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Titolo della tesi di Dottorato

Memory for faces and proper names: episodic and semantic aspects

Direttore della Scuola: Ch.mo Prof. Luciano Stegangno
Supervisore: Ch.mo Prof. Patrizia Silvia Bisiacchi

Dottorando: Dott. MARCO CALABRIA

‘…there is so complete a subjection to certain rules and formulas, that there result an art full of confusion and obscurity calculated to embarrass, instead of a science fitted to cultivate the mind. By these considerations I was induced to seek some other method [...]. And as a multitude of laws often only hampers justice, so that *a state is best governed when, with few laws, these are rigidly administered*; in like manner, instead of the great number of precepts of which logic is composed, I believed that the four following would prove perfectly sufficient for me, provided I took the firm and unwavering resolution never in a single instance to fail in observing them.

The first was *never to accept anything for true* which I did not clearly know to be such; that is to say, carefully to avoid precipitancy and prejudice, and to comprise nothing more in my judgement than what was presented to my mind so clearly and distinctly as to exclude all ground of doubt.

The second, *to divide each of the difficulties under examination into as many parts as possible*, and as might be necessary for its adequate solution.

The third, to conduct my thoughts in such order that, by commencing with objects *the simplest and easiest to know*, I might ascend by little and little, and, as it were, step by step, to the knowledge of the more complex; assigning in thought a certain order even to those objects which in their own nature do not stand in a relation of antecedence and sequence.

And the last, in every case *to make enumerations so complete*, and reviews so general that I might be assured that nothing was omitted.’

René Descartes, *Discourse on Method*, 1637

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Introduction

Encoding and retrieval of the names associated with people's faces is a daily task that is mastered with less than perfect success by most normal subjects. Although a huge number of such associations can be stored during a lifetime, and often can be retrieved after several decades, the task also regularly seems to reach the limits of human cognitive abilities if one has brief contact with many people. To date, we have accumulated some knowledge of the cognitive processes involved (Valentine, Brennen, & Brédart, 1996), but the neurophysiological bases of face-name pair learning is still lacking.

So, the first aim of this thesis is to investigate, through event-related potentials (ERPs), the encoding and retrieval of faces and proper names. First, an experiment was carried out on young adults to define the neurophysiological pattern during an associative learning and retrieval of face-name pairs, using a two alternatives task. Then the same experiment was conducted in older adults. The rationale of this latter experiment is based on the fact that one of the main reported and observed age-related changes of cognitive functions is in episodic memory. And in particular, the deficiencies in the episodic memory of older adults manifests as their relative inability to form and retrieve links between single bits of information, such as an associative deficit (see the 'associative deficit hypothesis' proposed by Naveh-Benjamin (2000)). So, face-name associative learning seems to be a good tool to test the associative deficit hypothesis. At same time, it is a relevant task which older adults are confronted with in their everyday life and for which they show some deficit (James, Fogler, & Tauber, 2008; Naveh-Benjamin, Guez, Kilb, & Reedy, 2004).

The last step of this project concerns the semantic aspects of face-name representation. If episodic memory accounts for the acquisition and retention of information in a particular context, semantic memory concerns general knowledge of the world (Tulving, 1972, 1984).

These semantic aspects were investigated in a patient with a neurodegenerative disease characterized by a breakdown of semantic memory, semantic dementia. The hypothesized degradation of semantic memory for famous faces and proper names will be investigated through explicit and implicit tasks, such as repetition priming.

The *fil rouge* of this project is to take into account the evidence present in the literature concerning what is known about cognitive psychology, neurophysiology and neuropsychology from the young to adults and brain-damaged patients. To achieve this goal, in the first part of this thesis a brief review of published studies in the field of memory is considered, especially for faces and names. This is the backgound from which this entire project started and on which the discussion of results was based.

Chapter 1

Face processing and proper naming: cognitive correlates and neural bases

Vertumnus
Giuseppe Arcimboldo, 1590

Everything is in the **face**
Cicero

We must find the minimal mental fact whose being reposes directly on a brain-fact; and we must similarly find the minimal brain-event which will have a mental counterpart at all. Between the mental and the physical minima thus found there will be an immediate relation, the expression of which, if we had it, would be the elementary psycho-physic law. But in taking the entire brain-process as its minimal fact on the material side it confronts other difficulties almost as bad.
In the first place, it ignores analogies on which certain critics will insist, those, namely, between the composition of the total brain-process and that of the *object* of the thought.
The second difficulty is deeper still. *The 'entire brain-process' is not a physical fact at all.*

What shall we do?

The Principles of Psychology
William James, 1890

1. Cognitive Psychology of Face Processing

Cognitive models were conceptualised according to data collected from laboratory experiments and in braindamaged patients. A number of information-processing models of face recognition were published during the 1980s.

The first tentative model describing components was made by Bruce (1979), but this period culminated with cognitive architectures proposed by Ellis (1986) and the most known theoretical framework for face recognition by Bruce and Young (1986).

These authors proposed a serial model as depicted in Figure 1. Basically, this model is conceptualised as made up of functional components, in the sense of any constraint of brain area involved (see below for more details about neural basis).

First of all, Bruce and Young postulated that we can use at least seven different information *codes* from faces: pictorial, structural, visually derived semantic, identity-specific semantic, name, expression, and facial speech codes. These codes are product of functional operations and not functional components per se. A pictorial code is a description of a picture: it is not equivalent to the viewer-centred information derived when a picture is seen. But it is conceived at a more abstract level, basically it is used when we made a yes/no recognition in a episodic memory task for a picture encountered before. But the pictorial code can act only for a restricted range of physical variation. So, structural code captured those aspects of the structure of a face essential to distinguish it from other faces. When a subject is presented with a face in a study session and in a consequent test session the recognition is partially impaired, even if the picture portrayed a familiar face. This effect is due to pictorial code.

What about structural code? It is more abstract and probably mediates the everyday recognition of familiar faces. It represents the face as a configuration, rather than single units. It that sense, recognition depends on the arrangements of the features rather than on the features themselves: for this reason, we could recognize famous faces even when single part are distorted or blurred. Consequently, structural codes for familiar faces differ from those formed to unfamiliar faces. Internal features are more important for recognition of familiar faces whereas internal and external features are equally important.

In Marr view 1982[1], when a face is perceived, primal sketch and viewer centred descriptions are constructed and they are, respectively, the layout of the image of the face, and the layout of the surfaces which gave rise to this image. It is not yet clear what description is needed for the recognition: a configurational and whole part based representation, or both. For example, Bruce and Young (1986) stated that several descriptions are needed for face recognition that are interconnected, some describing the whole face, some other the details of particular futures. So, a face is recognized as familiar when a match between an encoded representation and a stored structural code.

Some other information can be obtained even for unfamiliar faces: for example, we can judge sex and age even if we do not know people who we are confronted with. This kind of information is called *visually derived semantic code.* By contrast, *identity-specific semantic code* might describe semantic information of familiar faces: person's occupation, which his/her friends are, and so on.

All authors do not always use this distinction, but one reason to distinguish these two codes is the ways are made up. By the first we can infer information using physical features, by the latter we can derive information that are not dependent upon surface form, such as person's occupation.

Finally, Bruce and Young (1986) postulates a separate code for *names.* Name codes are conceived as output codes which allow a name to be generated. They could be considered a subclass of identity-specific semantic code, even if empirical evidences (everyday, laboratory studies and neuropsychology) support the hypothesis that they are separate.

These codes are considered as product of facial processing: what about the procedures generating and accessing to these codes?

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[1] Marr (1982) distinguished three representational stages beyon the retinal image. The *primal sketch* makes explicit the intensity changes present in the image; the *2 ½ sketch* is a viewer-centred representation that describes the surface layout if a viewed scene relative to the viewer. Finally the *3D model* defined as an object-centred representation allowing the recognition of objects from any point of view.

The answer is given by the Bruce and Young (1986). This model (see Figure 1) is conceived as a functional model, represented as a 'box and arrows' system, experimentally derived. First, a structural encoding is postulated that subserve a set of descriptions of the presented faces. It includes view-centred descriptions as well more abstract descriptions. View-centred descriptions provide information for the analysis of facial speech and expressions. Whereas expression analysis is independent, at a more abstract representation, providing information for the face recognition units (FRUs). This latter contains stored structural codes describing one of the faces known to a person. The FRUs allow the access to person identity nodes (PINs): it is a store containing one person identity node for each person known. The nature of these units is conceived of as analogical representations. For some researcher these representations emphasize characteristic features of the face, or for some others they are conceptualised as a multidimensional space where the central point correspond to a facial prototype and in which face is a specific point Brédart & Bruyer (1994). This hypothesis could explain a classical effect found in face recognition: 'other race effect'.

The last stage of the face processing is the *name* retrieval. The fact that names are stored separately explains because it is particularly difficult to retrieve them Brédart & Valentine (1998).

Bruce and Young's model postulated that FRUs, PINs, and name codes are processes that are activated sequentially, and this is well supported by empirical evidences: from mental cronometry to neuropsychology.

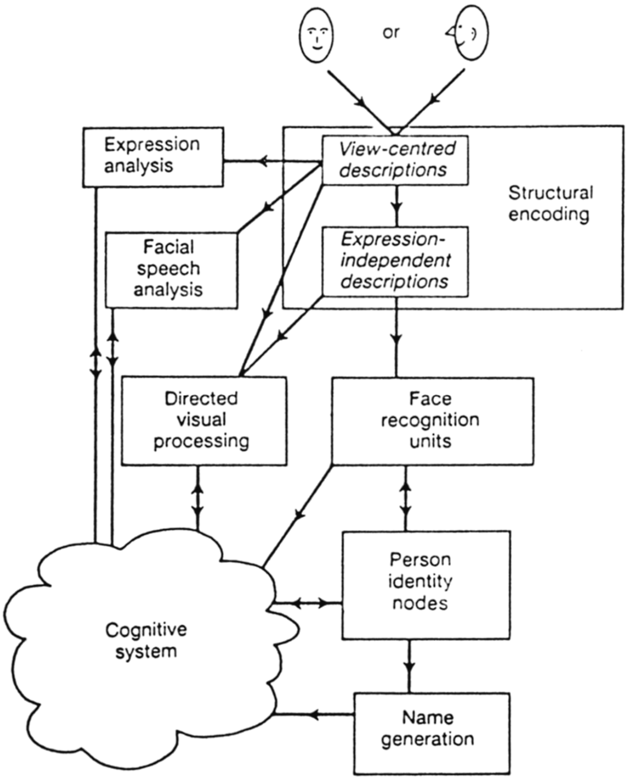

Figure 1. Bruce and Young's model of face processing (1986).

Another alternative model was hypothesised by Burton, Bruce & Johnston (1990) (see Figure 2). These authors designed an interactive activation and competition (IAC) network in order to explore the microstructrure of Bruce and Young's model. It comprises a number of units organized into pools or clusters. All the units belonging to the same pool are interconnected whit inhibitory links, whereas excitatory connections are between different pools. As for other connectionist models, input units receive the input from an experimenter an learning of the network is modulated by the number of the cycles and unit activations. Activation passes along excitatory links into the different pools so the level of activation increases. In particular, in Burton et al. (1990)'s model contains three kinds of units: face recognition units (FRUs), person identity Nodes (PINs) and semantic information units (SIUs). Basically, the first node is a store conceptualised as in the Bruce and Young's model. PINs are just cross-domain and modality free to biographical information[2] (for this model familiarity decision is taken at these levels). SIUs store the information describing the identity of individuals. This is one of the major differences between Burton et al.'s implementation and the Bruce and Young (1986).

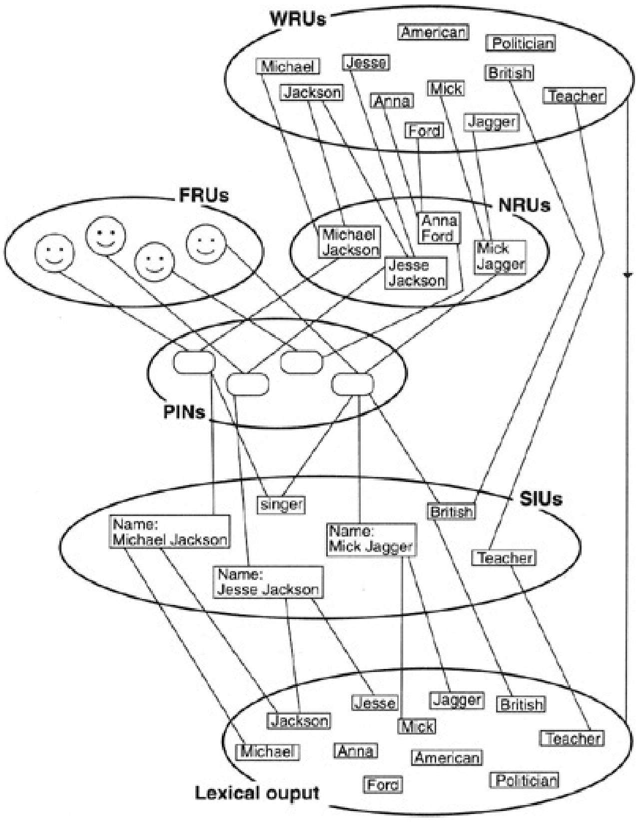

Figure 2. IAC model by Burton, Bruce & Johnston (1990).

Several advantages gives this model in terms of face processing. First of all, the model can account for the differences in the time-course and modality specificity of repetition and semantic priming. Burton et al. (1990) proposed that the mechanism for the repetition priming of face recognition was an increase of the weight of the connections between the FRU and PIN of a stimulus face. When a face is seen, the strength of the connection increases, and when the same face is encountered again, the activation of the PIN reaches threshold more quickly

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[2] Bruce and Young (1986) did not explicitly indicate that PINs include identity-specific semantic information or PINs allow the access to semantic information.

because more activation is pased to the PIN from FRU via the increased weight on the connection. Semantic priming is explained as an advantage of the spreading action of PINs via SIUs.

A further advantage of this model is that it can explain covert recognition of faces in patients without requiring any other processing mechanisms or pathways to be hypothesized. In that sense, prosopagnosic patients show a reduction of activation between connections (FRUs and PINs), instead of a disconnection. Simulations of 'lesioned' networks show that this approach can provide a parsimonious account of covert recognition in prosopagnosic patients.

> 'Because each facial part is the sum of its individual details
> and the whole face is the sum of its sections,
> the total assessment of it requires a careful visual addition'
>
> Penry, 1971

Beside the functional aspects of the face processing, one another aspect concerns the nature of representation of faces within the cognitive system. Two main hypotheses are advised to explain the representational aspects of perception and memory of faces: features-based and/or configurational approach.

In a recent review, Rakover (2002) proposed four main hypotheses: 1) the featural hypothesis; 2) the configurational hypothesis; 3) the holistic hypothesis; and 4) the norm hypotheses (the norm-based hypothesis and the 'hierarchy of schemas' hypothesis).

According the *featural hypothesis*, we perceive and remember faces by means of facial features. For example, we say that this is a picture of the face of Cyrano de Bergerac because only he has such a big nose. The face as a whole is perceived only as the sum of features, and the face is nothing but the joining of isolated facial features.

The *configurational hypothesis* claims that we perceive and remember faces by means of two kinds of information, namely featural and configurational, where the importance of the latter is generally conceived of as greater than of the former (e.g. Diamond & Carey, 1986; Rhodes, Brake, & Atkinson, 1993).

Diamond and Carey (1986) proposed this hypothesis as a solution to the facial inversion effect and as an alternative to the hypothesis that facial information is processed through a special cognitive mechanism. They stress that faces are visual forms 'sharing the same configuration'—hair above brow above eyes, and so on. Not all visual forms share the same configuration. Landscapes, for example, are not given this quality as one scene may include water and sky and another houses and trees.

Visual forms that do not share the same configuration are distinguishable by 'first order relational properties', namely according to the spatial relations between similar parts that constitute them. It is possible to distinguish faces by the spatial relations between the facial elements that define the shared configuration: these are called 'second-order relational properties'. In a similar way, Rhodes (1988) differentiated first-order features as those that may be described independently from other parts of the face (e.g. eyes, nose, mouth) from second-order features, characterized by the spatial relations between them, their position on the face and the shape of the face.

The third hypothesis is the *holistic* one. According to this hypothesis, we perceive and remember faces by using two kinds of information—featural and configurational—where these kinds are perceived as a single entity, the whole face. This perceptual wholeness is difficult to break down into its parts without seriously harming perception and remembering a face and its parts. The holistic hypothesis has two interpretations concerning the relation between feature and configurational information. According to the accessibility interpretation, the whole face is more accessible in the memory than its parts; according to the configurational coding interpretation, configurational information is more important than featural information—an interpretation not greatly different from the preceding hypothesis (e.g. Farah, Wilson, Drain, & Tanaka, 1995; Tanaka & Farah, 1993).

The *norm hypothesis* suggests that, all facial information, featural and configurational, is presented in a cognitive system as deviations from the norm (prototype), as distances from the abstract prototype face. These deviations emphasize the featural or the configurational qualities of a given face with respect to the norm.

One other long debate concerns the *face specificity* and the role of *expertise* in face processing. Gautheir and Logothetis (2000) some years ago wrote 'Is face recognition no so unique after all?'; and more recently, Gauthier and Bukach (2007) discussed the opportunity to reject the hypothesis accounting for face specificity in humans. The long debate of face specificity of face processing started some times ago and it is still vivid. Basically, two main theories have emerged in literature.

The domain-specificity hypothesis (e.g., Kanwisher, 2000; McKone & Kanwisher, 2005; Rhodes, Byatt, Michie, & Puce, 2004; Yin, 1969) suggests that the 'special' processing used for faces occurs only for faces. This hypothesis does not, per se, propose a mechanism for the origin of the special processing. It is possible, however, that special processing for faces has an innate component (de Haan, Humphreys, & Johnson, 2002; Morton & Johnson, 1991) and/or that it is necessary to obtain appropriate face experience at a particular time in development (e.g., a sensitive/critical period during infancy for the development of normal face processing, Le Grand, Mondloch, Maurer, & Brent, 2001, 2003, 2004).

In contrast, the expertise hypothesis (e.g., Carey, 1992; Diamond & Carey, 1986; Gauthier & Tarr, 1997; Meadows, 1974) suggests that 'special' processing for faces is a potentially generic ability that arises for faces because of substantial experience in individual level discrimination; this predicts that the special processing can also arise for any other object class through the same mechanism (e.g., in expert dog show judges looking at dogs from their breed-of-expertise). An important assumption of the expertise hypothesis is that the period of life when this experience is obtained is irrelevant: object expertise can be developed entirely as an adult, and the predictor of processing style is merely the amount of practice. This assumption was made explicit by the original proposers of the hypothesis (e.g., Diamond & Carey, 1986; Carey, 1992), and has remained implicit in subsequent research, which tests for face-like processing in subjects who have in many cases obtained their expertise as adults or teenagers (e.g., Gauthier, Skudlarski, Gore & Anderson, 200; Gauthier & Tarr, 1997; Grill-Spector et al., 2004; Xu, 2005).

2. Neuropsychology of Face Processing

"Prosopagnosia," which is derived from the Greek words for "face" (*prosopon*) and "not knowing" (*agnosia*). The term of this spectacular impairment was introduced by Bodamer in 1947 (Ellis & Florence, 1990), described an injury to a 24-year old man who suffered a bullet wound to the head.

One of the first review of lesion studies (De Renzi, Perani, Carlesimo, Silveri, & Fazio, 1994) clearly evidenced the role of right hemisphere. The lesions that cause prosopagnosia are usually found in ventral occipito-temporal cortex, involving the lingual and fusiform gyri, and are bilateral in most of the cases (Damasio, Damasio, & Van Hoesen, 1982; Sergent & Signoret, 1992), although right unilateral lesions can be the cause of the syndrome (e.g. Landis et al., 1988; Wada and Yamamoto, 2001; Uttner et al., 2002). However, since the advent of neuroimaging there has been good evidence of prosopagnosia from unilateral lesions of the right occipitotemporal cortex.

Since then, despite its rarity, a certain number of cases with a major deficit of face recognition have been described (see Farah, 1990; for more recent cases, e.g. Sergent and Signoret, 1992; Clarke et al., 1997; Gauthier et al., 1999; Laeng and Caviness, 2001). However, establishing relationships between structures and function based on clinical studies alone has always been problematic; the lesions of prosopagnosic patients are not always clearly identifiable, can be highly variable from case to case, and are usually very large and not limited to the structures subtending face processing. Relative to the study of patients with naturally occurring brain lesions, neuroimaging thus affords far greater anatomical precision and avoids the confounding factors associated with patient studies, such as any compensatory functional reorganization of the brain (Sergent et al., 1992).

There are two main impairments in face processing. The first is linked to a deficit in discrimination or matching unfamiliar faces (appercetive), whereas the second is related to the inability ot identify a face as a familiar person (Benton & Tranel, 1993).

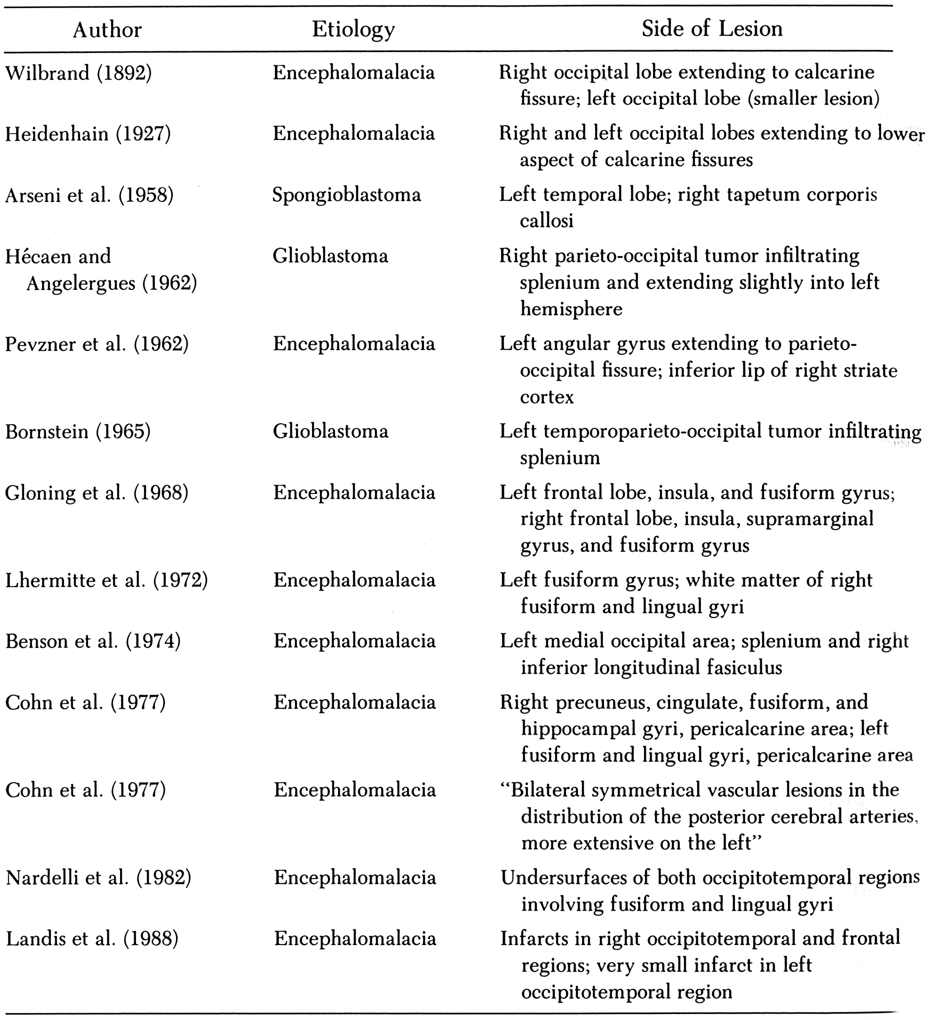
The defect to recognise a familiar face usually occurs for anterograde and retrograde periods: patients failed to judge familiar faces both people previously seen and newly presented ones. It is distinguishable to a proper naming defect because patients no longer experience the sense of familiarity related to those familiar faces.

When this defect is 'purely' defined, patients are free of major defects in visual perception and scored within normal limits in neuropsychological assessment testing visuo-spatial and perceptual abilities. Other modalities are intact, and it happens that these patients could recognise relatives on the basis of the voice. Or sometimes patients used some body or external face features (such as hairstyle, posture) in order to recognise familiar faces (Damasio et al., 1982; Damasio, Tranel, & Damasio, 1990).

The lesion site is generally a bilateral damage in inferior occipital and temporal visual associative cortices. Most case reported are caused by cerebrovascular disease, head injury, cerebral tumors (especially glioma), herpes simplex encephalitis (see Figure 3), and recently as in neurodegenerative disorders, such as Alzheimer's disease (Werheid & Clare, 2007) and frontotemporal dementia (Keane, Calder, Hodges, & Young, 2002).

It is important to distinguish these defects to those previously described. Sometimes some other visuo-perceptual abilities are affected, such as line orientation discrimination or pattern discrimination. It is commonly associated to with damage in right visual associative areas within the occipital and parietal lobes. In particular, inferior and superior components of areas 18 and 19 are critically involved of appercettive prosopagnosia.

In recent years, attention has been paid to an analogous impairment, congenital prosopagnosia (CP), which refers to the impairment in face processing that is apparent from birth in the absence of any brain damage, and occurs in the presence of intact sensory and intellectual functions. CP individuals are typically able to acknowledge that a face is present but are unable to identify the face and, hence, rely on voice or other cues such as clothing, gait or accessories for person identification.



Author	Etiology	Side of Lesion
Wilbrand (1892)	Encephalomalacia	Right occipital lobe extending to calcarine fissure; left occipital lobe (smaller lesion)
Heidenhain (1927)	Encephalomalacia	Right and left occipital lobes extending to lower aspect of calcarine fissures
Arseni et al. (1958)	Spongioblastoma	Left temporal lobe; right tapetum corporis callosi
Hécaen and Angelergues (1962)	Glioblastoma	Right parieto-occipital tumor infiltrating splenium and extending slightly into left hemisphere
Pevzner et al. (1962)	Encephalomalacia	Left angular gyrus extending to parieto-occipital fissure; inferior lip of right striate cortex
Bornstein (1965)	Glioblastoma	Left temporoparieto-occipital tumor infiltrating splenium
Gloning et al. (1968)	Encephalomalacia	Left frontal lobe, insula, and fusiform gyrus; right frontal lobe, insula, supramarginal gyrus, and fusiform gyrus
Lhermitte et al. (1972)	Encephalomalacia	Left fusiform gyrus; white matter of right fusiform and lingual gyri
Benson et al. (1974)	Encephalomalacia	Left medial occipital area; splenium and right inferior longitudinal fasiculus
Cohn et al. (1977)	Encephalomalacia	Right precuneus, cingulate, fusiform, and hippocampal gyri, pericalcarine area; left fusiform and lingual gyri, pericalcarine area
Cohn et al. (1977)	Encephalomalacia	"Bilateral symmetrical vascular lesions in the distribution of the posterior cerebral arteries, more extensive on the left"
Nardelli et al. (1982)	Encephalomalacia	Undersurfaces of both occipitotemporal regions involving fusiform and lingual gyri
Landis et al. (1988)	Encephalomalacia	Infarcts in right occipitotemporal and frontal regions; very small infarct in left occipitotemporal region

Figure 3. Autopsy findings in prosopagnosia (from Benton & Tranel, 1993).

Damage to structures that interact with temporal lobe neocortical storage sites during face memory encoding and retrieval should also be accompanied by recognition memory impairment. For example, anterograde memory impairment for novel faces has been documented following right temporal lobectomy in patients with epilepsy (Crane & Milner, 2002). Epilepsy patients with right medial temporal lobe pathology or lobectomy also show evidence of retrograde memory loss for famous faces (Seidenberg et al., 2002). The deficit involves all components of face memory, including the recognition of facial familiarity and the retrieval of identity-specific semantic and name information. By contrast, patients with left medial temporal lobe pathology or lobectomy are able to recognize famous faces as familiar, although they may have difficulty remembering precise biographic information and are often disproportionately impaired in recalling the person's name.

Gainotti (2007) extensively reviewed the involvement of temporal lobes in famous people recognition disorder. In revising single-case and group studies, he found mainly three converging results:

a. familiarity decisions were more impaired in right than left hemisphere damaged patients;
b. right brain damaged patients were also more impaired in faces than in names recognition, and in accessing to person specific knowledge;
c. familiarity related to other 'unique entities' (such as monuments) seems to be not necessarily correlated to an impairment of famous face recognition. Patients with temporal lobe lesion even if they were pathological in monument recognition, their score were higher than that obtained in face recognition task.

There are some other studies showing that damage to prefrontal cortex can also be associated with anterograde and retrograde face memory impairment (Rapcsak et al., 2001). However, the memory deficit of frontal patients is usually not as severe and may be qualitatively different from what is typically observed in patients with prosopagnosia following right ventromedial temporal lobe damage. The prefrontal cortex may implement the types of memory control functions that we have ascribed to the "executive system". Rapcsak (2003) in his review have summarized lesion data and have provided aschematic representation of brain regions involved in face memory and recognition (see Figure 4).

Other insight into neuropsychology of face processing comes from neurodegenerative diseases. In particular, some studies are now available regarding Alzheimer disease (AD) and Semantic Dementia (SD). The core of neuropsychological impairment in AD is essentially for episodic memory, associated to categorical naming defects (Rascovsky, Salmon, Hansen, Thal, & Galasko, 2007). So, the most prominent deficit in face processing concerns the acquisition of newly learned faces.

At the onset of disease famous face recognition is not impaired, and it seems more related to the semantic memory impairment (Werheid & Clare, 2007). AD patients suffer from a temporal gradient of retrograde memory deficits: faces from remote decades are better recalled than faces of recent celebrities (Hodges & Graham, 1998).

Whereas Semantic dementia is a neurodegenerative disease characterized by anomia, semantic errors (paraphasia) and word comprehension deficits (Snowden, Goulding, & Neary, 1989). The more prototypical lesion site at the onset is the left anterior temporal lobe (Hodges & Patterson, 2007). But sometimes, this syndrome is characterized by a predominant right-sided lesion, always within the temporal lobe. In these cases, deficits are prominently of visuo-spatial type. One of the most documented deficits at this regard is a prosopagnosia of associative type.

Along the evolution of neuropathological degeneration, a bilateral atrophy is associated to SD. In this case, a partial dissociation of impaired recognition of face and name could be found in relation of predominance of the site atrophy (Snowden, Thompson, & Neary, 2004).

Another degenerative disease in which face recognition is affected (especially familiar faces) is posterior cortical atrophy (PCA). PCA patients have an isolated but catastrophic disruption to visual and spatial, including Balint's syndrome, simultanagnosia, visual inattention, alexia, and topographical disorientation (see Caine (2004) for a review). They are also affected in face recognition associated to a visual agnosia for objects (De Renzi, 1986; McMonagle, Deering, Berliner, & Kertesz, 2006).

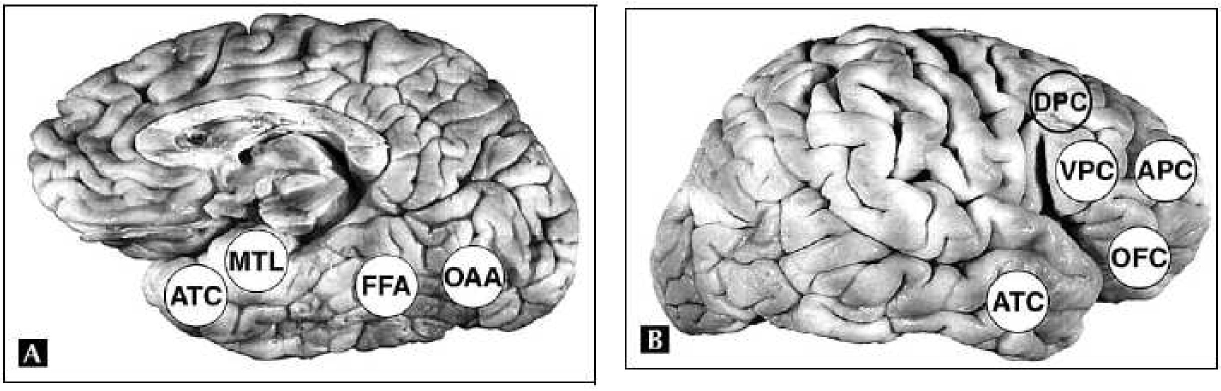


Figure 4. Neuroanatomic regions implicated in face perception and memory by functional imaging and cortical electrical recording studies. **A**. Image of ventral occipito-temporal cortical areas. **B**. Image of prefrontal and lateral temporal cortical areas. (APC—anterior prefrontal cortex; ATC—anterior temporal cortex; DPC—dorsolateral prefrontal cortex; FFA—fusiform face area; MTL—medial temporal lobe; OAA—occipital association areas; OFC—orbitofrontal cortex; VPC—ventrolateral prefrontal cortex.) (adapted from Rapcsak, 2003)

3. Cognitive Psychology of Proper Naming

> "A proper name [is] a word that answers the purpose of showing what thing it is that we are talking about", "but not of telling anything about it".
>
> John Stuart Mill, *A System of Logic* (1843)

Cognitive psychology studies concerned the mental representations and processes required to recognise and recall proper names (Valentine, Brennen, & Brédart, 1996). As for face processing, models were build up according to data from laboratory experiments, reports of everyday naming failures and braindamaged patients. For example, in diary studies, researchers asked subjects to monitor and record their naming difficulties experienced in real life (Burke, MacKay, Worthley, & Wade, 1991; Burke & Martin, 1988), whereas in laboratory studies, research attempted to provoke tips-of-the-tongue (TOTs) by definitions. Valentine, Brédart, Lawson, & Ward (1991) proposed a functional model that postulate a set of name recognition units (NRUs), the analogous of FRUs for faces (see Figure 5). NRUs represent the names of each individual and they mediate between the word recognition units (WRUs) and the semantics.

