Available online at www.sciencedirect.com
ScienceDirect
Journal of Physiology - Paris 100 (2006) 142–153
Journal of Physiology Paris
www.elsevier.com/locate/jphysparis

Dissociating episodic from semantic access mode by mutual information measures: Evidence from aging and Alzheimer's disease

Elisa Ciaramelli [a], Rosapia Lauro-Grotto [a], Alessandro Treves [b,c,*]

[a] Dipartimento di Psicologia Generale, Università degli Studi di Firenze, via S. Niccolò 93, 50125 Firenze, Italy
[b] SISSA, Cognitive Neuroscience, via Beirut 2, 34014 Trieste, Italy
[c] NTNU, Centre for the Biology of Memory, Trondheim, Norway

Abstract

Re-thinking the semantic vs. episodic distinction with new experimental paradigms, we have designed a simple classification task to assess episodic and semantic access modes to memory for famous faces. The task requires to post 54 cards into nine mail boxes arranged in a 3×3 (nationality by field of activity) array, allowing for a quantitative analysis of the distribution of their responses, in particular of their classification errors. By using an information theoretical approach, we have developed an index of the concentration of errors, i.e. the metric content index. High levels of metric content indicate strong dependence of the classification performance on perceived relations among the set of stimuli, and therefore a preferred semantic access mode. We have found (1) a significant effect of age on the metric content, indicative of a shift from episodic to semantic access in older subjects (Experiment 1); (2) a significant correlation between the metric content and relevant measures assessing episodic and semantic retrieval mode in the Remember (*R*)/Know (*K*) paradigm introduced by Tulving [Tulving, E. 1985. Memory and consciousness. Can. Psychol. 26, 1–12] (Experiment 2); (3) a significant increase in metric content in early Alzheimer's disease patients compared to normal controls, consistent with their specific impairment in episodic access (Experiment 3).

Keywords: Hippocampus; Neocortex; Semantic memory; Episodic memory; Famous faces; Neural networks

1. Introduction

1.1. Different access to information in memory

Human memory is being increasingly described as a heterogeneous system, relying on the storage of information in multiple locations in the brain. Distinct brain regions may hold different memory material, or similar material but at different times along the processes of initial acquisition, consolidation, and long-term storage. Of particular interest is the situation in which the same material is stored at the same time in multiple locations. In this case, the logic of multiple storage may have to do, beyond mere redundancy, with different facilities for access and use of the material deposited in memory.

Tulving proposed a first distinction between *episodic* and *semantic* memory systems, the former dealing with unique, temporally-dated events and the latter involving general, timeless knowledge that a person shares with others (Tulving, 1985, 2002). According to Tulving, episodic retrieval (i.e. remembering) is associated to *autonoetic awareness*, that is, a sense of travelling back in time to re-experience past events. Conversely, semantic retrieval is associated to *noetic awareness*, that is, a state of knowing and familiarity that does not encompass any re-experiencing of past events (Tulving, 2002). Episodic and semantic retrieval modes have been operationalized in the Remember (*R*) /Know (*K*) paradigm (Tulving, 1985), in which participants

* Corresponding author. Address: SISSA, Cognitive Neuroscience, via Beirut 2, 34014 Trieste, Italy. Tel.: +39 (0) 40 3787623; fax: +39 (0) 40 3787615.
E-mail addresses: grotto@psico.unifi.it (R. Lauro-Grotto), ale@sissa.it (A. Treves).

0928-4257/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jphysparis.2006.09.008

are asked to indicate, for each recognized item, whether they recollect some aspects of its presentation (i.e. *R* response) or whether the item is merely familiar (i.e. *K* response). Numerous behavioural and neuroimaging studies have provided evidence supporting the existence of two distinct access modes to memory, which have different neuroanatomical substrates and can be differentially affected by brain damage. For example, compared to normal controls, patients with medial temporal lobe (MTL) lesions typically give fewer *R* responses to recognized stimuli, but a similar amount of *K* responses (Moscovitch and McAndrews, 2002; Dalla Barba, 1997). This evidence suggests that the episodic access mode is mediated by the MTL. Accordingly, patients with Alzheimer's disease (AD), who show MTL damage, may exhibit a 'semantization' of autobiographical memory, being able to provide semantic information about their life, but not to re-live spatio-temporal and phenomenological details of past events (Westmacott et al., 2001; Piolino et al., 2003). Interestingly, recent research focusing on person-related knowledge demonstrated that whereas normal controls are better able to recognize and identify famous names with high (compared to low) autobiographical significance, i.e. those linked to personal memories (Westmacott and Moscovitch, 2003), patients with AD and patients with MTL lesions do not show such performance advantage (Westmacott et al., 2004). This finding again supports the view that the episodic access to knowledge would be mediated by the MTL.

A consistent reduction of *R* responses in recognition memory experiments is also observed in healthy elderly adults (Parkin and Walter, 1992; Java, 1996; Bastin and Van der Linden, 2003). Moreover, a study investigating autobiographical memory retrieval showed that whereas younger adults favoured episodic details (i.e. locations, perceptions, etc.) older adults were biased toward semantic details not localized in time and place (Levine et al., 2002). Similarly, Piolino et al. (2002) found that older adults were disproportionately impaired in recalling personal episodic events compared to personal semantic information (see also Borrini et al., 1989; Holland and Rabbitt, 1990). The observed shift to semantic access mode with aging may be related to volume loss in the temporal and prefrontal cortex (Raz, 2000; Van Petten et al., 2004). In line with this suggestion, neuroimaging studies confirm a primary role of MTL and prefrontal cortex in episodic access mode: in a fMRI study, Eldridge et al. (2000) found that activity in the hippocampus and medial and ventral prefrontal regions increased only when retrieval of words was accompanied by recollection of the learning episode (*R* responses), whereas it did not increase for items recognized based on familiarity (*K* responses). Moreover, recent fMRI and PET studies have demonstrated a crucial role of the MTL and prefrontal cortex in the retrieval of episodic compared to semantic autobiographical memories (Piolino et al., 2004; Maguire and Frith, 2003; Addis et al., 2004; Levine et al., 2004).

The studies reported so far have estimated separate episodic and semantic contributions to retrieval on a *qualitative* ground, based on the type and the vividness of reported details (Borrini et al., 1989; Holland and Rabbitt, 1990) and on the subjective feeling of remembering that characterizes the episodic access mode (Piolino et al., 2002). It is worth noting, however, that the capability to report on past events, as well as to label a retrieved memory as 'remembered' vs. 'known', depends not only on memory, but also on participants' verbal production and comprehension skills. Therefore, in order to obtain a more accurate estimate of episodic contribution to memory retrieval, tasks have to be designed that place little demands on the verbal skills of participants. This is particularly important when investigating patients with pronounced deficits in language, such as those with AD. Note, also, that although in normal subjects *R* responses seem to indicate the actual recovery of contextual information (Perfect et al., 1996; Yonelinas et al., 1998), there is a current debate about the relation between subjective and objective measure of recollection in some patient populations (Duarte et al., 2005; Ciaramelli and Ghetti, in press).

