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Semantic memory impairments: models and experimental investigations

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Introduction

The list of the disciplines that are involved in the study of brain functions is extremely rich, including physics biophysics, biochemistry, molecular biology, neuroendocrinology, electrophysiology, neurochemistry and pharmacology, citology, neuroanatomy, neurology, and, in the domain of behavioural sciences, experimental psychology, neuropsychology, cognitive neuropsychology and neurolinguistics. Scientists from different disciplines usually take advantage of a well established pool of methodologies and develop their theories on the base of a domain-specific background.

This multidisciplinary approach has proven to be extremely fruitful for the progress of brain sciences, as documented by the amount of collected information. From a methodological point of view it implies that it is reasonable to consider different levels of scientific descriptions for the brain, going from behavioural sciences to biophysics, as at each level it is possible to set well defined scientific problems. This is by no means trivial as the setting of the problem is a fundamental step in research. However, once the problem is appropriately set, the question arises of the level at which an appropriate explanation must be provided.

The reductionist approach states that any valid explanation of a given phenomenon will finally be provided in terms of lower level mechanisms. Other approaches tend to stress the independence and the validity of explanations which do not refer to lower level mechanisms.

I will consider here as a specific example the case of the distinction between storage and access deficits in semantic memory impairments, which is extensively treated in the first chapter of this thesis. Semantic memory (Tulving and Donaldson, 1972) is the store of all that knowledge which allows us to recognize the stimuli we perceive from the world as meaningful ones: it includes the meaning of the words, the knowledge about the objects and tools we perceive and use, and, in general, the global amount of information about the world that we collect in our life. It is known since the seventies that semantic memory can be selectively impaired due to brain damage (Warrington, 1975).

One of the most frequent evidence of a semantic memory impairment is a word comprehension deficit: the patient, although able to perceive and repeat a spoken word or to read it aloud, does not understand its meaning. According to some authors (Warrington and Shallice, 1979; Shallice, 1988) the comprehension deficit can be due to two different pathological phenomena: either the representation of the meaning of the word is lost, or it is temporary unavailable. Warrington and Shallice (1979) claimed that it is possible to distinguish between the two alternatives on the basis of some empirical criteria which can be used to define the patterns of performance of the typical 'impaired access' and 'degraded storage' patients[1]. Given the rarity of the access patients however, it took around twenty years to have an exhaustive definition of the two pattern of performance, and this was only after specific experimental tools were devised. During that period many influential cognitive

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[1] It is not necessary to go into the details of the proposed distinction now, as the point I would like to make here is not concerned with them.

neuropsychologists even denied that such a phenomenon had to be explained.

The neuropsychological differentiation of the two types of semantic memory impairment is an example of the laborious process of correctly setting the term of a problem to be addressed. The next step, in this specific case, is to explain how the two different types of impairment may arise from neural damage.

A neuropsychological account of the phenomenon has recently been provided by Warrington and Cipolotti (1996). The authors ascribe the storage impairment to a degradation of the semantic representations and the access impairment to a temporary 'refractoriness' of the representation: once a representation has been accessed, it becomes unavailable for a given interval of time thereafter. Refractoriness is an entirely appropriate neuropsychological concept, as it provides an exhaustive explanation of the experimental evidence. An indirect proof of the credit that has been tributed to the refractoriness hypothesis is in the increasing number of case reports that have been published by other research groups in the very last years which document the same phenomenon and explain it in the same way (Forde and Humphreys, 1995; Forde and Humphreys, 1997).

Warrington and Cipolotti claim that this explanation is biologically plausible as the refractory state could be ascribed to a temporary shortage of metabolic supply to the neuronal activity, which would produce the a reversible silencing of the neurons. However this claim is not supported by any particular evidence; the discipline-specific consistency of the hypothesis is assumed to provide sufficient evidence, and the possible physiological base of the phenomenon is just mentioned *en passant*.

A different approach to the same problem is considered in chapter 1 of this thesis, where a very preliminary attempt is made to provide a physiological background to the refractoriness hypothesis. In fact, although it is evident that the refractoriness hypothesis is well founded from a neuropsychological point of view, in my opinion its appeal is grounded on the plausibility of the underlying physiological assumptions, which nevertheless are payed so little attention.

In order to collect some more specific suggestions on the mechanisms that could produce the refractory state, a very simple, but explicit model of storage and retrieval for associative memory, as semantic memory probably is, has been considered. The model is based on a neural network of the Hopfield type (Hopfield, 1982), in which the computational units are intended to represent, at a very schematized level, the behavior of real neurons. Furthermore the network is endowed with a learning rule of the Hebbian type (Hebb, 1949), the only type of learning for which a plausible neurobiological basis has been suggested (Braitenberg and Schuz, 1992). The advantage of this type of modeling is that it allows for a rudimentary verification of the effects that highly simplified but plausible biological mechanisms may have on the neural computation processes which ultimately result in cognitive performance. As a consequence, a better definition of the characteristics of the physiological mechanism that could be at the basis of a a given phenomenon, such as the existence of refractory states in semantic memory in our example, can be obtained. Once the mechanism is defined with respect to the model, the problem of the selection and the evaluation of possible realistic candidates for their biological implementation becomes hopefully more tractable.

The style of neural network modeling that is adapted in this work may be contrasted with connectionism, in which the units or nodes performing the computations are often not intended to model individual neurons, and the variables that are used in the simulations are not considered to correspond to biological quantities. Moreover connectionist networks are often trained with algorithms using backpropagation of information from the output to the inner layers, a non local process whose biological plausibility is dubious (But see (Plaut and Shallice, 1993) for a different approach). Connectionist models (McClelland,J.L. and Rumelhart,D.E., 1986) are valuable for they show what can be computationally achieved with networks in which the strength of the connections between simple units determins the nature of the computation performed by the system. They are a possible starting point for understanding how very complex computations could be implemented in brain-like systems. However they often use learning algorithms that are in some sense too powerful with respect to the ones that are presumably available to brain computation. Hence neural networks of the more realistic type must be preferred when the aim of modeling is to provide a link between two different levels of descriptions of a given cognitive phenomenon (Rolls and Treves, 1998).

In order to clarify further the differences between the two styles of modeling with neural networks, I will consider David Marr's three level description of information processing in cognitive systems. According to Marr the higher level of description of a given cognitive system is the level of the computational theory, that is the computational problem that the system is meant to deal with. The next level of description is the level of the representations and the algorithm by which a given computation is achieved. Finally there is the level of the neural implementation of the representations and of the algorithm. In Marr's view the three levels of description are in fact independent one from the other, so that the structure of the computational theory should be defined irrespective of the algorithm which instanciate it. and the algorithm in turn should be explained without reference to the neural implementation. In my opinion connectionist models fit rather well within Marr's schema, as they should be considered as possible computational theories describing the type of problem that a cognitive system is meant to deal with.

The neural networks of the more realistic type on the contrary do not fit with any of the levels of description proposed by Marr. Furthermore in this type of modeling the assumption on the independence of the levels of description is rejected: the structure of the neural system is considered to pose strict limitations to the nature of the computation that the system is able to perform, and ultimately, it is thought to determine it.

In the absence of a precise localization and of a detailed description of the neurological substrate of a given function however, it is nevertheless possible to produce reasonable neural network models of cognitive functions. In fact, it is known from neuroanatomy that the structure of the neocortex and in particular the pattern connectivity, at a first approximation can be considered to be a rather uniform one (Braitenberg and Schuz, 1992). The major source of diversity appear to arise from the physical separation of the information channels belonging to different context (sensorial modalities, subcortical areas etc.), and originating in different regions. Apparently one could say that the syntax of the neural messages is universal across the neurons of the cortex, while the content of the message varies according to where it comes from. This being the case, in general it is possible to build up neural network models that are based on a reasonable schematizations of the cortical circuitry. It is clear that if more detailed evidence is collected on the localization of the function and on the anatomical and physiological characteristics of the specific area (or areas) involved in the function, it would be important to incorporate it in the model and use it to generate appropriate constraints for its behaviour.

This is indeed the case for the neural network model of semantic memory that is described in the second chapter of the thesis. Neuropsychological literature and more recently, imaging experiments, agree in pointing to the inferotemporal regions as the crucial areas over which the semantic network would extend, although for specific categories, such as the one of living items, the occipitotemporal regions seems to be involved. In the absence of a more precise description of the anatomical substrate of the semantic system, a conservative approach has been adopted here to neural network modeling: the semantic network has been assumed to be composed a set of interconnected associative neural networks in accordance with one of the current hypotheses on the structure of the semantic system, the so called multimodal semantics hypothesis. Each network is meant to store information that is qualitatively different, such as modality-specific knowledge, encyclopedic knowledge etc.. The format of the memories, the learning rule, and the network dynamics are nevertheless the same over all the networks, so that each subsystem performs basically the same type of computation (associative retrieval). The second chapter of this thesis is devoted to the study of the equilibrium properties of the dynamics of the system of interconnected networks.

The following part of the thesis concerns with a neuropsychological assessment of the multimodal semantic hypothesis. A single case study is presented of a patient suffering from a degenerative condition mainly involving the temporal lobes, the so called Semantic Dementia syndrome. The peculiarity of the case is a marked modality-specific performance in semantic tasks. In fact the patient consistently demonstrates the preserved ability to support specific types of semantic judgements from visual, but not from verbal, input. In addition the representations accessed from visual input were found to trigger complex behavioural schemata, while on verbal material the patient performed almost invariably at chance level. The experimental investigation on the residual semantic competence of this patient allows a preliminary description of the nature of visual semantic representations to be derived.

Here I would like to stress the complementary role that the neuropsychological investigation and the computational approach can have in the description of a cognitive system, such as semantic memory. Neuropsychological evidence is crucial in determining the global structure of the system at a first approximation. In the present case for example the system of associative networks is thought to represent an implementation of the multimodal semantics hypothesis. The study of the (biologically plausible) explicit computational model is then necessary in order to verify if, and under what conditions, the proposed architecture is indeed able to solve the type of problems the real brain system is thought to deal with. In fact, as the model is intended to be a simplified version of the real biological network, its performance must be robust and stable in that range of values of the parameters, such as the connectivity and the mean level of activity in the network, that are consistent with the values taken by the biological factors they schematize. Once the plausibility of the architecture is verified on computational grounds, more specific neuropsychological investigations may be planned in order to gain better insight on the nature of the representations that are involved in the computation performed by the system.

In the last part of the dissertation the issue of the hemispheric localization of the semantic system is addressed. As reviewed in chapter 4, the literature on semantic memory functions in the right hemisphere is vast, but the evidence collected is still insufficient to derive any solid conclusion on the relevance of the supposed right hemisphere contribution to semantic processing.

In the discussion of the single case study presented in chapter 3, the hypothesis was raised that the selective preservation of the visual semantic representations documented in that patient could be related to the marked asymmetry of the temporal lobe atrophy which was evident from imaging data: in fact the right hemisphere of the patient appeared to be distinctly less atrophic than the left. In order to test this hypothesis some of the experiments performed with the Semantic Dementia patient were proposed in an appropriately modified version to a commissurotomized subject. Furthermore the same subject was submitted to other investigations devoted to assessing the level of semantic processing of visually presented stimuli in the isolated right and left hemispheres.

The interpretation of the result obtained with this patient has been somewhat laborious, as the level of performance reached by the right hemisphere was often found to be statistically different from chance, but rather low in most of the experiments. However, the pattern of performance of the isolated right hemisphere was found to be qualitatively different from the pattern of performance of the Semantic Dementia patient.

The split brain population is characterized by a marked variability in performance, which is possibly a consequence of the variability in the medical history of the patients. Generalizations of results obtained with these patients to the behaviour of a healthy right hemisphere require a careful assessment. Maybe more converging evidence from neuropsychological investigations and imaging experiments will provide the suitable base for understanding the role that the right hemisphere might play in non pathological semantic processing.

Chapter 1

1.1 The storage versus access distinction: a brief historical review.

The selective impairment of Semantic Memory was first documented in three patients suffering from a cortical progressive degenerative disease (Warrington, 1975), whose knowledge of word meaning was found to be disproportionately poor when compared with other intellectual skills, and in particular with their phonological and syntactic abilities. The representation of the meaning of some words had entirely disappeared from their vocabulary, and for many other words some degree of preservation of *superordinate* information was detected. *Consistency* of performance across words was later documented in comprehension tasks (Coughlan and Warrington, 1981). A major factor in determining which representations were more fragile and which were more robust, was found to be the word *frequency* class. This pattern of performance was ascribed to a *degradation* of the semantic store, due to the neural cell loss typically found in these pathologies. Since then, a similar pattern of performance has been described in many patients suffering from cortical degenerative conditions such as Dementia of the Alzheimer Type (D.A.T.) (Chertkow and Bub, 1990) and Pick's Disease (Hodges et al., 1992a), but also in some cases of recovery from Herpes Simplex Encephalitis (Warrington and Shallice, 1984; Sartori et al., 1993).

In 1979 Warrington and Shallice described a patient suffering from acquired dyslexia whose ability to read aloud single words was extremely *inconsistent*; furthermore in this case word frequency did not influence the probability of correct reading. Related results were soon after found in a second dyslexic patient (Warrington, 1981). In particular Warrington and Shallice (1979), on the grounds of the contrast in performance between patient E.M. (Warrington, 1975) and patient AR (Warrington and Shallice, 1979) introduced a theoretical distinction between *storage* and *access* impairments. According to them, four *experimental criteria* could be used to distinguish degraded storage and impaired access patients:

- item consistency vs item inconsistency across trials;
- presence or absence of major frequency effects;
- presence vs absence of selective loss of subordinate level information;
- effectiveness vs ineffectiveness of semantic cueing.

In a network approach semantic processing can be impaired either due to the *irreversible degradation* of the memory traces corresponding to a given semantic representation. or due to a *temporary retrieval difficulty*. which can be caused by the network parameters exceeding their stability ranges. According to Shallice (1988), the first case corresponds to the storage impairment while the second corresponds to the access impairment.

Patient V.E.R., suffering from an infarct of the left middle cerebral artery, was the first global dysphasic patient in which an impairment of oral and written word comprehension was attributed to an access deficit (Warrington and McCarthy, 1983). V.E.R. was extensively investigated with word-object matching techniques, in which the same arrays of stimuli were repeatedly tested. The basic characteristics of his performance were *inconsistency* across trials, *category specificity*, with performance on living items better than on objects, and a significant effect of *presentation rate*: the patient appeared to benefit from disproportionately long response-stimulus intervals. As the rate of presentation effects are rather unusual, it may be useful to summarize what is the actual experimental manipulation that has been introduced in order to detect them: the patient is presented with an array of m pictures, then the experimenter names one of the items presented in the pictures and the patient is instructed to point to it. All the m presented items are named by the experimenter one after the other in pseudo-random order, and the entire set of m trials is repeated for n times. So the same m pictures are used for $(n \cdot m)$ subsequent trials, n trials for each. Then another set of m items is tested. The response-stimulus interval is calculated from the moment in which the patient provides an answer to the presentation of the subsequent stimulus.

A significant *decrement in performance across subsequent presentations* of the same items was noticed, together with a negative effect of *semantic relatedness* between target and distractors in the word-matching task. Unfortunately frequency effects were not properly investigated (except in one test in which they were found to be significant). Although with respect to the distinction between storage and access already proposed by Warrington and Shallice (1979), V.E.R would better fit in the pattern of the access impairment, the relevance of the rate effect, which was interpreted as an *interference* effect, led the authors to suggest that the deficit could be better described in terms of a temporary, possibly category specific, *refractoriness* of the semantic representations.

The rate of presentation, semantic relatedness and inconsistency effects were replicated and extended in a second case of global dysphasia of vascular origin, patient Y.O.T. (Warrington and McCarthy, 1987).

In 1994 a putative case of an access deficit disproportionately severe for the semantic class of proper names was described in a tumor patient, M.E.D. (McNeil et al., 1994). In this case performance also appeared to be unrelated to word frequency. However patient H.E.C., a vascular case recently described by (Cipolotti and Warrington, 1995), is the first access patient in which the absence of word frequency effects has been extensively documented. This lack of frequency effect is particularly striking in that word frequency effects are usually pervasive in language impairments; furthermore, as will be discussed in section 1.4, it is not easy to imagine how this could not be the case from a computational perspective.

Rapp and Caramazza (1993) voiced a rather diffuse skepticism on the validity of the proposed criteria for distinguishing between storage and access deficits: they questioned the empirical basis of the distinction, in particular by pointing out that the co-occurrence of the characteristics of each type of pattern is not at all mandatory in the literature. Among other less interesting criticisms, they cited two patients, P.W. (Howard, 1985) and K.E. (Hillis et al., 1990) exhibiting consistency together with lack of frequency effects, and they argued that the evidence about consistency in many so called storage patients is not conclusive Shallice (1988, p.285) however argued that in P.W.'s case the level of impairment was so mild that loss of only limited attribute information could be expected even for low-frequency items. With respect to the frequency effect Rapp and Caramazza (1993) appropriately observed that *"even granting that more frequent events are more likely to be resistant to damage, it does not follow that this increased resilience should apply only to stored repres-*

entations and not to aspects of mechanisms or operations of access" (p.128). Furthermore they argued that it would be possible to accommodate the experimental evidence in the context of very different theoretical accounts, by considering the level at which the various phenomena should be placed in different models of semantic memory and of lexical access, so that, according to them, the distinction cannot be treated as a pre-theoretical one, as claimed by Shallice (1988).

The criticisms listed here surely deserved serious consideration. Empirically Warrington and Cipolotti (1996) produced a detailed and exhaustive description of four storage and two access patients, whose performance has been directly compared on identical tests, namely different versions of the word-picture matching task, designed to investigate the effects of word frequency, rate of presentation and semantic relatedness, and to assess consistency. The results clearly confirmed that it is possible to distinguish the two patterns of impairments on solid experimental grounds: the performance of the storage patients, which is consistent across trials and influenced by word frequency, is not influenced by the rate of presentation (response-stimulus interval), and by semantic relatedness (between target and distractors), while the opposite pattern holds for the access patients. Tables 1.1 and 1.2 reproduce the evidence on frequency and rate of presentations effects. Consistency data are presented in Table 1.3.

The absence of any effect of frequency is a striking phenomenon, as it is known that frequency effects are the rule in the literature on aphasia (Shallice, 1988). The rate effect also is very rare, and in fact it has been documented in this type of globally aphasic patients only.

It is now evident that a fundamental distinction between the two groups of patients

FREQUENCY EFFECTS

$\%$ $correct$	$High$	low	χ^2 $(d.f. = 1)$	p
$H.E.C.$	76	78	0.07	$n.s.$
$A1$	62	60	0.003	$n.s.$
$A2$	64	70	1.01	$n.s.$
$S1$	96	39	109.40	< 0.001
$S2$	87	42	62.17	< 0.001
$S3$	92	40	87.44	< 0.001
$S4$	97	36	117.65	< 0.001

Table 1.1: Statistical effect of the word frequency class (high and low) at the word-picture matching test. Percentage correct is reported for three access and four storage patients: all the patients are described in (Warrington and Cipolotti, 1996), except for H.E.C. (Cipolotti and Warrington, 1995).

can be found in the *aetiology* of the disease: storage impairment is invariably associated with a neurodegenerative condition (chronic in the case of Alzheimer and Pick's disease and post-acute in the case of Herpes Simplex Encephalitis), while all the access patients presented in the literature were suffering from vascular accidents or from tumors.

In conclusion, 'even granting' that solid experimental evidence for the dissociation has been definitely produced - and I will consider the two groups of patients described by Warrington and Cipolotti (1996) as prototypical of the storage and access types of impairment - two other issues discussed by Rapp and Caramazza (1993) still remain to be addressed: the first is how to produce conclusive evidence about consistency, the second is how to interpret the quite surprising lack of frequency effects and presence of rate effects documented in access patients.

RATE OF PRESENTATION EFFECTS

$\%$ *correct*	*Fast* ($1s$)	*Slow* ($15s$)	χ^2 ($d.f. = 1$)	p
$A1$	49	73	16.89	< 0.001
$A2$	58	76	10.60	< 0.01
$S1$	67	69	0.143	$n.s.$
$S2$	63	66	0.24	$n.s.$
$S3$	64	69	0.77	$n.s.$
$S4$	63	69	1.25	$n.s.$

Table 1.2: Statistical effect of the rate of presentation at the word-picture matching test, measured as response-stimulus interval: the fast rate is 1 second, the slow rate is 15 seconds. Percentage correct is reported for two access and four storage patients. From (Warrington and Cipolotti, 1996).

1.2 Consistency Measures.

1.2.1 Short and long time scale consistency.

Consistency has possibly been considered the key criterion for distinguishing between storage and access impairments. It is generally assumed that if a given semantic representation is lost, a patient will fail to score in whatever semantic task would require it; however inferring that performance will be consistently good if a given representation is not lost, requires further assumptions on the efficiency of the access procedures.

For patients suffering from degenerative processes, the time interval elapsing between successive assessments must be taken into account. If trials are repeated on a time scale which is much shorter than the time scale of the progressive impairment then complete consistency can be found. I will indicate this pattern as one of *short time scale consistency*. If temporally distant trials are compared, as it is the case for the study of the Semantic Dementia patient J.L. in (Hodges et al., 1995), then consistency must be interpreted as a condition in which a given item, once failed, is consistently failed thereafter. I will indicate this pattern as one of *long time scale consistency.*

LONG TIME SCALE CONSISTENCY at naming

	April 91	*Sept* 91	*March* 92	*Sept* 92	*March* 93
lorry	+	+	+	+	+
bike	+	+	+	+	+
telephone	+	+	+	+	−
airplane	+	−	+	+	−
motorcycle	+	+	+	−	−
bus	+	+	−	−	−
fish	+	+	−	−	−
monkey	+	−	−	−	−
duck	+	−	−	−	−
cooker	+	−	−	−	−
toaster	+	−	−	−	−
helicopter	+	−	−	−	−
deer	+	−	−	−	−
rabbit	+	−	−	−	−
mouse	+	−	−	−	−
tiger	+	−	−	−	−
chicken	+	−	−	−	−
kettle	−	+	−	−	−

Table 1.3: An example of long time scale consistency in Semantic Dementia: patient J.L.'s naming consistency on the 18 over 48 pictures that he was able to name at least once correctly. From (Hodges et al., 1995), Table 4, p.474

A typical example of *long time scale consistency* is given in table 1.4: patient J.L. was submitted to a longitudinal study of his progressive semantic memory deterioration. The naming task of the Semantic Memory Battery devised by Hodges at al. was administered five times over a two years period in order to assess consistency. Of the 48 stimuli proposed, 30 were never named, 2 were always named and all the other except two showed the typical pattern of *long time scale consistency*, e.g. once failed they were always failed thereafter (See (Hodges et al., 1995), Table 4, p.474). The analysis of consistency produced by (Hodges et al., 1995) is qualitative, and self-evident due to the clear cut pattern presented by the patient.

Long time scale consistency is typical of the Semantic Dementia syndrome and of D.A.T. (Hodges et al., 1992b); however this does obviously not exclude that such patients may exhibit *short time scale consistency* when tested on time scales shorter than the ones characteristic of the pathology progression. This is the case, for example, of the Warrington and Cipolotti (1996) storage patients, but also of patient R.M. whose single case study is presented in Chapter 3.

(Chertkow and Bub, 1990) performed a group study on 10 D.A.T. (Dementia of the Alzheimer's Type) patients, which confirmed that their pattern of performance basically fitted with the criteria of impaired storage. Consistency was assessed across two repetitions of a picture naming task. Although the time delay between the two sessions is not specified, from the fact that the overall performance remained stable one can infer that this was the case of a short scale consistency measure. Data were analyzed with the Kappa coefficient measure, which is derived from the χ^2 statistics. The Kappa coefficient ranges between -1 (complete inconsistency) and +1 (complete consistency). The Kappa values for the D.A.T. were found to lay between +0.75 and +0.91, indicating an overall pattern of highly consistent performance.

Naming has often been used as the elective task for consistency assessment. This is due to the fact that the probability of correct naming by guessing is virtually null, so any statistics derived from the χ^2 statistics can, as a first approximation, be employed to assess consistency (for criticisms see (Faglioni and Botti, 1993)) across two repeated trials. Naming however is not such crucial evidence in the case of access impairments, which, with the exception of the acquired dyslexia cases, have been described in the context of comprehension deficits. In these cases the most widely used test is the multiple-choice word-picture matching task. Multiple-choice arrays imply a non-null probability of correct guessing, which renders inappropriate all statistics derived from the χ^2 statistics. Also the Markovian model proposed by Faglioni and Botti, that will be discussed later, is not appropriate for forced-choice tests.

(Warrington and McCarthy, 1987) and (Warrington and Cipolotti, 1996) use a simple method for assessing consistency in the multiple-choice word-picture matching task, which is unfortunately unsathisphactory. It is based on the assumption that, if independence across n repetitions of the same test holds, then the probabilities of obtaining $0, 1, 2, ..., n$ correct answers can be estimated from the terms of the binomial expansion $(p+q)^n$, in which the probability of success p is estimated from the overall experimental frequency of correct answers and the probability of failure is $q = 1 - p$. Independence can expected only if there is no trial by trial correlation; so the better the experimental frequencies approximate the corresponding binomial expected values, the more realistic is the independence assumption, e.g. the more inconsistent is performance. The statistical significance of the discrepancies between the obtained and the expected values is then evaluated with the χ^2 method. In fact this method *only provides a decision between complete independence and dependence across repeated trials; it does not provide any direct measure of consistency.*

Furthermore the overall procedure does not take into account the following points: first, in the presence of a *non-null probability of correct guessing* the binomial expansion does not provide a good approximation of the expected frequencies of $1, 2, ..., n$ successes; second, the substitution of an a priori probability with an experimental frequency introduces a

SHORT SCALE CONSISTENCY at word-picture matching

	vvv	xxx	xvv	xxv	$\chi^2(d.f.3)$	P
$A1$ *obs.*	20	14	19	27		
$A1$ *exp.*	11	9	31	29	6.6	*n.s.*
$A2$ *obs.*	26	8	24	22		
$A2$ *exp.*	19	5	35	22	3.8	*n.s.*
$S1$ *obs.*	39	23	9	9		
$S1$ *exp.*	17	5	34	23	40.8	< 0.001
$S2$ *obs.*	36	15	14	15		
$S2$ *exp.*	20	4	32	21	18.9	< 0.001
$S3$ *obs.*	34	12	20	14		
$S3$ *exp.*	22	3	35	19	12.8	< 0.01
$S4$ *obs.*	41	17	8	14		
$S4$ *exp.*	21	4	35	20	52.5	< 0.001

Table 1.4: An example of a short scale consistency measure: two access patients (A1 and A2) and four storage patients (S1, S2, S3, S4) performed a word-picture matching test for three times (n=48, Chance level=25%); only for the storage patients performance is significantly different from what would be expected if the trials were independent, suggesting consistency. From (Warrington and Cipolotti, 1996), p.620.

systematic bias in the estimate of non-linear quantities, the so called *limited-sampling bias*. These methodological flows make the method quite unsafe: it can be seen as providing only a first approximation of the required experimental evidence on consistency.

In the next section a new method allowing more precise consistency measures by taking into account both the non-null probability of correct guessing and the limited-sampling bias, is described.

1.2.2 Storage and Retrieval Indices.

In 1993 Faglioni and Botti proposed a statistical analysis of consistency in naming experiments, which provides an estimate of the degree of storage degradation and retrieval efficacy. The aim was to allow one to assess the degree of storage and access impairments on the basis of the key consistency evidence alone.

The basic assumption of the model is that, in the presence of a semantic deficit and once major perceptual and phonological problems are excluded, failure to name can be due to two *independent processes*: the first is that the semantic representation of the to be named item is so degraded that it cannot support naming; the second is that, if the representation is not degraded, a retrieval failure occurs. The crucial remark is that the link between observable events (the sequences of successes and/or failures) and the unobservable psychological determinants (storage and/or retrieval deficits) is not deterministic as all the traditional statistical approaches assume, but *stochastic* in nature. In fact consistent failures are possibly, but by no means necessarily, due to a storage deficit, since there is always some probability that they would follow from a retrieval deficit.

In the case in which only successes or failures are considered as possible outcomes, the link between observed facts and unobservable causes can be unambiguously described by a two parameter stochastic model:

- the parameter s is an estimate of the fraction of the total number of semantic representations which can support correct performance in the test;
- the parameter r is an estimate of the probability of correct retrieval of one of these (non-degraded) representations.

The Markovian approach assumes independence of storage and retrieval, so that the probability of correct naming in one trial, p_1, can be considered as the product sr, e.g. the product of the probabilities of the representation being able to support performance and of it being correctly retrieved. Failure can be due to two possible events: either the representation is not stored - and I will use the short-cut expression 'it is not stored' in the sense that 'is not able to support performance' - or it is stored, but a retrieval failure occurs. So the probability of failing one trial, p_0, is given by $(1-s)+s(1-r)$.

When more than n trials are considered, the extra assumption that the storage and retrieval functions are not altered across trials is required. The probabilities of getting $1, 2, ..., n-1, n$ successes can be expressed as functions of the storage and retrieval indices, and can eventually be estimated with the experimental frequencies of $1, 2, ..., n-1, n$ successes[1]. Faglioni and Botti provide the expressions of r and s as functions of the probabilities of getting $1, 2, ..., n-1, n$ successes up to $n = 4$.

This approach can be extended to the cases in which the probability of correct guessing is sensibly different from zero, as it is always for multiple-choice procedures. One has to take into account that both when a given semantic representation is not stored and when it is stored, but a retrieval failure has occurred, a correct response can still be provided due to guessing. Guessing is assumed to be a third independent event that can produce a correct answer. So, for example in the case of one single trial with guessing probability a, one obtains: $p_1 = sr + s(1-r)a + (1-s)a$ and $p_0 = (1-s)(1-a) + s(1-r)(1-a)$.

In what follows the formulas for 2 and 3 repetitions of a multiple-choice experiment with chance probability equal to a are presented; the formulas presented here will be applied in the experimental studies of Chapter 3 and Chapter 5, and to some experimental data presented in the literature.

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[1] The limited-sampling bias is not considered in the Markovian model.

1.2.3 s and r for $n = 2$

Given 2 repeated trials on a forced choice task with chance probability equal to a, the probabilities of obtaining 2, 1 or 0 correct responses, p_2, p_1 and p_0 respectively, as a function of the storage parameter s and of the retrieval parameter r are given by the following expressions:

$$\begin{aligned} p_2 &= s[r+(1-r)a]^2+(1-s)a^2 \qquad (1.1) \\ p_1 &= 2s[r+a(1-r)](1-r)(1-a)+2(1-s)(1-a)a \\ p_0 &= s[(1-r)(1-a)]^2+(1-s)(1-a)^2 \end{aligned}$$

$$(1.2)$$

These equations can be solved for s and r by substituting the a priori probabilities p_2, p_1 and p_0 with the corresponding experimental frequencies of successes.

Given the following definition of the parameters Δ_1 and Δ_2

$$\begin{aligned} \Delta_1 &= a[p_0-(1-a)^2]+(1-a)[p_2-a^2] \qquad (1.3) \\ \Delta_2 &= [p_2-a^2]-[p_0-(1-a)^2] \end{aligned}$$

one obtains an estimate of the parameters s and r

$$\begin{aligned} s_{est.} &= \frac{(1-a)\Delta_2^2}{4\Delta_1} \qquad (1.4) \\ r_{est.} &= \frac{2\Delta_1}{(1-a)\Delta_2} \end{aligned}$$

These values of s and r are not corrected for limited-sampling.

1.2.4 s and r for $n = 3$

Given 3 repeated trials at a forced choice task with chance probability equal to a, the probabilities of obtaining 3, 2, 1 or 0 correct responses (p_3, p_2, p_1 and p_0 respectively) as a function of the storage parameter s and of the retrieval parameter r are given by the following expressions:

$$\begin{aligned} p_3 &= s[r + (1-r)a]^3 + (1-s)a^3 \\ p_2 &= 3s[r + a(1-r)]^2(1-r)(1-a) + 3(1-s)(1-a)a^2 \\ p_1 &= 3s[r + a(1-r)][(1-r)(1-a)]^2 + 3(1-s)(1-a)^2 a \\ p_0 &= s[(1-r)(1-a)]^3 + (1-s)(1-a)^3 \end{aligned} \tag{1.5}$$

These equations can be solved for s and r by substituting the a priori probabilities p_3, p_2, p_1 and p_0 with the corresponding experimental frequencies of successes.

Given the following definition of the parameters Δ_1 and Δ_2

$$\begin{aligned} \Delta_1 &= 3(1-a)^3 p_3 + a(1-a)^2 p_2 - a^2(1-a)p_1 - 3a^3 p_0 \\ \Delta_2 &= 3(1-a)^3 p_3 - a(1-a)^2 p_2 - a^2(1-a)p_1 + 3a^3 p_0 \end{aligned} \tag{1.6}$$

one obtains an estimate of the parameters s and r which is *biased* due to limited sampling:

$$\begin{aligned} r_{biased} &= \frac{2a\Delta_2}{\Delta_1 - \Delta_2(1-2a)} \\ s_{biased} &= \frac{[\Delta_1 - \Delta_2(1-2a)]^3}{24a^3(1-a)^3\Delta_1\Delta_2} \end{aligned} \tag{1.7}$$

In fact the numerical values of r and s are calculated by substituting the probabilities of $0, 1, ..n$ successes with the corresponding experimental frequencies. The smaller is the number of items tested in each trial, N, the bigger is the effect of the systematic error induced by the evaluation of the probabilities by means of the experimental frequencies.

The effect of the bias can be evaluated. Consider a general quantity $X(\{p_i\})$ depending from a set of parameters $\{p_i\}$, $i = 0, ..., n$, that are only known with a certain approximation due to limited sampling: $p_i = f_i + \delta p_i$. Here $\{f_i\}$ are the estimates of the parameters obtained from the data. If the parameters are *a priori* probabilities, as in the case of the access and storage indices, then they can be approximated with the experimental frequencies. In general if $\{f_i\}$, $i = 0, ..., n$ is the estimate of the parameters obtained from a given sample of the data, the effect of limited sampling can be evaluated by introducing an expansion of X around $\{f_i\}$ in the form:

$$X(\{p_i\}) = X(\{p_i\}) \mid_{\{f_i\}} + \sum_{j,i} \frac{\delta X(\{p_i\})}{\delta p_j} \mid_{f_i} \delta p_i + \sum_{j,i,k} \frac{\delta^2 X(\{p_i\})}{\delta p_j \delta p_k} \mid_{f_i} \delta p_i \delta p_k \qquad (1.8)$$

When this expression is averaged over the distribution of the parameters, the first order term disappear because $< \delta p_i >= 0$, while the second order term is the bias ΔX:

$$\Delta X = \sum_{j,i,k} \frac{\delta^2 X(\{p_i\})}{\delta p_j \delta p_k} \mid_{f_i} < \delta p_i \delta p_k > \qquad (1.9)$$

In the same way in the case of the r and s indices the bias amounts to a correction that must be subtracted from the biased values (Lauro-Grotto, Treves and Shallice *in preparation*):

$$\begin{aligned} s &= s_{biased} - \Delta s \qquad (1.10) \\ r &= r_{biased} - \Delta r \end{aligned}$$

The expressions for Δs and Δr are:

$$\Delta r = \frac{16a}{ND_1^3}[aF_1F_2 + F_3F_4] \qquad (1.11)$$

$$\Delta s = \frac{2s}{N} + \frac{D_1}{24ND_2^3}[F_1F_6 + F_5F_7]$$

where the quantities D_1, D_2, F_1, F_2, F_3, F_4, F_5, F_6 and F_7 are defined as follows:

$$\begin{align} D_1 &= \Delta_1 - \Delta_2(1-2a) \tag{1.12}\\ D_2 &= [a(1-a)\Delta_1\Delta_2] \nonumber\\ F_1 &= [9(1-a)^6p_3 + a^4(1-a)^2p_1] \nonumber\\ F_2 &= 3a^3p_0 - a(1-a)^2p^2 \nonumber\\ F_3 &= (1-a)[3(1-a)^3p_3 - a^2(1-a)p_1 \nonumber\\ F_4 &= 9a^4p_0 + a^2(1-a)^4p_2 \nonumber\\ F_5 &= a^2(1-a)^4p_2 + 9a^6p_0 \nonumber\\ F_6 &= (\Delta_1^2 - 4\Delta_1\Delta_2 + \Delta_2^2)(\Delta_1 - \Delta_2 + 2a\Delta_2)^2 + 6(1-2a)\Delta_1\Delta_2(\Delta_1 - \Delta_2)^2 \nonumber\\ F_7 &= (\Delta_1^2 + 4\Delta_1\Delta_2 + \Delta_2^2)(\Delta_1 - \Delta_2 + 2a\Delta_2)^2 + 6(1-2a)\Delta_1\Delta_2(\Delta_1 + \Delta_2)^2 \nonumber \end{align}$$

This analysis of consistency has been applied in order to compare the performance of the Semantic Dementia patient R.M. to that of the Warrington and Cipolotti' storage and access patients (For more details see Chapter 3). Table 1.5 shows the original data, the raw estimates $r_{est.}$ and $s_{est.}$, the corrections for limited-sampling $\Delta\ r_{est.}$ and $\Delta\ s_{est.}$ and the corrected values for r and s.

The pattern of results for the storage patients, except perhaps in patient S3, is quite clear-cut: the retrieval index is much higher than the storage index, indicating that the storage impairment is the critical aspect of the deficit. In the case of R.M. r is near to its theoretical maximum value, while s is less than 0.5, so virtually any failure to perform the task can be ascribed to a degradation of the semantic representations.

The pattern of the three "access" patients is more complex. In the case of patient H.E.C. the retrieval impairment is clearly documented. In the case of the two access patients A1 and A2, although the values of r are definitely smaller than what is found in the storage pattern, a rather substantial storage deficit is superimposed on the retrieval one. While from the point of view of the theoretical interpretation this poses some problems that will be addressed later in this chapter. by contrast from the point of view of the validation of the stochastic approach these results show the sensitivity of the method: a traditional analysis of consistency would not have differentiated the two separate contributions of the storage and retrieval deficit to the global pattern of performance, it would simply have signaled the inherent inconsistency of the results.

In Table 1.6 the storage and retrieval indices are evaluated for two different spoken word/written word matching tasks performed by patient M.E.D. (McNeil et al., 1994). As expected from the analytical expressions of the limited sampling corrections Δr and Δs , in which the leading terms scale as $\frac{1}{N}$, it is evident that the relevance of the correction for limited-sampling increases as the number N of available stimuli decreases. As result of the availability of the limited-sampling correction procedure, stronger evidence can be obtained from less data.