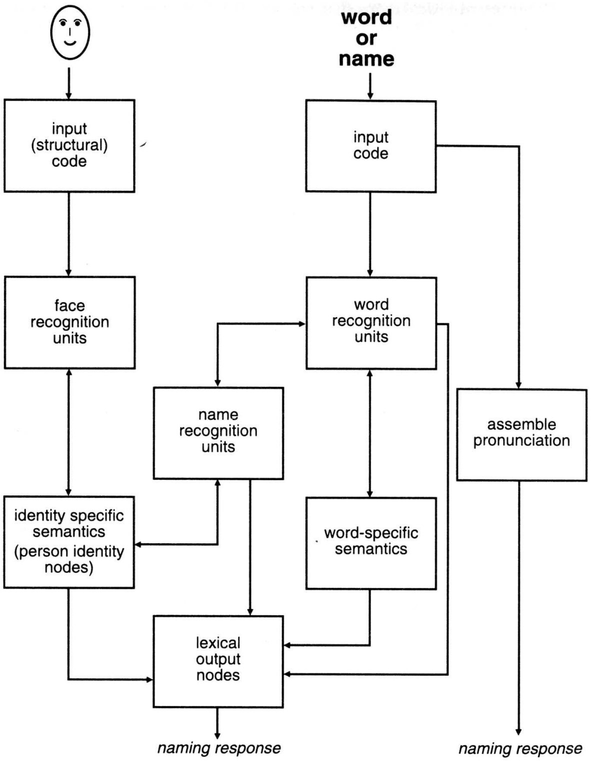


Figure 5. Valentine et al. (1991)'s model of proper name processing.

According to this model proper names are initially processed by the word recognition system. When a people's name is encountered, person recognition begins by activation of name recognition units.

As briefly described above, in Bruce and Young model (1986) proper names are stored separately from other systems. And from a functional point of view, name retrieval comes after the FRUs and the PINs; this means that it can receive excitatory and inhibitory connections from these two stores.

Burton et al. (1990) implemented a connectionist model from the Bruce and Young model (1986), the IAC (interactive activation and competition, see Figure 2). This model considers four interconnected pools of units connected by bi-directional excitatory connections to the PINs. Thus, the PINs provide a means of accessing SIUs that can accumulate evidence from different input domains (FRUs for faces, NIUs for names, etc.). The PINs are also used to determine familiarity; an input to an FRU or NIU is only categorized as familiar if the activation in the person's PIN exceeds a threshold.

One of the main difference between the two models regards the stored of proper names. In the Bruce & Young (1986) model, they are sequentially represented after faces, where in this latter model they are a pool of units in a wide neural network. This implies different cognitive mechanisms both in representation and in processing.

These models could explain the difficulty of name retrieval because proper names are retrieved after the related biographical information. But they did not explain why these are more susceptible to the tip of the tongue (TOT) phenomenon than common names (Bredart, 1993; Bredart & Valentine, 1998). Psycholinguistics explain these difficulties in terms of meaningless and arbitrarily of these items (Cohen, 1990). In that sense, proper names are considered as 'tokens': the label has nothing about the identity of the belonger. If you know somebody and he is a plumber, one can derive a number of information related to this semantic category (such as, a man working with tubes), where his surname is 'Mr. Plumber' this does not convey anything about him. Proper names denote individuals and not categories, for this reason they cannot share properties or attributes with other members.

Another similar view is adopted by some other authors. Semenza & Zettin (1989) define proper names as *pure referring expressions*: their functions are to be referred to an object per se and not to describe it.

4. Neuropsychology of Proper Names

> *"What's your name?" – "Auguste."*
> *"Last name?" – "Auguste."*
> *"What's the name of your husband?" –*
> *"I think… Auguste."*[3]

The idea that proper names are 'pure referring expressions' (for a recent review see Semenza, 2006) and they do not entail any description of the entity they designate posits in principle for a cognitive modularity of the their access and representation.

In fact, double dissociations between common and proper names are described in neuropsychology literature. Cases were described of selective anomia for proper names, with normal retrieval of common names, and cases of the reverse pattern were observed in different syndromes.

Semenza (2006) described the proper anomia in four varieties in relation to the level of processing which is impaired (Figure 6). The first type of anomia is the deficit in *accessing to the phonological lexicon*, to a post-semantic level. Two varieties within this type of anomia are distinguishable: one including all categories of proper names (persons' names and geographical names) and one restricted to names of people. These patients never commit semantic errors and their failures are omissions, often accompanied by circumlocutions. Semenza & Zettin (1989) described a patient, PC, presenting the first kind of impairment; and Lucchelli & de Renzi (1992) describe another patient, TL affected by a anomia limited to people's names. In these patients, semantics in itself is preserved: they can report all the information related, but the problem seems to access and retrieve a proper name from semantic memory.

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[3] Initial interview of Auguste D. by Dr Alois Alzheimer. Source: Patient record, Hospital for the Mentally Ill and Epileptics, Frankfurt am Main (Germany), November 26th, 1901 (cited in Maurer, Volk, & Gerbaldo, 1997).

The second type is the *anomia due to loss of semantic information.* Patients show a selective anomia for the names of familiar people, without any other disorder for common and other proper names. APA, a patient described by Miceli et al. (2000) had a proper anomia and a deficit in reporting person knowledge information, but spared semantic knowledge of common objects.

The third is in the case of the *isolation of information about individual entities.* It is the case of C.B., a patient described by Semenza (1998)that he could retrieve information about an individual only once provided with the name of that individual. This patient presented a deficit also in reporting person related knowledge.

Face-specific anomia (Prosopanomia) is the fourth subtype of anomia described by Semenza (2006). The author indicates that this term is correctly used only to patients unable to name a person on presentation of the face, with a spared ability provide the name upon definition.

Besides the study reporting deficits in speech output, there are also some evidence of braindamaged patients with comprehension deficits in proper names. Data reported in literature support dissociation between comprehension of proper names and common names. Van Lancker & Klein (1990) described four patients with global aphasia tested in proper name comprehension through a task that required to match a face in an array of four with a spoken name. These patients performed within normal ranges in that task, whereas they showed a pathological performance when the match was for common names. Similar results are reported by Wapner & Gardiner (1979).

Warrington & McCarthy (1987) reported a patient (YOT) with an impaired comprehension of common and proper nouns, but the deficit for nouns was category-specific. Other dissociations in aphasic patients have been reported for geographical names compareed to body part names, the former ones preserved and the latter ones compromised (Goodglass & Wingfield, 1993).

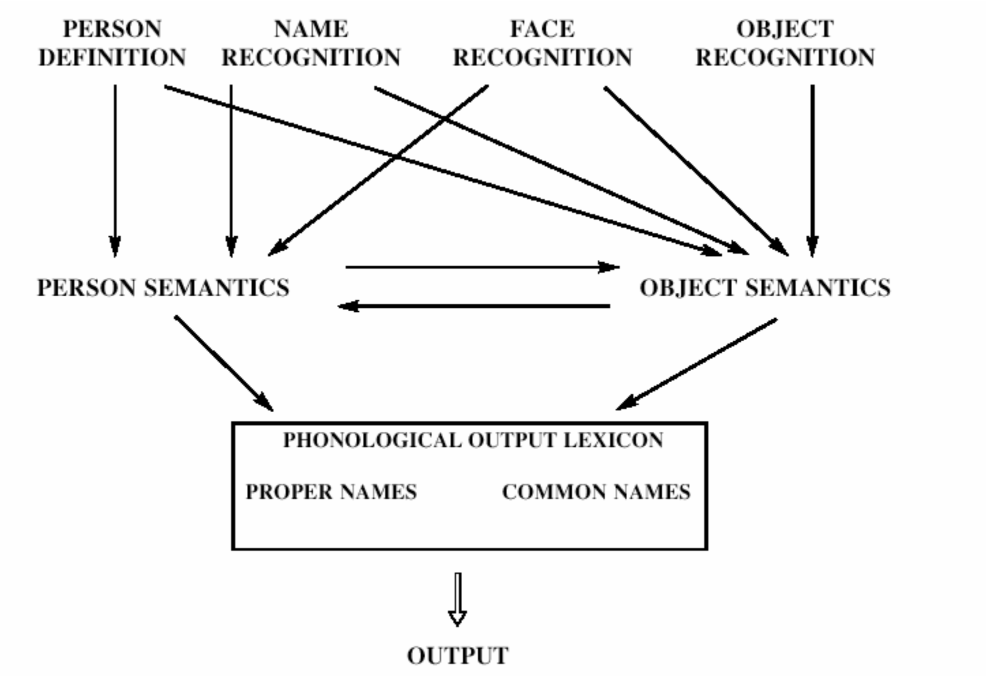


Figure 6. Proper naming from neuropsychological studies
(Adapted from Semenza, 2006)

In particular, some studies are now available regarding Alzheimer disease (AD) and Semantic Dementia (SD). The core of neuropsychological impairment in AD is essentially for episodic memory, associated to categorical naming defects (Perry & Hodges, 1996; White & Ruske, 2002). As reported, in AD patients familiarity judgement is preserved, whereas it seems that these patients had more difficulty in recalling a person's name than person related information (Werheid & Clare, 2007). Due to early episodic memory deficits, AD patients are also imparied in the face-name association learning (Fowler, Saling, Conway, Semple, & Louis, 2002).

Semenza, Mondini, Borgo, Pasini, & Sgaramella (2003) studied proper names in patients with early AD. They found that proper name retrieval tests were more sensitive to early AD than any other test or battery. Delazer, Semenza, Reiner, Hofer, & Benke (2003) also carried out a study in a group of AD patients and the preclinical phase of this disease, namely the Mild Cognitive Impairment (MCI). These authors found that the post-semantic aspects of processing underlie a significant proportion of AD patients' failures with people names. AD patients were able to deliver semantic information specific to retrieve with some extent the proper name through some cues. So, it seems reasonable to hypothesise that pre-semantic and semantic deficits should not play a major role; but also to problems in accessing the phonological representation, as well as to a degradation of phonological representations.

The other neurodegenerative disease in which proper naming is impaired is semantic dementia (SD). This is a neurodegenerative disease characterized by anomia, semantic errors (paraphasia) and word comprehension deficits (Snowden et al., 1989). SD is named also the 'language' variant of the frontotemporal lobar degeneration (FTLD, Neary et al., 1998). As described above, the more characteristic lesion site is the left temporo-polar lobe. And when the atrophy is more prevalent on the left, person semantic knowledge (biographic information) and proper naming aare impaired (Poeck & Luzzatti, 1988; Papagno & Capitani, 1998; Schwarz, De Bleser, Poeck, & Weis, 1998; Tyrrell, Warrington, Frackowiak, & Rossor, 1990a; Schwarz et al., 1998; Graff-Radford et al., 1990; Hodges, Patterson, Oxbury, & Funnell, 1992). In this case, SD patients are affected by a anomia due to deficits in person semantics, according to Semenza (2006) description. It is quite rare that the deficit is limited to the output level, because in these patients semantic degradation is present since the onset of the disease.

5. Neural basis of face processing: neurophysiology and neuroimaging studies

Numerous studies have shown that faces elicit a much larger ERP of negative polarity between 130 and 200 ms than other object categories. This component peaks at occipito-temporal electrode sites at about 170 ms following stimulus onset and has accordingly been termed the N170 (Bentin et al., 1996). A corresponding positive component is found on the vertex (Figure 7).

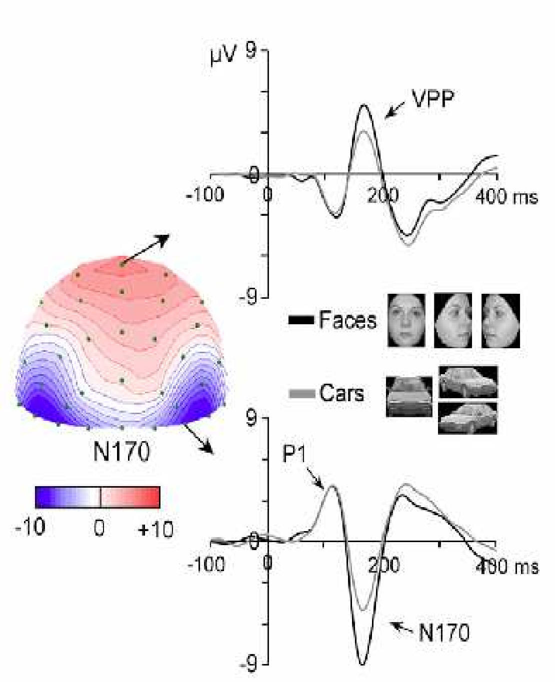


Figure 7. The early ERP components (N170 and VPP) of face processing.
(from Rossion & Jacques, 2008)

Since the first studies (Jeffreys, 1989; Jeffreys & Tukmachi, 1992; Bentin, Allison, Puce, Perez, & McCarthy, 1996) has been reported these two complex. Bentin et al . (1996) found a negative potential peaking at about 170 ms from stimulus onset from scalp of normal subjects responding preferentially to human faces and isolated eyes, but not to human hands, animal faces, furniture, cars or nonsense stimuli. Jeffreys (1989) reported the positive component (VPP) recorded over Cz, also preferentially for all face and face-like stimuli, such as line drawings or fragmentary figures. Interestingly, changes in stimulus size did not affect the amplitude of VPP, conversely face inversion or removing particular facial features produced a marked increase in latency and slightly in amplitude. This 'inversion effect' has been reported also for the N170 (e.g., Bartlett & Searcy, 1993; Itier & Taylor, 2004). N170 is usually delayed and larger for inverted than for upright faces and this effect reflects the disruption of configurational information at the encoding stage of face perception. The role of this early component is related to those mechanisms associated with face identification. It has been reported that N170 amplitude (Bentin and Deouell, 2000) is not affected by familiarity: see a famous face or an unfamiliar one elicit the same amplitude and latency on N170. For this reason it has been linked to 'structural encoding' as suggested to Bruce and Young (1996). Some modulation of this ERP component could be found in some context of stimulus ambiguity (such as recognition of Mooney-like faces), and in this case familiarity enhances N170 amplitude (Jemel, Pisani, Calabria, Crommelinck, & Bruyer, 2003).

The second main component found in face processing is the N250. This component is more evident when an explicit task of familiarity is required: familiar faces elicit more negative potentials than unfamiliar faces (Bentin & Deouell, 2000; Itier & Taylor, 2004). This data was confirmed also in repetition priming studies with familiar faces (Schweinberger et al., 2002; Jemel et al., 2006). This component is considered the precursor of the well know 'semantic' component N400, centro-frontally distributed (Barrett, Rugg, & Perrett, 1988; Yovel & Paller, 2004 Pickering & Schweinberger, 2003), extensively reported in language literature.

The specificity of the ERP components for faces raised a debate around the modular neural correlates of face processing. As long as cognitive psychologists are questioning about a 'face-specific module' in human cognitive system, in neurophysiology is still open the debate of a distinction of ERP component (especially for N170) for face and object processing. Recently, Thierry et al. (2007) claimed that 'the N170 effect' is due to a methodological artifact in stimulus selection, in particular, the different physical variance between objects and faces should account for it, and when eliminated the effect disappears. Rossion and Jacques (2008) reply to this claim proposed some arguments in favour of a N170 specificity for face processing. First, when interstimulus invariance is controlled, the larger N170 amplitude for faces is not abolished at all (i.e., Goffaux, Gauthier, & Rossion, 2003). Second, it seems that high-level perceptual processing drives N170, so low-level features of stimuli do not lead to significant change over this component (Arcimboldo's famous paintings of face made up vegetable indeed elicit larger N170). Third, variations of this component (e.g. face inversion effect) are larger for faces as compared to nonface stimuli, indicating that the N170 is particularly sensitive to faces.

The development of functional brain imaging techniques have permitted the identification of brain regions that respond more to face images than to other objects. In particular, these studies have shown that there is a specific region labelled the Fusiform Face Area (FFA), corresponding to the lateral and middle fusiform gyrus. This region has been found to have an increased activation to face compared to other objects (Kanwisher, McDermott, & Chun, 1997; Spiridon & Kanwisher, 2002). The involvement of this area has been demonstrated both in passive viewing tasks and in tasks that focus attention on invariant aspects of the facial configuration (e.g., simultaneous and delayed matching of pictures of the same individual, gender judgement). In addition to the face-responsive fusiform region, functional imaging studies have identified other face-responsive regions, usually consistently located in the lateral inferior occipital gyri and the posterior superior temporal sulcus (Haxby et al., 1999; Ishai, Ungerleider, Martin, & Haxby, 2000). These latter brains area may reflect the perception of the changeable aspects of a face that vary with movement, eye gaze, angle of profile, and expression (Perrett et al., 1984).

The most comprehensive model of neural basis of face perception is described by Haxby, Hoffman, & Gobbini (2000) (see Figure 8). The model is divided into a core system, consisting of three regions of occipitotemporal visual extrastriate cortex, and an extended system, consisting of regions that are also parts of neural systems for other cognitive functions.

Basically, it reflects the cognitive framework of the Bruce and Young's model (1986) and its further modifications. Three brain areas are included in the core system. The first area is the inferior occipital gyri devoted to the early phase of processing in the cognitive models (the structural coding system). Then, the superior temporal sulcus is related to the changeable aspects of face perception. This is the case of the module devoted to process unfamiliar faces: those aspects are independent to the recognition of faces, i.e. lip movement, expression, gaze. The extended system comprises the other non visually-derived aspects of face processing. In particular, the limbic system (especially, the amygdala) is related to emotional processing (Sergerie, Chochol, & Armony, 2008). The semantic and liguistic aspects, such as person identity and name retrieval, are related to the anterior temporal lobe.

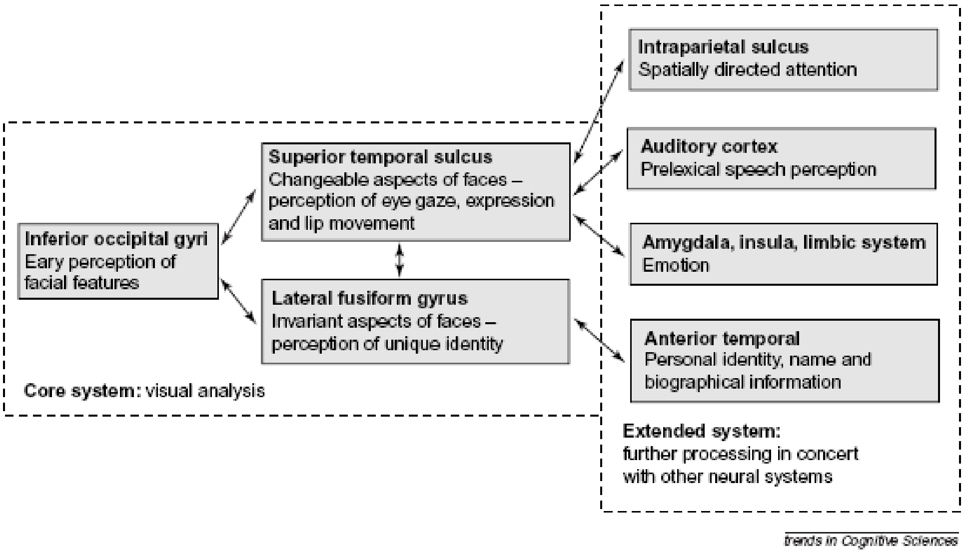


Figure 8. The human neural system for face perception (Haxby et al., 2000)

The area devoted to face processing, the fusiform gyrus, name fusiform face area (FFA) is more active during passive viewing of face-like stimuli than non-face stimuli such as objects (Kanwisher et al., 1997). Early studies (Halgren et al., 1999) have also indicated other areas involved in face processing such as: the superior temporal sulcus (STS) and the inferior and mid occipital gyri. More interestingly, recent studies in prosopagnosic patients have questioned the role of these brain regions. Steeves et al., (2006) studied a prosopagnosic patient (DM) affected by an acquired prosopagnosia as a result of accidental carbon monoxide poisoning. She showed a bilateral lesion of the lateral occipital cortex and a left hemisphere lesion near the top of the parieto-occipital sulcus. DM has a functionally active FFA area and she can differentiate faces from non-faces and she could discriminate well faces when presented upright. But she cannot make any higher level discriminations requiring recognition of known faces, emotion and gender. This results support the hypothesis that an intact complex network is necessary for higher level face processing and that the FFA is not sufficient for face recognition. According to this hypothesis, Rossion et al. (2003) studied a prosopagnosic patient with a bilateral occipito-temporal lesion. Despite the absence of any feedforward inputs from the right occipital face area (OFA), located in a damaged area of cortex, they found a normal activation of the right FFA in response to faces (using fMRI). Together, these findings show that the integrity of the right OFA is necessary for normal face perception and suggest that the face-sensitive responses observed at this level in normal subjects may arise from feedback connections from the right FFA. Sergent et al. (1992), in a PET study, found an activation of the striate cortex for a gender discrimination task, whereas extrastriate areas (middle gyrus of the left temporal cortex and the right parahippocampal gyrus) were also active when a face-identity task was required. In object recognition task involved more the left occipito-temporal cortex.

Many studies have compared the unfamiliar faces to other categories of stimuli, such as complex pattern, animal and artifacts. Few studies attempted to investigate the brain areas involved in fame, contrasting famous faces versus unfamiliar ones. Gorno-Tempini et al. (1998) carried out two PET experiments to study the metabolism linked to famous entities. They found that the middle temporal gyrus (Brodman's area 21), precuneus and temporoparietal junction were more active for famous stimuli (faces and names) compared to unknown ones. In a further PET study, Gorno-Tempini & Price (2001) compared famous faces and buildings in a pair matching task. The results of this study showed that the right anterior middle temporal gyrus was active during matching faces but not for buildings. Those data confirmed the role of temporal lobe in storing of long-term representation of famous faces. Other functional neuroimaging studies have demonstrated that the recognition of famous faces (actors, media celebrities and politicians) as compared to unfamiliar faces activates extensive frontal and temporal regions (Sergent et al., 1992; Kapur, Friston, Young, Frith, & Frackowiak, 1995; Kapur et al., 1995; Leveroni et al., 2000; Bernard et al., 2004). The results are somewhat mixed: for example, Gorno-Tempini et al. (1998) found a widespread activation in the left frontotemporal but not in the medial temporal lobe. Conversely, other studies showed a hippocampal activation during a famous face recognition task (Leveroni et al., 2000; Bernard et al., 2004). These authors concluded that the hippocampus was involved in mediating effective access to conscious recollection of semantic information. But some difference has been found regard to lateralization of hippocampus activation: Sergent et al. (1992) found a right activation in a right, whereas Kapur et al. (1995) found a left one.

More recently, Elfgren et al. (2006) in a fMRI study investigated famous face processing using two tasks: categorisation for fame or for gender. In the fame task, the subjects were required to identify the person when seeing his/her face and also to try to generate the name of this person. In the gender task, the subjects were asked to conduct a judgement of a person's gender when seeing his/her face. The main effect of the processing of famous faces (intentional and incidental recognition) yielded activation in left medial temporal lobe as well as in right parahippocampus. Thus, the current results clearly support the finding that retrieval of information from the long-term semantic memory is related to increased activity in medial temporal lobe.

But how is person-specific information represented in the brain? Person recognition requires more than the structural analysis of a face. Paller et al. (2003) performed a fMRI experiment asking subjects to learn a set of faces associated to biographical information and their own name. After this study phase, subjects were required to categorise with a yes-no judgement a new series of faces made of half of faces previously seen and half of faces never seen before. Subjects also performed a gender judgement as a control task. fMRI comparisons between gender and memory tasks showed an activation of three areas: the right precuneus, the right dorsolateral prefrontal cortex and the right insula. A left hippocampus activation was associated with successful retrieval of person-specific information, as previously reported in an other study (Paller, 2002).

The activation of prefrontal cortex is related to retrieval processes. Buckner, Koutstaal, Schacter, Wagner, & Rosen (1998) demonstrated that the right prefrontal cortex are more active in a task where a large number of items were successfully retrieved. And it is also the area involved in the episodic retrieval (Buckner & Petersen, 1996) and its activation could be modulated by the context, suggesting that it is more in engaged in high demand task and not in mere recognition (Wagner, Desmond, Glover, & Gabrieli, 1998). Conversely, the activation of other areas within the frontal lobe, such as the frontal-opercular region and the left dorsolateral prefrontal cortex are supposed to be modulated by the retrieval effort, i.e. when an item demanded the most effort to be retrieved and when the retrieval was rarely successful. Hofer et al. (2007) found a bilateral prefrontal and anterior cingulate activation during encoding of unfamiliar faces.

6. Neural systems of proper names and faces-names associations

Several reports suggest that the temporal lobe in the language-dominant hemisphere is one of the most critical structures in the neural network for the retrieval of people's names. Gorno-Tempini et al. (1998) in a PET study compared the famous face and name activation. Subjects had to decide whether the two stimuli, displayed simultaneously, were the same or different. They found that names greater activated the left hemisphere (from superior temporal gyrus to the angular and supramarginal gyri), whereas famous faces activated striate and extrastriate cortices in the right hemisphere.

Damasio, Grabowski, Tranel, Hichwa, & Damasio (1996) conducted word-retrieval experiments with a large population of brain-damaged patients and a positron emission tomography (PET) study with normal subjects. They found that the retrieval of words signifying different categories of entities depended on different regions in the left temporal lobe: the rostral part of the temporal lobe for the names of famous people, the lateral inferior temporal area for the names of animals, and the lateral temporo-occipitoparietal area for the names of tools.

Tsukiura et al. (2002) studied patients with language-dominant temporal lobectomy (DTL) and non dominant temporal lobectomy (NDTL) in retrieval of names from photographs and from verbal definitions. This task was performed for newly learned face-name associations and for famous names. They found interesting results respect to group patients. First, DTL group was significantly impaired in their ability to retrieve famous people's names both from their photographs and from their verbal descriptions; whereas the NDTL group was not impaired in these tasks. Second, the DTL group showed impairment in retrieving newly learned people's names and other types of information from corresponding faces. In particular, lesion data from this study showed the anterior part of the left temporal lobe plays a critical role in the retrieval of famous people's names as previous studies found (i.e., Damasio et al., 1996), but interestingly, this is true irrespective of the stimulus familiarity (famous or newly learned). Prefrontal areas were activated in the retrieval of newly learned information but not of familiar information. This different hemispheric asymmetry was also found in the Tsukiura, Mochizuki-Kawai, & Fujii (2006)'s study. These authors found that the left anterior temporal lobe was significantly activated in the retrieval of people's names encoded with person-related semantics, whereas the right anterior temporal lobe was activated in the retrieval of people's faces encoded with person-related semantics. This suggests that the three components of faces, names, and person-related semantics may be mutually mediated by the bilateral anterior temporal lobe, and the retrieval of people's names from faces after sufficient learning of face name associations may be achieved without the mediation.

In another study the contribution of the right anterior temporal lobe related to person identity knowledge was confirmed. Tsukiura, Suzuki, Shigemune, & Mochizuki-Kawain (2007) asked subjects to recognize job titles (semantic information) previously associated with faces and names, and compared neural activations of those in case of successful retrieval of semantic information and associated face and name, semantic information with only the face, or only the semantic information with no memory for the face or name. First, the left anterior temporal activation significantly increased in the successful retrieval of semantic information and face-name associations, compared to retrieval accompanied only with face memory or neither face nor name memory. Second, the right anterior temporal showed a significantly increased activation in the successful retrieval of semantic information. Third, activation patterns in the right medial temporal lobe (hippocampus) were the same as those in the right anterior temporal lobe. These findings demonstrate that the bilateral anterior and medial structures may differentially contribute to process memory for person identity.

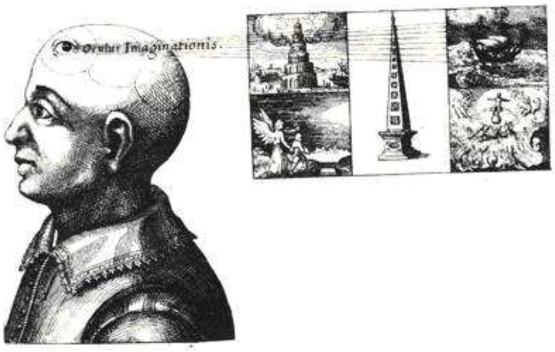
Grabowski et al. (2003) undertook a functional imaging study of a group of patients after temporal lobectomy for medically intractable epilepsy in order to shed light on the neural systems that participate in residual naming of unique entities, such as proper names.

Those studies that have investigated the neural basis of face-name associations indicate that anterior part of the hippocampus is always involved. In particular, it has been found related to encoding processing (Sperling et al., 2003; Sperling et al., 2001). More recently, Chua, Schacter, Rand-Giovannetti, & Sperling (2007) found that the anterior hippocampal formation showed increased activation for subsequently remembered face-name associations compared with pairs that were forgotten. In contrast, the posterior hippocampal formation showed activation above baseline during attempted encoding of face-name pairs, but no evidence of differential activation based on subsequent memory. Further analyses revealed that a parahippocampal region, most likely corresponding to perirhinal cortex, showed subsequent memory effects for faces.

Few studies have investigated the neurophysiological bases of proper names. Müller & Kutas (1996) reported difference in N1/P2 complex when subjects listen to their own name respect to common names. This complex was followed by a prominent negativity at parieto-central site around 400 ms and a late positivity between 500-800 ms over left lateral-frontal sites. Dehaene (1995), using a task of word categorization, found that ERPs elicited for proper names differed to other categories (animals, verbs and numerals) between 280 and 356 ms. The topography was specific as well: proper names evoked a temporal negativity extended towards left inferior temporal sites, without a clear hemispheric asymmetry. By contrast, a more left temporal involvement was found when subjects are required to retrieve a proper name by a definition (Proverbio, Lilli, Semenza, & Zani, 2001). These authors reported larger amplitude of N1 over the left temporal sites when proper names are provided, whereas common names elicited a stronger activation of visual cortex later, at 250 msec.

Chapter 2

Neurophysiological bases of episodic memory in young adults



The memory can be enormously enhanced by transmuting concepts into visual and spatial images: herein lies the secret of the Ars Memorativa of Antiquity, the Middle Ages, and the Renaissance… Here the three ventricles are shown… but the things to be memorized are brought from the obscurity of the back of the head and exposed to the eye of imagination. The images are the Tower of Babel, Tobias and the Angel, an obelisk, a storm at sea and the Last Judgement.

Robert Fludd
Utriusque Cosmi, Maioris scilicet et Minoris,
metaphysica, physica, atque technica Historia (1617—1619)

1. Episodic memory: the story so far

Episodic memory is memory related to events over limited periods of time (Mayes & Roberts, 2001). Events that are later remembered are, therefore, initially consciously experienced as a serie of perceptual and semantic representations of objects that interact in space and time within a larger spatio-temporal context. Theories of episodic memory have tried to specify the encoding, storage, and retrieval processes that underlie this form of memory and indicate the brain regions that mediate these processes and how they do so.

Typically, encoding episodes involves representing a sequence of linked scene that occurs over a period of time. The major feature of episodic representations, therefore, is that they associate together very different kinds of information, which include perceptual and semantic aspects of objects and how these are located in space and time relative both to each other. Tulving (2000) have argued that episodic encoding depends on information being processed successfully through semantic memory. This is not exactly true because patients suffering from breakdown of semantic memory could indeed encode spatio-temporal information (e.g., Scahill, Hodges, & Graham, 2005). Only one part of the experienced episodes are put into long-term memory storage, and only a small part of this is later retrievable.

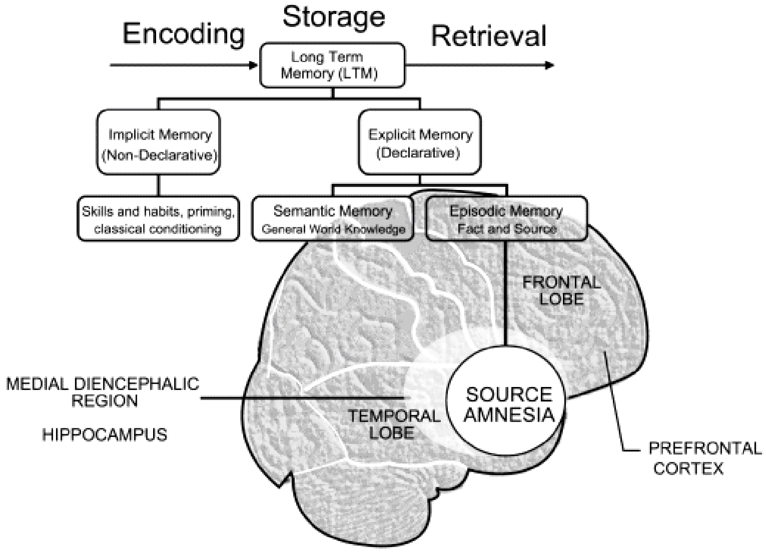


Figure 9. Schematic representation of Squire's model of long-term memory (Squire, 1987)

One of the modern concept regard to the episodic retrieval is based on the distinction of two main processes: familiarity and recollection. Along this idea, human memory is conceived as a dual-process system. The most common situation describing this is when we encounter a person, we have the feeling of knowing to recognize him/her (familiarity), or we can recollect when and where we met him/her the first time (recollection). A number of memory models have been proposed that assume that recognition memory judgments can be based on two distinct forms of memory. However, they differ in critical ways and in many cases make conflicting predictions about the functional nature and the neural substrates of the underlying processes or systems (for an exaustive review see: Yonelinas, 2002).

One of the first model has been proposed by Atkinson, Hertmann, & Wescourt (1974). In this model, familiarity is assumed to reflect the activation of nodes in a lexical store in which each node represents an individual word or object. Basically, the idea is that a node activation lowers the threshold and in a recognition test the studied items are more active than the unstudied ones. The gaussian distribution of these two classes of stimuli, and mainly the overlapping area is where the criterion set up by the subject falls in. Familiarity and recollection differs because they support memory for perceptual and semantic information, respectively.