1.2. Hippocampal and neocortical representations

The qualitative difference between episodic and semantic memory representations may can be traced back to differences in the structural organization of the hippocampus and the neocortex. Following an approach based on the quantitative analysis of the constraints imposed on the structure of a neural system by its function (Marr, 1971), the CA3 region of the hippocampus, at the core of the MTL system, can be understood in terms of its function as an autoassociator, temporarily storing the trace of episodes in a recurrent attractor network (Treves and Rolls, 1994). Elements of episodic memories, processed in distinct neocortical regions, are relayed through the entorhinal cortex to CA3 via the dentate gyrus, which may help in producing the sparse and orthogonal representations (Leutgeb et al., 2004) that optimize the use of the available storage space in the small CA3 network (Treves and Rolls, 1992). Such network models describe the role of the hippocampal complex as an on-line, but limited and temporary repository of episodic memories. They identify the origin of the Ribot (1882) gradient of amnesia in the capacity limits of the CA3 network, which can be related to the number of recurrent collaterals, to the sparseness and to the rate of acquisition of new information (Treves and Rolls, 1991). During the recall of an episode, activation is transferred from CA3 to the CA1 region, possibly losing already some of the orthogonality of its representation to that of related episodes (Leutgeb et al., 2004), and from there to neocortex, where hebbian plasticity supports the formation and consolidation of large distributed patterns of cortical memories. According to such network models (in this aspect similar to connectionist models such as the Trace Consolidation Theory and the Multiple Trace Theory), a degenerative process which damages the hippocampal network (as in normal aging, Barnes et al., 1994 , and more seriously in dementia) reduces the possibility of episodic recall. If cortico-cortical connectivity is better preserved, however, part of the content of the very same memories that cannot be 'remembered' could still be accessed from consolidated and more semantic neocortical representations.

Note that CA3 is described as a simple network (Marr, 1971), but the distribution of afferent connections endows it with some internal functional organization, as evident in the contrast between dorsal and ventral correlates in rats (Jung et al., 1994; Moser and Moser, 1998). Cortical connectivity is vastly more structured than CA3 connectivity and, in contrast to hippocampal memories, cortical memories are described as relying on a much larger and distributed network of interconnected modules, with a graded variation from modality specificity to highly multimodal and associative areas (Braitenberg and Schüz, 1991). The intrinsic 'compatibility' of memories sharing overlapping anatomical substrates, in contrast to the 'arbitrarity' and sparseness of hippocampal episodic memories, would underly the semantic structure, that is, the 'mental image' of the cortical connectivity. This image would then be bound by the complex set of links of association, opposition, exemplification and abstraction which define the reciprocal connections of meaningful cortical representations, and, on the other hand, it would impose a structural compatibility constraint on the new memories to be stored.

1.3. Semantic access influences the distribution of errors

The episodic-semantic access distinction could be characterized in terms of the relevance of relationships of inclusion, similarity and pair-wise association to the process of retrieval. For example, one can 'semantically' know that a particular car was likely made in Germany, because it appears to be as sturdy and carefully crafted as most German cars, or because it looks very similar to a known Volkswagen model, or because it displays a detail typical of many German cars, or even because one can read and recognize its name. Alternatively, one could 'episodically' remember the scene of a friend showing the new German model.

All the relationships aiding semantic retrieval can be collectively described as the *structure* embedded in semantic representations, while episodes can be individually recollected based solely on the auto-associative completion of the configuration of elements characterizing each episode (Marr, 1971), thus essentially without relying on semantic structures. One might further speculate that, in normal subjects, the cueing stimulus may influence the propensity to adopt the 'episodic' or 'semantic' strategy (see also Westmacott and Moscovitch, 2003). The former would be engaged when the cue is strong enough to elicit retrieval via a content addressing mechanism (Treves and Rolls, 1992), whereas the latter would be invoked when episodic recollection fails or is not available (Curran et al., 2006). The picture is probably somewhat different in neurological patients, where the availability of the two strategies may be differentially compromised by brain damage (Westmacott et al., 2001). Thus, semantic access to information should especially help when episodic retrieval is not available, consistent with findings in AD patients, who have been reported to show hyper-priming (Chertkow et al., 1994; Giffard et al., 2002) and to make errors that maintain the correct superordinate information (Hodges et al., 1993).

It follows from the above discussion that the distribution of errors incurred in during retrieval can serve as an efficient indicator of the way information is accessed. A qualitative analysis of this type has been performed in other contexts by Shallice et al. (2000), who found it useful to distinguish between *single* errors, and *double* errors, the latter being a combination of the former. We propose to pursue this line of research by establishing a more *quantitative* framework, based on measures drawn from information theory (Shannon, 1948; Treves, 1997), which allows systematic analysis of groups of patients, using methods that can be used also with neurophysiological recordings in monkeys or rats (Treves et al., 1998).

1.4. The present report

Our first goal has been to design a task that enables a quantification of the distribution of errors. We have chosen a task involving the classification of famous faces because faces are ecologically highly relevant visual stimuli, which can lead to retrieve various attributes of the individuals pictured both in episodic and non-episodic modes. We introduce a measure of the relative concentration of errors derived from information theory, i.e. the metric content (see below). In order to verify whether such a measure is effective in distinguishing episodic from semantic contributions to memory retrieval, we have focused on two different source of variability in memory performance: normal aging and AD.

In Experiment 1, the task has been administered to a sample of healthy adults varying in age. Based on previous findings (Parkin and Walter, 1992; Java, 1996; Bastin and Van der Linden, 2003), we expected to find a prevalence of semantic access in older compared to younger adults. In Experiment 2, we have provided evidence for the validity of our approach, by comparing our measure of metric content with subjective indicators of episodic and semantic access mode, i.e. R and K responses in a R/K paradigm. Finally, in Experiment 3 we have administered the task to a group of early AD patients and a group of healthy control subjects. Based on previous findings (Dalla Barba, 1997; Westmacott et al., 2004), we expect to find a prevalence of semantic access in AD patients compared to age-matched controls.

2. Materials and methods

2.1. The famous faces multiple choice test

The Famous Faces Multiple Choice Task (FFMCT; Lauro-Grotto et al., 1997; see Fig. 1) requires the subject to classify a set of 54 pictures of famous people into nine disjoint categories according to *nationality* (Italian, Other European and American) and *field of activity* (Sportspeople, Politicians, Actors and Singers). The picture categories are the nine combinations of nationality by field of activity. Each category includes six famous faces from across the 20th century, two of whom became famous roughly in the 40–50s, 2 in the 60–70s and 2 in the 80–90s. Prominent personalities were chosen on the basis of their fame, whereas they were portrayed in pictures spanning a range from easily recognizable to quite difficult. As a result, famous faces from the 50s were in principle recognizable even by subjects who were not alive when they became famous, and at the same time it was very difficult for any subject to achieve nearly perfect performance (see Appendix A). Ensuring a substantial number of errors is of course a prerequisite in order to examine their distribution.

The performance of each subject can be described by a matrix $Q(s,s')$, i.e. the 'Confusion Matrix', reporting the frequency with which an image belonged to category s and was classified by the subject as s'. A first summary measure of performance is obviously percent correct classification, which can be expressed as the cumulative fraction distributed along the diagonal, $f_{\mathrm{corr}} = \sum_s Q(s,s)$. A second summary measure of the correspondence between the actual categories and those that were assigned by the subject is mutual information, $I = \sum_{s,s'} Q(s,s')\log_2[Q(s,s')/P(s)Q(s')]$-$C_1$, where $P(s) = 1/9$ is the *a priori* frequency of each category, $Q(s')$ is the marginal frequency of responses in category s' (cumulated over the actual category of each picture), and C_1 is a correction term that removes most of the bias due to using frequencies rather than probabilities (Panzeri and Treves, 1996).

