Two months earlier, a SPECT was performed revealing a concentration deficit of the tracer in the left temporal lobe. A more recent NMR (march 2005) scan revealed a diffused cerebral atrophy (see Figure 3.4.).

Figure 3.4. Selected images from the MR scan performed on patient AM in March 2005. The diffused amplitude of liquoral spaces is evident in the ventricular and subaracnoidal spaces and in the fronto-temporo-parietal regions bilaterally, more pronounced in the left hemisphere. This neuroradiological finding fits well with a diagnosis of a dementia of Alzeheimer's type



Control participants

Since the demented and apraxic patients differed in age and educational level, two groups of healthy controls took part in the study. The first group (N = 10) had a mean age of 67.7 years (±3.6) and 8.8 years (±2.2) of education. The second group (N = 9) had a mean age of 51.7 years (±2.8), and 12.3 years (±1.7) of education.

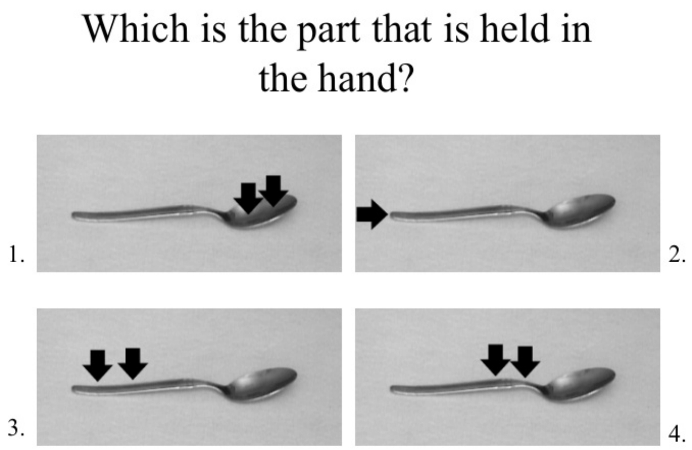
MATERIALS AND METHODS

Experiment 1: semantic questionnaire. Twenty-two objects were presented visually (coloured picture) or verbally (spoken name) to patients and controls, one at a time, according to an ABBA design. Five or six questions were posed orally to the subjects for each item, without giving them any feedback, following the procedure used by Laiacona et al. (1993). The aim was to test different hierarchical levels of object knowledge (e.g. *hammer*; correct responses are underlined): 1) higher-level superordinate information (e.g. is it an <u>object</u>, a vegetable or an animal?); 2) lower-level superordinate information (e.g. is it a <u>tool</u>, a musical instrument or a gem?); 3) subordinate perceptual information (e.g. is it made of glass, of <u>metal</u> or of cement?); 4) subordinate structural information (e.g.

is it smaller than a screw?); 5) functional information (e.g. is it used for cutting, screwing or sticking nails?); and 6) the prototypical use of the object (e.g. is it used by the house-painter, the carpenter, the glazier?).

Experiment 2: knowledge of object parts. A set of 47 questions concerning the functions of different parts of 23 objects (the same 22 stimuli used in Experiment 1, plus the matchbox), were read aloud by the experimenter. This experiment specifically aimed at testing patients' functional knowledge of the relevant parts of the same 22 objects presented in the other tasks. They were given four choices in which arrows pointed to different parts of the object. They were asked to point to the picture where the arrows indicated the part relevant for the action described by the experimenter (see Figure 3.5). Patients performed the experiment twice, with about a four-week interval between the two sessions.

Figure 3.5. Example of a stimulus of Experiment 2. Patients were asked to point to the picture corresponding to the sentence written on the top of the page, while the sentence was also read aloud by the experimenter.



Experiments 3a: Object Use. Patients were asked to use 23 objects in simple common actions such as lighting a match or pouring liquid from a bottle into a glass; one or two objects were employed at a time. Objects were put on the table in front of patients for each trial, and then removed after use.

Experiment 3b: MOTs . Patients engaged in more complex actions in which more than two objects were involved such as: preparing coffee using an Italian coffee machine (water, coffee, spoon, a disassembled coffee machine), preparing an envelope to post (envelope, letter, and stamp), and lighting a candle (candle, candle holder, a match-box containing matches).

The performance of patients on experiments 3a and 3b was video-recorded and subsequently scored independently by three raters. Actions were scored as either correct or incorrect. For the incorrect actions, raters used a classification developed by Rumiati et al. (2001) to categorize patients' errors. The inter-raters' agreement was 100% as far as accuracy and error classification were concerned.

Experiment 4a: **Object Naming.** Patients had to name the 23 real objects used in experiments 1 and 2. Objects were placed one after the other in front of the patients. No feedback was given and no time constraints were imposed.

Experiment 4b: Name-Picture Matching. Patients had to match the name of each object (N = 23) to the corresponding stimulus presented together with two semantically-related stimuli used as distractors (e.g. *glass*; bottle, vase). On each trial, the experimenter placed the three objects on the table and said the name of one of them. After each trial, the objects were replaced by the experimenter with the subsequent triplet of stimuli.

Experiment 5a: Pantomime Naming. Patients were presented with pantomimes of object use (N = 23) and asked to identify them by either naming them or matching them to one of three action verbs. The pantomimes where performed by the experimenter, one after the other.

Experiment 5b: Pantomime Recognition. Patients had to match each pantomime (N = 23) to the corresponding object presented together with two semantically-related stimuli used as distractors (e.g. *glass*; bottle, vase). The procedure was otherwise the same as in Experiment 4b.

RESULTS

Neuropsychological profiles

Table 3.1. illustrates the performance on standardized neuropsychological tests.

Patient FG had no language impairments except for mild difficulties in language comprehension as indicated by the Token Test (AAT). Testing did not reveal any visual processing or semantic knowledge deficits. With regard to memory, his verbal auditory short-term memory was somewhat pathological, as shown by his performance on digit span. He also had memory retrieval problems: FG's immediate and delayed recall of 15 words were both impaired, but his recognition memory was intact. FG had also indications of frontal dysfunction as shown by his performance on the Wisconsin Card Sorting Test (WCST). Concerning his motor control abilities, FG performed accurately a Goodale-Milner posting task making only 1 perseverative error, and could correctly reach most of the times (29/32) for a target (a disk of a diameter of 2 cm) placed at eight different locations from the patient while fixating the nose of the experimenter. His ability to imitate novel and known gestures was normal. However, as in previous extensive testings6 (see Rumiati et al., 2001), FG had many difficulties in using real objects.

Patient DR had extensive language problems affecting his spontaneous speech, repetition of words and sentences, written language and naming (see Table 3.1). In contrast, his verbal comprehension was unimpaired (Token test). This clinical pattern is compatible with a diagnosis of Broca's aphasia. He did not show signs of visual or spatial agnosia, but a mild deficit in a recognition memory task was observed. Although his reaching and grasping abilities resulted to be normal on testing, and his ability to imitate was borderline, he was apraxic when using objects. His performance on the WCST was satisfactory, indicating preserved executive functioning.

Patient DL was severely impaired on naming tasks, producing frequent semantically related words (i.e. semantic paraphasias) and several omissions. That DL's naming deficit lay in the semantic system was suggested by his pathological performance on the Pyramids and Palm Trees test (Howard and Patterson, 1992) in which he was required to match either words or pictures based on their meaning. By contrast, DL's repetition of words was remarkably spared, as was his word reading, though making few errors in writing. Early visual processing was also relatively spared. Interestingly, despite his difficulties in identifying and naming objects, DL did not show any problem when using common objects (Ideational Apraxia test). His verbal auditory short-term memory was preserved; in contrast long-term memory was dramatically impaired as shown by his pathologically poor performance on a word recognition test as well as on a recognition memory test for faces. This pattern of cognitive impairments fits well as Semantic Dementia, a form of fluent progressive aphasia primarily affecting word meaning and object identity knowledge (see Hodges et al., 1992, Snowden et al., 1989).

Patient AM's results on the neuropsychological assessment are also summarised in Table 3.1. The evaluation of AM's linguistic abilities revealed many anomias and semantic paraphasias in spontaneous speech as well as in naming, and a moderate deficit on the Token Test. No noticeable deficits in writing, reading and repetition were found. AM performed pathologically on only one subtest (i.e. Incomplete Letters) of the Visual Object and Space Perception Battery (VOSP), that investigates visual-spatial processing. Significant Impairments were also observed on tests assessing her long-term memory and semantic knowledge (both from pictures and words), however, she was not apraxic.

Overall, the behavioural pattern shown by DL and AM in 2002 was consistent with previous descriptions of patients affected by so-called Semantic Dementia (Warrington, 1975, Hodges et al., 1992, Snowden et al., 1989). However, when AM was assessed again two years later (study 3B), her clinical symptoms seemed to have evolved toward a Dementia of Alzheimer Type (DAT), but her praxic skills were still significantly better than her semantic knowledge about objects. As a result, patient AM likely represents one of those cases with an atypical DAT onset, as suggested by Galton et al. (2000).

Table 3.1. Results on the neuropsychological assessment administered to all four patients is summarized here. Bold font indicates pathological scores, as individuated by means of Z-scores or cut-offs. R% = percentile rank; a.s. = adjusted score; n.a.= not administered.

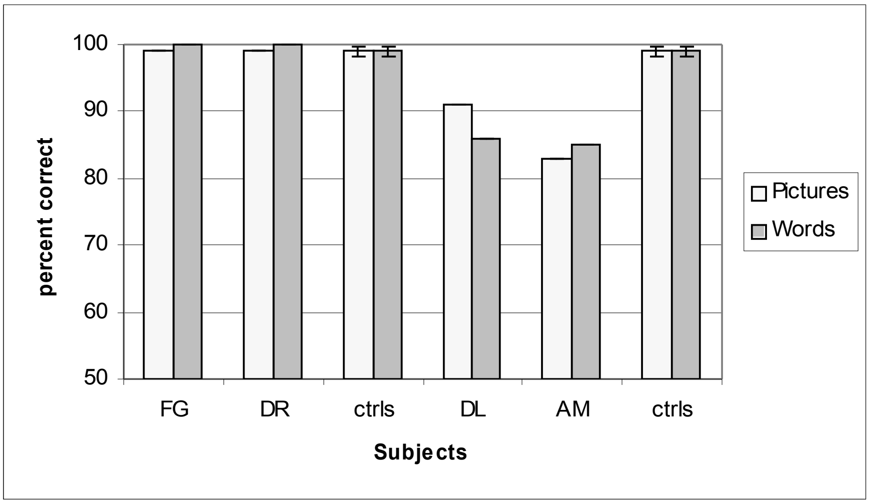
			FG	DR	AM	DL	Cut-offs
Language	***AAT (R%)***	Token Test	81	99	68	*91*	60
		Repetition	91	**36**	74	*94*	59
		Writing	93	**19**	84	*75*	58
		Naming	100	**41**	61	60	59
		Comprehension	91	100	81	*85*	55
	Laiacona et al. (1993)	Naming	77/80	**12/20***	**40/80**	**32/80**	61/80
		Comprehension between cat.	80/80	80/80	79/80	79/80	74/80
		Comprehension within cat.	78/80	80/80	73/80	65/80	74/80
Intelligence	***Raven's CMT***	Total score	29	34	**17.4**	31	18.9
Linguistic Fluencies		For letters	n.a.	n.a.	20.6	18.2	17.35
		For semantic categories	n.a.	n.a.	11.5	8.25	7.25
Visual Processing	VOSP	Screening Test	20	20	18	18	15
		Incomplete letters	n.a.	20	**12**	17	16
		Object decision	19	19	16	16	14
Memory	Short-term	Corsi test	5	5	2.25	5	3.75
		Digit span forward	**4**	4	5.5	4	3.75
	Long-term	Rey-words Imm. recall	**25**	n.a.	18	33 a.s	28.53
		Delayed recall	**1**	n.a.	3.4	5.4 a.s.	4.69
		Recognition corr.	40/46	n.a.	12/46	11/15	
		false	7		23	12	
		Story Recall	**4/16**	n.a.	n.a.	n.a.	
		Word recognition memory	n.a.	36/50	28/50	28/50	
		Face recognition memory	n.a.	19/25	5/25	12/25	
	Semantic	Pyramids & Palm Trees Test					
		words	52/52	Na**	41/52	40/52	48/52
		pictures	52/52	51/52	35/52	38/52	48/52
Praxis		Imitation	60/72	54/72	60/72	67/72	53
		Object Use	14/14	**8/14**	14/14	14/14	14
		Posting	19/20	20/20	n.a.	n.a.	
		Reaching	29/32	32/32	n.a.	n.a.	
Frontal Functions	WSCT	Categories	**2**	6	n.a.	n.a.	
		Total errors	13	4			
		Perseverations	3	1			
	Attention	Attentive Matrices	**27/60**	**25/60**	**27/60**	**28/60**	31/60

* shortened version

BEHAVIORAL RESULTS

Experiment 1 (semantic questionnaire). The overall accuracy of patients and controls on these questions is plotted on Figure 3.6. FG and DR performed excellently on all the different dimensions of object knowledge, regardless of the input modality. Both FG and DR scored 130/131 (99%) with line drawings of objects, and 131/131 (100%) with their spoken names. FG's and DR's performance on both versions of the questionnaire was as accurate as that of individuals without brain-damage of comparable age and education (control mean and SD: 130.4 ±0.83 for both verbal and visual presentation). In contrast, DL and AM had not retained full semantic knowledge concerning all the objects either following visual (119/131, 90%; 109/131, 83% respectively) or auditory-verbal (113/131, 86%; 112/131, 85% respectively) presentation of the stimuli. DL's and AM's failures occurred on all dimensions of object knowledge in both conditions. Overall, DL's and AM's performance was worse than that of controls, and more importantly, they performed worse than FG and DR, both in the verbal and visual versions of the task (Wilcoxon, $p < .01$ in all comparisons, see Figure 3.6).

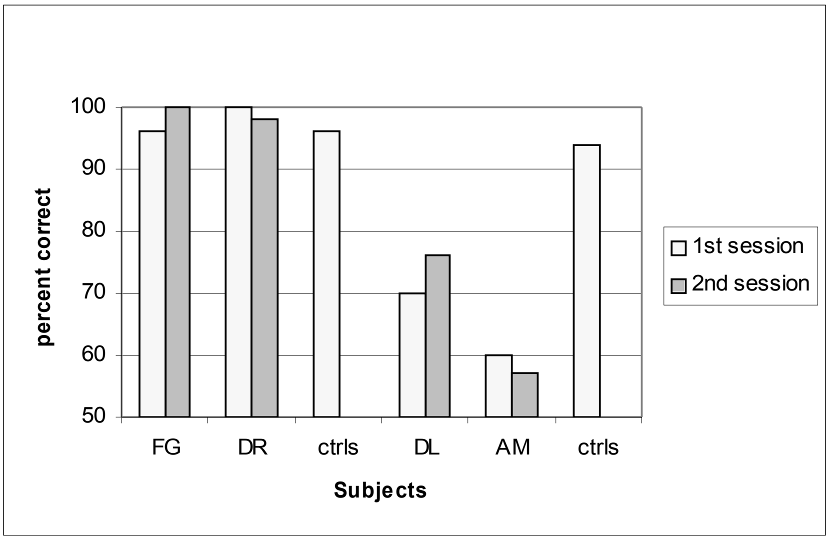
Figure 3.6. Overall accuracy of all patients as well as of the two control groups on Experiment 1.



Experiment 2 (Knowledge of Object Parts), The scores of the patients on this experiment are reported in Figure 3.7. Both apraxic patients performed equally well on this task (FG:

45/47, 96%, and DR: 47/47, 100%). In contrast, DL gave correct responses to 33 (70%) and AM to 28 questions only (60%). DL and AM performed significantly worse than both FG (Wilcoxon, p < .01 and p < .001 respectively) and DR (Wilcoxon, both p <.001). The experiment was administered for a second time to all patients replicating the same results (FG: 47/47, 100%, and DR: 46/47, 98%; DL: 36/47, 76.5% AM: 27/47, 57%) (see Figure 3.7).

Figure 3.7. Patients' and controls' overall accuracy on Experiment 2. The task was performed twice, in two different sessions. FG and DL performed the two sessions one month apart, whereas AM and DR were tested two years later.



Experiment 3a (Simple Object Use). The four patients were required to use 23 objects in a simple context. The errors of the patients are reported in detail in Table 3.2. FG and DR committed 18 and 11 errors respectively, as evaluated by three independent raters. This was in sharp contrast with their performance on the semantic tasks (Experiments 1-2).

As to the demented patients, DL's performance in Experiment 3a was errorless, whereas AM made 2 errors: one was an argument error (she twisted the pencil sharpener instead of the pencil), and one orientation error (she used the saw with an appropriate movement but keeping the blade upside-down).

Table 3.2. Patients' errors in experiment 3a (simple object use)

Type of error	AM	DL	FG	DR
Misuse	-	-	2	6
Argument	1	-	4	-
Mislocation	-	-	7	-
Tool substit.	-	-	1	-
Sequence	-	-	2	1
Grasping	-	-	2	3
Orientation	1	-	-	-
Body Part as Tool	-	-	-	1

Experiment 3b (Multiple Object Tasks). FG executed the first two activities flawlessly although he had some problems in folding the paper to put it inside the envelope when preparing the letter to post. When lighting the candle, FG first had difficulty in opening the matchbox, then he broke the match and initially attempted to light the wrong end of the candle. To avoid burning his fingers, he lit another match with which he now approached the candle holder; then he put the match into his mouth. He made a second attempt to light the candle at the wrong end and then eventually succeeded. As far as DR's performance was concerned, he was able to make coffee and to prepare the letter to post, but when requested to light the candle he made many mistakes, including scratching the match using an inappropriate movement and trying to light the candle with the unlit match. The type of errors committed by FG and DR has been previously observed in other ideational apraxic patients (De Renzi and Lucchelli, 1988). DL and AM instead were surprisingly competent when using objects both in a simple and complex context, despite their lack of knowledge of the functions of a number of objects. DL made no errors, while AM made one step omission (she did not seal the envelope) and one misuse error (she folded the letter in a wrong manner). AM's type of errors were comparable to those of normal subjects doing the same tasks (see Table 4.d. In Chapter IV). Combining the performance on the two Experiments we found that FG made significantly more errors

than either DL ($\chi^2 = 7.53$, $p < .01$ one-tailed) or AM ($\chi^2 = 24.23$, $p < .001$ one-tailed). DR also made more errors than DL ($\chi^2 = 3.33$, $p < .05$ one-tailed) and AM ($\chi^2 = 17.5$, $p < .001$ one-tailed).

Experiment 4a (Object Naming). FG correctly named all the objects employed throughout the study (23/23, 100%), and DR named correctly only 12/23 objects (52%). FG's performance suggests that it is possible to retain a perfect ability to name objects and yet being unable to use them properly. DR was impaired in object naming due to his severe Broca's aphasia, but when the task required pointing (Experiment 2) or simple yes/no responses (Experiment 1), he showed full knowledge of objects and their parts. DL could name only 56% (13/23) of the objects correctly, and AM 15/23 (65%), and they also showed a significant loss to their semantic, functional and parts knowledge (see Experiments 1 and 2).

Experiment 4b (Word-Picture Matching). This task was devised to verify whether the naming problem of patients DR, DL and AM was a purely nominal one. FG and DR correctly matched the name of each object to the target when it was presented together with two semantically related items (23/23, 100%). DL, however, was successful on 83% (19/23), and AM on 100% of the trials. These data confirm that DR's deficit in Experiment 4a was due to a retrieval problem, whereas the performance of one of the two demented patients was pathological compared to that of normal controls.

Experiment 5 (parts a and b). These experiments were carried out in order to verify whether IA patients were able to name or recognize the actions that they could not perform. In Experiment 5a (Pantomime Naming), patients were asked to name the pantomimes of object use performed by one of us without the object. FG performed more accurately (20/21, 95%) than DR (9/21, 43%), DL (15/21, 71%) and AM (12/21, 57%)

(Wilcoxon, p < .05 in all comparisons). Unlike DR, DL, and AM, FG was able to correctly retrieve the action names associated with the pantomimes. Experiment 5b (Pantomime-Object Matching) was administered to ascertain whether the difficulties emerged in naming pantomimes were purely due to aphasia or to a faulty pantomime recognition. In this test, FG and DR performed at ceiling (both 21/21, 100%) while DL and AM both scored 19/21 (90%).

LESION ANALYSIS

Procedure

<u>Patient FG.</u> This lesion reconstruction was performed in two main steps:

Step 1: MRIcro software[10] was used by an expert neuroradiologist (Dr. Maja Ukmar), who was unaware of the patients' symptoms, to draw FG's lesion on his original MR scan.

Step 2: FG's brain scan and his lesion have been spatially normalized to the stereotaxic space using SPM2 software[11]. In order to prevent its possible effect on SPM normalization routines, the cerebral lesion was masked using cost function masking as described by Brett et al. (2001). This procedure allows aligning the patient's scan to the stereotaxic space, and avoids possible distortions caused by the presence of the lesion. The resulting image is shown in Figure 3.1. (red area).

<u>Patient DR.</u> For DR, the software did not allow us to perform the same normalization procedure as it could not overcome the considerable size of his lesion. Therefore, the neuroradiologist (M.U.) drew DR's lesion directly onto the standard MRI template provided by MRIcro. The resulting image of DR's lesion is reported in Figure 3.2. (red area).

---

[10] http://www.mricro.com

[11] http://www.fil.ion.ucl.ac.uk/spm/

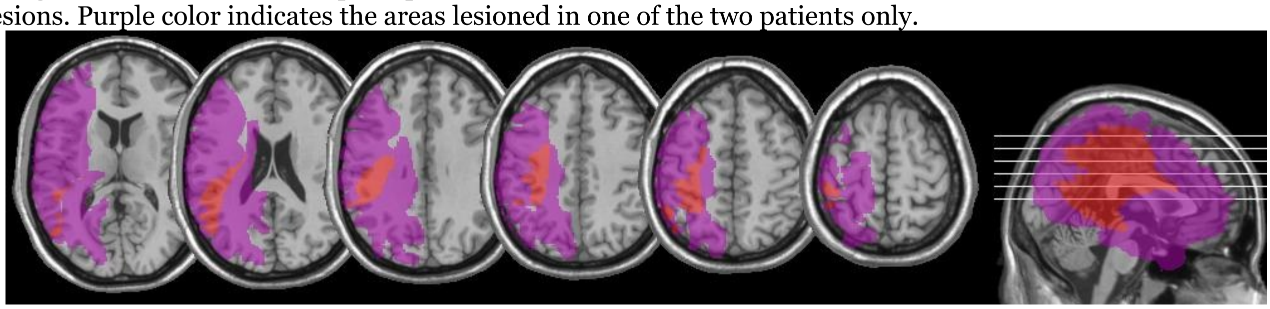
FG's and DR's lesions overlap. The previous steps allowed us to map FG's and DR's lesions as Regions Of Interests (ROIs) aligned on the same stereotaxic space. The following procedure allowed us to overlap them and identify the brain areas lesioned in both patients.

Step 1. Using the ROI Intersection option provided by the software, it was possible to identify a new ROI consisting of the areas lesioned in both the patients: the resulting image is provided in Figure 3.8.

Step 2. The lesioned areas have been identified both using the Automated Anatomical Labelling map (Tzourio-Mazoyer et al., 2002) provided by the MRIcro software and with reference to the atlas of Duvernoy (1991).

AM and DL**.** The ROI reconstruction procedure was not appropriate for AM and DL due to the fact that they had atrophy instead of localized lesions. The brain scans have been therefore interpreted by the neuroradiologist, as reported in the following paragraph.

Figure 3.8. Lesions overlap for patients FG and DR. The red area indicates the intersection of the two lesions. Purple color indicates the areas lesioned in one of the two patients only.



Lesions Results

Both demented patients showed brain atrophy in frontotemporal regions (see Figures 3.3. and 3.4.), consistently with their degenerative disease (Mummery et al. 2000; Mummery et al., 1999). Figure 3.3. shows a MR-scan performed on DL on September 2000, which revealed bilateral temporal lobe atrophy, greater in the left temporal pole and Perisylvian areas. Two neuroradiological scans were available for patient AM: a

SPECT, performed in 2002 (not reported here) revealed cortical atrophy restricted to the left temporal region; and a new MR scan performed 2005, that revealed widened liquoral spaces in the ventricular and subaracnoidal areas and in fronto-temporo-parietal regions bilaterally, greater in the left hemisphere (see Figure 3.4.).

For the two apraxic patients, the MR scans have been analyzed using MRicro software: the procedure to identify the cortical brain structures involved in the lesions is described in detail in the previous section. Results show that the brain areas lesioned in both FG and DR included the superior part of the left middle temporal gyrus, superior temporal gyrus, angular gyrus, supramarginal gyrus, inferior parietal cortex, postcentral gyrus and precentral gyrus (see Figure 3.8.).

