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The role of the prefrontal cortex in familiarity and recollection processes during verbal and non-verbal recognition memory: An rTMS study

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ABSTRACT

Neuroimaging and lesion studies have documented the involvement of the frontal lobes in recognition memory. However, the precise nature of prefrontal contributions to verbal and non-verbal memory and to familiarity and recollection processes remains unclear. The aim of the current rTMS study was to investigate for the first time the role of the DLPFC in encoding and retrieval of non-verbal and verbal memoranda and its contribution to recollection and familiarity processes. Recollection and familiarity processes were studied using the ROC and unequal variance signal detection methodologies. We found that rTMS delivered over left and right DLPFC at encoding resulted in material specific laterality effects with a disruption of recognition of verbal and non-verbal memoranda. Interestingly, rTMS over DLPFCs at encoding significantly affected both recollection and familiarity. However, at retrieval rTMS did not affect recollection and familiarity. Our results suggest that DLPFC has a degree of functional specialisation and plays an important role in the encoding of verbal and non-verbal memoranda.

Introduction

Familiarity and recollection are thought to be components of recognition memory (Jacoby, 1991; Jacoby and Dallas, 1981; Mandler, 1980). Familiarity refers to the feeling that a stimulus has been previously encountered, without the retrieval of any specific details. Recollection, on the other hand, involves consciously remembering the specific experience in which an item was encountered (Tulving, 1985; see also Yonelinas, 2002). The issue of whether familiarity and recollection are best conceptualised by single process theory assuming quantitatively different levels of confidence for memory traces belonging to the same memory system (the unequal variance signal detection model—UVSD) or by dual process theory assuming two functionally distinct processes (the dual processes signal detection model—DPSD) underpinned by different neuronal structures is hotly debated (e.g., Aggleton and Brown, 2006; Aggleton et al., 2005; Eichenbaum, 2000; Donaldson, 1996; Dunn, 2004; McClelland and Chappell, 1998; Shiffrin and Steyvers, 1997; Wais et al., 2006; Brown and Aggleton, 2001; Eldridge et al., 2000; Verfaellie and Keane, 2002; Yonelinas et al., 1998; Yonelinas, 1994, 2002; Manns et al., 2003; Squire and Zola, 1997; Wixted and Squire, 2004). Several neuropsychological and neuroimaging studies have examined the role of medial temporal lobe structures in familiarity and recollection. However, the results so far have been inconclusive (see for review for Aggleton and Brown, 2006; Cipolotti and Bird, 2006).

The frontal lobes receive direct projections from the enthorinal/perirhinal cortex, hippocampus and the medial portions of the thalamus (Aggleton and Brown, 2006; Simons and Spiers, 2003). For example, regions such as the dorsolateral and orbitofrontal cortices are known to have strong reciprocal connections with the perirhinal and entorhinal cortices (e.g. Lavenex and Amaral, 2000). Unidirectional projection exists from the hippocampus to medial prefrontal cortex (MPFC, Rosene and Van Hoesen, 1977). It is also well known that the thalamus projects into prefrontal cortex (Aggleton and Brown, 1999). Thus it is possible that the frontal lobes play a role in familiarity and recollection (e.g., Aggleton and Brown, 1999; Yonelinas et al., 2002; Davidson and Glisky, 2002; Knowlton and Squire, 1995; Tulving, 1989).

Lesion studies have confirmed that the frontal lobes play a role in recognition memory. For example, Delbecq-Derouesné et al. (1990) reported a frontal patient with markedly impaired recognition memory. Frontal patients have also been reported to have higher false alarm rates (e.g., Alexander et al., 2003; Rapcsak et al., 1996, 1998; Schacter et al., 1996; Swick and Knight, 1999). A similar pattern

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was observed in a patient with a right frontopolar lesion and in another patient with right ventrolateral prefrontal lesion (Rapcsak et al., 1999; Curran et al., 1997; Schacter et al., 1996). Material-specific laterality effects have also been reported, although more rarely. For example, patients with left frontal lesions were found impaired in recognition memory tasks employing words (e.g. Milner et al., 1991; Warrington, 1984). Patients with right frontal lesions were found impaired in recognition memory tests using abstract designs and words (Milner et al., 1991). Warrington (1984) reported that patients with left frontal lesions obtained poor scores in recognition memory tests for words whereas patients with right frontal lesion were impaired in recognition memory tests for faces.