When a picture is misclassified by the subject, it can still be assigned to the correct nationality or to the correct field of activity; it is also possible that the subject has a tendency to confuse, solely among Politicians, Americans with Other Europeans, or else, solely among Americans, Politicians with Actors and Singers; more in general, errors can be entirely random or they can be concentrated, to a varying degree, by incomplete semantic cueing. Unlike f_{corr}, I is sensitive to the concentration of the categories s' mistakenly assigned to each actual category s. However, since I measures the *total* (average) concentration of responses s' for each category s, it is expected to largely covary with f_{corr}, which measures their average concentration in the correct category s itself. Thus, to turn it into an effective measure of the concentration of errors only, the main dependence of I on f_{corr} can be removed by using, as explained below, the metric content index λ, which simply reflects the range of values I can take for a fixed f_{corr} (Treves, 1997).

2.2. The metric content index

For a given f_{corr}, I takes its theoretically minimum value when incorrect responses are evenly distributed (Treves, 1997). Neglecting their discreteness, that means that

$$Q(s,s' \neq s) = (1 - f_{\mathrm{corr}})/(S-1), \quad \text{and}$$
$$I_{\min} = \log_2 S + f_{\mathrm{corr}}\log_2 f_{\mathrm{corr}} + (1 - f_{\mathrm{corr}})\log_2[(1 - f_{\mathrm{corr}})/(S-1)].$$

The absolute maximum value of I for a given f_{corr}, on the other hand, is attained when all incorrect responses are grouped in a single category s' (different for each correct category s), in which case $I = \log_2 S + f_{\mathrm{corr}}\log_2 f_{\mathrm{corr}} + (1 - f_{\mathrm{corr}})\log_2(1 - f_{\mathrm{corr}})$. This maximum however would correspond to a perverse systematic misclassification by the subject. A more useful reference value can be obtained by assuming unbiased classification (incorrect categories can at most be chosen as frequently as the correct one) and, for mathematical simplicity, a real (not integer) number of categories. Then the largest information value corresponds to the case in which all pictures are categorized in clusters of size $1/f_{\mathrm{corr}}$ and, at each trial, the cluster is correctly identified but the category inside it is selected at random (Treves, 1997). One finds in this case $I_{\max} = \log_2 S + \log_2 f_{\mathrm{corr}}$.

If one interprets the probability of misclassification as a monotonically decreasing function of some underlying perceived 'distance' between the categories, in the first situation categories can be thought of as drawn from a space of extremely high dimensionality, so that they all tend to be at the same distance from each other; while in the second case (which can be realized for example by an ultrametric or taxonomic classification, Treves, 1997) categories which are at a distance less than some critical value from

Fig. 1. The test mail-boxes.

each other form clusters, while the distance between any two members of different clusters is above the critical value. In the first case, corresponding to the lower limit on I, the subject behaves as if not perceiving any particular similarity among the famous people represented in the pictures, other than among those in the very same category, and the classification, when incorrect, is random. In the second case, instead, the subject can detect similarities among some of the famous people of the data set, and therefore errors in classification are more concentrated. This increases the mutual information value of the classification for a given f_{corr}. Intermediate situations can be conveniently described by quantifying the relative amount of information for a given f_{corr} with the parameter $\lambda = (I - I_{min})/(I_{max} - I_{min})$.

This *metric content* index ranges from 0 to about 1, and in all generality it quantifies the degree to which relationships of being 'close' or 'distant' among stimuli have been relevant to their perception and classification (Treves, 1997). For $\lambda \sim 0$ such relationships are irrelevant, and if a stimulus is misclassified the probability of assigning it to any of the wrong categories is the same. For $\lambda \sim 1$, categories can be thought of as clustering into an arbitrary but systematic semantic structure, while the particular category within each cluster is chosen at random. The metric content index is therefore a measure of the amount of structure embedded in the neural representations that inform subject choice: It is high when individual memory items are classified using semantic cues, which leads to a more concentrated distribution of errors. It is low either when performance is random (in which case performance measures are also low), or when episodic access to the identity of each famous face is prevalent, semantic relationships remain largely unused, and errors, when made, tend to be more randomly distributed.

It is important to note here that any tendency towards *systematic* misclassification, not only the correct identification of super-ordinates, is reflected in an increased metric content. For example, if a subject systematically confuses American Politicians with Italian Actors and Singers, due to their good looks, the corresponding λ value will be larger. Furthermore, subjects might be able to detect similarities in the data set that are more fine-grained than the explicit super-ordinates of nationality and field of activity: for example they could be prone to confuse Italian Politicians with Other European Politicians, but not with American Politicians. For these reasons, λ appears to represent a more effective and model-free measure of perceived semantic structure than the mere access to super-ordinate information.

To visualize the metric content measure, it is useful to plot f_{corr} and I with the additional lines indicating $I_{min}(f_{corr})$ and $I_{max}(f_{corr})$ (see Fig. 2). The relative vertical excursion of a data point between these two lines represents the *metric content* of the classification by that subject. This kind of representation is particularly suitable to compare and analyse the performance of groups of subjects at the FFMCT, in that quantitative differences in the joint $f_{corr} - \lambda$ distribution are reflected in the different positions they occupy in the 'leaf' diagram.

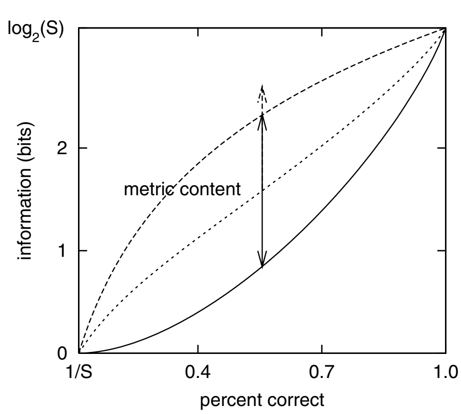

Fig. 2. The I vs. f_{corr} 'leaf' diagram and the metric content index. The lines corresponding to $\lambda = 0$, 0.5, and 1 are indicated. Note that values $\lambda > 1$ can occur, with systematic errors in the classification.

3. Results

3.1. Experiment 1

3.1.1. Participants

Ninety-three healthy Italian adults (45 women and 48 men), distributed for age from 40 to 70 (age = 54.9 ± 8.7) and with a mean education of 11 years (SD = 4) took part in the study. Participants had not any neurological or psychiatric medical history or symptoms of dementia, as assessed by the Mini Mental State Examination (MMSE $\geqslant$ 29; Folstein et al., 1975). All participants had normal or corrected-to-normal vision. Participants were grouped into three age-groups: Younger Adults (YA Group, $N = 30$), aged between 40 to 49 years (mean age = 44.5; SD = 2.3); Middle Aged Adults (MAA Group, $N = 31$), aged between 50 and 59 years (mean age = 54.5; SD = 2.7); and Older Adults (OA Group, $N = 32$), aged between 60 and 70 years (mean age = 65.0; SD = 2.9). The gender variable was balanced in each of the three groups.