DISCUSSION ON STUDY 3A

On a variety of occasions, FG and DR failed to use common objects correctly. Moreover, their impairment was at a higher level within the system controlling actions (*i.e.* they did not show ataxia or motor deficits in the ipsilesional hand). However, both patients could identify the objects and they retained a very substantial amount of specific functional and manipulation knowledge as well as general semantic information. Indeed they both performed virtually at ceiling on all these tests. DL and AM, on the other hand, could use almost perfectly objects that were problematic for the two apraxic patients. Unlike apraxic patients, DL and AM did not have a full detailed semantic knowledge about objects. This classical double dissociation pattern (see Shallice, 1988) strongly suggests that a higher-level motor knowledge of manipulable objects may be represented separately from semantic knowledge. The double dissociation reported here is in contrast with the embodied theories of conceptual knowledge, for which the semantic meaning of a concept is highly dependent on its re-enactment (also called *simulation*) in the sensory-motor system (e.g. Gallese and Lakoff, 2005). Instead, such a pattern of results is in line with models that postulate a separation between conceptual knowledge and motor abilities, like the distinction between the “what” and “how’ pathways described in the Introduction, but also like Rothi et al.’s (1991) model of apraxia. In particular, DR and FG’s error profiles in using objects (Rumiati et al., 2001) have been analyzed and discussed in a similar framework by Cooper (2007), which hypothesizes in these apraxic patients a disconnection between the action schema network and the object network, within Contention Scheduling.

Study 3B

A Follow-Up Study on Patients AM and DL

Introduction

In this section we report a two-year longitudinal study in which we assessed the ability to use objects of DL and AM two years after the assessment reported in study 3A, as well as their lexical-semantic knowledge concerning the same objects. The aim of this second study was to verify whether the dissociation observed in study 3A maintained consistency over time, given the possible worsening of their symptoms. Evidence that the integrity of semantic knowledge is not sufficient to support tool use comes from observation of patients with IA (see study 3A and Rumiati et al., 2001; Buxbaum et al., 2000; Hodges et al., 1999; Ochipa et al., 1989).

METHODS

Participants

Patients. AM and DL were tested first in April-July 2002 (see study 3A) and subsequently in May-August 2004. The testing was carried out in the hospital's neuropsychology room as well as at the patients' home, in three-four different sessions that lasted about two hours each.

Controls. The performance of patients in Experiments 2-5 of the study was compared with that of twenty individuals (10 males and 10 females) matched for age (mean = 61.1 years, SD = 9.45 years) and education (mean = 9.7 years, SD = 3.3 years).

General Neuropsychological Assessment

Results of AM and DL on the neuropsychological assessment are reported in Table 3.3.

•*Orientation in time and space*. AM was well-oriented in space and time in 2002, while in 2004 she was slightly disoriented in time (she was unsure about the current year but showed no problem in reporting the season as well as the month), but not in space. DL was well-oriented in time and space in both evaluations.

•*Language*. Linguistic abilities were affected in both patients on the Aachener Aphasie Test (Luzzatti et al., 1996); in particular, their naming ability was severely impaired. In 2002, repetition, comprehension, reading, and writing skills were well-preserved in patient DL. In 2002 AM showed a deficit in repetition particularly of long sentences, suggesting a deficit in maintaining verbal information for short time periods. She was also impaired in the Token subtest of the AAT, revealing a deficit in comprehension of simple orders. In 2004 only a short version of the AAT could be administered to DL, whereas AM resulted impaired also in writing and in sentence comprehension, as compared to the previous evaluation.

•*Memory*. Spatial (Corsi test, De Renzi and Nichelli, 1975) and verbal short-term memory (digit span, WAIS), and working memory (backwards digit span, WAIS) were in the normal range for both patients, in 2002 as well as in 2004 evaluation. However, they were both found to have severe anterograde memory deficits, as suggested by their performance on a recognition memory test which employs words as well as faces (Warrington, 1996), and as indicated by the results on the Auditory Verbal Learning test (Rey, 1964). During the clinical interview, both patients had no difficulty in reporting autobiographical data and information about their relatives. They were also accurate in describing their usual daily activities and recent personal events.

•*Non-verbal intelligence* (Raven CPMs, 1984). Non-verbal intelligence was stable across evaluations, being within the normal range for DL and in the low average range for AM.

• *Vision.* In contrast to AM, who performed below the cut-off on the Incomplete Letter test (VOSP, Warrington and James, 1991) in 2002 as well as in 2004, DL's visual processing resulted well-preserved in both evaluations.

In the following paragraphs, a brief description of the tests aimed at investigating the semantic memory and praxic abilities of the two patients is provided, followed by the results.

Table 3.3. Patients' scores on the general neuropsychological assessment. The **bold** character indicates pathological scores. Symbol "*" connotes skills that deteriorated in the second evaluation; "a.s." = adjusted score; "PR" = percentile rank; "n.a." = test not administered.

			AM		DL		Cut Off
			2002	**2004**	**2002**	**2004**	
	MMSE			**15/30**		**21/30**	
Intelligence	Raven's CMT	Total score	**17.4 a.s.**	19.2 a.s.	31	32.5 a.s.	18.96
Language	AAT	Token Test (PR)	**68**	77	91	n.a.	
		Repetition (PR)	**74**	**64**	94	46/50	
		Writing (PR)	84	**71**	75	n.a.	
		Naming (PR)	**61**	**56**	**60**	n.a.	
		Comprehension (PR)	81	**39**	85	9/10*	
Linguistic Fluencies		For letters	20.6	**14.4**	n.a.	**0**	17.35
		For semantic categories	11.5	7.25		**0**	7.25
Visual Processing	VOSP	Screening Test	18	17	18	20	15
		Incomplete letters	**12**	**10**	17	n.a.	16
		Object decision	16	**7**	16	15	14
Memory	Short-term	Corsi test	**2.25 a.s.**	4.25 a.s.	5	5	
		Digit span forward	5.5 a.s.	4.5 a.s.	4	5	
		Backward	3	3	n.a.	3	
	Long-term	Rey-words Immediate recall	**18**	**16 a.s.**	n.a.	n.a.	28.53
		Delayed recall	**3.4**	**0**	n.a.	n.a.	4.69
		Recognition corr.	**12/46**	**17/46**	n.a.	n.a.	
		False recognitions	**23**	**27**	n.a.	n.a.	
		Word recognition memory	n.a.	**28/50**	**28/50**	**26/50**	
		Face recognition memory	**16/25**	**16/25**	**12/25**	n.a.	

*reading words

Semantic Memory Assessment

• *Picture naming* (Laiacona et al., 1993). Patients were asked to name 80 line drawings presented in a random order. As in the original study (Laiacona et al., 1993), synonyms and other acceptable nouns were scored as correct responses. AM's and DL's performance on this task was severely impaired in both evaluations (see Table 3.4.), making semantic paraphasias and omissions.

Following Laiacona et al. (1997) procedure, patients' scores were submitted to a logistic regression including a categorical variable (category: living vs. non-living items) and continuous variables (familiarity, word frequency and prototypicality) in order to partial out the effect of possible confounds. AM did not show a significant effect of category neither in 2002 nor in 2004 ($P > .05$ for both comparisons on a Chi-square test, df = 1), even when the effect of psycholinguistic variables was partialled out. However, her performance was affected by word frequency in 2002 (Chi-square = 4.8, df = 1, $P < .05$) as well as in 2004 (Chi-square = 8.54, df = 1, $P < .01$).

DL showed, both in 2002 and in 2004, a significant effect of category, in that he named nonliving better than living items (in 2002: Chi-square = 5.99, df = 1, $P < .05$; in 2004: Chi-square = 7.4, df = 1, $P < .01$), as well as a significant effect of word frequency (in 2002: Chi-square = 10.29, df = 1, $P = .001$; in 2004: Chi-square = 18.88 df = 1, $P < .001$). In 2004 his naming performance was significantly predicted also by the familiarity of the stimulus (Chi-square = 4.22, df = 1, $P < .05$).

Patients' accuracy in naming was consistent over time (DL: consistency coefficient = .40, Chi-square = 14.9, $P < 0.001$; AM: consistency coefficient = .49, Chi-square = 25.2, $P < 0.001$). As compared to 2002, DL's naming performance in 2004 worsened significantly, but not that of AM (Mc Nemar test, $P < .05$, and $P > .05$, one-tailed, respectively). Results are reported in Table 3.5.

• *Word to picture matching* (Laiacona et al., 1993). Patients were asked to point, among five pictures (one correct and four foils), to the one named by the examiner. This task was presented in two different conditions: within-category, with foils belonging to the same category of the target, and between-categories, with foils belonging to categories different from that of the target. Patients' scores and cut-offs are reported in Table 3.4. Both patients performed below the normal range in 2002 as well as in 2004 in the within-category, but not in the between-categories condition. Compared to that in 2002, AM's performance worsened in 2004 in the within-category condition (McNemar test, $P < .05$) but not in the between-categories condition ($P > .05$). DL scored worse in 2004 than in 2002 in the within-category condition ($P < .05$). In 2004 he was not administered with the between-categories condition (see Table 3.4.).

• *Pyramids & Palm Trees test* (Howard and Patterson, 1992). In this test, patients were required to indicate, between two foils, the one semantically related to the target (e.g. pyramid: palm tree or pine?). Two versions of the test were administered, one using written words and the other using pictures as stimuli. AM and DL scored below the normal cut-off in performing either versions in 2002 as well as in 2004, but only DL's performance on the second evaluation was significantly lower than that on the first evaluation (McNemar test, $P < .05$) performing at chance level when pictures were used (the verbal version was administered only in 2002). Results are reported in Table 3.4.

• *SISSA Object Semantics* (SOS). This test was created in order to investigate the patients' integrity of the knowledge about function and manipulation of objects. Three line drawings depicting objects were shown on a sheet to the patient, who was required to identify the two objects that shared either the same manipulation (e.g. a typewriter and a piano) or the same function (e.g. a piano and a radio). The same test was administered also verbally using written words as stimuli, according to an ABBA design. Results are reported in Table 3.4. AM made more errors in 2004 than in 2002 (McNemar test, $P < .001$ for both verbal and visual versions). DL was administered the test only in 2002 and he made errors. No differences between the performance in the verbal and the performance in the visual condition were found for either patient (see Table 3.4.).

Table 3.4. Patients' performance on different tests assessing semantic memory. The **bold** character indicates pathological scores.

SEMANTIC MEMORY		AM 2002	AM 2004	DL 2002	DL 2004	Cut-off
Laiacona et al. (1993)	Naming	**40/80 (50%)**	**30/80 (38%)**	**32/80 (40%)**	**18/80 (23%)**	61/80
	Comprehension between-cat.	79/80 (98%)	75/80 (93%)	79/80 (98%)	n.a	93%
	Comprehension within-cat.	**73/80 (91%)**	**71/80 (89%)**	**65/80 (81%)**	**40/80 (50%)**	93%
Pyramids & Palm Trees Test	Words	**41/52 (79%)**	**38/52 (73%)**	**40/52 (77%)**	n.a	48
	Pictures	**35/52 (67%)**	**39/52 (75%)**	**38/52 (73%)**	**26/52 (50%)**	48
SISSA Object Semantics:						
Manipulation knowledge	Words	**8/17 (47%)**	**6/17 (35%)**	**9/17 (53%)**	n.a	
	Pictures	**10/17 (59%)**	**7/17 (41%)**	**9/17 (53%)**	n.a	
Function knowledge	Words	**15/17 (88%)**	**8/17 (47%)**	**10/17 (59%)**	n.a	
	Pictures	**13/17 (76%)**	**10/17 (59%)**	**11/17 (65%)**	n.a	

Semantic Memory: Discussion

Based on the results on the naming task, the within-category and across-categories word-to-picture matching tasks, the Pyramids and Palm Trees test and the S.O.S, we conclude that both AM and DL had a deficit affecting their semantic memory and that this deficit is progressively worsening.

The deficit is not modality specific, as patients have comparable difficulties when pictures and words are used as stimuli. Moreover, the logistic regression analyses revealed an influence of word frequency on naming accuracy, and patients' performance was consistent over time. The effect of word frequency increased with time, compatibly with the progression of the illness. The multi-modality of the deficit, the word-frequency effect and the consistency across evaluations are three criteria that Warrington and Shallice (1979) proposed for correctly diagnosing a semantic deficit at the central level, as opposed to a mere deficit in accessing semantics. Thus our analyses confirmed that the deficits of AM and DL are within the semantic system.

Apraxia Assessment

• *Ideational Apraxia* (De Renzi and Lucchelli, 1988). This test is commonly used in the clinical assessment for establishing the presence IA. Patients are asked to show how they would use seven common objects. For each item, 2 scores are assigned if patients perform correctly on the first attempt, 1 if they succeed on the second attempt, and zero if they fail on all occasions (maximum score = 14). In 2002 both patients performed normally but in 2004 they both made a few errors thus falling below the normal cut-off (see Table 3.5.).

• *Ideomotor Apraxia* (De Renzi et al., 1980). This test has been devised in order to diagnose the presence of ideomotor apraxia, defined as a selective deficit in imitating actions. Patients were requested to imitate the gestures performed by the examiner. They were given three attempts to imitate an action correctly, scoring from 3 to 0 points, for a maximum of 72. AM was borderline in 2002, whereas in 2004 she performed below the cut-off, being unable to imitate both meaningful (e.g. the sign of the cross and the military salute) and meaningless actions, such as alternating the fist and the open palm consecutively. DL performed within the normal range in both evaluations (see Table 3.5.).

Table 3.5. AM's and DL's results on the clinical assessment of praxis. The **bold** character indicates pathological scores.

			AM		DL		
			2002	**2004**	**2002**	**2004**	**Cut-off**
Praxis	Imitation	Ideomotor Apraxia (De Renzi et al., 1980)	60/72	**48/72**	67/72	64/72	53
	Object use	Ideational Apraxia (De Renzi and Lucchelli, 1988)	14/14	**10/14**	14/14	**11/14**	14

Experiment 1: Object Use

AM and DL were asked to show the correct use of twenty-three common objects (see Appendix 3a) by performing 21 actions (see Appendix 3b). Performance of AM and DL was videotaped and subsequently scored by two independent judges and use was classified as correct/incorrect with 0 or 1 score. Even partially incorrect actions (e.g. doing the correct distal movement but holding the object in a clumsy fashion, or vice-versa) were scored as 0. The inter-rater agreement revealed no discordances between the two raters (Kappa-Cohen test, $P > 0.05$ for all comparisons). AM scored 20/22 (91%) in 2002, and 19/23 (83%) in 2004, indicating that her ability to perform everyday activities with common objects was largely preserved (McNemar test, $P > .05$). DL performed flawlessly (23/23; 100%) in 2002, and two years later he could use 20/23 (87%) objects correctly (McNemar test, $P > .05$), six[12] of which he claimed not to be able to use because he did not know what they were. However, when he was persuaded to try, he resulted surprisingly skilful. According to the error classification criteria put forward by De Renzi and Lucchelli (1988) and Rumiati et al.(2001), AM in 2004 made two *omissions* and two *mislocations*[13]. In contrast, DL refused to use three objects (orange squeezer, pencil sharpener and cigarette) even after several requests made by the experimenters.

Under normal circumstances, healthy individuals are at ceiling when they use familiar objects, making no errors. These findings indicate that both patients' ability to use objects did not decline significantly over time, despite a trend toward worsening.

Experiment 2: Object Naming

Patients were requested to name the same 23 objects used in Experiment 1, without the possibility to touch them. AM named 15/23 (65%) objects in 2002 and 11/23 (48%) in 2004, with no significant difference between the two evaluations (McNemar test, $P > .05$). DL named 13/23 (56%) and 2/23 (9%) objects in 2002 and 2004 respectively, indicating that his lexical retrieval worsened dramatically during this period (McNemar test, $P < .001$).

---

[12] Toothbrush, light bulb, match and matchbox, key and padlock, screwdriver, comb.

[13] *mislocations*: she turned the socket instead of the light bulb; she placed the spanner above the bolt head. *Omissions:* she did not remove the cap of the toothpaste before squeezing it on the toothbrush; she tried to open the padlock without inserting the key.

Experiment 3: General Semantics

Coloured pictures of objects (N = 22) as well as their written names (N = 22) were presented to patients and controls, one at a time on a single card. The 22 items were the same as in Experiment 1 except for the matchbox. Five or six questions were posed orally to the subjects for each item without giving them any feedback (see Laiacona et al., 1993), for a total of 131 questions for both visual and verbal condition. For the item *"hammer"* the questions asked were the following:

- general superordinate: *is it an object, an animal or a plant?*;
- same category superordinate: *is it a tool, a musical instrument or a precious stone?*;
- perceptual subordinate *is it made in glass, in metal or in cement?*;
- comparative perceptual subordinate: *is it smaller than a screw?*;
- associative functional subordinate: *is it used for screwing, for cutting or for driving nails?*;
- associative contextual subordinate: *is it used by the painter, by the carpenter or by the glassworker?*.

Table 3.6. Results on Experiment 3 (Object general semantics). Z-scores are calculated based on the control group. Symbol * indicates scores significantly worsened in 2004 evaluation (McNemar test, p<.05). The **bold** character indicates pathological scores. Controls: verbal: M=130,37, DS=0,83; visual: M=130,42; DS=0,9.

	DL			AM			
	2002		2004	2002		2004	
	Verbal	Visual	Visual	Verbal	Visual	Verbal	Visual
Raw score	**113/131**	**119/131**	**107/131**	**111/131**	**109/131**	**89/131***	**96/131**
%	**86%**	**91%**	**81%**	**85%**	**83%**	**67%**	**73%**
Z scores	**(z= -20)**	**(z=-8.4)**	**(z=-17.5)**	**(z=-22.3)**	**(z=-16)**	**(z=-47.7)**	**(z=-25.8)**

Patients' accuracy on the semantic questionnaire is summarised in Table 3.6. Comparing patients' evaluations in 2002 and 2004, AM's performance when words where used as stimuli worsened with time (McNemar test, $P < .05$). In contrast, in 2004 DL did not show a significant decrease in performance compared to 2002 (McNemar test, $P > .05$). Compared to the control group, AM and DL performed pathologically in all conditions, both in 2002 and in 2004 (Z scores are reported in Table 3.6). The differences in performance on the visual and the verbal versions of the test were not found significant for either patient (see Table 3.9.).

Experiment 4: Knowledge of Parts

In this experiment, a set of 47 questions concerning the functions of different parts of the same 23 stimuli used in Experiment 1, were read aloud by the experimenter. For each question, patients and control subjects (N = 20) were presented with four colour photographs of identical objects differing only in the position of arrows pointing to different parts of the object itself (see Figure 3.5.). They were required to point to the photograph with the arrows indicating the part of the object corresponding to the described function. AM scored 8/23 (35%) in 2002 (z = -5.7) and 9/23 (39%) in 2004 (z = -5.1), and DL 16/23 (69%) in 2002 (z = -2.5) and 13/23 (57%) in 2004 (z= -3.1). The difference in performance between the two sessions was not significant for either patient (McNemar test, $P > 0.05$).

AM and DL performed worse than the control group in both evaluations but their accuracy did not decrease significantly in the second as compared to the first evaluation.

Experiment 5: Manipulation Knowledge

In this experiment patients and the twenty controls saw on a computer screen either the photographs of 20 objects used in Experiment 1 or, in a different block, their names, as well as three videotaped pantomimes, each lasting about 6 seconds, in sequence. Their task was to say which video demonstrated the correct use of the target object.

In 2002, AM identified correctly 11/20 (55%) manipulations in the verbal condition (z = -10.9) and 17/20 (85%) in the visual condition (z = -2.9), whereas in 2004 she scored 14/20 (70%; z = -6.9) in the verbal (McNemar test, $P > .05$) and 9/20 (45%; z = -13.1) in the visual condition (McNemar test, $P < .01$). The difference in accuracy between verbal and visual condition was not significant neither in 2002 nor in 2004 (see Table 3.9).

In 2002, DL identified 16/20 (80%) manipulations in the verbal condition (z = -4.26) and 18/20 (90%) in the visual condition (z = -1.64), whereas in 2004 he scored 12/20 (60%; z = -9.3) in the visual condition (McNemar test, $P > .05$). There was no difference between verbal and visual presentation (see Table 3.9). The verbal version was not administered in 2004.

These results indicate that, compared with normal controls, the two patients were impaired in recognizing actions. The same deficit, called pantomime agnosia, has been reported before by Rothi et al. (1986) and by Cubelli et al. (2000).

Further Analyses

Object use and semantics

In this section, performance of object use (Experiment 1) has been compared to that of the other experiments in which different aspects of object knowledge were tested (on a Wilcoxon signed rank test). The results are summarised in Table 3.7. Object use was significantly better than performance on many of the other experimental tasks. Patients' ability to use objects and that to choose their correct manipulation (Experiment 5) seem to be equally affected, irrespective of whether words or pictures were used. The fact that in Experiment 5 patients were not as impaired as in the other semantic tasks reflects the intactness of a praxicon component (see Rothi et al., 1991), independent of verbal and visual semantic object knowledge.

Table 3.7. P-values associated to a Wilcoxon signed rank tests are reported. In this test AM's and DL's performance on object use was compared to performance on the other experiments. Given the high number of comparisons, the α value was set at .01. The key result is that performance on object use is better than that on the other tasks in most contrasts. "n.a." = not administered; "n.s" = not significant.

	Object Use (Exp. 1)			
	AM		DL	
Experiment	**2002**	**2004**	**2002**	**2004**
Exp.2 (object naming)	n.s.	n.s.	<.01	<.001
Exp. 3 (general semantics/words)	<.01	<.001	<.001	n.a.
Exp. 3 (general semantics/pictures)	<.01	<.001	<.001	<.05
Exp.4 (semantic of parts)	<.01	n.s.	<.01	n.s.
Exp. 5 (manipulation/words)	n.s.	n.s.	n.s.	n.a.
Exp. 6 (manipulation/pictures)	n.s.	n.s.	n.s.	n.s.

Consistency item-by-item analysis between tasks

An item-by-item consistency analysis across tasks was carried out with the aim of establishing whether patients failed or succeeded with the same items across tasks, or whether the deficit randomly affected different items in different tasks. None of the statistical tests led to a significant result (see Table 3.8.), clearly indicating that the lack of semantic and functional knowledge about objects does not necessarily prevent correct object use.

Table 3.8. Consistency analysis comparing the performance in object use with the other experiments. Object use can be considered largely independent from the other abilities. C = Contingency coefficient; "n.a." = not administered.

	Object Use (Experiment 1)			
	AM		DL	
Experiment	2002	2004	2002	2004
Exp.2 (object naming)	C = .29 Chi-square = 1.95 *P* > .01	C = .20 Chi-square = 1.01 *P* > .01	C = .22 Chi-square = 1.23 *P* > .01	C = .14 Chi-square = .46 *P* > .01
Exp. 3 (general semantics/words)	C = .04 Chi-square = .04 *P* > .01	C = .10 Chi-square = .22 *P* > .01	C = .13 Chi-square = .37 *P* > .01	n.a. in 2004
Exp. 3 (general semantics/pictures)	C = .23 Chi-square = 1.21 *P* > .01	C = .08 Chi-square = .15 *P* > .01	C = .15 Chi-square = .56 *P* > .01	C = .04 Chi-square = .04 *P* > .01
Exp.4 (semantic of parts)	C = .29 Chi-square = 1.99 *P* > .01	C = .32 Chi-square = 2.62 *P* > .01	C = .28 Chi-square = 2.09 *P* > .01	C = .06 Chi-square = .08 *P* > .01
Exp. 5 (manipulation/words)	C = .35 Chi-square = 2.59 *P* > .01	C = .05 Chi-square = .06 *P* > .01	C = .37 Chi-square = 3.36 *P* > .01	n.a. in 2004
Exp. 6 (manipulation/pictures)	C = .15 Chi-square = .42 *P* > .01	C = .20 Chi-square = .81 *P* > .01	C = .48 Chi-square = 6.3 *P* >.01	C = .34 Chi-square = 2.55 *P* > .01

Table 3.9. P-values associated to a Wilcoxon signed rank test, comparing AM's and DL's performance on the verbal and the visual version of the tasks. Bold character indicates significant differences. "n.a." = not administered.

	Patient AM		Patient DL	
Experiment	**2002**	**2004**	**2002**	**2004**
Exp.3 (General semantics)	>.01	>.01	>.01	*
Exp. 5 (Manipulation knowledge)	>.01	>.01	>.01	*
SISSA Object Semantics				
function	>.01	>.01	>.01	n.a.
manipulation	>.01	>.01	>.01	n.a.