Other dual-process models have stressed the neuroanatomical bases of the long-term memory. Specifically, most part of studies showed the involvement of the medial temporal lobes (e.g., hippocampus, parahippocampal gyrus). These theories start data issued from lesion studies, from patients suffering from amnesia. According to these authors (e.g., Mayes, 1988; Mayes, Montaldi, & Migo, 2007), recognition memory in amnesic patients is restricted to familiarity, whereas in healthy people could be dependent both to recollection and familiarity. Specifically, a contextual information retrieval accounts for the amnesic syndrome. In that sense, hippocampal region is critical for recollection, whereas the medial temporal lobes are important for familiarity. These neuroanatomical models have the limit to not take into account other brain areas really important for memory processes. It is known that the anterior prefrontal cortex, is implicated in episodic retrieval (Buckner, 2004; Buckner et al., 1998; Buckner & Petersen, 1996), and that the superior and inferior regions of parietal lobe are closely linked to successful recollection (Vilberg & Rugg, 2008).

One other influential point of view is of Jacoby (1983; 1991). According to this author, recollection reflects an analytic and conscious process, whereas familiarity is a relatively automatic process. Familiarity arises when a fluent processing of an item is attributed to a past experience. This means that in perceptual identification familiarity plays a central role, but also in conceptual processing (i.e, for the meaning of the words). It is faster than recollection, but in supposed to act in parallel.

Tulving and colleagues proposed a multicomponent model (Figure 10), including episodic memory, wich gives rise to the conscious experience of 'knowing', and semantic memory, which gives rise to the conscious experience of 'knowing' (Tulving, 1985; Tulving, 1987; Tulving, 2000). This is not a standard dual-process memory system, but it is conceptualised as two main components. The episodic system stores experienced events and their temporal features and is more related to recall performance, where the semantic system stores general world knowledge. Frontal and temporal lobes are the neural bases underlying the episodic system, and thus damage to these structures leads to deficits in recollection. A more fine-grained division is made within the temporal lobe: hippocampus is critical for episodic memory, whereas the surrounding temporal lobe regions are critical for semantic memory (Tulving & Markowitsch, 1998). Another important subdivision is within prefrontal areas. The right prefrontal are critical for retrieval from episodic memory, whereas left prefrontal regions are important for retrieval from semantic memory and encoding into episodic memory (Nyberg, McIntosh et al., 1996).

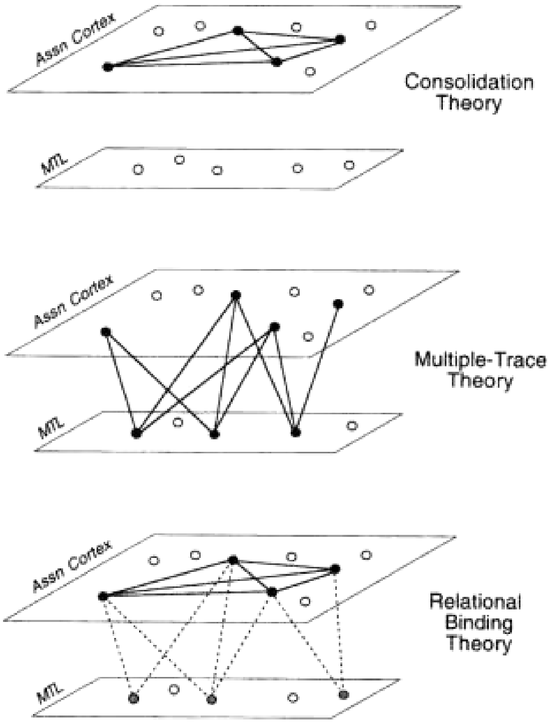


Figure 10. Three different theories of memory consolidation and retrieval processes in medial temporal lobe (Squire & Schacter, 2003).

1. Episodic memory: neurophysiology of encoding and retrieval processing

a. Encoding processing and ERPs

ERPs have been used in memory processes investigations for several reasons. First, because they have high temporal resolution: this can permit to investigate the time-course of memory processing. The second advantage is that is possible to record ERPs even in covert tasks, when no behaviourally response is required, such as during encoding of new information. Third, looking at the spatial representation of the brain activity permits to investigate how the subcomponents of memory occur respect to the different cognitive processes.

Regarding to encoding tasks, it has been usually used a typical paradigm. The idea on this paradigm relies on the idea that stimuli correctly retrieved later are accompanied by a different electrical activity to those not retrieved. So, after the test phase (retrieval) the ERPs recorded during encoding are labelled according to the successfulness of retrieval. The electrical difference is referred as 'subsequent memory effect', or difference due to memory ('Dm'), as reported by Paller, Kutas, & Mayes (1987). Actually, the first paper describing this procedure was by Sanquist, Rohrbaugh, Syndulko, & Lindsley (1980). In that paper, subjects were required to make a 'same-different' judgment on word pairs sequentially presented on the basis of of orthographic, phonological or semantic features. Data on ERPs were analysed according to the subsequent memory performance. Semantic and phonological task elicited a more positive-going waveform for studied pairs subsequently recognized, compared to those did not.

Another variant of this paradigm is the use of the 'Von Restorff' procedure (Fabiani, Karis, & Donchin, 1986, 1990). This effect is referred to a better memory shown for isolates than for the other members of a word list. Isolates are created in changing features of the words, such as varying the font size. Basically, it seems that P300 component indexes the extent of item revision of the memory, and/or the extensive revision per se boost up the memory trace. Karis, Fabiani & Donchin (1984) also found an interesting correlation between P300 amplitude and encoding strategies. In their experiment of learning new items under an intentional procedure in a Von Restorff paradigm they found that those subjects that used a 'rote' mnemonic strategy show smallest P300 amplitudes for isolates correctly retrieved, especially over the parietal sites. Also in an incidental memory task, Fabiani et al. (1986) found that items correctly retrieved show a more positive-going ERP respect to those not retrieved. P300 complex is elicited in the 'oddball' paradigm, whereby a target stimulus is presented amongst more frequent standard background stimuli. The classic oddball paradigm has seen many variations, but in the end most protocols used to evoke the P300 involve some form of conscious realization or decision making (Pritchard, 1981).

In a direct experimental manipulation of memory strategies subjects were required to alternatively adopt a rote or elaborate strategy to learn items (Fabiani et al., 1990). More positive-going ERPs were elicited to correctly recognized words as prevoiusly reported, but with different spatial distribution. During the elaborate condition of learning more positivity over frontal site was evident, whereas during rote learning the effect was distributed more posteriorly, involving the P300 component. The larger effect found for the non-elaborate words have been explained by the 'distinctiveness'. This is because without an elaborative processing, physical features become the determinant of the efficacy of learning. This is the explanation proposed by Donchin and Fabiani, and these authors proposed also that the marker of this effect is P300 component.

Other authors carried out some investigations to study late components of ERPs, such as N400. Neville et al. (1986) used a semantic judgement task to study ERPs and subsequent memory effect. The task used, basically, was a sentence completion with two alternatives. In the test phase, subjects were required to recognize the word presented in the study phase. ERPs were more positive going for correctly retrieved words that were correctly complete the sentence. Same results were found also for the words recognized but not congruent to the sentences presented in the encoding phase. But the difference is that in this latter condition ERP difference started from 400 ms post-stimulus. Similar results has been found in the hallmark paper on language and semantics, by Kutas & Hillyard (1980). This famous study was specific semantics: subjects presented a larger N400 component when they were presented with a word that did not fit the incomplete sentence presented before.

The nature of this difference related to the Dm has been mapped (Friedman & Johnson, 2000). This has been done through CSD maps: this method calculates the topographic distribution of current density emphasizing local differences (Nunez & Pilgreen, 1991). Because local generators are represented by this technique, CSD maps are particularly useful for forming hypothesis about neural sources in superficial cortex. Friedman and Trott (2000) found a negative current density over left inferior prefrontal scalp for two temporal windows (500-800 and 810-1,100 ms). This activity was related to successful encoding of words.

Paller and colleagues reported several papers on the subsequent memory effect. In a first study, ERPs were obtained during encoding of items using a matching task based on semantic attributes or non-semantic attributes (Paller et al., 1987). They found a positive-going component for recognized words, larger for those in the semantic task.

Beside this procedure, another one has been applied using the Remember/Know technique. The idea proposed by Friedman and Trott (2000) considers the hypothesis of differential encoding processes as a function of subjects' awareness of the subsequently retrieved items. If a Remember response indicates 'recollection' because contest-dependent information are retrieved, whereas Know responses indicate familiarity-based retrieval, these difference could be found also during encoding. ERPs elicited by study items subsequently classified as Remember elicited greater amplitude from about 400 to 1000 ms than those were missed. Topography of CSD maps showed that this effect is evident over the left prefrontal sites. In contrast, ERPs elicited by study items subsequently classified as Know did not differ to those missed.

The timing of the Dm effect has been confirmed also by intracranial EEG recording (Fernandez et al., 1999). These authors recorded from medial temporal lobe structures in pre-surgical epileptic patients during a single word study task. They found that item subsequently recalled elicited during encoding larger N400-like potential than those were missed.

b. Priming and ERPs

In a broad sense, priming could be defined as the facilitation of the processing of a stimulus (target) when the same or related stimulus is encountered before (prime). The prime preactivates the related items, and by the way the subject is faster to respond to target respect to a control condition where no relation stands between prime and target. It is an implicit measure to investigate representation, especially for the semantic features.

The advantage of this technique is that it does require explicit response, thus it is very useful in those patients where a covert response is impossible or not reliable. A repetition effect on ERPs can only occur if the brain is in some way responding differentially to repeated and unrepeated items, if it is exhibiting some form of memory. The fact this effect could occur over long lags means that long-term representation is involved.

One typical experiment is characterised by an initial incidental study task followed by a recognition test memory, in which words from the study task had to be discriminated from new words (Bentin, Moscovitch, & Heth, 1992). ERPs recorded in this latter task are more positive as a function to prior exposure, independent of whether they had been correctly classified in the recognition memory test. The 'ERP repetition effect' onsets around 200 ms poststimulus, and has been found in response to words and pictures. Given that this effect is elicited in indirect tasks in which there is no requirement for intentional memory, it is tempting to interpret as a neural correlate of implicit memory. By now, there is no agreement about this statement, because this effect could reflect incidental explicit memory. One way to disentangle this point is to employ prime and test in different modalities. Findings issued from these studies report a modulation of neural activity around 200-400 ms, compatible with a modulation of perceptual processes that contribute to data-drive implicit memory for stimuli.

Another way to investigate this effect is to compare neural activity elicited by studied items that subject misclassified as new (misses) with those elicited by new items correctly judged as new, in a direct memory task. According to this idea, item missed are those which do not reach the explicit processing.

c. Retrieval and ERPs

Recognition of episodically stored material has most often been modelled as consisting of the two distinct processes, such as familiarity and recollection, as described above. The majority of ERP memory studies have investigated the neural basis of explicit recognition and recall, and have demonstrated differential ERP responses depending on the study status of the item being recognized (for a review see Rugg & Curran, 2007).

Several studies have shown that items judged as old (previously seen in the study phase) elicit a more positive-going deflection in comparison to those judged as new (Rugg & Allan, 2000). This effect is called the *left parietal ERP old/new effect*, it onsets at about 400 ms and it lasts till 600 ms, and it larger over the temporo-parietal sites. This effect is also referred by some authors as the episodic memory effect (EM) (Friedman & Johnson, 2000). One proposal by Rugg and Doyle (1992) was that this effect is the neurophysiological marker of familiarity-based recognition, but successive research pointed out the some aspects of recollection were involved as well (e.g., Paller & Kutas, 1992; Wilding & Rugg, 1996; Rugg & Yonelinas, 2003).

The use of high-resolution mapping has allowed evidencing that the old/new effect consists of a number of functionally different subcomponents, each with its own spatio-temporal features. Three main components have been described (see Figure 11). One early appears as a negative peak at 400 ms, maximal over the left prefrontal-central scalp (sometimes called also FN400). For example, it has been reported that old words elicit less negativity than new words (see Johnson, Kreiter, & Russo, 1998). This is ubiquitous over the scalp and it has been reported that disappeard as long as the lags the items are repeated (e.g., Van Petten, Kutas, Kluender, Mitchiner, & McIsaac, 1991).

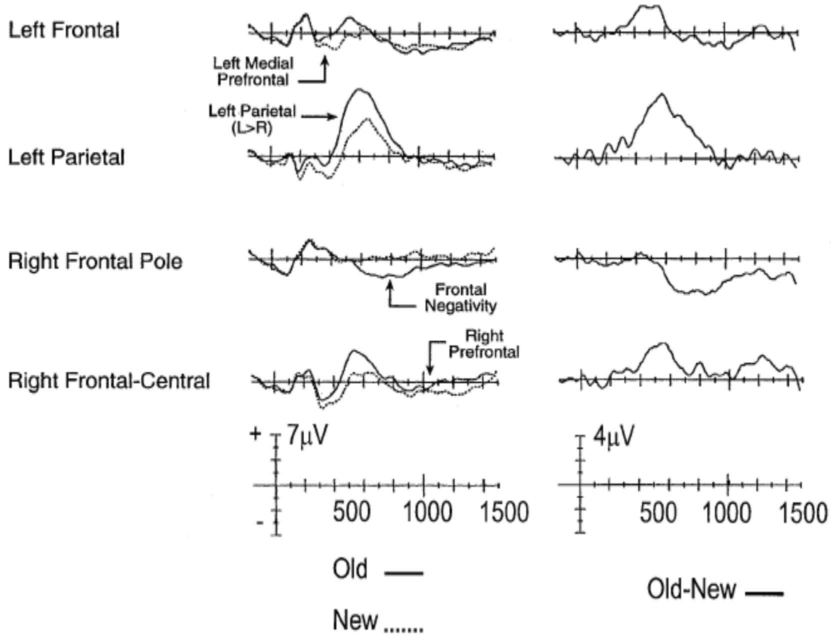


Figure 11. Schematic representation of three main components elicited during the retrieval processing. The left column displays Grand average of ERPs of old and new items, and the right column displays the ERP difference of these two activities (adapted from Friedman and Johnson, 2000).

In general, this effect has been interpreted as an index of familiarity in memory recognition (Curran, Tepe, & Piatt, 2006). More recent studies (e.g., Yovel & Paller, 2004) has cast some doubt on the proposed relationship between the FN400 and familiarity. The experiment used face stimuli to explore the "butcher-on-the-bus phenomenon," or the intuitive feeling experienced when a familiar person is encountered in an unfamiliar situation (such as seeing one's butcher on a bus). Subjects were required to discriminate old/new faces and if "old" they were presented with three subsequent choices: "occupation," "other specifics" and "no specifics". Rather than differentiating correctly classified old and new faces regardless of whether or not occupations or other details were recollected, the FN400 old/new differences were only observed when occupations were recollected. But more recently, Curran and Hancock (2007) chose a more heterogeneous set of faces, including color photographs of people who varied in ethnicity (or race), age, facial hair and glasses. This was done to reduce the similarity between old and new items, and increase familiarity-based discrimination. The same procedure of Yovel & Paller (2004) study was applied. And actually, they found than FN400 for the new faces did not differ according to subject's ability to recollect occupations that had been previously associated with correctly recognized faces.

One other hypothesis that has been advanced is that this frontal component is linked to a form of implicit memory called conceptual priming (Paller, Voss, & Boehm, 2007; Voss, Reber, Mesulam, Parrish, & Paller, 2008). Conceptual priming refers to a form of repetition priming that depends on repeated access to semantic, rather than perceptual, representations. According to Paller et al. (2007), most of the experimental manipulations used to isolate or modulate the neural correlates of familiarity are not 'process pure', and instead exert parallel effects on conceptual priming. The fact that the frontal effect can be elicited by meaningless items is a first evidence that is not possible to explain this phenomenon trough the conceptual priming (Paller et al., 2007). Moreover, evidence comes from studies in which the format of material is manipulated. Curran & Dien (2003) reported that the magnitude of the mid-frontal effect was not significantly affected by a shift in sensory modality (auditory to visual), although a non significant attenuation was reported in the between-modality condition. A second line of evidence comes from studies in which the strength of this frontal effect correlates with the behavioural performance, smaller for misses than for hits (Curran & Hancock, 2007).

Tsivilis, Otten, & Rugg (2001) proposed a recent functional hypothesis to explain this the frontal effect. According to these authors, then mid-frontal effect reflects processes downstream from those responsible for computing the familiarity of the different elements in an episode, and that an earlier old/new effect might be a more direct reflection of the accumulation of familiarity information. Thus, the effect reflects attentionally mediated processing of multiple sources of familiarity information.

The second subcomponent temporally overlapping the left prefrontal positivity is maximal over left parietal occipital scalp. It occurs from 400 and 800 ms, and it is sometimes divided into two main parts, one early component from 400 to 500 ms and a later one from 500 to 800 ms. The left parietal effect has been the most studied, and hence much is known about its relation to episodic retrieval. Findings indicate that the amplitude of this parietal effect increases with study-test repetitions (Johnson, Kreiter, Zhu, & Russo, 1998), is larger in association with those items rated as being consciously remembered (Smith, 1993), is larger for correctly recognized items that are subsequently recalled (Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1996), and is larger for words whose study context is correctly retrieved (e.g., Wilding & Rugg, 1996). Taken together, these data indicate that the presence of the parietal effect is closely allied with recollection and its amplitude is related to retrieval success (Vilberg & Rugg, 2008).

Some studies have used a source assessment along the recognition memory task. The idea is that recollection is stressed because the retrieval of contest information is the core process of episodic memory. ERPs are sorted along the behavioural performance (hits and misses) related to the source memory. Tipically, in this task is required to report if the item has been previously presented in study phase ('old) or not ('new'), and if it is categorized as old, if wich list was presented. Some studies (e.g., Trott, Friedman, Ritter, Fabiani, & Snodgrass, 1999; Wilding & Rugg, 1996) found that when subjects correctly recognized ad old item and they identified its source, the left parietal effect was larger than when the source was incorrectly identified.

Some other studies used a Remember/Know procedure to disentangle recollection and familiarity over parietal sites. Trott et al. (1999) found a larger parietal old/new effect to items that were correctly recognized and given a remember judgment compared to that associated with correct recognition and given a know judgment.

A third subcomponent of the old/new effect, maximal over right central-frontal scalp, begins between 500–590 ms and may last until the end of the recording epoch (e.g., Trott, Friedman, Ritter, Fabiani et al., 1999; Wilding & Rugg, 1996). The timing of this right prefrontal subcomponent is such that, although it typically begins soon after the left parietal old/new effect, its duration exceeds the posterior activity by several hundred milliseconds. At present, a consensus on the functional role of the right prefrontal subcomponent is still lacking. Given that the frontal lobes play a major role in the retrieval of source information, episodic memory seemed a likely candidate of the successful retrieval of source information, as it has been found that this activity was larger when the source was correctly identified. Wilding (1999) manipulated the kinds of source information that had to be retrieved. At study, subjects heard words presented in either male or female voice and made an active/passive judgment or a pleasant/unpleasant judgment. In one retrieval test, subjects had to retrieve the gender of the voice in which the word had been spoken at study, while in another study they attempted to retrieve the kind of task (action or liking) they had performed on the given word during the study phase. The results revealed larger right prefrontal effects in the retrieval of task compared to the retrieval of voice condition. Importantly, this difference also obtained for the ERPs elicited by correctly rejected new items. As these items had not been seen during study, no episodic mnemonic information could have been retrieved. Wilding (1999) concluded that the right prefrontal EM effect could not have reflected retrieval success, suggesting instead that it reflected processes that "monitor for certain kinds of retrieved information". Some other evidence against the idea that the right prefrontal EM effect reflects successful retrieval has been provided by Ranganath and Paller (1999). These investigators employed a different approach, in which highly distracting environmental sounds were delivered while subjects retrieved either autobiographical or semantic memories. Based on neuropsychological and experimental evidence, the ERP response to novelty, the "novelty P3," is thought to depend upon intact frontal cortex. Hence, Ranganath and Paller (1999) predicted that the novelty P3 would be reduced in amplitude to the extent that novelty detection and memory retrieval interfere with one another. In line with their prediction, novelty P3 amplitude was reduced over right prefrontal scalp sites during episodic retrieval, whereas a similar but less lateralized pattern was obtained during semantic retrieval. This was not the case during a control, tone counting condition. Although not clarifying the role that these frontal activations might play during retrieval, these data are important because they demonstrate that right prefrontal activations may occur not only during episodic retrieval but also during semantic retrieval. One possibility is that the reduction in novelty P3 amplitude observed by Ranganath and Paller (1999) has more to do with the strategic aspects of memory retrieval, than it does with a mnemonic function per se.

So, although a number of ERP researchers have investigated the relation between the right prefrontal activity and source memory, they have met with mixed success. One problem in interpreting this frontal effect is that is much extended in time course (from 500 to 2000 ms approximately), and those who have studied it have never looked to single component for short intervals.

The functional significance of the parietal old/new effect is equally obscure as well (Rugg & Curran, 2007). For some authors (Wilding & Rugg, 1996), the effect reflects processes that contribute to the representation of recollected information. Some others (Rugg & Henson, 2002) claim that the effect might index attentional orienting to recollected information, rather than processes supporting its representation or maintenance. Recent findings indicating that the effect varies according to the amount of information recollected, and so it is more consistent with the first of these two proposals (Vilberg, Moosavi, & Rugg, 2006). Besides this dual-processes theory, it is noteworthy to say that there are some other theories supporting different points of view. Yonelinas (2002) claims that recollection is best conceptualised as representing a discrete, threshold mnemonic state (as a all or none phenomenon), whereas others have suggested that both familiarity and recollection are continuously varying memory signals that are combined before a recognition judgement is made (Wixted, 2007). According to these different theories, ERP effects that differentiate 'recollected' and 'non-recollected items' items (in the sense of 'remember' or 'know' procedure) might reflect differences in overall memory strength rather than in underlying memory processes.

2. Integrating neurophysiological and neuroimaging studies

There is a good congruence between results issuing from ERP and homodynamic studies investigating the brain activity related to memory processes. HERA model (Hemispheric Encoding Retrieval Asymmetry), proposed by Tulving, Kapur, Craik, Moscovitch, & Houle (1994). These authors postulated that during encoding left inferior prefrontal cortex is more activated. This early finding has been extended in several studies (for a review see Gabrieli, Poldrack, & Desmond, 1998). And in revised version of this model, Habib, Nyberg, & Tulving (2003), support the idea that both a material-specific and a process-specific asymmetry can even appear in the same region (most left lateralized for verbal material, and most right lateralized for non-verbal material). The two kinds of asymmetry certainly can appear in different regions. It follows, therefore, that material-specific and process-specific models of hemispheric asymmetry can co-exist (see Figure 12).

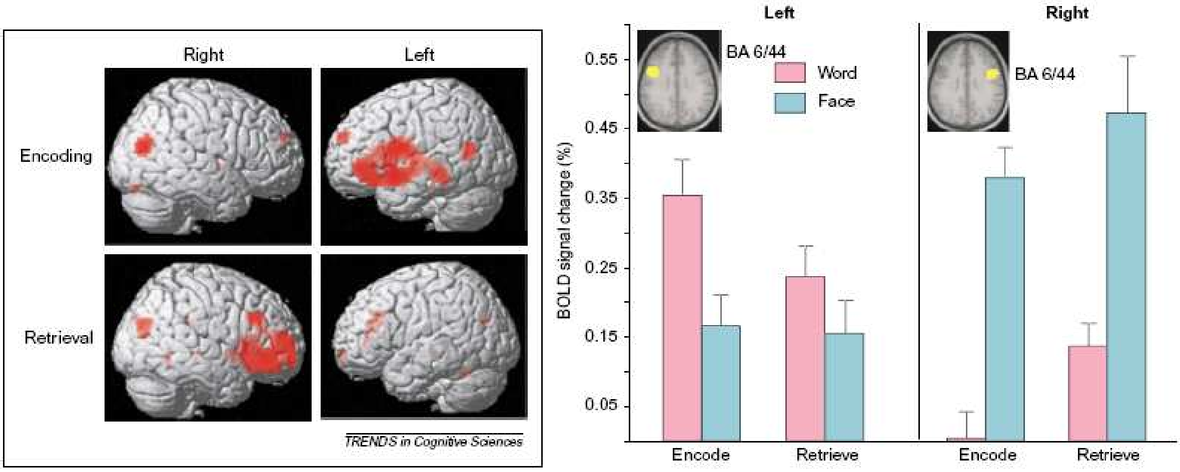


Figure 12. *Left*. Activations of encoding and retrieval The pattern shows that encoding information into episodic memory activates the left hemisphere more than the right, whereas retrieval of information activates the right hemisphere more than the left. *Right*: Percentage fMRI BOLD signal change in the left and right inferior frontal gyrus (BA 6/44) as a function of type of material (words vs. faces) and type of processing (encoding vs. retrieval). (adapted from Habib et al., 2003)

In a PET studies review, Nyberg, Cabeza, & Tulving (1996) report that when the blood flow associated with shallow encoding is subtracted with the deeper encoding, an extensive region in the left prefrontal cortex was differentially activated. This association stands for a relation between the level of processing and brain metabolism. Also, deeper processing at encoding resulted in higher recognition of the studied items. The activation is clearly asymmetrical: no difference regard to the encoding conditions was found within the right prefrontal cortex. Nyberg, Cabeza et al. (1996) reviewed also 25 studies to summarize data about episodic retrieval. These studies evidence two main results: first, activation on the right prefrontal cortex, no activation on the left, or, second, greater activation on the right than on the left. Some distinctions are reported when the kind of material studied is taken into account. Lee, Robbins, Pickard, & Owen (2000) compared brain activity during verbal and visual memory tasks, and they found that the former was associated with blood flow change predominantly located in the left later frontal cortex whilst the latter was associated with change predominantly located in the right lateral cortex. However, some other studies (i.e., Thompson-Schill, M., Aguirre, & Farah, 1997) proposed that the left prefrontal cortex is more concerned in the *selection* of information among some other alternatives, rather than a semantic retrieval per se.

Temporal lobe is also involved in long-term memory, specially the medial temporal lobe structures, such as hippocampus (Moscovitch et al., 2005; Mayes et al., 2007). According to the standard model (Squire & Alvarez, 1995), memory consolidation begins when information, registered initially in the neocortex, is integrated by the hippocampal complex/medial temporal lobes (HC/MTL) and related structures in the diencephalon to form a memory trace that consists of an ensemble of bound hippocampal complex–neocortical neurons. This initial binding into a memory trace involves short-term processes, the first of which may be completed within seconds and the last of which may be completed within minutes or, at most, days. The importance of the hippocampus is that it has a lot of inputs and projections from/to medial temporal lobe subregions, such as the parahippocampal region and the perirhinal cortex (Diana, Yonelinas, & Ranganath, 2007). Moreover, the projects are extended to the frontal lobes and to associative areas as well, such as the parietal regions. Perirhinal cortex receives the majority of its inputs from unimodal visual association areas and roughly a third of its inputs from unimodal, non-visual, semantic association areas. The parahippocampal region receives its strongest inputs from visuo-spatial areas in the dorsal stream, dorsolateral prefrontal cortex and retrosplenial cortex, in addition to unimodal inputs. Both project to entorhinal cortex. Entorhinal cortex provides the majority of the cortical input to the hippocampus, which in turn projects back. The hippocampus is the site of convergence of 'what' and 'where' information in the processing stream. In Figure 13 it is summerized a unified account based on Multiple Trace theory, proposed by Moscovitch (2005).

The data from temporal lobe involvement fit well with those issuing from intracranial EEG recording. Fernandez et al. (1999) recorded from medial temporal lobe structures in pre-surgical epileptic patients during a single word study task. They found that item subsequently recalled elicited during encoding larger N400-like potential than those were missed. Other studies have evidenced that the rhinal N400 component followed by hippocampal positivity are the markers of successful memory formation (Elger et al., 1997; Fell, Ludowig, Rosburg, Axmacher, & Elger, 2008).

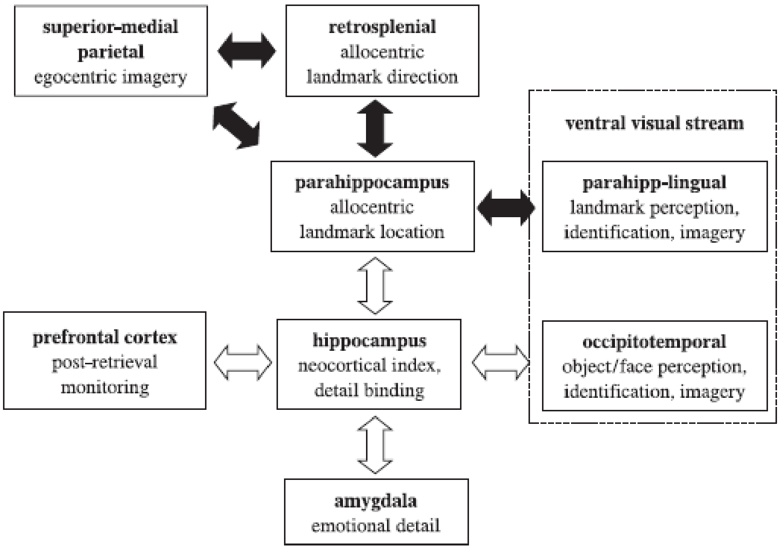


Figure 13. Graphic illustration of a hippocampal–neocortical framework of long-term memory.

Also for the retrieval processes there is a good agreement between the results from hemodynamic and ERPs studies. In recognition memory of prior episodes, human neuroimaging studies have indicated that prefrontal, parietal, and medial temporal cortices are involved, but the functional roles that these regions play in recognition are widely debated.

It is not possible to compare data from ERP and imaging studies along the time processing, due to poor temporal resolution of functional anatomy techniques. However, it is interesting to find overlapping results between these two techniques. Several imaging studies have found activation on right prefrontal cortex in episodic memory retrieval, as shown for ERPs (for a review see Buckner & Koutstaal, 1998). Typically, the regions most commonly involved in this effect include anterior lateral cortex (BA 10) and dorsolateral cortex of the middle frontal gyrus (BA 46/9). Once confirming the HERA model, proposed by Tulving et al. (1994), postulating a predominant right prefrontal activation in episodic retrieval. But the functional role of these areas is still matter of debate.

In an ERP/fMRI study, Duzel et al. (1999) studied the neural correlates of task-related and item-related processes of memory retrieval. Two retrieval tasks, episodic and semantic, were crossed with episodic (old-new) and semantic (living-nonliving) properties of individual items to yield evidence of regional brain activity associated with task-related processes, item-related processes, and their interaction. The results showed that episodic retrieval task was associated with increased blood flow in right prefrontal and posterior cingulate cortex, as well as with a sustained right-frontopolar-positive ERP, but that the semantic retrieval task was associated with left frontal and temporal lobe activity. Retrieval of old items was associated with increased blood flow in the left medial temporal lobe and with a brief late positive ERP component. These results provide converging hemodynamic and electrophysiological evidence for the distinction of task- and item-related processes, show that they map onto spatially and temporally distinct patterns of brain activity.

As seen before for ERP studies the parietal lobe is involved in retrieval related processing. The left parietal lobe effect spanning from 400 to 800 ms seems to have a corresponding counterpart as reported in fMRI literature. Wagner, Shannon, Kahn, & Buckner (2005) recently revised the functional studies and the parietal lobe. The authors reported that, early PET and fMRI studies that compared extended epochs (blocks) of episodic retrieval with non-memory control conditions consistently revealed activation in poster parietal cortex, including during recognition of words, sentences, and pictures (e.g. Tulving, 1994). Initial studies emphasized retrieval-related activations in the precuneus with one hypothesis being that precuneus participates as part of the 'mind's eye' to reinstate visual content during retrieval. Nowadays, the basic phenomenon that has sparked interest in parietal contributions to episodic retrieval is that differential parietal responses are observed when individuals correctly recognize previously encountered old items (hits) as compared with correctly identifying new unstudied items. Recent fMRI data indicate that PPC activation can be modulated by (a) the subjective perception that items are old, (b) recollective- as compared with familiarity-based recognition, and (c) retrieval oriented towards the recollection of episodic details versus detecting differential stimulus familiarity (Wagner, Schacter et al., 1998).

Vilberg and Rugg (2008) in their meta-analysis addressed the question if this brain region can disentangle familiarity to recollection. As reported in Figure 14, many loci have been found sensitive to these two processes. Although this finding can be explained on the assumption that a high proportion of recollected items are also familiar, it is equally compatible with the possibility that activity in this region is modulated not by the nature of the memory signal elicited by a test item, but by some more general distinction between correctly classified old and new test items.

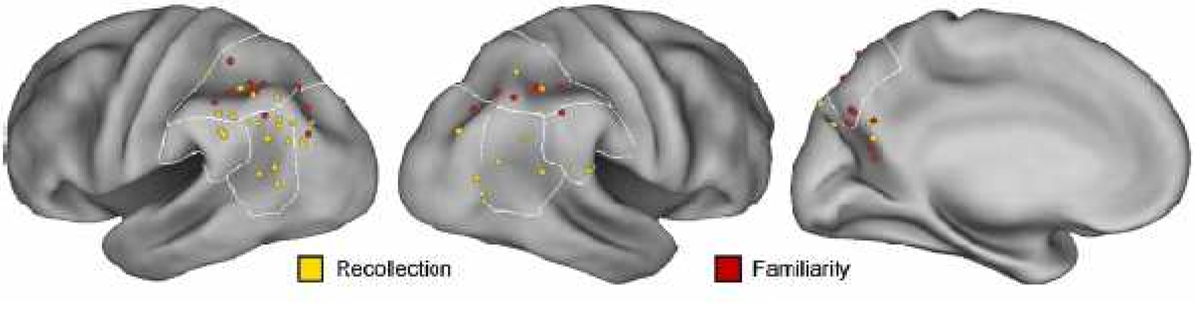


Figure 14. Parietal loci sensitive to recollection vs. familiarity. Displayed from left to right are the left lateral, right lateral, and left medial surfaces of the inflated brain. The borders of Brodmann areas 7, 39, and 40 are demarcated by white lines. (adapted from Vilberg and Rugg, 2008).