3.1.2. Procedure

Subjects were tested individually. Subjects sat at a table, with the FFMCT in front of them, and were instructed to place each of the 54 cards in one of the $S = 9$ boxes, the one they felt the most appropriate. The experimenter was not allowed to provide any help or feedback, and, in case of failed recognition, subjects were instructed to guess. No time limit was given for the performance, which usually lasted between 15 and 35 min.

3.1.3. Results: percent correct and mutual information

Table 1 presents the estimates of central tendency and variability for percent correct (f_{corr}), mutual information (I) and metric content (λ) in Younger Adults (YA), Middle Aged Adults (MAA), and Older Adults (OA). As can be seen in the Table, f_{corr} was similar between YA and MAA, whereas it slightly decreased in the OA. The distribution of individual values was roughly Gaussian, and the absence of ceiling effects indicates that the difficulty of the task has been chosen appropriately to allow a reliable analysis of the errors made by the subjects. Mutual information, somewhat in contrast to f_{corr}, was approximately constant across participant groups, suggesting that, compared to younger subjects, older individuals made fewer fully correct responses but more partially correct responses,

Table 1
Group averages and standard deviations for different measures of performance, for the three age groups

	f_{corr}	I	λ
Group YA	0.69 ± 0.11	2.12 ± 0.41	0.61 ± 0.13
Group MAA	0.69 ± 0.12	2.15 ± 0.41	0.61 ± 0.14
Group OA	0.64 ± 0.12	2.11 ± 0.34	0.70 ± 0.15

in such a way as to approximately compensate each other in a measure of average consistency or concentration of responses (I).

As expected, a significant correlation emerged across subjects between f_{corr} and I ($r = 0.87$; $p < 0.001$). This large correlation confirms that f_{corr} and I reflect the same aspect of performance, i.e. its overall accuracy, even though I *also* reflects the concentration of errors. From an univariate point of view, the 3 groups appear to be strongly overlapping. We therefore turned to a multivariate approach in data analysis. As in our experimental data f_{corr} and I appear to be strongly correlated, we performed a Multivariate Analysis of Covariance (MANCOVA) in order to clarify the effect of aging on these two variables. The possible confounding effect of education was controlled by introducing this variable in the design as a continuous regressor while we compared 3 different Age Groups (YA, MAA, OA). In order to apply the MANCOVA model, we excluded significant deviation from the assumption of equality of covariance matrices in the sample (Box $M = 6.82$; $p = 0.35$). The MANCOVA taking f_{corr} and I as dependent variables showed a significant effect of age (Wilks' $\lambda = 0.86$; $p < 0.01$) but not of the level of education ($p = 0.27$) on performance. It is worth noting that neither the univariate effect of age on I ($p = 0.73$) nor on f_{corr} ($p = 0.16$) reached the significance level in our analysis, while the manipulated factor clearly revealed its effects when the bivariate distribution of the dependent measures was taken into account. This means that the three groups are not distinguishable in terms of f_{corr} or I alone, but only when considering the combination of the two variables, pointing at the need to examine the distribution of errors, the factor affecting I but not f_{corr}.

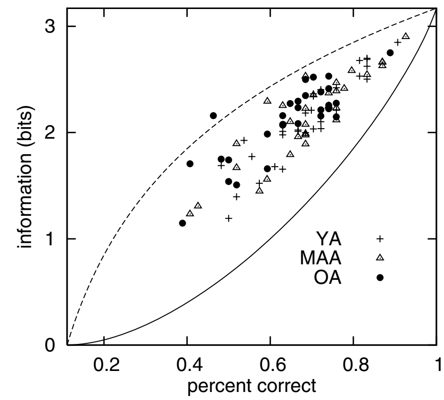

Fig. 3. The scatter of the 3 age groups on the I vs. f_{corr} 'leaf' diagram. The lines corresponding to $\lambda = 0$ and 1 are indicated.

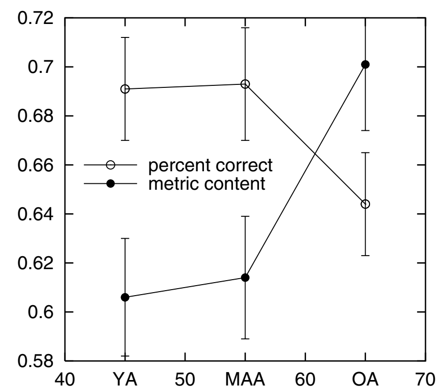

Fig. 4. Percent correct and metric content for the three age groups of subjects.

3.1.4. Results: metric content

Consistent with the definition of λ as the component of I not tracking f_{corr}, the Pearson correlation between λ and f_{corr} was close to null ($r = -0.02$), suggesting that λ solely quantifies the concentration in the distribution of errors. When λ was used to describe performance, the ANCOVA revealed a significant effect of age [$F(2,88) = 4.13$; $p < 0.05$)], without any effect of level of education ($p = 0.48$). Simple contrasts showed a higher metric content in the OA Group compared to the YA Group (0.70 vs. 0.61; $p < 0.001$) and to the MAA Group (0.70 vs. 0.61; $p < 0.001$), whereas no difference was found between the YA Group and the MAA Group. In Fig. 3, quantitative differences in the joint $I - f_{corr}$ distribution among the YA Group, the MAA Group and the OA Group are reflected in the not fully overlapping positions they occupy in the 'leaf-like' graph, with the older subjects being characterized by a higher metric content (relative amount of I for a given level of accuracy f_{corr}) relative to the younger ones.

The results of Experiment 1 clearly indicate that the three age groups are not significantly different in terms of the level of accuracy they achieved, whereas they appear to be quite distinguishable by virtue of a measure, the metric content index, which quantifies the distribution of misclassification errors in performance, and reflects the preferred access mode during memory retrieval (Fig. 4). Specifically, our results show that in order to perform the task older adults resorted to a semantic access mode to a greater extent than younger adults did.[1]

[1] Note also that the choice of test material, i.e. of famous characters and of the pictures portraying them, while somewhat arbitrary, turned out to be remarkably well balanced for our sample of subjects. This was revealed, for example, by considering separately the performance for the faces of people famous in different epochs. We computed a 'diachronic index', Δ, as the difference between percent correct performance on characters famous mainly in the 40–50s and on characters famous mainly in the 80–90s (however loosely defined such categories were). Not only the grand average of Δ across subjects turned out to be close to zero, but so were its Pearson correlations with all the relevant variables, including education, except for the obvious one, age ($r = 0.40$, $p < 0.001$). The complete lack of correlation between Δ and λ ($r = -0.01$) indicates that the interesting aging effect on metric content does not arise simply from a tendency to resort more to semantic cues for older material, and reinforces the interest in analysing metric content also with other test material.

3.2. Experiment 2

3.2.1. Participants

Twenty-seven healthy Italian adults (12 women and 15 men), who had not taken part in Experiment 1, participated in the study. Participants had a mean age of 59.8 years (SD = 5.7) and had completed on average 11 years of formal education (SD = 5). None of them had any neurological or psychiatric medical history or symptoms of dementia (MMSE $\geqslant$ 29). Participants had normal or corrected-to-normal vision.