DISCUSSION OF STUDY 3B

In this section we have compared the two evaluations, in 2002 and 2004, of patients AM and DL, considering their general cognitive abilities as well as semantic and motor knowledge about a set of objects. The neuropsychological investigation revealed that the two patients had a semantic impairment but relatively normal non-verbal intelligence, visual and spatial short-term memory, visual processing and praxis (see Tables 3.3., 3.4 and 3.5.). While DL's severe language deficits remained his prominent impairment over the period in which he was examined, with little change in his general cognitive abilities, AM showed a more general deterioration at the second evaluation, involving also visuo-perceptual skills and praxis abilities. Given the extention of the impairment to non-semantic functions, it is possible that the case of AM is better described as a patient with a dementia of Alzheimer type with an atypical onset, whose early signs of pathology were focal and primarily involved language skills (see Galton et al., 2000; for a similar case Greene et al., 1996). The magnetic resonance performed in 2005 seems to support this interpretation showing a diffused cortical atrophy. Despite the fact that in 2004 AM's deficit was no longer "purely" semantic, the strong dissociation (see Shallice, 1998) between object use and object knowledge remained significant.

Overall, study 3B showed that AM and DL's performance on object use was significantly better than that on tasks tapping verbal and semantic knowledge about them, showing a strong dissociation (see Shallice, 1988), but it was as impaired as the ability to recognize the correct manipulation of objects (Experiment 5) (see Table 3.7.). Nevertheless, an item-by-item consistency analysis (Table 3.8.) showed that patients were also able to use objects (Experiment 1) for which they did not retain general semantic knowledge at all (Experiments 3 and 5) or even functional knowledge of their parts (Experiment 4). For example, in 2004, when requested to use a spanner, a match, a key and a light bulb, after showing distress for he did not know what those objects were, DL managed to use them correctly. Though it could be argued that object use may also rely on a non-semantic route in which affordances are elicited directly from the object structure (see Hartmann et al., 2005; Hodges et al., 2000; Goldenberg and Hagmann, 1998; Gibson, 1977), this explanation cannot account for instances in which object manipulation cannot be inferred from its shape. For example, in 2004, when a match -whose purpose and use cannot be readily inferred from its shape and structure- was posed in front of DL, he said: “I don’t know, I’ve never seen it before and I do not even know what this thing is used for”. Nevertheless, when the experimenter asked him to try to use it anyway, he could light it by scratching it against the matchbox, and then he blew it out correctly. Note that this is a task in which IA patients are highly prone to errors, despite their intact object knowledge about the objects presented (see Rumiati et al., 2001 and study 3A). In addition, DL in 2004 clearly showed to know very little about the aforementioned objects, as he failed to name them in Experiment 1 and to answer to specific questions concerning them in the Experiments 3-4-5. Similarly, in 2004 AM was able to use six objects for which formal testing demonstrated that she did not retain neither semantic, nor functional or manipulation knowledge (Experiments 3-4-5). Thus our findings are at variance with the claim that the conceptual knowledge and problem solving abilities play a critical role in determining the success of object use (Bozeat et al., 2002; Hodges et al., 2000; Coccia et al., 2004; Goldenberg and Hagmann, 1998).

DISCUSSION OF CHAPTER III

In order to account for the neuropsychological findings reported in these two studies, the functional dichotomy put forward by Goodale and Milner needs to be extended beyond low-level perception and reaching-grasping activities respectively. Thus, besides perception, the ventral "what" system may also carry the conceptual knowledge used, for instance, in tasks tapping functional-semantic knowledge of objects, as well as in naming tasks. By contrast, the dorsal "how" system may contain the representation of affordances, namely the learned associations between objects and the basic motor components necessary for their use, such as the orientation and the shape of the hand grip (Grèzes et al., 2003; Tucker and Ellis, 1998; 2001; Ellis and Tucker, 2000). In addition, these findings suggest that the "how" system also involves higher-level action representations acquired by past experience, which are selected at appropriate times when elicited by environmental triggers (Cooper and Shallice 2000; Rumiati et al., 2001; Cooper, 2007). In his computational model of DR and FG's behaviour, Cooper (2007) predicts indeed that the action-relevant object representations (storing the visual and perceptual features of objects) and the action schemas (coding the appropriate movement for a given goal) are two separated networks. Such object representations can also be considered separate from semantic-encyclopaedic knowledge, which is impaired in patients with temporal lesions like AM and DL. Considering the patients that we tested, normal performance in semantic tasks is possible in the presence of a deficit in action tasks, and *vice versa*. Based on these observations, one can suggest that the two systems are at least partially separable and that, although in some circumstances they may interact (e.g. in a SRC task), damage to one of them does not lead to a significant damage to the other. In particular, I have shown that a deficit in tool use and manipulation does not necessarily affect neither the verbal/functional knowledge of objects, nor the recognition of the relative pantomimes. The imaging data on tool use (see Chapter V for a discussion, but also Johnson-Frey,

2004) are in line with the behaviour of patients like FG and DR, whose lesions overlapped in the left posterior parietal cortex.

Some authors have argued that patients who are still able to use objects despite having a semantic loss may rely on visual and/or tactile affordances or on trials and errors strategies (e.g. Hodges *et al.*, 2000). It has also been proposed that the loss of knowledge about an object is generally associated to the failure in its use (e.g. Coccia et al., 2004; Bozeat et al., 2002; Hodges et al., 2000). Our results with AM and DL (studies 3A and 3B) seem to be at variance with the above view: we propose that semantic and motor knowledge of an object, although they usually interact, may be represented separately in the brain. In our patients the two abilities seem to decline independently. AM and DL's performance on object use is significantly better than on other semantic tasks and they are still able to use objects for which the semantic properties are lost. Their failure of object use is not simply because this task is easier than the semantic tasks, as their performance double dissociates (see Shallice, 1988) with that found in patients with IA, in whom the ability to use objects is impaired despite a preserved semantic knowledge about the same objects (Rosci et al., 2003; Rumiati et al., 2001; Rapcsack et al., 1995; Schwartz et al., 1995). We cannot excude that AM and DL's spared ability to use objects is based on preserved visuomotor transformations that rely on parietal lobe structures. In any case, this would further confirm the idea of fractionation of the system components. It would be in conflict with the embodied view that considers the motor system necessarily ingaged in semantic processing. Still, The object-actions associations (praxemes and/or action schemata) can be seen as motor properties of a "leopard spots" distributed object representation, and they are held to be at fault in IA patients (see Rumiati *et al.*, 2001), whereas they are preserved in AM and DL.

So far, we have seen that models that postulate a separation between input and output praxicons (e.g. Rothi et al., 1991) are most suited to explain the dissociations among the different components of praxis and conceptual system, and in particular between input and output modalities. However, a more detailed model of the interactions between action and object representation is needed in order to account for the specific patterns of errors found in apraxics, which may qualitatively differ across patients (e.g. Rumiati et al., 2001). In the next chapter I will describe a group study aimed at testing the validity of such a model, originally proposed by Norman and Shallice (1986) and developed by Cooper and Shallice (2000), which may explain the qualitative differences among apraxic patients in terms of damage within the Contention Scheduling System (Cooper, 2007).

Appendix 3a. List of the 23 objects used in Experiments 1-5. Items in italic were not used in Experiments 3-5.

1	knife
2	squeezer
3	*pencil*
4	glass
5	tea spoon
6	cigarette
7	match
8	hammer
9	pencil sharpener
10	mug
11	teapot
12	saw
13	scissors
14	*nail*
15	pliers
16	screwdriver
17	spanner
18	axe
19	comb
20	toothbrush
21	key
22	lightbulb
23	*match box*

Appendix 3.b. List of actions that patients were required to perform in Experiment 1 (object use). Object(s) were posed in front of the patients who were asked to use them, without any further instruction.

1 Cutting an orange with a knife
2 Squeezing an orange with the squeezer
3 Pouring the juice from squeezer to glass
4 Drinking from the glass
5 Pouring from a teapot in a mug
6 Stirring sugar with a teaspoon in the mug
7 Screwing (screwdriver + screw)
8 Cutting a wooden board with an axe
9 Putting the toothpaste on the toothbrush
10 Brushing teeth
11 Using a pencil sharpener and pencil
12 Using a spanner and a bolt
13 Cutting paper with scissors
14 Screwing a lightbulb
15 Hammering a nail in a wooden board
16 Sawing a wooden board
17 Lighting a match (match + matchbox)
18 Lighting a cigarette (match + cigarette)
19 Removing a nail with pliers
20 Combing oneself
21 Using a key (key + padlock)

Chapter IV

A Neuropsychological Investigation of the Contention Scheduling Model

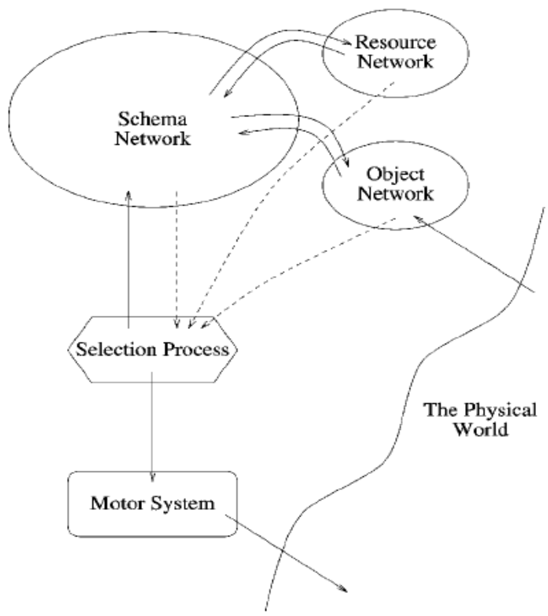
Abstract. In this chapter I will present results from a group study on 15 left-brain damaged patients, aimed at testing the validity of the computational model that can account for Ideational Apraxia proposed by Cooper (2007). The model postulates a modular organization of the components that contribute to the organization of routine actions, and explains FG and DR's behavior (Rumiati et al., 2001) as due to a disconnection syndrome. In this study, we were able to find several dissociations at the single case level that would suggest a separation between information on action schemata and on object features.

Theoretical Background of the Study

In Chapter II we were able to show that there are double dissociations between the ability to produce object-related actions and that to recognize them, as well as between object use and object recognition. The study reported in Chapter III further demonstrated that the two systems, "what" and "how", can be selectively damaged following brain disease. Such data are in line with previous neuropsychological findings and with models holding that the production systems and the input systems are separated. Moreover, the double dissociation between action production and object knowledge found in Study II is congruent with theoretical claims which predict that the semantic system and the action system are separate in the brain (e.g. Rothi et al., 1991), rather than sharing similar neural structures and subserving processes (Gallese and Lakoff, 2005). However, in order to account for the qualitative differences in the errors made by patients with ideational apraxia, one needs to refer to a model that allows more specific predictions as to the nature of the links between object knowledge and the action production systems.

The study described in this chapter is based on the theoretical considerations arising from Cooper's (2007) simulation of patients' errors and its implications in the Contention Scheduling model, which I described in more detail in Chapter I (see also Norman and Shallice, 1986; Cooper and Shallice, 2000). The main goal of these experiments was to test the existence and separateness of two components of contention scheduling -object schema network and action schema network- and their connections, by studying patients with left brain damage and ideational apraxia. As exposed in Chapter I, Cooper (2007) proposed that the error patterns of FG and DR might arise from a disconnection either between the action schema and the object schema (as in the case of FG) or between object representations and action schemas as in the case of DR (see Figure 4.1.).

Figure 4.1. The figure depicts the Contention Scheduling model proposed by Cooper and Shallice (2000).



These different patterns of errors were observed when patients used common objects in a familiar context (e.g. preparing coffee).

Thus, in patient DR, the partial disconnection from object representation to the action schemas led to a high proportion of errors classified as *misuse*$_2$, namely gestures that would be appropriate for the object at hand but inappropriate in that particular context (e.g. cutting an orange by pushing downwards the knife instead of making a sawing-like movement). Conversely, the disconnection of action schemas from object representations would give rise to a pattern of errors similar to that of patient FG: here *mislocation*$_2$ errors will be more likely to occur (e.g. scratching a match inside the matchbox rather than on the appropriate sandpaper strip).

In the present chapter, I will report a study in which I tested patients with left brain damage, who are more likely to have object use apraxia (De Renzi and Lucchelli, 1988) and analyzed the errors they made in performing a series of experiments. The deficits that these patients may show will allow me not only to test the validity of the Contention Scheduling model, but also of the Supervisory Attentional System. In fact, some tasks (in particular the Multiple Object Task) may also be influenced by the ability of the patients to plan action sequences: patients with lesions in the frontal lobes may fail in such Activities of Daily Living (ADL). This profile has also been described as “action disorganisation syndrome” (Duncan, 1986; Humphreys and Forde, 1998; Schwartz et al., 1995).

MATERIALS AND METHODS

Eighteen left brain damaged and 12 control participants, matched for age and education, were recruited from the Rehabilitation Unit of the A.O. Ospedali Riuniti di Trieste. Consecutively admitted patients were selected for the study if they met the following criteria:

-left unilateral stroke, as reported from the neuroradiological notes

-absence of previous neurological disorders

- at least five years of education

- age less than 80 years

-MRI or CT scan available

Three patients were excluded from the study: Mi.B. and Mo.T., because they had prior multiple vascular lesions found through a CT scan reexamination made by an expert neuroradiologist (Dr. Maja Ukmar); Ba.C. because of the severe comprehension deficit that made impossible for her to understand even simple task instructions. The final sample consisted of 15 patiens (age 69,13 $\pm$ 6,81; education 8,57 $\pm$ 3,18, see Appendix 4-I).

Twelve control subjects (age 67.18 $\pm$ 7.69; education 9.72 $\pm$ 4.63) were in-patients of the rehabilitation ward following orthopedic surgery, and before participating in the study they were assessed for handedness (Edinburgh inventory) and cognitive impairment (MMSE, Italian norms). Patients and controls participated in the experimental tasks, but only patients were administered with an extensive neuropsychological assessment (see Appendix 4-II). All patients and controls, or their closest relatives in case of severe reading/writing impairments, gave written informed consent to participate in the study.

Experiments 1a, 1b and 1c: object use tasks

Patients and controls had to perform three object use tasks. In all tasks, objects were placed on the table in front of the subjects with the following verbal instructions: "Please show me how you would use this/these object/s".

Experiment 1a.Multiple Object Tasks (MOT) This task consisted of five activities that were repeated in 4 different sessions (20 trials in total). These activities were the following:

Preparing Italian coffee: a disassembled moka (filter, upper part, lower part), a teaspoon, a can of coffee, an opened bottle containing water;

Lighting a candle: a matchbox containing matchsticks, a candle, a candlestick

Preparing orange juice: a knife, a glass, an orange, a squeezer;

Opening a bottle and drinking water: a bottle sealed with a crown cap, a bottle opener, a glass;

Preparing a letter to post: an envelope, a stamp, a stick glue, a pen, a white paper sheet.

Experiment 1b. "Multi-schemata" objects. This experiment specifically tested the ability to use a set of tools that are linked to more than one action schema. A knife, for example, can be used to cut by pushing if it is presented with butter, or to cut by sawing with an orange. Six tools and their possible targets (for a total of 14 trials, listed below) were presented to the patients who were asked to show how to use them. By hypothesis, such tools should elicit a higher number of *misuse*$_2$ errors in those patients with a type of apraxia similar to that of DR (Rumiati et al., 2001). I predict that patients such as DR would fail with tools associated with more than one action schema, as in these patients the links connecting the object representation network to the action schema network are supposed to be damaged. The list of stimuli of experiment 1b is the following:

Multi-schemata object	**Target Objects**	**Expected action**
Knife +	Orange	Cut by sawing
	Swiss cheese	Cut by pushing
	Marmalade	Spreading
Corkscrew +	Bottle with crown cap	Use the upper part of the corkscrew as a lever
	Bottle with cork	Use the twisted part to extract the cork

Pinch+	Nail	Extract by pulling
	Bolt	Extract by twisting
Teaspoon+	Coffee mug	Stir
	Ice cream cup	Take icecream and bring to the mouth
	Sugar pot	Lift sugar, move it from the pot
Toothpick+	Olive	Picking the olive and bringing it to the mouth
	(alone)	Cleaning teeth
Bottle+	Glass	Pouring in the glass
	(alone)	Drinking from the bottle

Experiment 1c. Single Objects. Twenty-eight objects of common use, all of unimanual use (listed in Appendix 4.III) were presented to the subjects. This number of items is larger than in the clinical test used for the Neuropsychological assessment, which contains 7 items only and does not distinguish between multiple and single objects.

Experiments 2a and 2b: action-target matching for multi-schemata objects

These experiments investigated the possible connections from the action network to the representations of multi-schemata objects and their targets. In particular, patients like DR should be impaired on these tasks, given that they cannot perform the correct action for a given tool/target combination.

Experiment 2a. Patients were presented with a movie of an actor using a tool appropriately for a given target (e.g. video: *cut by sawing with a knife*), in absence of the target (e.g.: *an orange*). Subsequently, four possible targets appeared on the screen and subjects were asked to point to the correct target for that action. The distractor targets were a semantically related one (*pasta*), one requiring a similar manipulation (*a log*) and one requiring a different manipulation but appropriate for the tool (*cheese*).

Experiment 2b. Subjects were presented first with a picture of a target object on the laptop screen (e.g. an *orange*), then with two movies of object use (e.g. using the knife to *cut by sawing* vs by *pushing*). They had to decide which of the two pantomimed actions was more appropriate for that target object for a total of 14 trials, the same as in Experiment 1b.

Experiment 3a and 3b. action-object matching

These experiments were designed with the aim of assessing the ability of patients to associate a correct action schema once the object representation was activated, and vice-versa. It is possible that both DR-like and FG-like patients fail in performing these tasks, given their hypotheized impaired connections between action schemas and object representations.

Experiment 3a. The picture of a tool is presented on the upper side of the screen. Subsequently, a videotaped pantomime of use (in absence of the object) appears below, while the picture of the tool is still present. The subject is asked to judge with a yes/no response whether the pantomime is correctly associated with the object. The foil pantomimes are related to objects that share semantic and functional features with the correct one, but are used with different action schemas (for example: object: *knife*; pantomimes: *cutting* -correct trial- or *shaving* -incorrect trial-). Cooper's model (2007), in fact, holds that objects with similar semantic information have overlapping representations in the object network. Therefore, it may be possible that patients with impaired links between action schemas and object representations fail to activate the correct object starting from a schema, while they are likely to activate semantically related objects. Object-pantomime pairs are presented in a randomized order, 50% correct and 50% incorrect, for a total of 66 pairs.

Experiment 3b. This experiment is identical to 3a but the object and pantomime are presented in the reverse order (pantomime first and object second).

Experiment 4a and 4b. Object Knowledge

Experiment 4a. Object Naming/Multiple choice. Patients were required to name 56 objects used in Experiments 1a, b and c, presented as pictures on a computer screen. In case of aphasia/anomia a multiple choice comprehension was been administered, in which patients had to choose between a target (e.g. *hammer*), a semantically related distractor (e.g. *nail*) and a phonologically related distractor (e.g. *martello/cartello* = hammer/ signpost)

Experimenti 4b. Functional-perceptual questionnaire. According to the CS model (Cooper and Shallice, 2000), the object features are represented in an object network, separately from the action schema network. This questionnaire, similarly to that described in Chapter II, aims at investigating the integrity of this information by tapping on the fine-grained functional and perceptual knowledge of the objects used in the other experiments of the study. Objects were presented as pictures and subjects were verbally presented with a short question requiring a yes/no answer. There were three types of questions assessing three different levels of object knowledge of the tool (e.g. *hammer*): the prototypically associated action (*Is it used for sawing?),* its material (*Is it made in wood?*), and the object usually associated (*Is it used with a screw?*). The questionnaire had in total of 138 questions: 50% required a Yes response, and the order of the question-object pairs was randomized.

RESULTS

Group level analyses

Correlational analyses

a) Correlations among praxis tasks

Nonparametric correlations were calculated among patients' scores on five praxis tasks, including the three object use tasks (Experiments 1a, 1b and 1c) and the two clinical tests for praxis assessment, the IMA and IA tests. The IMA (Ideomotor Apraxia) test investigates the ability of the patients to imitate meaningful and meaningless gestures, whereas the IA (Ideational Apraxia) test investigates the ability to use objects and it includes two multi-step tasks and five single objects (see Appendix 4-II). The results are displayed in Table 4.a.: applying a Bonferroni correction for the significance level (new critical p=.005), none of the correlations resulted statistically significant. However, if we use a less restrictive criterion of $p<.01$, the results are the following:

- Scores on the IMA test correlate with those on the IA test, but not with performance in the other three experimental tasks. It is possible that a general problem of the action production system would affect both tasks; however, since the comparison between IMA and Experiment 1c (in which a higher number of items with respect to the IA test is used) is not significant, one may hypothesize that performing De Renzi and Lucchelli (1988) test for IA requires several functions that need to be disentangled, as it includes also multiple object use tasks (i.e. lighting a candle and closing and opening a lock with a key). Furthermore, the number of items of the IA test might be too small, thus producing a high rate of false negatives.
- Experiment 1c correlates with the IA test: Experiment 1c includes 28 objects of common use, like the IA test devised by De Renzi.
- Experiment 1a correlates significantly with experiment 1b but not with experiment 1c. This result is in line with the hypothesis that patients with IA do not have difficulties only with multi-step actions, but also when they are presented with objects that may potentially activate several action schemas. In Experiment 1b, in fact, subjects were not required to generate a series of steps and sub-goals but only to perform the appropriate action for the tool-target pair presented.

Table 4.a. Correlation matrix among the five praxis tasks used in the assessment and in the experimental session. (*) indicates significant correlations for p<.01

		1b. Multisch	1c. Single	IA	IMA
1a. MOT	Spearman's rho	,655 (*)	,569	-,432	-,322
	Sig. (2-tailed)	,008	,027	,108	,242
1b. Multisch	Spearman's rho	-	,567	-,395	-,424
	Sig. (2-tailed)	-	,027	,145	,115
1c. Single	Spearman's rho	-	-	-,656 (*)	-,505
	Sig. (2-tailed)	-	-	,008	,055
IA	Spearman's rho	-	-	-	,603 (*)
	Sig. (2-tailed)	-	-	-	,017

b) Correlations between object use tasks and recognition/semantic tasks

We have calculated nonparametric correlations also between the praxis experiments and the two experiments (4a and 4b) that we devised to investigate the lexical-semantic knowledge of the objects. Keeping the significance level used above (p<.01), only the correlation between task 4a and task 4b is significant, suggesting that the performance in recognizing the objects on a comprehension task is closely related to the semantic knowledge of the objects themselves. Very importantly, the two semantic tasks did not correlate with performance on any of the object use experiments, suggesting again the relative independence of the semantic and action systems, more extensively discussed in Chapter III.

Table 4.b. Correlation matrix with praxis Experiments (1a, b and c) and the lexical-semantic experiments (4a and 4b). (*) indicates significant correlations for p<.01

		1b. Multisch	1c. Single	4a. compr	4b.question
1a. MOT	Spearman's rho	,655 (*)	,569	,241	,164
	Sig. (2-tailed)	,008	,027	,387	,559
1b. Multisch	Spearman's rho	-	,567	,305	,281
	Sig. (2-tailed)	-	,027	,268	,310
1c. Single	Spearman's rho	-	-	,305	-,013
	Sig. (2-tailed)	-	-	,270	,964
4a. compr	Spearman's rho	-	-	-	,737(**)
	Sig. (2-tailed)	-	-	-	,002

Single Case Approach

In order to compare patients' performance with the results of Rumiati et al. (2001) and to test Cooper's (2007) predictions, the error profiles of individual patients were analyzed. We compared the average number of errors that each patient made when they performed MOTs, with those made by FG and DR (Rumiati et al., 2001). This comparison is reported in Table 4c.

Case-by-case comparison with FG and DR.

First of all, we have looked at possible similarities between behaviour in the MOTs of the patients in the present study and the two patients described by Rumiati et al. (2001). One of the aims of the present study was to identify patients who behave similarly to FG or DR, and analyze their performance on the other experiments we devised. In Appendix 4.IV. we report the full description of the errors made by the 15 patients.