A somewhat different application of the same analysis is described in Chapter 5, where it has been used to analyze the data obtained with the split brain patients M.E. in order to compare the performance of the Left and Right Hemispheres at a lateralized version of some semantic tasks: a dissociation in the values of the storage and retrieval indices for the two hemispheres strongly suggests independence of performance. A very similar deduction can be derived by considering R.M.'s performance on a visual semantic task in the visual

STORAGE AND RETRIEVAL INDICES

$Patient:$	$R.M.$	$S1$	$S2$	$S3$	$S4$	$A1$	$A2$	$H.E.C.\ I$	$H.E.C.\ II$
$freq.(3)$	0.50	0.49	0.45	0.43	0.51	0.25	0.32	0.40	0.54
$freq.(2)$	0.17	0.11	0.17	0.25	0.10	0.24	0.30	0.46	0.31
$freq.(1)$	0.06	0.11	0.19	0.17	0.17	0.34	0.28	0.10	0.15
$freq.(0)$	0.28	0.29	0.19	0.15	0.21	0.17	0.10	0.04	0.00
$r_{est.}$	1.04	0.98	0.90	0.82	0.97	0.73	0.71	0.63	0.78
$\Delta\ r_{est.}$	0.07	0.02	0.01	0.00	0.01	0.00	−0.01	−0.01	−0.01
r	0.97	0.96	0.89	0.82	0.96	0.73	0.72	0.64	0.79
$s_{est.}$	0.45	0.50	0.57	0.65	0.54	0.47	0.67	1.04	0.92
$\Delta\ s_{est.}$	0.02	0.03	0.03	0.03	0.02	0.03	0.04	0.05	0.03
s	0.43	0.47	0.54	0.62	0.52	0.44	0.63	0.99	0.89

Table 1.5: Comparison of the indices of ”retrieval” (A1, A2 and H.E.C.) and ”storage” for patient R.M., and for the typical ”storage” (S1, S2, S3 and S4) and ”access” (A1, A2 and H.E.C.) patients described in (Warrington and Cipolotti, 1996) and in (Cipolotti and Warrington, 1995). In the first four raws the frequence of m successes ($freq.(m)$) is reported. The values of r and s reported for R.M. are derived from the ordinate level categorization (Experiment 4) and from ordinate level sorting (Hodges' Battery for Semantic Dementia - See Sec. 3.3) of the same verbal material (chance probability a=1/3, n = 36: see Chapter 3). The values reported for S1, S2, S3, S4, A1 and A2 are estimated from the results obtained in a word-picture matching test described in Warrington and Cipolotti (1996), Table 13, p.620 (chance probability a=1/4, n = 30). The values reported for H.E.C. are estimated from the results obtained in a word-picture matching test described in Cipolotti and Warrington (1995) (chance probability a=1/4, n = 48), in which the entire experiment consisting of three subsequent trials has been replicated. The analysis is performed separately on the two repetitions (I and II). The estimates of r and s are corrected for limited-sampling according to the formulas: $r = r_{est.} - \Delta\ r_{est.}$ and $s = s_{est.} - \Delta\ s_{est.}$.

modality: while the retrieval index remains close to one, the storage index is sensibly higher in the visual then in the verbal task, a finding suggestive of a selective impairment of the verbal semantic storage (See Chapter 3, Experiment 7).

LIMITED-SAMPLING CORRECTIONS: dependence from n

$M.E.D.$	$f.(3)$	$f.(2)$	$f.(1)$	r_{est}	$\Delta\ r_{est}$	r	s_{est}	$\Delta\ s_{est}$	s
$n = 24$	0.31	0.40	$O.24$	0.64	−0.03	0.67	0.90	0.10	0.80
$n = 12$	0.39	0.39	0.19	0.70	−0.05	0.75	0.92	0.18	0.74

Table 1.6: Different relevance of the correction for limited-sampling bias as a function of the number of experimental trials n. Two experiments, with $n = 24$ and $n = 12$, and three trials have been considered by the authors. Data (the frequences of 1, 2, and 3 successes) are derived from spoken/written word matching tasks, performed by patient M.E.D. (McNeil et al., 1994). Chance level is 1/6.

1.3 Storage and Access in the Attractor Neural Network approach.

Table 1.7 summarizes the main characteristics of the typical patterns of performance of the storage and access impairments.

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	Storage	*Access*
consistency	*yes*	*no*
frequency effects	*yes*	*no*
rate of presentation effects	*no*	*yes*
semantic similarity effects	*no*	*yes*

Table 1.7: Summary of the main characteristics of the storage and access impairments.

The actual co-occurrence of the four characteristics has been recently assessed in the Warrington and Cipolotti (1996) set of four 'storage' and two 'access' patients. In order to gain some theoretical insight into this complex experimental evidence it is useful to consider some computational constraints that could enlighten the links between the various characteristics of the storage and the access impairments. As Rapp and Caramazza (1993) pointed out, discussing these issues in the absence of a specific theoretical framework can be unsafe.

so the discussion will be restricted to a class of models, namely attractor neural networks implementing Hebbian learning, e.g. storing patterns in the form of *content addressable* memories. A network of this type has been used as the building block for the Multimodal Model of Semantic Memory proposed in (Lauro-Grotto et al., 1997) and is discussed in Chapter 3. However any result which is not expected to hold in other kinds of attractor networks will be explicitly indicated.

1.3.1 Attractor networks.

Attractor networks can be viewed as dynamical systems which encorporate the principal characteristics of the neural dynamics at a highly schematized level. Neurons are represented by stochastic variables whose activity is determined by the balance of excitatory and inhibitory signals received from other neurons: when the total signal exceeds a given threshold the firing probability of the neuron increases dramatically. In biologically relevant models global inhibition has a determinant role in keeping the activity of the net in the low range that appears to be optimal for associative storage and retrieval (Braitenberg and Schuz, 1992). What allows such a system to work as a memory system is the possibility to define *learning rules* which ensure that the network dynamics, given appropriate initial conditions, and appropriate ranges of values for the parameters of the model, will evolve towards stable self-reproducible states, the so called attractors. These stable patterns of neural activity are highly correlated with the patterns of activity found in the net during the first stimulus presentation, so that after learning has taken place, a stimulus can be entirely retrieved from a very partial initial cue. *Hebbian learning* is based on the hypothesis, now generally accepted, that the crucial modification is realized at the synaptic level in the form of a strengthening of the synapses between neurons that are simultaneously activated during the presentation of the to be learned stimulus.

I will consider here a model of an associative attractor network storing *binary patterns*. whose behavior has been studied analytically (Buhmann and Schulten, 1987; Lauro-Grotto. 1993). I will discuss how the storage and retrieval pattern of performance could be explained in the context of such type of model, as the analytical knowledge of the network behavior is helpful in understanding the computational meaning of the described phenomena.

The basic computational unit of a neural network is the so called *formal neuron*, which incorporates the fundamental characteristics of the real neural computation: at each time t the formal neuron receives many signals from other neurons as its input, each scaled with a given synaptic efficacy; it adds up these scaled signals, and finally switches to the *firing* or the *non firing* state according to a *firing rule*. The firing rule is usually a threshold rule: if the total signal in input is higher than the *activation threshold*, the neuron will fire with a given probability f, which is usually function of the difference between the incoming signal and the threshold. If $f = 1$ the neuron fires if and only if the incoming signal is over threshold. In this case the network dynamics is said to be deterministic. The firing state of the formal neuron corresponds to the emission of spike train from a real neuron: although more complex schemes have evident advantages ((Panzeri et al., 1996)). for many computational derivations it is sufficient to consider binary neurons, e.g. neurons that can be found in either of two states: firing and non-firing. The output of each neuron contributes to the signal in input to all the neurons on which it makes *synaptic contacts*.

The model I will discuss presents N binary units $S_i = \{1, 0\}, i = 1, , N$ whose dynamics is described by the following stochastic (asynchronous) *firing rule*:

$$\begin{aligned} f\{S_i(t+\Delta t)=1\} &= \frac{1}{1+\exp\left(h_i(t)-U\right)/T} \\ f\{S_i(t+\Delta t)=0\} &= 1-p\{S_i(t+\Delta t)=1\} \end{aligned} \qquad (1.13)$$

$h_i(t)$ is the global signal received by neuron i at time t: the state of the neuron at the successive time $(t+\Delta t)$ is determined by the difference $h_i(t)-U$ where U is the neural activation threshold. This firing rule is probabilistic: in fact the probability of firing is basically a sigmoid function of the difference $h_i(t)-U$: so even if the signal is under threshold there is a non-null probability of firing, as well as a non-null probability of firing failure if the signal is over threshold. The sigmoid function changes into a step function if $T \to 0$ (noiseless or deterministic dynamics): the T parameter in fact controls the shape of the sigmoid function and hence the level of the the so called *fast noise*[2] in the network.

In the model the to be learned stimuli are represented by binary patterns ξ_i^μ, where $i = 1,,N; \mu = 0,,p-1$, which are stochastically determined by the prescription that $p(\xi_i^\mu) = a\delta_{Dirac}(\xi_i^\mu - 1) + (1-a)\delta_{Dirac}(\xi_i^\mu)\ \ \forall \mu, i$, where a specifies the average proportion of firing neurons when the network is retrieving a given pattern and the function $\delta_{Dirac}(x)$ is defined as usual ($\int \delta_{Dirac}(x)dx = 1$ if $x = 0$, $\int \delta_{Dirac}(x)dx = 0$ if $x \neq 0$). If $a \neq 0.5$ the patterns are said to be *polarized*. the choice $a \sim 0.1$ is considered biologically plausible for associative areas (Miyashita and Chang, 1988; Miyashita, 1988; Sakai and Miyashita, 1991; Braitenberg and Schuz, 1992): This level of activity corresponds to a neural network in which, during a memory task, 10% of the neurons in average are emitting spike trains at a given time.

This type of noise is called 'fast noise' because it is related to the network dynamics; a different type of noise, the so called 'quenched noise' is related to the presence of the stored patterns in the network: it may be considered as built in during learning.

The *learning rule* defines the value of the *synaptic efficacy* $W_{i,j}$ as a function of the p to be learned patterns (Buhmann and Schulten, 1987):

$$W_{i,j} = \sum_{\mu=1}^{p} \frac{(\xi_i^\mu - a)(\xi_j^\mu - a)}{a(1-a)N} - \frac{\gamma}{aN} \tag{1.14}$$

The first term implements the Hebbian learning mechanism (Hebb, 1949) for polarized patterns, while the second models global inhibition as a function of the mean activity in the net ($\gamma > 0$). Global inhibition is a way of introducing a soft constraint in the network dynamics, which stabilizes the mean activity around a. Each neuron in the network receives a signal $h_i(t) = \sum_{i=1}^{N} W_{i,j} S_j$.

In the limit of very low fast noise level, $T \rightarrow 0$, and in the relevant range of the parameters values, the dynamics exhibit stable attractor states corresponding to the memorized patterns (Lauro-Grotto, 1993). The stable states can be described by introducing some mean field variables which globally describe the state of the network: M and m^μ. M is the global level of activity in the network, while the *overlaps* m^μ $\forall \mu, \mu = 1, .., p$ are measures of the degree of correlation between the actual state of the network and each memorized pattern:

$$\begin{aligned} M &= \ll \sum_{i=1}^{N} \frac{< S_i >}{aN} \gg \\ m^\mu &= \ll \sum_{i=1}^{N} \frac{(\xi_i^\mu - a) < S_i >}{aN} \gg \qquad \forall \mu \end{aligned} \tag{1.15}$$

In these expressions " $< \cdots >$ " is the mean on the *fast noise* due to the probabilistic nature of the updating rule (which, for $T \neq 0$ can produce neural activation even if the signal is under threshold and viceversa); " $\ll \cdots \gg$ " is the mean on the *quenched noise* produced by the various ξ_i^μ: the quenched noise arises from the fact that when a pattern is presented to the network for retrieval, at the beginning of the retrieval phase the network is found in a state which has a macroscopic overlap with the corresponding stored pattern, but also, due to the statistical structure of the patterns, a minimal degree of overlap with every other stored memory: the sum of all the microscopical overlaps with patterns that are not involved in the retrieval is responsible for the quenched noise, while the macroscopic overlap with the to be retrieved pattern produces the signal leading the network dynamics into the attractor state.

In general the amount of quenched noise is linked in a non-trivial way to the number of stored patterns, p. The *storage capacity* of the network, α, is defined, in the thermodynamic limit, as the ratio of the maximum value of p that the network is able to sustain, to N: $\alpha = \frac{p}{N}$. In a standard Hopfield network storing uncorrelated patterns $\alpha = 0.138$ (Crisanti et al., 1986; McElice et al., 1987); in a network of the type I am considering, the existence of a non-null correlation between stored patterns produces significant cancellations in the noise, so that one finds that α is proportional to $\frac{1}{a \ln a}$ (Buhmann and Schulten, 1987).

The self-consistency equations in the low temperature limit can be easily derived if p does not exceed the storage capacity limits of the network. If pattern ξ^1 is presented for retrieval the equations can be derived by explicitly performing the means in the definitions of m^1 and M:

$$\begin{aligned} m^1 &= \ll \sum_{i=1}^{N} = \frac{(\xi_i^1 - a) < S_i >}{aN} \gg \\ &= (1-a)(< S >_1 - < S >_0) \end{aligned} \tag{1.16}$$

$$\begin{aligned} M &= \ll \sum_{i=1}^{N} \frac{< S_i >}{aN} \gg = \\ &= < S >_1 + \frac{1-a}{a} < S >_0 \end{aligned} \tag{1.17}$$

where $< S >_1$ and $< S >_0$ are the means over the fast noise of S over the sites where $\xi_i = 1$ and $\xi_i = 0$ respectively. In their explicit form the equations read:

$$\begin{aligned} m^1 &= (1-a)\{\frac{1}{1+\exp-\frac{m \;\; -\gamma M-U}{T}} - \frac{1}{1+\exp-\frac{-\frac{a}{-a}m \;\; -\gamma M-U}{T}}\} \\ M &= \frac{1}{1+\exp-\frac{m \;\; -\gamma M-U}{T}} + \frac{1-a}{a}(\frac{1}{1+\exp-\frac{-\frac{a}{-a}m \;\; -\gamma M-U}{T}}) \end{aligned} \quad (1.18)$$

The solution can be derived in the limit $T \rightarrow 0$, in which

$$\begin{aligned} < S >_1 &\longrightarrow \vartheta(m^1 - \gamma M - U) \\ < S >_0 &\longrightarrow \vartheta(-\frac{a}{1-a}m^1 - \gamma M - U) \end{aligned} \quad (1.19)$$

and the self-consistency equations become:

$$\begin{aligned} m^1 &= (1-a)(< S >_1 - < S >_0) \\ M &= < S >_1 + \frac{1-a}{a} < S >_0 \end{aligned} \quad (1.20)$$

where $\vartheta(x)$ is the usual ϑ-function defined as equal to 1 for positive values of the argument x and equal to 0 for negative values of x.

When only one pattern is presented for retrieval, for example pattern ξ^1, according to the values of the parameters of the model, two stable solutions can be found: $\{m^1 = 1-a; M = 1\}$, for $1-a-\gamma > U > 0$, and $\{m^1 = 0; M = 0\}$, for $0 < 1-a-\gamma < U$. The first corresponds to successful retrieval while the second corresponds to a state of *no-recognition*, e.g. a state in which the network does not retrieve any pattern. The existence and stability of the state of no-recognition is a characteristic of the network having 0, 1 variables and constrained dynamics (Amit, 1989). Networks exhibiting stable no-recognition states are said to be *non − opinionated* (Buhmann and Schulten, 1987).

The simple case of retrieval of a single memory is sufficient to discuss the issues of the storage and access types of impairments. The storage pattern will be discussed first.

1.3.2 Impaired storage.

The characteristics of the storage impairments have been recapitulated in Table 1.7 on the basis of the results of repeated administrations of a word-picture matching task: performance is consistent across trials and strongly influenced by the frequency class of the stimulus word; furthermore there is not beneficial effect of long delays between the patient's answer and the presentation of the subsequent stimulus. According to (Warrington and Cipolotti, 1996) performance is independent of the nature of the distractors presented together with the target picture in the word-picture matching task: the semantic similarity between target and distractors does not compromise performance. This last evidence however is less well established, and in fact Warrington and Cipolotti (1996) point out that better results may be obtained if distractors from very remote semantic categories are used. In order to include the investigation on the effects of semantic similarity in the computational study of the storage and access impairment, it is necessary to formulate specific assumptions on the nature of the similarity relationships across representations and on the representation of semantic categories in the model. This point will not be addressed in the present work.

The interpretation of the described storage pattern of performance is in terms of a permanent neural loss due to a neurodegenerative process. This account can be modeled in terms of a random elimination of a given percentage of units from the network. In the neural network model just described this means that, after learning, N is decreased because a given number of units are lost due to the pathological process. As a first approximation I will model damage as a random loss of neurons, with each neuron being either damaged with probability d or intact with probability $(1-d)$. Damage is intended to involve permanent loss of the neuron, so that if neuron i is lost, then $S_i(t) = 0\ \forall t$.

Using the geometrical interpretation described in (Lauro-Grotto, 1993) it is easy to find that the self-consistency equations for the case of retrieval of a single pattern, for example $\xi^{\mu=1}$, at low loading, are modified so as to be:

$$\begin{aligned} m^1 &= (1-a)(1-d) < S >_1 -[(1-a)(1+d)] < S >_0 \\ M &= (1-d) < S >_1 + \frac{(1-a)(1-d)}{a} < S >_0 \end{aligned} \tag{1.21}$$

The two stable solutions, and the corresponding stability conditions, in the low temperature limit become:

$$\begin{aligned} m^1 &= (1-a)(1-d) \\ M &= (1-d) \quad for\ (1-a)(1-d) - \gamma(1-d) > U > 0 \end{aligned} \tag{1.22}$$

for the solution corresponding to correct retrieval, and

$$\begin{aligned} m^1 &= 0 \\ M &= 0 \quad for\ 0 < (1-a)(1-d) - \gamma(1-d) < U \end{aligned} \tag{1.23}$$

for the solution corresponding to no-retrieval.

So the retrieval quality decreases due to neural loss. Furthermore the stability condition for retrieval $(1-a)(1-d)-\gamma(1-d) > U > 0$ can be written in the form: $(1-a)-\gamma > \frac{U}{1-d} > 0$, and if an *effective threshold* [3] damage to in the presence of damage is defined in the form:

$$U_d = \frac{U}{1-d} > U \tag{1.24}$$

the stability conditions for retrieval becomes:

$$1 - a - \gamma > U_d > U > 0 \tag{1.25}$$

So the effect of neural loss can be seen as an increase of the activation threshold of the surviving neurons, which favors the stability of the solution of no-retrieval. This amounts to reducing the *basins of attraction* of the solutions corresponding to retrieval and enlarging the basin of attraction of the solution corresponding to no-retrieval (Amit, 1989; Lauro-Grotto, 1993).

But are these kind of difficulties expected to produce item consistency? Surprisingly enough the answer is *in general: No.* If one assumes random damage, as usually done, all the representations are expected to be affected in the same way on average by the signal reduction, and failure or success in retrieval depends on the details of the dynamical evolution of the network state in a given retrieval process. So inconsistency rather than consistency should be expected! As the description of the network that has been proposed is exact only in the so called mean field limit, e.g. for $N \to \infty$ it is always possible that the statistical fluctuations around the average to be expected for finite N values would produce a certain degree of specificity with respect to a given damage: some representations could be more sensitive to the damage because more of their active neurons have been eliminated due to random damage. Also the effect of fluctuations will be more and more evident as

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[3] The term 'effective threshold' is introduced because in the presence of neural damage the stability conditions corresponding to retrieval of a given memory are equivalent to those of an undamaged network with threshold U_d.

long as N is decreased due to damage as they are proportional to $\frac{1}{\sqrt{N}}$ (Amit, 1989). But this explanation is quite unsatisfactory if compared with the robustness of the consistency effects.

A more appropriate way to 'escape from inconsistency' is to break the symmetry across the stored memories. There is a trivial way of doing it, e.g. by saying that the pathology would produce not only neural loss, but also synaptic damage, so that the memory trace of some patterns are lost. This kind of explanation would just reproduce the original question at a different level: why some representations and not others? The less trivial way is by realizing that the symmetry across memories is an oversimplification of the model. Consistency should be seen as an evidence against this oversimplification. If one assumes the the strength of the memory trace can vary across the patterns, so will the robustness of the signal.

The factors influencing the strength of the memory traces can be related to the different experiences that a subject might have about the various stimuli: for instance some may be encountered and/or retrieved more often than others. One way of taking this into account is by considering the *frequency class* of a word or the *familiarity* of a visually presented stimulus. These global factors my account for the 'zero order' effect, but more fine-grained differentiations are to be expected due to individual differences, and these one would be responsible for the long scale consistency pattern found in storage patients.

In a neural network model the natural way of thinking about frequency and familiarity classes is by considering a differential robustness in the signal for different stimuli. It is possible to think of two different factors which would alter the robustness of a signal: the first is the strength of the memory traces and hence the deepness of the attractors; the second is the number of neurons involved in a given representation[4]. It is obvious that the more neurons are involved in given representation the more robust is that representation to neural loss. Furthermore the bigger is the network involved in a given representation the higher is the possibility to assign different neurons to different representations, thus minimizing the interference across elements of the same class. Reducing interference is indeed another mean to increase the quality of the signal. One can think of the case of faces representations as an example in which frequent and relevant stimuli have been evolutionary allocated to a specific neural area. It is however at least plausible to assume that if a given subject, due to his his personal experience, is specifically familiar with a given category of stimuli - say plants, if one devoted his life to botanic sciences - he might have devoted specific networks in the brain to store the information about that class of stimuli.

However I will consider here the simpler case in which the frequency effects are considered within a given category of semantic representations. In this case frequency can be introduced by altering the the strength of the memory traces; in the model this can be achieved by introducing more sophisticated learning rules. I will consider for the sake of simplicity only two word frequency classes, high and low, and assign half of the patterns to each class. One can then differentiate the learning rules for the two classes by adding an appropriate multiplicative factor in the synaptic matrix:

$$W_{i,j}^{h+l} = \sum_{\mu_h=1}^{p_h} (1+h)\frac{(\xi_i^{\mu_h} - a)(\xi_j^{\mu_h} - a)}{a(1-a)N} + \sum_{\mu_l=p_h+1}^{p} (1-h)\frac{(\xi_i^{\mu_l} - a)(\xi_j^{\mu_l} - a)}{a(1-a)N} - \frac{\gamma}{aN} \quad (1.26)$$

where the pattern indices μ_h and μ_l run over the patterns of the high and low frequency classes respectively ($\mu_h = 1, , p_h; \mu_l = p_h + 1, , p$), $p = 2p_h$, and $h (0 < h < 1)$, is the factor determining the advantage for the high frequency patterns (in fact the corresponding energy

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I owe this idea to a conversation with Prof.M.A. Virasoro.

levels are lowered so that the attractors become more stable).

The explicit form of the self-consistency equations in the case of retrieval of an high frequency pattern (e.g. $\mu = 1$) at low loading is:

$$\begin{aligned} m^1 &= (1-a)\{\frac{1}{1+\exp-\frac{(1+h)m \ -\gamma M - U}{T}} - \frac{1}{1+\exp-\frac{-\frac{a}{-a}(1+h)m \ -\gamma M - U}{T}}\} \\ M &= \frac{1}{1+\exp-\frac{(1+h)m \ -\gamma M - U}{T}} + \frac{1-a}{a}(\frac{1}{1+\exp-\frac{-\frac{a}{-a}(1+h)m \ -\gamma M - U}{T}}) \end{aligned} \qquad (1.27)$$

If an high frequency pattern is presented for retrieval, the stable solution of the self-consistency equations corresponding to retrieval remains unaltered, but the corresponding stability conditions are modified as follows: $(1+h)(1-a)-\gamma > U > 0$ for the retrieval solution $\{m^1 = 1-a; M = 1\}$ of the high frequency class. The stability condition for no-retrieval remains unaltered. Similarly one can derive the stability conditions $(1-h)(1-a)-\gamma > U > 0$ for the solution $\{m^{p_h+1} = 1-a; M = 1\}$, corresponding to the retrieval of the pattern ξ^{p_h} from the low frequency class. As $h > 0$ the effect of the modification of the learning rule is to increase the stability and the basin of attraction of the solution corresponding to the high frequency patterns and decrease the ones corresponding to the low frequency patterns.

If neural damage is introduced according to the schema just proposed the following stable solutions are obtained for the high and low frequency patterns respectively:

$$\begin{aligned} m^1 &= (1-a)(1-d) \\ M &= (1-d) \quad for\ (1+h)(1-a)-\gamma > U_d > U > 0 \end{aligned} \qquad (1.28)$$

$$\begin{aligned} m^{p_h+1} &= (1-a)(1-d) \\ M &= (1-d) \quad for (1-h)(1-a)-\gamma > U_d > U > 0 \end{aligned} \qquad (1.29)$$

So even if all of the two classes were stable before the damage, for every value of h there will be a value of the damage d (remember that $U_d = \frac{U}{1-d}$), for which high frequency patterns only will be attractor states of the network dynamic.

It is interesting to note that in this very preliminary picture the low frequency representations are not 'lost', but are successively and permanently destabilized as long as d increases.

The absence of rate of presentation effects is not a peculiar phenomenon: it is their presence in the context of the access pattern that has to be explained, and this will be addressed in the next section.

1.3.3 Impaired access and 'refractoriness'.

The pattern of performance of the 'access' patients is described in Table 1.7; again the evidence is derived from repeated administrations of a word-picture matching task (Warrington and Cipolotti, 1996; Warrington and McCarthy, 1987). Performance is not consistent across trials and there is no evidence of any frequency effect; furthermore the very peculiar phenomenon of the significant influence of response-stimulus interval has now been clearly documented.

In the last section we have seen that it is plausible to assume that different memories are encoded with different synaptic efficacy, and that familiarity and word frequency classes are expected have an influence on the stability of a given attractor state. And in fact such an assumption is necessary in order to explain the consistent pattern of performance shown by the storage patients. Now if one has assumed that there is a difference in the memory trace of high and low frequency stimuli in order to explain the consistent pattern of performance of the storage patients, in the case of the access patients one will have to explain what type of deficit would result in a performance independent from the frequency class of the stimuli and so produce inconsistency across trials.

According to the original argument by Warrington and Shallice, inconsistency originates from a retrieval impairment, e.g. from a failure to reach the attractor state once the stimulus has been presented to the network. A possible way of inducing retrieval deficits in an associative neural network is by increasing the noise level over given critical values. How behavior of a network like the one we have just proposed changes at different noise levels is known: as long as T increases from zero toward the *critical value* $T_c = 1$ above which the system dynamics becomes ergodic, the overlap decreases. This can be easily seen from the self-consistency equation for the overlap in the Hopfield network by considering the geometric solution of the equation $m =\ll \xi tanh(\frac{m}{T} \gg$. For the more complex network we are considering, in which the neurons have $\{0, 1\}$ instead of $\{-1, +1\}$ as possible states, the same picture holds, except for the fact that at the critical temperature $m = \frac{1}{2}$.

At $0 < T < T_c$ the attractor state is substituted by a distribution of states fluctuating around the memorized pattern with an overlap $m_T < m_{T=0}$ (Amit, 1989): this is because, even if the network is in the attractor state, due to the fast noise, some neurons can temporary flip and become misallined with the retrieved pattern; the average value in any case the overlap between the network state and the pattern remains quite high ($> 90\%$) for relatively high T values, so that the system can realize associative recall.

Although it reduces retrieval quality, the fast noise has a beneficial influence from a different point of view: it destabilizes *spurious attractor states* (Amit et al., 1985). Spurious states correspond to an attractor having a macroscopic overlap with more than one pattern in the network (Gardner, 1986). When the network state evolves towards a spurious state retrieval fails because more than one memory is partially activated, and ambiguity follows. When the noise level is raised from zero, the spurious states corresponding to mixture of several patterns, that are local minima of the energy function at $T = 0$, are subsequently destabilized, until for $T > \frac{1}{2}$ only the global minima, corresponding to the retrieval of one memory pattern, are found to be stable attractors (Amit, 1989) (See Table 1.8). At this noise level the attractor states are characterized by overlap values ranging around 95% of the corresponding zero noise values ($m_{T=0.5} \sim 0.95 m_{T=0}$). In conclusion a moderately noisy situation not only is more plausible from the biological point of view, but also is optimal for the the retrieval abilities of the network. Similar results were found in a biologically more plausible network in (Buhmann et al., 1989), where the noise was introduced in the form of fluctuations in the membrane potential of the simulated neurons.

NOISE, RETRIEVAL and SPURIOUS STATES

T range	*retrieval quality*	*spurious states*
$T = 0$	*optimal*	*metastable*
$0 < T < 1/2$	*good*	*metastable*
$T = 1/2$	*good*	*unstable*
$1/2 < T < T_c = 1$	*good → poor*	*unstable*
$T = T_c$	*null*	*absent*
$T > T_c$	*null*	*absent*

Table 1.8: Effect of the noise level on retrieval quality and on the stability of the spurious states in the Hopfield network (Amit, 1989). In the range $1/2 < T < T_c$ if T is near $1/2$ there is an optimal range for associative recall: retrieval quality is good (with an overlap around 95% of the $T = 0$ value) and all the spurious states are unstable.

However if the fast noise level is further increased towards T_c, the overlap decreases towards zero, and so does the signal which stabilizes the corresponding attractor; as a consequence the basin of attraction also is reduced in amplitude, and the retrieval dynamics is slowed (Amit, 1987). This situation fits with the retrieval impairment postulated by Shallice (1988): when the basins of attraction of the stored memories are reduced in size, the probability of correct retrieval is also reduced: retrieval will be successful or fail just due to the particular initial conditions of each process (Amit, 1989). In this situation inconsistent performance is expected. Furthermore, if the noise level is high, both high and low frequency stimuli (according to the definition given in the previous section) can be affected by the retrieval impairment: although high frequency patterns have deeper basins of attraction, they do not have better retrieval quality from the point of view of the overlap. In fact, as we have shown in the previous section, frequency has an influence on the stability conditions and not on the solutions of self-consistency equations.

It is interesting to note that in this simple picture retrieval failure has two main characteristics: from the point of view of the temporal evolution of the dynamics, it is plausible to assume that retrieval is successful only if the network is able to reach the attractor state in a reasonable amount of time. Furthermore, if the attractor is reached in a reasonable amount of time, the retrieval quality, measured by the overlap, could be insufficient to allow systems downstream to detect that the net reached an attractor state, i.e. to sustain the cognitive performance.

A different way of eliminating the beneficial effect of frequency and obtaining inconsistent performance, is by considering a kind of impairment which emerges when the network has already reached the stable attractor state: if the system was then in a condition in which, for some physiological reasons due to the pathology, sustained activity was difficult to maintain, the difference in stability due to frequency would become irrelevant. Such an impaired network would have troubles in sustaining its own activity both while reaching the attractor and while in the attractor state. In this case the network model just described is too simple to produce relevant evidence because the state of the dynamical variables at time t is entirely determined by the signal at time $t - 1$ and there is no memory of the preceding states.

A relevant hypothesis has been considered by (Warrington and Cipolotti, 1996) in their proposal about *refractoriness*, which has has been put forward in order to explain the rate of presentation effect. Rate of presentation effects, and the related phenomenon of decreasing performance across single items in repeated trials (Warrington and Cipolotti, 1996) are very peculiar phenomena, because they clearly document the existence of a *negative auto-correlation* in performance: the probability of correct performance on the same item decreases in subsequent trials. Furthermore if the items are presented at a very low response-stimulus interval (15s) the overall performance is significantly higher than if the rate of presentation is fast (2s). The 'refractoriness' hypothesis is based on physiological considerations: the typical etiology found till now in the access deficit is either vascular or oncological. They argue that in both cases a compressive lesion would be expected to produce negative interference to the blood supply of the surrounding tissue, and hence possible *oxygen and energy deprivation*, which would be responsible for *reversible conduction failures*. In this condition neurons would have difficulties in maintaining sustained activity. This proposal is extremely appealing but also underspecified from the physiological point of view. Brain hypoxia and hypoglicemia in fact are known to have very complex consequences, and even different ones according to the duration and the severity of the deprivation. Furthermore in the case of the access patients a *chronic state of very mild deprivation* has to be considered. Most of the experimental evidence on the consequence of hypoxic brain insult on the contrary has been produced with respect to the acute or subacute state.

In order to collect evidence that could be relevant to the case it is therefore necessary to consider that *reversible conduction failures* imply a lack of permanent neural damage, so *endogenous neuroprotective factors* must play a crucial role in the phenomenon. Among these, the hypothesis to be explored in this thesis is that the most relevant effect for very mild and short-term hypoxic conditions is the effect of *endogenous Adenosine.*

1.4 The Adenosine Hypothesis.

Removing the oxygen supply to a given brain area leads to a fall in intracellular ATP levels, and thus to a slowing of the sodium/potassium exchange pump. As a result there is a slow rundown of the ionic and voltage gradients across the cell membrane lasting for about 2 minutes, after which the extracellular potassium concentration $[K^+]_o$ suddenly jumps up to about 50-60mM, which depolarizes cells to about -20mV and completely suppresses action potential production(Attwell, 1988). During the slow depolarization phase a constant release in excitatory aminoacids (glutamate and aspartate) is produced throughout vescicle exocitosis. Excitatory aminoacids are known to have dramatic neurotoxic effects at high extracellular concentrations(Szatkowski and Attwell, 1994; Martin et al., 1994), eventually triggering cell death. In normal conditions a glutamate carrier is responsible for glutamate reuptake. If severe anoxia is prolonged for more than two minutes, the changes in transmembrane ion and voltage gradients (that is an increase in $[K^+]_o$ and $[Na^+]_i$ and a decrease in $[K^+]_i$ and $[Na^+]_o$, and membrane depolarization) produce a reversal of the glutamate re-uptake mechanisms, the carrier will pump glutamate out of cells into the extracellular space until a new equilibrium is reached with the extracellular concentration of glutamate at highly neurotoxic levels ($[glu]_o > 100\mu M$) (Attwell, 1988). In this situation further prolongation of the anoxic state will produce irreversible damage. If one wants to consider reversible conductance failures only phenomena occurring before the reversed uptake of glutamate takes place must be considered (Martin et al., 1994; Santos et al., 1996).

The most relevant evidence comes from experiments on artificially induced hypoxia (oxygen deprivation) and ischemia (oxygen and glucose supply shortage) in rats and pigs (Santos et al., 1996; Gribkoff and Bauman, 1992). In the very early phase of ischemia a pronounced increase in the level of endogenous extracellular Adenosine has been documented (Rudolphi et al., 1992) (See Table 1.9). Adenosine is released in the extracellular space probably because ATP (Adenosine Triphosphate) is stored as a co-transmitter with some neurotransmitters: the released ATP is converted to Adenosine by extracellular ectonucleotidases. Furthermore during initial brain anoxia Adenosine is also formed intracellularly as mitochondria stop their production of ATP, which consequently is dephosphorilated into ADP (Adenosine DiPhosphate), AMP (Adenosine MonoPhosphate) and finally into Adenosine. Adenosine is then extruded in the extracellular space on a special nucleoside carrier. There are though two different mechanisms which link Adenosine level to the presynaptic activity: first, the ATP release through vescicles is obviously activity dependent; second, presynaptic activity induces faster ATP depletion, unbalancing the ATP/ADP ratio, with the consequence of a rise in the concentration of AMP and intracellular Adenosine (Attwell, 1988; Rudolphi et al., 1992).

ADENOSINE LEVELS IN THE BRAIN

Intervention	*Species*	*Basal*	*Stimulated*
		$[\mu M]$	$[\mu M]$
K^+ *depolarization*[1]	*Rat*	0.9 – 1.1	2
Bicuculline seizures[2]	*Pig*	0.5	3.5
Hypoxia[3]	*Rat*	1 – 2	5
Hypoxia[4]	*Pig*	1.3	2.1
Global ischemia[5]	*Rat*	1.9	40
Global ischemia[6]	*Rat*	2.1	39
Middle cerebral occlusion[7]	*Rat*	0.7	20
Chronic implantation[8]	*Rat*	0.05 – 0.2	

Table 1.9: Extracellular Adenosine level in the brain as measured by microdialysis. Initial estimates of the basal concentration (1,2,3,4,5,6,7) in the unanesthetized freely behaving animal may represent an overestimation due to the trauma induced by the microdialysis probe itself. After prolonged implantation lower basal levels are obtained (8). Different types of stimulation produce a dramatic increase in the level of extracellular Adenosine. List of references: 1-(Ballarin et al., 1987); 2-(Park et al., 1987); 3-(Zotterstrom et al., 1982); 4-(VanWylen et al., 1986); 5-(Hagberg et al., 1987); 6-(Busto et al., 1989); 7-(Hillered et al., 1987); 8-(Ballarin et al., 1991).

Adenosine is known to have a powerful neuromodulatory effect on excitatory, and especially glutamatergic synaptic conduction, which appear to be mediated by at least two independent mechanisms. At the presynaptic level Adenosine's interaction with its A_1 receptor, via activation of a G-protein, leads to the block of Voltage-dependent Ca^{++} channels, and then to silencing of the synaptic activity (Dunwiddie, 1985; Fredholm and Dunwiddie, 1988; Phillis and Wu, 1981; Greene and Haas, 1991). At the postsynaptic level the membrane-stabilizing effect that limits the activity-evoked depolarization and leads to hyperpolarization of the neurons, has to be attributed to an Adenosine-mediated increase in K^+ conductance (Trussel and Jackson, 1987).

Inhibition of activity is thought to have a double neuroprotective effect: by reducing the energy demands and the potentially neurotoxic release of glutamate, it increases the probability of survival to brief hypoxic periods and diminishes the possibility of partial neural damage.

Most of the evidence on the neuroprotective effect of Adenosine has been collected with in vitro preparations using hippocampal slices from rats and other animals, and in experimental models of transient global ischemia in vivo (See (Rudolphi et al., 1992) for review). However two studies with rats and cats used permanent middle cerebral artery occlusion, a clinically relevant model of stroke (Hillered et al., 1987; Matsumoto et al., 1992). In the cat study the Cerebral Blood Flow (CBF) threshold for ischemia-induced increase of extra-cellular Adenosine and glutamate concentration was measured in the ischemic cortex using microdialysis: the adenosine concentration was transiently elevated if CBF fell below 25ml/100g/min, while glutamate concentration started to increase only at lower flow level of 20ml/100g/min, reflecting the inherent but time-limited protective action of Adenosine against glutamate excitotoxicity. In 1994, Boissard, Lindner and Gribkoff produced an anatomical and behavioral study in which two groups of rats that had been trained in the Morris Water Maze were submitted to a very mild hypoxic condition. Only one group was treated with a specific A_1 antagonist, CPT (8-cyclopentyltheophylline); while this group reported substantial anatomical damage and consequent behavioral impairment, the group that was able to benefit from the effect of endogenous Adenosine did not. It was concluded that the Adenosine dependent silencing mechanisms has a crucial role in determining neurons survival to brief and mild hypoxic insult in vivo.