3.2.2. Procedure

In this Experiment, as in previous studies (Westmacott et al., 2004), we adapted the R/K paradigm (Tulving, 1985) and applied it to the assessment of memories acquired outside the laboratory. Participants were presented with the 54 famous faces of the FFMCT, one at time. They were instructed to give a R responses to a face if they could re-experience a particular episode in which they watched, listened to or heard about the famous person, or if seeing the person's face triggered some other personal memory. Otherwise, if the participants judged a face familiar but they could not recall a specific memory involving him or her, they were instructed to give a K response. Finally, if they did not recognize the face they had to say 'I don't know' (i.e. N response). After a time interval of about 5 days, the same subjects performed the FFMCT with the same procedures as described for Experiment 1.

3.2.3. Results

On average, participants gave 27.6 ± 11 [mean ± st.dev] R responses, 14 ± 8 K responses, and 12.5 ± 8 N responses to the stimulus set. The frequency of R responses was quantified simply as $F(R) = (\text{number of } R \text{ responses})/54$, and likewise the frequency of K responses $F(K)$ and the frequency of N responses $F(N) \equiv 1 - F(R) - F(K)$. Table 2 reports mean $F(R)$, $F(K)$, $F(N)$, f_{corr}, I, and λ scores obtained by participants. Table 3 reports the Pearson correlations between $F(R)$, $F(K)$, $F(N)$, and f_{corr}, I, and λ (Fig. 5).

The results showed that $F(R)$ significantly correlates with f_{corr} ($r = 0.56$; $p < 0.002$) and also, but only marginally, with I ($r = 0.32$; $p < 0.1$), indicating that an episodic access mode leads to a high level of accuracy at the FFMCT.[2] An important result is that $F(R)$ is negatively correlated with λ ($r = -0.66$; $p < 0.001$; see Fig. 6), supporting our hypothesis that a preferred episodic access mode during performance translates into low metric content values. That is, when subjects retrieve memories mainly via the episodic route, which may be hypothesized to be the default route (Curran et al., 2006), they obtain a great number of correct identifications, but their errors do not reflect much structure, as expected when not relying on semantic retrieval.

With regard to K responses, no significant correlation whatsoever emerged between $F(K)$ and f_{corr}, or I ($p > 0.25$ in both cases). In contrast, $F(K)$ is positively correlated with λ ($r = 0.45$; $p < 0.02$). These results suggest that although a mere feeling of familiarity is not enough to improve correct performance at the FFMCT, it does elicit the use of semantic cues to help in the classification task, resulting in a high metric content.

Considering now how subjects behave when they are forced to 'post' unknown items, the correlations F(N) of course just mirror those of $F(R)$ and $F(K)$ combined: a strong negative correlation with the percent of correct responses ($r = -0.58$; $p < 0.001$) and with mutual information ($r = -0.41$; $p < 0.05$). Importantly, $F(N)$ presents a

Table 2
Performance measures for the subjects in Experiment 2

	Mean	St. dev
$F(R)$	0.51	0.20
$F(K)$	0.26	0.14
$F(N)$	0.23	0.15
f_{corr}	0.69	0.13
I	2.20	0.35
λ	0.67	0.17

Table 3
Correlations between R, K responses and classification measures in Experiment 2

	$F(R)$	$F(K)$	$F(N)$
f_{corr}	0.56**	−0.18	−0.58**
I	0.32	−0.03	−0.41*
λ	−0.66**	0.45*	0.47*

* Denotes significance $p < 0.05$, $^{**}p < 0.01$.

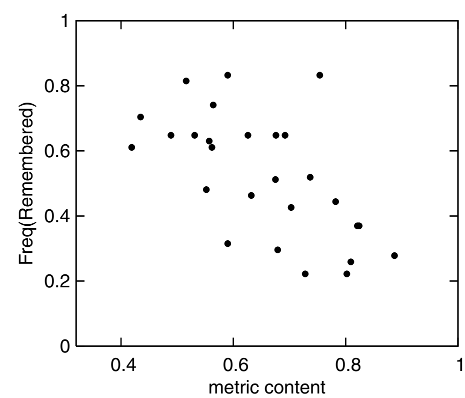

Fig. 5. The anti-correlation of $F(R)$ with λ for the limited group of subjects of experiment 2.

[2] As a consequence, $F(R)$ has a strong negative correlation with the amount of partial errors, i.e. the fraction of responses where only one of the two superordinate categories is chosen correctly ($r = -0.55$; $p < 0.005$); which is itself strongly anti-correlated with f_{corr} ($r = -0.93$; $p < 0.001$ in this dataset). A detailed analysis of partial errors will be published elsewhere.

positive correlation with metric content ($r = 0.47$; $p < 0.02$). Thus, as expected, unfamiliar faces lead to a high number of errors in performance. However, when subjects have to decide where to classify them, they still invoke semantic structures to try and accomplish the task, in that they show concentrated rather than random errors.

The correlation analysis shows that for this limited sample of subjects the metric content index does not correlate either with age or with education (for the latter, $r = -0.29$; $p = 0.14$). In contrast, $F(R)$ does not correlate with age, but it has a positive correlation with the level of education ($r = 0.48$; $p < 0.011$), suggesting that more educated subjects could explicitly recollect faces more than less educated ones. It seems unlikely that education affects episodic retrieval processes per se, such that more educated subjects found it easier to recollect personal episodes connected to the famous faces. Perhaps, they more often interpret as explicit recollection the same association of a face with some of its attributes that less educated subjects merely used as a semantic cue. Whether the correlation observed reflects more salient explicit memories in educated subjects, or merely their self-confidence when interrogated, the evidence that education has only a weak, if any, anti-correlation with λ, suggests that this measure is relatively robust to such artifactual influences.

3.3. Experiment 3

3.3.1. Participants

Eleven patients with early Alzheimer's disease (5 women and 6 men) and 22 healthy control subjects (9 women and 13 men) participated in the study. Patients had a mean age of 65 years (SD = 5 years). Healthy subjects had been matched to patients for age (mean age = 64.6; SD = 4 years). All participants had normal or corrected-to-normal vision.

3.3.2. Procedure

Procedures were the same as described in Experiment 1. Patients were tested twice, from 9 to 12 months apart, while performing routine clinical neuropsychological evaluations at the Center for Dementia of the Neurology Department of Florence University. Results from the second testing session will be reported in full elsewhere.

3.3.3. Results

Results are reported in Table 4, while the 'leaf' diagram in Fig. 6 presents the individual f_{corr} and I estimates (relative to the first administration of the test) for patients and controls.

Table 4
Group averages and standard deviations for different measures of performance, for the AD and Control group

	f_{corr}	I	λ
AD	0.41 ± 0.11	1.62 ± 0.35	0.89 ± 0.39
Control group	0.66 ± 0.11	2.12 ± 0.33	0.67 ± 0.11

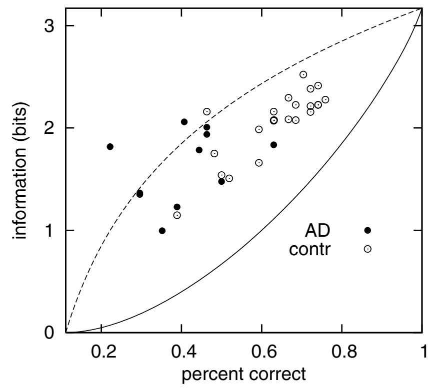

Fig. 6. The scatter of the AD (first test) and Control groups on the I vs. f_{corr} 'leaf' diagram. The lines corresponding to $\lambda = 0$ and 1 are indicated.