DR-like patients. Two patients, Bu.S. and St.V, made a similar number of *Misuse2* errors to DR in performing the MOTs (see Table 4c). In particular, patient Bu.S. shows an error profile in the MOTs very similar to that of DR, with a high rate of *Sequence* errors (mean = 7.5 per session), *Misuse2* errors (mean = 2.5 per session), and low rate of *Mislocation2* errors (mean = 0.75 per session). Patient St.V. instead makes a smaller number of *Sequence* errors but a similar number of *Misuse2* (mean = 1.75 per session) compared with Bu.S. and D.R (mean = 0.5 per session),. We think that Bu.S.' pattern of performance can be explained in terms of nonspecific resource limitations (see Buxbaum et al., 1988). Bu.S. makes a very large amount of sequence errors (see Table4c and Figure 4.2a), similarly to patients with frontal apraxia described by Schwartz et al. (1991). In general, both her neuropsychological profile and her scores in all the other experimental tasks indicate a general widespread damage that involves all the main cognitive functions: her performance falls below normal range in the language assessment (AAT test), semantic memory (Pyramids and Palm Trees Test) in short-term memory (Corsi test), logic abilities

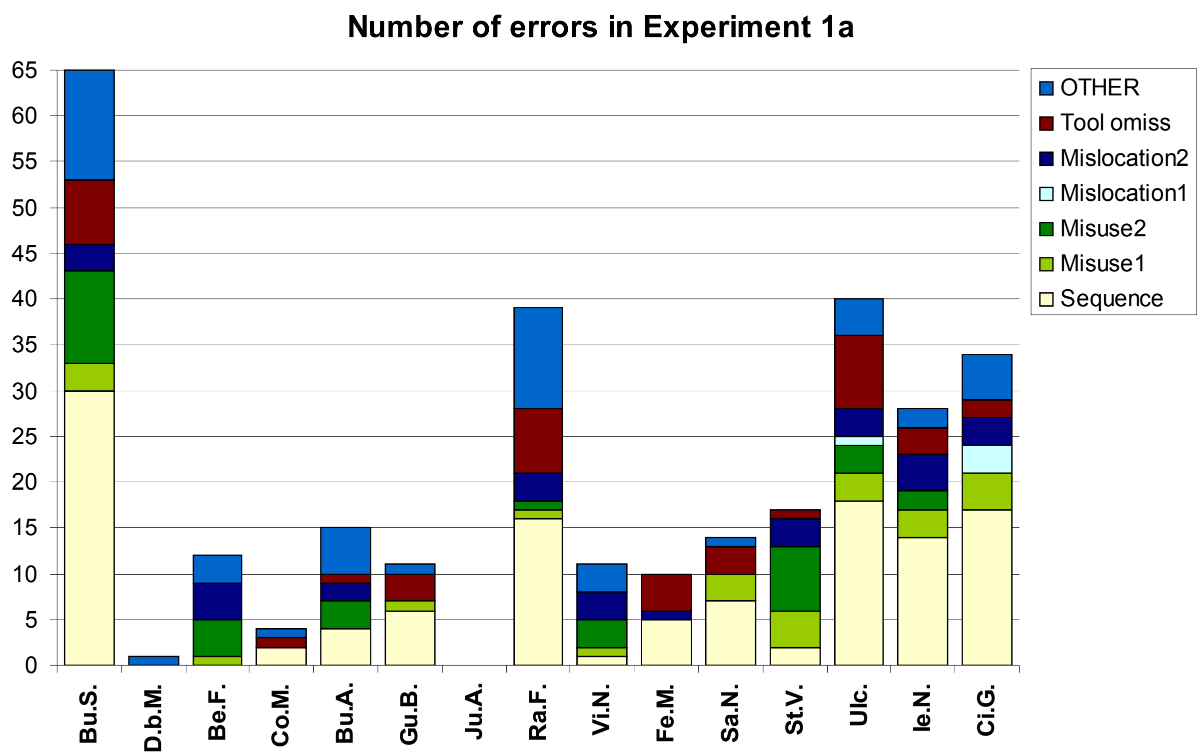
(Raven matrices) and attention (TMT-A), besides all the experimental tasks (see Table 4d). More interesting is the profile of patient St.V., who makes a high number of *Misuse2* errors in the MOTs, despite a rather preserved neuropsychological context: his attention, logic abilities and semantic memory are normal (see Appendix 4-II). As far as the other experimental tasks are concerned, patient St.V. shows an interesting dissociation between his impaired performance in experiments 2a-2b (involving action knowledge for objects that elicit multiple action schemata) and his normal scores in experiments 3a and 3b (testing action knowledge for single objects). This pattern of results suggests that this high rate of Misuse2 errors was somewhat related to a altered knowledge of the action/target links, specific for multischemata objects. This is confirmed by the fact that St.V. performs below cutoff also in Experiment 1b (that requires to use multischemata objects together with possible targets), but not in Experiment 1c (the single object use).

FG-like patients. None of the patients of this group performed similarly to FG, namely making a high number of Mislocation2 errors in Experiment 1c.

Table 4c. Average number of errors on four MOTs for our 15 patients compared with FG and DR. Symbol ♥ indicates patients similar to DR. Note that FG and DR were asked to perform ten MOTs, whereas our patients performed five MOTs, so we halved FG and DR's scores reported in Rumiati et al., 2001 (grey rows).

	Sequence	**Misuse1**	**Misuse2**	**Misloc1**	**Misloc2**	**Tool Om**	**Pantom**	**Perplex**	**Toying**
F.G.	5.25	.36	0.62	1.25	**2.87**	0.75	0.37	2.87	1.25
D.R.♥	2.37	-	**2.5**	0.87	-	.36	-	.12	-
BE.F.	0	0.25	1	0	1	0	0	0	0
BU.A.	1	0	0.75	0	0.5	0.25	0.25	0.25	0
BU.S.♥	7.5	0.75	**2.5**	0	0.75	1.75	0	0	0
CI.G.	4.25	1	0	0.75	0.75	0.5	0	0.5	0.25
CO.M	0.5	0	0	0	0	0.25	0	0	0
DB.M.	0	0	0	0	0	0	0	0	0
FE.M.	1.25	0	0	0	0.25	1	0	0	0
GU.B.	1.5	0.25	0	0	0	0.75	0	0.25	0
IE.N.	3.5	0.75	0.5	0	1	0.75	0	0	0
JU.A.	0	0	0	0	0	0	0	0	0
RA.F.	4	0.25	0.25	0	0.75	1.75	0.25	1	0
SA.N.	1.75	0.75	0	0	0	0.75	0	0.25	0
ST.V.♥	0.5	1	**1.75**	0	0.75	0.25	0	0	0
ULC.	4.5	0.75	0.75	0.25	0.75	2	0.5	0	0.25
VI.N.	0.25	0.25	0.75	0	0.75	0	0.25	0	0

Figure 4.2.A. Number and percentage of errors (divided by type) made by the 15 patients in Experiment 1a.



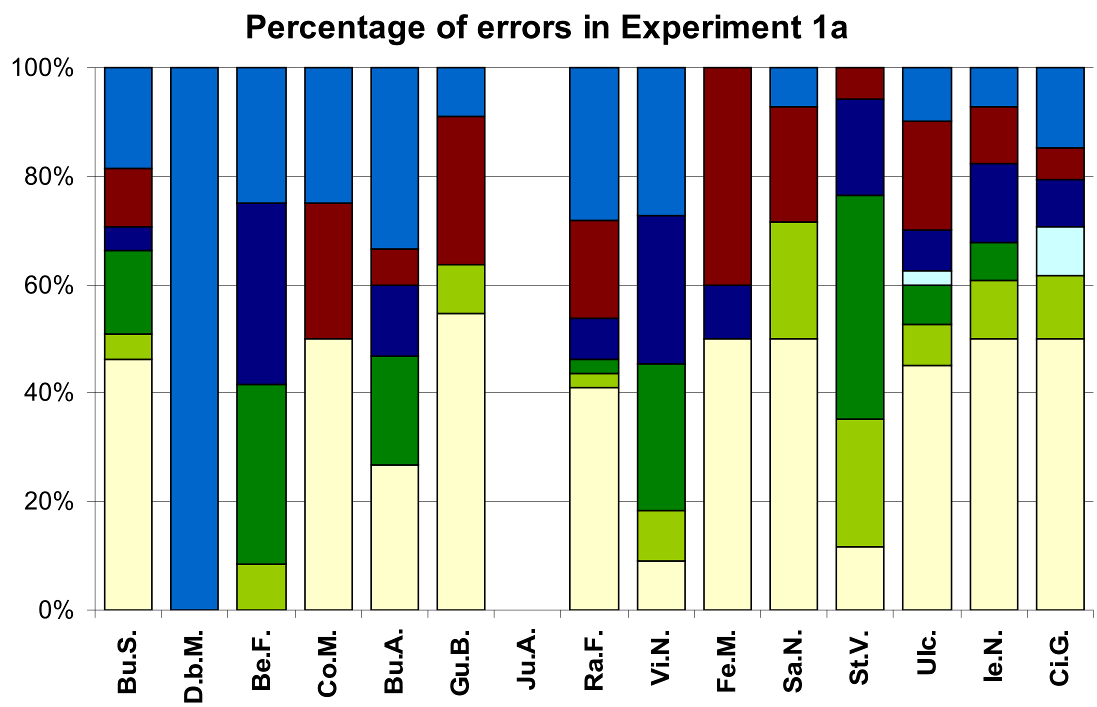
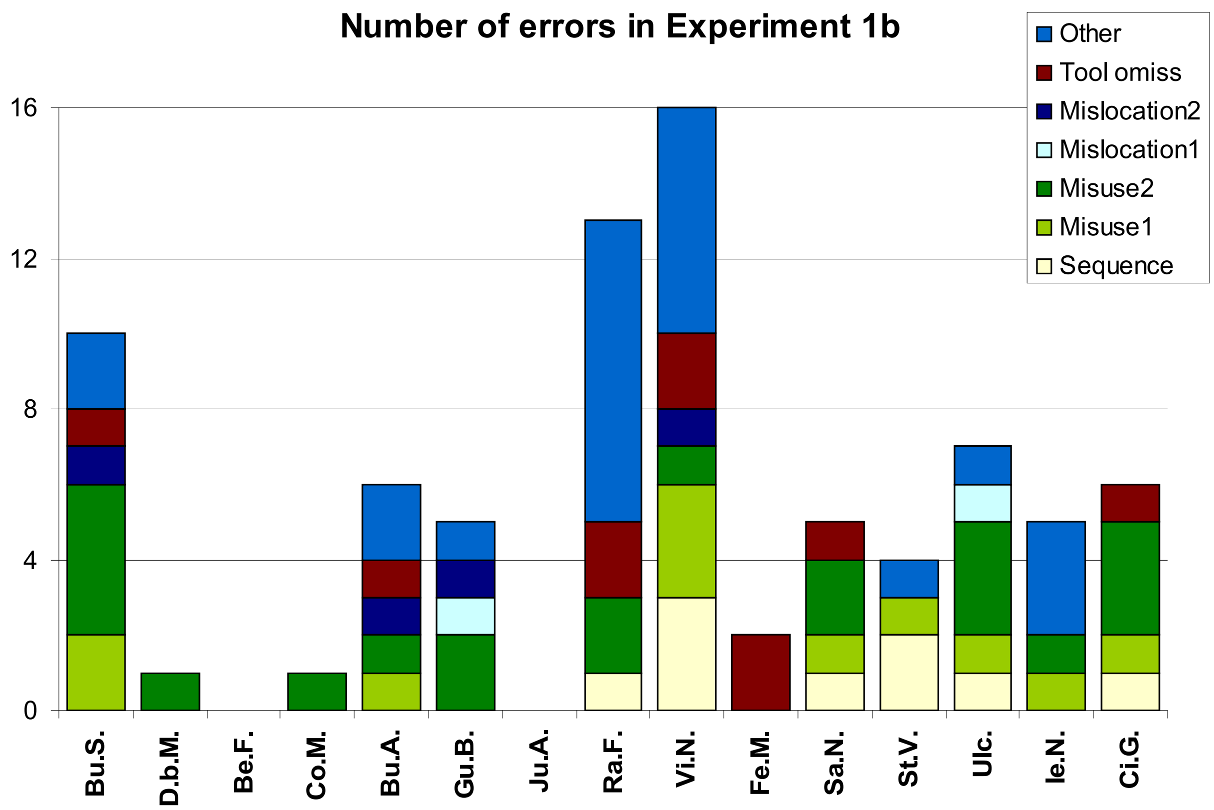


Figure 4.2.B. Number and percentage of errors (divided by type) made by the 15 patients in Experiment 1b.



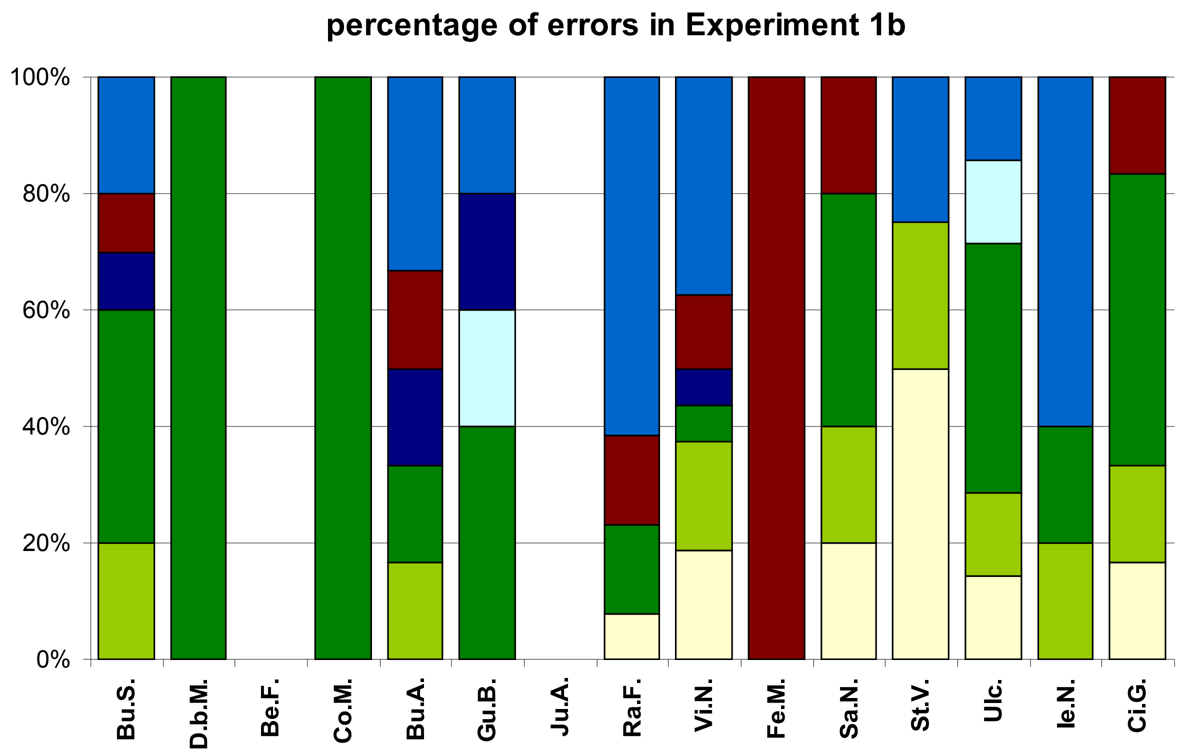
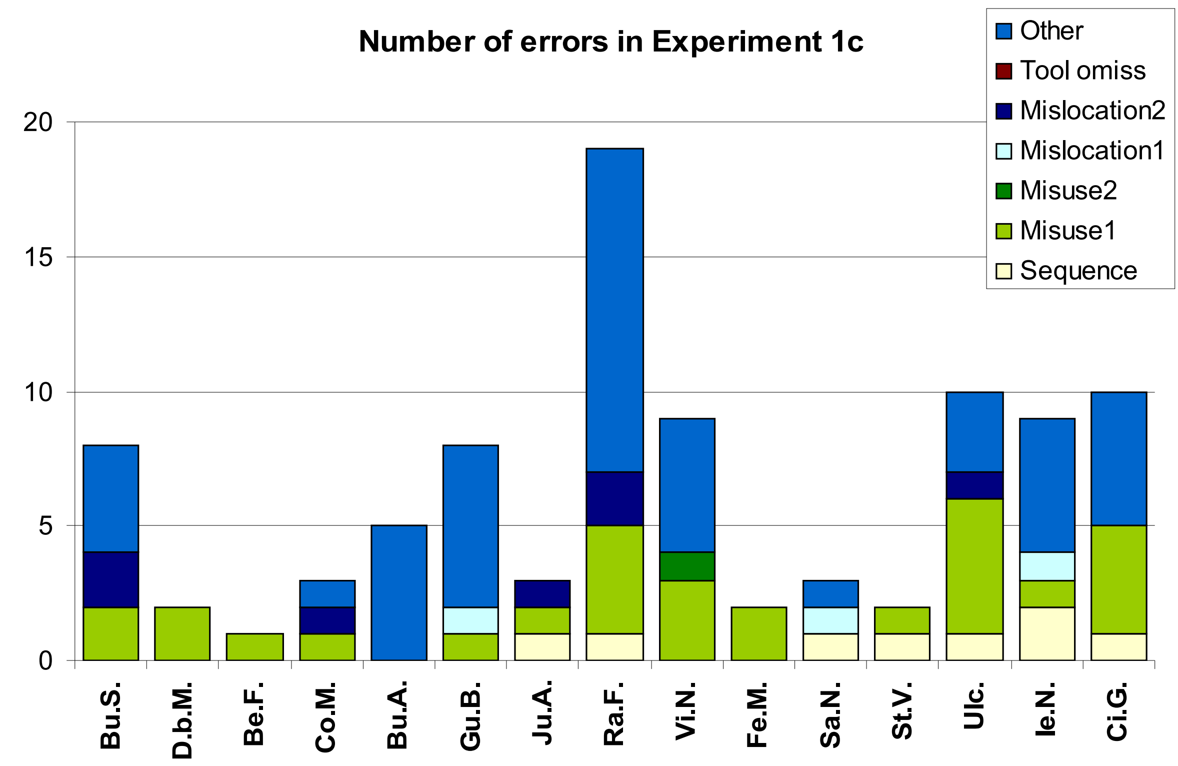
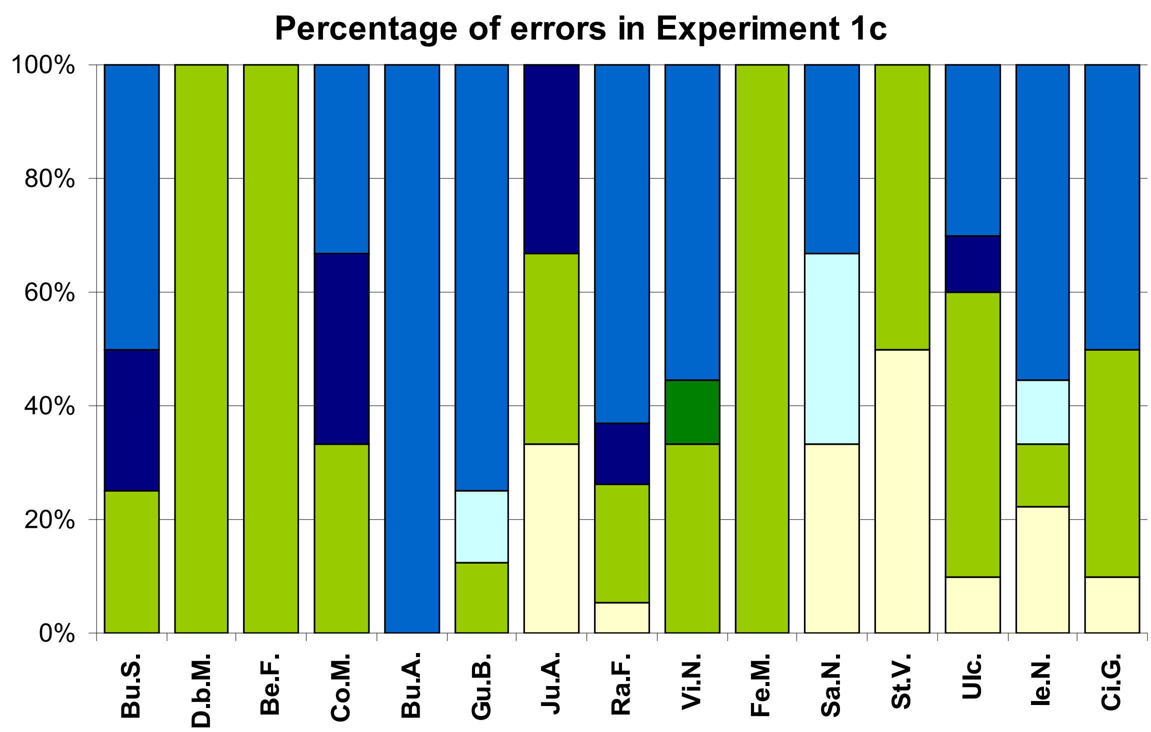


Figure 4.2.A. Number and percentage of errors (divided by type) made by the 15 patients in Experiment 1c.





Considerations on Experiments 1a, 1b and 1c

Patients Bu.S., Ra.F. And Vi.N. made the highest number of errors in Experiment 1b. However, their patterns of performance in the three object use tasks look quite different from each other. While Bu.S. is the most impaired patient in MOTs, making in total 65 errors, she is not the most impaired in the simple object use task, in which she makes 8 errors only. Patient Ra.F. instead makes 20 errors in the single object tasks, but less errors than Bu.S. in the MOTs. Patient Vi.N. is the most impaired in experiment 1b, he is also quite impaired with single objects, but he has a relatively good performance in MOTs.

Such data allow to think that there is not just an effect of difficulty of the tasks or severity of damage, because in this case we should not observe double dissociations. Instead, it could be that these experiments are able to elicit different patterns of errors because they tap different abilities. MOTs are more involved with action sequencing and the organization of routine behavior. Multischemata objects can be prone to error because, in case of damage within the CS, more schemas compete for activation when the tool is held in hand. Single object use is more prone to errors like errate grasping, timing, misuse and so on, which are related to low-level action schemas (like pick up, put down).

Dissociations in Experiment 2 and Experiment 3.

In this section, we will consider the possible existence of dissociations between performance on Experiment 2 and performance on Experiment 3 and we will try to relate the results to the patients' behavior on Experiments 1a, b and c. Since Experiments 2a and 2b had a different number of alternatives, we operated a linear transformation[14] on the subjects' score. We thus obtained a new score (see Table 4d), that we called "criterion", that reaches a maximum of 1 (if all the responses are correct). Zero corresponds to a

[14] $[(X_p*N)-1]/(N-1)$, where Xp is the proportion of errors made by the patient, and N is the number of alternaticves in the task

random performance, like 25% in case of a task with four alternatives like in Experiment 2a.

Double dissociation between Experiment 2a and Experiment 2b. Three patients (Bu.S., Ra.F. and Ulc.) performed relatively better in Experiment 2a than in Experiment 2b (Crawford and Garthwaite's RSDT test[15], p<.05 one-tailed). It is interesting to note that Bu.S, Ra.F. and Ulc. made the largest number of *tool omissions* in Experiment 1a (mean per session = 1.75, 1.75 and 2 respectively). This result seems to suggest that, if one is no longer able to associate the correct action schema for the use of a tool combined to the object-target, then he/she would attempt to act on the object-target without the using a tool (e.g. trying to remove a cap with the hand instead of using the bottle opener). Appendix 4.IV.B. shows the overlap of the three patients' lesions, reconstructed with MRIcro software: this corresponds to a small subcortical portion of the left temporal lobe.

On the other hand, four patients (Fe.M., Gu.B., Ie.N., and Ju.A) performed on Experiment 2b better than on Experiment 2a (RSDT test, p<.05 one-tailed). In this case, the pattern of errors made by the patients is not homogeneous and we will not give a neuropsychological interpretation of this result. Lesions are reported in Appendix 4.IV.B: three out of four patients have a lesion overlapping in a subcortical area adjacent to insula.

The fact that there are patients whose performance in Experiment 2a double dissociates from that in Experiment 2b rules out the explanation that one task is more difficult than the other. In contrast, it is possible that the two tasks rely on cognitive abilities that are at least functionally separable (see Shallice, 1988 and the discussion in chapter III of this thesis). In this case, we observed that the connections from action schemas to target representations can be selectively spared despite damage to the connections from object representations to action schemas, and *vice versa*.

[15] Crawford, J. R., & Garthwaite, P. H. (2005). Testing for suspected impairments and dissociations in single-case studies in neuropsychology: Evaluation of alternatives using Monte Carlo simulations and revised tests for dissociations. *Neuropsychology*, 19, 318–331.