In conclusion, the Adenosine-dependent silencing of synaptic transmission is a very appealing neurophysiological substrate for refractoriness for the following reasons:

- it induces temporary failures of excitatory synaptic transmission;

- it is activity-dependent, so that neurons that are externally excited are the most likely to be inhibited;
- it has a neuroprotective effect: it reduces the energy demands of the cells and prevents the neurotoxic accumulation of extracellular glutamate;
- its time course is compatible with the time course of the behavioral phenomena.

In principle the effect of Adenosine release at synapses can be studied with a computational simulation of a neural network such as the one described in Sect.1.4.1. One way of introducing this supposed silencing mechanism could be by substituting the neural activation threshold U with a dynamic variable $U_\imath(t\jmath)$, with $\imath = 1, \ldots, N$, defined for each neuron $\imath$ and varying with time as a function of the state of activation of the neuron in such a way that the threshold value is enhanced if the neuron remains active for more that a given time interval. In the simulations time is a discrete variable $t\jmath$ defined by the updating cycles of the neural dynamics (see eq.1.11). If for example a neuron were to be silenced after m subsequent cycles in which it has been firing, one could define

$$U_\imath(t_\jmath) = U_\imath(t_\jmath = 0)\Big(1 + A * \prod_{\ell=0}^{\jmath} S_\imath(t_\jmath)\Big) * \vartheta\Big(\sum_{\ell=0}^{\jmath} S_\imath(t_\jmath) - m\Big) \tag{1.30}$$

and keep the threshold value fixed to $U_\imath(t_\jmath)$ for any time thereafter. $A > 1$ is the parameter determining the increase of the activation threshold, and $\vartheta(x)$ is the usual ϑ-function defined as 1 for positive values of its argument and 0 for negative values of its argument. If the value of A is sufficiently high, the silenced neuron will not be able to fire, irrespective of the exciting signal it receives, that is irrespective of the strength of the attractor corresponding to a given representation. This is why, at the level of the patient's behavior, no effect of frequency or familiarity is detected.

The parameter m is linked to the time course of the silencing mechanism. In this zero order approximation only subsequent time intervals in which a neuron is firing have been considered to be able to produce the silencing effect. This is just one of various possibilities: the dynamics of the threshold can be varied in order to take into account, for example, the mean firing rate in a given time interval, which would render the neuron more sensible to its remote activation states, and would allow to include in the simulations different trials in which the same item is presented for retrieval.

In my opinion, both an experimental investigation of the *physiology of refractoriness* and serious computational work are needed in order to give a comprehensive account of the *phenomenology of refractoriness.* The Adenosine Hypothesis should be seen as a possible guideline in this research.

Chapter 2

2.1 Dissociations in Semantic Memory impairments.

Important evidence on the organization of the semantic system has been obtained from investigation of neurological patients. Since Warrington's 1975 paper, in which the selective impairment of semantic memory was first documented, different patterns of semantic impairments have been considered (See (McCarthy and Warrington, 1990) for a review). In the previous chapter I have discussed the evidences which favor the dicothomy between access and storage impairments. Even more relevant from the point of view of the implications for modeling semantic memory function have been the experimental findings on *category-specificity* (Warrington and McCarthy, 1983; Warrington and Shallice, 1984; Sartori et al., 1993) and *modality specificity* (McCarthy and Warrington, 1988; Chertkow and Bub, 1990), including modality-specific naming impairments (Lhermitte and Beauvois, 1973; Beauvois, 1982; Manning and Campbell, 1992; Endo et al., 1996).

The dissociations in performance on different semantic categories have now been extensively documented in patients suffering from different types of neurological impairment, such as neural damage secondary to Herpes Simplex Encephalitis, neurodegenerative illness and cerebro-vascular disease. In a recent review of single case studies [1], R. McCarthy

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[1] Presented in the course of the Post-Doctoral School on Semantic Memory Functions, S.I.S.S.A. - Trieste

produced the following summary of the semantic categories for which dissociations can be found: abstract words and concrete words (Warrington, 1975; Warrington, 1981), common names and proper names (Semenza and Zettin, 1989; Ellis et al., 1989; McNeil et al., 1994) (but see (Shallice, 1993) for a different interpretation of this dissociation), proper names with and without unique referent (Shallice, 1993), country names (McKenna and Warrington, 1978) object names and action names (McCarthy and Warrington, 1985), living and non-living items (Warrington and Shallice, 1984; McCarthy and Warrington, 1988; Hillis et al., 1990; Farah et al., 1991; DeRenzi and Lucchelli, 1994), animals (Sartori et al., 1993) fruit and vegetables (Hart et al., 1985), food (Humphreys and Riddoch, 1987), body parts (Ogden, 1985; Semenza and Goodglass, 1985; Sacchett and Humphreys, 1992), colors, tools and non-manipulable artifacts (Warrington and McCarthy, 1987; Sacchett and Humphreys, 1992; Sartori and Job, 1993), musical instruments and vehicles (Warrington and McCarthy, 1987). Also specific patterns of impairment that cross the boundaries of general categorizations have been reported: so usually musical instruments tend to be impaired together with living items, while body parts ofter follow the fate of non-living items (Warrington and McCarthy, 1987; Sartori and Job, 1993). Category-specific effects have been documented in the context of both storage and access impairments (Warrington and McCarthy, 1983; Warrington and Shallice, 1984; Riddoch and Humphreys, 1987; Sartori et al., 1993; McNeil et al., 1994); furthermore in some cases the category-specific deficits were restricted to given modalities of stimulus presentation (Warrington and McCarthy, 1994; Hart et al., 1985; Hart and Gordon, 1992).

Some authors have raised the possibility that category-specific effects could be found as

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1996.

a byproduct of different characteristics of the experimental stimuli, such as word frequency and familiarity (Funnell and Sheridan, 1992; Stewart et al., 1992; Parkin and Stewart, 1993). in particular the class of living items should be less robust due to lower familiarity values when compared to the categories of non-living items such as tools, vehicles or furniture, which are higher in familiarity. Since these relevant observations were made, case studies have been performed using carefully balanced sets of stimuli. Furthermore a regression analysis, taking into account familiarity and frequency of the stimuli, as well as the semantic category, can be used to assess the genuinity of the phenomenon if normative data on the set of stimuli are available. For example this approach was used in the analysis of the performance at Hodges' Battery for Semantic Memory (Hodges et al., 1992a) in the case study of patient R.M., as described in Section 3.3.

Although less frequent than the converse dissociation, the occurrence of selective preservation of performance on living items with respect to non-living items is reported in the literature: (Hillis and Caramazza, 1991) documented a double dissociations of the robust type between two patients, a finding which speaks in favor of functional independence in the way the two class of stimuli are actually treated in the brain[2].

Possibly the dissociation across modalities of stimulus presentation (McCarthy and Warrington, 1988; Warrington and McCarthy, 1994) is an even more common pattern of impairment, and it is one with which the next chapter will be entirely concerned. Among

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The classification of double dissociations in terms of *classical*, *robust* and *trend* type is provided in (Shallice, 1988), chap.10. In a *classical* double dissociation patient A performs in the normal range in task I and is impaired in task II, while patient B performs in the normal range in task II and is impaired in task II; it is the strongest evidence of functional separability of the cognitive systems supporting the two tasks. In a *robust* double dissociation patient A performs much better than patient B on task I and much worse than patient B on task II; this type of evidence also provides support for functional separability. Finally a *trend* double dissociation differs from a robust one in that the difference of performance just reaches the level of statistical significance; Shallice argues that theoretical conclusions based on trend dissociations can be unsafe.

these the most relevant one is selective preservation of performance in the visual or verbal modality (the first being more often encountered than the second) (Chertkow and Bub, 1990; Chertkow et al., 1992). The issue of whether the knowledge bases for visual and verbal material is unitary or to some extent separable is one of the crucial points on which theoretical effort has been concentrated (Shallice, 1988; McCarthy and Warrington, 1988; Caramazza et al., 1990; Chertkow et al., 1992; Shallice, 1993).

The findings on category-specific and especially on modality-specific dissociations have been used to argue for the view of the semantic system as a multimodal, highly structured system, comprising modality-specific subdomains (Shallice, 1988; McCarthy and Warrington, 1990). On the version of the multiple storage account adopted in (McCarthy and Warrington, 1988), which has been referred to as the *input account* of multiple semantics (Riddoch et al., 1988), considerable duplication of semantic knowledge accessible from different modalities of input, has been proposed. A less strong version holds the semantic system to be a highly interconnected multimodal network in which the modality of the acquisition process together with the intrinsic nature of the stored information determines the final structure of the semantic representations (Shallice, 1988). This version, that I will call the *multimodal semantics* hypothesis, has been implemented in a neural network model that will be described in the final sections of the chapter.

Within the multiple system framework, at least to a first approximation, however, dissociations are thought to emerge as a direct consequence of selective damage to one or more components or subregions of the network, or to the pattern of connections among them. In the case of optic aphasia (Lhermitte and Beauvois, 1973; Beauvois, 1982; Manning and Campbell, 1992), a syndrome characterized by a deficit in naming visually presented objects, with knowledge of the visually presented object being manifest, the impairment in naming to visual confrontation is held to arise from a difficulty in accessing the verbal semantic subsystem, which is assumed to be necessary for naming, from the visual semantic subsystem.

Some authors however have questioned the necessity of assuming separable domains of knowledge in the different modalities and argued in favor of the possibility of accommodating all the described dissociations in the context of an unitary amodal semantic system, accessible from each input modality (Caramazza et al., 1990; Humphreys and Riddoch, 1987). In particular in a series of papers Caramazza and co-workers have argued that if it is possible to accommodate all the experimental evidences in the framework of an amodal semantic system, for the sake of simplicity there is no reason to move to more articulated proposals. The crucial issue is then to verify that the all the current evidences can indeed be accommodated in the context of the amodal semantics proposal.

On the unitary storage system account, the observed pattern of better performance with visual than verbal presentation of the stimuli (Chertkow and Bub, 1990), has been explained by assuming that for visual presentation, some features of the item can have *privileged access* to the semantic system and so support for example, correct miming of the use of that object; in the case of verbal presentation on the contrary, no such privileged link exists between the lexical and the semantic representations (Hillis and Rapp, 1995), as the former are arbitrary labels and do not have any intrinsic link with the semantic representations. This proposal has been referred as the Organized Unitary Content Hypothesis of semantic memory (Caramazza et al., 1990; Rapp et al., 1993). It states that the semantic system is an amodal store, and that the semantic representations are lists of *abstract predicates* which include the entire set of properties constituting the meaning of a word. In this model perceptual, functional and associative properties, but also information about the category membership, is represented in a unique format, *abstract predicates.* Although no explicit position is taken about the neural localization of the system, it is possible within the theory that some types of semantic features would have different neurological substrate, without any appreciable consequence from the point of view of the functional architecture of the system (Caramazza et al., 1990).

In a relevant paper Roelefs explicitly argued against the assumption of *decompositionality of word meaning* (Roelefs, 1997). Decompositionality assumes that word meaning is represented in terms of a collection of features; abstract predicates would be an example of this position. Roelefs first pointed out the theoretical flaws in the arguments that have been used to reject *chunked* mechanisms of lexical access, that is the hypothesis that lexical access is produced via activation of a non-decompositional representation of word meaning; then he showed that the computational models assuming decompositionality, of which the most creditable is Dell's model (Dell and O'Seaghdha, 1992), are indeed unable to deal with problems such as the generation of hyperonyms and hyponyms, word-to-phrase synonymy, context dependence of word meaning and *reductio ad infinitum* in the conceptual analysis of word meaning among others, while models assuming non-decompositionality, or chuncked access, such as WEAVER++ (Roelefs, 1992b; Roelefs, 1992a; Roelefs, 1993), do not suffer from these limitations. Note that in WEAVER++ the chuncked representation of word meaning is also connected to a set of featural representations specifying the sensory attributes of the item: the important assumption is however that lexical access can only be produced via the activation of the chuncked representation, which is the only node directly connected to lexical representations. I believe that chuncked lexical access, that is one of the crucial assumptions in the powerful computational model of speech production WEAVER++, should be related to the neuropsychological claims on the existence of verbal semantics representations: in particular, it should be seen as a computational jiustification for the existence of non-decompositional verbal semantics representations.

However, decompositional representation of word meaning can be criticized also on neuropsychological grounds. If one assumes the existence of such a thing as an *abstract predicate*[3], and the possibility that such a thing as a collection of abstract predicates could exhaust a semantic representation, there is virtually no limit to the types of category-specific dissociations that can be accounted for by such a model. To give an example consider the explanation provided for the category-specific impairment (living worse than non-living) of patients JBR and SBY (Warrington and Shallice, 1984) in (Hillis et al., 1990): "These patients' performance may be explained by proposing damage to a single semantic system in which only enough information to identify the superordinate category of living thing was available but more information was available for inanimate objects (p.231)." This is no more than a description of the experimental facts, that is that in these patients only superordinate knowledge is preserved in the living domain while more information is available for non-living items. There is no hint to how such a pattern could emerge from neural damage.

Apparently even the authors are aware of the overfitting capacities of the O.U.C.H., in that they observe "It would seem therefore that none of the existing observations requires that O.U.C.H. be modified. One would not want, however, to have a model so powerful that it cannot be falsified." (Rapp et al., 1993). The only type of evidence which could be

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What are the abstract predicates for the word "Red"? How does the child learn to extract a list of abstract predicates from his very concrete experience of the world?

problematic to the O.U.C.H. according to the authors comes from the domain of modality-specificity. This is hardly surprising as the only substantive assumption contained in the O.U.C.H. is the one on privileged access. The privileged access hypothesis restricts the field of the modality-specific dissociations to ones characterized by better performance in the visual than in the verbal domain. However, as noted by (Shallice, 1993), the opposite pattern occurs in visual associative agnosia: such patients, despite intact visual perceptual processes, can fail to identify visual stimuli, while demonstrating better comprehension of words (Hécaen and Albert, 1978; McCarthy and Warrington, 1990; Warrington and McCarthy, 1994). Supporters of the unitary hypothesis ascribe associative agnosia to fine grained, and often undetectable, misperception of visual stimuli (Caramazza et al., 1990; Farah, 1990), or to disconnection of the structural description system from the semantic one (Humphreys and Riddoch, 1987; Humphreys and Riddoch, 1988). Also Farah has questionned the possibility of empirically distinguishing apperceptive from associative agnosias (Farah, 1990). However a case of category-specific associative agnosia has been recently described (Warrington and McCarthy, 1994) in a case with bilateral but asymmetric infarcts in the right parietal lobes and inferior left occipital lobe: patient D.R.S. is disproportionately impaired in semantic tasks involving objects presented in the visual modality, while his performance improves on living-items [4]. Although he could flawlessly name objects from description, he was unable to name them by sight nor to mime their use. On two visual matching tasks in which he had to match an object item with a physically dissimilar synonym or with a semantically related item, he was impaired and affected by semantic proximity. In a sound to picture matching task, as well as in word-picture matching tasks,

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[4] In the next chapter I will present a single case study of a patient showing selective preservation of object knowledge in the visual modality.

he performed much better with living than with non-living items. Given his otherwise excellent verbal abilities, the authors ascribe these deficit to misidentification of the pictures. Warrington and McCarthy argue that the domain specificity in performance renders implausible any account of the deficit in terms of perceptual limitations or difficulties in accessing semantic representations from visual input.

Along similar lines, the interpretation of the optic aphasia syndrome in the context of unitary models of semantic memory is based on the supposition that from existing evidence it is impossible to exclude relevant damage at the level of the semantic representations accessed from visual input. In fact most of the evidence produced in favour of correct object identification in optic aphasia, is based on performance in miming tasks in which the subject is requested to show the use of an object he has failed to name. On Humphreys and Riddoch's position it is assumed that simple actions can be produced as *affordances* from the structural descriptions level in the absence of any semantic access (Riddoch et al., 1988): for example the presence of a handle, or the shape of a glass would be able to elicit the correct hand posture for grasping the object. In the O.U.C.H. it also assumed that the semantic feature describing the perceptual characteristics of object could have privileged links with the simple action production (Caramazza et al., 1990). So on this hypothesis simple actions are directly elicited by some types of semantic features and not at the presemantic level of structural descriptions. In order to account for optic aphasia it is assumed that even if exactly those features useful for miming are accessible from the visual modality as a consequence of their privileged relationships with structural descriptions, some other features in the semantic representation could nevertheless be inaccessible from visual input and as a result a pattern of dissociation between naming and miming would emerge. In any case miming is not the only task that has been used in order to test the integrity of semantic representations from visual input in optic aphasia, and different capacities have been tested in different patients. For example the Japanese patient H.O. (Endo et al., 1996), who presented with both optic and tactile aphasia, performed 100% correct in a grouping task in which performance could not be supported by perceptual cues (e.g. grouping 3 tea-related tools vs rice-related ones), and 93% correct in selecting among four objects (e.g. a metal comb, a pair of scissors, a spanner and a comb) the one which forms a semantic couple with the stimulus (e.g. a fork). Another optic aphasic patient, A.G. (Manning and Campbell, 1992) not only had identical abilities to produce appropriate gestures to input in the visual and verbal modalities, but also showed preserved performance in a wide variety of other visual semantic tasks. He was 90% correct on a picture-spoken word matching task with very close semantic distractors (the same level as three control subjects), and 91% correct on Probe questions tapping perceptual knowledge non directly represented in the drawn stimuli such as dimension and color. He performed in the normal range on the Pyramids and Palm Tree test with visual material, and finally was able to classify not only animals as 'dangerous or tame', but also drinks as 'suitable or unsuitable for children' and 'clothing as 'washable or non-washable', which clearly demonstrates access to fine grained subordinate level knowledge from visual input. Clearly this patient does not fit in the account of optic aphasia proposed in the context of the O.U.C.H. A characteristic of this patient, is the preservation of action naming, a finding that has been replicated in other optic aphasic patients.

(Chertkow et al., 1992) produced an intriguing analysis of the experimental evidence on modality-specificity, and of the different theoretical proposals that have been put forward in order to account for it (See Hillis and Rapp (1995) for a critique of their approach to the unitary semantics position). They presented findings from patients with progressive dementia which they argued were relevant to the different hypotheses on semantic memory structure. The patients were held to have storage deficit using the criteria of Warrington and Shallice (Warrington and Shallice, 1979; Shallice, 1988). However they produced better performance with visual than with verbal material. This result was established by Probe Questions relating to both the perceptual and the associative aspects of items in different semantic categories. The patients also performed better with questions tapping perceptual than associative knowledge, but this was not correlated with the modality of input. In order to investigate further this lack of interaction, given main effects of both modality of input and type of knowledge, the authors focussed their attention on a subset of the stimuli (the animals), on which correct identification could be assessed by two different tests (categorization and front-back matching test). Their critical argument was based on an error analysis of the Probe Question findings on this subset of items. The one patient who completed the tests, failed to answer 45% of the questions correctly with verbal presentation, but only 25% of them with a picture of the stimulus; moreover, 91% of the questions failed with visual presentation were also failed with verbal presentation. The authors argued that this pattern of performance is only compatible with the relevant information being retrieved from a single amodal semantic memory system.

In fact this conclusion is not mandatory. What the data clearly evidentiate is that there is no duplication of information unrelated to its strength in the two sub-systems. From this evidence no conclusion can be derived with respect to the nature of the corresponding semantic representations: an amodal representation and multimodal representations in which knowledge is not duplicated across modalities would both produce the same pattern of results.

The evidence of better preserved performance on visual stimuli was explained by adapting a theory put forward by Miller and Johnson-Laird and differentiating an *'identification semantics'*, which was assumed to be relatively intact, from the impaired amodal semantic memory (Miller and Johnson-Laird, 1976). In using the term 'identification semantics' Chertkow et al. hold that the system contains only the semantic information crucial for the identification of a visually presented item. They also assume that this information is sufficient for correct naming. For living items it would include a type of perceptual description, while for man-made objects it would contain more functional than perceptual information. All other kind of semantic information pertaining to a given item, are assumed to be held in the 'associative semantic store', thought to be amodal and directly accessible from the presemantic lexical representations. This proposal holds that identification semantics, although is a modality-specific component, is also accessible from the amodal semantic system if information about perceptual structure is required.

In another group study (Hodges et al., 1996) both D.A.T. and control subjects were requested to name pictures of 48 living and non-living items, and to produce spoken definitions of the corresponding names. The spoken definitions were then analyzed in order to compare the knowledge of physical and functional-associative information separately for 'named' and 'un-named' items. D.A.T patients produced less informative definitions both for named and unnamed items when compared to controls; in particular a disproportionate reduction of physical with respect to functional-associative information was found for the unnamed items, while no such disproportion was found for the functional-associative information. The authors claim that these finding support the hypothesis that successful naming depends on a subset of semantic knowledge comprising physical features.

However in the context of a model of semantic memory in which physical (visual) features and associative-functional features (non-visual) are segregated, this conclusion does not appear to be straightforward. In fact assume to have a model of semantic memory composed of two subsystems, the visual semantic subsystem and the non-visual semantic subsystem. In the picture naming task correct performance requires that both the visual and the non-visual components are activated: the visual component is needed for identification of the picture, while the non-visual component has to be accessed for naming, as it is the only component which gives access to the output lexicons (and which is accessed from the input lexicons). Assume[5] that each of the two subcomponent can be damaged independently from the other, and that the probability of damage to the 'visual semantic component', which is the store of the physical features, is p_1, and the probability of damage to the 'non-visual semantic component', storing associative-functional features, is p_2. Within this assumption the overall probability that a visually presented item is not named is simply $1 - (1 - p_1)(1 - p_2) = p_1 + p_2 - p_1 * p_2$. In the definition task the subjects are required to retrieve both visual and non-visual features. However, as in the definition task the non-visual representation is accessed first, the visual features will be accessed only if the non-visual features of the same semantic representation are substantially unimpaired. As a consequence the classification of the definitions obtained from the patients for the unnamed items will inevitably produce an overestimation of the damage to the visual semantic subcomponent.

I owe the following argument to Prof.Tim Shallice

In the next chapter I will present a single case study providing strong evidence against the identification semantics hypothesis. The patient is suffering from a degenerative process mainly affecting the inferior part of the left temporal lobe. Despite a profound deficit in all tasks requiring verbal comprehension, she shows relatively intact performance both in everyday life activities and in experimental conditions designed to investigate the preservation of non verbal knowledge. In particular the patient is able to access complex behavior schemata in response to visual, but not to verbal, stimuli. The profound impairment of verbal comprehension provides the opportunity to investigate the limits of the abilities supported by non-verbal semantic systems. I will argue that the richness and complexity of the behavior elicited by visual stimulation cannot be explained as a by-product of preserved 'identification semantics'; also an attempt to accommodate the experimental evidence in the context of the O.U.C.H. would force one to extend the privileged access hypothesis well beyond its current content. Instead the data will be interpreted in the context of the multimodular model of semantic memory described in the next section.

2.2 A neural network model for Multimodal Semantics.

In Chapter one I described an associative neural network storing memories in the form of distributed patterns learned by means of an Hebbian learning rule. This type of network has been used as the building block of an implementation of the multimodular model of semantic memory (Lauro-Grotto, 1993; Lauro-Grotto et al., 1997). In this model the semantic system is represented by a set of interconnected neural networks comprising modality-specific subcomponents, each of which is either directly accessed from the corresponding input modality, or providing access to output, such as output lexicons, and action schemas. The possibility that for some networks access is only provided via activation of other subcomponents of the system is also considered.

The computational model was originally designed in order to study the equilibrium properties of the system, e.g. what types of attractors can be found when several networks are connected together. The results are described in general for an arbitrary number M of neural networks. It is actually for neuropsychological research to find evidence in favour or against the multimodal hypothesis and to specify the nature and the particular properties of the various semantic subsystems. A step in this direction is provided by the single case study of patient R.M. presented in the next chapter.

For the sake of simplicity I will first summarize some analytical results obtained in the simpler case of $M = 2$ [6], then simulations of a system comprising more than two networks are described[7].

2.2.1 A system of two coupled neural networks.

The first modification to be introduced in the model presented in the first chapter in order to describe the dynamics of two coupled networks is synaptic dilution (Derrida et al., 1987; Sompolinsky, 1986). Technically synaptic dilution is realized by introducing a symmetric matrix $T_{i,j}$, $i, j = 1, \ldots, N$, $T_{i,j} = \{0, 1\}$, which eliminates some synapses $J_{i,j}$ in such a way as to have a fixed mean value of the connectivity, C. The connectivity is defined as the ratio of the mean number of neurons connected to a given neuron in the network, and the total number of neurons N:

$$C = \frac{\sum_{i,j=1}^{N} T_{i;j}}{N^2} \tag{2.1}$$

These results are derived from (Lauro-Grotto, 1993)

The simulations were performed in collaboration with Prof.M.A.Virasoro; the results of the simulations are published in (Lauro-Grotto et al., 1997)

Consider now two neural networks having N formal neurons each. A capital letter will be used in order to index quantities referring to a given network. So the state of the $i-th$ neuron in network A at time t is represented by the binary variable $S_i^A(t)$. Coupling between two networks, A and B, is realized by connecting each neuron in network A to a given proportion of neurons in network B: intramodular connectivities (C^{AA} and C^{BB}), representing the connections among neurons of the same brain areas, are taken to be higher than the connectivities across different areas ($C^{AB} = C^{BA}$):

$$C^{AA} \cong C^{BB} \gg C^{AB} = C^{BA} \tag{2.2}$$

For a given modul, for example A the intramodular connectivity is defined by the matrix $W_{i,j}^{AA}$, while the inter-modular connectivity is defined by the matrix $W_{i,j}^{AB}$:

$$\begin{aligned} W_{i,j}^{AA} &= T_{i,j}^{AA} J_{i,j}^{AB};\ \text{dove } i = 1, \ldots, N^A = N\ ;\ j = 1, \ldots, N^B = N \\ W_{i,j}^{AB} &= T_{i,j}^{AB} J_{i,j}^{AB};\ \text{dove } i = 1, \ldots, N^B = N;\ j = 1, \ldots, N^B = N \end{aligned} \tag{2.3}$$

where $T_{i,j}^{AA}$ and $T_{i,j}^{AB}$ express the synaptic intra-modular and inter-modular dilutions, and $J_{i,j}^{AA}$ and $J_{i,j}^{AB}$ are the matrices of the synaptic strength expressed as functions of the memories stored in the two networks according to a Hebbian learning rule which is the direct extension of the one introduced in the last chapter:

$$\begin{array}{ll} J_{i,j}^{AA} = \displaystyle\sum_{\mu=1}^{p^A} \frac{(\xi_i^{\mu^A} - a)(\xi_j^{\mu^A} - a)}{a(1-a)N} - \frac{\gamma}{aN} & i \neq j \\ & i, j = 1, \ldots, N \\ J_{i,j}^{AB} = \displaystyle\sum_{\mu=1}^{p} \frac{(\xi_i^{\mu^A} - a)(\xi_j^{\mu^B} - a)}{a(1-a)N} - \frac{\gamma}{aN} & i \neq j \end{array}$$

$$i, j = 1, \ldots, N$$

$$p \leq p^A \tag{2.4}$$

Inframodular synapses realize the storage of the patterns in each network (ξ^{μ^A}, $\mu = 1, \ldots, p^A$ in network A and $\xi^{\mu^B}, \mu = 1, \ldots, p^B$ in network B), while the intermodular synapses implement the associative link between them. Associative links are meant to implement the relationship between two modality-specific representations in the semantic system. An associative link across patterns in different modules can be exemplified by the visual and the motor-functional semantic characterizations of a given stimulus, e.g. a pair of scissors. The patterns ξ^{1^A} and ξ^{1^B} for example can be seen as the modality-specific semantic representations of the scissors that become associatively linked in the course of experience: one pattern would store for example the visual information that allows recognition of all the possible instantiations of scissors as such and may be some information about the visual environment in which they are usually seen, another pattern would store the action schema appropriate to the use of a pair of scissors as a tool, and hence the information about its use[8]. When one of the two pattern is retrieved in one module (e.g. during visual presentation of the stimulus) a signal is sent to the second modul, which drives the network dynamics into the attractor corresponding to the functional specification of the stimulus. In general not all the patterns stored in module A are associated with a pattern stored in module B. One can think of many items that can be recognized in the visual modality, but that do not have any functional-motor characterization, such as trees or clouds for example. Another example could be the case of abstract words, that do not have perceptual meaning and are represented only in the verbal semantic subsystem. In what follows I will assume that of the

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Evidence in support to this position is provided in chapter 3; see specifically the general discussion.

p^A patterns stored in module A only p ($p < p^A$), will be associated to patterns in module B.

The mean field approach to the dynamics of two coupled networks goes along similar lines to that for the dynamics of a single network, but the actual derivation of the mean field equations is complicated by the presence of the dilution matrices. The dynamic variables that describe the collective behavior of the system however can be defined in exactly the same way as for the single network. So for each module it is possible to define the *overlaps* $m^{\mu^A}, \mu^A = 1, ..., p^A$ between the network state $\{S_i^A\}, i = 0, ..., N-1$ and each of the stored patterns $\xi^{\mu^A}, \mu^A = 1, ..., p^A$, as effective measures of the quality of retrieval; the global magnetization M^A is the measure of the activity in network A.

In the limit of zero fast noise, the stable solutions for the self consistency equations correspond to the global minima of the following *energy* function (Lauro-Grotto, 1993):

$$\begin{aligned} E &= -\frac{a}{2(1-a)}[\sum_{\mu^A=1}^{p} C^{AA}(m^{\mu^A})^2 + \sum_{\mu^B=1}^{p} C^{BB}(m^{\mu^B})^2 + 2\sum_{\mu^A=\mu^B=1}^{p} C^{AA}(m^{\mu^A})(m^{\mu^B})] + \\ &+ \frac{\gamma a}{2}[C^{AA}(M^A)^2 + C^{BB}(M^B)^2 + 2C^{AB}M^A M^B] + aU(M^A + M^B) \end{aligned} \tag{2.5}$$

It is worthwhile to note that the associative link between memories of different modules contributes to lowering the energy of the solution corresponding to the retrieval of two associated patterns by the mean of the negative term $\frac{-a}{(1-a)} \sum_{\mu^A=\mu^B=1}^{p} C^{AB} m^{\mu^A} m^{\mu^B}$. So from the point of view of the entire network the memories that are represented on all the modules are the more stable ones.

In the next session I discuss the stable solutions of the global network dynamics corresponding to different initial conditions for the retrieval process, obtained in the noiseless limit with the mean field approach described in the previous chapter.

2.2.2 Retrieval dynamics for two coupled networks. A summary of results.

The simplest case to be considered in the case of the two coupled networks is the one in which a given memory has a representation in both modules. Patterns corresponding to modality-specific representations of a single memory are indicated with the same μ index (μ is the index running over the set of patterns stored in the system). Let ξ^{1^A} and ξ^{1^B} be the associated patterns. In order to derive the selfconsistency equations and the corresponding solutions, a situation in which the stimulus represented by the associated patterns is presented to the system for retrieval must be considered. In this case in the initial condition each module is set in a state that is created by the input, in which it has a substantially non-null overlap (m^{1^A} and m^{1^B} respectively) with only one of the stores memories.

As I have discussed for the case of the single network (Sections 1.4.1. and 1.4.2), if $\lim_{N\to\infty}\frac{p}{N}=0$, that is if the system is operating at *low loading*, the contribution of the overlaps with the other stored pattern is averaged out, and the entire dynamics of the system can be described by the four global variables: m^{1^A}, m^{1^B},M^A, M^B. The self-consistency equations for the global variables of the two modules are coupled. The equation for overlap in module A, m^{1^A}, is also dependent from the overlap of the associated pattern in module B, m^{1^B}, which contributes to driving the dynamics into the attractor:

$$\begin{aligned} m^{1^A} &= \frac{\xi^{1^A}-a}{1-a}\{1+exp-\beta[\frac{(\xi^{1^A}-a)}{1-a}(C^{AA}m^{1^A}+C^{AB}m^{1^B})+ \\ &- \gamma(C^{AA}M^A+C^{AB}M^B)-U]\}^{-1} \\ m^{1^B} &= \frac{\xi^{1^B}-a}{1-a}\{1+exp-\beta[\frac{(\xi^{1^B}-a)}{1-a}(C^{BB}m^{1^B}+C^{BA}m^{1^A})+ \\ &- \gamma(C^{BB}M^B+C^{BA}M^A)-U]\}^{-1} \end{aligned}$$

$$\begin{aligned} M^A &= \frac{1}{a}\{1+exp-\beta[\frac{(\xi^{1^A}-a)}{1-a}(C^{AA}m^{1^A}+C^{AB}m^{1^B}+ \\ &- \gamma(C^{AA}M^A+C^{AB}M^B)-U]\}^{-1} \\ M^B &= \frac{1}{a}\{1+exp-\beta[\frac{(\xi^{1^B}-a)}{1-a}(C^{BB}m^{1^B}+C^{BA}m^{1^A})+ \\ &- \gamma(C^{BB}M^B+C^{BA}M^A)-U]\}^{-1} \end{aligned} \qquad (2.6)$$

The parameters γ and U are the *lateral* inhibition constant and the *neural activation threshold*, defined as in Sect.1.4.1. The higher the intermodular connectivities C^{BA} and C^{BA}, the stronger is the reciprocal influence between the two networks.

In the noiseless limit, the solution can be obtained with the same geometrical method used for the single network; it corresponds to the the correct retrieval of two associated memories:

$$\begin{aligned} m^{1^A} &= 1-a \\ m^{1^B} &= 1-a \\ M^A &= 1 \\ M^B &= 1 \end{aligned} \qquad (2.7)$$

The stability conditions are also very similar to the ones found for a single network, the only difference coming from the presence of the connectivity terms $(C^{AA}+C^{AB})$ for module A and $(C^{BB}+C^{BA})$ for module B.

$$\begin{aligned} (1-a-\gamma)(C^{AA}+C^{AB})-U &> 0 \\ (1-a-\gamma)(C^{BB}+C^{BA})-U &> 0 \end{aligned} \qquad (2.8)$$

As I said, the system is also able to store memories that are represented in a single modality, that I will call *unimodal patterns*. A unimodal pattern in module A (according to the notation just introduced this would be for example pattern $\xi^{(p+1)^A}$) can be formally viewed as being associatively linked to the state of ’no recognition’ of module B, e.g. the state of zero activity of modul B. This situation corresponds to the following solution of the self-consistency equations:

$$\begin{aligned} m^{(p+1)^A} &= 1-a \\ M^A &= 1 \\ M^B &= 0 \end{aligned} \tag{2.9}$$

which is found to be stable under the condition

$$(1-a-\gamma)C^{AA} - U > 0 \tag{2.10}$$

The system of coupled networks as well as the single network is said to be *non-opinionated*, because it can signal that a given semantic representation is not stored: the solution corresponding to the state of ’no-recognition’ is simply $\{m^{1^A}=0; m^{1^B}=0; M^A=0; M^B=0;\}$, which is always a stable solution if the neural activation threshold U is positive.

Finally in (Lauro-Grotto, 1993) an analytical description has also been provided for the case in which a given stimulus presented for retrieval has non-null overlaps with two different stored patterns either in one or in both modules. This can be seen as a first step for the introduction of the concept of *semantic distractors* in this model. Here the first relevant difference from the simple case of a single network is found: in fact, while in any single associative network there cannot be any stable solution in this case because of symmetry constraints, the coupled networks exhibit stable solutions corresponding to the retrieval of two different patterns in both modules, the so called (Σ, Σ) solutions ((Σ, Σ) standing for 'Sum' of two patterns in both modules), and also to the retrieval of the intersection of the two patterns in both modules, the so called (Π, Π) solutions ((Π, Π) standing for 'Product' of two patterns in both modules). Furthermore both Σ and Π solutions in a module can be coupled to the solution corresponding to the retrieval of a single pattern in the second modul, giving rise to the so called $(\Sigma, 1)$ solution and $(\Pi, 1)$ solution respectively. Before considering possible cognitive consequences for these types of attractor states, it is important to note that the ranges of stability for these types of solutions, and especially in the case of the Π ones, are extremely narrow, e.g. they require *fine tuning* of the parameters of the model. This characteristic makes them a rather implausible possibility from a biological point of view, at least in a model in which the global parameters are set to fixed values.

2.3 A system of M coupled modules. A summary of results.

The results described in the previous session have been generalized to the case of an arbitrary number M of coupled networks, in which every neuron in a given network is connected to a given proportion C^{infra} of neurons in the same modul, and to a different proportion C^{inter} of neurons in the other modules of the system. So for example synaptic matrices will be either *inframodular* (of the $J^{AA}_{i,j}$ type) , e.g. representing synaptic contacts between neurons of the same modul, or *intermodular* (of the $J^{AB}_{i,j}$ type), e.g. representing contacts between neurons belonging to two different modules:

$$J^{AA}_{i,j} = \sum_{\mu=1}^{p^A} \frac{(\xi_i^{\mu^A} - a)(\xi_j^{\mu^A} - a)}{a(1-a)N} - \frac{\gamma}{aN} \qquad i \neq j$$

$$i, j = 1, \ldots, N$$

$$J_{i,j}^{AB} = \sum_{\mu=1}^{p} \frac{(\xi_i^{\mu^A} - a)(\xi_j^{\mu^B} - a)}{a(1-a)N} - \frac{\gamma}{aN} \qquad \begin{array}{l} A \neq B, i \neq j \\ i, j = 1, \ldots, N \\ p^{AB} \leq min(p^A, p^B) \end{array} \tag{2.11}$$

p^{AB} is now the number of pattern associatively linked in the two modules (A, B).