Only very few lesion studies have investigated familiarity and recollection processes in patients with frontal lobe lesions. The results are somewhat inconsistent (Duarte et al., 2005; MacPherson et al., 2008; Wheeler and Stuss, 2003). Thus, Wheeler and Stuss (2003) compared patients with medial and lateral lesions in a remember/know task. They reported that neither patient group were impaired at know judgments. In contrast, in a relatively small sample of unilateral frontal patients, Duarte and colleagues found that familiarity estimates were significantly reduced only when items were presented in the contralesional visual field.

MacPherson and colleagues (2008) documented familiarity impairment in a study investigating a large group of patients with focal frontal lesions. They argued that the apparent deficit in familiarity may be due to a more general difficulty in distinguishing between target and distractor items that have a high degree of similarity. Although parallels between non-demented Parkinson's patients and focal frontal lesion patients have been discussed at length (e.g. Owen, 2004), most qualitative reviews of Parkinson's disease have focused on dysfunction of prefrontal cortex as the predominant characteristic of the disease. Davidson et al. (2006) reported a selective impairment in familiarity in Parkinson's disease patients.

The contribution of frontal lobes to familiarity and recollection has been investigated also in a number of neuroimaging studies. Skinner and Fernandes (2007) in a meta-analysis of neural correlates of familiarity and recollection, reviewing both neuroimaging and lesion data, concluded that both familiarity and recollection tap similar DLPFC-based cognitive control processes (but see, Kirwan et al., 2008). This conclusion is in broad agreement with some of the results reported in a recent large meta-analysis of fMRI studies (Spaniol and colleagues, 2009).

Neuroimaging studies have also reported that the frontal lobes contribute to encoding and retrieval, two processes which have proved rather difficult to investigate with lesion studies. A well known model has been proposed, the HERA model—Hemispheric Encoding Retrieval Asymmetry (e.g. Habib et al., 2003; Tulving et al., 1994). According to this model the left prefrontal cortex plays a crucial role in encoding, whereas right prefrontal cortex is necessary for retrieval. However, a recent large meta-analysis of fMRI studies failed to lend support to this model, although some regional differences were reported between encoding and retrieval activation. Specifically left VLPFC appears to be more strongly involved in encoding whereas left DLPFC and anterior PFC was more strongly involved in retrieval (Spaniol et al., 2009).

Neuroimaging studies cannot reveal whether prefrontal regions are truly necessary for recollection and familiarity during encoding and retrieval. Given their correlational nature, they cannot distinguish whether task-related activations are indeed necessary or whether they are simply associated with other aspects of task performance. This issue can be resolved to an extent by applying repetitive Transcranial Magnetic Stimulation (rTMS). This unique technique is used to elicit a brief and reversible interference in a given brain region in vivo. Such interference would lead to a decline in task performance only if the stimulated area is causally engaged in the task under investigation (e.g., Walsh and Cowey, 2000; Rossi and Rossini, 2004). To the best of our knowledge, so far, only one study has examined familiarity and recollection in healthy participants using event-related rTMS applied over left and right DLPFC (Turriziani et al., 2008). This study adopted a Remember/Know (R/K) task employing only a non-verbal recognition memory test using unknown black and white faces. At encoding rTMS on the right DLPFC was detrimental both to R and K judgments. rTMS on the left DLPFC had a detrimental effect only for K judgments. At retrieval rTMS over right or left DLPF had no effect on R/K judgments.