Dissociation between Experiment 3a and Experiment 3b. We observed two patients (Co.M. and Ci.G.) who performed Experiment 3b better than Experiment 3a (Chi-square = 4.86 and 4.08 respectively, $p<.05$). Their lesion overlap is depicted in Appendix 4.IV.C.: the areas commonly lesioned are more posterior with respect to the patients showing dissociations between Experiments 2a and 2b. They involve, among others, cortical parietal structures associated with tool-use abilities (see Johnson-Frey, 2004 for a review). Co.M and Ci.G. did not make similar errors in experiments 1a, 1b and 1c. Moreover, the opposite side of this dissociation was not found in this sample, therefore we will not make further neuropsychological considerations about this dissociation because it might be due to a task difficulty effect.

Object Knowledge (Exp. 4) and its relation with the other Experiments.

Using this new series of experiments, we were able to partially replicate the findings described in Chapters II and III, in which we reported double dissociations between the fine-grained semantic knowledge of tools (or at least their visual recognition) and the actual ability to use them. The correlational analyses showed that performance on the experiments tapping on semantics did not correlate significantly with that in experiments action production. Moreover, within this sample, three patients (Be.F., Co.M. and Fe.M.) performed above the cutoff on the semantic questionnaire, despite showing apraxia when performing the MOTs, showing intact semantic and functional knowledge of the tools that they failed to use in the Experiment 1a. Such findings strengthen the view that the motor knowledge of tools is not necessary for the intactness of fine conceptual representation of the tools. In particular, the questions contained in Experiment 1c were devised in order to explicitly tap the functional and action knowledge of the items presented, as it overtly investigated object features like its prototypical action, its material and the associated objects. On the other hand, we were not able to find patients showing a semantic impairment in answering questions contained in the questionnaire (such as AM and DL, described in Chapter II) but normal performance in performing object use tasks. This result may be due to the nature of the disease of the patients of this sample, as the most common lesions associated with strokes are usually caused by infarction or hemorrhage of the middle cerebral artery, which supplies the outer surface of the cerebral hemisphere. Instead, AM and DL's atrophy mainly involved the temporal poles.

Table 4d. Results in experiments 2, 3 and 4. Symbol * represents performances below cutoff (controls' lowest score); Nam = Naming; MC = Multiple Choice; crit = patients' score linearly transformed, considering the number of alternatives of the task.

	MOT	multi-sch	single	Exp2a		Exp2b		Exp3a		Exp3b		Exp4a		Exp4b
initials	**n.err**	**n.err**	**n.err**	**%**	**crit**	**%**	**crit**	**%**	**crit**	**%**	**crit**	**Nam %**	**MC%**	**%**
BE.F.	12*	0	1	92.8	0.90	100	1.00	87.9	0.76	87.9*	0.76*	--	98.2	96.4
BU.A.	15*	6*	5	78.6	0.71	92.9	0.86	92.4	0.85	90.9	0.82	--	92.9*	79.7*
BU.S.	65*	10*	8*	71.4*	0.62*	71.4*	0.43*	74*	0.48*	74.2*	0.48*	0	92.9*	91.3*
CI.G.	34*	6*	10*	28.6*	0.05*	57.1*	0.14*	57.6*	0.15*	74.2*	0.48*	0	42.9*	60.9*
CO.M	4*	1	3	78.6	0.71	85.7	0.71	86.4	0.73	97	0.94	--	100	97.8
D.B.M.	1	1	2	85.7	0.81	92.8	0.86	98.5	0.97	98.5	0.97	--	96.4	97
FE.M.	10*	2	2	42.9*	0.24*	78.6*	0.57*	63.6*	0.27*	72.7*	0.45*	--	89.3*	97.8
GU.B.	11*	5*	8*	35.7*	0.14*	85.7	0.71	77.3*	0.55*	86.4*	0.73*	58.9	89.3*	82.6*
IE.N.	28*	5*	9*	35.7*	0.14*	78.6*	0.57*	87.9	0.76	87.9*	0.76*	0	98.2	94.2*
JU.A.	0	0	3	71.4*	0.62*	100	1.00	90.9	0.82	93.9	0.88	--	96.4	99.3
RA.F.	39*	13*	19*	85.7	0.81	64.3*	0.29*	84.8*	0.70*	87.9*	0.76*	--	91.1*	88.4*
SA.N.	14*	5*	3	42.9*	0.24*	64.3*	0.29*	77.3*	0.55*	75.8*	0.52*	--	75*	72.5*
ST.V.	17*	4*	2	50*	0.33*	71.4*	0.43*	86.4	0.73	84.8*	0.70*	0	83.9*	87*
ULC.	40*	7*	10*	57*	0.43*	50*	0.00*	77.3*	0.55*	78.8*	0.58*	44.6	91.1*	88.4*
VI.N.	11*	16*	9*	57.1*	0.43*	78.6*	0.57*	83.3*	0.67*	90.9	0.82	--	96.4	94.9*
cutoffs	**3**	**3**	**5**	**78.6**	**0.71**	**85.7**	**0.71**	**86.4**	**0.73**	**90.9**	**0.81**		**94.6**	**96.4**

DISCUSSION

Of the 15 patients who took part in this study, six were found to be apraxic as assessed with the De Renzi and Lucchelli (1988) test for object use. All the patients that failed in the De Renzi test were also below cutoff in experiment 1c. However, five patients who were normal when performing the IA test (Be.F., Bu.A., Sa.N., St.V. and Ulc.) performed below cutoff in the MOT task, and two patients (Gu.B. and Ulc.) normal when performing the De Renzi test, were instead below cutoff in Experiment 1c. As suggested also by the correlational results, we hypothesize that the IA test devised by De Renzi and Lucchelli (1988) used in the clinical practice is probably influenced by several confounding variables, in addition to the fact that it contains a small number of items.

The pattern of distribution of errors performed by each patient in Experiments 1a, 1b and 1c is very heterogeneous: it includes patients who made few errors (like Ju.A. or DB.M.) and patients who produced a much higher error rate (e.g. Bu.S. or Ulc.). The error profile analysis has shown that the majority of them cannot be considered similar either to FG or to DR, suggesting that their errors in MOTs may originate from damage to a different module within contention scheduling, or outside CS itself (see for example the discussion about patient Bu.S.).

As reported in Figure 4.2. and 4.3., the most frequent type of errors made by patients are sequence errors, including step omissions, action anticipations and perseverations.

The documented double dissociation between performance in Experiment 2a and performance in Experiment 2b suggests that, for the multischemata objects, there might be selective deficits in activating the correct object representation starting from the action schemas in presence of intact connections in the other direction, and vice versa. Moreover, patients who performed Experiment 2a better than 2b also shared common features as far as their performance on the MOTs is concerned.

As for Experiments 3a and 3b, we were able to find dissociations only for patients who performed 3b better than 3a. Although we cannot rule out the explanation of the difficulty of the task (controls also performed slightly better in 3b, although not significantly), we are skeptical in accepting it because Experiment 3a has exactly the same structure and items (re-randomized) as Experiment 3b.

We observed dissociations among the tasks that we have devised in order to tap on the different modules and links within CS. We showed that not all apraxic patients behave in the same way when they are asked to perform recognition tasks tapping action and semantic knowledge. Although the explanation of apraxia proposed by Buxbaum and colleagues (1998) holds for one of the cases presented (Bu.S.), the individual differences among patients in the dissociations that emerged and in the error profiles suggest a modular interpretation of the action organization systems.

To conclude this chapter I would like to use the present data in order to compare the CS model with another model that has been proposed to explain action slips in normal and apraxic behavior. Botvinick and Plaut (2004) trained a recurrent connectionist network in a task very similar to that used by Cooper and Shallice (2000). The important difference from the CS approach is that Botvinick and Plaut propose that the structure of the task is not hierarchically organized, and the sequencing of the different task subgoals is achievable also by a network that does not support hierarchical structures. The authors compare the network results with that of patients with action dysorganization syndrome due to closed head injury (CHI), described in Schwartz et al (1998) and, since the pattern of errors of the network is similar to that of the CHI sample, they conclude that their model is suitable to explain action disorganization deficits.

We have plotted in Figure 4.3 and 4.4. the two samples of patients: those participating in this study and the patients of Schwartz et al. (1998). We have modified the colors in order to consider only two type of errors: a) those called by Botvinick and Plaut “*substitution*” errors (in white), in which the correct action is done with the wrong object, or the wrong action is performed with the correct object (correspoding to our mislocations and misuses); b) *sequence* errors, that include step omissions, perseverations, anticipations, repetitions etc.

Figure 4.3. Data from Schwartz et al. (1998), showing the relationship between overall error rate and types of errors, divided into sequence and substitution errors (modified graph)

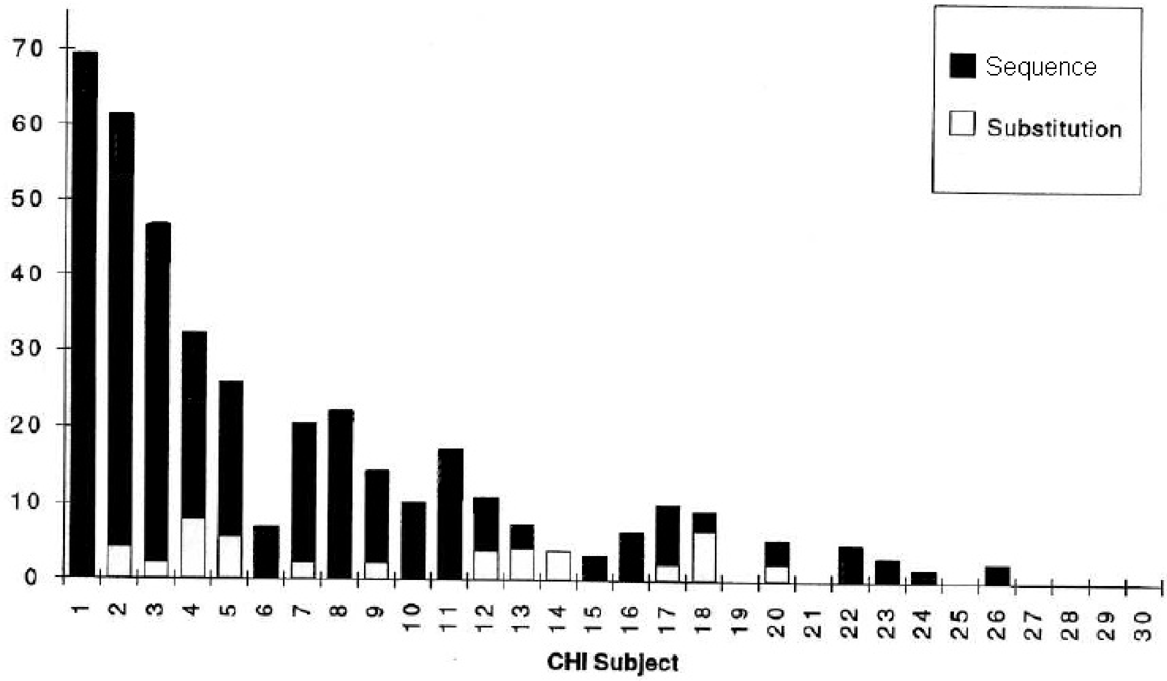
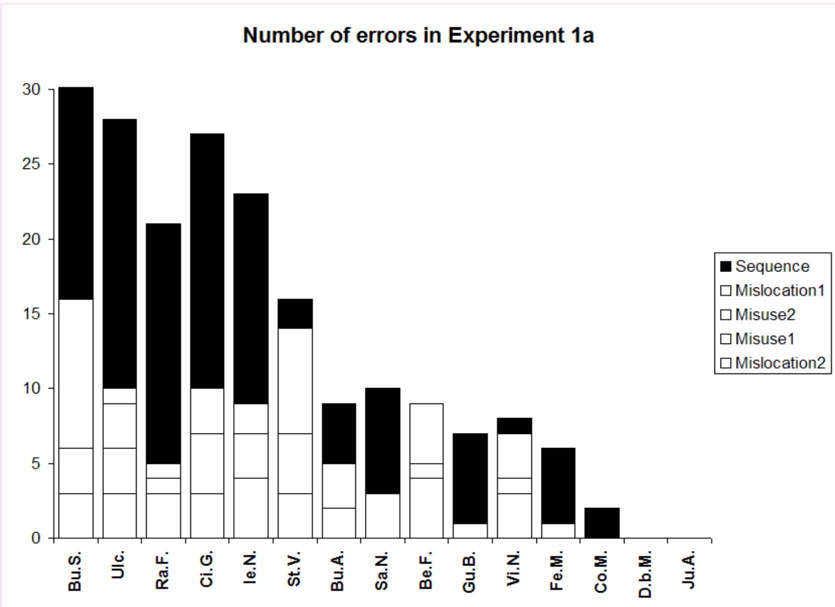


Figure 4.4. this graph reports the proportion of sequence (black) and substitution (white) errors in MOTs for our sample of 15 left unilateral stroke patients.



It is evident at first sight that, in our sample, the proportion of substitution errors compared to sequence errors is much higher, as our stroke patients make in proportion much more substitution errors than Schwartz (1998)'s CHI patients. In the simulation of Botvinick and Plaut (2004), the authors are able to reproduce CHI error patterns by adding noise to the network connections. More problematic would be to obtain a high proportion of substitution errors in this kind of network. In the context of the SAS/CS model however, by altering the top-down control coming from the SAS to the CS, we should provoke something more similar to the "frontal" apraxia. The pattern of errors of our left brain damaged patients can be accounted for by hierarchical models of routine actions, but it is not easily explained in the framework of recurrent networks that consider the MOTs as sequences of actions. In the recurrent network model, lesions to the hidden units cause increase of substitution errors only at high stages of damage. In left stroke patients however there are cases (Be.F., Vi.N.), which show high proportion of substitution errors even in presence of mild impairment in the MOTs. These data are also at variance with studies that conclude for the absence of qualitative differences across patients (reft, right or frontal) as to the types of error they make in multi-step actions (Buxbaum, Schwartz and Montgomery, 1998).

Further investigation is needed in the future, in particular new computational simulations of the novel error profiles will be necessary, in order to see whwther the model can account for both frontal and ideational apraxia. Moreover future work will allow us to clarify whether the Contention Scheduling hypothesis fits with the data that we found and, in case of affirmative response, we could find the locus of damage within CS for the new patients who behaviorally differ from FG and DR.

APPENDIX4-I. Patients' demographic and lesion data. BG = Basal Ganglia, P= Parietal, O= Occipital, F = Frontal, T= Temporal

INITIALS	AGE	EDU	handedness coeff	ONSET	AETIOLOGY	LESION SITE (left)	DATE EVALUATION	DIAGNOSIS APHASIA (AAT test)
BE.F.	67	8	100	05/04/2004	emorr	BG	04/05/2006	NO APHASIA
BU.A.	71	7	92	02/10/2005	isch	P-O	09/11/2005	WERNICKE severe
BU.S.	76	5	100	07/04/2005	isch	T-P	11/05/2006	GLOBAL
CI.G.	77	17	100	24/11/06	isch	T-P	15/12/06	WERNICKE severe
CO.M	59	10	83	08/07/2005	emorr	P	26/10/2005	WERNICKE moderate
D.B.M.	58	13	100	27/12/05	isch	Semioval center	05/03/2006	output phonological buffer deficit
FE.M.	61	12	100	18/02/2006	tce+emorr	F-T-P	17/03/2006	TRANSC MIXED mild
GU.B.	67	11	100	18/11/2005	emorr	T	19/12/2005	WERNICKE (96,5%) mild
IE.N.	71	8	100	05/06/2007	isch (+emorr)	F-P	06/04/2007	WERNICKE severe
JU.A.	74	15	83	02/07/2005	isch	P	21/02/2006	CONDUCTION
RA.F.	72	7	100	27/01/2006	emorr	T-P-O	02/03/2006	TRANSC SENSORIAL mild
SA.N.	64	8	100	18/04/2006	isch	BG + F-T	30/05/2006	BROCA severe
ST.V.	67	5	100	04/05/2006	isch(+emorr)	BG + P	30/06/2006	BROCA severe
ULC.	71	6	83	09/07/2006	isch(+emorr)	BG+ int. & est. capsula +claustrum	16/08/2006	BROCA mild
VI.N.	82	5	100	25/01/2006	isch(+emorr)	T-P	01/03/2006	BROCA mild

APPENDIX 4-II. Patients' neuropsychological profiles. Red colour indicates severe impairment. Blue indicates mild impairment. "n.a." = not administered

	AAT												
				Written Language			*Comprehension*		*LTM*		*STM*		
Patient	Token	Rep.	Read.	Writ.1	Writ.2	Nam.	Oral	Written	Verb.	Vis.	Verb.	Vis.	P&P
BE.F.	7	140	30	27	27	107	51	50	41	22	4.25	4	50
BU.A.	50	9	22	0	0	15	43	48	n.a.	24	n.a.	4	49
BU.S.	36	44	9	0	0	15	26	14	n.a.	16	n.a.	2.25	46
CI.G.	50	0	0	0	0	0	22	0	n.a.	n.a.	n.a.	----	47
CO.M	25	102	14	14	19	61	49	43	n.a.	25	n.a.	4.75	50
D.B.M.	39	71	24	8	12	83	51	48	31	25	n.a.	4	51
FE.M.	41	95	23	14	21	34	31	31	n.a.	20	2.75	4	47
GU.B.	29	134	30	16	25	29	34	21	32	23	4.25	4.25	32
IE.N.	30	31	5	0	0	43	49	37	n.a.	24	n.a.	4.5	51
JU.A.	6	134	26	24	24	109	58	60	36	16	2.75	4	52
RA.F.	40	139	0	0	22	59	44	0	n.a.	19	6.25	3.25	46
SA.N.	36	101	16	3	0	29	28	18	n.a.	21	n.a.	6.25	39
ST.V.	40	94	16	12	3	43	42	21	n.a.	22	n.a.	1	47
ULC.	36	122	15	0	0	88	39	11	n.a.	3	4.5	3	47
VI.N.	7	100	22	14	7	98	52	56	n.a.	25	n.a.	3.5	52

APENDIX 4-II (continued)

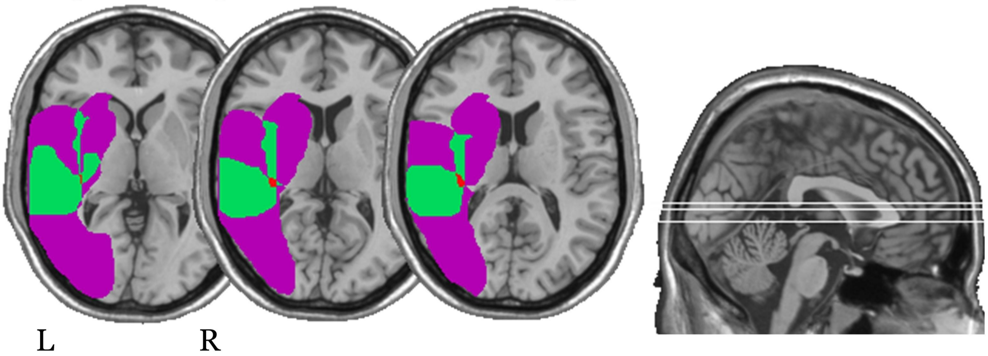
	IA	*IMA*			*ATTENT.*	*EXECUTIVE FUNCT.*				*VISUAL PERC.*	
INITIALS		**MF**	**ML**	**total**	**TMT A**	**TM T B**	**BWD DIGIT**	**WEIGL**	**RAVEN**	**SCREEN**	**OBJ DEC.**
BE.F.	14	MF=28	ML=31	59/72	118	n.c.	2	6.75	27	20	17
BU.A.	14	MF= 19	ML= 25	44/72	22	275	n.s.	10	32.6	20	16
BU.S.	9	MF=17	ML=19	36/72	n.s.	n.s.	n.s.	7.25	21.2	14	16
CI.G.	7	MF=12	ML=19	31/72	194	n.s.	n.s.	1.5	20.8	19	12
CO.M	13	MF= 34	ML= 31	65/72	10	92	n.s.	8.5	36	20	17
D.B.M.	14	MF=36	ML=36	72/72	48	76	n.s.	13 (p.g.)	31	20	16
FE.M.	14	MF=28	ML=28	56/72	133	303	2	3	21.8	20	15
GU.B.	14	MF=35	ML=34	69/72	238	n.c.	2	3.75	32	20	14
IE.N.	5	MF= 17	MF= 17	34/72	94	n.c.	n.s.	5	20.6	20	16
JU.A.	14	MF=15	ML=20	35/72	39	134	2	11.75	29.8	20	17
RA.F.	5	MF= 21	ML= 26	47/72	n.s.	n.s.	3	5	18.6	19	11
SA.N.	14	MF=26	ML=29	55/72	94	n.s.	n.s.	9.75	28	20	13
ST.V.	14	MF=33	ML=32	65/72	63	n.s.	n.s.	4.75	28.9	20	16
ULC.	14	MF=29	ML=28	57/72	n.c.	n.s.	0	5	23.5	20	17
VI.N.	10	MF=18	ML=16	34/72	79	n.c.	n.s.	--	22	20	17

APPENDIX 4-III. list of the objects used in experiment 1c.

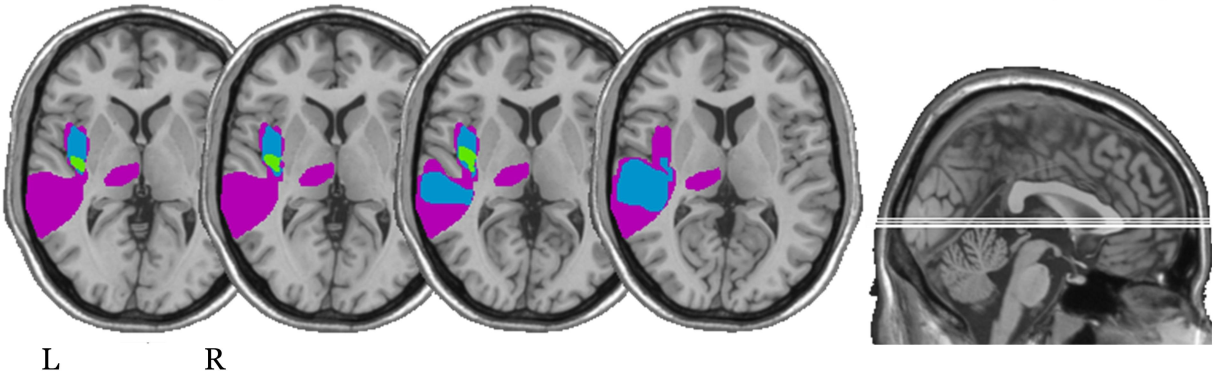
axe
bolt and screw
carpet beater
cigarette
coffee mug
drawing pin
dropping bottle
fish net
flywisk
glass
gun
hammer
key
ladle
light bulb
lighter
lipstick
liquid soap
match
paint brush
painting roll
pen
razor
saw
screw cap
spray
squeegee
tweezers

Appendix 4.IV. Brain lesions of the patients reported in the single case analysis. Red=area lesioned in all patients. Purple=area lesioned in one patient.

A)Patients performing 2a better than 2b (Bu.S., Ra.F., and Ulc.)
Overlap in a small portion of insula and Heschl gyrus (red)



B) Patients performing 2b better than 2a (Fe.M., Gu.B., Ie.N., and Ju.A)
3 out of 4 lesions (green) overlap in a small portion of the insula; there are no areas with 4/4 overlap



C)Patients performing 3b better than 3a (Co.M. and Ci.G.)
Red area: rolandic operculum, insula, middle occipital gyrus, supramarginal gyrus, angular gyrus, superior temporal gyrus, middle temporal gyrus, Heschl gyrus

Appendix 4.IV. errors description of the patients in Experiments 1a, 1b and 1c

Patient BE.F

MOT 1

Preparing a letter: he tries to write without opening the pen but then he succeed (*conduite*). He folds the letter in a wrong manner (*misuse2*). He glues the stamp on the edge of the envelope, like a seal (*misuse1 and mislocation2,* qualitative)

MOT 2

Preparing a letter: he tries to write without opening the pen but then he succeed (*conduite*). He folds the letter in a wrong manner (*misuse2*). He glues the stamp on the wrong corner of the correct side of the envelope (*mislocation2,* quantitative)

MOT 3

Preparing a letter: he writes on the sheet keeping it in a landscape orientation (*orientation*). He folds the letter in a wrong manner (*misuse2*). He glues the stamp on the wrong corner of the correct side of the envelope (*mislocation2,* quantitative)

MOT 4

Preparing a letter: He folds the letter in a wrong manner (*misuse2*). He glues the stamp on the wrong corner of the correct side of the envelope (*mislocation2,* quantitative)

MULTI-SCHEMATA OBJECTS

No errors.