A semantic representation is formed by a set of associatively linked patterns, that may involve only some of the modules in the system, and even only one in the case of unimodal patterns. In the noiseless limit, the structure of the attractor states is similar to what found in the case of $M = 2$, but the stability conditions for the various solutions are altered according to the number of patterns associatively linked in a given semantic representation. And in fact, as a consequence of the learning rule 2.11, every module during associative retrieval of a given representation receives a stabilizing signal (e.g. a signal that helps convergence toward the right attractor) from each of the other networks involved in the representation, and therefore the higher is the number of modules on which a given memory is represented, the greater is its stability. This can be verified by studying the variation in energy across solutions in which a different number n of modules are activated. For the sake of simplicity I take all inframodular connectivities equal to a single value C^{infra} and all the intermodular connectivities equal to a second fixed value C^{inter}; The energy in the noiseless limit $(T = 0)$ is given by (Lauro-Grotto, 1993):

$$E(T=0) = -\frac{a}{2}(1 - a - \gamma)[C^{infra} + C^{inter}(n-1)]n + aUn \tag{2.12}$$

as in the solution corresponding to correct retrieval $\frac{1}{2}(1 - a - \gamma) > 0$, the energy of the solutions diminishes with increasing n. The stabilizing effect of intramodular connections will be evidentiated also by the simulations presented in the next sections. To a first approximation this is equivalent to saying that the more distributed representations are also the more robust ones.

In the multimodular model of semantic memory, a natural way of implementing semantic similarities of items belonging to the same category is by making the hypothesis that the semantic representations of items from the same categories are represented across the same subset of modules in the semantic system (Lauro-Grotto, 1993). But semantic proximity may also have an effect at the level of single modules, e.g. in modality-specific representations. In order to capture the effect of similarities inside a modul, the concept of 'semantic distractors' has been introduced (Lauro-Grotto, 1993; Lauro-Grotto and Virasoro, 1995). A *semantic distractor* of a pattern ξ^{μ} is defined as a pattern $\xi^{\bar{\mu}}$ such that:

$$\ll \xi_i^{\bar{\mu}} \gg = a \qquad [\ll \xi_i^{\mu} \xi_i^{\bar{\mu}} \gg] = b \gg a^2 \tag{2.13}$$

This means that while two patterns selected at random share on average a fraction a of their active neurons, for the case of a pattern and its distractor the proportion of shared active neurons is much higher than what would be predicted by the statistics of the set of patterns. In particular there is a critical value b^* of the fraction of shared neurons between a pattern and its distractors, over which the two cannot be separately retrieved: e.g. instead of retrieving the pattern presented, the network will retrieve the Σ solution corresponding to the sum of the stimulus and its distractors. A Σ solution in which a pattern and its distractor are retrieved together is said to be an *ambiguous* solution. In the case of a single network it has been shown that $b^* \cong \frac{1}{2}a$, which means that two patterns that share more than around 10% of their active neurons cannot be retrieved separately.

The problem of ambiguous solutions arises not only in associative networks, but also in multilayer networks. Many proposed solutions are based on variations of the learning rules which aim to enhance the relevance of the unshared components of the patterns. Unfortunately with these types of rules the learning of a new pattern strongly influences the already learned memories, in such a way that optimal solutions can be found only by iterative and slowly convergent algorithms. In any case in the context of this model of multimodal semantics anyway it has been shown that a simple way of reducing ambiguity (e.g. the tendency to erroneously retrieve the Σ solution) is by associatively linking a pattern and its distractor to two non-overlapping patterns in another modul. This amounts to saying that multimodal representations are less sensitive to the detrimental effect of semantic distractors than unimodular ones. In particular it has been shown (Lauro-Grotto, 1993) that even in the case of a representation distributed over two modules, b^* can reach values as high as 50%.

In the next section many of the previous analytical results will be illustrated with examples derived from simulations. Analytical results are derived in the so called *thermodynamic limit*, $N \to \infty$ that is in an ideal situation in which the number of units in the network is so high that, because of the Law of Large Numbers, the effect of fluctuations can be neglected. Simulations on the contrary are realized with finite, although very large, numbers of units, allowing for a control of the effects of fluctuations.

Another issue that the computational work will address is the relative robustness of attractors distributed over a different number of modules.

2.4 Simulations with Multimodal Semantics.

In the analytical approach just described results are derived in the so called *thermodynamic limit*, $N \rightarrow \infty$ that is in an ideal situation in which the number of units in the network is so high that, because of the Law of Large Numbers (Feller, 1968), the effect of fluctuations can be neglected. Simulations on the contrary are realized with finite, although very large, numbers of units, allowing for a control of the effects of fluctuations.

Another issue that only the computational work can address is the relative robustness of attractors distributed over a different number of modules. In order to work as a model of semantic memory, the multimodular network must allow for the storage and retrieval of representations containing different distributions of modality-specific information: for example, abstract words will be represented over just one module (the verbal semantic subsystem), colors will be represented over two (visual and verbal semantics), tools over three at least, and so on.As during the retrieval process the networks that are not involved in a given representation nevertheless produce some noise, it is important to assess the effect of this type of noise on the various type of representations.

The simulations[9] were performed on an IBM 550E with 128 Mbytes of RAM. We first discuss numerical experiments done on a single isolated module. They provide a good example of correct functioning of a neural network and help us understand the role of the parameters γ, the lateral inhibition parameter, and U, the neural activation threshold, defined in Sect.1.4.1.

Results in this section are derived from (Lauro-Grotto et al., 1997)

2.4.1 One Isolated Module.

The simulations of the single network dynamics were performed with a choice of the parameters that define the structure of the system based on the computational reasons and on biological plausibility assumptions discussed in Sect.1.4.1. The fraction of active neurons in each pattern a, corresponding to the fraction of neurons firing during recognition of a given stimulus, was set to 0.1. The connectivity parameter C_{intra}, representing the probability of a synaptic contact between two neurons chosen at random in the network, was set to 0.05. The total number of neurons the system, $N = 4000$, was selected in order to have a a computationally reasonable approximation of a biological network, and in order to allow for the storage of a relevant number of patterns p. We chose $p = 71$, a value of p which is below the theoretical limit of capacity. The simulations are then performed in the low loading range.

We considered different values of γ and U. We observed the following behavior:

- For γ and U both large (≥ 0.5) the only stable configuration corresponds to the zero state in which all neurons are inactive.

- For γ and U both small all the patterns are stable. However "unions" of patterns are also stable. These are states in which all the neurons that would be active in each individual pattern in the union are simultaneously active. We consider this situation unsatisfactory because the module does not discriminate.

- For γ between 0.2 and 0.4 but U small (≤ 0.1) the unions of patterns become unstable while the patterns themselves are stable. However if we start the module from an initial condition that is orthogonal to any stored pattern the system still converges either to one of the patterns themselves or to a spurious attractor that has a large number of active neurons. This situation is also unsatisfactory. The module is "recognizing" when there is nothing to recognize. Furthermore if this situation reappears once we couple the M modules, the spurious activity will generate noise that will be difficult to treat.

- Finally for $0.2 < \gamma < 0.3$, $0.3 > U > 0.2$ the patterns are stable, the zero state is stable and if the initial state is far from any stored pattern the module converges to the zero state with no active neuron. This is the ideal situation: non-recognition corresponds to a zero state that transmits minimal noise to other parts of the brain.

Therefore, this preliminary experiment teaches us that both the inhibition parameter and the threshold must be tuned. Theoretical analysis confirm these results: γ prevents the stabilization of states with too many active neurons while U controls the stability and the basin of attraction of the zero state.

2.4.2 Multimodule Model Simulations.

The numerical experiments involved 5 modules with 1333 neurons each. The intramodule connectivity C_{intra} was equal to 5% while the intermodule one $C_{inter} = 2.5\%$.

How a pattern is represented depends on its semantic content. The semantic category, as defined in the previous section, determines the modules that will be active for the specific pattern. The remaining modules should converge to the zero state. For instance an abstract concept cannot evoke a visual component; some other concepts may not be associated with information in the motor modules etc. The model must therefore guarantee the existence and stability of attractors corresponding to patterns that are distributed over many modules and of those that are present only in a limited small subset. It is this requirement that will prove difficult to satisfy.

For the sake of simplicity we have compared only two extreme categories of patterns: a first one in which patterns are distributed in all modules and a second one composed of patterns that are present in a single module. It is evident, and we have checked it in the simulations, that the first class is more stable than the second one. Thus when we increase the number of stored patterns, near the limit of capacity, the distributed patterns will be the last to be destabilized. Furthermore, the noise produced by a distributed pattern on an isolated one is larger. Therefore at constant number of stored patterns, the signal to noise ratio will increase if we increase the percentage of distributed patterns. It is therefore necessary to analyze the behavior of the model in terms of two parameters: the total number of patterns and the ratio of distributed over isolated patterns.

We began considering 17 patterns distributed over 5 modules and 2 isolated ones in each different module (in total, 27 patterns). The distributed patterns were stable for U around 0.3 and $\gamma = 0.2$. It was enough to start with a signal in one of the modules for the system to reconstruct the whole pattern. The zero state was also stable. However, the isolated patterns could not be recalled at all. Even starting with the initial state coinciding with an isolated pattern the system would evolve towards meaningless configurations.

We then repeated the experiments reducing the number of distributed patterns. When this number reached 5 while those isolated were more than 14, we enter into a transition regime in which a larger fraction of isolated patterns became stable. Finally with 1 and 18 all the representations were stable. Therefore decreasing the number of more distributed patterns strengthens the isolated patterns.

This scenario is not acceptable. It seems implausible that any appropriate model for semantic memory would impose limits on the number of distributed patterns that are to be stored. In the next section we discuss possible modifications to improve the performance.

2.5 Possible Modifications on the Model.

The strategies that one can follow include modifying the learning mechanism and/or the retrieval dynamics. They are not mutually exclusive.

2.5.1 Modification of the learning mechanism.

If the poor performance is due to the larger effect of signal and noise for the distributed patterns one may try to depress their impact on the synaptic efficacies. We observe that the noise of M incoherent sources adds to a total value of order $\sqrt{M}$ while the signals add coherently and is therefore of order M. It would thus be ideal to divide the signal and noise terms by a factor proportional to M. When the different degrees of connectivity are taken into account an exact calculation yields a dividing factor equal to $(C_{intra} + (M-1)C_{inter})$. In this case the signal of distributed patterns and of isolated ones are equal while the noise produced by the former is smaller[10].

Unfortunately it is difficult to imagine how this ideal solution could be realised. Let us consider, for instance, the case where an old pattern is complemented with new information.

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[10] A similar type of modification of the learning rule has been discussed in Section 1.4.1. as an implementation of the frequency classes of the stimuli. In that case the idea was to enhance the synaptic traces of some patterns (the more frequent stimuli) with respect to others. As I discussed in Section 1.4.2. this procedure increases the interference of the frequent patterns over the unfrequent ones. In the present case the modification goes in the opposite direction, because it is the strength of the attractors distributed over many modules that has to be reduced. From the computational perspective, the synaptic strength and the number of neurons involved in a given representation are two independent factors that can be altered in order to modify the signal to noise ratio and hence the strength of the attractor. However I assume that in this model the number of neurons involved in a given representation is constrained by the semantic category of the stimulus, that is by the number of modules over which it is distributed.

The synaptic trace left by the original information must be depressed to compensate for the new association that perhaps involves other modules.

The only biologically inspired proposal specifically designed to balance basins of attraction is the so called *unlearning* mechanism. In its original version there was an explicit reference to the REM dream phase. In (Hopfield et al., 1983) the mechanism was implemented in a Neural Network. The net effect was to decrease the interference among patterns and to increase the storage capacity. The idea that such a mechanism exists is attractive because of its automatism. During the REM phase the system is supposed to be activated spontaneously starting from a random configuration and evolving into an attractor. Once the latter is reached the synaptic couplings are modified following a rule similar to the one in equation 2.11 but with the opposite sign. Larger attractors will be reached more often and therefore they will be depressed more. Unlearning must stop at a certain moment otherwise all of the traces would disappear. The automatic tuning of this moment is problematic because it cannot depend on checking whether the goal of equal basins of attraction has been reached. A safe conclusion is that the difference among basins of attraction will be reduced but will not disappear.

In fact there is independent evidence that the basins of attraction of different patterns do not become equal. The differential robustness against damage of certain categories and the existence of factors like *familiarity* (Funnell and Sheridan, 1992) and *frequency* on the strength of a representation could not persist if that was not the case.

2.5.2 Modification of the Retrieval Dynamics.

We now discuss the possibility of changing the parameters of the retrieval dynamics.

Redesigning the inhibition.

Inhibition is supposed to be mediated by an independent class of neurons. In the model the inhibition term is proportional to the overall activity in the whole network. This could be improved in several ways. The most general case would be to substitute the unique parameter of lateral inhibition γ with a matrix $\gamma(a, b)$ that would generate an inhibition effect in module a proportional to the activity in module b. To implement such a mechanism signals coming from other modules should remain sufficiently segregated so as to be independent inputs to different aggregates of inhibitory neurons. Surprisingly enough the anatomical structure of the biological network that has been proposed as an implementation of an auto-associative system, seems to be designed to satisfy these constraints. In fact it has been found[11] that in the hippocampus the total external signal and the internal one project into different parts of the excitatory neurons. Reassured by this evidence and in order to obtain the correct functioning of the hippocampus as an associative memory, Treves and Rolls have suggested that the external signal should be renormalized so that it is of the same order as the internal one (Treves and Rolls, 1994). In this way the external system selects but does not deform the internal attractor.

This idea goes in the right direction, but does not solve the problem we face in the multimodular cortex . It treats external signals and external noise in the same way and in some cases it even amplifies the noise (we have observed this effect in the simulations). For instance if a pattern activates modules A and B and is absent in the $M-2$ remaining modules, the external signal on A will mix the signal (and noise) from B plus the pure noise from the other $M-2$ modules. It is clear that renormalizing the total external signal will

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E. Rolls personal communication.

not change the signal to noise ratio much. We believe that the mechanism is useful when the origin of the signal is essentially always the same.

Modulating Intermodular Synapses (or Thresholds).

In a Content Addressable Memory, retrieval uses input information to reconstruct the whole pattern. In Section 2.1 we have identified a new type of information: the category to which the pattern belongs, defined as the set of coactive modules. It is natural to expect that such information can be used as input.

For this purpose we propose a mechanism that, on the basis of the category information, modulates the thresholds and/or the intermodules synapses. Its effect will be to depress the activity on the modules where the pattern is supposed to be absent and/or to disconnect them from the rest.

In the simulations we multiplied all the synaptic couplings that connect two given modules by a common factor and simply reduced it to zero[12] when needed. This mechanism reduces to zero the noise coming from inactive modules. It improves dramatically the efficiency of retrieval. Acting together with some form of unlearning the system reaches the optimal storage capacity. A biologically plausible way of implementing it could be via a neuromodulator acting partially through diffusion.

Reduction to zero was assumed to simplify the simulations; in the biological implementation of the mechanism a strong depression of activity should be considered.

Chapter 3

3.1 Introduction.

In this article [1] we present a single case study of a patient with a clear cut visuo-verbal dissociation. The patient was suffering from a degenerative process mainly affecting the inferior part of the left temporal lobe. Despite a profound deficit in all tasks requiring verbal comprehension, this patient showed relatively intact performance both in everyday life activities and in experimental tests designed to investigate the preservation of non verbal knowledge. The profound impairment of verbal comprehension in this patient provides the opportunity to investigate non-verbal knowledge and the nature of the tasks that can still be supported by the semantic system in the presence of this type of damage.

In the investigation we experimentally characterize some types of semantic judgements that the patient is able to perform on visual material only. By devising certain "ecological" tests, we show further how the patient is in fact able to access complex behavioral schemata in response to visual, but not to verbal, stimuli. Finally we investigate subordinate level visual knowledge and show that it is preserved.

These data are interpreted in the context of the neural network multimodal model

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[1] Lauro-Grotto, Piccini and Shallice: "Modality-specific operations in Semantic dementia" in press on Cortex.

of semantic memory (Lauro-Grotto, Reich and Virasoro, 1997) described in the previous chapter: in this model the semantic system is thought as a multimodal network in which different areas are accessed by each modality, and store modality-specific information. In non-pathological conditions the various components of the net are connected to each other so that it is always possible to retrieve the entire representation from any input channel, via previous activation of the corresponding modality-specific one. In pathological conditions one or more components of the net can be preferentially damaged or become inaccessible, which gives rise to neuropsychological dissociations. In the model the Verbal Semantic component is thought to mediate on-line verbal comprehension and to support access to lexical output channels. Our findings suggest that this Verbal Semantic component is profoundly degraded in the present patient. It is interesting to note that not all kinds of semantic tasks can be performed in the absence of the Verbal component even when the material is not presented in the verbal modality. This reflects the distribution of information in the semantic network and possibly the presence of different coding processes. The present experimental investigation allows us to provide a preliminary sketch of the content of another Non-Verbal component, the so called Visual Semantic sub-system.

As a final point, we compare our account of the Visuo-Verbal dissociation with another account, the so called "Identification Semantics" hypothesis proposed by Chertkow, Bub and Caplan (1992). These authors also based their model on findings from patients with progressive dementia, who showed qualitatively similar modality-specificity effects, in having performance on verbal material worse than on visual. They argued that this pattern of performance can be explained by assuming that the information that allows perceptual identification of visually presented items is segregated in a separate modality-specific component of an otherwise amodal semantic system. This information is held to be sufficient to support naming, but not to allow for any other semantic operation, such as the ones that require the linking of a concept to other concepts in an associative semantic net. they hold that better performance in the visual modality is best explained by damage to the amodal associative semantic store, which is directly accessed from verbal input, together with selective preservation of the modality-specific "Identification Semantics". This might also appear to be a plausible account for the pattern of performance of our patient, who is severely impaired in the verbal modality. However we argue that the richness and complexity of behaviors elicited in our patient by visual stimuli is not compatible with this type of development of Identification Semantics hypothesis, and fits better in the context of models that assume a different fractionation in the semantic system.

3.2 Case Report.

R.M., a right-handed woman, born in 1931, left school at the age of 12. Until 1991, when she retired, she had worked in her husband's texile manufacturing business. Around that time, she started complaining of difficulties in remembering the names of common objects, phone numbers and well known people's names. Family members also noted the occurrence of mood changes and increasing irritability, egocentricity and a slightly decreased involvement in her family's daily problems. In 1992 neither a cranial CT scan nor an EEG revealed any abnormality, but an MRI scan indicated atrophy in the temporal lobes and frontoparietal cortices, with minimum enlargement of the ventricular system and Virchow-Robin spaces. R.M. was referred to the Neurology Department in Careggi(Florence) for further assessments in February 1994. Her objective neurological examination was normal. A second

MRI scan (Feb.1994) showed some mild generalized atrophy, with a few scattered areas of high signal in the cerebral white matter, which could just be age related changes. The striking finding was inferolateral atrophy of the left temporal lobe, most marked anteriorly but with some early focal atrophy posteriorly (See Figure 3.1). The left temporal pole was also distinctly atrophic compared to the right. The atrophy seemed to spare the superior temporal gyrus except for the most anterior part.

The asymmetric nature of the atrophy was later confirmed by a PET scan, performed at S.Raffaele Hospital (Milano) in December 1994, where a hypometabolism of the left polar and mesoinferior temporal lobe was detected, as well as a slight metabolic asymmetry of the inferolateral frontal regions, the basal ganglia and the thalamus, again with left hemisphere structures being more compromised. The appearance of the atrophy is compatible with left temporal lobe Pick's disease; its localization and time course is typical of the semantic dementia syndrome, having as cognitive counterpart the break-down of semantic knowledge.

In February 1994 the patient was alert, lucid and cooperative; she was able to deal appropriately with people, and continued to take care of herself, her house and family. She could drive and go shopping alone. Insight was well maintained. She complained of increasing word finding difficulties, which started to affect her daily communication with other members of her family. At a preliminary assessment, spontaneous speech was fluent, but with frequent word finding problems. No phonemic paraphasias were noted.

As an initial neuropsychological examination the patient was tested on a battery originally devoted to assessing mental deterioration in probable DAT patients (Bracco et al., 1990). This battery utilizes 16 subtests, many existing as independent tests; it explores orientation in time and space, concentration capacity, verbal and spatial memory, simple arith-

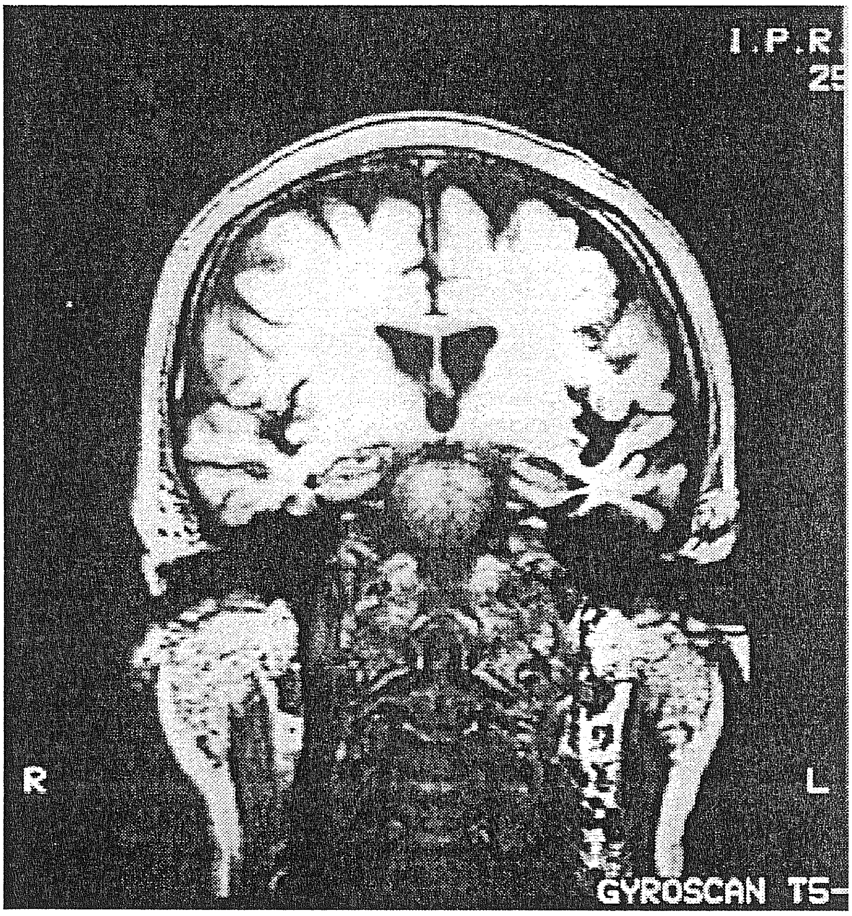

Figure 3.1: Nuclear Magnetic Resonance scan of patient R.M. carried out in February 1995. The Section shown is -20mm from the planum temporale. The inferolateral left temporal lobe is distinctly atrophic compared to the right. Right and Left are reversed in the picture.

methycal skills, language (verbal comprehension, fluency, writing and reading capacities), and visuomotor functions. Scores, as well as normal performance ranges for comparison, are reported in Table 3.1.

The patient was well oriented in time and space; she retained knowledge about her personal history, but performed poorly on questions tapping knowledge of well-known people and events. She was impaired on tests requiring verbal comprehension and long term verbal memory. In reading she showed a surface dyslexic pattern of performance, with stress errors. Writing was preserved. She also performed poorly in the category fluency task. By contrast, her performance on non-verbal tests was preserved: she had normal spatial memory for her age, and good visuo-spatial abilities. She was also able to perform simple additions and subtractions, although she used counting strategies. No sign of buccofaccial apraxia was recorded. The patient was able to imitate meaningful gestures (such as to hitchhike, to salute, "O.K." and "crazy") but could not produce them to verbal command. Further details on miming abilities are given in Section 4.4.

This preliminary investigation revealed a dissociation between tests requiring verbal comprehension or other verbal semantic memory functions, where performance was severely compromised, and other tests relying on visuo-spatial abilities, in which performance was entirely preserved. The dramatic impairment in naming and word comprehension, together with the reduced category fluency and the surface dyslexic error pattern in reading, suggested that the impairment should be located at the level of the semantic memory system. As she did not have a primary clinical amnesia, her low performance on verbal memory tests can also be attributed to semantic memory problems (Warrington, 1975).

Some time later (February-March 1995), a more detailed evaluation of R.M.'s language skills was carried out. In a two choice spoken sentence-picture matching task designed to assess syntactic competence (Bisiach, Cappa and Vallar, 1983) the patient scored 11/12 correct (Feb.1995), demonstrating normal syntactic comprehension. The patient was then given the Italian version of the AAT (Aachener Aphasie Test) (Luzzatti, Willmes, De Bleser, 1991). The equivalent T scores for the different subsections are shown in Table 3.2. At this time the impairment profile was classified as that of Wernicke's Aphasia. The reading performance again showed occasional surface dyslexic errors. The mild level of deficit on repetition and on the Token Test could be attributable to a primary auditory-verbal short memory problem, with no evidence of phonologic processing deficits. She did however show phonemic paraphasias very occasionally in spontaneous speech. Most critically comprehension and naming were the most seriously impaired functions; statistical comparison between subsections showed significantly poorer performance in naming and comprehension than in the other subsections (Psychometric Single Case Analysis $p < 0.01$).

At this stage of her progressive disease, a deficit of semantic functions appeared to be at the core of the patient's pattern of impairment. In addition she had some problems with auditory-verbal short term memory and made very occasional phonemic paraphasias. However even as late as February 1996, the patient scored 29.5 on the Raven Matrices (A,B,C,D), which is more than one standard deviation above the mean for aged matched controls (27.0 ± 2).

Overall R.M. presents with a specific semantic memory problem with other cognitive functions much less impaired. The experimental investigations which follow are concerned with a detailed analysis of her semantic memory problem. As it will be evident by looking at the experimental results, the time course of R.M's pathology as regard the semantic memory deficit is rather slow; the progression involved addition of new systems rather than the semantic memory impairment itself becoming rapidly more severe. When the same test has been repeated within a month performance was always found to be at the same level (See Tables 3.5, 3.6, and 3.8). When the same task, or a very similar one, has been repeated several months (See Table 3.8) and even one year apart (Compare Table 3.4 and Table 3.6) the level of performance was also found to be stable. However as the patient had a degenerating condition we distinguished four different periods in the time course of the investigation: I) February-May 1994; II) November 1994; III) February-June 1995, IV) October 1995-February 1996.

3.3 An initial assessment of semantic memory functions (Period I, May 1994).

Experiment 1. Part I.

Methods and Materials.

Experiment 1 used a test battery which is basically an Italian version of the one introduced by Hodges to assess semantic dementia (Hodges et al., 1992a). Six semantic categories (12 household items, 6 vehicles, 6 musical instruments, 12 land animals, 6 birds, and 6 sea-water animals) are tested in five different tasks: fluency, naming, word-picture matching, multiple level sorting, and definition of spoken names. The stimuli are taken from the Snodgrass and Vanderwart (Snodgrass and Vanderwart, 1980) set of line drawings.

Results.

R.M.'s results on the different subtests are summarized in Table 3.3. On fluency, R.M. was unable to produce a single word in any of the categories. The patient was not able to define any of the spoken words, although she was able to repeat them without difficulty. Only 6 items were correctly named; R.M. also produced 5 circumlocutions specifying the function, a possible phonemic paraphasia ("becchia" for "bicicletta" (bicycle)) and 2 perseverative errors. Phonemic cueing did not improve performance. In the word-picture matching task there were five distractors belonging to the target category for each target item. The patient was asked to repeat the spoken word before the selection of the target picture. Repetition was correct on all the items. Performance was perfect on the household objects and vehicles categories, while being at chance on the others. The dissociation between living and non-living items reached statistical significance in a logistic regression taking into account visual agreement, name agreement, imageability, lexical frequency and familiarity ($p < 0.05$).

The multiple level picture sorting included three sections. In the living vs non-living section the percentage of correct answers was 93%. What we will call the ordinate level section (e.g.: land animal vs water animals vs birds and household items vs vehicles vs musical instruments) was performed separately on living and non-living categories. Performance was 100% correct on living and 92% correct on non-living items. In the subordinate section[2].

R.M. was 67% correct on non-living and 84% correct on living items. While the results reproduce the well known trend for greater impairment of subordinate level knowledge (Warrington, 1975), it should be noted that the different subtasks are not equally balanced

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Including 'electric vs non-electric' (10/12 correct), 'smaller or bigger than a T.V. monitor' (5/12 correct), 'found in the kitchen or not found in the kitchen' (9/12 correct) for household items, and 'smaller vs bigger than the well known dog Rocky', R.M.'s neighbours' German Shepherd', (11/12 correct), and 'fierce vs domestic' (9/12 correct) for land animals.

for the possibility of the patient using presemantic information.

Experiment 1. Part II.

Methods and Materials.

A verbal version of the sorting task, employing the same items, categories and classification criteria as for picture sorting, was given to the patient in the same period (May 1994). The patient first had to read the name on a card, being corrected if she made a reading error; in this case she was asked to repeat the correct pronunciation. Then she had to sort the card. Examples from the groups in which the items had to be sorted were presented in the same format as the stimuli, and included only frequent words; verbal descriptions of the different categories were also provided.

Results.

R.M. performed 58% correct at living vs non-living sorting (at chance: Binomial test $p > 0.05$), 62% correct at the ordinate level (better than chance (33%), Binomial test $p < 0.01$), and 64% correct at subordinate sorting (not different from chance (50%), Binomial test, $p > 0.05$). R.M.'s performance is significantly worse with verbal than visual stimuli, even excluding all stimuli on which reading errors occurred (Sign test $p < 0.01$) (See Table 3.4). With respect to the reading performance, the patient made 8/48 errors, 4 involving the misplacing of stress (e.g.: 'lampáda' instead of 'lámpada'=lamp), which is typical of the surface dyslexic error pattern for Italian (Chiacchio et al., 1993).

The initial investigation confirmed the evidence of a semantic memory deficit. Perfect performance on repetition of single words, and the nature of the few reading errors - half involving misplacing of stress, possibly due to lack of semantic support (Patterson and Hodges, 1992; Chiacchio et al., 1993; Miceli, Capasso and Caramazza, 1994) - also suggested that more peripheral phonological and orthographic deficits, if any, were not crucial in defining the pattern of impairment.

R.M.'s performance appeared to be dependent on the type of semantic knowledge required by the task: the experimental results pointed to a dissociation between tasks requiring verbal comprehension, which seemed to be dramatically compromised, and tasks relying mostly on non-verbal semantics, such as picture sorting (McCarthy and Warrington, 1988), which were relatively intact.

3.4 Visual and Verbal Semantics.

In the previous section it was suggested that R.M. might show different degree of impairment for visual and verbal material. The following experiments explored this possibility more formally.

3.4.1 The Pyramids and Palm Tree test (Period II: Nov. 1994): verbal and visual presentations.

Experiment 2.

Methods and Materials.

The patient was given the original version of the Pyramids and Palm Trees test and, two days later, the corresponding verbal version. The same tests were given again ten days later in the opposite order. In both the verbal and visual presentations the cards, with line drawings or words respectively, were arranged in a triangular set, with the stimulus at the upper vertex and the target and the distractor randomized at the bottom. For the verbal administration the same procedure was used as in the verbal sorting experiments.

Results.

The patient scored 31/54 on visual and 35/54 on verbal presentation on the first occasion, and 26/54 with visual and 33/54 with verbal presentation on the subsequent administration. On the first verbal administration the patient produced just one reading error. On the second verbal administration 16/54 words were not properly read: errors included 5 stress misplacing errors, 7 single phoneme substitutions and 4 additions of an 's' at the beginning of the word [3].

As the Pyramids and Palm Tree Test involves somewhat uncommon items, some fairly abstract references, and was derived for use with English patients, we developed a version using a similar structure, in which the inferences were of particular predefined types.

3.4.2 The Semantic Judgement Type Test (Period III: Feb. 1995).

Experiment 3.

Methods and Materials.

The material for the test was a collection of household items, foods, clothes, jewels, cosmetics, commonly used personal objects, such as cheques and identity cards, and some familiar items used outside the house, like a windscreen wiper and a tax stamp. During the first session, which was videotaped, a preliminary assessment of the patient's recognition abilities was produced by asking the patient to mime the use or give any other kind of

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In these last cases, which occurred in sequence, ('criceto', 'trapano', 'chiodo' and 'ghianda') the patient was not able to produce the right pronunciation even after the experimenter's correction. These errors could be related to a phonological phenomenon, which is peculiar to syllabification in Italian. Current theory holds that CCCVX syllables do not exist in the basic structure of Italian syllables (Nespor, 1994). However, words starting with S+CCV do exist (e.g.:'stretto'), and for them it has been proposed that the initial 'S' is added by a special mechanism as a C syllable.

indication she could about the object. Some objects were excluded at this stage because they were unfamiliar. For each of the 60 remaining objects a 3 alternative forced choice set was formed.

The proposed 60 forced choice sets were classified by 3 independent judges. They had to decide, for each set, which of six possible kinds of semantic judgements was relevant for providing the correct response. On 51 occasions all the judges agreed. On 9 occasions one judge gave a divergent assessment. In these cases the majority assessment was used. The decisions of the judges led to the following semantic classes being adopted for the forced choice experiment:

- 14 judgements were classed as simple common category judgements (e.g.:earrings: bracelet vs belt vs lipstick);
- 7 were classed as involving the matching of items which are typically seen together but not related by common use or function (e.g: windscreen wiper: car tax sticker vs scarf vs detergent);
- 12 were classed as requiring pure semantic inferences (e.g.: cork: raisin vs pepper vs scissors);

The broad class of functional relationship was further fractionated into:

- 10 cases in which the stimulus and target were judged to share the same function, and with it being achieved by a similar kind on action (e.g.: brush: comb vs sponge vs glove)

- 7 cases in which the same function was judged to be achieved by a very different action (e.g.:button: zip fastener vs belt vs glove).
- 10 cases in which the stimulus and target were judged to be used jointly in the achieving of the same function or goal (spring clip: hair curler vs shampoo vs bottle opener).

Exemplars from the different classes were presented in random order, but with the same order being followed in the visual and verbal sections, which were administered on successive days. Both the visual and verbal presentations were repeated 3 weeks after the first assessment, in reverse order with respect to the first administration. In the object presentations, the stimulus was placed on a colored sheet of paper to enhance its role; the target and two distractors were placed on the table in front of it, in randomized positions. For the verbal administration, the procedure used in the Pyramids and Palm Tree test was applied.

Results.

The overall performance on verbal material was at chance (33%) in both sessions while with real objects the percentage of correct answers was 65% on the first and 73% on second evaluation, significantly better than chance on both occasions (See Table 3.5). Considering the different kinds of semantic judgement, the performance with verbal input was at chance on all subsections. The performance with visual and verbal material was compared for each of the different subsections (See Table 3.5). Two consistent patterns could be distinguished. For three classes of semantic judgements, performance was at chance on visual as well as verbal presentation, and there was no statistical difference between visual and verbal material; these classes were semantic inferences, detection of common category and detection of common abstract function[4] . For three other classes of semantic judgements however, performance was significantly above chance with visual presentation on both testing sessions but not on either for verbal presentation. Moreover with these classes of semantic judgements R.M.'s overall performance was significantly better with visual than with verbal material. These latter classes are detection of common concrete function, joint use of a function and spatial co-occurrence.

Discussion.

The dissociation in performance between visual and verbal presentation obtained using the Hodges' Battery, was confirmed in the present experiment. R.M.'s performance on verbal material was at chance for all subsections of the Semantic Judgement Type Test. On the visual version, however, performance was significantly above chance and significantly better than on the verbal version in the sections concerning spatial co-occurrence, similar function and action, and joint use in a function. On the other sections, the performance on the visual version was not better then chance. These were the sections where the question could not be answered on the basis of common location or similarity of action. Could one assume that this dissociation can be accounted for by assuming that presemantic information is supporting performance? For example could one argue that retrieval of a visual scene would indeed be sufficient to perform the task; but this hypothesis would not explain the overall pattern because in the classes of judgements where performance is at chance there are also many items that can be found together on some occasions; this is particularly true for items belonging to the same category, like fruits (e.g. apple and banana *vs* onion *vs* cork), clothes (e.g. gloves and pullover *vs* belt *vs* hammer) etc., but also for items that

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On one of the two testing sessions performance with verbal presentations was just significantly above chance on this judgement.

share the same 'abstract' function (e.g. zip fastener and button *vs* skirt *vs* plate). Also the distractors in the critical test where performance was preserved were often chosen expressly as items belonging to the same loose context of the target (e.g. hair pin and roller *vs* shampoo *vs* bottle opener. What therefore we would claim is that information about the typical context in which an item is found should be considered as part of the semantic representation (see Shallice,1993). If this was not the case one would be obliged to assume that the context is also represented at the level of structural descriptions, which does not fit with the experimental evidences found in agnosic patients (Humphreys and Riddoch, 1987).

It should be noted that R.M. spontaneously provided some support for her choice on almost one third of the errors on visual presentation, often based on her personal experience. For example, while incorrectly matching earrings with a lipstick instead of a bracelet, she showed how she would have put on earrings and some make up before going out. In these cases, although the retrieval of a personal experience is incorrect with respect to the kind of judgement formally required in the test, it does reveal access to the semantic system, because the retrieved experience clearly relates to the meaning of the stimulus, and the selected pairing is linked by proximity.

3.4.3 Visual and verbal categorization (Period III: June 1995).

Experiment 4.

Methods and Materials.

In view of the difficulty the patient had in the common category part of the Semantic Judgement Type Test, R.M. was given a simplified version of the sorting task from in Hodges' Battery. The same items were used. For each item, the picture or the written name was presented on a card, and a simple question was asked. For written material, the same procedure was used as for the original Pyramids and Palm Tree test. For the living vs non-living classification the patient was asked if the item was an animal or not. Then for what we will call the "ordinate level" classification she was asked if the item was found in a house or outside in the case of man-made objects, and if it was found in water or not for animals. This last classification could not be carried out on the base of the structural description of the items. The categories of 'musical instruments' and 'birds' were not included in this last session of the test. The test was repeated twice in an ABBA design.

Results.

The results are summarized in Table 3.6. The dissociation in performance between visual and verbal input was significant at both the superordinate (Sign test: $p < 0.01$) and ordinate levels (Sign test: $p < 0.05$) on both testing sessions. The results of the two ordinate level classifications with verbal material and of the corresponding ordinate level sorting task of Hodges' Battery (on the same items) were analyzed using a statistical procedure which extends the stochastic approach of Faglioni and Botti (1993) to the case of multiple choice tasks (Lauro-Grotto, Treves and Shallice *in preparation*). Based on the assumption that consistency of results in repeated trials is a feature of storage deficits while inconsistency is a feature of access impairments, this analysis produces two indices ranging from zero to one, s and r, which correspond to estimates of the probability of correct storage and the probability of correct retrieval (given correct storage) respectively. In the present case the analysis produced s=0.44 and r=0.94 which correspond to a degraded storage type of impairment.