Few studies have investigated the contribution of DLPFC to encoding and retrieval using rTMS. It has been reported that when rTMS was applied at encoding to the left or right DLPFC or at retrieval to the right DLPFC subjects' performance was significantly disrupted (e.g., Miniussi et al., 2003; Rami et al., 2003; Sandrini et al., 2003; Floel et al., 2004; Kohler et al., 2004; Rossi et al., 2001, 2006). To the best of our knowledge, so far, there have been no rTMS studies examining the contribution of the DLPFC to recollection and familiarity processes during encoding and retrieval of non-verbal and verbal recognition memory tasks.

The aim of the present study was to evaluate for the first time the effects of rTMS over DLPFC to recollection and familiarity using non-verbal and verbal memoranda. rTMS was applied at encoding and retrieval during a non-verbal (Experiment 1) and a verbal (Experiment 2) recognition memory tasks. The results were analysed according to the dual process signal detection (DPSD) and the unequal variance signal detection (UVSD) models.

Experimental investigation

2 rTMS experiments employing non-verbal and verbal memoranda were used. In each experiment subjects received rTMS over left and right DLPC at encoding or retrieval. A baseline condition with no rTMS was included. See Fig. 1 for a schematic diagram.

Experiment 1. Non-verbal recognition memory.

Materials and methods

Participants

Sixty right-handed Italian psychology students (25 males, 35 females; mean age = 22.6 ± 2.1 years) were recruited from the University of Palermo. All participants were in good health and had no previous history of neurological or psychiatric illness. Written informed consent was obtained from all participants prior to participating in the study in accordance with the ethical committee regulations of the Santa Lucia Foundation (Rome, Italy).

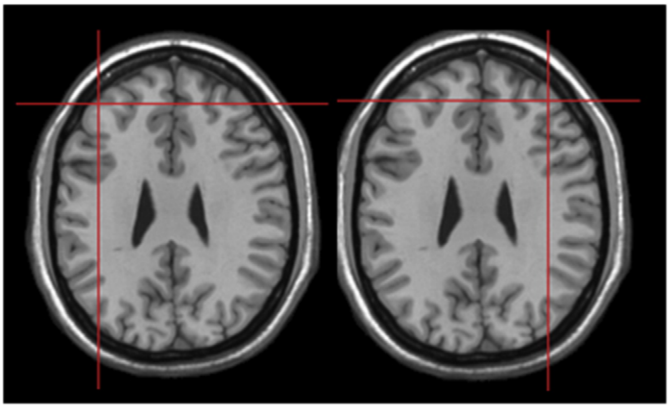


Fig. 1. Axial MRI-constructed stereotaxic template of a representative subject indicating the left and right site of stimulation. Crosses indicate the position of the TMS coil at which rTMS was administered.

Materials

The materials used have been employed in previous studies where they have been described in detail (Cipolotti and colleagues, 2006, 2008). Therefore we will only provide a brief outline. The stimuli were 120 black and white photographs of outdoor scenes that depicted unfamiliar buildings. These photographs did not contain any verbal cues (e.g. street names) or obvious distinguishing features (e.g. people)The photographs were randomly divided in two sets – one set of 60 study items and one set of 60 unstudied distractor items. The study items set was used at the encoding. Both sets were used at retrieval. All photographs were presented in the centre of a computer screen on a white background.