The questioning role of parietal lobe comes from evidence that patients with lesion in this site do not present memory impairment. Only one recent study (Berryhill, Phuong, Picasso, Cabeza, & Olson, 2007) reported patients with parietal lesions were required to recollect various autobiographical memories. In the first phase, the participants freely recalled events from their lifetime in as much detail as possible. In a second phase, they answered specific questions about the recalled memories. The results showed that parietal lobe damage decreased the vividness and amount of details freely recalled. By contrast, there are several studies reporting negative results on the relation of parietal lesions and episodic memory impairment (Vilberg & Rugg, 2008).

So, the exact functional role of parietal lobe is yet to be defined. One proposal of Vilberg & Rugg (2008) is that the role of this region supports something to akin to the episodic buffer described by Baddeley (2000). According to this proposal, by contributing to the generation and maintenance of an integrated representation of retrieved information, inferior parietal cortex acts as an interface between episodic memory and the executive systems that monitor and control on-line processing. Second, the mnemonic accumulator hypothesis posits that parietal regions temporally integrate a memory-strength signal. Wagner et al. (2005) linked this idea to signal-detection models of recognition memory that postulate that old–new memory decisions are determined by a continuous memory magnitude. Finally, the the internal representation hypothesis states that parietal regions shift attention to, or maintain on, internally generated mnemonic representations.

As noted by Wagner et al. (2005), each of these hypotheses can account for some but not all available functional neuroimaging evidence. The output buffer hypothesis fits well with evidence that certain parietal regions are associated with recollection (vivid remembering of an event including specific contextual details) rather than with familiarity (vague feeling of oldness in the absence of specific details). The idea is that these regions hold the qualitative content of retrieved information, which by definition is greater for recollection than for familiarity. However, the output buffer hypothesis cannot easily explain why activity in some parietal regions increases as a function of perceived oldness, which refers to the tendency to respond "old" regardless of the true nature of the stimuli. This finding fits better with the mnemonic accumulator hypothesis, which assumes that parietal regions do not hold actual memories but rather signal summarizing information coming from other brain regions, which is eventually used to make memory decisions. Thus, these regions show high activity not only for "old" responses to old items (hits) but also for "old" responses to new items (false alarms). Nevertheless, the mnemonic accumulator hypothesis cannot readily accommodate evidence that certain parietal regions show greater activity when participants attempt to recollect source information than when they try to retrieve item information, regardless of responses and accuracy. This recollective-orienting pattern suggests that these regions track the intention to remember, that is, voluntary attention to memory contents.

Along this line of evidence it has been proposed a new hypothesis. This account postulates that the role of the superior parietal lobe is the reflections of processes downstream of retrieval, the engagement of which depends on the salience or task-relevance of the eliciting item. Cabeza, Locantore, & Anderson (2008) have recently proposed attention to memory (AtoM) model. According to this model, dorsal parietal cortex activity maintains retrieval goals, which modulate memory-related activity in the medial temporal lobe, whereas ventral parietal cortex activity, like a circuit breaker, signals the need for a change in the locus of attention following the detection of relevant memories that have been retrieved by the medial temporal lobe (Figure 15). Relevant memories include not only the realization that an event is old, but also the certainty than an event is new.

Because ventral parietal cortex activity reflects the attentional adjustments that are triggered by the products of ongoing medial temporal lobe activity, it fluctuates continuously over time. The relevant information generated by the medial temporal lobe but does not hold or accumulate this information (as the output-buffer and mnemonic-accumulator hypotheses propose). Basically, these authors propose that the dorsal parietal cortex is associated with the allocation of attentional resources to memory retrieval according to the goals of the remembered (top-down attention), whereas the ventral cortex is associated with the capture of attentional resources by relevant memory cues and/or recovered memories (bottom-up attention).

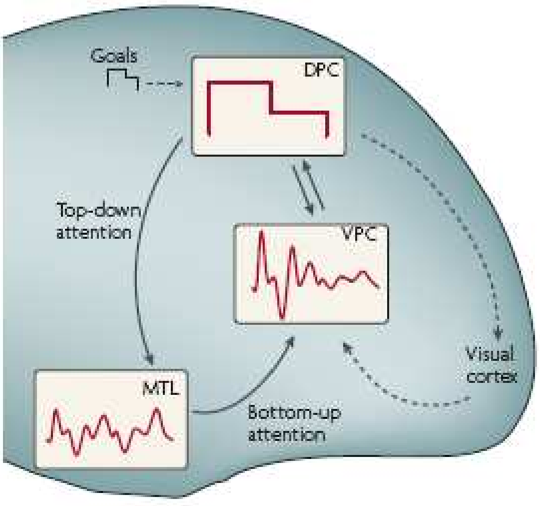


Figure 15. A simple graphical description of the attention to memory (AtoM) model (DPC: dorsal parietal cortex, VPC: ventral parietal cortex, MTL: medial temporal lobe; Cabeza et al., 2008).

Chapter 3

Neurophysiological bases of episodic memory in aging

Unitled (1982) and Untitled VII (1985)
De Kooning, 1904-1997

> Memory is the benefit from our experience.
> *Tulving, 1983*

1. Episodic memory and aging

It is well established that older adults, relative to younger adults, have more difficulty with episodic memory than with semantic memory (Balota, Dolan, & Duchek, 2000; Dalla Barba, Boller, & Rieu, 2008). These deficits might occur at three distinct stages of episodic memory: encoding (the initial storage of the memory), retention (the maintenance of the memory across time), and retrieval (the utilization of the stored memory). In particular, this effect could be due to deficits in encoding and retrieval particular details or the context of events. Older adults appear affected by factors that impoverish contextual support of content memory and task conditions that require access to contextual information only loosely associated with the stimulus. When contextual information is closely related to the target, age differences in memory for context are reduced almost by half (Spencer & Raz, 1995).

Regarding encoding, it appears that even when instructions encourage the formation of rich, elaborate memory traces, older adults are less likely to do so. And regarding retrieval, there is clear evidence of age-related changes. In particular, there is considerable evidence that age differences in memory performance diminish when retrieval is facilitated by providing additional cues at the time of the memory test. For example, largest age differences are found in tests of free-recall, diminished age differences in cued-recall, and often times little or no age differences in tests of recognition (Balota et al., 2000).

Researchers have proposed several mechanisms to account for age-related changes, these are: general slowing, reduced processing resources, loss of inhibitory functions, and lack of cognitive control. According to the general slowing account, aging is accompanied by a general reduction in processing speed that in turn leads to declines in a broad range of cognitive functions, including memory performance (Salthouse, 1996). Processing speed clearly plays a role in many cognitive functions, and it is plausible that complex tasks involving multiple types of processing should suffer more from slowing, showing greater age-related declines. But this theory does not account, for example, for age-related declines found in tasks such as free recall that do not obviously have a speed component. Second, allowing unlimited processing time (for example, self-paced study) does not reduce memory problems for older adults, but instead improves performance in younger adults more. Third, aging is associated with differential effects on tasks that do not apparently involve different amounts of processing (for example, greater effects on source recognition than on item recognition).

The processing resources hypothesis proposes that the amount of attentional resources available for cognitive processing declines with age. Attentional resources are seen as a type of so-called mental energy, with difficult cognitive tasks requiring more resources than simpler tasks. As a result of reduced processing resources, older adults are less likely to carry out the effortful and strategic memory processes associated with good performance (Craik, 1986, 2006; Craik & Byrd, 1982). Thus, older adults have greater difficulties with working memory tasks than with simple span tasks, with remembering specific names than with general facts, and with free recall than with recognition tasks. However, this view has been criticized as too vague about its core construct: attentional resources.

One other proposal is that older adults show working memory deficits caused by less efficient inhibitory mechanisms (Hasher & Zacks, 1988). According to their view, inhibition serves primary functions that are of relevance to memory performance: preventing irrelevant information from entering working memory, and deleting no-longer-relevant information from working memory. The inhibition view is appealing in that it fits well with the fact that older adults often have great trouble dealing with interference and distractions, and that aging is associated with an increased rate of false recognitions and memory intrusions. However, it does not explain the difficulties that older adults have with prospective memory tasks, where their problem seems to reside in initiating rather than inhibiting the execution of planned intentions.

And finally, one other point of view relies on the distinction between automatic and consciously controlled processing in memory tasks. Jacoby (1991) differentiates recollection, a controlled form of memory use, from familiarity, an automatic type of memory process. Aging is accompanied by declines in controlled processing, while automatic processing is largely spared. Thus older adults have few problems in finding information familiar; however, they have substantial difficulty in recollecting details of the original experience. Jacoby has developed ingenious methods to provide independent estimates of recollection and familiarity; these studies demonstrate that familiarity holds up with age, whereas recollection does not (Jennings & . 1993). In this account it is proposed that memory is a dual-process system, neurally segregated mechanism that are affected in different manner by aging. Although parsimonious, the single-process theories have trouble explaining many findings.

To specifically explain the context (episodic) deficits, more frequently reported (Spencer & Raz, 1995), it is proposed that older adults have trouble binding pieces of information into complex memories (Chalfonte & Johnson, 1996). Such results suggest that there is a distinction between memory for single units of information and memory for associations among those units and that aging affects those two types of memory differently. Naveh-Benjamin (2000) extended and clarified this idea by proposing the *associative deficit hypothesis* (ADH), which holds that a major contributor to older adults' deficiencies in episodic memory is their relative inability to form and retrieve links among single bits of information.

Old & Naveh-Benjamin (2008) extensively revised this account. The major finding of this meta-analysis was that older adults are, in fact, more disadvantaged on memory tests of associations than on tests of item memory compared with young adults. An age-related associative deficit, then, indicates not only that older adults are impaired in memory for associative information but that this impairment is larger than the impairment in memory for item information. In particular, aging seems to impair memory for binding required in source, context, temporal order, location, and item pairs to a greater degree than memory for single units of information. Second, the results showed a clear age-related associative deficit when tested materials were learned intentionally, maybe because older adults have difficulty using self-initiated processes to bind together pieces of information. Additionally, it has been shown that providing participants with associative strategies reduces the age-related associative deficit (Naveh-Benjamin, Brav, & Levy, 2007a), indicating that older adults have difficulty using associative strategic processes. Third, older adults seemed to exhibit an associative deficit for both verbal and nonverbal information, providing evidence for the generality of the ADH. While familiarity is sufficient to perform well on an item recognition test, an associative recognition test requires recollection; that is, it is not enough to be familiar with two items, but one must recollect enough detail to determine whether those items were studied together.

Beside the cognitive theories of aging, neuropsychology have tempted to reconcile age-related differences along the neural bases involved. West (1996) has provided a review of the aging literature, and has suggested that both neurophysiological evidence and also neuropsychological evidence indicates that the frontal lobes are especially sensitive to increased aging.

Medial temporal and frontal lobes are the two main areas involved in aging and memory (Head, Rodrigue, Kennedy, & Raz, 2008). It is proposed that medial temporal areas are at the core of an associative system that relatively automatically binds together what is consciously apprehended (Moscovitch & Winocur, 1995; Mayes et al., 2007). The notion is that at any point in time a number of distinct neural networks/pathways are activated via both internally generated and externally available stimuli. The medial temporal system has been viewed as binding these distinct patterns to produce a record of the conscious experience.

If the medial temporal system is so important for declarative memory performance, then why is there the interest in age-related changes in frontal lobes? Some authors (Buckner & Petersen, 1996; Moscovitch et al., 2005; Moscovitch & Winocur, 1995) have argued that a second frontally-mediated system is also quite important in declarative memory performance. This system operates on both the input to the medial temporal system and the output from it. Presumably, the frontal areas provide control over the networks that become activated during encoding and become available during retrieval. In this sense, frontal control system can be viewed as a system that works with memory, providing the input and exerting control over the output. Older adults appear to be especially disrupted by aspects of memory tasks that involve frontal structures. In addition, there is now considerable evidence from imaging studies of strong involvement of frontal areas in memory performance (e.g., ; Buckner, 2004; Buckner & Petersen, 1996; Rajah & D'Esposito, 2005). Some other authors have argued that frontal system are important for executive aspects of memory (Elderkin-Thompson, Ballmaier, Hellemann, Pham, & Kumar, 2008), for inhibition, or cognitive control (Paxton, Bach, Racine, & Braver, 2008), and these appear to be partially disrupted in healthy older adults. These data are also consistent with studies demonstrating that older adults show deficits in source memory

(Dennis et al., 2008; Swick, Senkor, & Van Petten, 2006). Glisky, Polster, & Routhieaux (1995) reported a double dissociation in older adults between frontal vs. medial temporal functioning and item and source memory performance in healthy young and older adults. Specifically, when older participants were divided into high vs. low frontal groups based on neuropsychological test performance, the high frontal group exhibited better source memory performance. On the other hand, when participants were divided into high vs. low medial temporal groups based on neuropsychological measures, the high medial temporal group exhibited better item memory performance.

2. Episodic memory and aging: neurophysiology of encoding and retrieval processing

Some studies in ERPs started to investigate the 'frontal lobe deficits' hypothesis. According to this line of investigation researchers have investigated the integrity of frontal lobe in cognitive functions and aging. As a whole, the results of these investigations suggest that there are differences in physiological parameters of elderly participants, as manifested in ERP patterns. And some of these patterns may be 'compensatory', whereas other may be 'inefficient', and by now there is clear-cut evidence supporting one or another position (for a review see Friedman, 2003). In this chapter, age-related memory processing and ERPs will be reviewed and discussed.

In similar fashion see for young adults, encoding and retrieval related ERP activity has been investigated in older adults (for recent reviews see Friedman & Johnson, 2000; Friedman, 2007). A brief review of these studies is reported in following paragraphs.

a. Encoding processing and ERPs

As the Dm effect has been associated with elaborative encoding, and older adults are thought to be deficient in using this kind of encoding strategy spontaneously, some investigators have attempted to contrast this electrical activity in young compared with older adults (e.g. Friedman, 1996).

Friedman et al. (1996) asked young and old participants to study lists of words under either orthographic (detect words whose first and last letters were in exact alphabetic sequence) or semantic (detect animal words) encoding conditions. Participants were subsequently assigned to either direct (stem cued recall) or indirect (word stem completion) memory tasks. Friedman et al. (1996) recorded ERPs only during the study phase. For both age groups, depth of processing (semantic, orthographic) had a systematic effect on both indirect (stem completion) and direct (cued recall) memory performance, with semantic processing producing greater accuracy on both types of memory test. However, the depth of processing effect was larger for stem cued recall than for word stem completion. There was a small age-related difference (favouring the young) in proportion correct on both the direct and indirect tests. Dm is thought to reflect elaborative encoding processes, the larger Dm magnitudes observed in the waveforms of the young compared with those of the old suggested to Friedman et al. (1996) that the small, though unreliable, age-related performance differences that resulted during the direct and indirect test phases may have been mediated by greater elaborative processing on the part of the younger adults.

One of the hypotheses of this different ERP activity in aging is that when older adults have not specific encoding strategy, they do not use semantic elaboration spontaneously. To investigate the nature of these processes, Nessler, Johnson, Bersik, & Friedman (2006) have employed a semantic selection paradigm. Participants were asked to study words under low- and high-selection conditions. The low-selection condition task required a decision as to whether a previously presented picture (e.g., a tiger) matched the meaning of a to-be-remembered word. In the high-selection condition, a decision was made concerning whether a previously presented adjective (e.g., heavy) described a feature of to-be-remembered word (e.g., feather). The idea is that in this latter condition items require more semantic concepts in order to be processed. In subtracting the ERP activity related to this two selection tasks both young and older adults show significant negative activity in the early period from 400 to 800 ms over the frontal sites. The effect of selection persists until 1200-1400 ms in young adults, whereas dramatically attenuated in older adults. Behaviourally, older adults performed poorer than young ones in the recognition task. Consistent with the performance, it seems the initial semantic aspect of encoding is quite preserved also in older adults, whereas the attenuation of late ERP activity could be responsible of defective episodic memory encoding. The distribution of such an attenuation over frontal scalp demonstrates this brain region is associated of episodic memory is not engaged in the late interval in older adults.

But conversely, the Dm effect seems to not be affected by implicit or explicit tasks. Téllez-Alan & Cansino (2004) recorded in young and older adults during the performance of an incidental encoding task (subjects were unexpectedly given a recognition test) followed by an intentional task (subjects expected the recognition test). Both tasks consisted of an encoding stage in which subjects classified words (natural/artificial) and a recognition stage in which they indicated whether the words were old (presented during the encoding stage) or new. In both groups and tasks, the ERPs, during encoding, differed as a function of subsequent recognition: the old words correctly recognized generated greater amplitude potentials than the incorrect ones. But the ERP activity related to encoding did not differ between young and older adults.

Friedman and Trott (2000) had their participants to study two lists of sentences. Each sentence contained two unassociated nouns. At test, subjects made speeded and accurate old/new recognition decisions to paired noun sequences. For all nouns judged old, participants then made remember (context): know (familiarity) followed by temporal source (i.e. list) judgments. The ERPs at study were averaged as a function of the subsequent correctness of the recognition response (i.e. hit) in association with the judgments of remember and know. These waveforms were then compared with the waveforms associated with subsequently unrecognised trials (i.e. misses). These data appear in Figure 16.

Both young and old show reliable Dm effects for subsequent hits associated with a ‘remember’ (source) judgment. However, young and old differ with respect to the Dm associated with subsequent ‘know’ (item) judgments — only the old show a reliable subsequent memory effect in this condition. Whether remember and know judgments reflect cognitively and physiologically distinct processes, or two portions of a graded continuum separated by a ‘remember’/’know’ criterion is an open question. Regardless, it seems reasonable that, if this distinction is cognitively meaningful, the likelihood of making a subsequent judgment of remember or know should somehow be reflected at encoding. Hence, these data suggest that, at encoding, older subjects did not differentially encode those items that would be subsequently associated with retrieval of contextual details from those that would not. This, in turn, suggests both a difference in encoding between the young and the elderly and or an age-related difference in the way in which the remember/know criterion was applied during the subsequent memory test. Nevertheless, these data suggest the possibility that older adults show a deficit during the encoding phase of recognition memory paradigms.

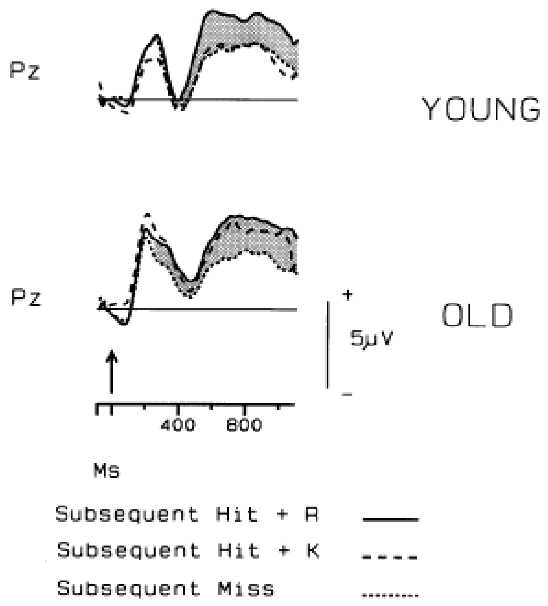


Figure 16. Grand mean ERPs averaged across young (top row) and older (bottom row) participants during the study phase of a study test paradigm. The ERPs have been averaged according to whether the studied items that were subsequently correct were associated with remember (R) or know (K) judgments. These waveforms are compared with waveforms associated with subsequently missed trials (from Friedman & Trott, 2000).

a. Retrieval processing and ERPs

As in young adults, the retrieval related ERP activity was specially investigated along the old/new parietal effect. In one of the first of these kinds of investigations, Friedman et al. (1993) used a continuous recognition memory paradigm, and recorded ERPs and reaction times from young, middle-aged, and older adults. The authors found that the ERP old/new effect and performance accuracy decreased in similar fashion as a function of lag for both young and elderly participants (however, the old performed more poorly than the young at each lag). The posterior ERP old/new effect had similar scalp topography in both age groups, and the early and late aspects of this effect were of similar magnitude in the waveforms of the young and old. However, a frontally-oriented positive slow wave (1200–1800 ms post-stimulus) was larger to new items and was larger in the ERPs of the younger participants.

However, the data indicated that, at prefrontal electrode sites, the elderly showed a statistically significant increase in positivity as a function of lag, in highly similar fashion to that observed in the young adult data at more posterior recording sites. The authors discuss this positive activity as indicative of greater effort to maintain task performance, and as consistent with a frontal lobe locus of age-related memory deficits.

Swick and Knight (1997) assessed verbal continuous recognition memory and indirect memory in a lexical decision task, in which repetition was incidental to task performance. These investigators reported a greater decrement in performance and ERP amplitude during the direct task as a function of lag in the older relative to the younger sample. This did not occur in the indirect task. They also observed larger old/new effects in the direct compared with the indirect task for the young, but the reverse relationship held for the elderly. The authors' interpretation relies on the idea that young placed greater reliance on recollective processes during continuous recognition while the older participants relied more on familiarity. Intuitively, this interpretation is attractive because relative to the young, older subjects have been reported to produce a greater number of recognition judgments based on familiarity rather than context.

Rugg, Mark, Gilchrist, & Roberts (1997) compared directly the ERP old/new effects recorded in a direct memory task (continuous recognition) with those recorded in an indirect task (semantic decision). During the indirect task both young and old produced robust repetition effects at both short and long lags, although for the old, the old/new effect associated with the long lag was smaller than that associated with the short lag. In the direct task, by contrast, the young showed reliable ERP old/new effects at both lags (with that of the long lag reliably smaller than that of the short lag) whereas, in the waveforms of the elderly, only the short lag produced a reliable old/new effect (which was smaller than its young adult counterpart). Rugg et al. (1997) concluded that it was the late aspect, and not the early aspect of the old/new effect that was age-sensitive. One recent report by Nessler, Johnson, Bersik, & Friedman (2008) used a shallow (match noun-verb) and a deep semantic (adjective- noun comparison) encoding. They recorded ERP at recognition during a recognition task in young and older adults. Behaviourally they did not find any difference, by contrast some age-related ERP activity differences were found. The frontal activity was the same in the two groups, where the parietal effect was dramatically attenuated in older adults. Nessler et al. (2008) concluded that in older adults familiarity-based ERP is preserved, whereas recollection is not.

More recently, Ally, Simons, McKeever, Peers, & Budson (2008) assessed the memory contribution of parietal cortex in younger and older adults, and in patients with circumscribed lateral parietal lesions. In a standard recognition memory paradigm, subjects studied colour pictures of common objects. One-third of the test items were presented in the same viewpoint as the study phase, one-third were presented in a 90 degree rotated viewpoint, and one-third were presented in a non-canonical viewpoint. Results revealed that the duration of the parietal old/new effect was longest for the canonical condition and shortest for the non-canonical condition. And they found that older adults demonstrated a diminished parietal old/new effect relative to younger adults. This is conflicting with the episodic-buffer hypothesis (Baddeley, 2000). According to this hypothesis, the expectation is that the parietal effect would be longest in duration for the non-canonical condition, as information would likely need to be held for a longer period of time for a memorial decision to be made and shortest in duration for the canonical condition, which likely requires a shorter period of time for a memorial decision to be made. Data from brain damaged patients show similar pattern as in older adults, suggestive that parietal lobe has only a supportive role in recollection. These authors proposed that parietal lobe index the magnitude of the subjective experience occurring at recognition. It has been suggested (Hassabis, Kumaran, & Maguire, 2007) that recollection entails a number of component processes, including both objective and subjective processes. The fact that parietal lesion patients are relatively unimpaired on tests of recognition suggests that parietal activity may support a subjective component of recollection rather than an objective one.

Some other interesting results come from studies using recognition memory task with source monitoring. Dywan, Segalowitz, & Webster (1998) used a paradigm in which participants studied a list and had to respond new to any new item even if it repeated during the test phase. Hence, as repetition engenders familiarity (and, therefore, a tendency to respond old to the repeated 'new' item), whereas a participant should only produce a response of old if the item had indeed appeared on the study list, these investigators pitted familiarity against recollection. The authors started to the hypothesis that if older adults based their old/new decisions more on familiarity than recollection, they would produce more false alarms to repeated foil words (as these would have elevated levels of familiarity by virtue of repetition), than would the younger adults. In fact, older subjects did produce more false alarms (40%) to the repeated foil words and these were associated with robust 'old/new' effects (i.e. greater positivity to repeated than unrepeated foil words) which, in turn, were greater than the old/new effects elicited by correctly recognized old items. The younger adults had a smaller false alarm rate and did not produce reliable 'old/new' effects to these foil items. These data add to the evidence of a source memory deficit in older adults.

One another evidence supporting the frontal lobe deficit hypothesis comes from Trott, Friedman, Ritter, & Fabiani (1999) study. These investigated memory for context with two different, but complementary techniques. At the heart of the experimental design was an assessment of episodic priming, which allowed a comparison of reaction time and ERPs to two previously unassociated nouns presented during a study phase depending upon whether, during a recognition test phase, the second noun was or was not preceded by the first noun with which it was associated in a sentence during the study phase (i.e. whether the two nouns were presented in same or different sentence contexts during the test phase). As the two nouns are unassociated prior to the experiment, any priming that results has to be due to the association being retained in memory. By contrast, the other method used for assessing contextual effects involved a list discrimination task (i.e. temporal source or recency). Participants saw two lists of sentences. During this test block, two nouns were presented sequentially and, for each noun, the participant made a speeded and accurate old/new reaction time judgment. Following the presentation of the second noun, if either noun had been judged old, it was re-presented and the participant made a temporal source judgment. Young and old show remarkably similar posterior old/new effects and a similar ordering of conditions; the ERPs associated with a hit trial on which the source was correctly judged are larger than those associated with a hit trial on which the source was incorrectly attributed, and both of these are larger than the ERPs elicited by new items (i.e. the ERPs associated with both of these behavioural outcomes show highly robust old/new effects). Because the core process of episodic memory is the retrieval of the context in which the item was initially learned, these data suggest that the posterior old/new effect has something to do with recollection. But no effect was found in prefrontal sites in old participants regarding the retrieval of context information (see Figure 17). Trott et al. (1999) concluded that the deficit in older participants is related to memory source (indexed by the frontal lobe activity) and not related to episodic memory.

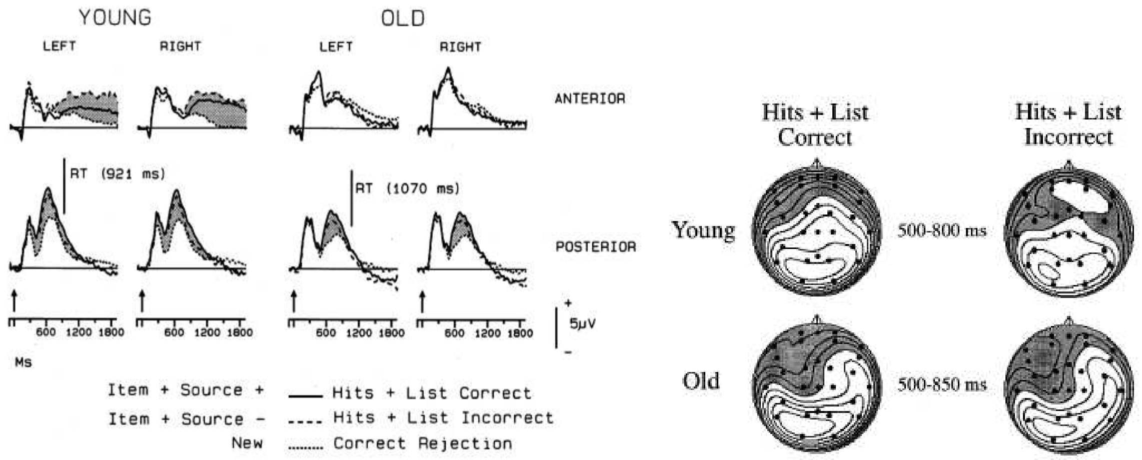


Figure 17. (Left) Grand mean ERPs averaged within the young and old age groups according to whether the correctly recognized old item was associated with a subsequent correct or incorrect judgment of temporal source. (Right) Surface potential scalp maps of the posterior old/new effects associated with hit trials that were accompanied by correct and incorrect temporal source attributions in young and old participants. (adapted from Trott, Friedman, Ritter, & Fabiani, 1999)

Other studies have replicated these latter findings. Wegesin, Friedman, Varughese, & Stern (2002) reported an absence of frontal effect of source retrieval in older partecipants, and by contrast they showed a central negative component not see in the young participants. And one recent paper by Swick, Senkor, & Van Petten (2006) show that healthy older participants and patients with prefrontal cortex lesions did not show the early old/new component of source retrieval that was prominent in the young. And older participants displayed a prominent left frontal negativity (from 600 to 1200 ms) not observed in the young.

To sum up, it seems difficult to get a firm conclusion about the ERP activity and memory processes in aging. This is due to small number of papers in literature and to mixed results reported as well. Basically, for encoding there is some evidence indicating that older adults did not differentially encode items that would be subsequently retrieved with context from those that would be retrieved without such attributes. And this it is indexed by an attenuation of ERP activity over left inferior prefrontal scalp.

For retrieval, there is some evidence to an early parietal old/new effect unchanged with aging, accompanied to a frontal lobe activity. The frontal lobe activity appears to be attenuated when source memory in involved in retrieval.

3. Episodic memory and aging: integrating neurophysiology and neuroimaging studies

Neuroimaging studies had the main goal to understand neural bases due to their higher spatial resolution compared with ERP studies, in which temporal resolution is much better.

Schacter, Savage, Alpert, Rauch, & Albert (1996) scanned young and older adults while they completed the three-letter stems of words (i.e. stem cued recall), under an explicit instructional condition, that they had studied either under semantic or non-semantic encoding conditions. PET subtractions revealed similar-magnitude activation of the hippocampal region in both young and elderly adults. Frontal activation was greater when participants attempted to retrieve items that were studied during the non-semantic compared with the semantic encoding condition, but the areas activated differed for young and old. For the young, activation was confined to Brodmann area 10 (right anterior frontal lobe), while in older adults activation occurred in more posterior frontal lobe regions and Broca's area on the left. Schacter and colleagues interpreted the hippocampal activation as reflecting age-invariant memory processing, whereas the difference in the site of frontal lobe activation was consistent with different retrieval strategies in the young and the old. Similar pattern of findings emerged from a study performed by Cabeza et al. (1997) reported right prefrontal activation in young adults, but a pattern of reduced bilateral frontal activation in their older adult subjects.

By contrast, there is also some other evidence against these results. Backman et al. (1997) found equal-magnitude right prefrontal activation in their young and old subjects during explicit cued stem completion of three-letter word stems seen during the study phase, but poorer performance in the older participants.

Grady (2000) reported reduced hippocampal activation in elderly relative to younger adult participants during face encoding, but equal-magnitude right prefrontal activations during face recognition in both young and older adults. Grady et al. (1995) data suggest that a hippocampal deficit during encoding may also contribute to the memory difficulties of older adults, at least with respect to face stimuli, but fail to replicate the lack of right prefrontal activation in the elderly seen by Cabeza et al. (1997).

Basically, Cabeza et al. (1997) found that old adults showed smaller differences in localized neuronal activity than young adults in some brain regions and larger differences in others. These preliminary results lead these authors to elaborate a new model for aging and memory functioning, based on HERA model. In 2002, Cabeza proposed the HAROLD Model (Hemispheric Asymmetry Reduction in Older Adults). The model starts to the idea of that asymmetry reduction plays a compensatory role in the aging brain. More specifically, it is proposed that activity during cognitive performances tends to be less lateralized in older adults than in younger adults. There are more evidence supporting this model in domains of episodic memory retrieval, episodic memory encoding/semantic memory retrieval, working memory, perception, and inhibitory control. In young participants activations tend to be left lateralized during encoding and right lateralized during retrieval, known as hemispheric encoding/retrieval asymmetry (HERA, Tulving et al., 1994). An age-related reduction in hemispheric asymmetry during episodic memory retrieval has been demonstrated for different kinds of tests (recall and recognition) and for different kinds of stimuli (verbal and pictorial) and therefore appears to be a robust and general phenomenon (Cabeza, 2002). In episodic memory encoding they demonstrated that age-related asymmetry reductions are not limited to the situation in which prefrontal cortex activity is right lateralized in young adults with an age-related increase in left prefrontal cortex activity (e.g., Stebbins et al., 2002); they may also occur when prefrontal acitivity is left lateralized in young adults with an age-related decrease in left prefrontal activity. This proposal is consistent with different aging theories. If it is assumed that prefrontal cortex performs inhibitory operations, then the inhibition view is consistent with the HAROLD model: older adults must recruit additional prefrontal cortex regions to reach the same level of inhibitory control young adults reach. The resources view (Craik, 1986) assumes that cognitive processes are fuelled by a limited supply of attentional resources and that aging further reduces this limited supply, producing deficits on demanding cognitive tasks. Older adults could accomplish this goal by engaging additional brain areas, such as homologous contralateral regions.