SINGLE OBJECTS

Lighter. He blows it out like a candle (misuse1)

Carpet beater. The movement is very quick (*frequency*)

Patient BU.A

MOT 1

Preparing an Espresso pot. He shows how to pour water in the coffee pot but without eventually pouring, although the experimenter repeats that he should actually use the objects (*pantomiming* and *step omission*). He does not open the coffee box (*step omission*) and he shows that he would pour the coffee from the box without using the spoon (*tool omission*).

Preparing an Orange Juice. He opens the squeezer (*action addition*), he cuts the orange holding it in his hand as one would cut an apple (*Misuse 2*).

Preparing a Letter. He writes on the paper sheet put in a wrong orientation (*orientation*), he folds the sheet in a wrong manner but he realizes that it does not fit in the envelope, so he folds it again (*conduite*). He glues the external edge of the envelope, on the part where one usually writes the sender's address (Mislocation 2. quantitative error?).

MOT 2

Preparing a Letter. He folds the paper sheet but it does not fit in the envelope, so he folds it again but in a wrong manner (*action addition*), he pretends to use the glue (*pantomiming*) then when he is asked to actually use it, he does not know what to do (*perplexity*). He glues the external edge of the envelope (*mislocation 2*), he writes on the envelope without opening the pen (*step omission*).

MULTI-SCHEMATA OBJECTS

Knife + Orange. He cuts the orange holding it in his hand, as it was an apple (*Misuse 2*).

Knife + Marmalade. He initially shows *perplexity*, then he drops the marmalade from the knife as he was using a spoon (*Misuse 1*), without spreading it.

Pliers + bolt. (the bolt is presented to the patients screwed in a piece of wood and they are supposed to remove it with the pliers. The experimenter holds the piece of wood so that it remains still) He grasps and rotates the piece of wood instead of the bolt (*Mislocation 2,* qualitative error), then he unscrews the bolt with his hand (*tool omission*).

Corkscrew + cork. He holds the corkscrew's arms while turning the upper part, and they cannot lift (*clumsiness*).

SINGLE OBJECTS

Lighter. He pantomimes the use of the object (*pantomiming*).

Carpet beater. He grasps the object inappropriately (*grasping*) and the movement is too narrow (*frequency*)

Ladle. The *grasping* looks inappropriate.

Tweezers. He shows a movement similar to "cut with a knife" (*misuse 1*).

Patient BU.S

MOT 1

<u>Lighting a candle</u>. She scratches the match on the short external side of the matchbox – the one without glasspaper (*Mislocation2*. quantitative error?)

<u>Preparing coffee</u>. She pours water correctly, she does not put coffee (*step omission*) and she tries to close the moka twisting it in the wrong direction (*orientation*). She realizes that there is a mistake (*Conduite*) so she unscrew the moka, she wants to pour water from the base to the bottle (*action addition*) without removing the filter (*step omission*). The experimenter empties the basis because the patient expressed the wish to restart. She puts the filter without pouring water (*step omission*) or coffee (*step omission*), she closes the moka, then she reopens it and she adds coffee (*conduite*) but not water (*step omission*). She closes the moka.

<u>Preparing orange juice</u>. She attempts to squeeze the orange without cutting it (tool omission and step omission), then she self-corrects (conduite) and she attempts to cut the orange by pushing instead of sawing (Misuse2). She does not squeeze the orange (step omission) and she does not pour juice in the glass (step omission and tool omission).

<u>Preparing a letter to post</u>. She attempts to open the glue by twisting the wrong end (mislocation2 I think this is a qualitative error because she acts on the wrong part of the object- visually different from the correct one). She opens it (*conduite*), she glues the stamp first (*action anticipation*) and she says she has completed the task (*3step omissions*, *2 tool omissions*). Then she attempts to write on the envelope without opening the pen (*step omission*).

<u>Drinking from a bottle</u>. She uses the bottleopener as a lever (*Misuse 1*), then she removes the cap with her hand (*tool omission*).

MOT 2

<u>Preparing a letter to post</u>. She writes without opening the pen (*step omission*), then she opens the pen (*conduite*) and she writes on the envelope. She glues the stamp correctly (but action anticipation) and she twists the glue cap while closing it (*action addition*). Then she opens the glue and she closes it (*action addition*). She writes again (*perseveration*) with the closed pen (*step omission*). She folds the sheet in a wrong manner (*Misuse 2*), she tries to fit it in the envelope but she has to fold it again (*conduite*), in a wrong manner. Then she puts the sheet in the envelope and she licks the envelope to seal it.

<u>Preparing coffee</u>. She pours water correctly, she takes a spoonful of coffee but she goes back to the coffee can and takes another spoonful without having poured the first one (*perseveration 2*). The remaining steps are done correctly.

<u>Drinking from a bottle</u>. She removes the cap with the hand (*tool omission*)

<u>Preparing an orange juice</u>. She attempts to cut the orange by pushing the knife (*Misuse2*), she says that her hand hurts, so the experimenter cuts the orange. She squeezes the half orange with her hand, above the squeezer but without twisting it (*misuse2*).

<u>Lighting a candle</u>. She cannot light the candle because she scratches the match too slowly (*frequency*), she puts the unlit match vertically on the top of the candle (*action addition*), then she acts correctly with the correct end of the match close to the wick and she puts the match again vertically on the top of the candle (*perseveration2*, *spoiling*)

MOT 3

<u>Preparing orange juice</u>. She attempts to cut the orange by pushing the knife (*Misuse2*). The experimenter cuts the orange. She squeezes the half orange with her hand, above the squeezer but without twisting it (*misuse2*).

Preparing coffee. She puts the filter first (action anticipation) and she pours water in the filter. she understands that she made an error (*conduite*) the experimenter empties the pot. This time she puts coffee in the filter first (action anticipation) then she removes the filter and pours water in the basis (conduite).

Lighting a candle. She scratches the match with a slow movement (frequency)

Drinking from a bottle. She grasps the bottle opener but she removes the cap with her hand (tool omission). She puts the cap on the bottle again and she attempts to use the bottle opener (conduite) but she can only use it as a lever (Misuse 1).

Preparing a letter. She uses the pen upside-down (orientation) and without opening it (step omission). She folds the sheet correctly and puts it in the envelope. She tries to open the glue by twisting the cap instead of pulling it (misuse2), then she twists the wrong end (Mislocation2 again, qualitative). She opens the glue (conduite) then she glues the stamp correctly but she does not seal the envelope (step omission)

MOT 4

Lighting a candle. She cannot light the match because she scratches too slowly (frequency). She performs the task correctly with the unlit match.

Drinking from a bottle. She uses the bottle opener as a lever pushing the bottom of the cap (Misuse1). The other steps are correct.

Preparing coffee. She does everything correctly.

Preparing a letter to post. She grasps the pen and she puts it back (action addition). She glues the stamp (action anticipation), she attempts to open the pen by twisting it, but it is a pen with button (Misuse2). She folds the sheet correctly, she puts it in the envelope but she does not seal the envelope (step omission).

Preparing orange juice. She tries to cut by pushing (Misuse2) but her hand hurts so the experimenter cuts the orange for her. She squeezes the orange on the top of the squeezer, but without twisting the orange (*misuse 2*)

Patient CI.G

MOT 1

Lighting a candle. He tries to verbally explain what he would do with the objects (but Wernicke's aphasia). He brings the matchbox near the candlestick, then brings the candle close to the candlestick (toying), without actually doing the actions. He refuses to perform the task (3 step omissions, 1 tool omission)

Drinking from a bottle. He opens the cap correctly then he shows (perplexity). The experimenter encourages him and he terminates the task correctly

Preparing coffee. He shows (perplexity) at the beginning. He puts water in the bottom part of the moka correctly, then he puts the filter correctly. He takes the upper part of the moka and pretends to pour from this to the filter (action addition). He puts it down, then he puts correctly coffee in the filter. He takes again the upper part of the moka and pretends to pour from this to the filter (action addition). He wants to seal the moka correctly, but he does not succeed because of (clumsiness)

Preparing a letter. He places the stamp on the envelope without gluing it (step omission). He attempts to write with the glue (misuse 1). He folds the sheet correctly, he puts it in the envelope but he does not seal the envelope (step omission) and he writes the address with the pen.

Preparing orange juice. no errors

MOT 2

Lighting a candle. He puts the candle on the candlestick. He lights the lighter correctly. Then he lifts the candle (action addition) and put the lit match near the candlestick (mislocation1). He blows the match and puts the candle back in the candlestick.

Drinking from a bottle. He attempts to open the cap with the wrong end of the opener (mislocation2, quantitative). Then he self-correct (conduite).

Preparing Italian coffee. He pours water and the filter correctly. He pours coffee in the filter by pouring from the can, without using the spoon (tool omission). Then he grasps the spoon without using it (action addition), seals the moka correctly. At the end he opens and closes the lid of the moka (acrion addition)

Preparing a letter. No errors

Preparing orange juice. the task is done correctly but at the end he stirs the juice with the knife (misuse1 and action addition)

MOT 3

Lighting a candle. No errors

Drinking from a bottle. No errors

Preparing Italian coffee. He first puts coffee (action anticipation) in the bottom part of the moka (mislocation1). He adds water and puts the filter, he seals the moka correctly.

Preparing a letter. He writes on the sheet with the glue (misuse1). Then he understand the error and he takes the pen, but he wirites without opening it (step omission). He folds and puts the sheet in the envelope correctly. He attempts to write the address with the glue (misuse 1), he glues the stamp. He does not seal the envelope (step omission).

Preparing orange juice. he does not cut the orange in half. He cuts only a tiny part of the orange skin (mislocation2, quantitative) and he attempts to squeeze the whole orange. the rest is correct (he pantomimes the actions of pouring the juice in the glass and drinking)

MOT 4

Lighting a candle. No errors

Drinking from a bottle. No errors

Preparing Italian coffee. He first puts coffee (action anticipation) in the bottom part of the moka (mislocation1). He adds water and puts the filter, he seals the moka correctly.

Preparing a letter. He writes on the sheet, folds it and put it in the envelope correctly. He glues the stamp with the glue but he does not twist the glue in order to make it work (step omission). He does not seal the envelope (step omission).

Preparing orange juice. he does not cut the orange in half but he cuts only a tiny part of the orange skin (mislocation2, quantitative) and he attempts to squeeze the whole orange. The rest is correct (he pantomimes the actions of pouring the juice in the glass and drinking)

MULTI-SCHEMATA OBJECTS

Pliers + nail. He twists the nail (misuse 2)

Corkscrew + crown cap. He puts the corkscrew on top of the bottle, as with a cork (misuse 2)

Corkscrew + cork. He attempts to remove the cork with the hand (tool omission) then he uses the tool correctly, but before pulling out the cork he twists the tool (action addition)

Knife + marmalade. He uses it like a teaspoon, bringing it to the mouth (misuse1)

Knife + cheese. He cuts by sawing (misuse 2)

SINGLE OBJECTS

Axe. He moves it on the horizontal axis but the blade is facing down (orientation)

Dropping bottle. He cannot open it, he pantomimes the action (pantomiming)

Match. (perplexity)
Ladle. First (toying 2) then he shows the use but with an incorrect (grasping)

Makeup brush. He uses it like a brush for shaving foam (misuse1)

Tweezers. He uses them on the nails, like scissors (misuse1)

Fish net. He moves it in the air (frequency, timing and orientation)

Lipstick. He does not remove the cap (step omission)

Liquid soap. He pours as if it was a bottle (misuse1)

Flywhisk. He uses it as carpet beater (misuse 1)

Patient CO.M

MOT 2

Preparing a Letter to post. He folds the sheet in a wrong manner for that particular envelope, then he corrects the action (*conduite*), he does not use the glue (*tool omission*) and he closes the envelope by licking it.

MOT 3

Preparing an espresso pot. He stirs the coffee in the box before putting it in the coffee pot (*action addition*).

MOT 4

Preparing an Orange juice. He cuts the orange in two halves correctly but he does not completely separate them (*step omission*), so he squeezes one half while the other one is still joint.

MULTI-SCHEMATA OBJECTS

Knife + cheese. He cuts the cheese by sawing (Misuse 2)

SINGLE OBJECTS

Gun. He tries to shoot by pulling the hammer with his thumb (*Mislocation 2* the action is correct but it's done on a completely wrong part of the target object= qualitative error), then he succeeds (*conduite*).

Patient D.B.M

MOT 1

Preparing a letter. She folds the letter in two, then she realizes that it would not fit in the envelope and she folds it correctly (*conduite*)

MOT 2
No errors

MOT 3
No errors

MOT 4
No errors

MULTI-SCHEMATA OBJECTS

Teaspoon + ice cream cup. She stirs (*misuse2*)

SINGLE OBJECTS

Carpet beater. She uses it like a tennis racket (*misuse1*)

Fishing net. She uses it like a butterfly net (*misuse1*)

Patient FE.M

MOT 2

Preparing a Letter. She does not use the pen to write the address on the envelope (*tool omission* and *step omission*)

MOT 3

Preparing a Letter. She does not use the pen (*Tool omission* and *step omission*). She glues the stamp on the bottom of the envelope instead than on the top (*Mislocation 2,* quantitative error).

MOT 4

Drinking from a Bottle. She does not pour the water in the glass (*step omission* and *tool omission*).

Preparing a Letter. She glues the stamp as first step (*action anticipation*), she does not use the pen (*Tool omission* and *step omission*).

MULTI-SCHEMATA OBJECTS

Pliers and bolt. She does not use the pliers and she removes the bolt using the hand (*tool omission*).

Corkscrew and cork. She attempts to remove the cork with her hands (*tool omission*).

SINGLE OBJECTS

Fishing net. She uses it like a butterfly net (*Misuse 1*).

Liquid soap. She pours the soap, as it was a bottle (*Misuse 1*).

Patient GU.B

MOT 1

Making an Orange Juice. She cuts the orange in two (correct) but then she cuts one half in two parts (*perseveration or action addition*), she does not use the glass (*tool omission*)

Preparing a Letter to post. She does not glue the stamp (*step omission*), she does not recognize the glue (tool omission).

MOT 2

Preparing a Letter to post. She glues the stamp at the beginning of the sequence instead than at the end (*action anticipation*).

MOT 3

Preparing a Letter to post. She glues the stamp at the beginning of the sequence (*action anticipation*), she does not recognize the glue and she uses it as if it was an eraser (*Misuse 1*).

MOT4

Preparing a Letter to post. She glues the stamp at the beginning of the sequence (*action anticipation*), she does not use the glue (*step omission* and *tool omission*).

MULTI-SCHEMATA OBJECTS

Corkscrew + cork. She twists the corkscrew anticlockwise instead of clockwise, then she does the action correctly (*conduite*).

Corkscrew + crown cap. She attempts to use the corkscrew as if she is opening a cork (*Misuse 2*), then she tries to lift the cap using the curly part of the corkscrew as a lever instead of using its upper part (*Mislocation 2,* qualitative error).

Knife + marmalade. She attempts to use the knife as a lever to open the cap of the jar (*Misuse 1*).

SINGLE OBJECTS

Makeup brush. She uses it on the table (*mislocation 1*, I think that mislocation1 are all qualitative errors), as a paintbrush (*misuse 1*).

Flywhisk. She shows *perplexity* but eventually she uses it correctly (*conduite*.

Knife. She uses it correctly after several attempts (conduite).

Light bulb. She uses it correctly after several attempts (conduite).

Lipstick. She pantomimes the use of the object (pantomiming), and then she uses it correctly (conduite).

Patient IE.N

MOT 1

Drinking from a bottle. She removes the cap with her hand (*tool omission*). After several attempts she uses the bottle-opener in a wrong manner, as if she was opening with another type of tool[16] (*misuse 1*). She manages to open the cap, and then she pours correctly and drinks correctly

Preparing coffee. She first put the filter (*step omission*). She pours the coffee from the can without using the spoon (*tool omission*).

Preparing a letter to post. She does not click the pen button in order to use it (*step omission*). She shows clumsiness in using the pen with left and right hand. She pretends to use the glue on the external edge of the envelope (*mislocation2*), without actually gluing it (*toying*). She just lays the stamp on the envelope (*step omission*)

Preparing orange juice. She puts the whole orange on the squeezer (*action anticipation*), she tries to cut with her index finger (*body-part-as-tool*), then she sees the knife, she takes it, she cuts the orange in a wrong *orientation*. She squeezes the orange correctly. She drinks from the empty glass (*action anticipation*), then she pours the juice and she drinks again (*conduite*)

MOT 2

Drinking from a bottle. She attempts to use the bottle opener as if she was opening with another type of tool (*misuse 1*). The rest is done correctly.

Preparing coffee. She pours water and she puts the filter, then she closes the moka without putting coffee (step omission and action anticipation). She opens the coffee can, she takes the spoon and she stirs the grounded coffee in the can (action addition)

Preparing a letter to post. She folds the sheet in a wrong manner (misuse2), she glues the external part of the edge of the envelope (mislocation2). The rest is correct.

MOT 3

Preparing a letter to post. She folds the sheet correctly, she glues the external part of the edge of the envelope (mislocation2). She lays the stamp on the envelope without gluing it (step omission). She is extremely clumsy in using the pen.

MOT 4

Drinking from a bottle. She uses the bottle opener by pushing under the cap like a lever (*misuse1*). The rest is correct.

---

16  **This the kind of bottle opener used in the task, but the patient makes an action more appropriate to this kind of opener** 

Preparing coffee. She adds water and puts the filter, then she pours coffee in the filter directly form the can (tool omission). At the end she uses the spoon but to remove the exceeding coffee from the edge of the moka (action addition).

Preparing a letter to post. She lays the stamp on the sheet (*action addition*). She writes on the envelope (but she is agraphic), she glues the pictured side of the stamp (*mislocation2*). She glues the envelope correctly. She does not fold the sheet, she does not put it in the envelope and she does not seal the envelope (*3 step omissions*)

Preparing orange juice. She cuts the orange by pushing although she had started the movement correctly (*misuse 2* and *spoiling*). The rest is correct.

MULTI-SCHEMATA OBJECTS

Corkscrew + crown cap: clumsy but correct

Corkscrew + cork: she puts the corkscrew on top of the cork. She lifts and lowers the arms of the corkscrew without succeeding.

Toothpick alone: she moves it orizontally close to the mouth, like a toothbrush (misuse1)

Knife + marmalade: she stirs in the marmalade; the experimenter asks her to pretend to have a slice of bread in her hand: she stirs on the imagined slice of bread (misuse2)

SINGLE OBJECTS

Axe: wrong *orientation*, *timing* and *grasping*

Carpet beater: the *orientation* is wrong, but the rest is correct

Dropping bottle: first she squeezes the rubber part (*action anticipation*) then she opens the cap, she does not squeeze the rubber in order to make the drops go out (*step omission*)

Matchstick: the movement is correct but she execute it on her cheek (*mislocation1*)

Light bulb: wrong *grasping*, she rotates the arm in the air without moving the wrist (*frequency*? *Timing*?)

Hammer: wrong *orientation* (with the thinner part hitting on the nail)

Tweezers: the movement is similar to a razor, performed on the cheek and not pinching on the object (*misuse1*)

Drawing pin: she starts *toying* with the object; she performs an *unrecognizable* movement just moving the pin near to the table surface

Razor: the movement is *clumsy*. She moves the razor on a horizontal axis rather than perpendicularly to the blade (*orientation*?)

Lipstick: the movement is too wide, reaching the cheeks (*mislocation* or *frequency*?)

Painting roll: the *grasping* is upside-down, the movement is correct

Flywhisk: she moves it in the air (normal subjects usually flap it on the table or on a surface): *mislocation 1*

Saw: the *orientation* axis is parallel to the patient's chest, rather than perpendicular

Spray: (presented after the gun) she makes a *perseveration* like trying to pull the gun's hammer

Patient JU.A

MOT

No errors.

MULTI-SCHEMATA OBJECTS

No errors.

SINGLE OBJECTS

Dropping bottle. He tries to pour from the sealed dropper (*action omission*) similarly to a bottle (*Misuse 1*).

Makeup brush. He uses it on his hand (*Misuse 2*).

Patient RA.F

MOT 1

Drinking from a bottle. She does not use the bottle opener, she removes the cap with her hand (*Step Omission + Tool Omission*)

Making an Orange juice. She peels the orange (*action addition*) with her hand (*tool omission*), she opens the squeezer (*action addition*) before squeezing the orange

Preparing a Letter. She does not put glue on the envelope (*step omission*) but she uses the glue for the stamp.

MOT 2

Lighting a Candle. She lights the match before putting the candle on the candle-holder (*action anticipation*). The correct sequence would have been to put the candle on the holder first, then light the match, otherwise the match could burn your fingers while you make the other steps (but this is arbitrary).

Drinking from a bottle. She does not use the bottle opener, she removes the cap with her hand (*Step Omission + Tool Omission*)

Making an Orange juice. She peels the orange (*action addition*) and she opens it with her hand (*tool omission*), she opens the squeezer (*action addition*) before *pantomiming* the use of the squeezer, she does not use the glass (*tool omission*)

Preparing a Letter. She does not seal the envelope (*step omission*)

MOT 3

Drinking from a bottle. She does not use the bottle opener; she removes the cap with her hand (*Step Omission + Tool Omission*)

Making an Orange juice. She does everything correctly but she grasps the squeezer in a wrong manner (*grasping error*).

Preparing a Letter. She does not seal the envelope (*step omission*), she does not glue the stamp (*step omission*), and she tries to glue the stamp with the wrong end of the glue (*Misuse2*).

MOT 4

Drinking from a bottle. She does not use the bottle opener; she removes the cap with her hand (*Step Omission + Tool Omission*).

Making an Orange juice. She cuts away the bottom of the orange (*action addition*), she peels it (*action addition*), she uses the knife with the blade upside-down (*orientation*), she holds the squeezer in a wrong way (*grasping*)

Preparing a letter to post. She does not seal the envelope (*step omission*), she attempts to use the glue upside-down but she eventually succeed in gluing the stamp (*conduite*).

MULTI-SCHEMATA OBJECTS

Corkscrew + cork. She uncorks the bottle with her hand (*tool omission*) saying that the corkscrew has nothing to do with the task. She grasps the corkscrew and looks a t it (*perplexity*), toying with the object (*toying 2*).

Pliers + nail. She is perplex about what to do (*perplexity*), she toys with the pliers (toying 2) and she does not remove the nail from the wood (*step omission*).

Knife + cheese. She cuts the cheese by sawing (*Misuse 2*)

Spoon and coffee pot. She succeds after several attempts (*conduite*).

Corkscrew and cork. She removes the cork with her hand (*tool omission*)

Pliers and bolt. She pulls the bolt with the pliers, the same movement that should be used for a nail (*Misuse 2*)

Spoon and sugar jar. She brings the spoon to the mouth (*Misuse 2*).

SINGLE OBJECTS

Axe. She show perplexity before using it correctly (*perplexity*).

Razor. She uses it as a knife (*Misuse 1*).

Flywhisk. She shows *perplexity*.

Soap dispenser. She uses it as a spray (*misuse 1*).

Spray. She uses it as a soap dispenser (*Misuse 1* but also *perseveration*, as the dispenser was the previous item).

Makeup brush. She shows *perplexity*.

Squeegee. She shows *perplexity* and she toys with the object (*toying 2*).

Painting roll. She shows *perplexity* and she toys with the object (*toying 2*).

Hammer. She uses the tool in a wrong orientation (*orientation*).

Dropping bottle. She uses it as a perfume spray, pushing the cap with her index finger (*misuse 1*), then she tries to open it but she unscrews the rubber part of the cap instead of the hard part (*Mislocation 2,* quantitative error).

Gun. She pantomimes the use of the gun without actually shooting (*pantomiming*), she toys with the object (*toying 1*).

Lighter. She pushes on the button but not on the flint (*mislocation 2,* quantitative error?).