Given the limited sample, we excluded a multivariate approach and compared the group of patients with the control group using three univariate ANOVAs taking the FFMCT measures as dependent variables. The frequency of correct responses f_{corr} was significantly lower in patients than in controls [$F(1,31) = 34$; $p < 0.0001$] and so was I [$F(1,31) = 15$; $p < 0.0005$]. In contrast, λ was significantly higher in patients than in controls [$F(1,31) = 6$; $p < 0.02$]. Note that the same comparison, but performed with the results obtained at the second administration of the FFMCT, shows a even larger effect of group on λ [$F(1,31) = 12$; $p < 0.002$]. In order to explain the behaviour of the metric content in the patient group it is important to consider the individual data presented in Fig. 6. By inspection of the diagram, we note that the control group is mainly placed in the medial part of the leaf, in an approximately intermediate position between I_{min} and I_{max}; this is also the case for 4 of the AD patients, while the other 7 are placed around, in fact even over, the level for fully metric unbiased responses described by I_{max}. The results show a clear pattern: the memory impairment typical of AD patients is characterized by an increase of the metric content, suggesting a prevalent semantic access mode to knowledge, in the context of a general decrement in the ability to access information in memory, i.e. a lower correct performance.

We also explored the correlation between our relevant measures and a global index of the severity of dementia, i.e. the Gravity of Dementia Scale-corrected index (GDSC; Bracco et al., 1990). We found that the GDSC score correlated significantly with λ ($r_{Pearson} = 0.61$; $p < 0.05$), but not with f_{corr} or I ($p > 0.6$ in both cases). Thus, the metric content index is higher in the case of more severe dementia, and it appears to capture the progressive semantization of access mode in AD better than other measures of performance do.

4. General discussion

The analysis of declarative memory is gradually shedding its original localizationist bias in order to consider the complex web of interactions among distributed systems. One approach, in animal studies, is to dissect the distinct ensemble codes with which different areas, or even sub-regions of the hippocampus (Leutgeb et al., 2004), store the same information; another approach, mainly used with human subjects, is to focus on changes in the mode of access to information stored in memory following cerebral pathology or with normal aging (Westmacott et al., 2004; Piolino et al., 2003; Levine et al., 2002; Westmacott et al., 2004). To helpfully complement each other these approaches must be interpretable in similar terms, and notions that are specific to sophisticated behavioural studies in humans (e.g., the R/K paradigm) must be translatable in terms of the underlying neural representations.

In this paper we show how an information-theoretical measure which has been introduced to characterize neural representations in behaving monkeys, i.e. the metric content (Treves, 1997; Treves et al., 1998), can also be used to qualify the preferred access mode to knowledge in humans. We note that the proper quantification of metric content requires an *ad hoc* design, with several exemplars, or trials, for each of a limited number of classes. Similar designs can easily be applied to neurophysiological recording experiments in animals, in which neural activity is recorded while the subject, for example, is repeatedly exposed to stimuli drawn from a limited set (there is no need for a behavioural response in this case).

We have used a task (i.e. the FFMCT) obeying to these requirements, which involves the classification of famous faces according to their nationality and field of activity. We have argued that the distribution of errors in the FFMCT can be a valid index of the preferred access mode to person-related knowledge during performance: if the participants predominantly rely on a semantic access mode, they would extract similarities among test items and tend to form clusters of stimuli perceived as similar. In this case, classification errors will be concentrated in clusters of classes. In contrast, if the participants rely predominantly on an episodic access mode, their classification errors should be random, as expected if semantic structures remained unused. As the metric content specifically reflects the tendency to perceive clusters in the data set, a semantic access mode to person related knowledge should be characterized by high metric content values, indicating a strong dependence of the classification performance on perceived relationships among the set of stimuli.

In Experiment 1, we have investigated age-related changes in the preferred access to knowledge by submitting the FFMCT to a large sample of healthy individuals varying in age from 40 to 70. We have found that older adults were characterized by a similar frequency of correct classifications but a higher metric content value compared to younger ones. This finding suggests that, although younger and older adults attained similar levels of memory accuracy, they differed with respect to the predominant retrieval mode. Specifically, older adults resorted to semantic access to a greater extent then younger adults did, possibly due to defective episodic access mode. It is worth noting that the two variables f_{corr}, i.e. percent correct, and λ, indexing the relative use of semantic cues for a given level of performance, were unrelated ($r = -0.02$), which confirms they actually measure distinct aspects of performance. The evidence of a 'semantized' access to knowledge in older individuals compared to younger ones is consistent both with studies employing the R/K paradigm (Java, 1996; Souchay et al., 2000; Clarys et al., 2002) and with those focusing on autobiographical memory retrieval (Borrini et al., 1989; Holland and Rabbitt, 1990; Levine et al., 2002; Piolino et al., 2002). Note that episodic memory, like other cognitive abilities, is the result of integrated activity in distributed networks, and there is evidence that the functional connectivity changes with age (and more drastically with neural degeneration). In particular, the episodic retrieval decline with aging seems to be due to neurofunctional changes in the frontal and medial temporal brain regions (Van Petten et al., 2004; Raz, 2000; Moscovitch and Winocur, 1995; Grady and Craik, 2000).

At variance with age, we have found that the level of education had no effect on the metric content, and therefore, arguably, on the retrieval mode sustaining performance. This evidence is perhaps consistent with findings from Nyberg and co-workers, who have found that whereas after controlling for differences in the level of education age was no longer related to semantic memory performance, it remained a significant predictor of episodic memory performance (Nyberg et al., 1996). They have concluded that factors specific to episodic remembering, affected by aging-related neuronal changes, were the underlying difference between young and elderly people in episodic memory (Nyberg et al., 1996).

In order to provide evidence for the validity of our approach, in Experiment 2 we have investigated the correlation between our measures and those derived from the R/K paradigm. The results show that high rates of R responses, reflecting an episodic retrieval mode, translated into high levels of accuracy, but into low metric content values. Conversely, an increase in metric content, indicative of the use of semantic cues during retrieval, was found to covary with K (or N) responses, which reflect the failure of the episodic access mode to knowledge. Thus, when individuals claim to *remember* a famous person they are very likely to attain the correct identification of that person. Famous faces which appear only familiar, and even more so those which are reported as unknown, are less likely to elicit correct classification than remembered ones. Interestingly, the metric content increases for both known (i.e. K responses) and unknown items (i.e. N responses), that is, whenever episodic recollection is not available. This finding is in line with the proposal that episodic access would represent the default retrieval mode, whose failure may be compensated by invoking semantic structures.

One possible criticism to the validity of our approach is the observation that in the FFMCT the correct superordinate could be guessed also by virtue of episodic retrieval.

More precisely, a subject could remember having seen a famous person in a movie and thus correctly classify him among Actors. However, the pattern of correlations we obtained does not support this suggestion: The frequency of R responses is not significantly correlated with the relative frequency of partial errors in the task ($r = 0.19$; $p = 0.34$), and, most important, it has a significant negative correlation with the metric content. Thus, even if it is possible that at times the correct identification of the profession or nationality of famous faces may be achieved via episodic retrieval, a performance mainly sustained by an episodic retrieval mode leads to a low metric content, i.e. to a diminished tendency to cluster classification errors.