The neuroimaging and ERP studies differ with respect to the location, presence and/or absence of right prefrontal regions of activation in older adults. Two neuroimaging studies have reported equal-magnitude right prefrontal areas of activation and two have shown abnormal right prefrontal activations in elderly participants. Two of three ERP studies have shown reduced right prefrontal old/new effects in the waveforms of the elderly, while one has reported no difference. The differences within the ERP and within the neuroimaging data sets are not easily reconciled. Differences in subject age are not likely to account for these discrepancies, as mean ages of participants was roughly similar in both the ERP and neuroimaging studies (between 66 and 70). Although task parameters differed somewhat among studies (e.g. face recognition vs. word recognition for PET studies; voice judgments vs. list judgments for the ERP studies), it is unclear at this point if these discrepancies can account for the differences among studies. Differences between PET and ERP studies are also not easily reconciled. Observation of PET areas of activation relies on the subtraction of brain activity elicited during two different conditions averaged over blocks of trials, whereas ERP data result from the averaging of the relevant brain activity to events that are random by trial. The use of subtraction in PET may, therefore, provide results that cannot be interpreted unequivocally (Johnson et al., 1997).

Chapter 4

Experiment 1

Episodic memory of face-name associations in young adults

1. Introduction

Associating a name with a familiar face is a relevant aspect of our social life with which we are continuously confronted (Valentine et al., 1996). As seen in Chapter 1, different models have described the cognitive processes involved in this task. In Bruce and Young's (1986) functional model, names are stored separately and they are retrieved after access to the person's PIN (Personal Identification Nodes). Burton et al. (1990) proposed an interactive architecture with processing units clustered into pools of units with similar functions, and within the pool, units have inhibitory connections. Four pools are hypothesized: Face Recognition Units (FRUs), Person Identity Nodes (PINs), Semantic Information Units (SIUs, which represent specific biographical information) and Name Input Units (NIUs). In Valentine et al.'s model (1991) the processes involved in recognising and retrieving people's names are mediated by a set of name recognition units (NRUs, analogous to FRUs, Face Recognition Units). Neuropsychological investigations have shown category specific dissociations as well. A series of patients have been described as having impairment to the retrieval of famous names but not of common names (for reviews see Semenza, 2006; Semenza, Mondini & Zettin, 1995; Yasuda, Nakamura, & Beckman, 2000).

Few studies have investigated the neural bases of proper name retrieval and its representation. Müller & Kutas (1996) reported a difference in the N1/P2 complex when subjects listen to their own name with respect to common names. This complex was followed by a prominent negativity at the parieto-central site around 400 ms and a late positivity between 500-800 ms over the left lateral-frontal sites. Dehaene (1995), using a task of word categorization, found that ERPs elicited for proper names differed to other categories (animals, verbs and numerals) from 280 to 356 ms. The topography was specific as well: proper names evoked a temporal negativity extended towards the left inferior temporal sites, without a clear hemispheric asymmetry. By contrast, a more left temporal involvement was found when subjects are required to retrieve a proper name by a definition (Proverbio et al., 2001). These authors reported a larger amplitude of N1 over the left temporal sites when proper names are provided, whereas common names elicited a stronger activation of the visual cortex later, at 250 ms. Left prefrontal and central areas were also involved at 300 ms.

Other studies have investigated face and name recognition using indirect tasks, such as the priming paradigm. The basic idea is that the processing of stimuli could be enhanced when the same or a semantically associated stimulus have been previously encountered. Basically, for famous faces, two main effects have been found: the early repetition effect (ERE), or N250r, may be related to FRUs, and the late repetition effect (N400), over centro-parietal sites, found for longer lags, and related to semantically related primes (Boehm & Paller, 2006). Schweinberger (1996) found a priming effect on familiar names and faces starting at 300 ms, consisting of a reduced negativity over the vertex and a reduced positivity at prefrontal sites. Interestingly, the ERP effect was not affected by prime type, face or name: this implies a face domain-independent representation and a post-perceptual locus of priming. In a subsequent study, Schweinberger et al. (2002) investigated the neural bases of repetition priming for long lags. In particular, they found that when subjects have to judge the familiarity of a face or a name primed by the same or different stimulus, a parietal positivity around 500-600 ms was associated. They also found that the topography of priming for face and name was undifferentiated, confirming the hypothesis of a common representation for famous people. In Herzmann and Sommer's (2007) study, subjects were presented with the target faces or names primed by the same or different stimulus. They had to recognize the target as belonging to a list of stimuli previously studied. The authors found that the priming effect occurred only for studied faces and names both at the behavioural (reaction time) and electrophysiological level. In particular, they found an early repetition effect only for learned faces, and a late repetition effect for all stimuli presented. Learned names showed a stronger late repetition effect than unstudied names.

Some other studies have investigated the electrophysiological bases of the encoding and retrieval of proper names when a face is presented through direct tasks. Guo et al. (2005) investigated the neural bases of successful encoding of faces, names and face-name associations. Subjects were presented with novel faces paired to a spoken name during ERPs recording. Successful encoding was measured as the 'Dm effect'. The 'Dm effect', described by Sanquist et al. (1980) and Paller et al. (1987), is referred to as the neurophysiological difference based on the comparison of successfully retrieved/recognized items with those that are not. Basically, they found that the Dm effect for the successful retrieval of face-name pairs (Experiment 2) was characterized by a positive waveform from 200 to 800 ms.

Paller et al. (1999) studied the recollecting processes in comparing faces associated with brief biographical information and some others that were not. In order to stress recognition but not priming, subejcts were required explicitly to remember a set of faces and to forget another set. ERPs to targets recorded during the recollection phase showed a positive deflection peaking at 500 ms, with its maximal over the parietal region. Interestingly, the authors found some differences between ERPs for faces to be remembered and those to be forgotten. This difference was prominent over the frontal and parieto-occipital sites from 300 to 600 ms, whereas it was restricted over the parieto-occipital regions later, from 600 to 900 ms. A similar pattern of data was found in a subsequent study using a yes-no recognition test (Paller et al., 2000). They found that ERPs for retrieved items were more positive than for new ones from

300 to 600 ms. But for named faces (those associated with autobiographical information) the study effect was over both the anterior and posterior sites, and for unnamed faces was restricted to posterior sites. Moreover, ERPs difference between named and unnamed faces was found only over Fpz and Fz from 400 to 500 ms. This is evidence for an anterior network associated to person recollection connected to biographical information learnt before.

And finally, Joassin et al. (2004) found that the retrieval of face-name associations involved a network made up of the left inferior and medial frontal gyrus, and the left inferior parietal lobe, the same brain areas found in the PET study performed by Campanella et al. (2001) using the same experimental design.

So, the aim of this study is to investigate the neural network of encoding and retrieval of face-name associations through ERPs. To test this first hypothesis, we recorded ERPs while subjects were required to encode associations of face-name of famous and novel people and to retrieve them later. Famous and novel pairs were used in order to compare different neural processing in novelty learning against well-established recognition, as in the case of famous face-name associations. The advantange of recording both during encoding and retrieval is that ERP-related activity can be compared in the same subjects. A paradigm was used in which subjects had to make a choice between two different alternatives of proper names to associate to a face presented. This is not a typical recognition paradigm, but this has the advantage of being more similar to recollection-based processing. So, it is expected that during the retrieval phase, recollection-based ERP acitivity will be found, in particular over posterior sites. Sustained frontal acitivity (index of familiarity-based processing) is not expected to found, because the task requires more retrieval of context-based information.

2. Materials and Methods

2.1. Participants

Twenty-four (four male and twenty female) subjects took part in the experiment. The mean age was 27 (SD ± 6.1; range 19-38) years and mean education was 16.3 (± 2.2) years. They were all right-handed according to the Edinburgh handedness inventory test (Oldfield, 1971) and they had normal or corrected-to-normal vision. Participants reported being free of neurological disorders and they gave their written informed consent.

2.2. Stimuli

Stimuli included grey-scale faces and proper names. Faces were downloaded from electronic datasets and other resources on the web and processed by Adobe Photoshop 5.0. A set of 96 faces was collected (48 males, 48 females), scaled to 210 x 263 pixels and presented from a distance of 100 cm (subtending a visual angle of ~ 3.15° x 4°). The photographs portraying famous faces were of well-known politicians, movie stars and other famous celebrities, whereas novel faces where unfamiliar and chosen to resemble famous people.

We conducted a pilot study to define the set of pictures to use in the experiment. Pictures printed on an A4 format sheet were presented to young adults, who were asked to correctly name the famous people. We considered only pictures with a percentage of correct responses above 90%. A set of 48 proper names (Font Arial 24) was randomly assigned to novel faces.

2.3. Procedure

After electrode application, thebsubjects were seated in a comfortable chair in a dimly illuminated room, facing a computer monitor placed 100 cm in front of them. They were instructed to pay attention and to minimize eyeblink.

The experimental procedure was structured in an encoding phase followed by a retrieval phase. Each phase comprised three separate blocks of 32 trials each.

During the encoding phase, subjects were presented with a face (1000 ms), followed by the corresponding proper name (1000 ms), then a fixation point appeared and subjects were requested to respond if a male or female had been presented. During this phase, subjects were asked to associate the proper name with the face presented. Responses were collected via a response-box using both hands.

During the retrieval phase, subjects were presented with the face presented before (1000 ms), followed by a first proper name (1000 ms) and a second name (1000 ms), then the fixation point appeared. They had to respond by pressing the left button of the response-box if the first name was correct and the right one if the second was correct (see Figure 18. **Schematic representation of the experimental procedure.**Figure 18).

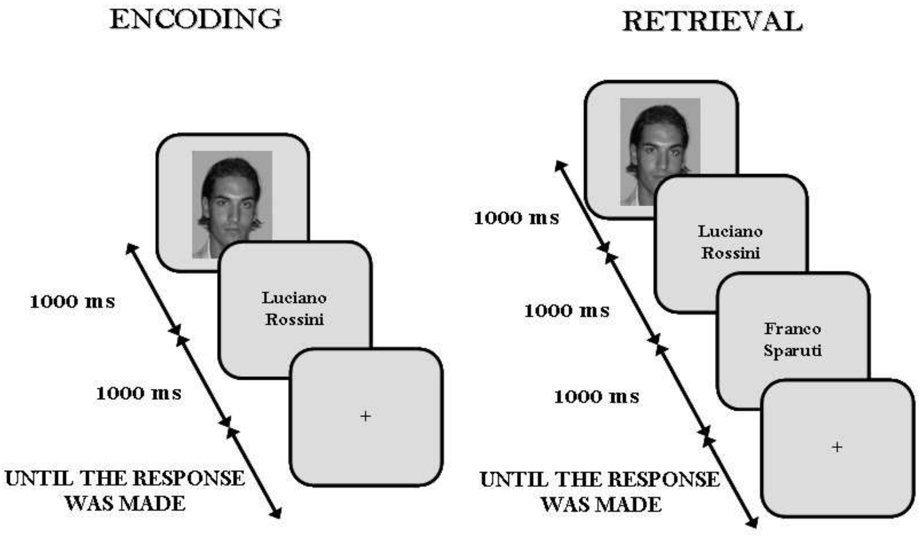


Figure 18. Schematic representation of the experimental procedure.

2.4. EEG Recording and Analyses

Continuous EEG activity was recorded from 19 scalp electrodes using an elastic cap and positioned according to the 10-20 International system (AEEGS, 1991).

The montage included 3 midline sites (FZ, CZ, PZ) and 8 sites over each hemisphere (FP1/2, F3/4, F7/8, C3/4, T7/8, P3/4, P7/8, O1/2). Horizontal eye movements were recorded using two electrodes placed at the external canthi of the eye; vertical movements were recorded with two electrodes, one placed above and one below the left eye. Left and right mastoid references were used. All signals were amplified, band-pass filtered between 0.03 and 100 Hz and digitized (0.1 μV resolution) at a rate 250 Hz. The electrodes' impedance was kept below 10 KΩ. Subsequent ERP analyses were performed, segmenting with a duration of 1200 ms (200 pre-stimulus and 1000 ms post-stimulus) per event (face and name). After segmentation, baseline correction (200 pre-stimulus and 1000 ms post-stimulus) was applied. Artefact rejection for trials including eye-blink and other artefacts was manually performed. An additional baseline correction (50 pre- and post-stimulus) was applied only for names. This procedure was motivated to a non-correct realignment of signal to baseline due to the preceding event. Separate averaged ERP waveforms were constructed. For the encoding analyses, averages were constructed according to *familiarity* (famous, novel) and *correctness* (correctly and incorrectly associated during retrieval) both for faces and names. For the retrieval analyses, ERPs were averaged for *familiarity* and *correctness*; whereas proper names were averaged for familiarity and type of *association* with face (old-correct, old-incorrect or new).

2.5. Statistical analyses

Behavioural responses were tested by analysing the percentage of correct responses. A three-way ANOVA was performed including as within factors, type of Stimulus (Familiar vs Novel) and Order of Presentation (first, second or third block).

For ERPs, the mean amplitudes of ERPs for each 50 ms time window were calculated for each subject. Analysis of variance with repeated measures was performed on the mean amplitudes as the dependent variable. Within-subject factors included in the analyses were: Electrodes (Prefrontal, Anterior Frontal, Posterior Frontal, Central, Temporal, Superior Parietal, Inferior Parietal and Occipital sites); Hemisphere (Left vs Right); Familiarity (Famous vs Novel). When the analyses considered correctness, this factor was also included in the ANOVA. Analyses were performed separately for faces and names.

In order to test any relationship between the level of the subject's performance and the amplitude of the ERPs components, bivariate correlations were performed and mixed ANOVAs with repeated measures, including Group as the between-subject factor (High vs Low), were performed.

The sphericity assumption was checked by performing the Mauchly's test, and Greenhouse-Greisser test (Geisser & Greenhouse, 1957) for the correction of degrees of freedom was applied when appropriated.

3. Results

3.1. Behavioural data

The percentage of correct responses for Famous items (99.4% ± 1.1) was significantly different from those for Unfamiliar items (66.5% ± 9.9) ($F_{2, 46} = 274.9$, $P < 0.001$). No significant effect of order presentation was found ($F_{2, 46} = 1.1$, $P = 0.3$), so we collapsed data over blocks for the subsequent analyses.

3.2. Encoding

3.2.1. Famous vs. Novel Faces

Encoding of Famous faces elicited a larger positive waveform than novel faces from 200 to 1000 ms (Fs ≥ 5.02, Ps < 0.05). In particular, from 250 to 450 it was centro-frontally distributed (Interaction Electrodes x Familiarity: $Fs \geq 3.96$, $Ps < 0.05$). Left hemisphere superiority over the occipital sites was found from 250 to 1000 ms (Electrodes x Hemisphere Interaction: $Fs \geq 2.94$, $Ps < 0.05$).

3.2.2. Famous vs. Novel Names

A posterior effect of Familiarity ($F_{1,23} = 8.04$, $P = 0.009$) from 250 to 350 ms was found, becoming more distributed from 400 to 550 ms, and then more centro-frontally distributed for the next 200 ms. Left hemisphere superiority was found from 400 to the end of the trial, in particular over fronto-temporal sites.

3.2.3. 'Dm' Effect for Novel Faces

The 'Dm' effect was defined as the amplitude difference elicited during the encoding phase between correctly and incorrectly retrieved responses. Correctly associated faces elicited a more positive waveform than incorrectly associated faces ($F_{1,23} = 4.31$, $P = 0.05$) from 250 to 350 ms.

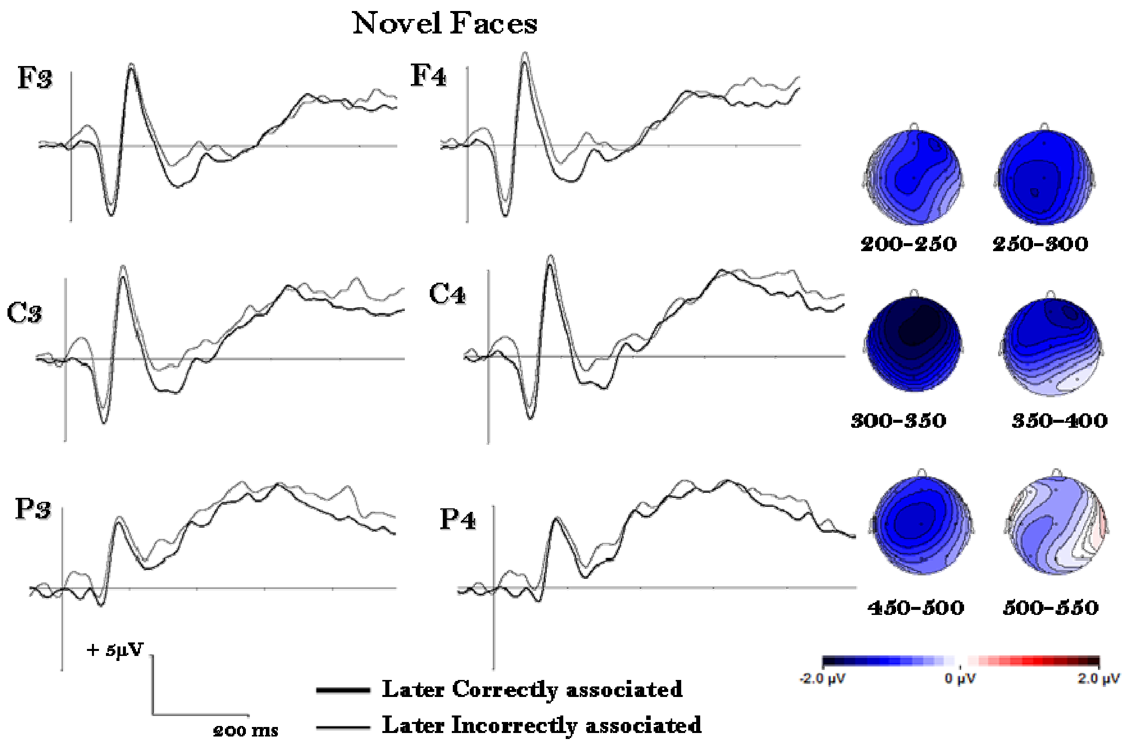


Figure 19. Grandaverage of ERPs during encoding for later correctly and incorrectly associated faces (left column). The voltage maps show the difference of mean distribution of later correctly and incorrectly associated names (right column).

3.2.4. 'Dm' Effect for Novel Names

Any effect of Correctness was found.

3.3. Retrieval

3.3.1. Famous vs. Novel Faces

Novel faces elicited more positive waveform than famous ones over centro-frontal sites from 250 to 450 ms (Familiarity x Electrode Interaction: Fs > 3.63, Ps < 0.01). From 500 to 750 ms these difference widespread over all electrodes being larger over posterior sites (Fs > 11.93, Ps < 0.01).

3.3.2. Famous and Novel Names

Novel names elicited a more positive waveform than famous ones from 150 to 350 ms over parietal sites (Familiarity x Electrode Interaction: $Fs > 3.20$, $Ps < 0.05$). From 400 to 450 ms, a larger negative waveform for novel names was found over the centro-posterior electrodes (Familiarity x Electrode Interaction: $F_{1.819,\ 41.842} = 3.40$, $P = 0.05$). From 600 ms the difference was larger over the left hemisphere, becoming restricted over the centro-posterior sites from 750 to 1000 ms (Familiarity x Electrode x Hemisphere Interaction: $Fs > 2.56$, $Ps < 0.05$). A clear left hemisphere superiority was found, being restricted to occipital and inferior parietal sites form 150 and 250 ms (Electrode x Hemisphere Interaction: $Fs > 3.20$, $Ps < 0.05$), and becoming widespread for the rest of the time window (Hemisphere Main Effect: $Fs_{1,23} > 7.12$, $Ps < 0.01$).

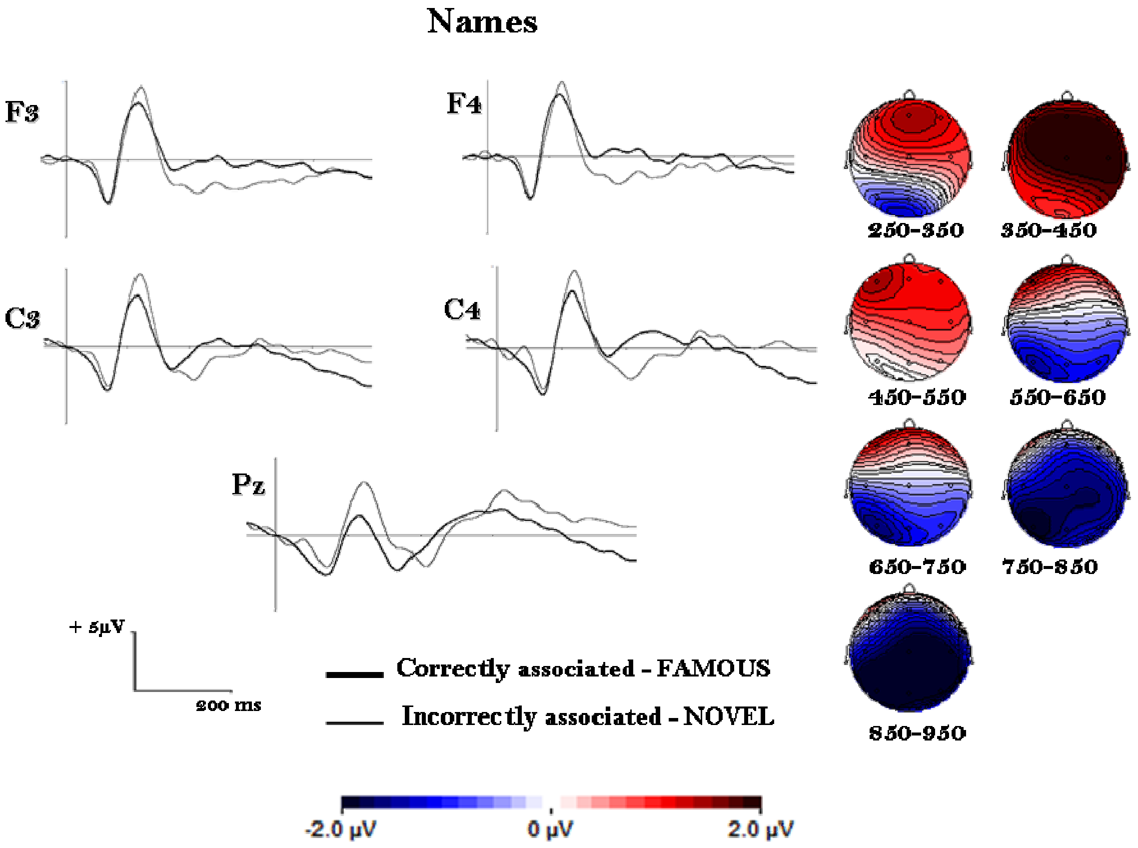


Figure 20. Grandaverage of ERPs during retrieval of famous and novel names (left column). The voltage maps show the difference of mean distribution of famous and novel names (right column).

3.3.3. Famous Names: Old and New

We further analysed data comparing New (those presented for the first time as distracters) with Old Famous names. We found that New Famous Names elicited a larger negative waveform than Old Famous names from 300 to 500 ms over the right centro-posterior sites (Electrode x Hemisphere x Stimulus Interaction: Fs > 2.94, Ps < 0.05). Clear left hemisphere superiority was found only for Famous names from 300 to 1000 ms (Hemisphere x Stimulus Interaction: Fs > 6.50, Ps < 0.05).

3.3.4. Novel Faces: Correctly vs. Incorrectly associated

Significant interactions of Electrode x Hemisphere x Correctness (Fs > 2.16, Ps < 0.05) were found from 600 to 1000 ms. Post-hoc analyses showed a difference between ERPs for faces correctly vs incorrectly associated over Fp1 for 600-650 ms, Fp2 for 700-750 ms, T8 for 700-750 and 950-1000 ms, C4 from 700 to 1000 ms. Right hemisphere superiority was found from 200 to 400 ms over central sites (Hemisphere x Electrode Interaction: Fs ≥ 2.35, Ps ≤ 0.05). Moreover, from 800 to 1000 ms, the left hemisphere showed slight higher positive-going activity than the right for correctly associated faces (Hemisphere x Correctness Interaction: $F\text{s}_{1,23} \geq 5.30$, Ps ≤ 0.05).

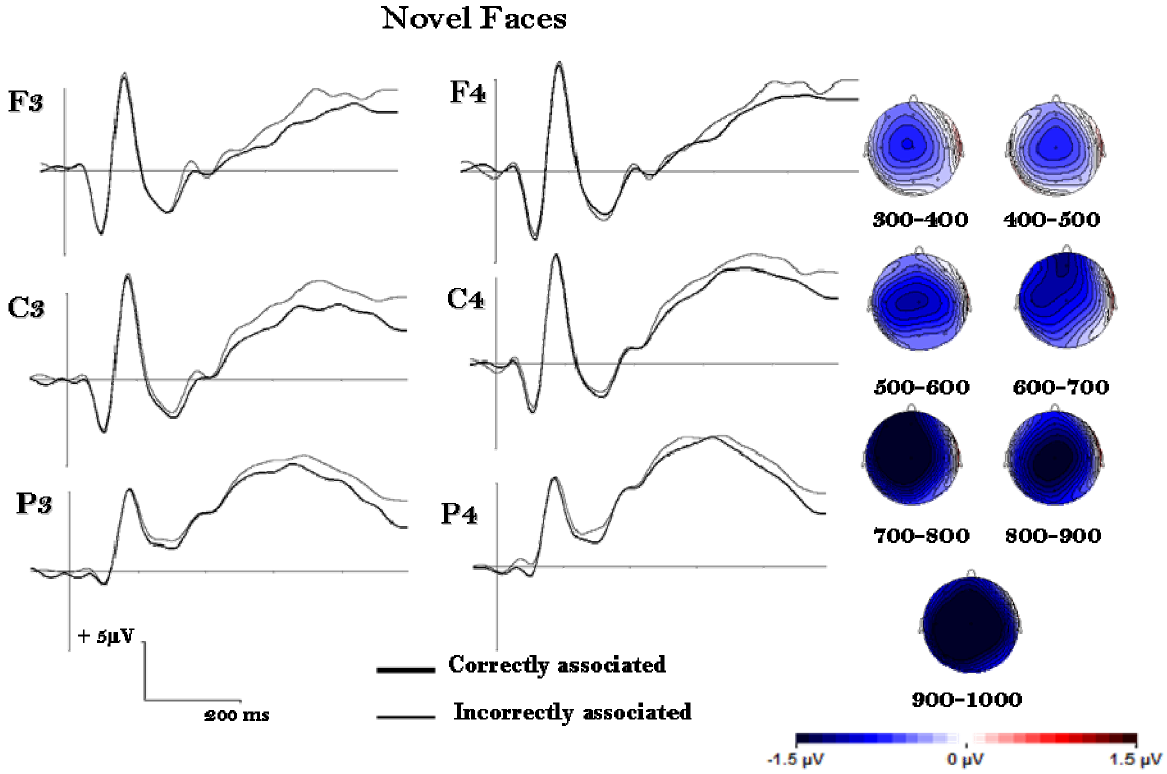


Figure 21. Grandaverage of ERPs during retrieval for correctly and incorrectly associated faces (left column). The voltage maps show the difference of mean distribution of correctly and incorrectly associated faces (right column).

3.3.5. Novel Names: Correctly vs. Incorrectly associated

Significant Electrode x Hemisphere x Correctness interactions were found from 650 to 900 ms (*F*s ≥ 2.10, *P*s < 0.05). Post-hoc analyses showed that names correctly vs incorrectly associated over F7 from 650 to 750, and over C4 from 700 to 900 ms. Correctly vs incorrectly associated names were significantly different over the left than the right hemisphere from 900 to 1000 ms (Hemisphere x Correctness Interaction: *F*s > 9.2, *P*s ≤ 0.05). ANOVAs performed adding New names did not show any further significance.

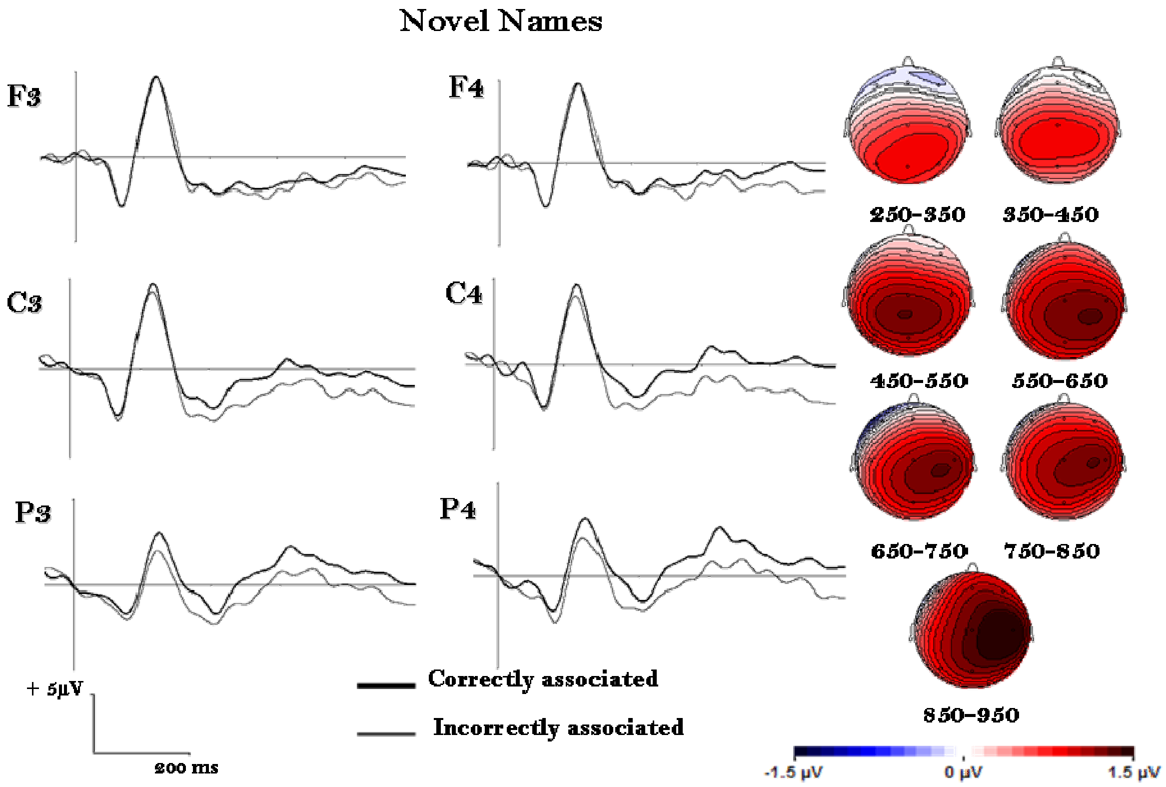


Figure 22. Grandaverage of ERPs during retrieval for correctly and incorrectly associated faces (left column). The voltage maps show the difference of mean distribution of correctly and incorrectly associated faces (right column).

3.4. ERPs and Performance

There are some reports that neurophysiological indices of memory correlate to the subjects' performance. Curran et al. (2001) studied the ERPs memory effect for words in considering the subjects' behavioural performance. They found that the ERP difference in recognition of old and new words, over the parietal sites, was more prominent for Low than High performers (defined using a median split method for correct responses). Only High performers showed a right frontal old/new effect from 1000 to 1500 ms.

In order to investigate the relationship between electrophysiological and behavioural patterns, correlation analyses were performed.

3.4.1. Correlations

Pearson's correlations were performed between ERP amplitudes for unfamiliar names (correctly associated, incorrectly associated and new ones) and the percentage of correct response in the name recognition task.

Names correctly associated. There were negative correlations between the percentage of correct responses and ERPs for name correctly associated over O2 (r = -0.43) between 100 and 150 ms, O2 (r = -0.55) and P4 (r = -0.41) from 200 to 250 ms. ERPs for name correctly associated correlated with behavioural responses over T7 (r = 0.49) from 350 to 400 ms. ERPs over frontal and prefrontal sites correlated with the percentage of correct responses from 350 to 1000 ms (rs < 0.41).

Names incorrectly associated. We found positive correlations between ERPs over central sites (C3-C4, rs ≥ 0.42) at 150-200, 350-400 and from 550 to 1000 ms. T8 correlated with the percentage of correct responses from 350 to 600 ms (rs ≥ 0.42), and from 700 to 800 ms (rs ≥ 0.43). Parietal sites (P3 and P4) showed positive correlations from 650 to 900 ms (rs ≥ 0.41).

New Names. Frontal sites (Fp2, F3 and F8) showed positive correlations from 400 to 900 ms (rs ≥ 0.41), and T8 from 400 to 650 ms (rs ≥ 0.45). Occipital sites (O1-O2) showed positive correlations from 750 to 1000 ms (rs ≥ 0.43).

Two groups were defined, splitting for the median percentage of correct responses (65.6%). 'High' performers were those who scored above the median value, and 'Low' performers were those who scored below the median value.

3.4.2. Encoding of Novel Faces

The positive waveform for correctly associated novel faces was affected by performance in several time windows (Correctness x Performer Interaction: $F_{1,22}$ > 4.59, Ps < 0.05).

Significant differences only for High Performers were found for these time windows: 50 -100 ms ($F_{1,22}$ = 7.76, P = 0.01), 150-250 ms (Fs > 4.83, Ps < 0.05), 500-550 ms ($F_{1,22}$ =6.56, P =0.02) and 800-900 ms (Fs > 5.33, Ps < 0.05). And from 750 to 850 ms, correct vs incorrect faces were significant only over the right hemisphere for High performers (Hemisphere x Correctness x Performer interaction: Fs > 4.36, Ps < 0.05). A more positive waveform was found for the left hemisphere over parieto-occipital sites from 650 to 1000 ms (Electrode x Hemisphere Interaction: Fs > 3.58, Ps < 0.05).

3.4.3. Encoding of Novel Names

A significant effect with respect to Group (High vs Low performers) was found. From 150 to 250 ms encoding of novel names, the left parieto-occipital areas showed a more positive waveform than the right (Electrode x Hemisphere Interaction Fs > 4.13, Ps < 0.01). For all other time windows, a clear superiority of the left hemisphere with a larger difference over the centro-frontal areas was found (Electrode x Hemisphere Interaction: Fs > 3.74, Ps > 0.05).