Patient SA.N

MOT 1

Drinking from a bottle. She handle the bottle opener with perplexity (*perplexity*), then she removes the cap with the hand (*tool omission*)

Preparing orange juice. She squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. She does not seal the envelope (*step omission*), she does not use the glue (*tool omission*), she does not open the pen before using it (*step omission*)

MOT 2

Drinking from a bottle. She removes the cap with the hand (*tool omission*)

Preparing espresso. She assembles the moka without coffee (*step omission*) and water (step omission). Then she redo everything correctly (*conduite*)

Preparing orange juice. She squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. She does not seal the envelope (*step omission*), she does not open the pen before using it (*step omission*)

MOT 3

Preparing a letter. She does not seal the envelope (*step omission*)

MOT 4

Preparing a letter. She does not seal the envelope (*step omission*)

MULTI-SCHEMATA OBJECTS

Corkscrew + cork. She does not lower the levers of the corkscrew (*step omission*)

Teaspoon + sugar. She eats like an ice cream (*misuse2*)

Corkscrew + crown cap. She puts the corkscrew on top of the bottle, as for a cork (*misuse2*)

Knife + jam. She eats like with a spoon (*misuse2*)

SINGLE OBJECTS

Dropping bottle. She does not press on the rubber part (*step omission*)

Makeup brush. She brushes the table and her chest (*mislocation1,* qualitative error)

Fishing net. She does correctly after few attempts (*conduite*)

Patient ST.V

MOT 1

Preparing orange juice. He cuts the orange by pushing (*misuse2*), he squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. He licks the stamp and he sticks it as first action (*action anticipation*). He folds the letter in a wrong manner (*misuse2*). He does not use the glue (*tool omission*)

MOT 2

Preparing espresso. He puts the water but not the coffee (*step omission*)

Preparing orange juice. He cuts the orange by pushing (*misuse2*). he squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. He folds the letter in a wrong manner (*misuse2*).

MOT 3

Preparing orange juice. He cuts the orange by pushing (*misuse2*). he squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. He licks the stamp and he sticks it as first action (action anticipation). He folds the letter in a wrong manner (*misuse2*).

MOT 4

Preparing orange juice. He squeezes the orange above the squeezer, like a half-lemon (*misuse1*)

Preparing a letter. He licks the stamp and he sticks it as first action (*action anticipation*). He folds the letter in a wrong manner (*misuse2*).

MULTI-SCHEMATA OBJECTS

Corkscrew + crown cap. He holds the corkscrew in a wrong orientation (*orientation*)

Toothpick + olive. He eats the olive (*utilization behaviour*?)

Teaspoon + sugar. He lift the sugar but does not pour it (*step omission*)

Knife + jam. He eats like with a spoon (*misuse1*)

SINGLE OBJECTS

Key. The movement is too wide (*frequency*)

Drawing pin. He perseverates with the movement for key (*perseveration*)
Soap dispenser. He uses it like a body deodorant (*misuse1*)

Patient ULC.

MOT 1

Drinking from a bottle. He shows the opening action without actually performing it (*pantomiming*), then he puts down the bottle opener and he pours without opening the bottle (*step omission*)

Preparing coffee. He seals the moka without putting water (*step omission*) and coffee (*step omission*). Then, after solicitation, he pretends to put coffee (*pantomiming*) but in the upper part of the moka (*mislocation 2,* qualitative error)

Preparing a letter. He puts all the objects on top of each other, without using them (*4 step omissions*)

MOT 2

Preparing a letter. He attempts to write without pushing the pen button (*step omission*), he folds the sheet in two but it cannot fit in the envelope, so hoe folds it again (*conduite*) but in an incorrect manner (*misuse2*). Then he glues the stamp on the side with the picture (*mislocation2*, quantitative or quantitative??) and he self-correct (*conduite*). He glues the stamp in the wrong side of the envelope (*mislocation 2,* qualitative). He does not seal the envelope (*step omission*), he does not write on the envelope (*step omission*), he does not use the pen at all (*tool omission*).

Preparing italian coffee. He pours too much water (*action addition*)

Preparing Orange Juice. He squeezes the orange with the hand, above the squeezer but without putting the orange on the squeezer, as a lemon (*misuse1* ?).

MOT 3

Preparing orange juice. He squeezes the orange with the hand, above the squeezer but without putting the orange on the squeezer, as a lemon (*misuse1* ?).

Preparing italian coffee. He pours too much water (*action addition*)

Preparing a letter. He does not push the pen button (*step omission*), he folds the sheet in an appropriate manner (*misuse 2*). He does not seal the envelope (*step omission*), he glues the stamp on the wrong side of the envelope (*mislocation2,* qualitative), he does not write on the envelope (*step omission*)

MOT 4

Preparing a letter. He folds the sheet in a wrong manner (*misuse2*). He does not write on the sheet nor on the envelop (*tool omission* and *step omission*). He glues the stamp on the wrong side of the envelope (*mislocation2*, qualitative)

Preparing orange juice. He squeezes the orange with the hand, above the squeezer but without putting the orange on the squeezer, as a lemon (*misuse1 ?*).

Drinking from a bottle. He does not use the bottle opener (*tool omission*) and he pours without opening the bottle (*step omission*)

MULTI-SCHEMATA OBJECTS

Coffee cup + teaspoon: he pretends to eat something from the cup (*misuse2*)

Toothpick: he pretends to eat an olive (*misuse2*)

Corkscrew + crown cap: he attempts to use the corkscrew like with a cork (*misuse 2*)

Knife + jam: he uses the knife to eat, as a spoon (*misuse 1*)

SINGLE OBJECTS

Tweezers: he uses on his fingernails (*misuse2*)

Cigarette: he breaks it in two parts (*toying1*)

Dropping bottle: he does not open it (*step omission*), he pretends to pour from it like a bottle (*misuse1*)

Flywhisk: he uses it like a ladle (*misuse 1*)

Makeup brush: he paints the table (*misuse 1*)

Lighter: he holds it in a wrong manner, twisting the lever in the wrong direction (*orientation*)

Soap dispenser: he pours on the table (*misuse1*)

Carpet beater: uses like a ladle (*misuse1*)

Saw: wrong grasping (*grasping*)

Patient VI.N

MOT 1

Preparing a Letter. She folds the paper sheet in a way that would be correct for a smaller envelope (*Misuse 2*).

MOT 2

Preparing a Letter. She writes on the paper sheet in a wrong orientation (*orientation*), she folds the paper sheet in a way that would be correct for a smaller envelope (*Misuse 2*).

MOT 3

Preparing a Letter. She folds the paper sheet in a way that would be correct for a smaller envelope (*Misuse 2*). She does not open the pen used to write (*step omission*).

Preparing Orange juice. She initially grasps the knife in a wrong manner (*grasping*) then she does everything correctly.

MOT 4

Lighting a Candle. She pretends to light the match (*pantomiming*)

Drinking from a Bottle. She does not use the bottle-opener properly (*misuse 1*)

Preparing a Letter. She tries to use the glue without removing the cap (*step omission*), she uses the pen upside-down (*orientation*).

MULTI-SCHEMATA OBJECTS

Corkscrew + cork. She tries to remove the cork with her hand (*tool omission*), then she pushes the corkscrew in the cork without twisting (*action omission*), finally she twists the bottle instead of the corkscrew (*Mislocation 2,* qualitative error).

Knife + cheese. She uses the knife with the blade upside-down (*orientation*).

Pliers + bolt. She uses the pliers with the same movement as a can opener (Misuse 1), then she uses her hand to remove the bolt (tool omission) and she finally succeeds (conduite)

Corkscrew + crown cap. She initially uses the corkscrew in a wrong orientation (*orientation*) then she corrects the action (*conduite*)

Knife + marmalade. She picks up the marmalade with the knife but she does not spread it (*action omission*) and she brings the knife to the mouth (*Misuse 1*).

Spoon + sugar. She does not put the spoon in the pot to pick up sugar, (*action omission*), but she just brings the spoon to the mouth (*Misuse 2*)

SINGLE OBJECTS

Lighter. She pushes the button without pushing the flint (misuse 2).

Match. She pretends to blow it but not to light it (Misuse 2).

Light bulb. She grasps the wrong end, then she pretends to screw it upside-down (grasping and orientation), the movement ha an inappropriate timing (frequency).

Hammer. She uses it in a wrong orientation (orientation).

Makeup brush. She brings to the face the brush in a wrong orientation.

Tweezers. She brings it to her head like a hairpin (Misuse 1).

Liquid soap. She pours from it like a bottle (Misuse 1).

Chapter V

General Discussion

The objective of the studies I presented was to directly address a recent divergence in theoretical claims that have been made with respect to the relationship between action systems and conceptual knowledge about actions and objects. On the basis of patient group studies, imaging and psychophysical results, it has been argued that motor production processes involved in using objects are critically involved in recognizing those same objects (Gallese and Lakoff, 2005) and in recognizing and imitating object associated pantomimes (Buxbaum et al., 2005). On the other hand, the theoretical claims based on single case dissociations hold that recognizing objects and actions does not require the reenactment of sensory-motor representations. Such different views may critically depend on the type of approach used: single case dissociations or group analysis. While both theoretical frameworks can explain the group patterns of correlations across tasks, single case dissociations are predicted only by those models which postulate a certain modularity of the system, such as the IPM and the SAS/CS .

In order to address this divergence, in Chapter II, I carried out analyses at both the group and the single case level in a sample of 37 brain damaged patients considering four tasks: action imitation, action recognition, object use and object recognition. We reproduced the associations at the group level that have been previously reported, as well as the dissociations at the single case level that are critical for cognitive neuropsychological methods (Shallice, 1988). Indeed, at the group level there were significant correlations (see also Buxbaum et al., 2005) between pantomime recognition and pantomime imitation, and between pantomime recognition and object use. These correlations have served as the basis for the argument from neuropsychological data that action production processes are constitutively involved in action recognition. However, within our group of patients, we also observed individual cases whose performance profiles are problematic for the Motor Theories of Action and Object Recognition. First, patients were observed who were impaired for object use but relatively unimpaired for action recognition, as well as the reverse. Second, patients were observed who were impaired for object use but relatively unimpaired for object recognition, as well as the reverse. Third, one patient was observed who was impaired for imitating pantomimes, but was relatively unimpaired for recognizing pantomimes and using objects. Such results are quite in disagreement with the embodied view, which postulates common neural and cognitive mechanisms to recognition and production of actions and object-related concepts.

In Chapter III, on the basis of single case analyses of two apraxic patients and two patients with semantic impairments, I have found that the former had intact fine-grained knowledge of the object that they failed to use, whereas the latter could use objects properly for which conceptual knowledge was lost. Based on these data, I have argued that motor production processes associated with object use are not necessary for successful object and action recognition, and that the loss of semantic visual and functional knowledge of tools does not affect significantly the ability to use them. Results support a separability of the "what" and "how" systems, in line with cognitive neuropsychological models that argue for a separate semantic system as well as input and output action systems (that we called IPM, Independent Praxeme Models, see also Heilman and Rothi, 2003).

In general, IPM models can account for dissociations between components within the praxis system. However, it has been shown that in those patients which show a selective disruption in action production, there may be qualitative differences between the error profiles in the use of common objects (Rumiati et al., 2001). In Chapter IV, I have reported a neuropsychological study that assesses, in particular, the validity of a computational model of routine action production, namely the Contention Scheduling Model. Such a model not only postulates the distinction between action and conceptual knowledge, but it provides an essential distinction is also able to account for qualitative differences in the error profiles of apraxic patients (Cooper, 2007). In order to test the predictions of this model, I have tested 15 left brain damaged patients on their ability to use objects in complex or simple tasks, as well as their fine-grained knowledge about those objects and their ability to associate action schemata to the corresponding objects. Dissociations at the single case level suggest not only that the action production systems are dissociable from object representations (as seen before), but also that the action production deficits may be affected by brain damage in qualitatively different ways, and that the classical object use tests used in clinical practice are not sufficient to individuate the locus of the damage within the action production system. In particular, it is possible to find disconnections between the ability to activate the correct object representation starting from the action schemata in the presence of intact connections in the other direction, and vice versa. Furthermore, the object representation network of the CS model does not overlap with the whole semantic memory. It is meant to encode action-relevant object features, and its neural bases are putatively based in the frontoparietal structures activated during SRC experiments (Grèzes et al., 2003).

The separation between action and conceptual system

As outlined above, in this thesis I have shown that actions and concepts representation are relatively independent processes that can be selectively impaired after brain damage. Considering the anatomical substrates of such processes, the relative separability of motor and semantic information about tools has also been supported by neuroimaging studies investigating their neural bases in human healthy adults (for reviews, see Johnson-Frey, 2004, and Lewis 2006). At least three cortical areas have been implicated in the *representation* of man-made objects/tools (Martin and Caramazza, 2003; Damasio et al., 2001): the left ventral precentral gyrus in the frontal lobe (or ventral premotor cortex, VPMC), the left posterior parietal cortex in the region of the intraparietal sulcus (IPS), and the posterior middle temporal gyrus (PMTG) either in the left hemisphere or bilaterally. Each of these areas seem to represent different features of object-related information. In a PET study subjects were asked to make judgments about the actions and functions associated with manipulable man-made objects contrasted with non manipulable objects (Kellenbach, Brett, and Patterson, 2003). Neither the left VPMC nor the PMTG were found to be selective for tool stimuli, although both regions responded more strongly to manipulable objects. The IPS, however, showed a clear selectivity for explicit *retrieval of action information* about manipulable objects. A comparable activation in the left posterior and inferior parietal cortex in 14 healthy subjects was found in another recent PET study (Rumiati *et al.*, 2004), where the subjects had to produce a wide range of skilled actions triggered by objects and effects of low-level perceptual, motor, semantic, and lexical processes were controlled. More importantly, the inferior posterior parietal region was found activated in the interaction term of the study of Rumiati et al. (-52; -44; +46). This area roughly corresponds to the supramarginal gyrus in Brodmann area 40, that is lesioned in both DR and FG, described in study 3A and in Rumiati et al (2001). Thus, the activation in the IPS found in the study of Kellenbach *et al.* (2003) may reflect implicit activation of sensory-motor transformations specific to individual object-types which have been explicitly triggered in the study of Rumiati *et al.* (2004). Similarly, Moll et al. (2000) found an activation of left Posterior Parietal Cortex (PPC) and IPS when subjects pantomimed or imagined tool-use gestures, as opposed to performing meaningless finger and limb movements.

In general, all these findings are in contrast with the strong embodied views that attribute a causal role of the motor knowledge in the processing of concrete (but also abstract, in some views) concepts. More plausibly, we think that the sensory-motor systems may play a critical role in the acquisition of concepts and perhaps, in some way, they drive the organization of visual knowledge in the ventral stream, computed over similarity metrics that also include motor features (see Mahon et al., 2007). However, the dorsal stream (here conceived as "how" system, extending the notion of "where" system) can still operate efficiently when the ventral stream is damaged, and the opposite dissociation is found too.

What is the Role of Motor Simulation in Action and Object Recognition?

In Chapters I and II, I proposed an operational definition of 'motor simulation': motor simulation refers to the automatic activation of motor production processes in the course of recognizing actions and objects. I chose this construal of the term 'motor simulation' because it is theoretically neutral regarding whether or not the activation of motor production processes is necessary in order for successful recognition of actions and manipulable objects to occur. According to this construal, the Motor Theories of Action and Object Recognition can each be decomposed into two separate assumptions. The first assumption, common to both hypotheses, is that observation of an action or a manipulable object automatically activates the motor system of the observer (for discussion of this 'direct matching hypothesis' as it applies to the Motor Theory of Action Recognition, see Prinz, 1997, Greenwald, 1970; Rizzolatti et al., 2001). The second assumption shared by the Motor Theories of Action and Object Recognition is that the activation of the motor system is required (i.e. necessary) for successful recognition of actions and manipulable objects. The validity of drawing a distinction between these two theoretical assumptions obtains only in the measure to which substance can be given to the notion of 'automatic' as opposed to 'necessary' activation.

As reviewed in Chapter I, there is a wealth of empirical data supporting the view that the motor system is 'automatically' engaged when observers view actions and manipulable objects. The Motor Theories of Action and Object Recognition are theories about the ways in which stimuli are processed, in that they claim that motor relevant information must be retrieved in order for successful recognition to occur. The neuropsychological data that have been reported and reviewed herein indicate that motor production processes are not necessary for successful recognition of either actions or objects. This conclusion sets in a new light the (undisputed) empirical fact that motor regions are automatically activated in tasks in which the retrieval of motor information is not necessary. In other words, the question is not: What role do motor production processes play in action and object recognition? A more basic question is: Why would there be activation of the motor system if that activation is not causally involved in the task?

To this point, discussions of the role of production processes in recognition have been very general (Buxbaum, Kyle, and Menon, 2005; Cubelli et al., 2000; Gallese and Lakoff 2005; Helbig, Graf, and Kiefer, 2006; Johnson-Frey, 2004; Kellenbach et al., 2003; Mahon and Caramazza, 2005; Martin et al., 2000; Pulvermüller, 2005; Rosci et al., 2003; Rothi et al., 1991). This generality respects our current knowledge in that it is not obvious how the term 'recognition' should be intended when discussing action and object recognition. The way in which the term 'recognition' is used may imply various commitments about the nature of the information that is required in order to accurately recognize (i.e., categorize) objects for use, and/or accurately identify objects for naming. One way in which we might be able to get some traction on this issue is by articulating the processes that are implicated by the term 'recognition'. How is it possible to observe a patient who is impaired at recognizing objects (e.g., for naming or conceptual judgments) but who can nevertheless use the objects correctly? Such dissociations suggest that the term 'recognition' may fractionate into 'recognition for use' and 'recognition for naming/conceptual access'.

Previous authors have proposed the IPM (Rothi et al., 1991; Cubelli et al., 2000) in which separate processes mediate action production, action recognition, and object recognition.

Left unspecified, however, this model is not satisfactory in that it provides no explanation of the fact that the motor system (e.g., output praxemes) is activated in tasks in which such activation would not apparently be required. For instance, naming pictures of manipulable objects differentially activates premotor and posterior parietal structures (e.g., Martin and Chao, 2001). However, the single case analyses suggest that such activation is not necessary. The IPM, in its strongest 'disembodied' form, provides no natural explanation of why there would be such activation. A further assumption would have to be made in order to explain why motor production processes are activated in task irrelevant situations when observers view actions or manipulable objects. With this model, such motor activation would be taken to be informative of the dynamics of activation flow throughout the system.

For discussion, let us assume a set of assumptions regarding the dynamics of activation flow throughout the cognitive system that collectively explain the activation of motor processes when observers view actions and manipulable objects. Even so, the ultimate reason for such an architecture would remain unresolved: it would remain unaddressed as to what purpose is served by such 'automatic' spreading of activation. One possibility is that the automatic activation of the motor system may serve the function of keeping the organism in a state of readiness. An alternative, and not mutually exclusive function, may concern feedback loops from motor processes to perceptual and conceptual processing (see Mahon et al., 2007, for discussion). In other words, it may be the case that motor information shapes the way in which non-motor relevant information is acquired by the system. It remains an open issue as to whether activation of motor information facilitates normal action and object recognition. We can now address this question with clear constraints on what might be implied by such facilitation, given the strong evidence provided by neuropsychological data, neurophysiological data, and functional neuroimaging data.

Alternatively, it might be argued from a strong Embodied Cognition perspective, that these neuropsychological data are not relevant to the embodied cognition hypothesis – that only activation evidence is relevant. This line of argument, however, does not go through. In the measure to which the activation data are taken as evidence for the embodied cognition hypothesis, then the neuropsychological data are problematic for that hypothesis. If the embodied cognition hypothesis were to be changed in such a way that the neuropsychological data were no longer relevant to that hypothesis, then one would have to reconsider what the activation evidence implies about the dynamics of information retrieval within the sensory/motor systems.

On the basis of the evidence available to date, it cannot be decided whether the automatic activation of motor information (i.e., motor simulation) contributes to the richness of conceptual experience. For instance, while the data we have reported from single case analyses indicate that output processes are not necessary for successful recognition, it remains an open question as to whether patients who have impaired output praxemes have, on some level, impoverished concepts of actions and manipulable objects. To this point, the associations at the group level and the dissociations at the single case level, that have been observed in neuropsychological studies, permit a model of praxis to be outlined in its basic features. An important issue that merits further research involves fleshing out the processes and content contained within the putative input systems that mediate action and object recognition.

The IPM model and the CS/SAS model: a possible integration.

In this thesis, we have shown that patients dissociations are better explained by models that conceive the action production system as modular and separated from the conceptual processing. Two models have been discussed throughout the chapters: the IPM proposed by Rothi et al. (1991) and the CS model by Cooper and Shallice (2000). Both aim at explaining normal and abnormal praxis. While the IPM was proposed to account for several phenomena and dissociations found mainly in the imitation domain, the CS model is most suited to explain disturbances in routine tasks involving objects.

Another model that comes into play for disorders of imitation is the dual route model presented in the Introduction (Tessari et al., 2007). This model can be considered as a modified Rothi (1991)'s model, as it postulates a separability of semantic and direct route. Since Tessari's model is not meant to explain also disorders in object use, we have not considered it in our patients discussion. The important difference with the IPM is that the notion of praxicons is not included and that in order to imitate well, one working memory must be intact. We agree that working memory plays an important role in the imitation of actions (especially in action sequences and pantomimes) and it should always be tested in patients study on Apraxia. In the CS/SAS model, working memory could be integrated in the concept of *resources* available to the system and in the top-dowm control that CS receives from the SAS.

As stated in the Introduction, we think that the CS/SAS and the IPM can be integrated and are not mutually exclusive, as they share important features: i) they consider the action production system separate from semantic representation; ii) they can predict patients' behaviour in terms of disconnections or damage to modules of the system; iii) complex action production can be fractioned in basic action representations, which are stored in the praxicon (IPM) or in the action schema network (CS).

References

Aglioti, S., Goodale, M.A. & DeSouza, J.F.X. Size-contrast illusions deceive the eye but not the hand. *Current Biology* 5, 679–685 (1995).

Allport, D.A. Distributed Memory, modular subsystems and dysphasia. In *Current Perspectives in Dysphasia*. Edited by Newman and Repstein. Churchill Livingstone, New York. (1985).

Bartolo, A., Cubelli, R., Della Sala, S., Drei, S., Marchetti, C. Double dissociation between meaningful and meaningless gesture reproduction in apraxia. *Cortex* 37, 696–699 (2001).

Barsalou, L.W. Perceptual symbol systems. *Behavioral Brain Sciences* 22, 577–660 (1999).

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

Bell, B.D. Pantomime recognition impairment in aphasia: an analysis of error types. *Brain and Language* 47, 269-278 (1994).

Binkofski, F, & Buccino, G. Motor functions of the Broca's region. Brain and Language 89, 362-369 (2004).

Bozeat, S., Lambon Ralph, M.A., & Patterson, K. When objects lose their meaning: What happens to their use? *Cognitive, Affective & Behavioral Neuroscience* 2, 236-251 (2002a).

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

Bozeat, S., Lambon Ralph, M. A., Patterson, K., & Hodges, J. R. The influence of personal familiarity and context on object use in semantic dementia. *Neurocase* 8, 127-134, (2002b).

Brass, M., Bekkering, H., & Prinz, W. Movement observation affects movement execution in a simple response task. *Acta Psychologica* 106, 3-22 (2001).

Brass, M., Bekkering, H., Wohlschläger, A. & Prinz, W. Compatibility between Observed and Executed Finger Movements: Comparing Symbolic, Spatial, and Imitative Cues. *Brain and Cognition* 44, 124-143 (2000).

Buccino, G., Binkofski, F., Fink, G. R., Fadiga, L., Fogassi, L., Gallese, V., Seitz, R. J., Zilles, K., Rizzolatti, G., & Freund, H. J. Action observation activates premotor and parietal areas in a somatotopic manner: An fMRI study. *European Journal of Neuroscience* 13, 400–404 (2001).

Buccino, G., Lui, F., Canessa, N., Patteri, I., Lagravinese, G., Benuzzi, F., Porro, C.A., and Rizzolatti, G. Neural Circuits Involved in the Recognition of Actions Performed by Nonconspecifics: An fMRI Study. *Journal of Cognitive Neuroscience* 16, 114–126 (2004).

Buxbaum, L.J., Kyle, K.M., & Menon, R. On beyond mirror neurons: internal representations subserving imitation and recognition of skilled object-related actions in humans. *Cognitive Brain Research* 25, 226-239 (2005).

Buxbaum, L. J., Veramonti, T., & Schwartz, M. F. Function and manipulation tool knowledge in apraxia: knowing 'what for'but not 'how'. *Neurocase,* 6, 83-97 (2000).

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

Buxbaum, L. J., Schwartz, M. F., & Carew, T. G. The role of semantic memory in object use. *Cognitive Neuropsychology* 14, 219–254, (1997).

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

Caffarra P, Vezzadini G, Dieci F, Zonato F, & Venneri A. Modified Card Sorting Test: Normative Data. *Journal of Clinical Experimental Neuropsychology*. 26, 246-50 (2004).

Caramazza, A., Capasso, R., Capitani, E., and Miceli, G. Patterns of comprehension performance in agrammatic Broca's aphasia: A test of the Trace Deletion Hypothesis. *Brain and Language* 94, 43-53 (2005).

Caramazza, A., Hillis A.E., Rapp, B.C., & Romani, C. The Multiple Semantics Hypothesis: Multiple Confusions? *Cognitive Neuropsychology*, 7: 161-189 (1990).