3.4.4 Further experimental investigations about visual semantics (Period III: May-June 1995).

The findings obtained with the semantic Judgement Type Test suggested that it was indeed still possible to explore R.M.'s residual semantic competence in dealing with visual stimuli. During a preliminary videotaped examination in Feb. 1995, the patient was recorded in the usual test room, while performing a series of daily activities elicited by visual stimulation. The patient was presented with some objects which were intended to elicit specific behaviors: a white coat with one button missing, an empty coffee machine, some spaghetti, a watch set to the wrong hour. The material necessary to carry out each of the related task was placed on a nearby table, mixed with many distracting items in order to see if the patient was able to distinguish what was needed. R.M. immediately and appropriately reacted to the stimulus. She was also extremely rapid and self confident. However it was evident that simple verbal request was almost completely ineffective in eliciting any kind of answer. For example when asked to show how to cook 'spaghetti', she simply stared at the experimenters, but when she was presented with the actual spaghetti she rapidly collected what was needed and gestured an extremely faithful and detailed account of the cooking procedure. She spoke at the same time, but virtually without using any relevant content words other than superordinates. The same kind of reaction was recorded on all the verbal requests. On the contrary a high standard of performance was attained in all the tasks with visual presentation.

In these videotaped sessions, it was possible to unmask complex levels of organized behaviors (schemata), that were elicitable by visual stimulation. This result, if confirmed, would help to explain one of the phenomenological observations that prompted our analysis, namely that the patient still had quite high standards in daily activities.

Experiment 5 (Period III: May 1995): the cooking procedures test.

Methods and Materials.

The cooking domain was selected as a relevant one to investigate, because cooking procedures have many specific requirements and are of a sufficient level of complexity. The patient was tested in a kitchen and asked to cook 8 different foods, and to mimic in the most detailed way the cooking procedure for 16 other foods. The whole section was videotaped. The patient was placed in front of a table where the materials necessary for cooking the whole set of 24 foods had been arranged randomly; the set included 7 different types of pans and related varieties of cooking dishes, with two exemplars of different dimensions for each type, 6 types of plates, 2 types of glasses, and common ingredients, including salt, pepper, oil, vinegar, sugar, butter, flour, ham, bread crumbs and eggs. On other surfaces of the kitchen 17 types of cooking implements, such as spoons, forks and knives of different dimensions, a wooden spoon, a tin-opener, a gas-lighter, some paper towels, some toothpicks, etc. were randomly arranged. On another table, placed next to the first, a big basket contained all the types of vegetable to be used in the test, plus onions, garlic, celery, parsley and carrots, which could be used as ingredients; another basket contained four types of fruit, oranges, lemons, apples and bananas.

When foods were actually cooked, the patient was shown the food she had to prepare on a chopping-board; she was not asked to name it, nor was the name pronounced by the experimenters during the whole session, but spontaneous naming was allowed. R.M. was asked to say if she could recognize the food and if it was one that she usually prepared at home or not; finally she was asked to cook it. First she had to select the quantity that would be appropriate for a given number of people from 3 to 7 (the size of her family); then she had to select the most suitable pan for that quantity and specific kind of food. She was instructed to collect whatever she needed from the two tables, without any feedback from the experimenters. She received no assistance during the cooking procedure. As she was rapid and self confident in carrying out the procedures, she was allowed to cook more than one food at a time.

The mimicking procedure was devised because the patient considered it inappropriate to cook more than a given number of different foods, which could not be eaten. The procedure applied was the same, except that, after the selection of the stove, the patient was required to gesture the rest of the cooking procedure: for example, she actually cleaned the artichokes and put them in the pan, but then she just selected the remaining ingredients from the basket and mimicked the action of adding water and putting them on the stove. All ingredients and implements the patient used in a given procedure were returned to their place before the beginning of the next trial.

Results.

In table 3.7 we have summarized the results of the videotaped section on cooking abilities. For every food, the level of performance reached by the patient is given, as assessed by three independent judges, two of whom were present at the experiment, while the third assessed the videotaped material. The judges were in 100% agreement in the categorization. The scores have been selected according to the following criteria:

'Perfect' is attributed to a procedure which is highly specific and appropriate in every single step;

'Good' refers to an appropriate and specific procedure that has been simplified in some passages without compromising the final result;

'Sufficient' refers to a procedure which is appropriate, but not specific to a particular food;

'Scarce' refers to an oversimplified procedure or to one where some crucial intermediate section was missed out;

finally 'Null' is attributed to a case where no response is elicited at all.

An example of a Good/Perfect procedure is one in which the patient correctly achieves each of the following steps:

a)general selection of the method of preparing the food (e.g.: the chicken breast must be cooked, it cannot be eaten raw);

b)selection of the appropriate stove for the given food;

c)selection of the appropriate type and dimension of the pan for a given quality and quantity of food;

d)selection of the ingredients needed for a given procedure (e.g. for the chicken breast: flour, ham, oil, salt);

e)organization of the subprocedures needed (e.g.:removing the central bones from the chicken breast; cleaning the ham slices; cutting the slices in the appropriate dimension to be stuffed in the chicken breast slices... and at least 7 other subprocedures of comparable complexity to complete the task.);

f)selection of the implements needed in each subprocedure (the big knife to cut the chicken breast, the toothpicks to close the slices together, the paper towel to coat the slices with flour);

g)timing and sequencing of the behaviors.

Over 24 foods presented, for 13 performance was rated as perfect; for 4 it was good;

for 2 it was sufficient; for 3 it was scarce and on 2 more it was judged as null (See Table 3.6). So in 71% of the cases performance was rated as at least 'good'.

The patient was usually self confident and rapid in carrying out the task. Ignoring the 'Sufficient' category, where the issue of the specificity of the response cannot be assessed, the patient gives evidence of specific knowledge of the procedures appropriate to a certain food: for example, in cleaning the artichokes the patient removed the external leaves, cut the top of the remaining leaves and the backs of the artichokes; then while she threw away the leaves that had been cut, she cleaned the backs by peeling away the hard external part and added them to the cleaned artichokes. This procedure is item-specific and cannot be inferred from general properties, like just 'being a vegetable', nor by affordances on perceptual features (why should the patient remove just a few of the leaves, which look exactly the same as the ones she is not going to remove?).

The behavior of the patient in the trials marked 'null' (aubergine and 'gnocchi') suggests that she is not sensitive to perceptual features which could prompt particular responses: thus she was not able to produce any response to the aubergines, which have a smooth violet part and a tough green more leaf-like part, that could be removed just on the base of an analogous perceptually based distinction. Nor did she respond to the 'gnocchi', which on color and texture share many perceptual attributes with 'tortellini', a food she cooked very well. Furthermore, if the patient was basing her selection of the correct procedure on the recognition of an item as a member of a given category (a vegetable, a kind of meat, a kind of pasta etc.), one would have expected to find a much greater proportion of the trials in the 'sufficient' class, where procedures not specific for a given item are applied. In this respect our results contrast with the 'identification semantics' position.

Discussion.

In this experiment R.M. showed not just recognition of the foods, but also good ability to select, among a large variety of closely related semantic distractors, the implements and the cooking dishes appropriate to a given procedure, and perfect recognition of the ingredients needed. The ability to use implements appropriately and to recognize ingredients has been considered as part of the correct execution of a given cooking procedure, and in consequence has not been independently scored. In the case of the foods actually cooked by the patient (8), the mean number of implements used is 6.5, while the mean number of ingredients is 5, which gives a quantitative idea of the richness of the procedures applied, as well as of the ease of the patient with respect to the use of the implements and to the knowledge of the peculiarities of the ingredients.

The patient did not appear to be confused or disturbed by the novelty of the material and surroundings: for example, she inferred correctly how to use the automatic gas-lighter of the oven, and she suggested keeping some kind of foods, such as fish and meat, in the refrigerator. During the whole videotaped section, R.M. spontaneously named only oil, salt, water, broth, rice, chicken and tomato sauce. On one occasion, she added that, while shopping, she could not remember names, but she had no problems in pointing to the items she intended to buy.

Experiment 6 (Period III: June 1995): the verbal 'counterpart'.

On initial pilot observations R.M. was unable to carry out the sequence of actions required in miming given the word instead of the object. However to gesture a complex sequence of actions from verbal command in the absence of the object is an intrinsically more difficult task than carrying it out with objects. We therefore decided to use the simplest control for the ability to identify this type of objects from verbal presentation, namely multiple choice word-object matching test. This experiment was performed two weeks after the cooking experiment.

Methods and Materials.

The experiment employed the same items as in the cooking procedure test. We selected a list of 56 items which consisted of all the foods tested in the cooking procedure (24), plus the essential ingredients (14), and the implements (18) that were necessary in the preparation of the different foods; they also included ingredients and implements that were necessary to cook those foods on which the patient's performance had been poor on the 'cooking procedures' test. In the word-real object matching test, each name had to be matched to the target inserted in a group of 5 distractors, chosen as the items most closely related semantically to the target among the whole set. For example, for a vegetable, other members of the same category were used as distractors. The patient listened to the spoken name, was asked to repeat it, and finally she had to select the matching object, within a time limit of 30 seconds after she repeated the name (this is quite long for a multiple choice test, but the task was made as easy as possible in order to provide more relevant data). R.M. then moved to another group of items, listened to another name and so on. The presentation order was random within each group, but cyclical across groups.

The whole test was administered twice to the patient.

Results.

The patient's percentage of correct answers was 53% (30/56) on the first trial and 62% (35/56) on the second (chance level 17%). Performance was consistent across trials (Contingency coefficient=0.47). On foods and ingredients performance reached 52% (20/36) and 72% (27/36) on the first and second testing sessions, while on implements the percentage of correct performance were 50% (9/18) and 44% (8/18) respectively. Neither frequency nor word-length was found to be predictive of performance in a linear regression analysis ($p > 0.05$). These levels of performance (30/56 and 35/56) are significantly worse than those occurring during the cooking procedures test: 86% of the same items (48/56) had been correctly employed by the patient during the videotaped section (Sign Test, $p < 0.01$ for the first session and $p < 0.05$ for the second). The value 48/56 is obtained by considering those items included in Experiment 1 on which R.M. reached a score of at least 'good', plus the ingredients and the implements which were used correctly and specifically in the cooking procedures (data derived from the videotape). So performance on this very simple task requiring verbal input (in fact the simplest we could think of!) was significantly worse than performance during the complex cooking procedures test. There was no correlation between the levels of performance reached in the cooking procedure test and the results on the same items in the word-object matching test (Wilcoxon Rank test ($p > 0.05$)). As only two weeks had elapsed between the cooking test and the word-object matching, and given the slow progression of R.M.'s pathology (See Case Report), it is highly unlikely that the difference can be attributed to worsening of the cognitive impairment.

In the subsequent experiment we investigated R.M.'s competence in dealing with visual stimuli in a domain different from the cooking one. We document the existence of another qualitatively different domain of preserved visual semantic knowledge. At the same time we show the richness of the semantic representation available from visual input; in particular we focus on the presence of subordinate level information.

Experiment 7: the "materials" multiple choice test (Period III: Mar.-Apr.1995;

Replicated in Period IV: December 1995).

Methods and Materials.

As the patient had been working in a texile manufacturing business it was assumed that she had a specific competence for clothes and fabrics. In the 'materials' multiple choice test, the patient was shown an article of clothes and asked to select among four given pieces of material the most suitable to create another exemplar of the same article; for example, when given a woman's silk blouse, R.M. had to select a piece of 'vyella' as another possible material with which to make a woman's blouse, instead of tweed or lycra. 22 different stimuli, ranging from clothes to lingery to house linen and 29 different materials were used in this test. Perceptual similarities between the stimulus and the target or distractors were always avoided: they never shared color, texture or the kind of design. So in order to perform the task, the patient must access subordinate level visual semantic knowledge about the stimuli and must perform fine grained visual semantic discriminations between the target and distractors.

The appropriateness of the 'ideal match' was confirmed by 2 judges, who were instructed to confer to reach an agreed assessment in case of initial disagreement. In fact they always agreed. On the first administration (Mar.1995), the patient was allowed to manipulate the materials; on the second (Apr.1995), she was forbidden to do so.

Results.

R.M. scored 19/22 correct (86%) on the first administration and 16/22 correct (73%) on the second, both significantly different from chance (25%) (Binomial test: $p < 0.01$). The results were consistent on 19/22 trials (86%); only 3 trials were successful on the first but not on the second administration, the two not being significantly different(Sign test,

$p > 0.05$).

Replication and Extension of Experiment 7 (Period IV: October 1995-February 1996).

In order to estimate performance with verbal input for the experimental material used in Experiment 7, a three choice Word-Object Matching Test on the names of the materials used was carried out in December 1995. In this task the patient was given the name of the material auditorily, and asked to repeat it; if necessary, she was corrected until perfect repetition was reached (correction was in fact only necessary once, with the word "taffeta"). Then she was instructed to point to the corresponding material. R.M. scored 6/21 (29%) in this task, not statistically different from chance (Binomial test: $p > 0.05$).

Given the progressive nature of R.M.'s dementing illness, the visual version of the 'materials' test was repeated again after the word-object matching test, this time presenting the patient with 16 colored pictures of the stimuli, while the targets and distractors were the same as in the previous sessions. The storage index and the retrieval index were evaluated by applying the statistical procedure described in Chapter 1 to the data from the three repetitions of the material test with visual input: this analysis produced $s = 0.78$ and $r = 0.94$.

Discussion.

The 'materials' test documents the existence of another domain of preserved semantic competence accessible from visual input. In this experiment, the patient was required to give a judgement on the basis of a specific ability. As the experiment was expressly devised to exclude the possibility of non-semantic cueing, such as by the use of visual similarities, the results demonstrate a fine grained preservation of knowledge about materials and access to subordinate level information on clothes as well. It is important to note that in the 'materials' test the "output" requirements were reduced to pointing to the target, so any privileged link between shape and function (Caramazza et al., 1990) is not relevant. The exclusion of tactile information did not lead to statistically worse performance, so the knowledge necessary for carrying out this task would appear to be entirely accessible from visual input. On the other hand performance on the Word-Object Matching Test, which was chosen as an easy comparison task, was once more at chance level. Although the names of some fabrics are of low frequency for the average member of the population, as the patient had been working all her life in her husband's texile manufactoring business, we can assume that her premorbid familiarity with the names of fabrics must have been particularly high. Data from this experiment also provided an estimate of the storage and retrieval indices given visual input, to be compared with the corresponding estimates obtained from data with verbal material (see General Discussion).

3.5 General Discussion.

We carried out extensive experimental work with patient R.M. in order to specify the nature of her deficit. The main characteristic of her impairment was a marked modality-specific effect, with the level of performance on verbal material almost never exceeding chance, in contrast to a much better level with visual presentation.

There are a number of findings which indicate that her difficulty on semantic tasks arises from an impairment at the semantic level. One problem in drawing such a conclusion is that distinguishing impairments of semantics from those of phonology is not straightforward because of the possible existence of semantic support for basically purely phonological processes (Caramazza and Hillis, 1991; Patterson and Hodges, 1992). However R.M.'s deficits in tasks involving orthography and phonology but not semantics were only mild or moderate even at a late stage in the evolution of the disease (as shown by her performance on the AAT). Thus late in the course of the illness she was able to reproduce words adequately when word-picture matching was grossly impaired (See Experiment 4). By contrast even early in the course of the disease if semantic processing was required, performance on tasks with verbal input was always at the severely impaired level. Moreover this degree of impairment was present when R.M. was provided with <u>both</u> orthographic and phonological inputs, <u>and</u> also when phonological output had to be accessed. Thus any explanation of her performance in terms of non-semantic processes would need to assume severe deficits in <u>three</u> phonological and orthographic systems. Moreover in the tests where performance lay between chance and ceiling with verbal input - the 'ordinate level' sorting and categorization (in Experiments 1 and 4) and the verbal the word-picture matching control experiment for the cooking procedures (in Experiment 6) - phonological dimensions such as word length did not correlate with performance. Phonetic cueing, as formally tested during Experiment 1, was ineffective.

All these findings fit in the assumption that the crucial impairment was at the semantic level, with phonological systems becoming involved only in the later stages of the illness. This hypothesis is also consistent with the anatomopathological findings, the results of MRI in particular: the locus of the atrophy was in the inferior and anterior parts of the left temporal lobe, as is typical for semantic dementia (Hodges et al., 1992a). The perisylvian region, responsible for phonological processes (Cappa, Cavallotti and Vignolo, 1981) appeared to be spared.

Secondly, given that the deficit is at the semantic level, then using the key criterion of consistency for distinguishing between access and storage deficits (Warrington and Shallice, 1979), the pattern of performance is of the degraded storage type. The possibility of distinguishing between these two patterns of impairments experimentally has been criticized (Rapp and Caramazza, 1993), but it has been effectively reaffirmed recently by Warrington and Cipolotti (1996) in at least a subgroup of patients. They provided an exhaustive description of a common pattern of performance in four typical "degraded storage" patients which contrast with one found in two "access" patients (using the term "refractory"). All four of the "degraded storage" patients suffered from a degenerative illness and indeed the diagnosis was the same as that for R.M., namely probable Pick's disease. One problem in this area though, is that effective estimates of storage and retrieval parameters have not been made in such cases from the key consistency evidence, and thus the differentiation of either of the putative 'basic' forms from 'mixed' varieties has not been rigorously made. Faglioni and Botti (1993) derived a technique for estimating both the degree of impairment of the representations in the semantic store and the probability of correct retrieval given that the representation is present, using repeated sessions of confrontation naming on which the same stimuli were presented on each occasion. This analysis produces two indices, s and r, which range from zero to one; the index s gives an estimate of the proportion of preserved items. i.e. where sufficient information remains in the store to support the forced choice judgement (s=1 corresponding to an intact semantic store). The index r is an estimate of the probability of retrieval of such preserved items on any given trials (r=1 corresponding to 100% correct retrieval). We have extended their approach to the case of multiple choice experiments, taking into account the possibility of correct guessing by chance (Lauro-Grotto, Treves and Shallice, *in preparation)*, described in Chapter 1. Values of r and s are most reliably calculated when the performance at the forced choice task is not at ceiling or floor and when the task has been repeated a number of times. In the present case the ordinate level three alternative verbal sorting task of Experiment 1 (one trial) was used together with the ordinate level categorization task of Experiment 4 (two trials). Chapter 1 provides the formulas for any value of chance probability a and for any number N of items presented. Table 3.9 gives the values of r and s obtained for R.M., together with the values of r and s obtained from the results of the word-picture matching performed by the four "degraded storage" patients described by Warrington and Cipolotti (1996) using the findings reported in their Table 3.13. The values obtained for R.M. are very similar to the the ones obtained by the "degraded storage" patients: in particular the s value is even lower, while the r parameter lies above the mean found for these patients. When the same analysis was performed on results obtained in a forced choice task using visual instead of verbal input, namely the materials test of Experiment 7, the retrieval index was found to be similar to the one in Table 3.9 (r=0.94), while the storage index was found to be much higher (s=0.78 vs s=0.44). In the other verbal condition which was not at chance level, R.M. again gave a consistent performance across repeated tests (see Experiments 6). We will therefore assume that R.M.'s impairment is at the semantic level and of the degraded storage type.

R.M.'s knowledge of the meaning of words is disproportionately poorer than her knowledge about the corresponding objects. As we discussed in the Introduction, different accounts of this pattern of performance can be given in the context of the range of divergent views on Semantic Memory that have been presented, such as the Organized Unitary Content Hypothesis of Hillis et al. (1990), the Multimodal Semantics Model (Warrington, 1975;

Shallice, 1988; Lauro-Grotto et al., 1997) and the Identification Semantics hypothesis (Chertkow et al., 1992). We have attempted to characterize further the nature of R.M.'s residual semantic representations experimentally, in order to assess the plausibility of these different accounts.

R.M.'s performance on the Semantic Judgement Type Test provides evidence on the nature of the semantic operations that the semantic system is still able to support. The results show that the impaired system still has the capacity to provide information on functional relationships, such as joint use or common function, and on the co-occurrence of objects. On the other hand, there is no evidence that it is able to support inferences, such as the one needed in linking "cork" to "raisin", which depend on an intermediate concept with which the stimulus and target have different conceptual relations. This dissociation observed in the Semantic Judgement Type Test is somewhat similar to that observed by (Semenza et al., 1992). Using verbal input, they found preservation of "thematic" but not "class" relationships in patients with more posterior left temporal lesions.

The following analysis was prompted by some observations on the variety of real life situations with which the patient dealt successfully. In the Cooking Procedures Test, we have shown that the semantic representations accessed from visual stimulation are sufficient to allow the triggering of higher level complex action procedures. In this task the patient displayed a large variety of organized goal directed behaviors - the cooking procedures, with all their highly specific components - which were elicited by the visual presentation of items to which she failed to respond appropriately in a verbal task as simple as word-picture matching.

The specificity of the procedure used is showed by the ratings of the judges. Only 3 out of 24 foods were cooked using quite general methods that could apply to many different foods. For 71% of the foods presented the procedure was considered to be highly specific. To cook well requires the selection of appropriate implements, pans and dishes, spices and other ingredients, that must be recognized for their very specific functions or characteristics: thus selecting garlic instead of onion as a flavouring for a given food (e.g.: the mushrooms) requires a subtle within-category discrimination. Moreover actions must be selected at the appropriate time to satisfy a subgoal when it is relevant.

Could the level of performance on the cooking procedures test be supported by affordances elicited by the structural descriptions of the objects presented? This could not be the case. The procedures elicited by visual input would need to have operated on at least three levels. First there were the specific procedures needed to carry out any subcomponent of the activity, e.g. the cleaning of the stalk of the artichoke. Here the particular actions carried out depend on the eventual taste of the cooked object, so it would seem implausible to characterize them in terms of a process like an affordance, which is driven only by the shape of an object and the general repertoire of one's actions. The second level of action procedures involves the sequencing of the set of first level activities. This is more appropriately considered a MOP level of control - to use Schank's terminology (Schank, 1982). Such sequencing of activities is not something implicitly inherent within the structure of an object; it cannot therefore be an affordance. Even more clear is the third level where the operations are varied to take into account the specific cooking implements available, the state of the food, the number of people for whom cooking has to be carried out, and so on. Here reasoning is clearly involved. In addition in daily life R.M. used to go shopping alone every day, and as she used to cook quite elaborate dishes, she necessarily had to keep in mind all the ingredients needed for any given recipe. The overall control of this type of behavior would not have been possible without a detailed semantic representation of the cooking procedures, and of the ingredients needed.

Our experimental findings indicate that even in the presence of a profound deficit in the representation of "word meaning", the Semantic System is able to support complex procedures that imply some preserved, and dissociable, knowledge about "object meaning". These results can be easily accommodated in the context of a Multimodal Model of Semantic Memory in which the semantic representations are distributed over different modality-specific subregions (Warrington, 1975; Shallice, 1988). The subregions can be considered as more or less strongly connected to each other as in the neural network model of Semantic Memory proposed in Lauro-Grotto et al.(1997). In non-pathological conditions, the whole semantic representation can be retrieved from a given input, given appropriate task demands, through a preliminary activation of the modality-specific subcomponent. In pathological conditions, however, the degeneration can differentially affect the various subregions of the semantic network, giving rise to neuropsychological dissociations, which in turn provide the opportunity to investigate the content of the different subcomponents. On such a model the present case corresponds to the Verbal subcomponent being damaged by the neurodegenerative process, and so one observes behavior sustained by the semantic network lacking one subcomponent, i.e. Verbal Semantics.

Considering the Multimodal Semantics position in more detail, it would seem inappropriate to assume that action procedures, which are relatively preserved in R.M., are represented in the modality-specific visual subcomponent, i.e. Visual Semantics. They are clearly more appropriately considered that part of semantic memory devoted to the organization of actions and indeed this view is compatible with De Renzi and Lucchelli's position that ideational apraxia represents the loss of semantic memory for actions (DeRenzi and Lucchelli, 1988). R.M.'s pattern of performance would though imply that Action Semantics can be accessed from Visual Semantics independently of Verbal Semantics. Thus the argument presupposes that Non-Verbal Semantics is also not unitary (for related discussions, see Shallice (1988) and Warrington and McCarthy (1988)).

Given the extensive disputes on the content of Visual Semantics (Caramazza et al. (1990); Shallice (1993); Rapp and Caramazza (1993)), can one specify more explicitly what Visual Semantics contains? First, we will assume that Visual Semantics contains distributed representations directly accessed from the 3-D structural descriptions. We will further presume, given our earlier argument that RM lacks verbal semantic representations, that if a capacity is preserved in R.M. and cannot be easily ascribed to another putative part of the semantic system (e.g. the Action Semantic component or the Encyclopedic Store), then it will be tentatively considered to be represented in the Visual Semantic subcomponent.

More specifically, one can use the criterion that if two items are given as stimulus and target in a test like the (visual) Semantic Judgement Type Test, and the target item is selected easily, then this is most plausibly carried out through the use of partially overlapping representations at a given level; for if two representations do have significant overlap, then, on a neural network approach such as that of Lauro-Grotto et al.(1997), it is easy to elicit one from the other because the activation of one involves the activation of a part of the other (and vice-versa).

From our experimental results we can only produce a preliminary analysis; at least for objects, three types of information would be represented in visual semantics:

- visual contextual contiguity (related to the habitual spatial context for an object, e.g.: car tax sticker and windscreen wiper);
- access to functional contextual contiguity (the way objects can be used as parts of the same functional process, e.g.: screwdriver and screw).
- subordinate level perceptual knowledge (e.g.: the type of fur for an animal and the type of tissue for clothings).

Visual contextual contiguity is a part of the Visual Semantic representation of the objects in the sense that objects *that we usually see together* appear to be linked to each other, even in the absence of other semantic relationships among them: that the semantic representation of an object can be elicited from that of another object sharing the same spatial context, implies that their representations should overlap to some extent[5]; so the context is represented at this level.

"Functional-contextual contiguity" refers to the relationships between objects that are used together: "functional"[6] refers to the fact that the visual representations of two objects that are used together for a given goal are typically "arguments" of the same action schema in the Action Semantics system (Cooper, Shallice and Farringdon (1995); Schwartz et al. (1991)). "Contextual" refers to the fact that the majority of the actions - at least the ones we normally attend to - are carried out under visual control. For the reason given above, this will introduce an overlap between their Visual Semantic representations, due to the shared visual context during monitored actions. For the Non-Verbal Semantic System as a whole

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This analysis assumes that unidirectional associations are sustained by post-semantic lexical associations or by an inference-based procedure.

In this context, as has already been pointed out by Laws et al. (1995) the adjective 'functional' has a different meaning from when it refers to the 'functional characteristics of living items (utility for man, etc.).

this is a very tight link, because if we look at the multimodal semantic representations of objects used together, they are also closely connected through the links between the action schema representations they activate in the Action Semantic sub-system. Finally subordinate level perceptual knowledge (e.g. textures of materials) is something that is not represented in the structural description system and that we have found to be preserved in all the categories that we have explored (See Experiments 2, 5 and 7).

It is also interesting to consider more abstract functional relationships, such as those not linked through a specific motor pattern. The present study provides no evidence that such a relationship is represented in the Visual Semantic component; perhaps it is the existence of a verbal semantic representation that provides a link between such concepts (e.g. the *verb* 'to cut' for scissors and knife), that supports the semantic connection between them.

The pattern of performance observed in R.M. can also be related to alternative perspectives on the origin of modality differences in semantic processing such as the Identification Semantics hypothesis (Chertkow et al., 1992) and the Privileged Access position of Hillis et al. (1990). Criticisms of the Privileged Access and Multimodal Semantics position, based on the experimental evidence they reported, were put forward by Chertkow et al. (1992). Their arguments on the Privileged Access position have been discussed recently (Hillis and Rapp, 1995). We will therefore restrict consideration to their critique of the Multimodal Semantics position. The objection to the Multimodal Semantics position that Chertkow et al. (1992) considered crucial, was based on the following experimental result: on testing their dementing patients with Probe Questions they found a large overlap between the questions that were failed with visual and with verbal presentations. While the error rate with verbal presentation was higher than with visual presentation, the overall deficit with verbal presentation seems unlikely to explain the degree of overlap. There was thus little evidence that information relevant to the questions they answered is stored independently in the Visual and Verbal Semantic stores.

What essentially this indicates is that virtually no information was available to the patient from verbal input alone. As is the case for the present patient this implies that in normal subjects the operation of any part of the semantic system putatively distinguished from the Verbal and Visual Semantic systems, such as the Store of Encyclopedic Knowledge (Laws et al., 1995), or our Action Semantics, can be accessed from the Visual as well as from the Verbal Semantic system. Then if the Verbal Semantic system is impaired the information can still be retrieved by access from the Visual Semantics. One also needs to make this assumption to explain the pattern of performance shown by patient T.O.B. described by Warrington and McCarthy (1988). As we have shown in discussing our model earlier, this assumption fits well with the Multimodal Semantic theory.

The "Identification Semantics" hypothesis assumes that access to the semantic system from visual channels occurs through a modality specific sub-system, called Identification Semantics, which stores the "schema mediating categorization and identification of visual instances" (Chertkow et al. (1992), p.359) i.e. sketched perceptual descriptions just sufficient for identification of the items, and for naming. The remaining semantic information is stored in an Amodal Associative System; in particular, the ability to link visually presented stimuli to "*other* concepts in an associative conceptual field" (Chertkow et al. (1992), p.359, italics in the original) is considered specific to this Amodal System. Chertkow et al. (1992) also state that whenever performance on visual input exceeds performance on verbal input, given that one can exclude an access deficit, the pattern of performance is due to preservation of Identification Semantics in the presence of damage to the Amodal Semantic System. In their own words "access (from the whole pictured object) to a partial semantic representation sufficient to support such identification (or access that was consistently retained only for this portion of semantic knowledge), would be associated with the phenomenon of better performance on pictures than on words on semantic tasks" (Chertkow et al. (1992), p.351). This should be the case for R.M., who shows a very profound impairment on verbal material and performed much better on visual material; this means that the present patient on their theory would be a typical case of selective preservation of "Identification Semantics". On Chertkow et al.'s hypothesis R.M. would be expected to have much more restricted semantic abilities than she does. In particular the patient should not be able to exploit knowledge about visual context, nor about detailed functional (in the sense just described in the text) properties to perform semantic tasks, because this amounts to linking a concept to another one, which is not a property of "Identification Semantics". Furthermore her residual modality-specific representations should not have been as rich in subordinate level content as the ones we have experimentally described, since that detail is not necessary for identification. Overall our findings provide no support for the idea of an 'Identification Semantics' tightly constrained in its content so as just to allow identification processes to operate.

In general the Privileged Access model appears to be more compatible with the findings. However one would need to specify it further to take into account the pattern of results obtained in R.M.. This would though require that privileged access goes well beyond the "privileged relationship between information about the *form* and information about the use of an object" (Our italics) (Caramazza et al., 1990; p.178). This may require such a constrained version of the Privileged Access hypothesis as to make it quite similar, in this fundamental respect, to access to a modality-specific component. The degree to which the theories are distinct is unclear without further specification of the Privileged Access theory. However the results fit naturally with a neural network approach assuming the existence of specialized sub-regions in the semantic network, each connected to specific input and output channels.

PERFORMANCE AT BRACCO'S PROTOCOL

SUBTEST	*R.M.(Max.)*	*Normal*	*Deficit*
MiniMental	15(30)	> 24	
Info. – Mem. – Concentr.(Blessed)	22(34)	33.4 ± 2.5	*Mild*
C.A.S. : Orientation	7(12)	8 ± 0.4	*Moderate*
C.A.S. : MentalCapacity	9(12)	10.2 ± 1.2	*Mild*
DigitSpan	4	4.2 ± 1.2	*Absent*
Randt : 5Words – Acquisition	0(15)	11.8 ± 1.9	*VerySevere*
Randt : 5Words – after10min	4(20)	17.6 ± 1.9	*Moderate*
Randt : 5Words – after24h	5(20)	15.4 ± 5.0	*Moderate*
PairedAssociates : Acquisition	3(18)	13.3 ± 2.5	*Moderate*
PairedAssociates : after10min	6(24)	21.2 ± 2.8	*Moderate*
PairedAssociates : after24h	14(24)	20.3 ± 3.1	*Mild*
BabcockStory : Aquisition	3(13)	9.1 ± 4.2	*Mild*
BabcockStory : after10′	0(13)	11.2 ± 5.0	*VerySevere*
CorsiTest	5(9)	4.2 ± 1.2	*Absent*
TokenTest	17(36)	33.1 ± 2.2	*Severe*
SetTest	18(40)	38.5 ± 1.6	*Severe*
3DigitSubtractions∗	8(10)		
CopyingDrawingsTest	16(16)	13.2 ± 1.9	*Absent*
GibsonMaze	10(12)	10.9 ± 0.8	*Absent*

Table 3.1: Performance on Bracco's Protocol for Dementia(Bracco et al., 1990). Comparison is made with a control group of 146 aged-matched controls. The degree of impairment (Deficit) is rated in 5 levels: Absent, Mild, Moderate, Severe, Very Severe. "Info.-Mem.-Concentr."=Information-Memory-Concentration (IMC) Test (Blessed et al., 1968), including Information, explored by means of 12 easy questions about time and space, Personal Memory, explored by means of 7 questions on personal semantics, Non-Personal Memory, explored by questions on well-known people and events, and Concentration, assessed by production of the months of the year forward and of the first 20 numbers backwards. "C.A.S." = Clifton Assessment Schedule (Pattie and Gilleard, 1975); its Subtest on Mental Capacity is composed of 4 parts: writing to dictation, reading, counting and producing the alphabet. "Randt" = Randt Memory Test involving delayed recall of a list of 5 words after a filled interval (Randt et al., 1990). "Babcock Story" = the Babcock Story Test (Babcock and Levy, 1930). "Corsi Test" = the Corsi Block Tapping test(Milner, 1971). The "Token Test" is used in the short version (DeRenzi and Faglioni, 1978). The "Set Test" is a category fluency task, with a time limit of 40", and with 4 categories: colors, towns, animals and fruits (Isaacs and Kennie, 1973). The task marked ∗ is the filler task of the Randt Test and has no standardization. The Copying Drawing Test includes drawings of increasing complexity (Arrigoni and De Renzi, 1964). The Gibson Spiral Maze is taken from the Clifton Assessment Schedule.

PERFORMANCE on the AACHENER APHASIE TEST

disturb – level(T – score)	*writt.lang.*	*repet.*	*token – t.*	*naming*	*compr.*
minimal/absent(63 – 80)					
slight(53 – 62)	56.0				
mild(43 – 52)		49.0	52.0		
profound(20 – 42)				40.7	41.9

Table 3.2: Classification of T scores obtained in the subsections (Token Test, repetition, written language, naming, and comprehension) of the AAT (March 1995) with respect to the level of impairment. T scores are derived from the actual results in the subsections, to allow a direct comparison between them.

SEMANTIC MEMORY BATTERY

	defin.	*cat.fl.*	*nam.*	*w. – p. – M.*	*pict.sort.*
land – animals(12)	0	0	2	3	12
water – animals(6)	0	0	1	1	5
birds(6)	0	0	1	1	5
household – items(12)	0	0	1	12	10
vehicles(6)	0	1	1	6	6
musical – instruments(6)	0	0	0	1	6
total(48)	0	1	6	24	44

Table 3.3: The number of correct responses for a given category of living (land animals, water animals and birds) and non-living (household-items, vehicles and musical instruments) items on the different subtests of the Hodges' semantic memory battery (Experiment 1. Part I. May 1994): definition of spoken names (defin.), category fluency (cat. fl.), naming (nam.), word-picture matching (w.-p.-M.; chance level 17%) and picture sorting (pict. sort.; chance level 33%). Results on picture sorting include only the ordinate level classification (land animals vs water animals vs birds for living items and household-items vs vehicles vs musical instruments for non-living items).

PICTURE and WRITTEN WORDS SORTING

	Pictures	*Words*	*ChanceLevel*
Superord.Class.	93%	53%	50%
OrdinateClass.	92%	62%	33%
SubordinateClass.	50%	64%	50%

Table 3.4: Percentage of correct answers at Picture and Written Word Sorting (Experiment 1. Part II. May 1994). Superordinate classification: living vs non-living; Ordinate classification: land animals vs water animals vs birds and household items vs vehicles vs musical instruments; Subordinate classification: 2 perceptual and 3 associative classes.

SEMANTIC JUDGEMENT TYPE TEST

	$real - obj.: 1st - -2nd$	$verb.: 1st - -2nd$	$vis. - verb.Diff.$
$co - occurrence(7)$	$6^{***} - -5^{*}$	$1 - -2$	< 0.05
$comm. - concr. - func.(10)$	$8^{*} - -10^{***}$	$5 - -1$	< 0.02
$joint - use - to - a - func.(10)$	$8^{***} - -9^{***}$	$2 - -4$	< 0.02
$comm. - category(14)$	$7 - -9$	$5 - -5$	$N.S.$
$comm. - abstr. - func.(7)$	$3 - -5$	$2 - -3$	$N.S.$
$sem. - inference(12)$	$7 - -5$	$3 - -5$	$N.S.$
$total(60)$	$39^{***} - -43^{***}$	$18 - -20$	
*	*	*	*
$overall$	65%−−73%	28%−−33%	
$chance - level$	33%	33%	

Table 3.5: Number of trials where matching was correct on the first and the second real object and verbal administrations of the Semantic Judgement type Test (Experiment 3. February1994). Results are given separately for each kind of semantic judgement in the test; judgements were classified as co-occurrence, common concrete function, joint use for a function, common category, common abstract function and semantic inference. In the first two columns levels of significance of the scores with respect to chance (Binomial test, one tail) are given by: * $p < 0.02$, **$p < 0.01$, and ***$p < 0.005$. In the last column, the statistical significance of the visual-verbal dissociation as measured by the Wilcoxon Rank test (N.S. = Not Significant) is given. In the last two rows, the percentage of overall correct answers is given for direct comparison.

VISUAL and VERBAL CATEGORIZATION

	VISUAL : 1*st* – 2*nd*.	*VERBAL* : 1*st* – 2*nd*	*VIS*. – *VERB.Diff*.
superord. – *class*.	47/48 – –46/48	30/48 – –29/48	< 0.01
ordinate – *class*.	34/36 – –35/36	28/36 – –23/36	< 0.05
chance – *level*	50%	50%	

Table 3.6: The proportion of correct classifications on the categorization task (Experiment 4. May 1995) using visual and verbal materials, on two administrations (1st and 2nd). Superordinate classification (superord.-class.) refers to correct answer to the question "Is it an animal?". Ordinate classification of living items (ord.-class.:living) refers to the question "Does it live in the water?". Ordinate classification (ord.-class.:non-living) of non-living items refers to the question "Is it found at home?".

THE COOKING TEST

Scores	*NumberOfFoods*
Perfect	13
Good	4
Sufficient	2
Scarce	3
Null	2

Table 3.7: Performance on the videotaped section on cooking abilities (Experiment 5. April 1995).