3.4.4. Retrieval of Novel Faces

ERP waveforms were significantly more positive for High than Low performers from 400 to 750 ms over parieto-occipital sites (Electrode x Performers Interaction: Fs > 2.25, Ps < 0.05). A significant larger ongoing positive activity for C4 from 600 to 750 ms and for right occipito-parietal sites from 800 to 1000 was found (Electrode x Hemisphere Interaction: Fs > 2.68, Ps < 0.05).

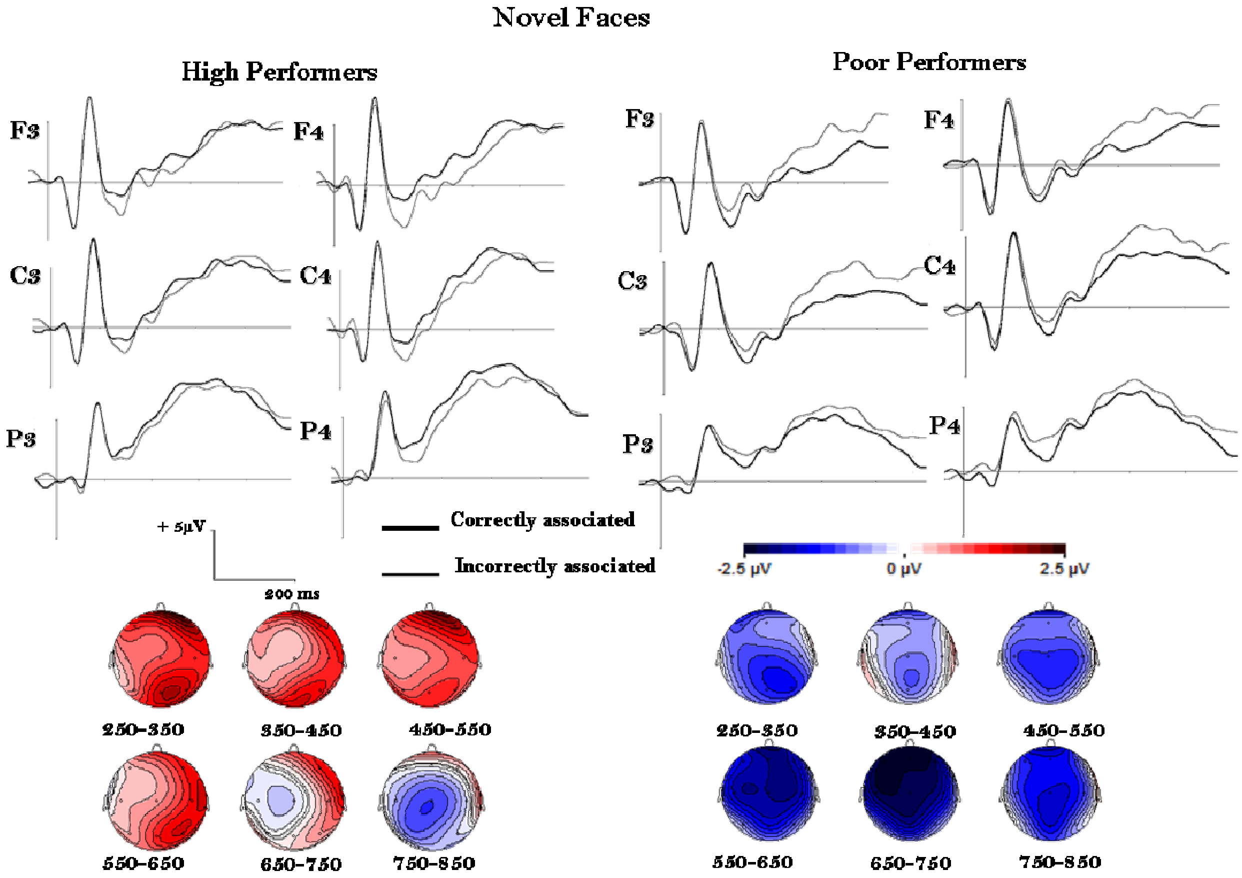


Figure 23. Grand average of ERPs during retrieval for correctly and incorrectly associated faces as a function of behavioural performance (top row). The voltage maps show the difference of mean distribution of correctly and incorrectly associated faces (bottom row).

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3.4.5. Retrieval of Novel Names

ERPs for correctly associated names were significantly different from incorrectly associated names only in High performers from 650 to 700 ms (Electrode x Correctness x Performers Interaction: $F_{2.627,\ 57.803} = 3.84$, $P = 0.005$), 750 and 800 ms (Electrode x Correctness x Performers Interaction: $F_{2.315,\ 50.940} = 3.03$, $P = 0.05$), 850 and 950 ms (Electrode x Correctness x Performers Interaction: *F*s > 3.70, *P*s < 0.05). This difference was significant only over centro-parieto-occipital sites.

A significant main effect of Hemisphere was also found ($Fs > 4.88$, $Ps < 0.05$) for 500-550 ms, 600-700 ms and 750-800 ms time windows, indicating more negative ongoing activity for the left hemisphere

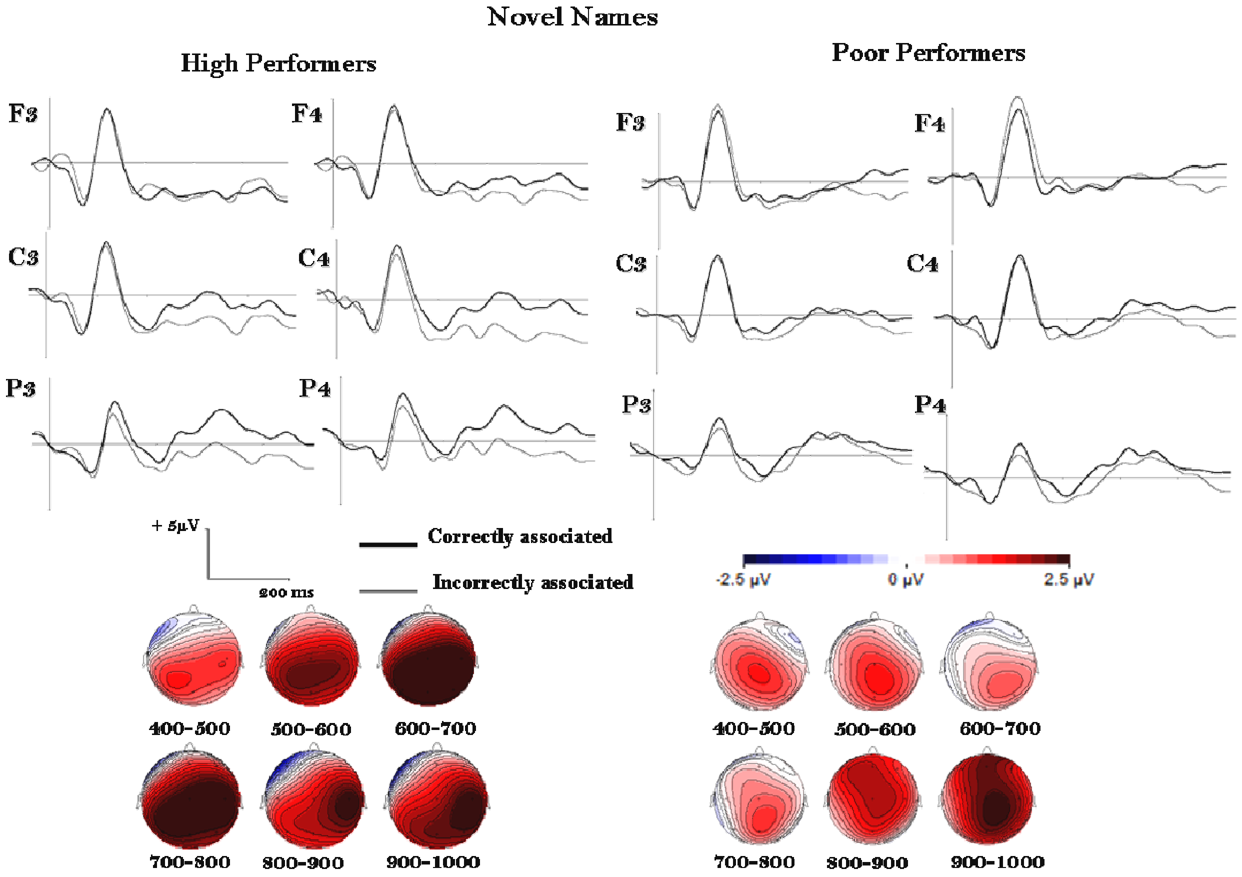

Figure 24. Grandaverage of ERPs during retrieval for correctly and incorrectly associated names as a function of behavioural performance (top row). The voltage maps show the difference of mean distribution of correctly and incorrectly associated names (bottom row).

Analyses of variance were run adding the new names. New names were significantly different from correctly associated ones only for High performers from 650 to 700 ms over centro-parietal sites (Electrode x Stimulus x Performers Interaction: $F_{4.562,\ 100.365} = 2.53$, $P = 0.04$); from 800 to 950 ms over parieto-occipital sites ($Fs > 2.92$, $Ps < 0.01$) and from 950 to 1000 ms over occipital sites ($F_{3.981,\ 87.584} = 2.67$, $P = 0.04$).

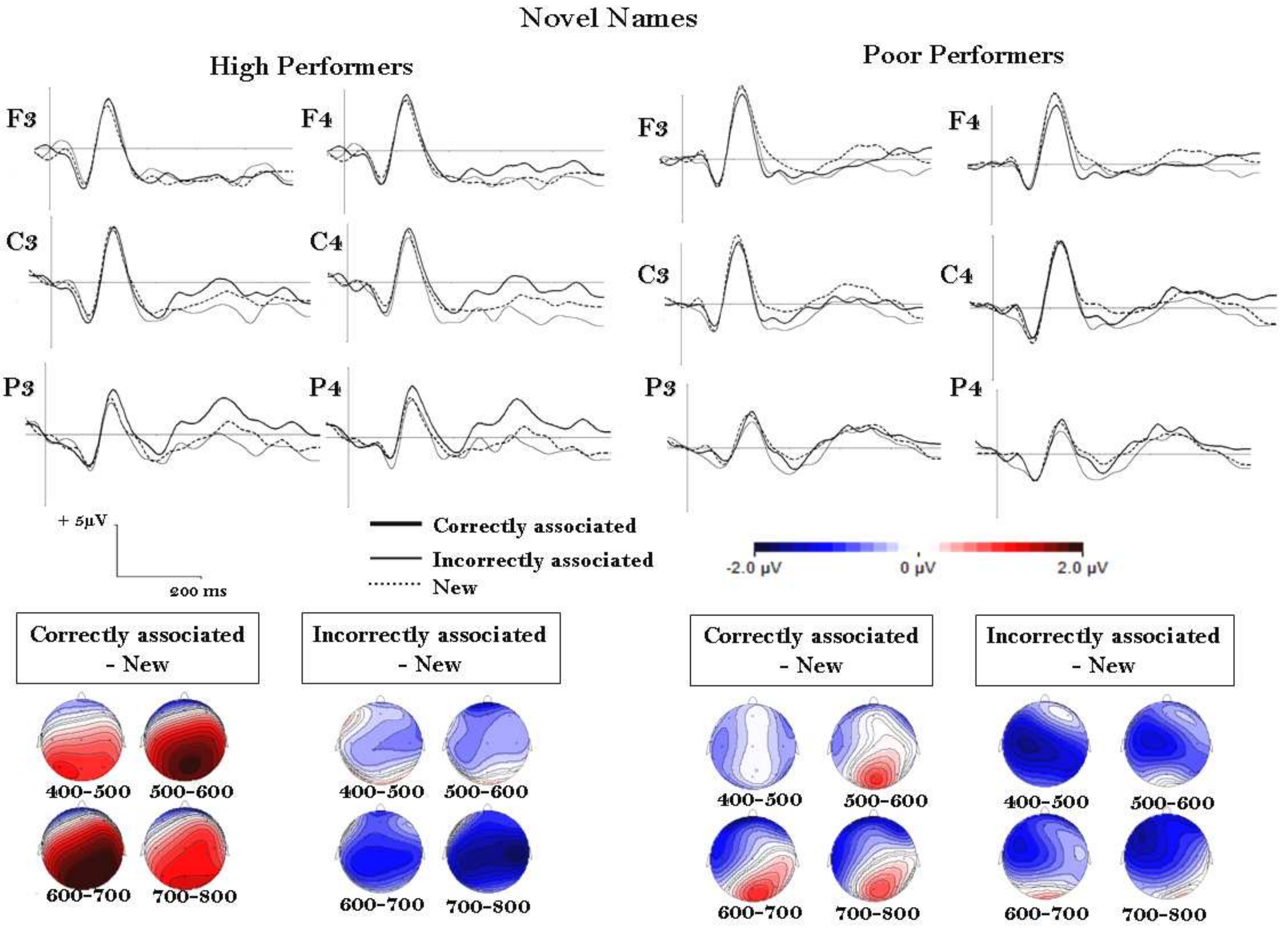

Figure 25. Grandaverage of ERPs during retrieval for correctly and incorrectly associated names as a function of behavioural performance (top row). The voltage maps show the difference of mean distribution of correctly and incorrectly associated names and new (bottom row).

4. Discussion

The aim of this study is to investigate the neural bases of episodic memory of face-name associations through event-related brain potentials. This was done by recording ERPs in young participants during a study phase (encoding) and retrieval of associations of famous and unfamiliar faces.

Encoding. ERP-related activity was studied by comparing brain activity for later correctly associated faces and names and for those incorrectly associated (namely the 'Subsequent memory effect'). An effect was found for novel faces: later correctly associated faces elicited a more positive-going waveform from 250 to 350 ms. This data is in line with results reported in previous studies. In particular, data from Guo et al.'s study (2005) reports the same effect from 200 and 800 ms over centro-posterior sites; and Sommer et al. (1991) found a positivity over the vertex from 300 ms. Conversely, a 'subsequent memory effect' for proper names was not found. This is possibly due to the experimental procedure. Guo et al. (2005) have shown that if subjects were required to retrieve face-name associations in each of the ten trials, the effect was clearly distributed over the entire scalp, whereas if they were required to retrieve face-name associations at the end of the experiment, the positive-going activity for correctly retrieved associations disappeared.

More interesting data were found regarding *retrieval* processing. First of all, correctly retrieved novel faces and names elicited a more positive-going activity from 600 to 1000 ms than incorrectly associated items over centro-posterior sites. This effect of recollection was confirmed also for famous names: they elicited a more positive-going waveform than novel ones over parietal sites. The earlier effect found for famous faces from 250 to 450 could be the sum of two main components related to familiarity, the N250 and FN400, as reported in other studies (i.e. Tanaka, Curran, Porterfield, & Collins, 2006).

This is the classical topography found for recollection opposed to familiarity (Friedman & Johnson, 2000; Rugg & Yonelinas, 2003). Paller et al. (1999) confirmed a similar pattern of results: novel faces classified as old elicited a more positive-going activity over parietal sites with its maximum at 600 ms. Also, Paller et al. (2000) found that ERPs for retrieved items were more positive than for new ones from 300 to 600 ms. But for named faces (those associated with autobiographical information), the effect was over both anterior and posterior sites.

These data support the role of the posterior and, in particular, parietal areas in episodic memory retrieval. Different hypotheses could accounted for this (for a review see Cabeza et al., 2008). First, the output buffer hypothesis postulates that parietal regions hold retrieved information in a form accessible to decision-making processes, similarly to one of Baddeley's (1987; 2000) working memory buffers. A second account, the internal representation hypothesis, claims that parietal regions have the role of shifting attention to, or maintaining, internally generated mnemonic representations.

And finally, a new account has been proposed by Cabeza et al. (2008) called the 'attention to memory (AtoM) model'. According to this model, the superior parietal lobe is the reflection of processes downstream of retrieval, the engagement of which depends on the salience or task-relevance of the eliciting item. Dorsal parietal cortex activity maintains retrieval goals, which modulate memory-related activity in the medial temporal lobe, whereas ventral parietal cortex activity signals the need for a change in the locus of attention following the detection of relevant memories that have been retrieved by the medial temporal lobe.

Results from this study are in agreement with the episodic memory buffer hypothesis (Vilberg & Rugg, 2008). According to this hypothesis, the effect over the parietal cortex should be modulated by the subjects' performance. To test this prediction, an analysis was run considering the behavioural responses and significant correlations with ERPs activity were found over these sites. To better characterize ERP activity, two groups were defined (High vs Low performers) using a median split method. High performers were those showing a greater distinct ERP component related to correctly vs incorrectly associated proper names. More interestingly, ERP activity related to new proper names (those excluded by subjects in case of correct responses) were statistically different to the other two activities. Conversely, Low performers did not show these dissociations on ERP activity. And they showed a right frontal component as a difference of ERP activity for correctly associated proper names and new ones. The topography of this effect may be an index of familiarity-based processing (Rugg & Yonelinas, 2003).

Taken together, this evidence supports recollection-based processes of episodic traces over posterior sites for novel names, whereas frontal activity was shorter lasting and left-side distributed. It is known that the successful recall of associative information is not always accompanied by the right frontal effect, but it is more associated with the explicit retrieval of contextual information about a prior episode (for a review see Allan, Wilding, & Rugg, 1998).

More frontally distributed ERP acitivity was found for novel faces. In this case, it could be claimed that this brain activity effect could be explained by a familiarity-based process, because an explicit recollection was not required at that point of the task.

Moreover, the central-parietal effect related to novel name retrieval seemed to be made up of two main components, the first with a maximum from 600 and 800 ms bilaterally distributed, and the second component being more right sided from 800 and 100 ms. Due to its topography, it could be attributable to post-retrieval processes. It has been reported that a late right frontal positivity could follow the parietal effect during memory retrieval. This posterior component could be a corresponding component more posteriorly distributed relating to control monitoring (Allan et al., 1998).

To sum up, it was found that the association of new face-name pairs entails specific ERP activity. Novel faces elicit a positive-going activity more centro-frontally distributed, whereas the association of the correct proper names elicits a more posterior positive-going activity from 600 ms. In the frame of the dual-process theory of memory, these two main effects could be explained as two different underlying processes. ERP activity related to faces could account for the familiarity-based process of recognition memory, whereas brain activity related to proper name association may account for a more recollection-based process of retrieval. This hypothesis is also supported by the correlation of posterior ERP activity and subjects' performance: the better the performance, the more ERP acitivity related to recollection was found.

Chapter 5

Experiment 2
Episodic memory of face-name associations in older adults

1. Introduction

As described in Chapter 3, age-related changes of cognitive functions are more related to episodic memory (Balota et al., 2000) than semantic memory (Spencer & Raz, 1995). To specifically explain the context (episodic) deficits, it is proposed that older adults have trouble binding pieces of information into complex memories (Chalfonte & Johnson, 1996). Such a hypothesis suggests that there is a distinction between memory for single units of information and memory for associations among those units, and that aging affects those two types of memory differently. Naveh-Benjamin (2000) extended and clarified this idea by proposing the associative deficit hypothesis (ADH), which holds that a major contributor to older adults' deficiencies in episodic memory is their relative inability to form and retrieve links among single bits of information.

Old & Naveh-Benjamin (2008) extensively reviewed this account. The major finding of this meta-analysis was that older adults are, in fact, more disadvantaged in memory tests of associations than in tests of item memory compared with young adults. An age-related associative deficit, then, indicates not only that older adults are impaired in memory for associative information, but also that this impairment is larger than the impairment in memory for item information. In particular, aging seems to impair memory for the binding required in source, context, temporal order, location and item pairs to a greater degree than memory for single units of information. Second, the results showed a clear age-related associative deficit when tested materials were learned intentionally, maybe because older adults have difficulty using self-initiated processes to bind together pieces of information. Additionally, it has been shown that providing participants with associative strategies reduces the age-related associative deficit (Naveh-Benjamin, Brav, & Levy, 2007b), indicating that older adults have difficulty using associative strategic processes. Third, older adults seem to exhibit an associative deficit for both verbal and nonverbal information, providing evidence for the generality of the ADH.

There is some evidence that older adults show deficits in recalling proper names that is larger than that for common names. This deficit could be related to retrieval processing being impaired by aging, but another explanation could account for it. According to Naveh-Benjamin's hypothesis (2000), the deficit could be due to a difficulty in binding a specific name to a specific face. In order to test this hypothesis, Naveh-Benjamin et al. (2004) required young and older participants to study name-face pairs and then they tested their recognition memory for the names, faces and their associations. They found a small deficit in recognizing faces but not proper names. But despite the shared ability for names, the results show that recognizing the associations between names and faces declines in old age. And the deficit is present even in a recognition task in which all information is provided to the participants and no free recall is required. The same pattern of results was confirmed by other studies using incidental vs intentional encoding (Naveh-Benjamin et al., 2008), strategies (Naveh-Benjamin et al., 2007) and using recognition memory tasks (James et al., 2008).

Few studies have investigated the neurophysiological basis of face-name associative memory processing. Pfutze et al. (2002) used a repetition priming paradigm to investigate ERP components in face and name recognition in older adults. Participants were required to classify each face and name as belonging to a famous or to an unfamiliar person. Each stimulus was presented twice at different lags between repetitions. The P100 component indexing early visual processing and N170 related to structural encoding of faces were not affected by aging.

Conversely, the early repetition effect reflecting access to existing representations in domain-specific memory appeared later with age, and it appeared for famous faces and names but not for unfamiliar ones. Furthermore, the late repetition effect was affected by age for faces but not for names. Its latency increased across the age groups, probably due to a slowed access to semantic memory. Age-related slowing was explained by these authors as a loss or a slowing of activation spreading from the perceptual system to the systems that store structural representation of faces (FRUs). The slowing related to the late repetition effect was as long as the early one, so the authors interpreted this result as the fact that there is no additional slowing in the recognition of familiar faces and names.

The ERP repetition effect, recorded during indirect memory paradigms, appears to be relatively intact with aging, suggesting spared repetition priming mechanisms and the brain substrates upon which they depend (Friedman & Johnson, 2000; Friedman, 2003). By contrast, during explicit memory testing, some age-related change was found. Most of the results are mixed, and more consistent results come from studies of retrieval.

Some characteristic neurophysiological patterns have been found in aging during explicit memory episodic tasks. As for the young adult studies, two classical phenomena have been considered: the *Subsequent memory effect*, which is the difference in amplitude between subsequently recalled and not recalled stimuli, and *old/new ERP effects*, describing the phenomenon that stimuli recognized as previously seen during the study test elicit greater activation than stimuli correctly classified as new (see Chapter 3). Concerning encoding, an age-related effect over the left inferior frontal sites was reported (Friedman & Johnson, 2000) with a reduced ERP activity for older adults compared to young adults. In older adults, this attenuation is modulated by task: episodic encoding is more affected than semantic selection tasks (Nessler et al., 2006). More studies from retrieval during episodic memory are available, even if the results are mixed. Two main findings are reported: the parietal old/new effect is sometimes attenuated in older adults (Ally et al., 2008; Fjell, Walhovd, & Reinvang, 2005; Nessler et al., 2008) accompanied by a frontal shift, such as more frontal distributed activity related to successful retrieval (for a combined MRI and ERP study see Walhovd et al., 2006).

As previously described, one of the hypotheses explaining these age-related changes is the associative deficit hypothesis (Naveh-Benjamin, 2000). So, in order to test this hypothesis it seems interesting to investigate the neurophysiological correlation of associative learning in older adults. Thus, the aim of this study is to investigate the encoding and retrieval of face-name associations in older adults through even-related brain potentials (ERPs). The predictions are basically that both encoding and retrieval are affected by age. Considering the results of Experiment 1 (see Chapter 4), it is expected that in older adults, retrieval-based processes are more affected. In particular, a frontal shift of ERP activity related to name association is expected over centro-posterior sites as found in young adults.

2. Materials and Methods

2.1. Participants

Fourteen (four male and ten female) participants took part in the experiment. The mean age was (69.7 ± 10; range 62-74) years and mean education was 11.4 (± 4.1) years. They were all right-handed according to the Edinburgh handedness inventory test (Oldfield, 1971) and they had normal or corrected-to normal vision. Participants reported being free of neurological disorders and they gave their written informed consent.

2.2. Stimuli

Stimuli included grey-scale faces and proper names. Faces were downloaded from electronic datasets and other resources on the web and processed by Adobe Photoshop 5.0. A set of 48 faces were collected (24 males, 24 females), scaled of 210 x 263 pixels presented from a distance of 100 cm (subtending a visual angle of ~ 3.15° x 4°). All the photographs portrayed novel faces (unfamiliar).

2.3. Procedure

After electrode application, subjects were seated in a comfortable chair in a dimly illuminated room facing a computer monitor placed 100 cm in front of them. They were instructed to pay attention and to minimize eyeblink.

Experimental procedure was structured in an encoding phase followed by a retrieval phase. Each phase comprised three separate blocks of 16 trials each. During the encoding phase, subjects were presented with a face (1000 ms), followed by the corresponding proper name (1000 ms), then a fixation point appeared and subjects were requested to respond if a male or female had been presented. During this phase, subjects were asked to associate the proper name with the face presented. Responses were collected via a response-box using the index finger of both hands.

During the retrieval phase, subjects were presented with the face presented before (1000 ms), followed by a first proper name (1000 ms) and a second name (1000 ms), and then the fixation point appeared. Subjects had to respond by pressing the left button of the response-box if the first name was correct and the right one if the second was correct (see Figure 18).

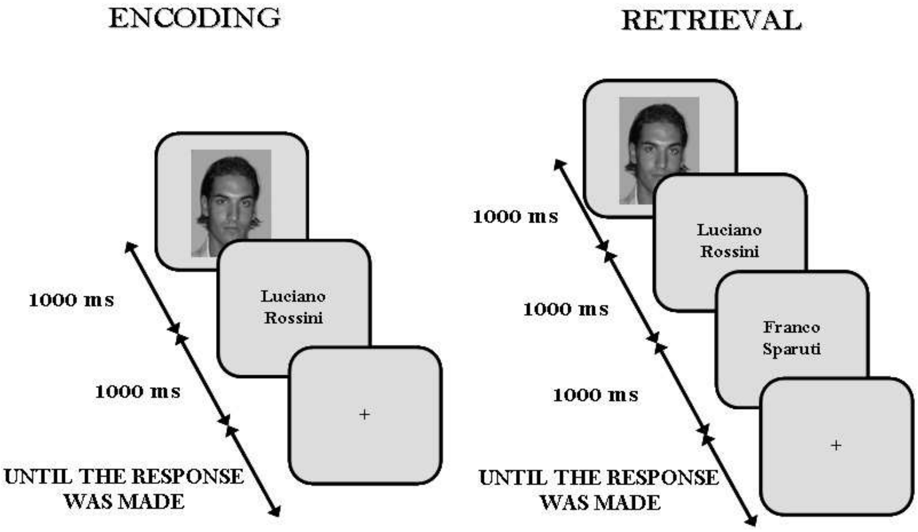

Figure 26. Schematic representation of the experimental procedure.

In a successive session, a neuropsychological assessment was used to test cognitive functions. The neuropsychological assessment included: Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975), Memory for Prose for Verbal Long-term Memory (Wechsler, 2004) and the Trial Making Test (Giovagnoli et al., 1996).

An adapted version of the Troyer & Rich (2002) metamemory questionnaire was used. This questionnaire includes three main subtests: Contentment (feelings regarding one's memory), Ability (self-appraisal of one's memory capabilities) and Strategy (reported frequency of memory strategy use). The *Contentmen*t subtest contains 18 items addressing a variety of emotions and perceptions that participants may have about their current memory ability. Statements address positive emotions (e.g. confidence, satisfaction), negative emotions (e.g. embarrassment) and subjective ability ratings. Respondents rated their level of agreement with each statement on a 5-point scale (i.e. strongly agree, agree, undecided, disagree and strongly disagree). For each item, 0 to 4 points were given on the basis of level of agreement. The *Ability* subtest contains 20 everyday memory situations, such as remembering appointments, names and telephone numbers. Respondents indicated the frequency with which each mistake occurred on a 5-point scale (all the time, often, sometimes, rarely, never), with higher scores indicating better subjective memory ability.

The *Strategy* subtest contains 14 items describing different memory aids and strategies applicable to everyday memory tasks, such as writing appointments on a calendar and repeating information to oneself. Respondents indicated the frequency with which they use each strategy using a 5-point scale (never, rarely, sometimes, often, all the time), with higher scores indicating more frequent use of memory aids and strategies.

An ad-hoc questionnaire was used for memory strategies. It was an adaptation from the Kirchhoff & Buckner (2006) study. It contains 12 items describing different memory strategies (i.e. 'I used a mental image to better remember study items'). Respondents indicated the frequency (0 to 9) with which they use each strategy using a 10-point scale (never to all the time), with higher scores indicating more frequent use of strategies.

2.4. EEG Recording and Analyses

Continuous EEG activity was recorded from 19 scalp electrodes using an elastic cap and positioned according to the 10-20 International system (AEEGS, 1991).

The montage included 3 midline sites (FZ, CZ, PZ) and 8 sites over each hemisphere (FP1/2, F3/4, F7/8, C3/4, T7/8, P3/4, P7/8, O1/2). Horizontal eye movements were recorded using two electrodes placed at the external canthi of the eye; vertical movements were recorded with two electrodes, one placed above and one below the left eye. Left and right mastoid references were used. All signals were amplified, band-pass filtered between 0.03 and 100 Hz and digitized (0.1 μV resolution) at a rate 250 Hz. The electrodes' impedance was kept below 10 KΩ.

Subsequent ERP analyses were performed, segmenting with a duration of 1200 ms (200 pre-stimulus and 1000 ms post-stimulus) per event (face and name). After segmentation, baseline correction (200 pre-stimulus and 1000 ms post-stimulus) was applied. Artefact rejection for trials including eye-blink and other artefacts was manually performed. An additional baseline correction (50 pre and post-stimulus) was applied only for names. This procedure was motivated to a non-correct realignment of signal to baseline due to the preceding event.

Separate averaged ERP waveforms were constructed. For the encoding analyses, averages were constructed according to *correctness* (correctly and incorrectly associated during retrieval) both for faces and names. For the retrieval analyses, ERPs were averaged for *correctness*; whereas, proper names were averaged for the type of *association* with face (correct, incorrect or new).

2.5. Statistical analyses

For ERPs, mean amplitudes of ERPs for each 100 ms time window were calculated for each participant from 200 to 1000 ms. Analysis of variance with repeated measures was performed on mean amplitudes as the dependent variable. Within-subject factors included inthe analyses were: Electrodes (Prefrontal, Anterior Frontal, Posterior Frontal, Central, Temporal, Superior Parietal, Inferior Parietal and Occipital sites), Hemisphere (Left vs Right), and Correctness. Analyses were performed separately for faces and names. The sphericity assumption was checked by performing the Mauchly test and Greenhouse-Greisser test (Geisser & Greenhouse, 1957) for the correction of degrees of freedom was applied when appropriated. Bivariate correlations between ERPs amplitude and subject's performance (percentage of correct responses), memory questionnaire and cognitive assessment scores were performed.

3. Results

The percentage of correct responses for name association was 59% (± 8) and did not differ significantly across blocks (F(2, 24) = 1.44, p = 0.26). **Errore. L'autoriferimento non è**

valido per un segnalibro. reports the cognitive assessment score and demographic variable of participants.

Table 1. Demographic variables and cognitive assessment of participants.

	Means	Standard Deviations	Cut-off
Gender (M/F)	**4/10**		
Age	**69.7**	*4.4*	
Education	**11.4**	*4.1*	
Mini Mental State Examination	**29.3/30**	*0.7*	> 24
Memory for prose	**14.1/28**	*2.4*	> 8
Wechsler Memory Scale (QM)	**118.2**	*12.1*	
TMT A	**35.9**	*12.0*	< 93
TMT B	**111.4**	*21.8*	< 282
TMT B-A	**75.4**	*21.5*	<186
Metamemory Questionnaire			
Contentment	**14.8/36**	4.2	
Ability	**27.9/68**	7.2	
Strategies	**20.2/52**	7.9	
Memory stategy Questionnaire	**18.4/108**	*5.2*	

3.1. Encoding

3.1.1. 'Dm' Effect for Faces

The 'Dm' effect was defined as the amplitude difference elicited during the encoding phase between correctly and incorrectly retrieved responses.

3.1.2. 'Dm' Effect for Names

Statistically significant differences between later correctly and later incorrectly retrieved responses were found from 500 to 600 ms (Electrode x Correctness interaction: F7, 91 = 2.8, p = 0.01) and from 600 to 700 ms (F7, 91 = 2.3, p = 0.03). Planned comparisons revealed that this difference was statistically significant over frontal sites (F7 and F8, p< 0.05). See Figure 27 for more details.