Carlesimo, G.A.; Caltagirone, C.; Gainotti, G. The Mental Deterioration Battery: Normative data, diagnostic reliability and qualitative analyses of cognitive impairment. *European Neurology* 36, (1996).

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

Coccia, M., Bartolini, M., Luzzi, S., Provinciali, L., and Lambon Ralph, M.A. Semantic memory is an amodal, dynamic system: Evidence from the interaction of naming and object use in semantic dementia. *Cognitive Neuropsychology* 21, 513-527 (2004).

Cooper, R. P. Tool use and related errors in ideational apraxia: The quantitative simulation of patient error profiles. *Cortex* 43, 319-337 (2007)

Cooper, R. P., Schwartz, M., Yule, P., & Shallice, T. The simulation of action disorganisation in complex activities of daily living. *Cognitive Neuropsychology* 22, 959–1004 (2005).

Cooper, R., & Shallice, T. Contention scheduling and the control of routine activities. *Cognitive Neuropsychology* 17, 297-338 (2000).

Coughlan, A.K., & Warrington, E.K. The impairment of verbal semantic memory: a single case study. *Journal of Neurology, Neurosurgery and Psychiatry* 44, 1079-1083 (1981).

Cubelli, R., Marchetti, C., Boscolo, G., & Della Sala, S. Cognition in Action: Testing a Model of Limb Apraxia. *Brain and Cognition,* 44, 144-165. (2000).

Craighero, L., Bello, A., Fadiga, L., & Rizzolatti, G. Hand action preparation influences the responses to hand pictures. *Neuropsychologia* 40, 492-502 (2002).

Crawford, J.R., & Garthwaite, P.H. Testing for suspected impairments and dissociations in single-case studies in neuropsychology: Evaluation of alternatives using Monte Carlo simulations and revised tests for dissociations", *Neuropsychology* 19, 318-331 (2005).

Crawford, J. R., & Garthwaite, P. H. Methods of testing for a deficit in single case studies: Evaluation of statistical power by Monte Carlo simulation. *Cognitive Neuropsychology* 23, 877-904 (2006).

Damasio, H., *et al*. Neural correlates of naming actions and naming spatial relations. *NeuroImage* 13, 1053-1064. (2001).

Damasio, H., Damasio, A., *Lesion Analysis in Neuropsichology* (Oxford University Press, New. York, 1989).

Decety, J., and Grèzes, J. Neural mechanisms subserving the perception of human actions. *Trends in Cognitive Sciences* 3, 172-178 (1999).

De Ajuriaguerra, J., Hécaen, H., & Angelergues, R. Les apraxies: variétés cliniques et latéralisation lésionelle. *Rev Neurol* (Paris) 102, 566–594. (1960).

De Renzi, E., & Lucchelli, F. Ideational apraxia. *Brain* 111, 1173–85 (1988).

De Renzi E, Motti F, & Nichelli P. Imitating gestures: a quantitative approach to ideomotor apraxia. *Archives of Neurology* 37, 6–10 (1980).

De Renzi, E., Pieczuro, A., & Vignolo, L. A. Ideational apraxia: a quantitative study. Neuropsychologia 6, 41-52 (1968).

Desimone, R., & Schein, S.J. Visual properties of neurons in area V4 of the macaque: sensitivity to stimulus form. *Journal of Neurophysiology* 57, 835-868 (1987).

Di Pellegrino, G., Fadiga, L., Fogassi, L., Gallese, V. & Rizzolatti, G. Understanding motor events: a neurophysiological study. *Experimental Brain Research* 91, 176-180 (1992).

Duncan, J. Disorganisation of behaviour after frontal lobe damage. *Cognitive Neuropsychology* 3, 271-290 (1986).

Dyde, R.T. & Milner,A.D. Two illusions of perceived orientation: one fools all of the people some of the time, but the other fools all of the people all of the time. *Experimental Brain Research* 144, 518–527 (2002).

Ellis, R., & Tucker, M. Micro-affordance: The potentiation of components of action by seen objects. *British Journal of Psychology* 91, 451-471 (2000).

Ferrari, P.F., Gallese, V., Rizzolatti, G., & Fogassi, L. Mirror neurons responding to the observation of ingestive and communicative mouth actions in the monkey ventral premotor cortex. *European Journal of Neurosciences* 17, 1703–1714 (2003).

Gaffan, D., Harrison,S., & Gaffan, E.A. Visual Identification Following Inferotemporal Ablation in the Monkey. *The Quarterly Journal of Experimental Psychology* 38B, 5-30 (1986).

Gallese, V. Embodied simulation: From neurons to phenomenal experience. *Phenomenology and the Cognitive Sciences* 4, 23–48 (2005).

Gallese, V., Migone, P., & Eagle, M.N. La simulazione incarnata: I neuroni specchio, le basi neurofisiologiche dell'intersoggettività ed alcune implicazioni per la psicoanalisi. *Psicoterapia e Scienze Umane,* 40: 543-580 (2006).

Gallese, V., & Lakoff, G. The Brain's concepts: the role of the Sensory-motor system in conceptual knowledge. *Cognitive Neuropsychology* 22, 455-479 (2005).

Galton, C. J., Patterson, K., Xuereb, J. H., & Hodges, J.R. Atypical and typical presentations of Alzheimer's disease: a clinical, neuropsychological, neuroimaging and pathological study of 13 cases. *Brain* 123, 484-498 (2000).

Geschwind, N. The apraxias: neural mechanisms of disorders of learned movements. *American Journal of Science* 63, 188-195 (1975).

Gibson, J. J. The theory of affordances. In *Perceiving, acting, and knowing: Toward an ecological psychology* (pp. 67-82). Shaw, R. & Bransford, J. (Eds.), Hillsdale, NJ: Erlbaum (1977).

Giovagnoli, A.R., Del Pesce, M., Mascheroni, S., Simoncelli, M., Laiacona, M., & Capitani, E., Trail making test: normative values from 287 normal adult controls. *The Italian Journal of Neurological Sciences*, 17, 305-309 (1996).

Goldenberg, G. Defective imitation of gestures in patients with damage in the left or right hemisphere. *Journal of Neurology Neurosurgery and Psychiatry* 61, 176–180 (1996).

Goldenberg, G. & Hagmann, S. The meaning of meaningless gestures: a study of visuo-imitative apraxia. *Neuropsychologia* 35, 333–341 (1997).

Goodale, M. A., & Milner A. D. Separate visual pathways for perception and action. *Trends Neurosci*. 15, 20-25 (1992).

Goodale, M. A., Milner, A. D., Jokobson, L. S., & Carey, D. P. A neurological dissociation between perceiving objects and grasping them. *Nature* 349, 154–156 (1991).

Goodale, M. A., Meenan, J.P., Bulthoff H.H., *et al.* Separate neural pathways for the visual analysis of object shape in perception and prehension. *Current Biology* 4, 604–610 (1994).

Grafton, S.T., Fadiga, L., A. Arbib, M.A., & Rizzolatti, G. Premotor Cortex Activation during Observation and Naming of Familiar Tools. *NeuroImage* 6, 231-236 (1997).

Greene, J.D., Patterson, K., Xuereb, J., & Hodges, J.R. Alzheimer disease and nonfluent progressive aphasia. *Archives of Neurology* 53, 1072-1078 (1996).

Greenwald, A.G. Sensory Feedback Mechanisms in Performance Control: With Special Reference to the Ideo-Motor Mechanism. Psychological Review 77, 73-99 (1970).

Grèzes, J., Tucker, M., Armony, J., Ellis, R., & Passingham, R. E. Objects automatically potentiate action: an fMRI study of implicit processing. *European Journal of Neuroscience* 17, 2735-2740 (2003).

Halsband, U., Schmitt, J., Weyers, M., Binkofski, F., Grützner, G., & Freund, H.J. Recognition and imitation of pantomimed motor acts after unilateral parietal and premotor lesions: a perspective on apraxia. *Neuropsychologia* 39, 200-216 (2001).

Hamanaka, T. *et al.* Cerebral laterality and category-specificity in cases of semantic memory impairment with PET-findings and associated with identification amnesia for familiar persons. *Brain Cogn* 30, 368–72 (1996).

Hartmann, K., Goldenberg G., Daurtmuller, M. & Hermsdorfer, J. It takes the whole brain to make a cup of coffee: the neuropsychology of naturalistic actions involving technical devices. *Neuropsychologia* 43, 625-637 (2004).

Heilman, K.M. Ideational apraxia: a re-definition. *Brain* 96, 861-864. (1973).

Heilman, K.M., & Rothi, L.J.G. Apraxia. In *Clinical Neuropsychology*, Oxford University Press New York. K.M. Heilman & Valenstein E. (Eds.), (2003).

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

Helbig, H.B., Graf, M., Kiefer, M. The role of action representations in visual object recognition. *Experimental Brain Research*, 174, 221–228. (2006).

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

Hodges, J. R., Bozeat, S., Lambon Ralph, M. A., Patterson, K., & Spatt, J. The role of conceptual knowledge in object use: evidence from semantic dementia. *Brain* 123, 1913-1925 (2000).

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

Hodges, J. R., Spatt, J., & Patterson, K. "What" And "How": Evidence for the dissociation of object knowledge and mechanical problem-solving skills in the human brain. *Proceedings of the National Academy of Sciences*, 96, 9444–9448 (1999).

Howard, D., & Patterson, K.E. *The Pyramids and Palm Trees test*. Bury St. Edmunds: Thames Valley Test Co. (1992).

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

Humphreys, G. W., & Forde, E.M. Disordered action schema and action disorganisation syndrome. *Cognitive Neuropsychology* 15, 481-815 (1998).

Humphreys, G.W., & Forde, E.M.E. Disordered action schema and action disorganisation syndrome. *Cognitive Neuropsychology* 15 (6-8), 771-811 (1998).

Jeannerod, M., Arbib, M. A., G. Rizzolatti, G., & Sakata, H. Grasping objects: the cortical mechanisms of visuomotor transformation. *Trends in Neurosciences* 18, 314-320 (1995).

Jeannerod, M., Decety, J., & Michel, F. Impairment of grasping movements following posterior parietal lesion. *Neuropsychologia* 32, 369–380 (1994).

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

Kellenbach, M. L., Brett, M., & Patterson K. Actions Speak Louder Than Functions: The Importance of Manipulability and Action in Tool Representation. *J Cogn Neurosci.* 15, 30-46 (2003).

Kohler, E., Keysers, C., Umiltà, M.A., Fogassi, L., Gallese, V., & Rizzolatti, G. Hearing Sounds, Understanding Actions: Action Representation in Mirror Neurons. Science 297, 846 – 848 (2002).

Kroliczak, G., Heard, P., Goodale, M.A. & Gregory, R.L. Dissociation of perception and action unmasked by the hollow-face illusion. *Brain Research* 1080, 9–16 (2006).

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

Laiacona, M., Capitani, E. & Barbarotto, R. Semantic Category Dissociations: a Longitudinal Study of Two Cases. Cortex 33, 441-461 (1997).

Lambon Ralph M.A., & Howard D. Gogi aphasia or semantic dementia? Simulating and assessing poor verbal comprehension in a case of progressive fluent aphasia. *Cognitive Neuropsychology* 17, 437-465 (2000).

Lauro-Grotto, R., Piccini, C., & Shallice, T. Modality-specific operations in semantic dementia. *Cortex* 33, 593-622 (1997).

Lawr, K.R., & Sartori, G. Category deficits and paradoxical dissociations in Alzheimer's Disease and Herpex Simplex Encephalitis. *Journal of Cognitive Neuroscience* 17, 1453-1459 (2005).

Lehmkuhl, G., & Poeck, A. A disturbance in the conceptual organization of actions in patients with ideational apraxia. *Cortex* 17, 153–158 (1981).

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

Liepmann, H. Apraxie. *Ergebnisse der gesamte Medizin* 1 , 516-543 (1920).

Liepmann, H. *The left hemisphere and action* (Trans. by D. Kimura). Munchener medizinische Wochenschrift, Nr. 48 and 49. (1905).

Luria, A.R. *Higher Cortical Functions in Man*. Basic Book, New York (1966).

Luzzatti C. Language disorders in Dementia. In: Denes G. & Pizzamiglio L. (eds) *Handbook of Clinical and Experimental Neuropsychology,* 809-846,. Psychology Press, Hove (UK) (1999).

Luzzatti C, Willmes K, & De Bleser R. *Aachener Aphasie Test (AAT)-Versione italiana*. Firenze: Organizzazioni Speciali (1994).

Mahon, B., & Caramazza, A. The Orchestration of the Sensory-Motor Systems: Clues From Neuropsychology. *Cognitive Neuropsychology* 22, 480–494 (2005).

Mahon, B., Milleville, S.C., Negri, G.A.L., Rumiati, R.I., Caramazza, A., & Martin, A. Action-Related Properties Shape Object Representations in the Ventral Stream. *Neuron* 55, 341-344 (2007).

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

Martin, A., & Caramazza, A. Neuropsychological And Neuroimaging Perspectives On Conceptual Knowledge: An Introduction. *Cognitive Neuropsychology* 10, 195-212 (2003).

Martin A., & Chao L.L. Semantic memory and the brain: structure and processes. Current Opinion in Neurobiology 11, 194-201 (2001).

Martin, A., Ungerleider, L.G., and Haxby, J.V. Category Specificity and the brain: The Sensory/Motor Model of Semantic Representations of Objects. In Gazzaniga, M. S. (Ed). *The new cognitive neurosciences*. Cambridge, MA, US: The MIT Press. (2000).

Martin, A., Wiggs, C.L., Ungerleider, LG. & Haxby, J.V. Neural correlates of category-specific knowledge. *Nature* 379, 649 - 652 (1996).

McCarthy, R.A., & Warrington, E.K. Evidence for modality-specific meaning systems in the brain. *Nature* 334, 428-430 (1988).

Michaels, C.F. S-R compatibility between response position and destination of apparent motion: evidence of the detection of affordances. *Journal of experimental psychology. Human perception and performance* 14, 231-240 (1988).

Milner, A. D., Perrett, D.I., Johnston, R.S., et al. Perception and action in visual form agnosia. *Brain* 114, 405–428 (1991).

Milner, A. D., & Goodale, M. A. Visual pathways to perception and action. *Prog Brain Res* 95, 317–337 (1993).

Milner, A. D., & Goodale, M. A. *The visual brain in action*. (Oxford Psychology Series, No. 27. Oxford University Press, Oxford, 1995).

Moll, J., *et al*. Functional MRI correlates of real and imagined tool-use pantomimes. *Neurology* 54, 1331-6 (2000).

Montomura, N., & Yamadori, A. A case of ideational apraxia with impairment of object use and preservation of object pantomime. *Cortex*, 30, 167-170 (1994).

Moreaud, O., Charnallet, A., & Pellat, J. Identification without manipulation: a study of the relations between object use and semantic memory. *Neuropsychologia* 36, 1295–301 (1998).

Morlaas, J. *Contribution à l'étude de l'apraxie*. Amédée Legrand, Paris (1928).

Mummery, C.J., Patterson, K, & Price, C.J. A voxel-based morphometry study of semantic dementia: Relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology* 47, 36-45 (2000).

Mummery, C.J., Patterson, K., Wise, R.J., Vandenbergh, R, Price C.J., & Hodges, J.R. Disrupted temporal lobe connections in semantic dementia. *Brain* 122, 61-73, 1999.

Negri, G. A. L., Lunardelli, A., Gigli G., & Rumiati R. I. Degraded Semantic Knowlegde and Accurate Object Use. *Cortex* 43, 376-388 (2007a).

Negri, G. A. L., Rumiati R. I., Zadini A., Ukmar M., Mahon B.Z. & Caramazza A. What is the role of motor simulation in action and object recognition? Evidence from apraxia. *Cognitive Neuropsychology* 24, 795-816 (2007b).

Norman, D., & Shallice, T., 1986: Attention to action: Willed and automatic control of behavior. In *Consciousness and Self Regulation: Advances in Research and Theory* (eds. Davidson, R., Schwartz, G., & Shapiro, D.), 1-18 (Volume 4. Plenum, New York, NY).

Ochipa, C., Rothi, L.J., & Heilman K.M. Conceptual Apraxia in Alzheimer's Disease. *Brain* 115, 1061-1071 (1992).

Ochipa, C., Rothi, L.J., & Heilman K.M. Ideational apraxia: a deficit in tool selection and use. *Ann Neurol* 25, 190–193 (1989).

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

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

Perrett, D.I., Mistlin, A.J., Harries, M.H., & Chitty, A. J. Understanding the visual appearance and consequence of hand actions, in *Vision and Action: The Control of Grasping* (ed. Goodale, M. A.), 163–342 (Ablex, Norwood, New Jersey, 1990)

Pick, A. Uber einen weiteren Symptomenkomplex im Rahmen der Dementia senilis, bedingt durch umschriebene starkere Hirnatrophie (gemischte Apraxie). *Monatsschrift fur Psychiatrie* 19 ,97-108 (1905).

Plaut, D.C. Granted modality-specific specialization in semantics: A computational account of optic aphasia. *Cognitive Neuropsychology*, 19, 603–639 (2002).

Poeck, K. Ideational apraxia. *Journal of Neurology* 230, 1-5 (1983).

Poeck, K., & Lehmkuhl, G. Ideatory apraxia in a left-handed patient with right-sided brain lesion. *Cortex* 16, 273-284 (1980).

Poeck, K., and Luzzatti, C. Slowly progressive aphasia in three patients. The problem of accompanying neuropsychological deficit. *Brain* 111, 151-168 (1988).

Pülvermüller F. Brain reflections of words and their meaning. *Trends in Cognitive Sciences* 12, 517-524 (2001).

Pülvermüller, F. (2005). Brain mechanisms linking language and action. *Nature*, 576-582.

Prinz, W. Perception and Action Planning. *European Journal of Cognitive Psychology*, 9, 129-154 (1997).

Rapcsak, S.Z., Ochipa, C., Anderson, K.C., and Poizner, H. Progressive ideomotor apraxia: evidence for a selective impairment of the action production system. *Brain and Cognition,* 27, 213-236 (1995).

Rey, A. *L'examen clinique en psychologie*. Paris: Presses Universitaires de France (1964).

Riddoch, M.J., Humphreys, G.W., Coltheart, M. & Funnell, E. Semantic systems or system? Neuropsychological evidence re-examined. *Cognitive Neuropsychology* 5, 3-26 (1988).

Rizzolatti, G, & Arbib, M.A.. Language within our grasp. *Trends in Neurosciences* 21, 188–194 (1998)

Rizzolatti, G., Fogassi, L., & Gallese, V. Neurophysiological mechanisms underlying the understanding and imitation of action. *Nature Reviews Neuroscience* 2, 661–670 (2001).

Rizzolatti, G., & Luppino, G. The Cortical Motor System. *Neuron* 31, 899-901 (2001).

Rizzolatti, G., Luppino, G., & Matelli, M. The organization of the cortical motor system: new concepts. Electroencephalography and Clinical Neurophysiology 106, 283-296 (1998).

Rosci, C., Chiesa, V., Laiacona, M., & Capitani, E. Apraxia is not associated to a disproportionate naming impairment for manipulable objects. N*europsychologia* 53*,* 412-415 (2003).

Rothi, L.J., Mack, L., & Heilman, K.M. Pantomime Agnosia. *Journal of Neurology, Neurosurgery, and Psychiatry* 49, 451-454 (1986).

Rothi, L.J.G., Ochipa, C., & Heilman, K.M. A Cognitive Neuropsychological Model of Limb Praxis. *Cognitive Neuropsychology* 8, 443-458(1991).

Roy E. A., & Square P. A. Common considerations in the study of limb, verbal and oral apraxia. *Advances in psychology* 23, 111-161 (1985).

Rumiati, R. I., & Humphreys, G.W. Recognition by action: dissociating visual and semantic routes to action in normal observers. *Journal of Experimental Psychology: Human Perception and Performance* 24, 631-47 (1998).

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

Rumiati, R. I., Zanini, S., Vorano, L., & Shallice, T. A form of Ideational Apraxia as a deficit of contention scheduling. *Cognitive Neuropsychology*, 18 , 617-642. (2001).

Schwartz, M.F., Montgomery, M.W., Fitzpatrick-Desalme, E.J., Ochipa, C., Coslett, H.B., & and Mayer, N.H. Analysis of a disorder of everyday action. *Cognitive Neuropsychology* 12, 863-892 (1995).

Schwartz, M.F., Reed, E.S., Montgomery, M.W., Palmer, C., & Mayer, N.H. The quantitative description of action disorganisation after brain damage: A case study. *Cognitive Neuropsychology* 8, 381–414 (1991).

Shallice, T. *From Neuropsychology to Mental Structure*. (Cambridge University Press, Cambridge, 1988).

Snowden, J. S., Goulding, P. J., & Neary, D. Semantic dementia: A form of circumscribed atrophy. *Behavioural Neurology* 2, 167-182 (1989).

Spinnler H., & Tognoni G. Standardizzazione e taratura italiana di test neuropsicologici. *Italian Journal of Neurological Sciences*. suppl. 6 al N°8, 1-20. (1987).

Steinthal, H. *Einleitung in die Psychologie und Sprachwissenschaft*. Berlin; Harrwitz and Gossman (1871).

Tessari A., Canessa N., Ukmar M., & Rumiati, R.I. Neuropsychological evidence for a strategic control of multiple routes in imitation. *Brain* 130, 1111-1126 (2007).

Tucker, M., & Ellis, R. On the relations between seen objects and components of potential actions. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 830-846 (1998).

Tucker, M., & Ellis, R. The potentiation of grasp types during visual object categorization; *Visual Cognition* 8, 769-800 (2001).

Tyler, L. K., & Moss, H. E. Towards a distributed account of conceptual knowledge. *Trends in Cognitive Sciences*, 5, 244–252 (2001).

Umilta`, M.A., Kohler, E., Gallese, V., Fogassi, L., Fadiga, L., et al. "I know what you are doing": a neurophysiological study. *Neuron* 32, 91–101 (2001)

Ungerleider, L. G., & Mishkin, M. Two cortical visual systems. In *Analysis of visual behavior* (eds. Ingle, D. J., Goodale M. A., & Mansfield R. J. W.) 549–586 (MIT Press, Cambridge, Massachusetts, 1982).

Von der Heydt, R., Peterhans, E., and Baumgartner, G. Illusory contours and cortical neuron responses. Science 224, 1260-1262 (1984).

Warrington, E.K. The selective impairment of semantic memory. *Quarterly Journal of Experimental Psychology* 27, 635-657 (1975).

Warrington E.K., & James M. *The Visual Object and Space Perception battery*. Bury St Edmunds: Thames Valley Test Company (1991).

Warrington E.K. *The Camden memory test*. Hove: Psychology Press (1996).

Warrington, E. K., & McCarthy, R. Multiple meaning systems in the brain: a case for visual semantics. *Neuropsychologia* 32, 1465-1473 (1994).

Warrington, E. K., & McCarthy, R. Categories of knowledge: Further fractionations and an attempted integration. *Brain*, 110, 1273–1296 (1987).

Warrington, E.K., & Shallice, T. Semantic access dyslexia. *Brain* 102, 43-63 (1979).

Wilson, M. Six views of embodied cognition. *Psychonomic Bulletin Review* 9, 625-636 (2002).

Zangwill, O. *Cerebral Dominance and its Relation to Psychological Function*. Edinburgh (1960).

Zanini, S., Rumiati, R.I., & Shallice, T. Action sequencing deficit following frontal lobe lesions. *Neurocase* 8, 88-99 (2002).

Acknowledgements

☺First of all I owe a big GRAZIE to my family, which always believed in my capacities.
☺I thank my supervisor Raffaella for her support in these four years.
☺I thank the two external examiners, Giuseppe Sartori and Rick Cooper, together with Tim Shallice, for the time dedicated to me and for their precious suggestions to improve my work (thesis aside).
☺ I thank Brad Mahon, who has been an excellent co-worker and helped me more than he could imagine.
☺ Special thanks to the people that most helped me with the patients work: Alberta Lunardelli, Alina Menichelli, Paola Mengotti, Anna Sverzut, Maja Ukmar and Antonella Zadini.
☺ I thank all the patients and controls that took part in the studies.
☺I am grateful to all past and present SISSA students, postdocs, professors, administration and technical staff... for being the most smart, friendly and fun people one can work with!
☺ I thank all my friends who could not come but are here with their heart.
☺ I thank my lovely flatmates who have cleaned the house in my place when I was too busy...
☺E ringrazio Roby perchè mi ha sopportato pazientemente in questi ultimi due lunghi mesi!

☼ This thesis is dedicated to Emiliano and his resuscitated academic career ☼