THE MATERIALS TEST

MaterialsTest :	%*Correct*	*ChanceLevel*
Ist – *Adm*. : *Jun*.1995	86	25
2*nd* – *Adm*. : *Jun*.1995	73	25
3*rd* – *Adm*. : *Dec*.1995	81	25
Word – *ObjectMatch*. – *Dec*.1995	29	33

Table 3.8: Performance on the three repetitions of the Materials Test (Experiment 7). Performance on the corresponding Word-Object Matching Test is also shown for comparison.

STORAGE AND RETRIEVAL INDICES

patient :	r	s
R.M.	0.94	0.44
$S1$	0.98	0.49
$S2$	0.89	0.56
$S3$	0.82	0.64
$S4$	0.97	0.44

Table 3.9: Comparison of the retrieval and storage indices for R.M. and for four typical "degraded storage" patients (Warrington and Cipolotti, 1993). The storage index s and the retrieval index r give an estimate of the proportion of representations in the semantic store which are sufficiently well preserved to support the forced-choice discrimination, and of the probability of correct retrieval of such representations from semantic memory. They are evaluated by extending the stochastic approach adopted by Faglioni and Botti (1993) to the case of multiple choice tasks (see Chapter 1). The values reported for R.M. are derived from the ordinate level categorization (Experiment 4) and from ordinate level sorting (Hodges' Battery) of the same verbal material. The values reported for S1, S2, S3 and S4 are estimated from the results obtained in a word-picture matching test by the "degraded storage" patients described in Warrington and Cipolotti (1996), Table 13, p.620.

Chapter 4

4.1 Hemispheric specialization: an historical introduction.

The notion that language impairments tend to co-occur with right hemiparesis more than with left was probably already known to ancient Egyptians and Greeks, but it is since the work of Dax first (1836), and of Broca around 25 years later, that the evidence of hemispheric specialization has entered the domain of modern scientific enquiry (Walsh, 1982). After the seminal work of Broca and Wernicke on language production and comprehension, Lissauer, in distinguishing between 'apperceptive' and 'associative' agnosia, assumed that the nature of the agnosic syndrome is related to the location of damage in the left or right hemisphere (Lissauer, 1890). On the base of his clinical observations of a single patient Jackson argued that the right hemisphere would be critical in "visuospatial" abilities (Jackson, 1876). Liepmann and Mass produced clinical evidence that severe dyspraxic symptoms could also be related to left hemisphere damage (Liepman, 1920). In the first half of the XX century the notion of *hemispheric dominance* was defined. According to this view the left and right hemispheres in man are considered to be identical from the anatomical, but not from the functional point of view: the left hemisphere in right-handed subjects is considered to be responsible for higher level cognition and praxis, while the right hemisphere is only capable of lower level perceptual activity; the dominance was held to be reversed in left-handed subjects.

The theory of hemispheric dominance has been reviewed in all respects during the last three decades. The regions of the brain responsible for language processes were the first to attract the attention of the neuro-anatomists, and Geschwind produced evidence on the asymmetry of the planum temporale, later confirmed by Galburda (Geschwind and Levitski, 1968). (Falzi et al., 1982) found on a cytoarchitectonic basis that Broca's area is more extended than the corresponding area in the right hemisphere. Other gross asymmetries are found in different areas: the left hemicortex is in general slightly thinner than the right one, and the left occipital pole and right prefrontal pole are slightly bigger than the homolateral regions. At the subcortical level an asymmetry of the crossing of the pyramidal motor fibers at the level of the medulla oblongata has been related to the pattern of manual dominance (Witelson, 1980).

However it is at the level of the functional asymmetries that more experimental work, and more speculations, have been produced. I will now briefly mention some speculations that have been produced in the past in an attempt to define what was thought to be a possible functional characterization of each hemisphere as a whole. Many of these speculations have been influential at their time, although they are clearly not tenable in the light of the current evidence about the heterogeneity and the modularity (Fodor, 1983; Shallice, 1988) of cortical functions.

According to Milner the left hemisphere can be considered as devoted to *'verbal processing'*, e.g. to any mental process requiring linguistic mediation to any extent, while the right hemisphere is maily devoted to *'visuo-spatial processing'*. Visuo-spatial processes are more difficult to be defined, but they can be seen as perceptual and mnestic processes that can be performed without any linguistic mediation (Milner, 1966; Milner, 1971). This view was also supported by Berlucchi and Moscovich who both stressed the irrelevance of the nature of the stimuli, either verbal or non-verbal, with respect to the nature of the task (Berlucchi et al., 1973; Moscovitch, 1979). A somewhat different interpretation was given by (Kosslyn, 1980), who put forward the hypothesis that left hemisphere is specialized in the production of a *propositional-linguistic* code, and the right hemisphere is specialized in the production of an *analog-spatial* code. The important point to be stressed is that in opposition to the hemispheric dominance theory, all these models have enlighted the influence of task requirements on the pattern of dominance.

(Semmes, 1968) tried to ascribe the functional differences in higher level cognition to differences in the structural organization of the simpler motor and perceptual functions in the two hemispheres: she assumes that the representation involved in the simple cognitive functions are well localized in circumscribed areas in the left but not in the right hemisphere. This distinction is usually referred as the *focal-diffuse distinction*; although in general the distinction is no more accepted, I'll show that it is still a rather influential conception in the domain of theories of semantic memory.

Different models have been proposed on the basis of the distinction between analytic (left hemisphere) and global (right hemisphere) processing. In the original view analytic processes are based on separate analysis of the component of the stimulus, while global processing is based on the structural characteristics of the stimulus as a whole, such as its symmetry, colinearity, etc. (Corcoran, 1971). For example (Cohen, 1973) specified the analytic-global distinction in terms of serial versus parallel processing; this specification had the advantage of being testable in experimental paradigms of visual search, which however demonstrated that both hemispheres are able to process information both in series and in parallel (White and White, 1975; Polich, 1980; Umiltá et al., 1979).

(Kimura, 1977) considered the left hemisphere specialization for language as a consequence of a phylogenetically older lateralization of fine praxic abilities: the left hemisphere would have specialized itself in the fine-tuned *sequential activation* of given motor districts of the hands first and of the mouth for phonation only later. This hypothesis has now been reconsidered by (Jeannerod et al., 1995; Rizzolatti et al., 1996) in the context of a neurophysiologically driven model of the development of linguistic skills in man from motoric skills in anthropoid monkeys. In Kimura's model the specialization of the right hemisphere is also primarily determined on motoric bases: it would concern the *simultaneous activation* of the districts responsible for posture and in general proximal limbs movements, and possibly also the ones responsible for facial expressions. The sequential-synchronous dicotomy has been extended to the perceptual domain: the left hemisphere would be preferentially involved in analysis of stimuli requiring fine temporal discriminations, such as linguistic ones, while the right hemisphere would be devoted to the simultaneous analysis of co-occurring stimuli.

In principle a different approach is taken by Sergeant: she proposed that the two hemispheres would be involved in the analysis of *different spatial frequencies*, high spatial frequencies being preferentially analized by the left and low spatial frequencies by the right hemisphere (Sergent, 1983; Sergent, 1985). Although this is the only model posing a kind of stimulus-specificity, in practice it is difficult to experimentally distinguish this proposal from the general global-analytic view.

Finally the hemispheric dominance theory has clearly proven to be wrong in its predictions about the functional differences between the right-handed and the left-handed brains. According to data from brain damaged patients, lateralization of language in the left hemisphere is confirmed for about 97% of right-handed subjects, but also for around 60% of left-handed, 30% would have language in the right hemisphere and 10% would have bilateral representation (Bryden, 1982). Similar figures were produced by Milner and co-workers, who used Wada's intracarotid sodium amytal test (Wada and Rasmussen, 1960) to localize language functions in patients that were to undergo removal of epileptic foci, and by (Warrington and Pratt, 1973), who studied depressed patients treated with unilateral electroconvulsive shocks. Data on lateralization of spatial functions are very few: according to (Hécaen and Albert, 1978), 69% of right-handed subjects would have spatial functions in the right hemisphere and 31% in the left; for left-handed subjects 43% would have a right representation of spatial functions, 28% would have it in the left hemisphere and 29% would have a bilateral representation of spatial abilities. Furthermore it is known that ideomotor apraxia, a deficit that can be evidentiated inter alia by spatial disorganization in copying drawings, can have different characteristics in patients with left and right hemisphere lesions (Warrington and James, 1967). However it is not simple to separate out the perceptual and the praxic component in complex tasks such as copying drawings.

I will now consider more in detail the issue of if and how is language represented in the right hemisphere of right-handed subjects. In fact the idea that right hemisphere could have some role in language processing is almost as old as Broca's observations on the predominant role of the left hemisphere: as early as 1874 Jackson hypothesized that it could play its part in the control of automatic, nonpropositional stereotyped speech (Jackson, 1958). Since then, the idea that the right hemisphere might be involved in recovery from aphasia and in reading has has been accepted by some researchers (Coltheart, 1985; Patterson et al., 1989; Coslett et al., 1993) and rejected by others (Shallice, 1988).

The evidence which would support the claim that some degree of language representation is present in the right hemisphere of normal subjects, has been collected in different types of neurological patients, such as split brain subjects, hemispherectomized patients, and, more specifically with respect to reading, patients with left occipital lesions manifesting pure alexia. The interpretation of this evidence remains however at debate. Other researchers have also performed priming experiments using lateralized stimuli with normal subjects and proposed an interpretation of their results in terms of models supposing the existence of distinct language processing systems in the two hemispheres. This literature, and the suspicious assumptions on which it is based, will be reviewed in the next section.

4.2 Lateralized priming experiments: what is similar and what is different across the hemispheres in normal subjects.

The literature on information structures in the hemispheres is notable for its contradictions rather than its areas of agreement. One of the more controversial issues in the literature on language lateralization is the belief that the lateralized priming procedure can provide a powerful tool for the investigation of the structure of the mental lexicon, if any, in the right hemisphere, and of its peculiarities with respect to the one represented in the left hemisphere.

Phonological or semantic priming is the facilitation in word recognition that occurs when a target word is preceded by a phonologically or semantically related word, with respect to an unrelated one (Neely, 1976). Priming can be considered an effect of *automatic activation* only if at least one of the following experimental conditions are fulfilled: prime-target stimulus onset asynchronies (SOAs) are short, the prime is pattern-masked or prime are much less frequent than unrelated words throughout the experiment. If longer SOAs are used, or if a high proportion of related primes are presented, the subjects can develop expectancies about the occurrence of related words: in this case, usually called *controlled processing*, the priming effect is greater, but it must be presumed to be an effect at least in part of cognitive control precesses (Chiarello, 1985).

In the lateralized version of a priming experiment both prime and target can be presented to either visual field. The belief that the lateralized priming procedure can provide a powerful tool for the investigation of the structure of the mental lexicon, if any, in the right hemisphere, and of how it differs with respect to the one represented in the left hemisphere, is based on Zaidel's claims on the possibility to experimentally distinguish between *callosal relay* and *direct access* tasks (Zaidel, 1986). According to Zaidel there are three main classes of models to account for behavioral laterality effects in normal subjects: the *direct access* models "assume that the hemisphere that receives the sensory information first will process it, for better or worse" (p.438, (Zaidel, 1986)); the *callosal relay* models assume that only one hemisphere can process information, so that if sensory information reaches the other hemisphere first, it will have to shuttle across the callosum prior to processing to occur; finally *dynamic shift* models, first proposed by Kinsbourne, assume that hemispheric activation is critical, and it is in turn dependent on a host of task parameters, so that for example, a dual task situation can increase hemispheric activation, but overloading can produce a shift in hemispheric control.

Zaidel produces a set of criteria for experimentally distinguishing callosal relay from direct access situations. Given the relevance of these assumptions for the interpretation of the literature on lateralized priming experiments I will consider these criteria in some detail. The first criterion, that I will call the *comparative criterion*, states that a direct access task should show small and comparable effects in the split and normal brain. A callosal relay task on the contrary would show a massive laterality effect in the split brain but only a relatively small if not insignificant effect in the normal brain. In terms of experimental design Zaidel characterizes the direct access model by a response hand x visual half-field interaction, while the callosal relay model would be characterized by main effects of both hand and visual field in the absence of a significant interaction.

The comparative argument seems to be reasonable in principle, however it is faced with the extreme variability of results that is found in the split brain population (to be addressed in more detail later): it is entirely conceivable that different split brain patients, differing for example in the age of onset of the illness, would produce different pattern of results on the same task. Furthermore, the presence of a significant response hand x visual half-field interaction could also be explained by a degradation of the signal or loss of information during callosal transfer, which could influence the rate and ease of processing in a lateralized system performing the task.

The second criterion is the so called *processing dissociation criterion* for direct access, stating that a significant interaction between visual hemifield and degree of stimulus complexity is a sign of direct access. Zaidel produces as an example the interaction between concreteness of the nouns and visual field that he detected in a lexical decision task (Zaidel, 1983), and explicitly rejects the possibility that concrete and abstract nouns could use different callosal channels or be relayed at different rates. This claim, which has never been submitted to experimental inquire, seems plausible at first sight. But if one considers the different levels at which lexical decision can be performed (visual-orthographic level, semantic level, phonological level) it seems less evident that experimental variables such as the frequency of an item in the orthographic lexicon, which might be different for abstract and concrete words would not influence the rate and efficacy of callosal relay. Finally the third criterion, that I will call the *interference criterion* assumes that a way to discover the nature of a given task is to couple it with a secondary task of known lateralization in a classical dual-task paradigm. Unfortunately this criterion, which appears to be the safer one, has never been systematically used to my knowledge.

In conclusion the grounds on which interpretation of the results of lateralized priming experiments are based appear to be unsafe. Nevertheless, I will describe some recent findings that would be interesting if replicated in the future, with and given that a more solid theoretical assumptions on the interpretation of the effects would become available in the future.

When phonological primes are used, a standard finding in the literature is that primes presented in the right visual field produce facilitation, while while primes presented in the left visual field do not (Abernethy and Coney, 90), but an example of a different type of finding is found in (Chiarello, 1985).

(Abernethy and Coney, 90) performed a priming experiment based on lexical decision both in the intrahemispheric condition (prime and target presented to the same visual field) and in the interhemispheric condition (prime and target presenter to different visual fields): they found a statistically significant priming effect (25 ms, $p < 0.05$) only in the left intralateral condition. Their subjects performed statistically better in the intrahemispheric condition, but only if the right visual field was stimulated. When the prime was presented in the left visual field and the target in the right however (Abernethy and Coney, 90) detected a trend toward facilitation both in reaction times and in the level of performance. These findings can be interpreted as evidence that the left hemisphere but not the right possesses a phonetic encoder which enables it to derive phonology from print and recognize phonological similarities, if one assumes that the lexical decision task is phonologically mediated. In the light of this assumption, it appears that the activation of phonemically related words in the left hemisphere is not related to any right hemisphere counterpart. This position is supported by some evidence collected with split brain patients, to be discussed later in the chapter. The non significant trend of facilitation detected for primes presented in the left visual field can possibly be explained with a perceptual facilitatory effect.

Lateralized semantic priming experiments in the older literature again do not provide consistent evidence. (Chiarello, 1985) found semantic priming in the left visual field when 20% of word pairs were related, but not when the percentage was augmented to 60%. (Zaidel, 1983) also found semantic facilitation in the left visual field, but only for associated concrete nouns, and as I have already discussed he rather dubiously assumed that this is evidence for direct access in lexical decision. (Hines et al., 1984) on the contrary detected significant semantic priming only when both prime and target were presented to the left hemisphere.

More recently several attempts have been produced in order to detect what are the origins of this variability. (Chiarello et al., 1987) stressed the relevance of keeping the subjects' expectancies under experimental control by taking into account the relevant criteria to distinguish between automatic and controlled processing. Her claim was that priming effects should be expected as long as only automatic spreading of activation is induced; even a minimal degree of controlled processing could mask the effect of automatic activation. A second source of confounding effects is due to the fact that some studies (Hines et al., 1984) used overt naming instead of lexical decision, a procedure that is usually held to involve a callosal relay component when target is presented to the right hemisphere (Zaidel, 1983).

More recently some authors have considered the influence that the type of semantic link between target and prime may have on performance in lateralized priming experiments (Abernethy and Coney, 90; Abernethy and Coney, 93; Chiarello et al., 1990; Beemn et al., 1994; Koivisto and Laine, 1995). (Drews, 1987) performed a divided visual field experiment where normal subjects had to decide whether two words were semantically related or not. Based on facilitation for judgements relating associated word pairs or members of the same semantic category, she proposed that the difference between *intra-conceptual vs inter-conceptual* relationships may be critical in the organization of the knowledge about word meaning. Intra-conceptual links are supposed to connect member of the same categories or in general items that share many relevant characteristics, as 'bus' and 'train' for example. Interconceptual links are held to arise as a consequence of repeated association in the experience (e.g. coffin-earth).

(Abernethy and Coney, 90) using a lateralized priming paradigm with a lexical decision task, found facilitation for prime-target couples of words belonging to the same semantic category only for pairs of words presented in the right visual field. In a subsequent study the same authors addressed the issue of the representation of inter-conceptual links (Abernethy and Coney, 93): they used prime-target couples of words that were linked by associative relationships but neither belonging to the same category, nor linked by superordinate-subordinate relationships. Orthographic similarity was carefully avoided by ensuring that the words in the couples did not have more than a single letter in common, which was never the first one (examples from the experimental set are: prime:wool, target:sheep; prime:church, target:nun). Using short SOAs (250 ms) they found a significant facilitation in response times when stimulus and target were presented in the right visual field, and a non significant advantage for unrelated pairs when stimulus and target were presented in the left visual field. However in a second experiment, performed with a different group of subjects but with the same material, prolonged SOA (450 ms) were employed. In this situation the significant results for the right visual field were replicated, but significant facilitation was also found for prime-target couples presented to the left visual field. In fact both (Zaidel, 1988) and (Chiarello et al., 1984), who found facilitatory effect in priming experiments with associated words, have used SOAs longer than 500ms. The lack of priming in the left visual field when short SOAs are used, has been interpreted by the authors as an evidence that the semantic activation process is slower when associated words are presented in the left visual field. From this they concluded that in the right hemisphere semantic system the associative links might be represented more weakly than in the left hemisphere semantic system. Again this conclusion is grounded on the quite unsafe assumption that lexical decision is a direct access task.

(Koivisto and Laine, 1995) observed that in the original Drews' experiment only locative relationships were used as exemplars of the inter-conceptual type of semantic link. Furthermore the associative strength of the link was not controlled. Anyway from longer response latencies found for locative pairs they deducted that locative relationships were in fact weaker than the categorical ones. (Koivisto and Laine, 1995) studied the representation of *locative and coordinate (=categorical) relationships* using a free association paradigm, which can be considered an implicit memory task (Schacter, 1987), taking the strength of the link under experimental control. They found a significant interaction between visual field and word pair type, and following the logic of Zaidel, they suggested a qualitative difference in the representation of the lexicon across hemispheres: in particular the coordinate relationships would be represented in both hemispheres, while the locative relationships would be principally represented in the right hemisphere. One possible explanation of why locative representations should be represented in the right more than in the left hemisphere may lie in the supposed different hemispheric modes of representing the visual context. (Zaidel, 1987) has shown that reaction times for recognition of common scenes is faster in the left than in the right visual field in normal subjects. Furthermore he found that the actual organization of the visual scene has an influence on performance only when stimuli presented to the left visual field. Zaidel has interpreted these findings as suggesting that the right hemisphere represents the meaning of the various components od a visual scene as their role in a spatial schema. This is an interesting hypothesis, consistent with the characterization of the right parietal cortex as a visuo-spatial processor; it could be more safely explored in studies with split brain subjects.

The strength of the semantic link is another variable that has been shown to have an effect in lateralized priming experiments using naming as a task (Beemn et al., 1994; Chiarello and Richards, 1992). In particular (Beemn et al., 1994) performed lateralized summation priming experiments in which a triplet of words are presented as prime, each of which has only a loose semantic link with the target (Example: primes: vault, jewelery, missing, target: theft), triplets of unrelated words were used as baseline (Example: primes: molasses, mother, moon, target: theft). The authors only analyzed the level of performance, finding that the subjects named right visual field target words 5.9% more accurately following summation primes (61%) than following unrelated primes and left visual field target words 14.7% more accurately following summation primes (66.0%) than following unrelated primes; furthermore this benefit from summation priming interacted with hemifield presentation. In a second experiment, the authors compared the effect of summation priming with the priming effect produced by a triplet composed by a strong associate and two unrelated items (Example: primes: blank, robbery, although, target: theft). They found that subjects that subjects named target words preceded by Summation primes more accurately (62%) than target words preceded by unrelated primes (52.6%), however hemifield of presentation did not exert any main effect nor iteraction with relatedness in the triplets. The authors claim that their results can be interpreted by assuming that the right hemisphere, but not the left, may use a *coarse semantic code*, that is it may weakly activate a large semantic field with distant associates of a given concept. The left hemisphere on the contrary would only be able to strongly activate small semantic fields. This would make the left hemisphere more competent in the comprehension of single words, but would leave open the possibility of a right hemisphere contribution to language comprehension when many words have to be simultaneously processed. Although this hypothesis is interesting, it is ill founded on the experimental grounds. In particular the authors offer a rather baroque and tautological argument to explain the results of the second experiment, which is based on the presumed asymmetry in relatedness judgements for two words, one of which is presented laterally:

subjects judge closely related word pairs as related more often when the lateralized word is presented to the right than to the left visual field (and viceversa) (Rodel et al., 1992).

Again, a word of caution on the interpretation of the data obtained with normal subjects and lateralized presentations of the stimuli must be given. The priming effects demonstrated in these type of studies range around 20 ms. These values should be compared to the current estimates of the mean callosal transfer time, which are around 3-4 ms (Marzi et al., 1991). A typical reaction time measure range over time periods long enough for several interhemispheric interactions to occur. As this is the case, it remains unclear what could be the neurophysiological interpretation of this type of results. This is one of the reasons why evidence on the possible role of the right hemisphere in normal language has been looked for in the domain of neuropsychological enquiry.

4.3 Language in hemispherectomized patients.

Surgical removal of one hemicortex is a radical and rather rare procedure that is undertaken only when the prognosis is very poor. The first reported cases of total hemispherectomy (this word is used as a synonym of hemidecortication) are 12 cases of infantile hemiparesis (Krynauw, 1950), of which 11 survived for long periods after the surgery. They were all reported to have benefitted from the operation. Krynauw speculated that the removed hemisphere in cases of infantile hemiparesis is always the non dominant one, because the neural damage at birth would have induced a process of functional reorganization of the neural substrates of higher cognitive functions. A well described patient with an early left hemispherectomy developed normal language and intellect: at the age of 26, he was found to have a performance I.Q. of 126 and a verbal I.Q. of 102 on the WAIS (Wechsler

Adult Intelligence Scale) (Smith and Sugar, 1975), with a notable difference between the two measures. Although this type of clinical reports suggests *equipotentiality* of the two hemispheres at a very early age, they do not directly address the issue of what are the characteristics of language in a normal right hemisphere, which has developed together with a healthy left hemisphere.

There are however at least two reports of some preserved speech abilities following left hemispherectomy in adulthood ((Zollinger, 1935; Hillier, 1954). In clinical descriptions of cases of left hemispherectomy performed to remove tumors, some preservation of single word comprehension has been frequently reported, indicating the presence of a limited auditory input lexicon; spontaneous speech was often limited to single words utterances, except in some cases for stereotyped expressions; the ability to repeat could be preserved to a minor extent and finally reading and writing abilities were usually found to be severely compromized (Smith, 1951; Smith and Burklund, 1966; Smith, 1974). However in this type of pathology it is difficult to infer the age of onset of the illness. In a series of 40 adult patients (McFie, 1961) it was found that irrespective of the hemisphere removed there was an increase in both verbal and performance I.Q. after surgery.

In the seventies Dennis and co-workers produced a series of studies on the characteristics of linguistic competence developed by patients who had an hemispherectomy in childhood. (Dennis and Whitaker, 1976; Dennis, 1980). They concluded that although the isolated right hemisphere acquires language after early left hemisphere injury, it seems to remain limited in its ability to process syntax. This claim was based on evidence in a syntactic test using voiced active and passive sentences with and without negation, and similar syntactic comprehension tests. The data however were re-analyzed by Bishop , who found weak statistical significance. Furthermore she pointed out that defective performance on the types of sentence used by Dennis is typically found in children and in subjects with low verbal I.Q., exactly the type of subjects that Dennis included in her studies (Bishop, 1983).

Odgen described two left hemispherectomized patients with long recovery periods. Their overall cognitive profiles are remarkably similar. They were in the borderline intellectual range, and showed commensurate vocabulary development. They could read and write albeit very slowly. They performed normally on the Token Test and showed preserved ability to manipulate syntax in production tasks, although they had some difficulties in tests of syntactic comprehension of the type used by Dennis (Odgen, 1988). Odgen commented that these profiles support the suggestion that recovery time may be a crucial factor in the sophistication of right hemisphere linguistic performance. According to (Corballis and Beale, 1976) this type of evidence supports the idea of a *left-right maturational gradient*: the right hemisphere would be very slow in reaching normal linguistic sophistication after early left hemisphere damage.

Not all the early left hemispherectomized patients however have such limited linguistic deficits. Patient R.S. for example (Gott, 1973; Zaidel, 1976) had mild comprehension impairments, with the interesting tendency of producing both semantic errors and semantic paraphasias in picture naming tasks. Her reading abilities were more severely compromized, but again she appeared to be prone to semantic errors. The tendency to produce semantic errors has been assumed to be typical of the right hemisphere performance, especially in the reading task (see section on right hemisphere reading); this patient however was also able to perform rhyming judgements on printed words, an ability that is considered crucial for showing the presence of grapheme to phoneme conversion processes.

Along similar lines (Patterson et al., 1989) studied the reading performance of the left hemispherectomized patient N.I. and noted that it was remarkably similar to the profile characteristics of deep dyslexia; they concluded that the right hemisphere might play a crucial role in determining the pattern of performance of deep dyslexic patients. However they failed to give conclusive evidence that N.I.'s phonological impairment was subsequent to the hemispherectomy, and some authors (Baynes, 1992; Plaut and Shallice, 1993) have criticized their conclusions by pointing out that N.I.'s performance could well be typical of a diminished reading system, irrespective of its laterality (for a computational support to this claim, see (Plaut and Shallice, 1993)).

To conclude, it is possible to summarize the observations found the literature on left hemispherectomies in the following points:

- patients surviving more than one year after left hemispherectomy performed in adulthood usually show severely limited spontaneous speech, some degree of preserved single word auditory comprehension, but at most very poor reading and writing;
- patients who had an hemispherectomy in childhood develop language skills that are commensurate to their general intellectual skills;
- at the moment there is no conclusive evidence on the more specific issue of the similarities in the reading abilities in this population of patients with the pattern typical of deep dyslexia.

More details on the issue of right hemisphere reading abilities and disabilities are produced in the next sections of the chapter, where the behavior of split brain subjects and pure alexic patients is analyzed.

4.4 Language and semantics in the Split Brain.

4.4.1 The anatomy of telencephalic commissures.

Telencephalic commissures are bundles of neural fibers which almost exclusively reciprocally connect cortical areas across the hemispheres. In placentate mammals there are three such connections: the *corpus callosum*, *the anterior commissure* and the *hippocampal commissure.*

The corpus callosum is estimated to contain fibers from at least 2-8% of the cortical neurons. Callosal fibers have their origins and targets in almost all functional area in the neocortex, although in segregated subportions. The vast majority of the fibers connects homologous areas across the hemispheres, and usually also the few heterotopic connections are found to link areas that are functionally related to each other. In fact there is an interesting correspondence between intra and interehemispheric connections: heterotopic callosal fibers never connect cortical areas that are not connected to each other intrahemispherically. In particular there are neither intra- nor interhemispheric direct connections between visual and auditory areas.

The topology of the human callosum was originally derived as an extrapolation from the data obtained in the macaque monkey (Pandya and Seltzer, 1986), but more recent results with in vivo imaging techniques and lesion studies are found to be in agreement with those predictions (DeLacoste-Utamsing and Holloway, 1982; DeLacoste et al., 1985). The callosum is divided into an anterior and a posterior part. In the anterior part the *rostrum* contains fibers connecting the prefrontal caudate-orbital regions and the inferior premotor areas; the *knee* connects prefrontal regions and the median part connects premotor and supplementary motor areas. In the posterior part the median section links motor areas in its most anterior section and somatosthetic parietal regions in the more posterior part; the *istmum* connects superior temporal and posterior parietal regions and finally the *splenium* connects occipital and inferoparietal areas.

The anterior commissure is the paleocortical commissure, linking the amygdalae and the olfactory bulbs; it also contains a few neocortical fibers. It is estimated to contain around 1/100 of the number of the callosal fibers (Demeter et al., 1988). The hippocampal commissure is the archicortical commissure, and in humans it runs just below the callosal bundle. Little is known about its functional structure, except the fact that its most developed section, the dorsal one, might be involved in the spreading of temporal epileptic seizures (Gloor et al., 1993).

Telencephalic commissure can be lesioned by traumatic, vascular, tumoral or degenerative pathological processes (such as demyelinization of callosal fibers in multiple sclerosis); they can be surgically sectioned in order to reach underlying structures or in an attempt to control the spreading of epileptic seizures. Furthermore the callosum might totally or partially fail to develop due to arteriovenous malformations. All the non surgical lesions anyway are incomplete. The only situation in which the two hemisphere are totally separated is in commissurotomized patients that have been operated in order to control generalization of epileptic seizures.

4.4.2 Neuropsychological profile of the disconnection syndrome.

The first surgeon to realize complete callosotomy was Van Wagenen in the early fourties. His group of 30 split brain patients was submitted to a standard neuropsychological investigation by Akelaitis, who failed to detect any systematic effect of the commissurotomy. The result were interpreted in the context of holistic theories that tended to deny any relevance of the actual anatomical connectivity with respect to function (Akelaitis et al., 1942).

Sperry and Myers were the first to employ the experimental protocol on perceptual equivalence of the visual fields (a stimulus presented in one visual field is later recognized if presented in the other visual field) as a tool to demonstrate the relevance of the commissures as the neural substrate of interhemispheric transfer of information in different animals (Myers and Sperry, 1953; Sperry, 1961). Inspired by this pioneering work in which simple but efficient techniques of lateralization of the stimuli had been finally introduced, (Geschwind and Kaplan, 1962) interpreted the symptoms of tactile anomia, left hand agraphia and lack of intermanual transfer in a patient with tumoral lesion of the anterior callosum in terms of a *disconnection syndrome.*

The work of (Gazzaniga et al., 1962) is the starting point of the analysis of a series of split brain patients operated by the californian neurosurgeons Bogen and Vogel, the so called *West Coast series.* In 1975 Zaidel devised a field occluding contact lens system which allows for unlimited presentation of lateralized stimuli. Patients N.G. and L.B. from the West Coast series were fitted with the lens, while the other patients of the West Coast series (A.A., R.Y. and N.W.) continue to be investigated with the traditional method of tachystoschopic presentation. A second series of commissurotomies, *the East Coast series*, was initiated by Wilson in the late seventies (patients P.S., J.W., D.R. and V.P.).

According to Berlucchi and co-workers however, the disconnection syndrome should be characterized not only looking at split brain patients but also taking into account the concomitant evidence from other populations suffering from callosal lesions of different origin (Berlucchi and Aglioti, 1996). Following their detailed discussion of the main findings on the disconnection syndrome, I will derive a brief sketch of its neuropsychological profile, to be considered as valid in general; a more specific discussion on language and semantics in the split brain will follow, together with a detailed review of some relevant single cases.

Disconnected patients presents with a dramatic *loss of perceptual equivalence of the two visual fields*: objects presented in one visual field are not recognized when presented in the other visual field; furthermore it is usually impossible to compare objects across fields. A common finding is *left visual hemianomia in the absence of agnosia.* Perceptual independence is not complete: in verbal expressions of split brain patients for example an emotional tone can be present which is appropriate to the content of terrifying stimuli presented in the left visual field, a behavior that is considered to be mediated by extracommessural visual pathways. Visual imagery has been investigated in an attempt to demonstrate a presumed specific role of the right hemisphere in generating visual images; however this assumption has never been proved, on the contrary there is some evidence of a preeminent role of the left hemisphere (Farah, 1988; Farah, 1990).

In the auditory domain the phenomenon of *extinction of the left ear* is well documented: patients presented with different stimuli to the two ears tend to verbally report only the ones presented to the right ear. Furthermore it has been shown that split brain subjects tend to preferentially follow a verbal command delivered in the left ear with respect to the one delivered to the right ear in the mean time (Milner et al., 1968). Some split brain patients (Musiek and Kibbe, 1985; Musiek and Reeves, 1986) have been shown to be impaired in the verbal description (of the type 'high-low-low') of sequence of tones presented to the left ear. In evaluating results from experiments in the auditory modality however it is important to remember that at the anatomical level the auditory pathways are not entirely crossed as are the visual ones.

In the somatoesthetic domain disconnected patients tend to show *poor resolution in the tactile localization of stimuli delivered on the left side of the body.* In parallel with the similar finding in the visual domain, the *loss of stereognosic equivalence of the hands* and *stereognosic left anomia without agnosia* are frequently reported. *Proprioception*, even in the distal areas, was found to be normal in two patients of the Californian series (McCloskey, 1973). This is apparently in contrast with the typical *difficulty in reproducing with one hand the posture imposed by the experimenter to the other hand out of view* frequently reported in the literature (Sperry et al., 1969; Bogen, 1985; Bogen, 1987; Bogen, 1993), which possibly requires fine grained discrimination of the posture imposed to many articulations at the same time. The left hand shows a pronounced superiority with respect to the right hand in both immediate and delayed matching to sample of meaningless shapes (Milner and Taylor, 1972).

In opposition to the other sensory pathways, the olfactory pathways have mainly uncrossed projections; in accordance with this, split brain patients may show *right narix hemianomia* and *loss of perceptual equivalence across narices* (Sperry et al., 1969; Gazzaniga et al., 1975; Gordon and Sperry, 1969).

The anatomy of the motor system allows for bilateral control of axial and proximal muscles, but the control shifts to the contralateral hemisphere for more distal segments (Berlucchi et al., 1995). Split brain patients are reported to show some evidence of *ideomotor apraxia of the left limbs on verbal command* even a long time after the commissurotomy; differently from patients with left hemisphere lesions however, they can easily imitate gestures (Gazzaniga et al., 1967; Sperry et al., 1969; Bogen, 1985; Bogen, 1987; Bogen, 1993). Axial movements such as smiling can be executed even on verbal command (Gazzaniga et al., 1967). A failure to execute a verbal command can arise both at the comprehension and at the execution level. According to (Gazzaniga, 1983) the right hemispheres of commissurotomized patients although always able to imitate gestures, can be divided into three classes with respect to their ability to follow verbal commands. The most representative one is that of right hemispheres that are unable to comprehend the commands; the other two groups include few patients that show good comprehension (at a word picture matching task with presentation of action words) but are unable to produce the gesture, and finally a very few patients with high linguistic and praxic competence that can perform the task. In view of these and similar results, (Berlucchi and Aglioti, 1996) conclude that

- the isolated right hemisphere of split brain patients must be considered able to control autonomously the praxis of the contralateral limbs;
- in general left hand dyspraxia on verbal command in commissurotomized patients has to be considered as a consequence of comprehension limitations and not a the result of disconnection of the right hemisphere from a supposed eupraxic center in the left hemisphere;
- each hemisphere has a limited degree of control on ipsilateral movements, the more proximal the better;
- the so called *callosal apraxia* in non surgical lesions, together with the severe left hand apraxia in the acute post-commissurotomy phase, can be explained in terms of summation of disconnection and intrahemispheric damage.

Interestingly the ability to reproduce complex sequences is severely limited with both hands and also with the facial musculature (Milner and Kolb, 1985). Motoric co-ordination is well maintained, but patients can fail if tasks are explicitly designed to stress the independence of movements of the two hands (Zaidel, 1977). Some split brain patients are able to *dysgraphically but legibly write* with their left hand, but possibly only under left hemisphere control. The few exceptions to this pattern will be described in the next session. Finally in the Californian series some patients are reported to have variable degrees of *right hand dyscopia and constructional apraxia* (Bogen, 1969; Zaidel, 1977). It is important to note that generalizations from findings in the commissurotomized population to the normal brain are not straightforward, as the possibility of functional re-organization and relateralization in patients where the onset of the illness is in childhood must be taken into account (this issue will be addressed in more details when some relevant single cases are reviewed in the next sections.).

Although a couple of patients became severely amnesic after commissurotomy (Ferguson et al., 1985), *memory* is considered to be at most slightly impaired in the split brain patient, and in particular only in subjects with complete section of all the commissures. It is known however that this population shows a selective difficulty with the subsection on verbal associations of the Wechsler scale; Milner (1990) has argued against the possibility that this deficit is due to a lack of visual imagery support in memorization. Agenetic patients have no deficit of memory (Chiarello, 1980).

Alertness is comparable to what could be expected on the basis of the clinical history of the subjects, often submitted to prolonged pharmacological treatment with barbiturates. In monotonous tasks of passive detection of non lateralized stimuli regularly presented in various modalities however, split brain patients can have periods of total unalertness, missing many subsequent stimuli presented to the right hemisphere.

Selective attention has been recently investigated. Split brain patients are facilitated by the absence of interference across hemifields in tasks requiring the analysis of conflicting information (Gazzaniga et al., 1987), so that the two hemispheres can perform in some tasks as independent information channels (Gazzaniga, 1987). When difficult stimuli are presented simultaneously to the two visual fields, patients tend to neglect the left visual field, but there is evidence that the effect arises at the level of the response and is not perceptual (Reuter-Lorentz et al., 1995). Voluntary control of visual attention is thought to remain unmodified after commissurotomy (Ladavas et al., 1994; Gazzaniga, 1987), but (Corbllis, 1995) suggests that *object-oriented attention*, being more cortically mediated than visual spatial attention, could be doubled in the commissurotomized brain.