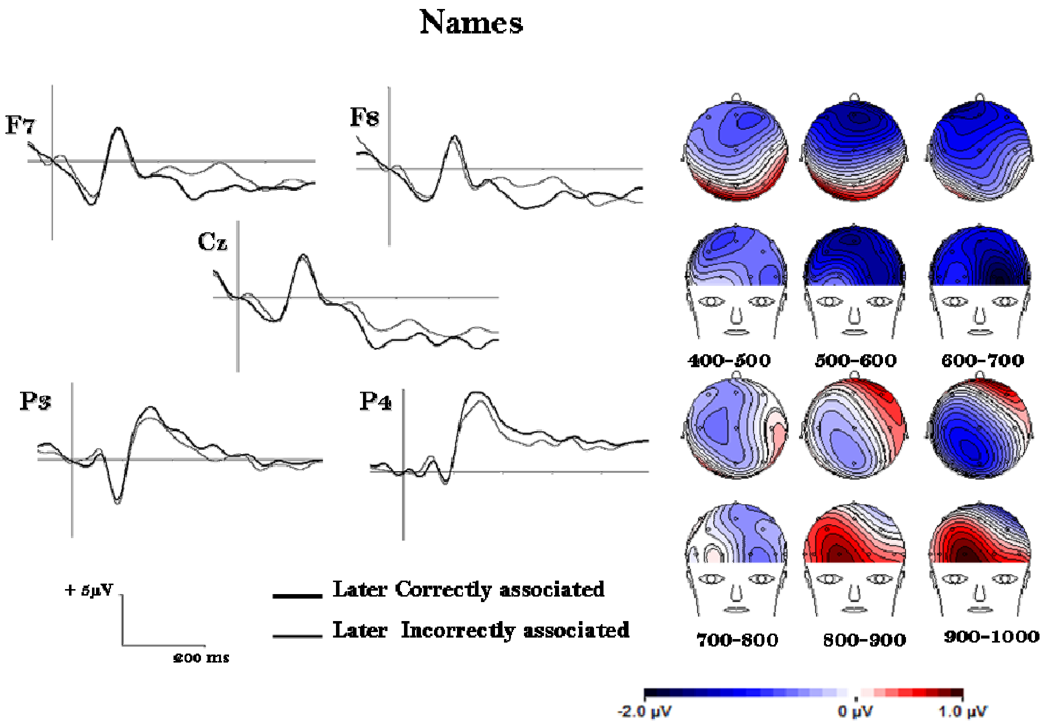

Figure 27. Grandaverage of ERPs during encoding for later correctly and incorrectly associated names (left column). The voltage maps show the difference of mean distribution of later correctly and incorrectly associated names (right column).

3.2. Retrieval

3.2.1. Faces: Correctly vs. incorrectly associated

Correctly associated faces elicited a more negative-going activity from 500 to 700 ms. Planned comparisons were carried out to better identify the sites of activity. From 500 to 600 ms (Electrode x Correctness interaction: $F_{7,\,91} = 3.2$, p = 0.004) this difference was significant over parietal sites (P3 and P4, p = 0.005). From 600 to 700 ms (Electrode x Correctness interaction: $F_{7,\,91} = 2.8$, p = 0.01), this difference was significant over temporal (p = 0.01), parietal ($p = 0.001$) and occipital ($p = 0.04$) sites. An analysis considering midline electrodes (Fz, Cz and Pz) was carried out separately. From 600 and 700 ms, a significant main effect of Correctness was found ($F_{1, 913} = 5.2$, $p = 0.03$). See Figure 28 for more details.

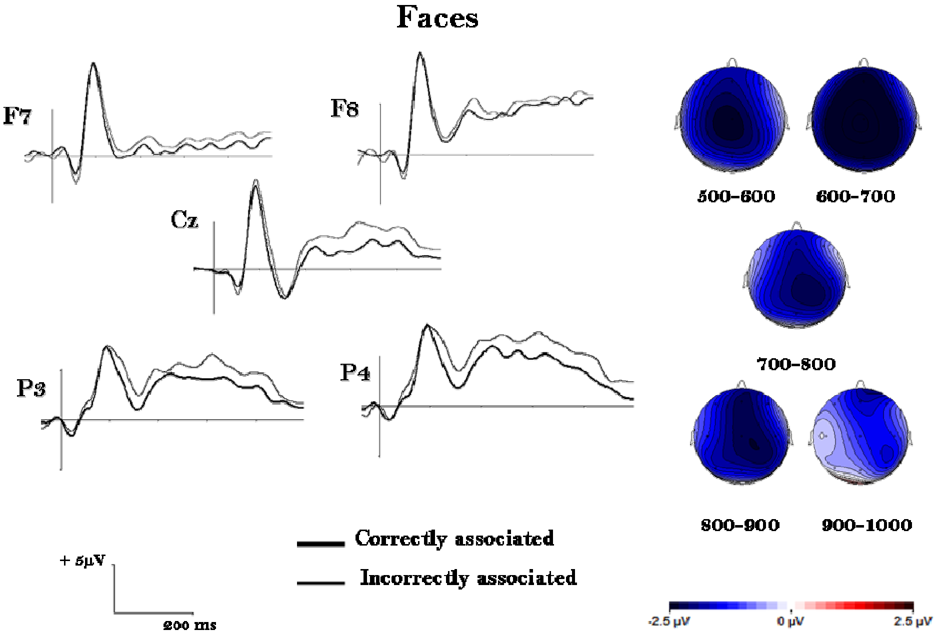

Figure 28. Grandaverage of ERPs during retrieval for correctly and associated faces (left column). The voltage maps show the difference of mean distribution of correctly and incorrectly associated faces (right column).

3.2.2. Names: Correctly vs. incorrectly associated

Correctly associated names elicited a more negative-going activity from 500 over the left frontal sites, as shown by statistically significant Electrodes x Hemisphere x Correctness interactions. From 500 to 600 ms ($F_{7, 91} = 2.4$, $p = 0.02$), this difference was significant over F7 ($p < 0.05$). From 700 to 800 ms ($F_{7, 91} = 2.3$, $p = 0.03$) this difference was still significant over F7 ($p = 0.05$). From 800 to 900 ms ($F_{7, 91} = 2.6$, $p = 0.016$) this difference was significant over F3 ($p = 0.05$) and F7 ($p = 0.001$). From 900 to 1000 ms the difference was significant over the left Hemisphere (Hemisphere x Correctness, $F_{1, 13} = 4.9$, $p = 0.04$), and in particular (Electrodes x Hemisphere x Correctness interaction, $F_{7, 91} = 2.8$, $p = 0.01$) over F3 ($p = 0.04$) and F7 ($p = 0.009$) and T7 ($p = 0.03$) and C3 ($p = 0.02$).

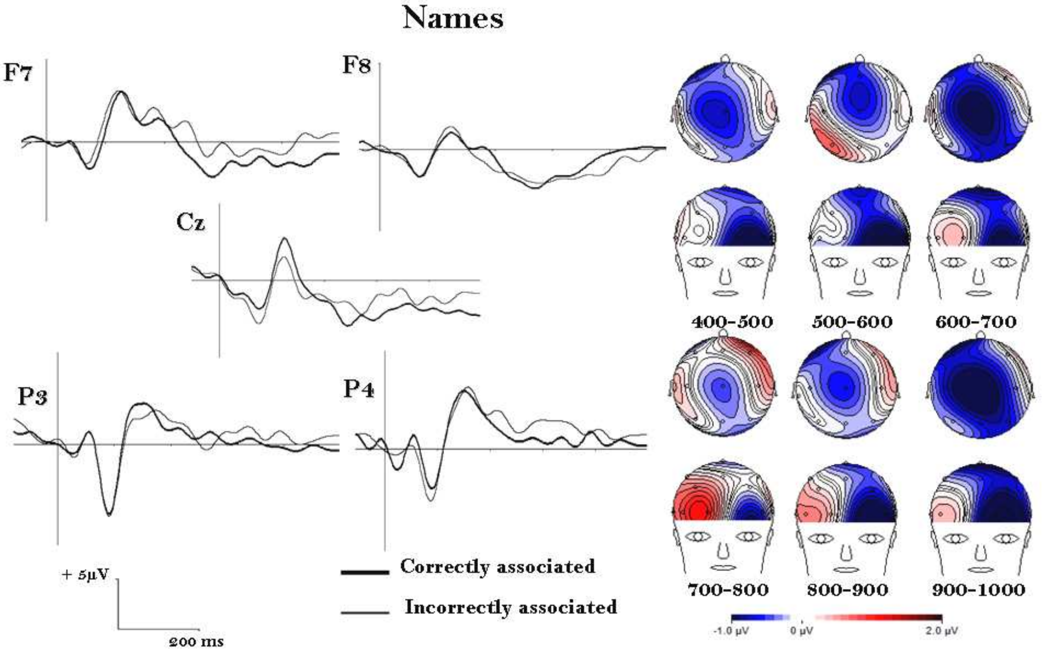

Figure 29. Grandaverage of ERPs during retrieval for correctly and incorrectly associated faces (left column). The voltage maps show the difference of mean distribution of correctly and incorrectly associated faces (right column).

3.3. Correlations

Encoding. ERP differences were calculated as the difference of ERP related to later correctly associated names minus those later incorrectly associated. Only the two significant time windows, such as from 500 to 600 and from 600 to 700 ms over F7 and F8, were considered. These differences were correlated with the percentage of correct responses, neuropsychological measures and metamemory questionnaires.

The amplitude difference over F7 from 500 and 600 ms correlated with the raw score of the Wechsler Memory Scale ($r = 0.58$, $p = 0.03$) and Logical Memory subtest ($r = 0.58$, $p = 0.03$).

The amplitude difference over F8 also correlated with the percentage of correct responses (r = -0.54, p = 0.05). The amplitude difference over F7 from 600 and 700 ms correlated with the raw score of the Logical Memory subtest (r = 0.63, p = 0.02).

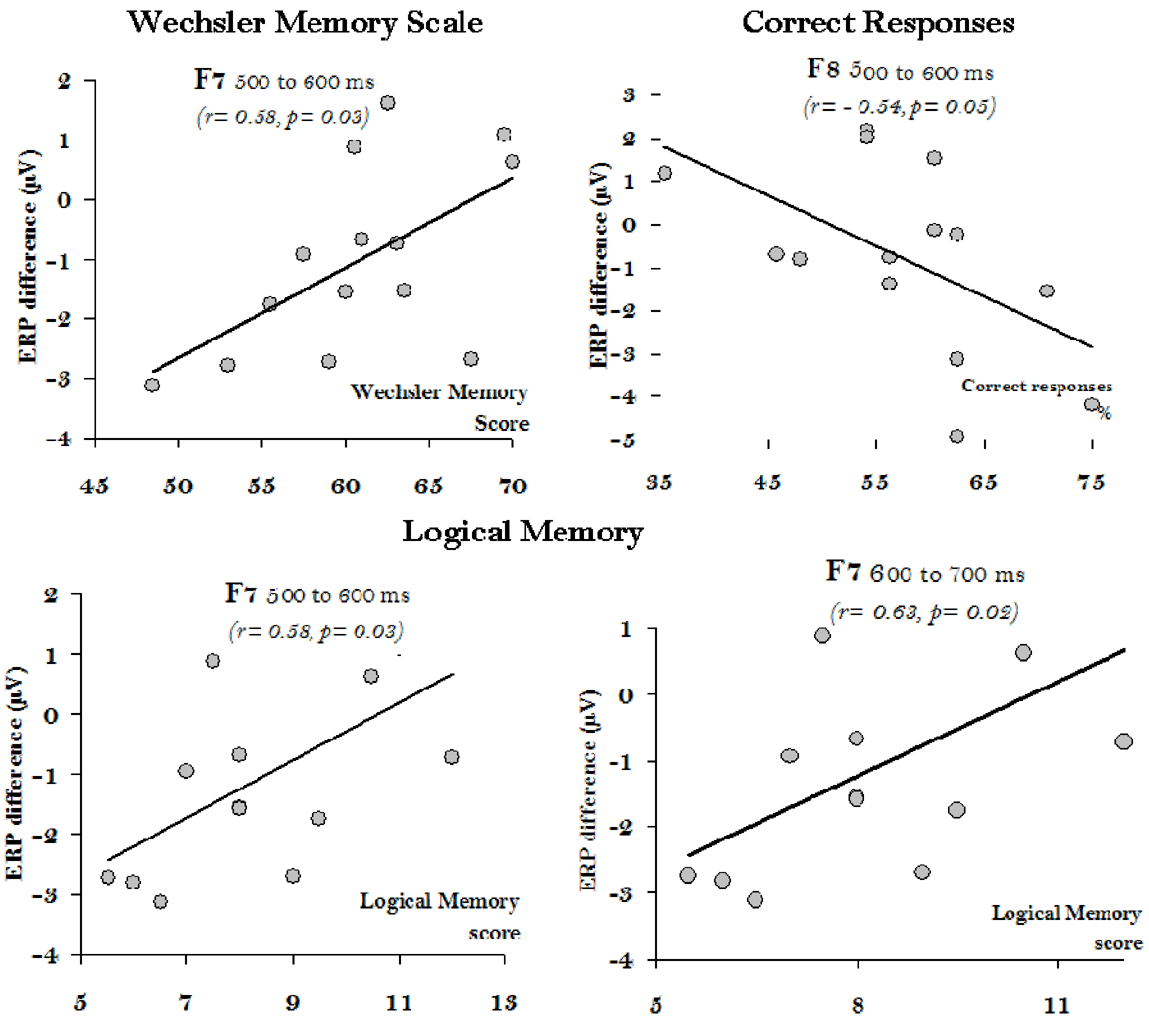

Figure 30. Scatterplots of correlations between ERPs activity over frontal sites during encoding, memory test scores and percentage of correct responses..

Retrieval. ERP differences were calculated as the difference of ERP related to correctly associated names during retrieval minus those incorrectly associated. Only ERP differences from 500 to 1000 ms over frontal sites were considered. Correlations were performed with the percentage of correct responses, neuropsychological measures and the metamemory questionnaires. Only frontal sites were considered because these are the only ones that were found to be statistically significant from previous analyses.

Significant correlations were found between ERP differences and the metamemory questionnaire score (Figure 31). The score of the Contentment subtest correlated with ERP difference over F3 from 500 to 600 ms (r = 0.59, p = 0.03). The score of the Ability subtest correlated with ERP difference over F7 from 800 to 900 ms (r = - 0.53, p = 0.05).

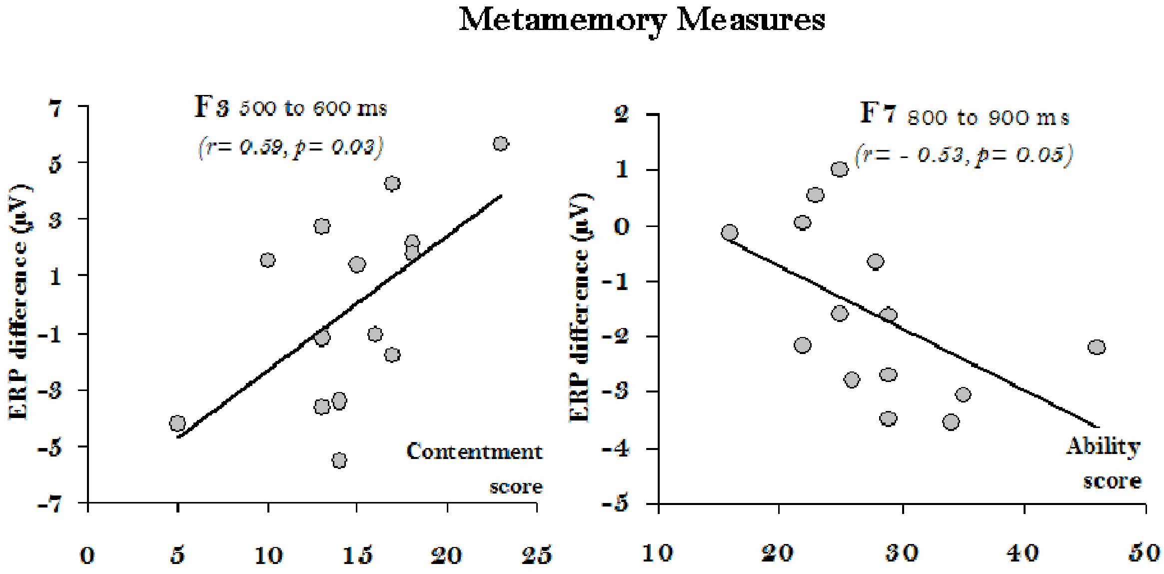

Figure 31. Scatterplots of correlations between ERPs activity over frontal sites during retrieval and metamemory questionnaire scores.

Other correlations were found between ERP differences and memory measures. The ERP difference over F7 correlated with Paired Associate Learning test, a Wechsler Memory Scale subtest, from 700 to 800 ms (r = -0.54, p = 0.04), from 800 to 900 ms (r = -0.70, p = 0.005) and from 900 to 1000 ms (r = -0.62, p = 0.02). The ERP difference over F7 from 800 to 900 (r = -0.60, p = 0.02) correlated with the Wechsler Memory Scale score, and from 900 to 1000 ms correlated with the Memory for prose test (Figure 33 and Figure 33).

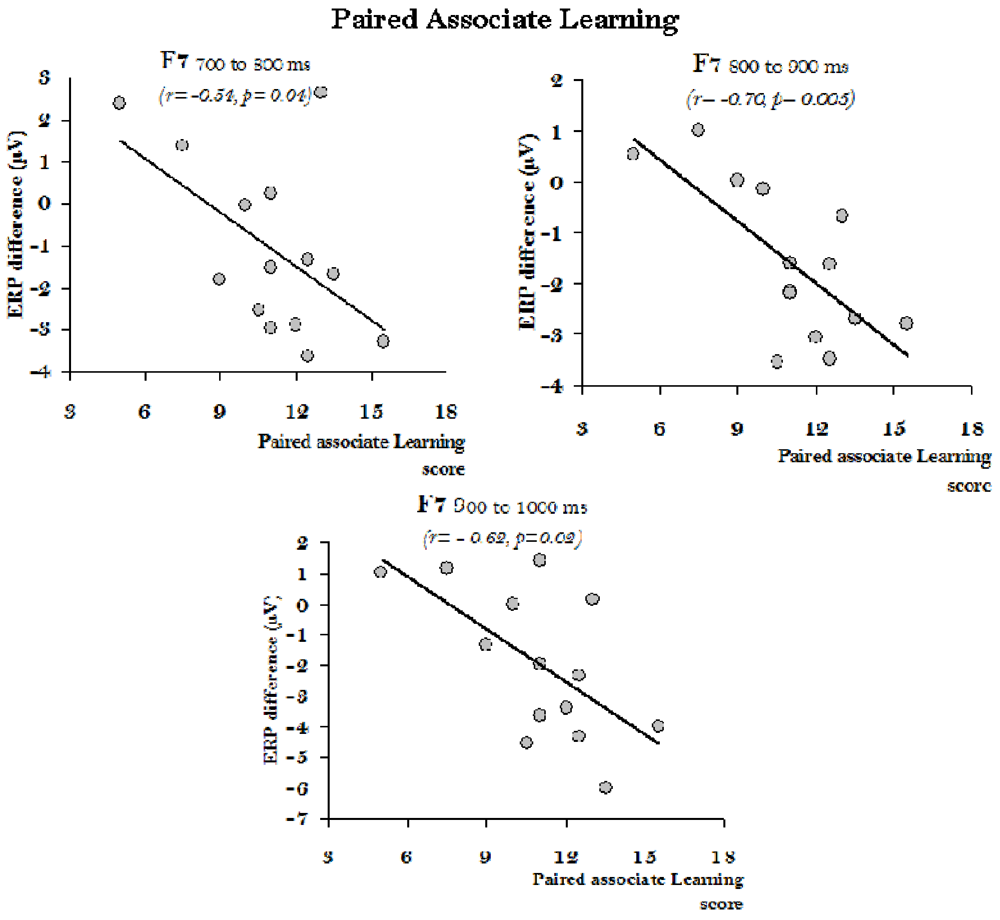

Figure 32. Scatterplots of correlations between ERPs activity over frontal sites during retrieval and memory test scores.

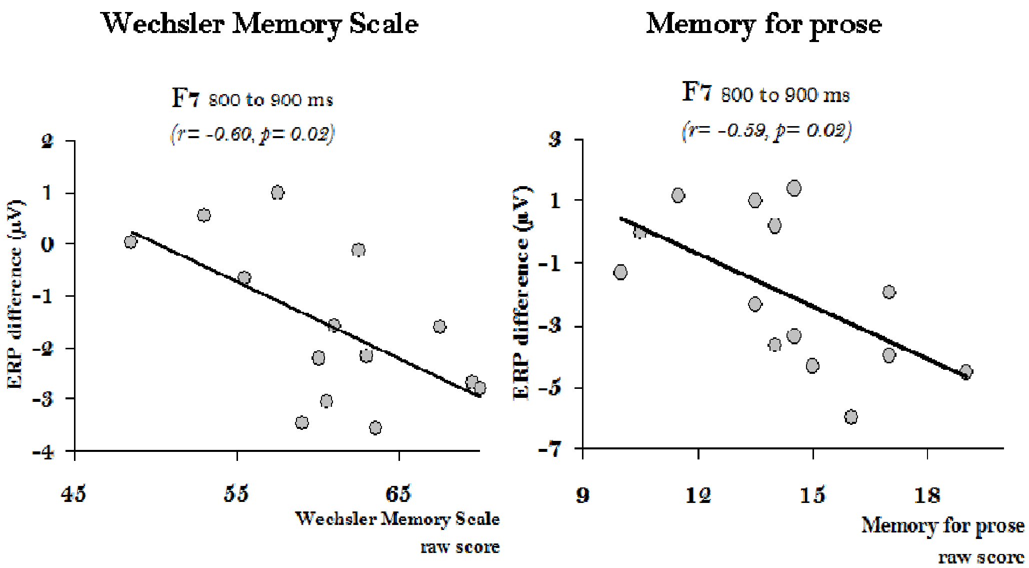

Figure 33. Scatterplots of correlations between ERPs activity over frontal sites during retrieval and memory test scores.

4. Discussion and Conclusions

In this study the neurophysiological correlates of encoding and retrieval for face-name pairs in older adults was investigated. Face-name learning was used because of its age sensitivity, as well documented in behavioural studies (i.e. James et al., 2008; Naveh-Benjamin et al., 2004). Secondly, only one other study (Pfutze et al., 2002) investigates age-related face and name recognition through event-related brain potentials, using an indirect measure of memory such as repetition priming. Here, a direct measure such as a recognition memory task was used: participants had to associate the correct name to unfamiliar faces previously studied. This paradigm has two advantages: first, it better identifies components related to the encoding and retrieval of information from episodic long-term memory (Rugg & Allan, 2000); second, it is much more similar to the everyday task of recalling a somebody's name.

The first result found was that *encoding* of proper names was characterized by a bilateral negativity over frontal sites. This negativity was the 'Subsequent memory effect' or 'Differential memory effect', the ERP activity calculated as the difference of electrical activity of stimuli correctly retrieved later to those not retrieved. An effect from 500 to 700 ms was found. This effect was positively correlated to the long-term memory test scores. Unfortunately, these results are not comparable with those in young adults (Chapter 5, Experiment 1), because we failed to find any effect in young participants, perhaps because of a slight difference in experimental design. But these results are in line with those of other studies: it is reported that in intentional learning (i.e. Friedman, 1996), older adults exhibit the same Subsequent memory effect as in young adults.

More interesting data was found during *retrieval*. The association of a proper name to an unfamiliar face in older adults was associated with a specific pattern of retrieval processes. In particular, it was found that the ERP differences between correctly associated and incorrectly associated names was over left frontal sites from 500 to 1000 ms, but not present over parietal sites. In young adults, it was found that the successful association of proper names to faces was accompanied by two components: a left frontal negativity from 500 to 600 ms and a large positivity from 600 to 1000 ms over centro-posterior sites.

These age-related differences in brain activity are associated with, respectively, familiarity- and recollection-related processing (Rugg & Curran, 2007; Yonelinas, 2002). This evidence supports the claim that whereas young adults use more recollection-related processes during face-name association (see Experiment 1), older adults appear to base their decisions primarily or entirely on familiarity. Even if Recollection/Familiarity were not directly tested by the paradigm employed, there are some arguments in favour of this claim. First of all, the negative-going negativity over frontal sites in older adults did not correlate with the percentage of correct responses, whereas in young adults the positive-going activity did. This indicates that the parietal lobe plays a role of an 'episodic memory buffer' (Baddeley, 2000) in memory retrieval (Vilberg & Rugg, 2008). Second, this difference positively correlates with contentment (the subjective perception of its own memory performance), and negatively correlates with memory test scores. Third, the topography of this effect suggests that is not directly related to recollection, as seen in young adults (and proposed by the dual process theory (see Rugg & Allan, 2000; Rugg & Yonelinas, 2003)). Taken together, this evidence could support a familiarity- rather recollection-based process of memory retrieval of proper names.

Several studies investigating age-related changes in neural activity associated with recollection and familiarity have reported the same pattern of results (Ally et al., 2008; Duarte et al., 2008; Fjell et al., 2005; Friedman & Trott, 2000; Gutchess, Ieuji, & Federmeier, 2007; Nessler et al., 2006, 2008; Wolk et al., 2008). In general, it is reported that the old/new ERP effect declines with age, despite age-invariant ERP activity during encoding (Nessler et al., 2008).

The nature of these familiarity-based processes means that the quality of memory retrieval in older adults is poorer than that of young adults, such as lower recognition memory capabilities. Thus, the frontal shift may indicate 'inefficiency': older adults perform less efficiently because their retrieval mechanisms are based on familiarity and not recollection (Walhovd et al., 2006). This hypothesis is also supported by the fact that high-performing older adults show intact recollection accompanied by a clear old/new parietal effect comparable to those of young adults (Duarte, Ranganath, Trujillo, & Knight, 2006).

Another explanation of this frontal shift could be based on a 'compensatory' hypothesis. It has been proposed that age-related changes in episodic memory retrieval engage more areas and less lateralized activations than those found in young adults (i.e. Cabeza, Anderson, Locantore, & McIntosh, 2002). Even if in this study a specific effect was found only within the left frontal sites, a more frontal area engagement was found in young adults (Experiment 1), in which a more posterior network was involved. Indeed, this frontal shift has been reported also in neuro-imaging studies in older adults. It has been shown that episodic memory retrieval engages more activation in the frontal lobes (Anderson et al., 2000; Grady, 2000; Grady, 2002), coupled with deactivation of the posterior areas, in particular for the occipital cortex. More recently, Davis et al. (2008) proposed a new model (PASA: posterior-anterior shift in aging) accounting for this data. These authors proposed that this posterior-anterior shift in aging could be attributed to a functional compensation and is not directly related to task difficulty.

To sum up, older adults showed a different and specific pattern of ERP acitivity in episodic memory of face-name associations. In young adults, a more posterior positive-going acitivity was found, an index of recollection-based processing. In older adults, a frontal shift was found, a possible index of familiarity-based processing of proper name association. This difference could account for age-related changes of brain area involved in episodic memory in face-name pair learning and retrieval.

Chapter 6

Experiment 3
Face-name repetition priming in semantic dementia: a case report

1. Face recognition, proper naming and semantic dementia

Famous face recognition and proper naming impairments are neuropsychological deficits occurring following a range of brain damage, including stroke, traumatic brain injury and neurodegenerative disease (Bauer, 2003; De Haan, 2000; Werheid & Clare, 2007; Semenza et al., 2003; Semenza et al., 1995). When impairments in famous faces and names occur in dementia they are characterised by an insidious onset and a progressive manifestation. In particular, these deficits are common in patients affected by the semantic dementia (SD), a subtype of frontotemporal lobar degeneration (FTLD) (i.e., Snowden et al., 2004).

Semantic dementia (SD) is characterized by speech output and word comprehension deficits (Snowden et al., 1989). Spontaneous speech is characterised by anomia, semantic errors (paraphasia), use of commoners, whereas phonology and grammar are relative spared (Hodges & Patterson, 2007). Semantic memory is affected whereas episodic memory appears intact, and this feature distinguishes SD from Alzheimer disease (AD) patients (Scahill et al., 2005). Studies with voxel-based morphometry (VBM) have shown that SD is characterised by the anterior temporal lobe atrophy (Gorno-Tempini et al., 2004, Patterson, Nestor, & Rogers, 2007). Hypometabolism related to the semantic memory impairment in SD patients involved selectively the bilateral rostral temporal lobes, in contrast to a widespread hypometabolism found in AD patients (Nestor, Fryer, & Hodges, 2006).

In single case study reports, SD patients presenting a progressive prosopagnosia always show unfamiliar face recognition and visual basic abilities preserved, in contrast to famous face recognition impaired. So, the prosopagnosic deficits are of associative-like type and never apperceptive in nature (Tyrrell, Warrington, Frackowiak, & Rossor, 1990b; Barbarotto, Capitani, Spinnler, & Trivelli, 1995; Evans, Heggs, Antoun, & Hodges, 1995; Gentileschi, Sperber, & Spinnler, 1999; Gainotti, Barbier, & Marra, 2003; Sperber & Spinnler, 2003; Joubert et al., 2003). The cortical atrophy was always within the temporal lobe (bilateral, greater on the right): in its antero-inferior parts (Gainotti et al., 2003), superior temporal gyrus (Tyrrell et al., 1990b) or the right fusiform gyrus (Joubert et al., 2003). Other studies have reported SD patients presenting proper naming deficit and person specific knowledge impairment (Poeck & Luzzatti, 1988; Papagno & Capitani, 1998, 2001; Schwarz et al., 1998). The presence in SD patients of these deficits might depend on the site of the brain atrophy. Snowden, Thompson, & Neary (2004) found that SD patients with predominant left temporal lobe atrophy were better to recognize famous names than famous faces, whereas those with right temporal predominance showed the reverse pattern. Moreover, Thompson et al. (2004) reported that specific person knowledge deficit could persist when the atrophy is predominantly on the right, whereas a general impairment knowledge is present when the temporal atrophy is predominantly on the left.

Two main theories explain these semantic deficits in SD patients. The semantic memory loss could be due to an impairment of explicit retrieval of knowledge or to a degradation of the internal representation of the semantic network (Hodges, Patterson et al., 1992; Hodges, Salmon, & Butters, 1992). Nowadays, the most consistent hypothesis refers to a representational deficit due to a progressive semantic degradation (Jefferies, Patterson, & Lambon Ralph, 2006; Rogers & Friedman, 2008). Besides the usual explicit measures of neuropsychological testing, the semantic system integrity has been investigated through implicit tasks, such as priming. The advantage of this technique is that it does not require a behavioural/covert response. In the case of repetition priming (RP), it is postulated that the processing of a stimulus (target) is facilitated when the same stimulus is encountered before (prime). Results issuing from studies of word priming in neurodegenerative disease patients are mixed. Cumming et al. (2006) found in SD patients a greater facilitation effect of priming (hyperpriming) for degraded words (those not identified in a explicit recognition task), when compared to controls. Conversely, some other authors found no effect of priming in SD patients in semantic tasks (Nakamura, Nakanishi, Hamanaka, Nakaaki, & Yoshida, 2000; Tyler & Moss, 1998). Conversely, in Alzheimer disease, some effects of facilitation has been found, because there is a preserved semantic memory, at least at the onset of disease (Nebes, 1989). Recently, Rogers et al. (2008) compared AD and SD patients using a priming task. AD patients showed a hypopriming whereas SD patients did not show any priming effect. This has been interpreted as a relatively spare semantic network in AD, in contrast to a clear semantic degradation in SD.

In order to study the face and name representation in SD it appears interesting to use a priming paradigm. Typically, in this task (see for example: Burton, Kelly, & Bruce, 1998; Johnston & Barry, 2006) subject is presented with a name of famous or unknown person (prime) preceded by a related or unrelated face (target). Subject is required to make a decision (for example, a familiarity judgement task) on the target. The prime preactivates the related items, and by the way the subject is faster to respond to target respect to a control condition where no relation stands between prime and target. According to this hypothesis, if in a patient explicit knowledge system is broken but some less activation still persists, facilitation in responses (reaction times, RTs) could be found in RP. Conversely, if a degraded representation occurred, any kind of facilitation could be found (Shallice, 1988).

In the present study we investigated face-name processing using a RP paradigm for faces and names in a patient with SD and in ten age-matched healthy controls. Repetition effect using name-name pairs (within domain) and face-name pairs (cross domain) was investigated. In order to investigate the semantic memory related to person representation it was decided to employ a repetition priming technique, exploiting the implicit processes. This paradigm permits to verify if such a representation is broken or only relatively spared but not accessible. An absence of priming effect could be considered as an index of a degraded representation of faces and names, instead of an impaired access to information.

First studies in healthy participants have shown that no priming effect occurred when prime and target are cross-domain (i.e., face–name, name–face) (Bruce & Valentine, 1985; Ellis et al., 1996). By contrast, more recent studies evidenced that priming can cross domain inputs when the face of a famous person is immediately preceded by the same person's name (or vice versa). Calder & Young (1996) demonstrated a clear effect of cross-domain repetition priming when short intervals occurred between prime and target of the same famous person ('self-priming'). The amount of priming was larger in within- than in cross-domain condition. Burton et al. (1998) reported evidence of cross-domain priming when task was semantic in nature (e.g.: nationality decision, dead/live).

There is also evidence in prosopagnosic patients, in which overt face processing is impaired. De Haan et al. (1992) described a prosopagnosic patient (NR) who overtly did not recognise famous faces but performed above chance in a forced-choice familiarity task. NR showed a priming effect in a cross-domain task (face-name), this effect was restricted to those faces categorised as 'familiar' in the forced-choice task. Also, Young, Hellawell, & De Haan (1988) described a prosopagnosic patient (PH) who cannot overtly recognise familiar faces but he showed facilitation to responses to targets (names or faces) preceded by semantically related primes.

It was hypothesised that in our SD patient no effect of priming will occurs in cross-domain priming: a famous face does not facilitate the access to its own name; and maybe no effect also in within-domain priming. Consequently, responses to target (names) will not be facilitated because primes (face and names) representation is degraded.

2. Materials and Methods

2.1. *Participants*

2.1.1. CMR

CMR, a 67-year-old woman with eight years of education was diagnosed with a semantic dementia according to frontotemporal dementia diagnostic criteria (Neary et al., 1998; McKhann et al., 2001). The patient underwent a structural brain MRI, and visual rating of MRI images was compatible with the clinical diagnosis. MRI scan (July 2007) detected a left temporal lobe atrophy with consequent enlargement of ventricles, associated to signal abnormalities within the right inferior parietal cortex (see Figure 34).

Extensive neuropsychological assessment was performed including: non verbal reasoning, language comprehension, verbal fluency, short-term memory, long term memory, constructional abilities, apraxia and attention and executive functions. Language functions were investigated with a detailed battery for aphasic deficits (AAT, Aachner Aphasie Test). A detailed description of CMR's performance is reported in Table 2.