In Experiment 3, we have investigated the performance of patients with Alzheimer's disease on the FFMCT (see also Lauro-Grotto et al., 1997). In line with previous research (Westmacott et al., 2004; Dalla Barba, 1997), we have found a significant increase in metric content index in AD patients compared to normal controls, in the context of a general memory impairment that leads to lower correct performance. This evidence is consistent with the well-documented disruption of episodic retrieval in AD, which is supposed to be due to MTL degeneration (Westmacott et al., 2004). Note, however, that whereas in normal aging we found an increase in metric content in the context of a stable overall level of available information, in AD the increase in metric content came in association to a significant information loss. Thus, whereas high metric content levels in aging can be safely read as a 'semantization' of memory, i.e. a shift to a semantic access mode to retrieve the required information, in the case of AD we cannot exclude that increases in metric content are in part the result of the progressive loss of subordinate information in semantic memory representations. In this case, we could say that the enhanced metricity, i.e. the perception of more similarity structure, reflects in fact the loss of resolution that prevents patients from discriminating many details of the memory representations. Nevertheless, we wish to emphasize that the metric content, but not the frequency of correct responses, was found to correlate with standard measures of severity of dementia, indicating that this measures is particularly suited to capture memory changes in AD.

4.1. Conclusion

We have introduced an information-theoretical approach to the study of memory retrieval. The metric content index, a measure of the relative concentration of errors, proved to be effective in distinguishing episodic from semantic contributions to memory retrieval: By using this measure, we detected a more pronounced semantic access to person-related knowledge in aging and AD.

One might ask what is the advantage of this method over classic methods aimed at distinguishing episodic from semantic access, such as the R/K paradigm. First, the metric content analysis appears to be consistent with insight obtained using the R/K paradigm, yet it can extend that insight to situations in which subjects cannot easily report whether they remember or know the items, for example because they have speech impairments or comprehension deficits. Second, metric content is largely independent from the level of performance. We can therefore compare on this dimension groups of subjects that markedly differ in their level of memory performance. In addition, this measure seems less susceptible to the influence of the educational level than R/K measures. Finally, the progressive increase in metric content is not tied to strictly follow the overt hierarchical classification scheme imposed by the task, and therefore it can reflect the idiosyncratic organization of memory and knowledge which is the endowment of any specific individual.

Further work using metric content to better understand memory processes includes comparing patients with Alzheimer disease with patients suffering from Herpes Simplex encephalitis or frontal dysfunction on the FFMCT (Lauro-Grotto et al, in preparation), and analyzing hippocampal and entorhinal cortex representations in rats foraging in an open arena (Treves et al, in preparation).

Acknowledgements

For their contribution and time we thank all the participants. We are grateful to Carolina Piccini for contributing to test patients, to Gianni Ciolli, Valerio Venturi and Augusto Ciaramelli for their help in data processing and editing, and to the photographic archives of the Trieste newspaper *Il Piccolo*, that let us borrow the shots used to prepare the cards for the test.

Appendix A

List of famous face stimuli

Italy

- Sportspeople: Fausto Coppi, Edoardo Mangiarotti, Pietro Mennea, Sara Simeoni, Roberto Baggio, Alberto Tomba;
- Politicians: Palmiro Togliatti, Alcide De Gasperi, Ugo La Malfa, Giovanni Leone, Irene Pivetti, Gianfranco Fini;
- Actors and Singers: Amedeo Nazzari, Anna Magnani, Mina, Claudio Villa, Mara Venier, Roberto Benigni.

Europe-not Italy

- Sportspeople: Emil Zatopek, Jacques Anquetil, Eddie Merckx, Ingemar Stenmark, Miguel Indurain, Steffi Graf.
- Politicians: Charles de Gaulle, Winston Churchill, Valery Giscard d'Estaing, Willy Brandt, John Major, Francois Mitterand.

- Actors and Singers: Jean Gabin, Marlene Dietrich, Brigitte Bardot, Jean Paul Belmondo, Isabelle Adjani, Gerard Depardieu.

USA

- Sportspeople: Rocky Marciano, Joe Di Maggio, Chris Evert, Mark Spitz, Jennifer Capriati, Earvin 'Magic' Johnson.
- Politicians: Dwight Eisenhower, John Fitzgerald Kennedy, Henry Kissinger, Jimmy Carter, George Bush, Bill Clinton.
- Actors and Singers: Gregory Peck, Marilyn Monroe, Robert Redford, Jane Fonda, Robert De Niro, Sharon Stone.

References

Addis, D.R., Moscovitch, M., Crawley, A.P., McAndrews, M.P., 2004. Recollective qualities modulate hippocampal activation during autobiographical memory retrieval. Hippocampus 14, 752–762.

Barnes, C.A., Treves, A., Rao, G., Shen, J., 1994. Electrophysiological markers of cognitive aging: region specificity and computational consequences. Semin. Neurosci. 6, 359–367.

Bastin, C., Van der Linden, M., 2003. The contribution of recollection and familiarity to recognition memory: a study of the effects of test formats and aging. Neuropsychology 17, 14–24.

Borrini, G., Dall'Ora, P., Della Sala, S., Marinelli, L., Spinnler, H., 1989. Autobiographical memory. Sensitivity to age and education of a standardized enquiry. Psychol. Med. 19, 215–224.

Bracco, L., Amaducci, L., Pedone, D., Bino, G., Lazzaro, M.P., Carella, F., D'Antona, R., Gallato, R., Denes, G., 1990. Italian Multicentre Study on Dementia (SMID): a neuropsychological test battery for assessing Alzheimer's disease. J. Psychiat. Res. 24, 213–226.

Braitenberg, V., Schüz, A., 1991. Anatomy of the Cortex: Statistics and Geometry. Springer-Verlag, Berlin.

Chertkow, H., Bub, D., Bergmann, H., Bruemmer, A., Merling, A., Rothfleisch, J., 1994. Increased semantic priming in patients with dementia of the Alzheimer's type. J. Clin. Exp. Neuropsychol. 16, 608–622.

Ciaramelli, E., Ghetti, S. What are confabulators's memories made of? A study of subjective and objective measures of recollection in confabulation. Neuropsychologia, in press.

Clarys, D., Isingrini, M., Gana, K., 2002. Mediators of age-related differences in recollective experience in recognition memory. Acta Psychol. 109, 315–329.

Curran, T., DeBuse, C., Woroch, B., Hirshman, E., 2006. Combined pharmacological and electrophysiological dissociation of familiarity and recollection. J. Neurosci. 26, 1979–1985.

Dalla Barba, G., 1997. Recognition memory and recollective experience in Alzheimer's disease. Memory 5, 657–672.

Duarte, A., Ranganath, C., Knight, R.T., 2005. Effects of unilateral prefrontal lesions on familiarity, recollection, and source memory. J. Neurosci. 25, 8333–8337.

Eldridge, L.L., Knowlton, B.J., Furmanski, C.S., Bookheimer, S.Y., Engel, S.A., 2000. Remembering episodes: a selective role for the hippocampus during retrieval. Nat. Neurosci. 3, 1149–1153.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. Mini mental state: a practical method for grading the cognitive state of patients for the clinician. J. Psychiat. Res. 12, 189–198.