4.4.3 Language in the split brain.

The results of the split-brain investigations are heterogeneous (Gazzaniga, 1983; Baynes, 1992). In general they are consistent with studies on unilateral lesions in indicating a major division of function between the hemispheres. The most relevant discrepancy however is that the right hemisphere of some right-handed split brain patients have been credited with a considerable level of linguistic skills. Variability has been explained with differences in the clinical history of the patients. In a review of 10 split-brain cases that were under investigation at that time (Whitaker and Ojemann, 1977) noted that 7 subjects (among with 2 cases showing hints of right hemisphere language) were reported to have sustained their lesions in infancy or early childhood, one sustained an injury at 15 and remained aphasic and another at 30. All 10 patients had evidence of structural damage to their brains before the commissurotomy. (McCarthy and Warrington, 1990) observed that generalizations about the language competence of the right hemisphere are based on a subset of population, most of whom sustained early brain damage, in which "a high incidence of bilateral language organization comparable to that observed in sodium amytal studies of patients with childhood lesions" should be expected (p.11). In the view of the evidence for plasticity in the developing nervous system, and (I add) possibly even in the view of the degree of functional plasticity that has been documented in the split brain population per se (Baynes et al., 1995), McCarthy and Warrington argued that the patterns of cerebral lateralization found in the commissurotomized patients "cannot easily be generalized to the developmentally normal adult brain. However, they can be very telling with regard to the potential and limitations of the right hemisphere in the development of certain types of linguistic abilities" (p.11., o.c.). This *caveat* has to be remembered in order to achieve a balanced evaluation of the results obtained from the studies of commissurotomized patients, that are reviewed in the next sections.

Semantics in the split brain.

In the early sixties Gazzaniga and his group started a systematic exploration of the linguistic abilities of the patients of the so called *West Coast series* (Gazzaniga et al., 1962). Although initially (Gazzaniga et al., 1967) it was impossible to obtain from these patients (N.G. and L.B. in the 1967 paper) any verbal response to left lateralized stimuli such as single letters, numbers, words or pictures, when multiple choice arrays were employed the right hemispheres ware found to be able to correctly identify single letters, digits and short words.

In the *the East Coast series* of commissurotomized subjects, the patients that have been more extensively investigated are P.S., J.W., and V.P.. P.S., a right-handed male, suffered from epileptic seizures with left hemisphere foci from the age of two, and had callosal section when he was 15 (Gazzaniga et al., 1977). Patient J.W., a right-handed male started experiencing staring spells between childhood and adolescence; his first major motor seizure occurred when he was 19, and soon after his seizures become intractable. His corpus callosum was sectioned in two stages when he was 25 (Wilson et al., 1978). V.P., a right-handed female, experienced her first seizures as a child after high fever. Seizures remained mild until the late 1970s when medical management failed to control them and a two stage callosotomy was performed (Sidtis et al., 1981).

These three patients of the East Coast have been tested on a variety of semantic tasks in order to study the nature of the right hemisphere semantic representations. All of these three patients show the ability to match written words presented to the right hemisphere with pictures at a reasonable level (having a right hemisphere level of performance reaching around 70-90% of the corresponding left hemisphere level); Word frequency and abstractness have a fundamental impact on the comprehension abilities of the isolated right hemisphere (Zaidel, 1982). P.S. was noted for the unusually high sophistication of the linguistic skills of his right hemisphere (Gazzaniga et al., 1977). One year after callosotomy P.S. developed the ability to initiate speech from the right hemisphere, which could also identify rhymes. Furthermore it was able to derive phonology from printing in order to read non-words. He was shown to be able to recognize semantic associates, antonyms and synonyms presented to his right hemisphere (Gazzaniga et al., 1977).

V.P. could identify synonyms, antonyms, functional relationships, and superordinate and subordinate category links (Sidtis et al., 1981). J.W. showed a similar pattern but with less accuracy; in particular he had difficulties with synonyms. (Gazzaniga and Miller,

1989) interpret this finding in the sense of an underspecification of the entries in the right hemisphere semantic lexicon, and speculate that this is the result of a lack of active manipulation of the semantic lexicon, and would have as a consequence the difficulty in addressing phonological representations from semantics.

In fact, in a study of inferential reasoning J.W. and V.P., despite their excellent single word comprehension and, for V.P., despite his ability to access speech, were both unable to show any inferential ability, nor other intellectual function operating on their right hemisphere lexicon (Gazzaniga and Smylie, 1984). In the test of inferential reasonning the patients were required to select the picture that best captured the consequence of two previously lateralized pictures (e.g. logs and matches were expected to induce selection of a picture of a bonfire more than a wood pile or a lit cigarette). A second test was devised in which two lateralized written words were presented and an appropriate target action word to had to be selected (e.g. stimuli: water+pan, target=boil, distractor=fry). Both right hemispheres performed at chance in these tests.

However performance was significantly better than chance, although worse than that of the left hemisphere, in another version of the previous task, in which pictures were used instead of written words; for example, after the presentation of the picture of a man and the picture of a fish, the picture of a fisherman had to be selected, the distractors being a picture of man swimming, of some boiling water and of a frying fish. This test was meant to show that the concept to be inferred in the reasoning test was in fact present in the semantic lexicon.

J.W. was shown to be able to derive the meaning of combined words like in selecting a piano keyboard after lateralized perception of the words 'key' and 'board' following each other (V.P. was not tested in this task). In a test of current events knowledge from news headlines both V.P. and J.W.' right hemispheres performed as well with their right hemispheres as with their left, showing a normal capacity to acquire new knowledge. The authors observe that in contrast to their apparently solid and updated knowledge base, the right hemisphere of J.W. is not able to perform inferential tasks of a type in which language trained chimpanzees do not fail (Premack, 1983). They claim that 'when increased abstraction of language stimuli is required, these demands are met not by the language system itself, but rather by other cognitive systems that carry out computations on the language stimuli' (p.151). These other cognitive abilities would be defective in the right hemisphere. However inferential reasonning is a very complex task, which probably requires componential analysis and the support of modality-specific working memory systems (Shallice, 1988); in fact it is even possible to speculate that a defective activation of the phonological short term memory system could explain the correlation between defective active manipulation of the semantic representations in inferential tasks and poor phonological abilities.

Some years after these results were derived, P.S. and V.P. developed the ability to transfer semantic information between hemispheres (Gazzaniga et al., 1982; Gazzaniga and Miller, 1989). J.W. was shown to have developed the ability to read aloud single number words presented to the left visual field 16 years after his commissurotomy (Baynes et al., 1995).

The presence of a semantic input lexicon has been investigated with semantic priming in a lexical decision task proposed to five commissurotomized patients (Zaidel, 1983). All but one could carry out lexical decision in both visual fields, but only one showed significant semantic facilitation from visual primes presented in the right visual field. Auditory semantic primes were effective for four out of five right hemispheres in this group.

The semantic structure of the lexicon has been also investigated using the effect of semantic incongruity on ERP (Event Related Potentials) (Kutas et al., 1988) in a series of experiments including both East and West Coast patients. The ending, either semantically congruent or incongruent, of an auditorily presented sentence was flashed tachystoschopically to the right and left hemisphere. All the left hemispheres presented the N400 response to semantic incongruence in the left hemisphere, but only P.S. and V.P. showed the N400 in the right hemisphere. The presence of this sign of the detection of semantic incongruence appears to co-occur with the possibility to initiate speech from the right hemisphere.

Morphology and syntax in the split brain.

[1] It is generally assumed that right hemisphere is very defective in syntactic abilities. (Gazzaniga and Hillyard, 1971) found little evidence of syntactic abilities in N.G.'s and L.B.'s right hemispheres: they could not distinguish active from passive sentences, single and plural words not the future tense; they could however understand negative sentences. In the same patients (Zaidel, 1978) demonstrated "rudimentary" syntactic competence (he assumed that such was a level of syntactic competence that can be compared to that of children aged 5) using more sophisticated linguistic tests: in a set of syntactic comprehension tasks, he found that the right hemispheres were more sensitive to length than to syntactic complexity when compared to a group of Broca's aphasic patients. Similarly to the isolated left hemispheres, the right hemispheres also found gerunds and verbs more difficult than nouns and verbs. Of all the split brain patients that have been submitted to the Token

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Although this thesis is not concerned with any issue related to syntax, this section is presented for the completeness of the review.

Test, only V.P. had good performance. All the other were impaired, but in contrast to Broca's aphasic patients, they seemed to be more sensitive to perceptual than to syntactic complexity on an error analysis (Zaidel, 1977; Gazzaniga, 1983). As V.P. is also the one patient with better speech abilities in his right hemisphere, a possible speculation is that he, unlike the other split brain patients, can benefit from a reasonable support of a phonological short term memory system in performing the Token test.

The ability to assign thematic roles has been assessed in J.W. and V.P. (Baynes and Gazzaniga, 1988). They tended to perform above chance on active voice sentences and below on passive, a pattern that has been seen in Broca's aphasic patients with poor syntactic competence. However both patients were able to make grammaticality judgements with their right hemispheres. In a study of the sensitivity to the grammatical information provided by the functor 'the', only V.P.was found to be able to exploit this type of cue to disambiguate sentence comprehension (Gazzaniga and Smylie, 1984).

Phonology and reading in the split brain.

The isolated left hemisphere of split brain subjects does not usually show any detectable linguistic deficit (Zaidel and Schweiger, 1984; Berlucchi and Aglioti, 1996). The first examples of expressive language from an isolated right hemisphere were in the written form: patient L.B. was able to spell words with his left hand using block letters out of view (Gazzaniga et al., 1967). P.S. was the first split brain patient to name lateralized stimuli; he started to show this ability only one year after surgery (Gazzaniga et al., 1979). He can recognize rhyming syllables and even read aloud homophones of real words presented in the left visual field (for example the non-word 'brane', which is homophone to the real word 'brain'). V.P.

also developed the ability to control speech with his right hemisphere rather late (Sidtis et al., 1981), but she was shown by MRI to have sparing of a few fibers of the rostrum and splenium (Gazzaniga et al., 1985). Her right hemisphere is able to discriminate CV structures, but not to identify them. Neither V.P. nor P.S. have ever been observed to produce paralexic or paraphasic errors with their right hemispheres. J.W. cannot produce speech from the right hemisphere, nor recognize rhyming words or CV structures (Sidtis et al., 1981). He is generally not prone to semantic errors.

The ability to derive phonology from pictures and from print has been extensively investigated in patients L.B. and N.G. of the West Coast series (Zaidel and Peters, 1981). Only L.B. was capable of matching pictures presented in his left visual field with words that sounded alike or that either rhymed or allitterated. N.G. however had some difficulties in these tasks even with the left hemisphere. When the same tasks were proposed with printed words, also L.B.'s performance decreased to chance level, indicating that his right hemisphere cannot exploit grapheme to phoneme conversion rules to perform the task. The absence of a phonological route in reading seems to correlate with the inability to initiate speech and the lack of the N400 response to semantic incongruity in the right hemisphere (Baynes, 1992).

The absence of grapheme to phoneme correspondence rules has been considered suggestive of a connection between reading in the isolated right hemisphere and reading in *deep dyslexia* (Coltheart et al., 1980; Coltheart, 1983; Coltheart, 1985). Deep dyslexia occurs after large left hemisphere damage, often in aphasic subjects: it is characterized by inability to read pronounceable non-words, abundance of semantic, visual and mixed errors, and significance of the abstractness and part-of-speech effects, with concrete and highly imageable words having the highest probability of been correctly read. According to Coltheart these characteristics could be explained by assuming that deep dyslexics read with their right hemisphere. This issue is extremely controversial. (Patterson and Besner, 1988) studied the reading performance of two split brain (L.B. and N.G.) and two deep dyslexic patients (D.E. and P.W.) and found that the isolated right hemispheres were so inferior to the deep dyslexic patients that no direct comparison could be made. Zaidel on the contrary tends to stress the similarities across the two groups: according to his meta-analysis collapsing data across the five split brain subjects of the West Coast series, he finds impaired grapheme to phoneme conversion, better performance on concrete words and a significant part-of-speech effect and a tendency to produce semantic errors in multiple choice reading tasks that he attributes to a certain looseness of the semantic representation in the right hemisphere; he also claims that the right hemisphere visual and auditory input lexicons would show a different ordering of preservation of the same semantic categories (objects, colors, actions, geometric shapes and numbers), with spoken object names comprehended best, and written object names worst (Zaidel, 1982; Zaidel and Schweiger, 1984). In the light of the extreme variability of linguistic skills reviewed here however, it is difficult to assign a conclusive value to results collapsed across the five patients.

Coltheart himself has acknowledged that if one wants to understand the role of the right hemisphere of aphasic patients in reading, and more in general in recovery from aphasia, it would be important to find some evidence of right hemisphere reading in subjects with supposedly normal neurological development prior to adult illness onset. The syndrome of pure alexia has recently been considered as the one providing this evidence.

4.5 Pure Alexia: a window on right hemisphere reading?

Pure alexia is a syndrome characterized by an extreme difficulty in reading (aloud or not) in the absence of other aphasic deficits, and in particular in the absence of agraphia. Patients are frequently left with letter by letter strategies as their unique reading resource (Geschwind and Fusillo, 1966). In his traditional account of pure alexia Dejerine (1892) attributed the disorder to disconnection of the system performing the visual analysis of the input from the linguistic center responsible for word recognition situated in the left hemisphere. However increasing evidence has been reported in the recent years of comprehension abilities in pure alexia that cannot fit with the traditional interpretation of the syndrome: some patients are reported to correctly match spoken to written words that they are unable to identify (Kreindler and Ionasescu, 1961; Albert et al., 1973; Grossi et al., 1984), or to perform correctly in a word picture matching with tachystoscopic presentation of stimuli from which they were unable to identify a single letter (Landis et al., 1980).

The first comprehensive demonstration of preserved covert reading in a pure dyslexic, patient M.L. is in (Shallice and Saffran, 1986): this patient performed well above chance in semantic categorization tasks with very short stimulus presentation and spontaneously went back to letter-by-letter reading if allowed to perceive the words for longer time intervals. (Coslett and Saffran, 1989) reported a couple of patients with the same pattern of performance; as both patients were sensitive to the imageability and the grammatical class of the stimuli, two variables that have been proved to greatly influence "reading" in the right hemisphere of split brain and left hemispherectomized patients (see previous sections), the authors proposed that their performance could be mediated by their intact right hemisphere. A second reason to suspect right hemisphere involvement is that many pure alexic have lesions that extend in the left occipital cortex, as demonstrated by the presence of various degrees of right homonymous hemianopia in this population, so that it would be reasonable to assume that the right occipital cortex is the only locus of early visual process in these patients.

Implicit lexical access was then demonstrated by one of two patients in an experiment exploiting the semantic cueing effect (Howard, 1991); (Bub et al., 1989) and (Reuter-Lorenz and Brunn, 1990) found an orthographic superiority effect in letter identification, again suggesting preserved access to an orthographic input lexicon in pure alexia.

Some alexic patients however do not show preserved implicit reading or lexical access (Warrington and Shallice, 1980; Patterson and Kay, 1982). One possible explanation of variability may be the intrinsic variability of competence perhaps as a consequence of the degree of lateralization in the representation of language (Shallice and Saffran, 1986). (Coslett et al., 1993) analyzed the effect of reading strategy on the performance of the pure alexic patient J.W.C.. They could demonstrate that he was reliably able to shift from letter-by-letter reading to a 'whole-word' reading strategy according to task requirements: when semantic but not phonological information was important to perform the task, for example in semantic categorization (animal vs non-animal, edible vs non-edible), the patient was able to suppress the tendency to derive a phonological representation from print, and only then was he able to succeed in the task (around 75% correct in both categorization tasks). If on the contrary he was asked to try to read the name aloud first, in which he succeeded in about 20% of the trials, and to perform the categorization only in case of an explicit reading failure, his performance inevitably dropped to chance level. The authors speculate that implicit reading is not at all a mandatory process; on the contrary, the subject has to learn to actively suppress letter-by-letter reading, that is considered to be the default reading strategy of the impaired left hemisphere reading system, in order to allow this putatively right hemisphere's competence to emerge. This would explain much of the variability in the data on pure alexia.

A different interpretation of implicit reading, based on computational findings, is provided by (Plaut and Shallice, 1993). In Shallice and Warrington's original account of pure alexia, the disorder is ascribed to a deterioration of a system which is held to be responsible for the visual analysis of letter strings as coherent units, the so called *visual word form* system, which would be accesses prior to any phonological information and which would mediate semantic access from print (Warrington and Shallice, 1980; Shallice and Saffran, 1986). In deriving their account of deep-dyslexia, (Plaut and Shallice, 1993) examined the type of impairment that a degraded input from the visual word form system to semantics would produce in a connectionist network. They found that when the correct response is not provided, there is a very high probability that the network dynamics would nevertheless settle down in a region of the semantic space very close to the correct solution. The authors interpret this result as an evidence that in the presence of a degraded input to the semantic system performance on categorization tasks can be preserved even if proper identification is not achieved. This account of pure alexia does not assign any role to the right hemisphere.

In conclusion, although the interpretation of implicit reading in pure alexia as a process realized in the right hemisphere and the at least partial recovery that pure alexic patients often do demonstrate have been considered as supportive of the general hypothesis that this hemisphere plays its role in recovery from aphasia, the specific pattern of interaction between supposedly left and right hemisphere reading strategies and the apparent possibility to shift at will between these strategies pose in my opinion more questions than provide solutions with respect to the issue of a right hemisphere contribution to normal reading processes.

Chapter 5

5.1 Semantic memory functions in a split brain subject.

In the discussion of the single case study described in Chapter 3, the possibility was raised that the type of semantic memory dissociation showed by that patient could be related to her degree of preservation of the right temporal lobe with respect to the left, that had been clearly documented in two M.R.I. scans and a P.E.T. study. A possible hypothesis was that her performance was sustained by a putative right hemisphere (visual) semantic system.

Patient R.M. presented with a profound impairment of the verbal semantic subsystem, and preservation of some types of semantic abilities in the non-verbal modalities. The preserved semantic abilities with visual material, that were possibly at the basis of her good standards of behavior in daily life, were investigated in the Semantic Judgement Type Test (S.J.T. test). In this test she showed preserved ability to match items according to various types of functional links, and also on the basis of co-occurrence in the same visual context. She was surprisingly poor at recognizing that two visually presented items belonged to the same category. This pattern could be related to the type of dissociation in the representation of allocative and categorical links proposed by (Koivisto and Laine, 1995) for the right and left hemisphere semantic systems. One should remember however that most of the results on right hemisphere semantics in normal subjects have been obtained using priming techniques and hence verbal material. The parallelism in any case remained, and it wold be important to find some evidence of a specialization of the right hemisphere semantic system.

The issue of the existence and the nature of semantic representations in the right hemisphere of split brain subjects has been experimentally addressed predominantly in the verbal modality (see Chapter 4 for a review). In split brain subjects the section of the cortical commissures allows for a complete lateralization of visual information and to a certain extent also of haptic information. In the literature on the disconnection syndrome the universally reported symptoms of inability to name stimuli presented to the left visual field or manipulated with the right hand out of vision, are often interpreted as purely *anomic* symptoms. It is generally assumed that the patient is indeed able to recognize the object and simply cannot access the corresponding phonological representation for output. Usually the ability to mime the use of the manipulated object, for example by appropriately handling it, is taken as evidence of normal recognition (Milner and Taylor, 1972; Milner et al., 1990).

The significance of this type of evidence however can be criticized for different reasons. First the split brain subject can be affected by a certain degree of left limb apraxia or dyspraxia that could compromize a correct execution of a miming gesture even if the object has been identified (Milner and Kolb, 1985; Berlucchi and Aglioti, 1996); secondly, even in the absence of apraxic symptoms, the issue of if and when the ability to mime the use of a tool can be taken as evidence of entirely normal identification - an issue that is central to the interpretation of optic aphasia and associative agnosia - has to be considered.

Another evidence of correct identification is taken to be the ability to perform delayed matching to sample with the left hand out of view: again if the target is physically identical to the distractor the task can be performed on perceptual basis in the absence of semantic processing (Milner and Taylor, 1972). Some patients however are able to perform delayed matching to sample also with non identical instantiations of the same concept, a task that is thought to require access to semantic information. Finally not all the split brain subjects are reported to be able to mime the use of objects manipulated out of view: some patients are reported to be agnosic in the left visual field, although there is a certain tendency in the literature to avoid statements on negative findings.

In the light of the varibility of results described, it would be relevant from a theoretical perspective to collect some data on the nature of the (visual) semantic representations in patients with different degrees of linguistic competence. Of particular interest are the cases of patients in which the origin of the disease prompting to callosotomy can be placed after childhood, in which case it is less plausible that reorganization of cognitive functions would have occurred. The single case study presented in this Chapter moves on these lines. Patient E.M. is a commissurotomized subject that started suffering from epileptic seizures as an outcome of a predominantly right hemisphere lesion suffered in a traffic accident at the age of eight. Since 1990 he has been periodically investigated at the Department of Neurology and Vision Sciences of the University of Verona, under the supervision of Prof.Giovanni Berlucchi. The present study was realized in the laboratories of this Department in collaboration with Prof.Giancarlo Tassinari.

5.2 Case report.

Patient M.E., male, right-handed (Briggs and Nebes' Laterality Index = +16) born in 1970, was submitted to removal of a right frontal subdural hematoma and partial right frontal polectomy following a traffic accident in 1978. He subsequently developed daily complex partial seizures with secondary generalization, resistant to pharmacological therapy. In 1989 the patient underwent a two step callosotomy with further resection of the right frontal lobe at the Neurosurgical Institute of the Catholic University in Rome (Prof.G.F.Rossi), resulting in a marked favorable change in severity and frequency of the seizures, under treatment with Phenobarbital and Phenytoin. Pharmachological treatment has been maintained since then. The completeness of the callosal section was documented by MRI, which also revealed a large defect in right prefrontal cortex, sparing most of the premotor cortex, the primary motor cortex, the basal ganglia and the internal capsulae, and in addition a smaller lesion on the orbital aspect of the left frontal pole, presumably to be attributed to the original trauma.

The patient was repeatedly submitted to neuropsychological investigations at the Department of Neurology and Vision Sciences of the University of Verona during the last years. On the standard clinical examination he presents with a stable condition characterized by left-hand anomia, alexia in the left hemifield, and left-hand ideomotor dyspraxia on verbal command, in the absence of other major neurological symptoms (for more details se (Berlucchi et al., 1997)).

Left-hand anomia was documented, in several sessions over the four years, in the haptic naming test, where the patient was required to name 34 common objects that were manipulated with the right or the left hand out of view: while performance was always correct with the right hand, virtually no object manipulated with the left hand was named. The issue of the presence of left hand agnosia will be addressed in the experimental investigation.

In the tactile localization test, requiring pointing to a location of one hand just stimulated by the experimenter with the thumb of the same hand (intramanual condition) or to the symmetric point on the other hand (intermanual condition), E.M. showed very good performance in the intramanual condition, and evidentiated a profound deficit in the intermanual condition.

The test for apraxia, involving the execution of 14 symbolic gestures with either hand upon an appropriate verbal command was invariably failed with the left hand and correctly performed with the right hand. However the patient was able to reproduce the gestures with the left hand on imitation.

Alexia in the left hemifield was assessed in the tachystoscopic reading test, in which 40 four letters words were presented to either visual field. The patient was completely unable to read words presented in the left visual field, while performance in the right visual field was normal. At an informal assessment, even tachystoscopic reading of single letters presented in the left hemifield was impossible.

Patient M.E. has been submitted to a prolonged investigation devoted to assess semantic memory functions in the left and right hemisphere. As this patient was only periodically available, the investigation has been performed on four separate sessions, spanning around one and a half years from January 1996 to June 1997:

- Session I: January 1996
- Session II: April-July 1996
- Session III: October 1996
- Session IV: June 1997

As stated in the introduction of the chapter, the principal aim of this investigation was to assess an hypothesis that was suggested by the pattern of performance of patient R.M. on the Semantic Judgement Type Test (Chapter 3) and by the asymmetry of her cortical atrophy. The hypothesis assumes that the right hemisphere would be able to sustain performance on some types of semantic judgements but not other, and that this performance would be specifically sustained by a visual semantic component.

In the course of the investigation however, many problems specific to the interpretation of the performance of the present case had to be addressed: some required more specific statistical analysis, some others lead to devising new tests in order to rule out alternative accounts of the results. In order to make the logic of the investigation fully appreciable, some theoretical issues are discussed along with the presentation of the experiments that have raised them.

5.3 Experiments on non verbal semantics in the left and right hemisphere.

As described in the case report, Patient E.M. was not able to follow verbal commands with his left hand; he was however able to imitate meaningful gestures with his left hand, and consequently he cannot be considered an apraxic subject. In different assessments he has been verbally requested to show the use of an object he was manipulating with his left hand out of view and usually has never been able to do so. The fact however that he has sometimes commented the request of miming the use of an object he had not been able to name with sentences like "How can I use it if I do not know its name" is indicative of a possible left hemisphere control during the task: the left hemisphere, but not the right, understands the verbal command, and it complains of its lack of information on the item as an excuse for its inability to perform the task. In order to assess the semantic identification of visual material, experimental procedures that minimize the need of verbal comprehension and the complexity of the praxic response are therefore preferable. These criteria were followed in devising a lateralized version of the Semantic Judgement Type test that has been described in Chapter 3, and also other tests of semantic identification.

5.3.1 A lateralized version of the Semantic Judgement Type test (Session II).

In the original visual presentation of the S.J.T.test the patient is asked to match a real object to one of three other real objects according to a criterion of maximal semantic proximity. Furthermore the proposed forced choice trials have been classified into six groups according to the nature of semantic judgement that is crucial in order to produce a correct matching. I summarize here the classification that has been adopted (all the details are in Chapter 3):

- common category judgements (e.g.:earrings: bracelet vs belt vs lipstick);
- matching of items which are typically seen together but not related by common use or function (e.g: windscreen wiper: car tax sticker vs scarf vs detergent);
- semantic inferences (e.g.: cork: raisin vs pepper vs scissors);
- matching on the base of same function achieved by a similar kind on action (e.g.: brush:comb vs sponge vs glove);
- matching on the base of same function achieved by a very different action (e.g.:button: zip fastener vs belt vs glove);

- matching on the base of joint use in the achieving of the same function or goal (spring clip: hair curler vs shampoo vs bottle opener).

In order to realize a version of the S.J.T. test that would allow to compare the performance of the right and left hemisphere, some major changes in the methodology were mandatory.

Methods and Materials.

In order to have lateralized presentation of the stimuli it was decided to produce suitable slides of the real objects used as stimuli in the original version of the S.J.T. test and of the corresponding triplets with the target and two distractors. As the original version of the S.J.T. test was devised for a female patient, we excluded some stimuli from the test that are less familiar to men (like 'roller' and 'lipstick'). Some other very uncommon items were also substituted. This produced a re-arrangement of the number of stimuli presented both in total an in each class of semantic judgement. Only prototypical objects were used to produce the slides, and pictures were taken from a canonical point of view.

In order to assess the appropriateness of the material of the test, seven aged-matched subjects were submitted to a slightly simplified version of the S.J.T test, in which tachystoscopic presentation (150 ms) of the stimuli was confined to one visual field. Their performance, expressed by the Mean Value ± the Standard Deviation, was $(62.4 \pm 0.6)/64$ ($(97 \pm 1)\%$ correct), irrespective of the visual field. The subjects were also asked to name each stimulus to explicitly assess correct identification. The three stimuli that were not named by the majority of the control subjects were excluded at this stage.

In the lateralized version of the test central fixation was maintained, and the objects were projected to the left or to the right side of the screen. Fixation was checked with an infra-red videocamera and trials in which fixation was not maintained were rejected and automatically repeated at the end of the session. Exemplars from the different classes of semantic judgements were presented in random order. Pseudo-random stimulation of the visual fields was adopted: side inversion of each slide, and alternation of the responding hand generated four different blocks. Asymmetric objects were photographated twice in order to present their canonical view in both visual fields.

The experiments were run in a sound-attenuated room illuminated by two red bulbs at 0.1 cd/m^2, with the subject sitting in an armchair in front of a white screen 171 cm distant from it. As the Carousel does not contain more then 80 slides, the test was divided into two half-tests for lateralized presentation, which usually followed each other in a block. The objects span a range of 10 degrees starting at 2.5 degrees from the fixation point.

The answering procedure was the following: a laser pointer was stuck on the index finger of one hand of the subject; as a group of stimuli was projected in the right visual field and the other group in the left, the responses were classified either as *crossed* or as *uncrossed*: responses given with the hand ipsilateral to the stimulated field were classified as *'uncrossed' responses* while the responses given with the hand contralateral to the stimulated field were classified as *'crossed' responses.* The test was repeated twice in order to collect both *crossed* and *uncrossed* responses to the entire set of stimuli: by combining the two repetitions, a complete set of uncrossed and crossed responses was obtained. The laser light was turned on after each tachystoscopic presentation to avoid interference with fixation, allowing the patient to point to the selected item in a triad that appeared on the screen in central view after the lateralized presentation of the stimulus. No time limit was imposed, but after around 30s the subject was forced to provide a guess.

Some familiarization trials were performed in free vision, with the left hand providing the answer. The sessions were videotaped.

M.E. performed the S.J.T. test twice, always in an ABBA design with respect to the hand providing the answer.

Results.

Results are shown in Table 5.1 and 5.2, separately for the Right and Left Visual Fields. It is interesting to note that from a statistical point of view the crossed and uncrossed responses can be considered as samples extracted from the same distribution (Kruskal Wallis test, $p > 0.05$), so that the results can be seen as four independent repetitions for each visual field.

Global performance in the Left Visual Field ranged between 48% and 54% correct, and it was found to be statistically better than chance (see Table 5.2), while performance in the Right Visual Field was higher, between 75% and 80%, even if it was worse than the performance of normal subjects ($(97 \pm 1)\%$ correct). In Table 5.3, results have been collapsed to compare the performance of the two hemispheres in the various classes of judgements: the right hemisphere always performed worse than the left, **except in the detection of co-occurrence**, were the level of performance was exactly the same. Performance in the right visual field was remarkably stable across the different types of semantic judgements. Interestingly, the left hemisphere showed a significant drop with respect to its mean performance in the detection of co-occurrence (Kruskal-Wallis test, $p < 0.01$) and a significant increase in performance in the detection of joint use in a function (Kruskal-Wallis test, $p < 0.01$) .

Comment.

The level of performance in the S.J.T. test was found to be rather low in both visual fields. In the lateralized version of this task some extra processing is required in order to keep in memory the stimulus during the presentation of the triplet. Furthermore the patient could have encountered specific difficulties in the identification of the stimuli during tachystoscopic presentation that could have impaired his performance irrespective of the type of semantic judgement to be performed. Before any theoretical inference could be derived from these data it was important to understand if factors other than the nature of the semantic judgement had influenced the results. In order to assess if the problems encountered in the S.J.T. test were due to misidentification of the lateralized stimuli, some tests of object identification were devised.

In the first experiment on objects identification in lateralized conditions, the patient was required to match a lateralized stimulus to a semantically identical one presented among two distractors in free vision. The stimuli for this test were the same used in the S.J.T. test in order to allow a direct comparison of the results.

5.3.2 The Identity Matching Test (Session II).

Methods and Materials.

In this experiment the same lateralization procedure described for the S.J.T. test was adopted, and the experiment was run in the same conditions. Stimuli were 53 slides of objects from the set used in the S.J.T. test, where some stimuli were presented twice to test different semantic relations. The triplets used for the test included two distractors and a target item, which could be either physically identical to the stimulus, although presented from a slightly different point of view, or another exemplar of the same item (e.g. a different

S.J.T. TEST - LEFT HEMISPHERE

Visual Field :	*Right*	*Right*	*Right*	*Right*
Tachystoscopic Time :	150*ms*	150*ms*	150*ms*	150*ms*
Response Type :	*uncrossed*	*uncrossed*	*crossed*	*crossed*
comm. category(12)	10^{**} (84%)	11^{**} (91%)	10^{**} (84%)	10^{**} (84%)
co − occurrence(9)	2 (22%)	6 (67%)	5 (55%)	4 (45%)
sem. inference(10)	7 (70%)	7 (70%)	8 (70%)	8 (70%)
comm. concr. func.(8)	7^{**} (88%)	6^{***} (75%)	7^{**} (88%)	8^{**} (100%)
comm. abstr. func.(13)	11^{*} (85%)	9^{*} (69%)	10^{*} (67%)	10^{*} (67%)
joint use to a func.(9)	9^{***} (100%)	9^{***} (100%)	8^{***} (89%)	9^{***} (100%)
total(61)	$46^{\star}$ (75%)	$48^{\star}$ (79%)	$48^{\star}$ (79%)	$49^{\star}$ (80%)

Table 5.1: Performance of M.E.'s left hemisphere at the various classes of semantic judgements included in the Semantic Judgement type Test (June 1996). Judgements are classified as common category, co-occurrence, semantic inference, common concrete function, common abstract function and joint use for a function. In the last raw global performance. In parentheses the percentage of correct answers. $(\star)$= significantly better than chance (Binomial test,$p < 0.0001$); $(\star\star)$= significantly better than chance (Binomial test,$p < 0.005$); $(\star\star\star)$= significantly better than chance (Binomial test,$p < 0.02$); $(*)$= significantly better than chance (Binomial test,$p < 0.01$); Chance level=33%.

ring). The stimulus and target were physically different in 12/53 cases [1]. The distractors could belong to the same semantic category of the target or be unrelated ones.

The test was performed in the crossed and uncrossed conditions, although these two had proven to be statistically equivalent at the S.J.T. test.

Results.

Results are given in Table 5.4. Performance at the Identity Matching test was very good (96% correct on both occasions) in the Right Visual Field but surprisingly poor(55% and 63% correct), although better than chance in the Left. The Identity Matching test was repeated in October 1996, during Session III, and the patient performed 50/51 (98%) correct in the Right Visual Field and 30/51 (61%) correct in the Left Visual Field, which is

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[1] These were the only items for which two physically different highly prototypical items could be found.

S.J.T. TEST - RIGHT HEMISPHERE

Visual Field :	*Left*	*Left*	*Left*	*Left*
Tachystoscopic Time :	150*ms*	150*ms*	150*ms*	150*ms*
Response Type :	*uncrossed*	*uncrossed*	*crossed*	*crossed*
comm. category(12)	7 (58%)	6 (58%)	5 (42%)	8^{*} (67%)
co – occurrence(9)	6^{*} (66%)	4 (44%)	4 (44%)	3 (33%)
sem. inference(10)	6 (60%)	6 (60%)	5 (50%)	4 (40%)
comm. concr. func.(8)	4 (50%)	4 (50%)	3 (38%)	5 (62%)
comm. abstr. func.(13)	8 (61%)	7 (54%)	7 (54%)	4 (31%)
joint use to a func.(9)	2 (22%)	4 (44%)	$7^{\star}$ (78%)	5 (56%)
total(61)	$33^{\star\star}$ (54%)	$31^{\star}$ (51%)	$31^{\star}$ (51%)	$29^{\star}$ (48%)

Table 5.2: Performance of M.E.'s right hemisphere at the various classes of semantic judgements included in the Semantic Judgement type Test (June 1996). Judgements are classified as common category, co-occurrence, semantic inference, common concrete function, common abstract function and joint use for a function. In the last raw global performance. In parentheses the percentage of correct answers. Chance level=33%. ($\star\star$)= significantly better than chance (Binomial test, $p < 0.005$); ($\star$)=significantly better than chance (Binomial test, $p < 0.01$); ($*$)=significantly better than chance (Binomial test, $p < 0.05$). All the other results re not different from chance level.

significantly better than chance (Binomial test, $p < 0.001$) and basically at the same level as in Session II in June 1996.

In order to identify the possible factors that could produce such a low performance, some hypotheses were advanced, and tested against experimental evidence.

The first dimension to be controlled was the physical identity of stimulus and target. The 12 cases in which stimulus and target were not identical were analyzed separately, but it was found that on these trials performance was not significantly different from performance in the other trials (Wilcoxon-Mann-Whitney test, $p > 0.05$), so it was found that physical identity was not a critical factor.

The second possibility to be considered was that performance was sustained by specific perceptual cues, so that, only when these cues were present would the trial be correctly

S.J.T. TEST - COMPARISON BETWEEN HEMIPHERES

Visual Field :	*Left*	*Right*
	N. correct(% *correct*)	*N. correct*(% *correct*)
comm. category (48)	26 (54%)	41 (85%)
co – occurrence (36)	17 (47%)	17* (47%)
sem. inference (40)	21 (53%)	30 (75%)
comm. concr. func. (32)	16 (50%)	28 (88%)
comm. abstr. func. (52)	26 (50%)	40 (77%)
joint use to a func. (36)	18 (50%)	35* (97%)
total (244)	124 (51%)	191 (78%)

Table 5.3: Comparison between performance of the right and left hemispheres at the various classes of semantic judgements included in the Semantic Judgement type Test (June 1996). Judgements are classified as common category, co-occurrence, semantic inference, common concrete function, common abstract function and joint use for a function. Chance level=33%. In the left visual field performance in the 'co-occurrence' class and in the 'joint use' class is statistically different from performance in the other classes (Kruskal-Wallis test, $p < 0.01$).

performed. In order to check this hypothesis, the stimuli were classed into three groups according to the number of correct responses obtained in the left visual field in the crossed and uncrossed conditions: 2 (23 trials), 1 (13 trials), and 0 (17 trials) respectively. The stimulus and target couples were then analyzed, and the number of couples in which the target and stimulus shared the color ('c') or the general shape ('s') were counted. Results of this analysis are shown in Table 5.5. As evident by inspection of Table 5.5, the 'c' and 's' couples were equally distributed along the classes, which made implausible an influence of these simple features on performance.

In Table 5.6 performance on the S.J.T.test is compared with performance on the Identity Matching on an item by item basis: the number of successes (a score that can range between 0 and 4) obtained for each stimulus at the S.J.T. test is reported according to its semantic according to the performance obtained on the same stimulus at the Identity Matching test

PERFORMANCE at the IDENTITY MATCHING

Visual Field :	*Left*	*Left*	*Right*	*Right*
Tachystoscopic Time :	150ms	150ms	150ms	150ms
	uncrossed	*crossed*	*uncrossed*	*crossed*
N. correct (53)	32^*	28^*	52	52
% *correct*	63%	55%	96%	96%

Table 5.4: Performance of E.M.'s left and right hemispheres at the Identity Matching test (June 1996). Chance level=33%. ($\star$)=significantly better than chance (Binomial test, $p < 0.001$).

IDENTITY MATCHING - Effects of color and shape

Visual Field :	*Left*	*Left*	*Left*
Classes :	2 *correct*	1 *correct*	0 *correct*
color	12/23 (52%)	9/13 (69%)	8/17 (47%)
shape	17/23 (74%)	11/13 (84%)	13/17 (76%)

Table 5.5: Effect of color and shape on right hemispheres performance in the Identity Matching test (June 1996): the table shows the fraction of trials in which stimulus and target shared the color or the general shape, with respect to a classification based on the number of successes obtained in the two repetitions of the test.