Baseline cognitive assessment included screening tests for dementia (MMSE; Clinical Dementia Rating, CDR), and neuropsychological tests as follows: non verbal reasoning (Raven Colored Progressive Matrices), language comprehension (Token Test), verbal fluency (Controlled Association Letter Test and Controlled Association Categories Test), short-term memory (Digit Span and Spatial Span), long-term memory (Story Recall, Rey Auditory-Verbal Learning Test, Rey-Osterrieth Complex Figure-Recall), constructional abilities (Rey-Osterrieth Complex Figure-Copy), apraxia (Buccofacial and Ideomotor Apraxia Tests), attention and executive functions (Trial Making Test, Cognitive Estimation Test and Pyramid and Palm Tree test (Lezak, Howieson, & Loring, 2004b).

Language functions. Repetition, naming, writing and comprehension were formally assessed with the full Italian version of the Aachener Aphasie Test (AAT) (Luzzatti et al., 1994). CMR showed pathological performances in comprehension and naming subtests, whereas repetition and writing were preserved.. CMR's spontaneous speech was fluent with severe anomia and semantic paraphasias. A baseline evaluation of action and object naming abilities was performed (Aphasic Battery for Analysis of Aphasic Deficits (BADA). In this evaluation the patient showed pathological performance both in action and in object naming. Also, oral comprehension of objects and actions end sentence comprehension were impaired (BADA).

Visuoperceptual and constructional abilities. Basic visuoperceptual abilities were assessed with the VOSP (The Visual Object and Space Perception; James & Warrington, 1991) battery. CMR scored within normal range for all but for Silhouettes and Object Recognition subtests. It is important to underline that the pathological scores in these two latter subtests could be biased by the language deficits.

Facial recognition test (Benton, Sivan, de S. Hamsher, Varney, & Spreen, 1990). In this test in which is required to match unfamiliar faces, CMR scored borderline (Correct responses 39 out of 54, cut-off score 41).

Gender judgement task. A set of 64 pictures portraying unfamiliar male and female faces were used. Half faces depicted all the face features, the other half was without external features (no hair). Stimuli were presented on the monitor of a PC and they remained on the screen until a response was made. CMR performed perfectly in this task (100% of correct responses).

Recognition of famous faces (Rizzo, Venneri, & Papagno, 2002). In this test half famous and half unfamiliar faces were presented and it was required to recognize famous faces, provide semantic knowledge and name them. In semantic knowledge and naming of famous people on picture presentation CMR had a pathological performance. In fame judgement subtest CMR performed within normal range, but because of score is obtained on the basis of false recognition of unfamiliar faces. CMR failed to recognise as famous 32 on 50 faces (64% of errors).

*Recognition of famous names (*Bizzozero, Lucchelli, Pozzoli, Saetti, & Spinnler, 2007). In this test is required to recognise famous name printed on a sheet, presented in a series half famous and half unfamiliar. CMR had a pathological performance in this test.

CMR showed a fluent progressive aphasia with naming and comprehension difficulties, loss of verbal and non verbal semantic knowledge about objects, concepts, people and meaning of words. Moreover, the patient obtained pathological scores on task that investigated executive functions and long term memory functions and recognition of famous names and faces, whereas visuo-spatial, perceptual and praxic abilities were spared.

In addition, behavioural and social changes were assessed with the Frontal Behavioural Inventory (FBI: Kertesz, Davidson, & Fox, 1997), a caregiver questionnaire designed to operationalize and quantify the personality and behaviour changes in FTLD. The FBI is a 24 item scale, composed of two subscales for negative (FBI-A) or positive behaviours (FBI-B). CMR showed clear pathological behavioural changes due to the disease (raw score of FBI (Italian version)= 36; Alberici et al., 2007). In particular, she showed apathy, indifference, disorganization, inattention, logopenia and semantic anomia (FBI-A), as well as irritability, impulsivity, aggression and hyperorality (FBI-B).

Table 2. Neuropsychological assessment

	Raw Scores	***Adjusted Scores***		***Cut- off***
Mini Mental State Examination	26/30	24	*Normal*	24
Non verbal Reasoning				
Raven Colored Progressive Matrices	21/36	23.5	*Normal*	18
Long-term Memory				
Story Recall	3/28	3.5	***Pathological***	8
Rey Auditory-Verbal Learning Test-Immediate recall	13/75	17	***Pathological***	28.52
Rey Auditory-Verbal Learning Test-Delayed Recall	4/15	5.3	*Borderline*	4.68
Rey-Osterrieth Complex Figure - Recall	0/36	0	***Pathological***	9.47
Short-term Memory				
Digit Span	4	4.25	*Normal*	3.75
Spatial Span	5	5,25	*Normal*	3.75
Language				
Token Test	25/36	24.75	***Pathological***	26.5
Controlled association letters test	1	5	***Pathological***	17
Controlled association categories test	3	7	***Pathological***	25
Visual and constructional abilities				
The Visual Object and Space Perception Battery (VOSP)				
Incomplete letters	17/20		*Normal*	15
Silhouettes	7/30		***Pathological***	16
Object Recognition	13/20		***Pathological***	17
Progressive Silhouettes	14/20		*Normal*	18
Dot Counting	10/20		*Normal*	8
Position Discrimination	19/20		*Normal*	18
Number Location	10/10		*Normal*	7
Cube Analysis	8/10		*Normal*	6
Rey-Osterrieth Complex Figure - Copy	31/36	32.5	*Normal*	28.88
Facial recognition test (Benton)	39/54		*Borderline*	41
Recognition of famous faces (Rizzo et al., 2002)				
Fame judgement on picture presentation	4/50	4	*Normal*	14.16
Semantic knowledge of famous people	7.75/50	12.5	***Pathological***	22.17
Naming of famous people on picture presentation.	0/50	0	***Pathological***	14.50
Recognition of famous names (Bizzozero et al., 2007)	2193.5	2257.96	***Pathological***	6666.46
Praxis				
Buccofacial apraxia	19/20	19	*Normal*	18
Ideomotor Apraxia - Right upper limb	67/72		*Normal*	62
Ideomotor Apraxia - Left upper limb	69/72		*Normal*	62
Attentional and executive functions				
Trial Making Test A	56	36	*Normal*	93
Trial Making Test B	321	253	*Borderline*	282
Trial Making Test B - A	265	217	*Pathological*	186
Pyramid and Palm Trees Test	22/30			
Cognitive estimation test				
Errors	20/42		***Pathological***	18
Bizzarreness	9/21		***Pathological***	4

Table 2 (continuing)

Aphasic Battery for Analysis of Aphasic Deficits(BADA)			
Oral Object Naming	6/30	***Pathological***	28
Oral Action Naming	12/28	***Pathological***	26
Oral Comprehension of Objects	35/40	***Pathological***	39
Oral Comprehension of Actions	16/20	***Pathological***	19
Sentence Comprehension	53/60	***Pathological***	58
Aachener Aphasie Test (AAT)			
Token Test	15/50	***Pathological***	
Ripetition	144/150	*Normal*	
Writing	88/90	*Normal*	
Naming	82/120	***Pathological***	
Comprehension	74/120	***Pathological***	

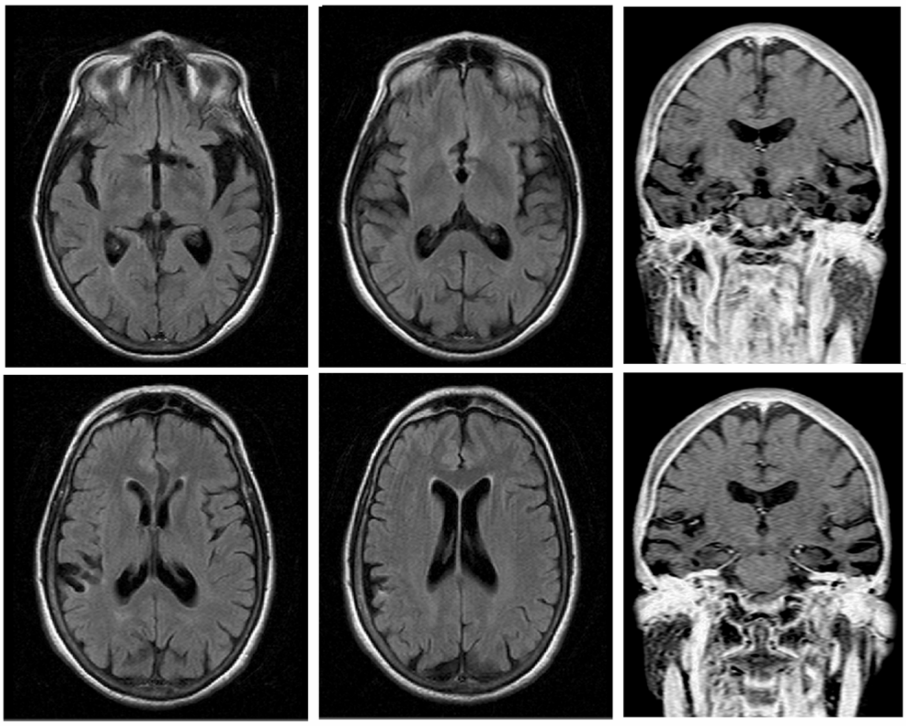

Figure 34. CMR'S MRI scan: coronal and horizontal sections showing temporal atrophy, greater on the left.

CMR was also tested in emotion recognition processing. It was used first the Emotion word knowledge questionnaire proposed by Werner et al. (2007). This questionnaire investigates the knowledge of emotion terms by asking patient to answer questions based on ecological situations. CMR scored correctly to all questions, confirming a perfect knowledge of emotions.

Second, to investigate recognition we employed The Ekman 60 Faces Test. This test uses a range of faces to test recognition of six basic emotions (anger, disgust, fear, happiness, sadness, and surprise). In this test photographs of the faces of 10 models (6 female, 4 male) selected from the Ekman and Friesen (1976) series are presented. For each model there are poses corresponding to each of 6 basic emotions. Each face is presented on a A4 sheet with six labels of basic emotions below the photograph. CMR was required to respond verbally deciding which label best described the facial expression shown. The maximum score was 10 for each basic emotion (60 total score).

In order to exclude any verbal bias in CMR's response, it was used a modified version of Ekman 60 Faces Test. The same photographs of the standard version were used but, instead of verbal labels, other six photographs displaying the six possible basic emotions were presented below the target stimulus (always 3 female and 3 male). CMR was required to indicate which photograph matches the target stimulus. The patient was assessed in this version one week later from the first one. As reported in

Table 3, CMR, in the stardard version, did not recognize any emotions. Conversely, in the modified version reported a perfect recognition of happiness.

Moreover, cognitive and emotional components of empathy assessed through the Interpersonal Reactivity Index. The Interpersonal Reactivity Index (IRI; Davis, 1983) is a 28-item questionnaire consisting of four 7-item subscales that measure both the cognitive and the emotional components of empathy. The four subscales are: 1) Perspective Taking (PT), i.e., the ability to adopt the viewpoint of others in everyday life; 2) Fantasy (FS), i.e., the tendency to project oneself into the place of fictional characters; 3) Empathic Concern (EC), i.e., the feelings of sympathy and concern for people involved in unpleasant experiences; and 4) Personal Distress (PD), i.e., the distress that results from witnessing another's negative emotional state. PT and FS subscales measure the cognitive aspects of empathy while subscales EC and PD the emotional aspects. In this study the IRI questionnaire validated on the Italian population was used (Albiero, Ingoglia, & Lo Coco, 2006). In order to assess the changes over time in CMR's empathy, it was asked her daughter and husband to indicate how well each item described on a 5-point scale the patient both prior to the onset of the disease and currently. Significant differences were found in both PT (score: before=54, current=34) and FS (score: before=43, current=31) subscales (z = 2,198, p = .028, and z = 1,968, p = .049, respectively). No significant differences were found in the EC (score: before=46, current=40) and PD (score: before=51, current=42) subscales. The total score comparison was significant (before=194, current=147; z = 3,122, p = .002).

In order to evaluate CMR's performance in the two components (cognitive and emotional) of empathy predicted by Davis (1983), in a further analysis the PT and FS subscales were summed together to provide a total cognitive empathy score, and EC and PD were summed together to provide a total emotional empathy score. A significant difference was found for the cognitive component (score: before=97, current=65) z = 2.948, p = .003). No difference was found in the emotional component between the pre- and the post-disease condition (score: before=97, current=82). See Table 4 for more details.

Taken together, these results indicate that in CMR still persists an ability to feel emotions even though the overt recognition is dramatically impaired.

Table 3. Correct responses for each basic emotion in the standard and in the modified version of the Ekman 60 Faces test. Scores marked in bold type are above the cut-off.

	Anger	**Disgust**	**Fear**	**Happiness**	**Sadness**	**Surprise**
Ekman 60 Faces						
Patient CMR	3	2	1	4	3	4
Modified Ekman 60 Faces						
Patient CMR	3	4	**4**	**10**	0	4
Cut-off	*4*	*6*	*3*	*9*	*5*	*6*

Table 4. IRI scores before the onset of the disease and currently with discrepancy.

	Before	**Current**	**Discrepancy**
Perspective Taking (PT)	54	34	-20
Fantasy (FS)	43	31	-12
Cognitive aspects of empathy*	97	65	***-32***
Empathic Concern (EC)	46	40	-6
Personal Distress (PD)	51	42	-9
Emotional aspects of empathy	97	82	***-15***
Total score	***194***	***147***	-47

** Score before and current statistically different (p<0.05)*

2.1.2. Healthy participants

Two different groups of ten healthy control subjects each were recruited for each experiment. No control had a history of neurological or psychiatric disease, head injury or alcohol abuse. They were neither under treatment for major illness. Controls were tested using Minimental State Examination Test, Trial Making Test for executive functions, Memory for Prose and Wechsler Memory Scale for memory abilities (Lezak, Howieson, & Loring, 2004a). All the controls performed within normal range for all the neuropsychological tests.

A pilot study with young participants showed that the percentage of priming effect was of 9.7 (± 3.9) compared to neutral conditions. So, the sample size of controls is over those estimated (n=9) considering an 80% of power and a 0.05 level test of significance on the expected mean difference found in the pilot experiment.

In the Experiment 1, the mean age of healthy participants was 67.5 (± 5.7) and mean years of education was 10.0 (± 2.9). In the Experiment 2 the mean age of healthy participants was 71.4 (± 5.7) and mean years of education was 11.2 (± 3.4). They did not differ significantly from the patient's age and education ($p > 0.05$).

2.2. Experimental tasks

2.2.1. Cross-domain priming for faces and names

2.2.1.1. Stimuli and procedure

Stimuli included grey-scale faces and proper names. Faces were downloaded from electronic free datasets and other resources on the web and processed by Adobe Photoshop 5.0. Image were scaled of 210 x 263 pixels and presented from a distance of 100 cm (subtending a visual angle of ~ 3.15° x 4°). The photographs portraying famous faces were of well-known politicians, movie stars and other famous celebrities. It was conducted a pilot study to define the set of pictures to be used in the experiment. Only pictures with a percentage of correct responses above 90% were considered.

Subjects were presented with a face for 500 ms (prime), followed by a proper name (target). Subjects were required to read aloud the names presented, and remained on the screen until the response was made. Vocal reaction times were recorded via a microphone.

The experiment consisted of three blocks of 24 face-name pairs each and a practise session. Three prime types were given to famous face targets, such as:

1. Same person prime: a famous face as a prime followed by the corresponding proper name as a target;
2. Unrelated famous prime: a famous face as a prime followed by an unrelated famous proper name as a target;
3. Unfamiliar prime: an unfamiliar face as a prime followed by a famous proper name as a target.

Only one prime type (unfamiliar face) was given to unfamiliar proper name targets.

In healthy participants, fame judgement for primes was performed offline when all the experiments were run. Stimuli that were not recognized as famous were excluded to calculation.

2.2.2. Within-domain priming for names

2.2.2.1. Stimuli and procedure

Subjects were presented with a proper name for 500 ms (prime), followed by a mask for 300 ms and a second proper name (target). Subjects were required to read aloud the names presented, and it remained on the screen until the response was made. Stimuli were presented in the centre of the screen, in 24 Arial font, over two lines (one line for the forename, and a second line for the surname, in capital letters). Targets were presented in bold. Vocal reaction times were recorded via a microphone. The experiment consisted of three blocks of 20 face-name pairs each and a practise session. The same Prime type as in the cross-domain priming experiment was considered. In the case of self-priming, two proper names were the same.

3. Statistical analysis

Reaction times (RTs) exceeding the two standard deviations above and below the means were excluded to computation. Statistical analyses were performed first on reaction times considering all the priming conditions. Then, analyses were performed on difference RTs calculated as follows: a) same-person prime condition minus unfamiliar prime-target condition; b) unrelated famous prime condition minus unfamiliar prime-target condition.

It was used only the 'unfamiliar prime-target condition' as control condition because there was not statistically different from the unfamiliar prime-famous target condition for the cross-domain (t(9)= 0.50, p= 0.63), and for the within-domain (t(9)= 0.47, p= 0.64). RTs for each condition are reported in Table 5.

The effect of priming in control participants was test using a T test for one sample considering an expected mean of zero (null hypothesis of no priming effect).

Additionally, t tests for independent samples were used to compare CMR and controls' performances. It was used a modified t test described by Crawford and Howell (1998), because is more appropriate when the individual as a sample is one and the control group is small. The level of significance was set at 0.05.

4. Results

4.1. Cross-domain repetition priming

Analyses performed on the priming effect revealed that in healthy participants the RT difference between the same-person and the unfamiliar prime-target condition was significantly different to zero (Mean= 50.5 ms; SD= 20.1; t(9)= 7.53, p < 0.0001). CMR's priming effect (-3 ms) was statistically different to controls in this condition (t(9)= -2.53, p= 0.02).

For healthy participants, there was no priming effect for RT difference between the unrelated famous and the unfamiliar prime-target condition (Mean= -3.9 ms, SD= 25.0, t(9)= -0.46, p= 0.65). No difference was found between CMR's priming effect (7 ms) and that of controls in this condition (t(9)= 0.41, p= 0.35). CMR in the forced-choice familiarity judgement task only the 36% of correct responses. Her performance were characterised by a high rate of missing, such as 52% (she did not recognise famous faces as famous ones) and 75% of false alarms (she categorised unfamiliar faces as famous ones).

4.2. Within-domain repetition priming

Analyses performed on the priming effect revealed that the RT difference between the same-person and the unfamiliar prime-target condition was significantly different to zero (Mean= 61.0 ms; SD= 27.7; t(9)= 6.61, p < 0.0001). CMR's RT difference (14 ms) was not statistically different from that of controls in this condition (t(9)= -1.54, p= 0.08). For healthy participants, there was no priming effect for RT difference between the unrelated famous and the unfamiliar prime-target condition (Mean= 5.0 ms, SD= 19.0, t(9)= 0.48, p= 0.64). No difference was found between CMR's priming effect (4 ms) and that of controls in this condition (t(9)= 0.04, p= 0.48). The effect of priming of Experiment 1 (cross-domain) and Experiment 2 (within-domain) in healthy participants did not differ statistically (t(18)= 0.92, p < 0.37).

Table 5. Vocal RTs (in milliseconds) in the within- and cross-domain priming experiment.. Values are reported as means and standard deviations in brackets.

	Familiar target			***Unfamiliar target***
Prime	Same	Unrelated	Unfamiliar	
Cross-domain				
CMR	646	654	658	654
Controls	676 (83)	731 (75)	729 (74)	727 (77)
Within-domain				
CMR	692	690	682	681
Controls	686 (94)	742 (89)	729 (83)	747 (100)

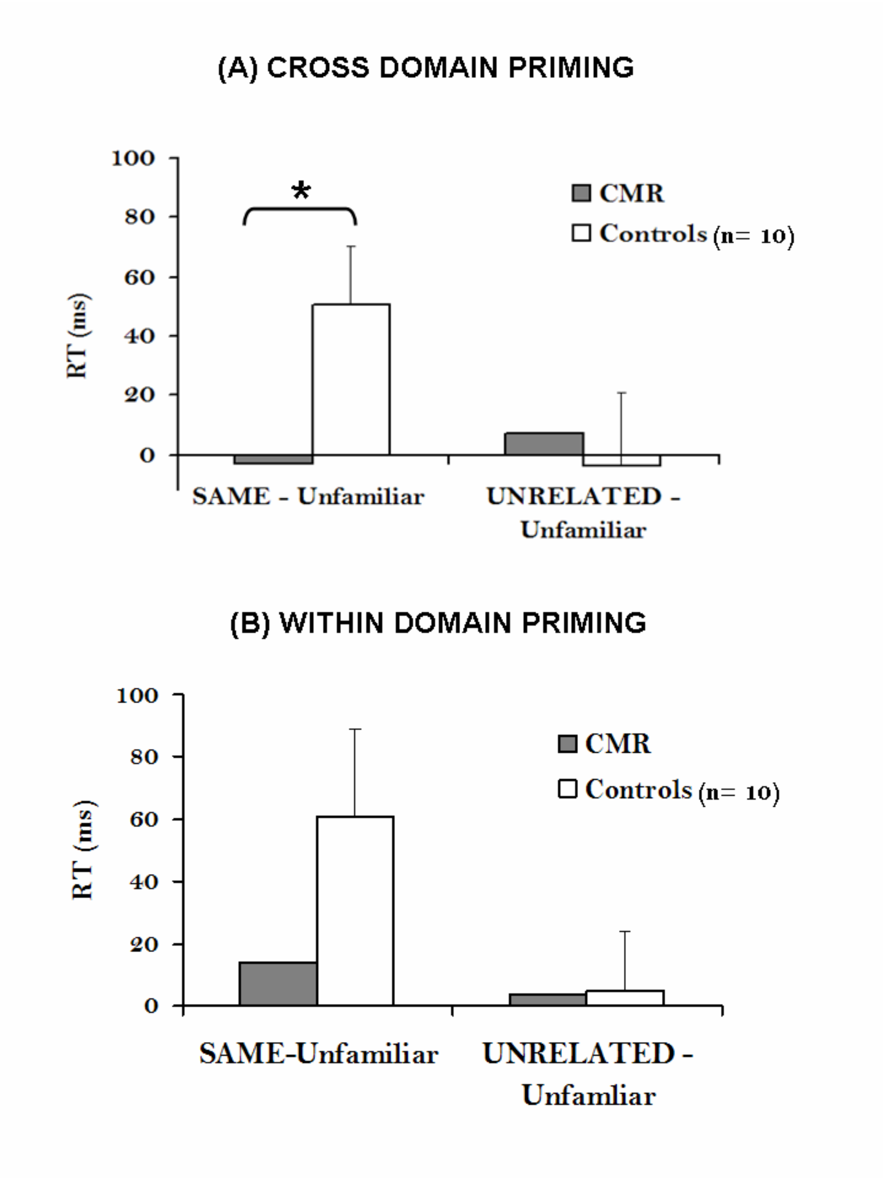

Figure 35. (A) Cross domain priming effect. Effect of priming calculated as a difference of conditions: same person prime and target, unrelated famous prime and famous name minus unfamiliar face prime and target. (B) Within domain priming effect. Effect of priming calculated as a difference of conditions: same person prime and target, unrelated famous name and famous name minus unfamiliar name prime and target. Values are means and standard deviations as bars.

5. Discussion

It was investigated implicit and explicit processing of famous faces and names in a SD patient (CMR) presenting a prominent proper anomia and person specific knowledge impairment. The association of these two deficits allows us to define the proper naming impairment as semantic in nature and not only at a post-semantic or at retrieval level (Semenza, 2006). Her famous face recognition was poor: she performed below chance (36%) in the fame judgement test. Conversely, her abilities to process configurational aspects of faces were preserved. CMR was relatively good in matching unfamiliar faces and excellent in gender judgement. Taken together, it could be claimed that her impairment of face processing was of 'associative' type, as those reported in the previous studies in literature (e.g. Snowden et al., 2004). These measures have permitted to investigate the explicit processes of conceptual knowledge of famous faces and proper names.

Implicit processing of the semantic memory was further investigated. In order to clarify the nature of this deficit it was used a paradigm of within- and cross-domain priming of faces and names. No effect of repetition priming in CMR was found, this could permit us to exclude a possible deficit of access of proper names. It was used a reading task instead of a behavioural response, such as familiarity judgement, in order to avoid a large drop of data. In famous face recognition test CMR performed below chance, this means that a large amount of data could have been missed if an explicit response was used. Other tasks, such as gender or facial expression judgement, were neither ideal because it is known that they do not produce any kind of priming effect (Ellis, Young, & Flude, 1990). The presence of a clear effect of priming in healthy controls supports our hypothesis that priming occurred in some way, even if the task was not semantic in nature. Moreover, other studies have used a similar task, such as threshold oral reading, in lexical priming task in AD patients (Glosser & Friedman, 1991; Glosser, Friedman, Grugan, Lee, & Grossman, 1998). These authors found significant effect of priming in associated and semantically related words in AD patients.

It was found that CMR did not show any kind of priming effect: a previous presentation of an item related to the target did not facilitate the processing of this latter. This was clear when the target (name) was preceded both by a face (cross-domain condition). The little effect in the within domain condition could be due to a physical identity effect of letters. Whereas controls showed a clear effect of priming for related pairs of faces and names.

These effects could be explained according to cognitive models of face processing and naming. In particular, the IAC (interactive activation and competition) developed by Burton, Bruce, & Johnston (1990), the connectionist model based on the Bruce & Young (1986)'s model makes some predictions in that sense. The IAC implementation postulates four types of units: one for faces (FRUs), one for names (NRUs, Name Recognition Units), one for classification of the person (PINs) and the last one is for semantic information (SIUs, Semantic Information Units). Burton et al. (1990) proposed that the recognition of a familiar name is speeded up when it is preceded by the same person's face only for semantic priming but not for repetition, because this latter is domain specific. But conversely, it was found the effect also when cross-domain self priming occurred. As Burton et al. (1990) pointed out, repetition priming is short-lasting, and in our experiment it was found the effect because prime and target occurred immediately. The locus of this priming could be explained as Burton et al. (1990)'s claim. They postulated that familiarity decision is made at PIN level, because these are units allowing the access to semantic information. So, for these authors priming occurs at this level. CMR showed semantic and person identity knowledge deficits, this precludes target to benefit of a previous exposure of the prime of the same individual. The non preactivation of the prime, due to a degraded representation in CMR, does not enhance the threshold at PIN level. Consequently, the target recognition was not facilitated.

The null effect for unrelated pairs needs some explanations. According to IAC model, only closed semantically related item could benefit of facilitation in recognition. Moreover, it is possible that some kind of inhibitory could exist, and the balance between excitatory and inhibitory contributes to the total effect. So, maybe that the two strengths of connection cancel one each other resulting in a null effect (Calder & Young, 1996). Other studies in young people (Jemel, Pisani, Rousselle, Crommelinck, & Bruyer, 2005) and in adults (Schweinberger, 1995) reported the same pattern of results at this regard.

Previous studies (Calder & Young, 1996; Johnston & Barry, 2006) found that within domain repetition priming is greater than cross-domain one. This is because different factors contribute to such a larger facilitation: the increased activation in the appropriate PIN, and the strengthened NIU - PIN connection for names, and FRU - PIN connection for faces. These processes occur both in the same domain, without a cost from switch to another different domain. It was not found such advantage for the within-domain condition, maybe because in elder people inhibitory effects are less strong.

To sum up, it was found that explicit measures of famous face processing and proper naming demonstrated a semantic deficit in our SD patient. Implicit measures, such as priming, revealed no effect of facilitation in the experimental task. The consistency of the results of these two measures could account for a semantic loss of representation, as previously found for language studies in SD (Nakamura et al., 2000; Rogers & Friedman, 2008; Tyler & Moss, 1998).

Further investigations in a group of SD patients are needed to explore this hypothesis of degraded knowledge for famous faces and proper names.

General discussion and conclusions

The aim of this thesis is to investigate the episodic and semantic aspects of memory for faces and proper names. Three experiments were carried out to explore these two different aspects of this specific associative learning. The first two explored the episodic aspects in young and older adults through event-related potentials, whereas the third one investigated the semantic aspects in a case of semantic dementia.

ERPs were recorded in young adults while they encoded and retrieved face-name pairs. The main result concerned the retrieval process: it was found that during the association of the names of unfamiliar people, two main components are distinguishable. The first, more transient, was a left frontal negativity over the left frontal site from 500 and 600 ms, and a second one, a positivity over centro-posterior sites from 600 to 1000 ms. According to the dual process theory, two main processes are responsible for episodic memory retrieval: 'familiarity' and 'recollection' (Yonelinas, 2002). Familiarity, basically, is when we have the feeling of knowing we recognize something or somebody; recollection is when we can recollect when and where we have seen it. The second component is that this posterior effect positively correlates with the subjects' performance. This data could not be explained by the difference of the trial used in the analysis. Even if the mean trials considered for Low performers differed significantly from that of High performers ($t_{20} = 2.15$, $p = 0.04$), they do not differ so much in size (mean trials: Low performers: 22 ± 3; High performers: 27 ± 5). Moreover, this data could be explained within the different hypotheses of the role of the parietal lobe. It has been proposed (Wagner et al., 2005) that parietal regions temporally integrate a memory-strength signal to summarize information coming from other brain regions ('mnemonic accumulator hypothesis'), or shift attention to, or maintain, internally generated mnemonic representations ('internal representation hypothesis'). More recently, Cabeza (2008) also proposed the 'attention to memory model (AtoM)'. According to this model, the superior parietal lobe is the reflection of processes downstream of retrieval, the engagement of which depends on the salience or task-relevance of the eliciting item.

And finally, the 'output buffer hypothesis' has been proposed. This hypothesis postulates that parietal regions hold retrieved information in a form accessible to decision-making processes, similarly to one of Baddeley's working memory buffers (Baddeley, 2000). According to this hypothesis, the relation of ERP measures over parietal lobes and recollection is sensitive to the amount of information recollected from episodic memory. Vilberg et al. (2006) have shown that correct recollection of the pairmate of the test item elicited a larger old/new effect over the parietal lobes. In that sense, the High performing subjects in Experiment 1 showed a larger positive-going activity for correctly retrieved proper names paired to faces previously studies. In summary, it seems that the results of Experiment 1 are more compatible with the 'output buffer hypothesis'.

The second step of this research aimed to investigate the age-related changes of associative learning. The same paradigm of face-name associations was used. The more interesting data in recollection is related to the 'frontal shift' of the ERP activity observed in the older adults. Correctly associated proper names elicited a more negative-going waveform than those incorrectly associated over the left frontal lobes. The same effect was not found over the parietal lobes, as previously seen in young adults. The second result is that the ERP activity related to this frontal shift does not correlate with older adults' performance, meaning that it is not directly related to recollection. Conversely, this frontal ERP activity positively correlates with the contentment test and negatively correlates with the long-term memory test scores. This effect could be explained by two hypotheses. The first one is within dual process theory (Yonelinas, 2002), and could be compatible with a familiarity-driven process. Even if it is reported that the neurophysiological correlation of familiarity is a positive-going activity over frontal areas, there is some evidence of left frontal negativity in older adults during memory retrieval not observed in the young (Swick et al., 2006). In that sense, a familiarity-based process during episodic retrieval entails less efficient memory retrieval in older adults. They used the feeling of having seen an item previously, instead of recollecting the context dependent information. This led to less efficient memory: older adults were slightly poorer than young adults in correctly associating proper names with faces (59% ± 8 vs 66% ± 10 of correct response; $t_{29} = 2.32$, $p = 0.03$).

The other hypothesis concerns the functional reorganization of brain activity through the lifespan, and especially in aging. A consistent observation from neuro-imaging studies is that older adults paradoxically increase activity in the frontal regions relative to young adults, sometimes in regions minimally active in young adults performing the same task (e.g. Cabeza et al., 1997; Logan, Sanders, Snyder, Morris, & Buckner, 2002). Recent findings further suggest that this increased recruitment may reflect a productive response to detrimental changes in aging, serving to mitigate performance decline (e.g. Cabeza, 2002). More recently, Davis et al. (2008) proposed a new model (PASA: posterior-anterior shift in aging) accounting for this data. These authors proposed that this posterior-anterior shift in aging could be attributed to a functional compensation and because older adults paradoxically increase activity in the frontal regions relative to young adults on tasks that place high demands on control processes (Velanova et al., 2007).

It should be interesting to investigate this neurophysiological pattern in a pathological population, for example, Mild Cognitive Impairment (MCI) (Petersen et al., 2001; Petersen & Negash, 2008) patients. MCI patients show a selective impairment of episodic memory. So, it should be interesting to study how this neurophysiological pattern changes in MCI in its temporal and topographical aspects with respect to physiological aging.

The Experiment 3 investigated the semantic aspects of face-name association in a case of semantic dementia. The aim of that study was to test the hypothesis of a degraded semantic system of these representations vs a deficit of access to knowledge. SD patients showed a semantic memory breakdown with a spared episodic memory, at least at the beginning of the disease.

The patient (CMR) showed a proper anomia associated to person specific knowledge impairment, as demonstrated by the neuropsychological test (explicit measures). But to be prone to a 'semantic degradation' hypothesis it is useful to have an implicit measure as well. For this purpose, a cross-domain priming paradigm for face-name pairs was adopted: participants were required to read aloud a proper name (target) preceeded by a face (prime). It was found that the semantic dementia patient did not show any kind of priming effect: reading a familiar name is not speeded up when it is preceded by the same person's face. Whereas control participants showed a clear priming effect in this condition called 'self-priming'. The locus of this cross-priming could be placed at the PIN (Person identity nodes) level where the familiarity decision is made, allowing access to semantic information (Burton et al., 1990). The patient showed semantic and person identity knowledge deficits, which precludes the target benefiting from previous exposure of the prime of the same individual. The non-preactivation of the prime in the semantic dementia patient, due to a degraded representation, does not enhance the threshold at PIN level.

Further investigations in a group of semantic dementia patients are needed to explore the hypothesis of degraded knowledge for famous faces and proper names, and to investigate if this degraded representation is present also for other unique entities, such as geographical names.

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