Giffard, B., Desgranges, B., Nore-Mary, F., Lalevee, C., Beaunieux, H., de la Sayette, V., Pasquier, F., Eustache, F., 2002. The dynamic time course of semantic memory impairment in Alzheimer's disease: clues from hyperpriming and hypopriming effects. Brain 125, 2044–2057.

Grady, C.L., Craik, F.I.M., 2000. Changes in memory processing with age. Curr. Opin. Neurobiol. 10, 224–231.

Hodges, J.R., Salmon, D.P., Butters, N., 1993. Recognition and naming of famous faces in Alzheimer's disease: a cognitive analysis. Neuropsychologia 31, 775–788.

Holland, C.A., Rabbitt, P.M., 1990. Autobiographical and text recall in the elderly: an investigation of a process resource deficit. Q. J. Exp. Psychol. 42, 441–470.

Java, R.I., 1996. Effects of age on state of awareness following implicit and explicit word-association task. Psychol. Aging. 11, 108–111.

Jung, M.W., Wiener, S.I., McNaughton, B.L., 1994. Comparison of spatial firing characteristics of units in dorsal and ventral hippocampus of the rat. J. Neurosci. 14, 7347–7568.

Lauro-Grotto, R., Borgo, F., Piccini C., Treves, A. 1997. What remains of memories lost in Alzheimer's disease and Herpes Simplex Encephalitis. American Society for Neuroscience Abstracts vol. 23, Part. 2, no. 734.

Leutgeb, S., Leutgeb, J.K., Treves, A., Moser, M.B., Moser, E.I., 2004. Distinct ensemble codes in hippocampal areas CA3 and CA1. Science 305, 1295–1298.

Levine, B., Svoboda, E., Hay, J.F., Winocur, G., Moscovitch, M., 2002. Ageing and autobiographical memory: dissociating episodic from semantic retrieval. Psychol. Aging. 17, 677–689.

Levine, B., Turner, G.R., Tisserand, D.J., Hevenor, S.J., Graham, S.J., McIntosh, A.R., 2004. The functional neuroanatomy of episodic and semantic remembering: a prospective functional MRI study. J. Cogn. Neurosci. 16, 1633–1646.

Maguire, E.A., Frith, C.D., 2003. Aging affects the engagement of the hippocampus during autobiographical memory retrieval. Brain 126, 1511–1523.

Marr, D., 1971. Simple memory: a theory for archicortex. Phil. Trans. R. Soc. B 262, 24–81.

Moscovitch, D.A., McAndrews, M.P., 2002. Material specific deficits in remembering in patients with unilateral temporal lobe epilepsy and excisions. Neuropsychologia 40, 1335–1342.

Moscovitch, M., Winocur, G., 1995. Frontal lobes, memory, and aging. Ann. NY Acad. Sci. 15, 119–150.

Moser, M.B., Moser, E.I., 1998. Functional differentiation in the hippocampus. Hippocampus 8, 608–619.

Nyberg, L., Backman, L., Erngrund, K., Olofsson, U., Nilsson, L.G., 1996. Age difference in episodic memory, semantic memory, and priming: relationships to demographic, intellectual, and biological factors. J. Gerontol. Psychol. Sci. 4, 234–240.

Panzeri, S., Treves, A., 1996. Analytical estimates of limited sampling biases in different information measures. Network 7, 87–107.

Parkin, A.J., Walter, B.M., 1992. Recollective experience, normal aging and frontal dysfunction. Psychol. Aging. 7, 290–298.

Perfect, T.J., Mayes, A.R., Downes, J.J., Van Eijk, R., 1996. Does context discriminate recollection from familiarity in recognition memory? Q. J. Exp. Psychol. 49, 797–813.

Piolino, P., Desgranges, B., Benali, K., Eustache, F., 2002. Episodic and semantic remote autobiographical memory in ageing. Memory 10, 239–257.

Piolino, P., Desgranges, B., Belliard, D., Matuszewski, V., Lavalee, C., de la Sayette, V., Eustache, F., 2003. Episodic memory and autonoetic awareness: triple dissociation in neurodegenerative diseases. Brain 126, 2203–2219.

Piolino, P., Giffard-Quillon, G., Desgranges, B., Chetelat, G., Baron, J.C., Eustache, F., 2004. Re-experiencing old memories via hippocampus: a PET study of autobiographical memory. Neuroimage 22, 1371–1383.

Raz, N., 2000. Aging of the brain and its impact on cognitive performance. In: Craik, F.I.M., Salthouse, T.A. (Eds.), The Handbook of Aging and Cognition. Lawrence Erlbaum, Mahwah(NJ), pp. 1–90.

Ribot, T., 1882. Diseases of Memory. Apppleton-Century-Crofts, New York.

Shallice, T., Rumiati, R.I., Zadini, A., 2000. The selective impairment of the phonological output buffer. Cogn. Neuropsych. 17, 517–546.

Shannon, C.E., 1948. A mathematical theory of communication. Bell Sys. Tech. J. 27, 379–423.

Souchay, C., Isingrini, M., Espagnet, L., 2000. Aging, episodic memory, feeling of knowing, and frontal functioning. Neuropsychology 14, 299–309.

Treves, A., 1997. On the perceptual structure of face space. Biosystems 40, 189–196.

Treves, A., Rolls, E.T., 1991. What determines the capacity of autoassociative memories in the brain? Network 2, 371–397.

Treves, A., Rolls, E.T., 1992. Computational constraints suggest the need for two distinct input systems to the hippocampal CA3 network. Hippocampus 2, 189–199.

Treves, A., Rolls, E.T., 1994. Computational analysis of the role of the hippocampus in memory. Hippocampus 4, 374–391.

Treves, A., Georges-Francois, P., Panzeri, S., Robertson, R.G., Rolls, E.T., 1998. The metric content of spatial views as represented in the primate hippocampus. In: Torre, V., Nicholls, J. (Eds.), Neural Circuits and Networks, NATO ASI Series F, Computer and Systems Sciences. Springer, Berlin, pp. 239–247.

Tulving, E., 1985. Memory and consciousness. Can. Psychol. 26, 1–12.

Tulving, E., 2002. Episodic memory: from mind to brain. Ann. Rev. Psychol. 53, 1–25.

Van Petten, C., Plante, E., Davidson, P.S.R., Kuo, T.Y., Glisky, E.L., 2004. Memory and executive functioning in older adults: relationships with gray matter volumes and white matter hyperintensities. Neuropsychologia 42, 1313–1335.

Westmacott, R., Moscovitch, M., 2003. The contribution of autobiographical significance to semantic memory. Mem. Cognit. 31, 761–774.

Westmacott, R., Leach, L., Morris, F., Moscovitch, M., 2001. Different patterns of autobiographical memory loss in semantic dementia and medial temporal lobe amnesia: a challenge to consolidation theory. Neurocase 7, 37–55.

Westmacott, R., Black, S.E., Freedman, M., Moscovitch, M., 2004. The contribution of autobiographical significance to semantic memory: evidence from Alzheimer's disease, semantic dementia, and amnesia. Neuropsychologia 42, 25–48.

Yonelinas, A.P., Kroll, N.E., Dobbins, I., Lazzara, M., Knight, R.T., 1998. Recollection and familiarity deficits in amnesia: convergence of remember/know, process dissociation, and receiver operating characteristic data. Neuropsychology 12, 323–339.