(2 correct responses, 1 or 0). If results at the Identity Matching test were predictive of results at the S.J.T. test, one would expect to find more of the higher scores (4 and 3) in the first column, and more of the lower ones (0 and 1) in the last column. By inspection of the table, it appears this is not what is found. This suggested that problems in performance were not correlaated with some quality of the stimuli per se.

5.3.3 An analysis of the runs.

An alternative explanation of low performance could be that some disruptive phenomenon could have happened during the task; for example, the right hemisphere could have undergone partial epileptic disturbances while performing the task and this could have negatively

IDENTITY MATCHING TEST vs S.J.T. TEST

Visual Field :	*Left*	*Left*	*Left*
Identity Matching :	2 *correct*	1 *correct*	0 *correct*
$S1^*$	4, 3, 3, 2, 1, 0, 0	3, 2, 2,	3, 3
$S2^*$	4	4, 3, 1, 1	3, 2, 1, 0
$S3^*$	3, 2, 1, 0	3, 1	4, 4, 3, 2, 2, 0, 0
$S4$	4	4, 1, 0	4, 0, 0
$S5$	3, 2, 1, 0	4	3, 1, 1, 1
$S6$	4, 4, 2, 1, 1, 0	4, 1	0

Table 5.6: Right hemisphere performance in the S.J.T. test is compared with performance in the in the Identity Matching test (June 1996). The number of successes (a score that can range between 0 and 4) obtained for each stimulus at the S.J.T. test is reported according to its semantic class (S1=same category; S2=semantic inferences; S3=common abstract function; S4=common concrete function; S5=joint use for a function; S6=co-occurrence;) and according to the performance obtained on the same stimulus at the Identity Matching test (2 correct responses, 1 or 0). If results at the Identity Matching test were predictive of results at the S.J.T. test, one would expect to find the higher scores (4 and 3) in the first column, and the lower ones (0 and 1) in the last column. By inspection of the data, it appears this is not what is found. The categories marked with $\star$ are the ones in which the semantic dementia patient R.M. performed significantly better than chance (See Table 3.6)

influenced the outcomes of the experiments. The mark of such a phenomenon, that would have been not detectable by the experimenters, would be an anomalous number of consecutive trials in which the patients performs at chance level. From a statistical point of view however, given the overall level of performance of the patient, and given the dimension of the sample, the detection of sub-samples in which performance is at chance level is not straightforward. As an inspection of the data revealed that long sequences of wrong answers were sometimes present, an analysis of 'runs' of failures was applied, in order to see if the sequences of responses could be considered to be *regular* from a statistical point of view.

The statistical analysis of 'runs' of successes or failures can be performed under the assumption that the sample of responses is extracted from a Bernoullian random process, that is a sequence of independent trials that have as unique possible outcomes either a success or a failure (Feller, 1968). Given a Bernoullian random process with probability of success p and probability of failure q, it is possible to estimate the size M and the standard deviation S of the number of trial that must be performed in order to obtain 'r' subsequent successes , e.g. a 'run of successes of rank r' [2]. In Probability Theory this number is called *recurrent time for runs of rank r*. Let the sequence have N trials. Given a sequence, one can estimate the probability od success, p, from the frequency of successes, and in fact there is no a priori hypothesis on this probability. For a given sequence, let 'r' be the size of the longest run of successes. The *mean M and the variance S^2 of the recurrence time of runs of rank r* are given by the following expressions (Feller, 1968):

$$M = \frac{1-p^r}{qp^r} \tag{5.1}$$

$$S^2 = \frac{1}{(qp^r)^2} - \frac{2r+1}{qp^r} - \frac{p}{q^2} \tag{5.2}$$

If N belongs to the interval $M \pm S$ then the sequence with a run of successes of rank 'r' is said to be statistically *regular*; if it is not, the sequence is said to be statistically *irregular*. If the rank 'r' is small with respect to the number of trials N it is possible that M is smaller than N, and in this case more than one run of rank 'r' is expected in the sample. A similar procedure can be applied to estimate the *recurrence time for runs of failures* by switching p and q in formula (5.1) and (5.2).

In Bernoullian random process however, the probability of a run of r failures, for $r \leq (N-2)$, can be directly calculated according to the formula:

$$prob(r) = [N - (r+2)]p^2q^r + 2pq^r \tag{5.3}$$

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[2] This analysis is described in (Feller, 1968), Vol 1. p.322 and following.

The probability of finding a run of rank r at least in a sample of N trials is therefore:

$$prob(rank \leq r) = q^N + pq^{N-1} + \sum_{\imath=r}^{N-2}\{[N-(\imath+2)]p^2q^\imath + 2pq^\imath\} \tag{5.4}$$

From where the probability of not finding in the sample a run of r failures is immediately calculated as $[1 - prob(rank \leq r)]$. A similar procedure can be applied to estimate the probability of runs of r successes by switching p and q in the formulas.

The analysis of the runs was applied to the sequences obtained in the Identity Matching test and in the S.J.T. test. More specifically the analysis was applied only to the longest run of each sequence, either of successes or of failures. The sequences of the S.J.T test and of the Identity Matching Test were all found to be statistically regular, which render the evidence of disruptive phenomena during the task rather implausible (the details of the sequences are reported in Appendix A).

An independent way of checking if aleatory phenomena, such as epileptic seizures, could have interfered with the performance of the Right hemisphere is to assess *consistency of performance*: as the disturbing event might have occurred at any moment during performance an inconsistent pattern cross trials should be found. Consistency of performance was assessed for both the S.J.T. test and the Identity Matching test by measuring *the storage and retrieval indices* using the method described in the first Chapter.

5.4 'Storage' and 'Retrieval' impairments in left and right hemisphere semantics.

As discussed in Chapter 1, Faglioni and Botti (1993) devised a statistical tool to measure the degree on consistency in repeated naming experiments. Their basic assumption was that in the presence of a semantic memory impairment, a failure to name an item can be due to a degradation of the corresponding semantic representation or, if the representation is not degraded, to a failure of retrieval, or both. If the impairment is due to a storage deficit, performance in repeated trials is expected to be consistent, while if retrieval is impaired, performance is expected to be inconsistent across trials. In Chapter 1 I have shown how this approach can be extended to the case of forced-choice paradigms, where the probability of correct guessing has to be taken into account. Given the results on repeated trials of the same experiment and the probability of correct guessing, the analysis produces an estimate of two indices, s and r: s is the fraction of semantic representations as preserved as to sustain correct performance in a given task, while r is the probability of correct retrieval of a preserved representation. These indices however can be interpreted as providing a direct estimate of consistency, as consistency is the only criterion that this approach takes into account in order to distinguish storage from access deficits.

The analysis has been applied to the results of the Identity Matching test collected in Session I and II, and to the results of the S.J.T. test, collected in Session II. As four repetitions of the S.J.T. test were available, all possible permutations of three over four trials were taken into account[3]

Results are summarized in Tables 5.7 and 5.8. In the case of the Identity Matching test the values of r and s for the Left hemisphere are very close to the maximum value (one), as expected from performance being almost at ceiling in this task. The Right Hemisphere showed a different pattern of performance: the storage index s is quite low, while the r index is much higher.

The S.J.T. test produced basically the same pattern of results, the only difference

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In fact the statistics for four repetitions of the same task is not available.

being a minor 'storage' deficit shown also by the Left Hemisphere, that can be attributed to the major intrinsic difficulty of the task. The s values for the Right Hemisphere (global performance) are very low, ranging between 0.23 and 0.36 for the various permutations of 3 of the 4 available trials, while the r values are much higher, between 0.79 and 1.00.

STORAGE and RETRIEVAL in Identity Matching

	r	s
Left Visual Field	0.79	0.36
Right Visual Field	0.96	0.98

Table 5.7: Estimate of the retrieval (r) and storage (s) indices obtained from the results of the three repetitions of the Identity Matching test (June and October 1996).

STORAGE and RETRIEVAL in S.J.T. test

Visual Field	*Left*	*Left*	*Right*	*Right*
	r	s	r	s
A B C	0.89	0.29	0.83	0.87
B C D	0.92	0.23	0.90	0.75
C D A	0.93	0.24	0.93	0.72
D A B	1.00	0.23	0.94	0.71
mean value	0.94	0.25	0.90	0.76

Table 5.8: Estimate of the retrieval (r) and storage (s) indices obtained from the results of the four repetitions of the S.J.T. test (April and July 1996). As the statistics is available up to three repetitions, all the possible permutations of three out of four trials have been considered. The trials are conventionally labeled with A, B, C and D. The mean of the four permutation is also given in the last raw.

Comment.

The patient definitely exhibits a consistent pattern of performance in both visual fields. The 'deficit' of performance in the left visual field - right hemisphere can be interpreted as a *deficit of storage* in the sense that **the semantic representations that would be needed to sustain performance are either lacking or somehow massively underspecified.**

Consistency can be taken as an indirect evidence of correct physical lateralization of the stimuli: an inconsistent pattern of performance would have authorized the speculation that correct performance was due to accidental spreading of information in the left hemisphere as a consequence of a failure in lateralization.

5.4.1 The 'Same' or 'Different' Visual test (Session III).

In the view of the difficulties that patient M.E. had in performing the Identity Matching task with stimuli lateralized to the left visual field, a test was designed in order to measure the ability to identify complex items with minimal task demands: the patient was simply required to indicate if two successive stimuli, the first being lateralized, were identical or not. This task can be performed at the perceptual level as well as at the semantic level; if performance with lateralized stimuli was found to be poor in this task, this would be evidence that the difficulties of the patient in performing semantic tasks could arise already at the level of the perceptual identification of the visual stimuli.

Methods and Materials.

40 pictures of objects, animals, vehicles and people were extracted from several magazines and books, and were reproduced on slides using the already described criteria for lateralized presentation. Two sequences of 40 stimulus and target couples were formed by alternating in a pseudo-random way 20 couples in which stimulus and target were different and 20 in which they were equal. The stimuli coupled with identical targets in the first sequence were coupled with different targets in the second sequence, and vice-versa. The two sequences were also balanced for side of presentation of the stimuli. The experiments were run in two conditions. In the *definite time condition* the stimulus and the target were both presen-

ted to either visual field for 200ms, one immediately after the other; in the *indefinite time condition* the target was presented in free vision. The subject was instructed to give his response by pressing a key on a board if the two items were identical, and another adjacent key if they were not. The wrist of the responding hand was fixed, so that only the index finger could be moved on the board. The experimental conditions were the usual ones. The experiment in the "indefinite time" condition was run first.

Results.

In the "indefinite time" condition the patient performed 33/40 (83%) correct in the Left Visual Field, which is statistically better than chance (Binomial test, $p < 0.0005$) and 39/40 (98%) correct in the Right Visual Field.

In the "definite time" condition the patient performed 24/40 (60%) correct in the left visual field, which is not different from chance level (Binomial test, $p > 0.05$), and 40/40 (100%) correct in the right visual field. Performance in the 'indefinite time" condition (left visual field) is statistically better than performance in the 'definite time" condition (Sign test, $p < 0.02$).

Comment.

Results at the 'Same' or 'Different' visual test differed according to experimental conditions. Performance in the right visual field was always at ceiling, while in the case of the stimuli presented to the left visual field the duration of the presentation of the target item had a clear influence on the results: performance was much better than chance only in the 'indefinite time' condition, i.e. when the target was presented in free vision. In this case it reached a reasonable level (83% correct). A possible explanation of this dissociation is in the difference in memory load across the two tasks. Furthermore the rapid presentations of two lateralized stimuli, that were flashed one immediately after the other, might have had a confounding effect. Anyway neither of these effects was present when stimuli were flashed in the left hemisphere, suggesting that the right hemisphere of M.E. could be more sensitive than the left to the perceptual qualities of the stimuli, such as time duration and/or to the memory load required for the task.

5.5 Complementary investigations: Naming experiments.

All the stimuli used in the visual experiments were also shown to M.E. in lateralized presentation to be named. The items of the S.J.T. Test were presented with the usual lateralization procedure (presentation time: 150 ms) in Session II (June 1996). This experiment was performed just after the S.J.T. Test. The two sequences of stimuli used in the 'Same' or 'Different' Visual test were presented for naming in Session III (October 1996). On this occasion the naming experiment was performed first, that is before the Identity Matching task.

Results.

The patient correctly named all the items from S.J.T. Test presented in his Right Visual Field except one (98% correct), and he also named 17/61 (28% correct) of the same items when presented in the Left Visual Field. He named correctly all (100% correct) the items used in the 'Same' or 'Different' Visual test presented in the Right Visual Field; 13/40 (33% correct) of the same items were named when presented in the Left Visual Field.

Comment.

The level of performance is very similar in the two naming experiments: in particular E.M. was able to name around 30% of the stimuli presented in his left visual field. The error analysis given in Table 5.9 however shows a substantial difference in the nature of the errors produced in the two experiments. In the experiment performed with the stimuli from the S.J.T. test there is a certain tendency to produce perseverations or to give information about the color of the stimulus, although this information is either wrong or aspecific ("A white thing"). In the experiment with the stimuli from the 'Same' or 'Different' test almost only "I did not see anything" responses were produced as errors. The difference may be due to the fact that the stimuli of the S.J.T. test were presented for naming just after the semantic test had been performed: in this case the patient was already very familiar with the set of items to be named, and seemed to be more keen to produce perseverative answers or to provide a kind of aspecific answer about the color of the stimulus. On the contrary the stimuli from the 'Same' or 'Different' test were presented to the patient for the first time in the naming task. In this condition almost no perseverative answers were obtained.

ANALYSIS of NAMING ERRORS

	old set	*new set*
perseveration	11	0
color	9	0
visual	3	1
semantic circumlocution	2	2
superordinate	1	0
"I didn't see anything"	13	27

Table 5.9: Analysis of the type of naming errors produced with the stimuli from the S.J.T. test (old set) and with the stimuli from the 'Same' or 'Different' test (new stimuli) presented to the Left Visual Field. The two set of stimuli are called 'old' and 'new' because in the first case the naming experiment was performed after the other experiments using the same stimuli, while in the second case it was performed first. The error type denoted as 'color' refers to an answer given in the following form: "A *..color..* thing". On 4 occasions the answer was just "A white thing". On the other occasions the information about the color was wrong.

5.6 Complementary investigations: experiments of object recognition in the tactile modality.

In this section a preliminary investigation on object identification using tactile input is described. The aim of this investigation was to provide some pilot results for the design of experiments with higher number of stimuli, which would be devoted to the investigation of semantic access from the tactile modality.

As documented earlier the patient has been reported to show left hand anomia, in that he has never been able to mime of the use of objects with his left hand out of view. As the instruction to mime the use of objects were given always only verbally, an inability to mime could have been due to a comprehension deficit: negative results in those task do not exclude the possibility that a correct identification of the item presented to the left hand has occurred. In the following two experiments verbal instructions were avoided. Furthermore many familiarization trials were performed in free vision and with feedback on the exactness of the responses in order to examplifie the task.

5.6.1 The 'Same' or 'Different' Tactile test (Session III).

This test was devised on the lines of the 'Same' or 'Different' visual test, but with two substantial differences: first only manmade items were used as stimuli, and second the patient was allowed to manipulate the object without any time limit.

Methods and Materials.

In this test 32 common manipulable objects were used. The patient was sitting in an armchair with the eyes occluded by a dark bandage and one hand on a table in front of him. The other wrist was blocked to the armchair. An object was given to him in the hand and he was allowed to manipulate it without time limits; he was prohibited to produce sounds by touching the table with the object. Then the object was removed. Immediately after another object, either identical to the first one, or different, was given to him for manipulation. After manipulation (again without time limits), the subject was instructed to hand the object back to the experimenter and then shift his hand toward the left side of the table if the two object were identical, or toward the right side if they were different. Many familiarization trials were performed in free vision and with a different set of objects before the testing sessions, in order to ensure that 'both hands' had understood the procedure well. 16 'Same' and 'Different' couples were presented in pseudo-random order to the right and then to the left hand; then 'Same' and 'Different' couplings were inverted and the test was presented to the left hand first.

Results.

The patient performed 32/32 (100%) correct with the Right hand, and 16/32 correct with the Left hand, which is exactly chance level (50%).

Comment.

The subject was not able to perform this simple tactile identification task with his left hand. To some extent this result is reminiscent of the result in the 'Same' or 'Different' visual task performed in the 'definite time' condition. Apparently when both stimulus and target were lateralized right hemisphere performance dropped to chance level. However the possibility that the right hemisphere had not grasped the meaning of the motoric response it was asked to provide cannot be ruled out.

In the next experiment a procedure that is more similar to the 'Same' or 'Different' visual task performed in the 'indefinite time' condition was adopted. Furthermore the 'symbolic' response ('left' or 'right' for 'same' or 'different') was substituted with a more 'concrete' pointing procedure.

5.6.2 The Tactile-Visual Matching test.

In this experiment the patient is required to choose among three visually presented objects, the one that he has just manipulated with one hand, out of vision.

Methods and Materials.

The patient was sitting in an armchair with his eyes occluded by a dark bandage and one hand on a table in front of him. The other wrist was blocked to the armchair. An object was given to him in the hand and he was allowed to manipulate it without time limits; he was prohibited to produce sounds by touching the table with the object. Then the object was removed. The same object and two distractors were placed on the table in randomized positions. After each presentation the bandage was removed and the subjected was required to point to the object he had just manipulated with the index finger of the same hand. 20 objects were presented as stimuli. The subject was provided with some familiarization trials performed with the left hand and in free vision.

Results.

The patient performed 12/20 (60%) correct in this test, which is statistically better than chance (Binomial test, $p < 0.01$, chance level=33%).

Comment.

As in the 'Same' or 'Different' visual test - indefinite time condition, performance in the left visual field was found to be better than chance. Overall the results of the right hemisphere in the tactile modality remained at the same level as in the visual modality. However for technical reasons these experiments were realized with a rather limited number of stimuli, so further experimental investigation would be necessary to derive conclusive evidence. The hint from the actual results was that semantic abilities were rather limited also when the tactile modality was employed as input channel.

5.7 General discussion.

In this experimental study the semantic abilities of the callotomized patient E.M. were investigated. At the age of 19 the patient underwent the callosal section to limit epileptic seizures that he developed after a traffic accident occurred when he was 8. Till that age, the patient had developed normal cognitive abilities and did not show any sign of neurological deficit. The present investigation started many years post-surgery, in a period in which the neuropsychological profile of the patient appeared to be stable. Patient E.M. presented with the classical symptoms of the disconnection syndrome, as manifested by the inability to transfer lateralized information across the hemispheres (see case report).

The experimental investigation focussed on the detection of the presence of semantic representations accessible from visual input in the right hemisphere, and on the comparison of the performance of the two isolated hemispheres in the same semantic tasks. The last point in particular was included in the investigation in order to verify an hypothesis on the structure of visual semantic representations, proposed as an explanation for the pattern of dissociation presented by the Semantic Dementia patient R.M., as discussed in Chapter 3. As during the years following the callosotomy the patient had never been able to access speech from his right hemisphere, all the experimental procedures used non verbal responses, usually pointing to the target in a multiple choice array.

It is generally assumed in the literature that the isolated right hemisphere is able to identify perceived items and to perform delayed matching to sample on the basis of non-verbal memory traces (Milner and Taylor, 1972; Milner et al., 1990). Furthermore, although the majority of the investigations on semantic memory function in the split brain have focused on the representation of word meaning, it is clear that whenever word-picture matching was used as an experimental procedure, indirect evidence was also obtained that the pictures were perceived as meaningful stimuli (Gazzaniga and Smylie, 1984; Gazzaniga et al., 1984; Gazzaniga and Miller, 1989). In some cases, the ability to mime with the left hand the use of objects presented to the left visual field was documented in the course of the preliminar neuropsychological assessments which precedes more specific experiments (Gazzaniga and Smylie, 1984; Berlucchi et al., 1997). This ability may co-occur with a complete left visual field anomia (Sidtis et al., 1981; Berlucchi et al., 1997).

E.M.'s ability to identify pictures of real objects tachystoscopically presented in either visual field was investigated in a series of experiments, in which the answering procedure was kept as simple as possible, in consideration of the possibility that a praxic deficit of the left hand might influence the outcome of the experiments. In tasks requiring only identification of the visual stimulus, such as the 'Same or Different' visual test, performance in the right visual field was at ceiling, while it was better than chance but not as good for stimuli presented in the left visual field. We observed that if stimulus and target were both lateralized, then performance of the right hemisphere dropped to chance level. This result was replicated when similar experiments were performed using the tactile modality for input (Sec.5.6); it seems to indicate some processing limitations in the right hemisphere.

We devised a lateralized version of the Semantic Judgement Type (S.J.T.) test (see chapter 3 for a detailed description), to which the patient was submitted in four different trials across the investigation. Contrary to the hypothesis that the right hemisphere could be preferentially involved in some types of judgements but not others, we found that performance with stimuli presented in the left visual field was not influenced by the nature of the semantic associations required. Although definitely better than chance, the right hemisphere's performance in this task was found to be rather low. It must be considered however that the patient's level of performance was not too high even with stimuli presented in the right visual field: in particular we found a significant drop of the level of performance with right visual field stimuli when the spatial co-occurrence of stimulus and target had to be detected in order to perform the task, and a significant increase in the level of performance in the class of judgements requiring to match items that are used together in the same action. The judgement of co-occurrence was the only type of judgement in which the two hemispheres performed at the same level. It is possible to speculate that the left hemisphere would be disadvantaged in this type of judgement due to his presumably inferior competence in the analysis of the spatial arrangement of the visual scene.

The same visual material utilized in the S.J.T. test was employed in a different task, the Identity Matching test, in which only semantic identification of the items was required. While the left hemisphere performed at ceiling in this task, thus supporting the hypothesis that failures in the S.J.T. test were due to actual inability to perform the judgement and not to misidentification of the stimuli, the right hemisphere performed only slightly better than in the S.J.T. test.

The results of the S.J.T. test and of the Identity Matching task were analyzed in detail in order to assess if the low level of performance of the right hemisphere was due to some experimental or epiphenomenal factors other than a semantic deficit. In fact while a positive result obtained with a split brain patient with stimuli lateralized to the right hemisphere is clear evidence that the right hemisphere is able to perform the task, a negative result is not a straightforward evidence that this is not the case. This is especially true in the case of split brain patients whose right hemisphere is deprived of linguistic competence, in which case only indirect evidence that the right hemisphere understood the task can be provided. In the present case for example, we noted that E.M. had a tendency to improve his level of performance with stimuli lateralized to the left visual field in the course of the task, both in the Identity Matching test and in the Semantic Judgement Type test. This result could be interpreted as the effect of an initial difficulty of the right hemisphere in grasping the task. A pattern of consistent performance across trials would be evidence against this interpretation if the stimuli are presented in different order in the different trials. This is the case of the Identity Matching test in which on one occasion stimuli were presented in reversed order: the estimate of the storage index for the right hemisphere indicate a high degree of consistency across trials. In the Semantic Judgement Type test on the contrary the same order of presentation was adopted in all four trials. Although the S.J.T. test employs the same procedure and the same stimuli as in the Identity Matching test in principle it is possible that the right hemisphere could have had more difficulties in understanding the semantic task, which is more abstract and intrinsically more difficult (as even the difference in performance of the left hemisphere across the two tasks suggests). Further repetitions of the S.J.T. test with random presentation of the stimuli are already planned to experimentally address this issue.

Another problem for the interpretation of negative results in the split brain is the presence of the so called "holes of consciousness": in the presence of stimulations delivered to both hemispheres split brain patients might have the tendency to miss some of the right hemisphere stimuli (Reuter-Lorentz et al., 1995). As split brain patients are usually constantly treated with antiepileptic drugs, it is possible to ascribe the phenomenon to a state of reduced alertness. We have preliminary evidence (to be described elsewhere) that the pharmacological treatment might have a profound influence on the cognitive behavior of our patient, as we detected a striking increase of performance of the right hemisphere (from chance level to 80% correct in four alternative word-picture matching task!) in correspondence to a change in the antiepileptic therapy[4]. However we also considered the possibility that the right hemisphere of our patient might have undergone partial epileptic disturbances during the tasks. We performed an analysis of the runs of failures in order to assess if they were statistically regular (that is, if such runs were to be expected given the dimension of the sample and the probability of failure), and we found that they were. Also consistency is evidence against the possibility of temporary random interferences with the execution of the task, because a random disturbance would produce inconsistent performance.

A post hoc analysis of the experimental material excluded that simple perceptual cues could have been used to sustain performance, and finally it was shown that the position of the target on the screen (which could be left, right or central with respect to fixation) was not predictive of performance, as would be the case if E.M. had shown a tendency to

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A global re-evaluation of the cognitive abilities of the patient is needed, together with a replication of the experiments in the non-verbal modality, in order to assess if the improvement is long-lasting, if it is language-specific or if it is generalized to all cognitive functions. Furthermore in this last case, an improvement of performance of the left hemisphere in the more complex tasks, such as the S.J.T. test should be also expected.

'neglect' the one of the three items presented in the right most position. As a result of these controls we can assume that the level of performance reached by the patient in the semantic tasks with lateralized stimuli provides a realistic estimate of the semantic abilities in the isolated left and right hemispheres.

In line with the evidence of some semantic processing in the right hemisphere, in the course of the last two sessions of experimental investigation, E.M. succeeded in naming about one third of the stimuli presented in his left visual field. The level of performance in naming, a task in which the probability of correct guessing is virtually null, was quite high if compared with performance in the non-productive semantic tasks discussed earlier, which all included at least 33% probability of correct guessing by chance. This result was unexpected given the well documented left hand anomia in this patient, but the emergence of some ability to name stimuli presented to the right hemisphere a long time after callosotomy has been recently reported for patient J.W. (Baynes et al., 1995).

Leaving aside this issue, that will be addressed with further experimental enquiry, we observed that the pattern of results obtained in the semantic tasks with stimuli presented to the right hemisphere was quite uniform across different experiments, documenting severe limitations in the semantic processing going on in the right hemisphere, which was however found to be definitely better than chance. The nature of the "deficit" of the right hemisphere semantic system has been described as being basically of the 'storage type': the consistency analysis revealed that the semantic representations in the right hemisphere were often either lacking or too underspecified to support performance. The picture we derived from the results seems to point to a right hemisphere semantic system which is basically a kind of degraded [5] semantic system. The current experimental investigation however cannot distinguish between the absence of a given semantic representation from the presence of a grossly underspecified semantic representation. This difference would be relevant in order to evaluate some recent proposals on the functions of the right hemisphere semantics, which tend to assign a specific role to the supposed 'looseness' of the right hemisphere representations (see Chapter 4 for a review) in sentence comprehension.

An interesting speculation can be proposed in the context of the neural network approach to give an account of the evidence, if one assumes that the right hemisphere semantic network is *much smaller* (including a smaller number of neurons) than the left hemisphere one. When an associative network is small with respect to the number of patterns it has to deal with, it is constrained out of the range of *low loading*, that, as discussed in the first chapter, is the optimal range for retrieval: in fact high loading produces an increase in *quenched noise* which has a detrimental effect on the network dynamics. In practice it increases the interference across the different patterns. A possible way of avoiding high loading could be by learning only some of the stimuli and 'forgetting' the rest. A sensible choice could be to only sustain the semantic representations of very frequent words or highly familiar visual stimuli, which are probably also the more relevant stimuli for the subject. In any case the role of this putative right hemisphere 'support' semantics in the intact brain would be unclear.

The well developed semantic functions of some split brain patients (Sidtis et al., 1981; Gazzaniga and Smylie, 1984; Gazzaniga et al., 1996) have been often attributed to a functional reorganization of the brain occurring early in childhood. At the same time we are

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How much degraded is a matter of future experimental investigation.

faced with the results of the imaging experiments showing a preferential left activation in different types of semantic tasks (Martin et al., 1995; Martin et al., 1996; Mummery et al., 1996; Price et al., 1996; Vandenberghe et al., 1996). For example, (Vandenberghe et al., 1996) used both living and non-living items as stimuli in a PET experiment in which associative and 'visual' semantic relationships were tested using either words or pictures; they found no task specific activation at all in the right hemisphere. However when living and non-living items were kept separate, a significant bilateral temporal activation has been detected. In particular (Mummery et al., 1996) found bilateral activation of the antero-medial temporal lobe specific for a fluency task with natural kind categories, and (Price et al., 1996) found bilateral medial anterior temporal (Brodman's Area 38) activation for object recognition. Unfortunately the level of agreement across different experiments is still limited, and more replications and extensions of the results would be needed.

It is interesting to note than when right hemisphere activation specific to the semantic component of the task has been detected, an homologous activation of the left hemisphere was always found (Martin et al., 1995; Martin et al., 1996; Mummery et al., 1996; Price et al., 1996), suggesting a possible relevance of the anatomical continuity of the involved temporal areas via the callosum. In the absence of anatomical continuity, as in the case of the split brain population, the 'normal' right hemisphere processing might be limited. The hypothesis of a smaller 'support' semantic system in the right hemisphere seems to provide an explanation for the lack of right activation in the PET experiments: in fact, this imaging technique is sensible to prolonged metabolic rises due to a robust and continuative activation of a given region (Roland, 1997), and it is possible that a 'limited' right hemisphere semantic system would not provide enough signal: this would be the case if for example only some of the items presented during the task were indeed adequately represented in right hemisphere semantics. If this is the case, it is possible that a more sensitive and faster technique, that is functional M.R.I., which has already proved to be suitable to detect activation of very small systems such as the hippocampal network (Gabrieli et al., 1997), will shed some light in the controversial field of right hemisphere semantics.

Appendix A

Estimate of the regularity of the samples from the Theory of Success runs.

Patient M.E. Test session II.

For each task (Identity Matching and S.J.T. tests) the sequences of responses are explicitly reported. The underlined 'runs' are the ones that have been studied within the statistical approach described in Chapter 5, Section 4.3.

In the line above the sequence, the stimulated visual field, the hemisphere supposed to perform the task and the hand producing the response are reported; furthermore as for technical reasons the tests are both divided into two parts that can be administered in different parts of the testing session, the two half-sequences are reported separately (marked first half and second half at the end of the line above the sequence).

In the first line under each sequence (marked Result:) it is specified the total number of successes 'tot(1)', the total number of failures 'tot(0)', and the probability of success in that sequence 'prob.(1)' ($prob.(1) = \frac{tot(1)}{N}$), to be used in the analysis. The probability of failure is obviously $[1 - prob.(1)]$.

In the line marked Global result:, the results of the two half-tests are collapsed (sum(1) and sum(0) are the sum of the number of successes and failures of each half test) and the longest run is analyzed using the probability of success of the entire test.

In the second line under each sequence (marked Feller Test:) it is specified:

- the rank (length) of the analyzed run, 'r';
- the estimated sample length, expressed as the mean M ± the Standard Deviation S;
- the actual sample length 'N';

- the probability of occurrence of a run of rank r, 'prob(r)';

Note that if $(M - S) < r$ the sequence are assumed to be regular by the analysis of the runs.

Identity Matching - Left Visual Field sequences

left visual field - right hemisphere - left hand - first half

1 1 1 0 1 0 1 0 1 0 1 1 0 1 1 0 1 $\underline{0\ 0\ 0\ 0\ 0\ 0\ 0\ 0}$ 1 1

Result: tot(1)=13 tot(0)=14 prob.(1)=0.48

Feller Test: r=8 M=(392.85±386.33) N=27 prob(r)=0.0205

left visual field - right hemisphere - left hand - second half

1 0 0 1 1 1 0 1 1 1 1 0 1 1 0 1 0 $\underline{1\ 1\ 1\ 1\ 1\ 1}$ 0 1 1

Result: tot(1)=19 tot(0)=7 prob.(1)=0.73

Feller Test: r=6 M=(20.77±16.46) N=26 prob(r)=0.2803

Global Result: sum(1)=32 sum(0)=21 prob.(1)=0.60 r=8 M=(2541.46±2534.62) N=53 prob(r)=0.0109

left visual field - right hemisphere - right hand - first half

1 0 0 1 1 0 1 1 1 0 1 1 0 1 0 0 0 0 1 $\underline{0\ 0\ 0\ 0\ 0\ 0}$ 1 1

Result: tot(1)=12 tot(0)=15 prob.(1)=.44

Feller Test: r=6 M=(71.42±66.86) N=27 prob(r)=0.0514

left visual field - right hemisphere - right hand - second half

1 1 0 $\underline{1\ 1\ 1}$ 0 0 $\underline{1\ 1\ 1}$ 0 1 1 0 1 0 0 1 0 1 1 0 1 0 1

Result: tot(1)=16 tot(0)=10 prob.(1)=0.61

Feller Test: r=3 M=(8.73±6.67) N=26 prob(r)=0.9020

Global Result: sum(1)=28 sum(0)=25 prob.(1)=0.53 r=6 M=(464.25±459.34) N=53 prob(r)=0.1477

S.J.T. test - Left Visual Field sequences.

left visual field - right hemisphere - left hand - first trial - first half

$\underline{0\ 0\ 0\ 0\ 0}$ 1 0 0 0 0 1 0 1 1 1 1 0 1 0 0 0 1 0 0 0 0 1 1 0 0 0 0 1

Result: tot(1)=11 tot(0)=22 prob.(1)=0.33

Feller Test: r=5 M=(19.41±15.83) N=33 prob(r)=0.4714

left visual field - right hemisphere - left hand - first trial - second half

$\underline{1\ 1\ 1\ 1\ 1\ 1\ 1}$ 0 1 1 0 1 1 0 1 1 0 1 1 1 1 1 1 0 1 0 1 1

Result: tot(1)=22 tot(0)=6 prob.(1)=0.78

Feller Test: r=7 M=(21.33±16.29) N=28 prob(r)=0.2769

Global Result: sum(1)=33 sum(0)=28 prob.(1)=0.54 r=7 M=(160.00±154.67) N=53 prob(r)=0.2388

left visual field - right hemisphere - left hand - second trial- first half

$\underline{0\ 0\ 0\ 0\ 0\ 0\ 0\ 0\ 0\ 0}$ 1 0 0 0 1 1 0 1 1 1 1 1 0 0 0 0 1 0 0 0 0 0 1

Result: tot(1)=10 tot(0)=23 prob.(1)=0.30

Feller Test: r=10 M=(114.67±106.95) N=33 prob(r)=0.0703

left visual field - right hemisphere - left hand - second trial - second half

1 1 1 1 0 0 1 0 1 1 1 0 1 1 1 1 0 1 0 $\underline{1\ 1\ 1\ 1\ 1\ 1}$ 0 1 1

Result: tot(1)=21 tot(0)=7 prob.(1)=0.75

Feller Test: r=6 M=(18.47±14.18) N=28 prob(r)=0.3115

Global Result: sum(1)=31 sum(0)=30 prob.(1)=0.51 r=10 M=(2455.4±2446.84) N=53 prob(r)=0.0110

left visual field - right hemisphere - right hand - first trial - first half

1 0 0 1 0 1 0 0 0 0 0 1 0 0 1 1 0 0 0 1 1 0 1 1 $\underline{0\ 0\ 0\ 0\ 0\ 0\ 0}$ 1 1

Result: tot(1)=12 tot(0)=21 prob.(1)=0.36

Feller Test: r=7 M=(60.38±55.11) N=33 prob(r)=0.1685

left visual field - right hemisphere - right hand - first trial - second half

1 1 1 1 0 0 1 1 1 1 0 $\underline{1\ 1\ 1\ 1\ 1}$ 0 0 0 0 1 1 0 1 1 0 1 1

Result: tot(1)=19 tot(0)=9 prob.(1)=0.68

Feller Test: r=5 M=(18.37±14.80) N=28 prob(r)=0.4057

Global Result: sum(1)=31 sum(0)=30 prob.(1)=0.51 r=7 M=(4278.51±4272.47) prob(r)=0.0986

left visual field - right hemisphere - right hand - second trial - first half

0 0 0 0 0 1 0 0 0 0 1 0 0 0 1 1 0 1 1 1 1 1 0 0 1 1 $\underline{0\ 0\ 0\ 0\ 0\ 0}$ 1

Result: tot(1)=12 tot(0)=21 prob.(1)=0.36

Feller Test: r=6 M=(37.64±33.22) N=33 prob(r)=0.2721

left visual field - right hemisphere - right hand - second trial - first half

1 0 1 $\underline{0\ 0\ 0}$ 1 0 1 1 0 1 1 0 1 1 0 1 0 $\underline{1\ 1\ 1}$ 0 0 1 0 1 1

Result: tot(1)=16 tot(0)=12 prob.(1)=0.57

Feller Test: r(1)=3 M=(10.23±8.17) N=28 prob(r)=0.9468

Feller Test: r(0)=3 M=(20.31±18.20) N=28 prob(r)=0.6848

Global Result: sum(1)=28 sum(0)=33 prob.(1)=0.46 r=6 M=(275.78±270.95) prob(r)=0.30

Conclusions

In this thesis three different issues concerning the study of semantic memory function have been addressed.

The first issue concerns the distinction between the so called 'access' and 'storage' type of impairments of the semantic system. The experimental evidence on which the distinction is grounded is discussed. In particular the crucial criterion for distinguishing the two types of impairments based on consistency of performance is considered, and a new statistical tool for the measure of consistency of performance in repeated trials of multiple choice tests is realized on the base of a stochastic model of retrieval from semantic memory. The application of this statistical technique, which allows for the estimate of two indices measuring respectively the proportion of preserved semantic representations and the probability of correct retrieval of these representation, is shown to be a useful tool for the empirical distinction between storage and access type of impairments.

More insight on the mechanisms underlying the two types of impairments is gained with the analysis of the pattern of performance typical of the storage and of the access impairments in the context of a neural network model of an associative memory. Furthermore the biological plausibility of the 'refractoriness' hypothesis is discussed, and a specific neurophysiological explanation for refractoriness is proposed.

The second part of the thesis addresses the issue of the structure of the semantic system. A neural network model is proposed on the base of the multimodal hypothesis on the structure of the semantic system: the model is composed of a set of associative neural network of the Hopfield type, and stores multimodal patterns of memories using a learning rule of the Hebbian type. The suitability of this architecture as a computational device for the storage of semantic memories is tested by simulations and an analytic treatment is made of the equilibrium properties of the system (in the context of a statistical mechanics approach using mean field equations).

A single case study of a patient with a modality-specific semantic memory impairment provides empirical support to the model. In particular the experimental investigation provides a preliminary definition of the nature of the visual semantic representations and of their privileged links with other cognitive components such as action schemata and more complex behavioural routines.

The last chapters of the dissertation address the issue of semantic memory processing in the right hemisphere: the literature is critically revised and an experimental investigation of semantic functions in a commissurotomized patient is described. In particular the ability to semantically process visual stimuli is analyzed. The experiments document a drastically reduced semantic competence of the isolated right hemisphere in this patient.

Finally from the point of view of the methodology, this work is meant to document the advantages that an interdisciplinary approach can provide in modelling brain functions.

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