Procedure

The paradigm consisted of a study phase and a test phase. In the study phase, each of the 60 study items was presented for 1000 ms and preceded by a fixation point that lasted for 100 ms. The interstimulus interval (ISI) was 2000 ms. Participants had to decide whether the architecture of the building was “pleasant” or “unpleasant”, and indicate their response by pressing one of two keys on a keyboard. This task was designed to engage the participants and focus their attention, and has been previously used (MacPherson et al., 2008; Cipolotti et al., 2006, 2008). The test phase was administered after an interval of ten minutes. In the test phase, study and distractor items were randomly intermixed and presented sequentially. The subjects were asked to remember if a stimulus has been presented before. Subjects were required to make recognition judgments for each item, according to a six-point confidence scale. They were instructed to give a response “6” only if they were able to recall something specific about seeing the stimulus at study (e.g., what they thought about when the stimulus was presented or what the stimulus looked like on the screen etc). If the subject could not recollect anything specific about the stimuli they were instructed to use the remaining 1-5 confidence ratings. Confidence rating “5” was to be used when the subjects were sure that the stimulus had been studied before, confidence rating “4” was to be used when the subjects thought that the stimulus had been studied before but were not entirely sure, confidence rating “3” was to be used when the subjects thought that a stimulus had not been studied before but were not entirely sure, confidence rating “2” was to be used when the subjects were fairly sure that the stimulus was not been studied before, and confidence rating “1” was to be used when the subjects were sure that the stimuli had not been studied before. The confidence rating procedure we adopted has been previously used in the fMRI literature (e.g., Yonelinas et al., 2005; Gonsalves et al., 2005). This type of rating procedure stresses the dissociation between recollection and familiarity processes and can be considered as a hybrid of confidence ratings and Remember/Know. Several studies have documented convergence of findings between studies employing confidence ratings and R/K paradigms (e.g., Carlesimo et al., 2007; Skinner and Fernandes, 2007; Vann et al., 2009; Wixted, 2007).

The subjects were instructed after the study phase by the same examiner (DS), throughout all experimental conditions. Instructions were repeated, if necessary. Subjects were encouraged to spread out their responses so that they used all confidence judgments. To ensure that the subject fully understood the need to use the entire confidence scale a small training study was administered to all subjects before the experimental session. There was an interval of approximately 10 min between the training and the experimental studies.

rTMS

We used repetitive transcranial magnetic stimulation (rTMS) trains at frequencies known to transiently inhibit the neural activity of a cortical area during the execution of a cognitive task. Stimulation was administered using a MagStim Rapid 2 magnetic stimulator (Whitland, UK), which is able to deliver trains to a maximum frequency of 50 Hz. The stimulator was connected to a focal 70 mm coil, so as to minimize discomfort from oral–facial muscle movements. For each participant, single pulse TMS was first applied at decreasing intensities to determine individual motor threshold, which was defined as the lowest TMS intensity capable of evoking a muscle twitch in the contralateral hand in 5/10 consecutive trials.

During the experimental task, rTMS was applied in trains of 1 Hz frequency for duration of ten minutes at 90% of motor threshold intensity. rTMS was applied over the left and right dorsolateral prefrontal cortex (DLPFC) prior to the encoding or the retrieval phase of the task in five groups of subjects. According to the guidelines of previous studies (Pascual-Leone and Hallett, 1994; Mottaghy et al., 2000), the tip of the intersection of the two coil loops was lined up with the F3/F4 sites of the 10-20 EEG system. To verify the localization of the stimulated site the SofTaxic Navigator system was used in each subject, from digitized skull landmarks (nasion, inion, and two preauricolar points) and about 30 scalp points (Fastrak Polhemus digitizer). Although individual magnetic resonance images (MRIs) were not available, the Talairach coordinates of the stimulated cortical site were automatically estimated from an MRI-constructed stereotaxic template and corresponded approximately at ±40, 45, 28 atlas coordinates (Talairach and Tournoux, 1988), a region assumed to correspond to the border of Brodmann areas 9 and 46 of the left and right hemispheres (Fig. 1) (e.g., Oliveri et al., 2001; Petrides, 2000; Hamidi et al., 2009).

Subjects were divided into five groups: before the encoding phase, ten subjects received rTMS over the right DLPFC and ten over the left DLPC. Before the retrieval phase ten subjects received rTMS over the left DLPFC and ten over the right DLPFC. Twenty subjects were our control group and performed the experiment without receiving rTMS (Fig. 2).

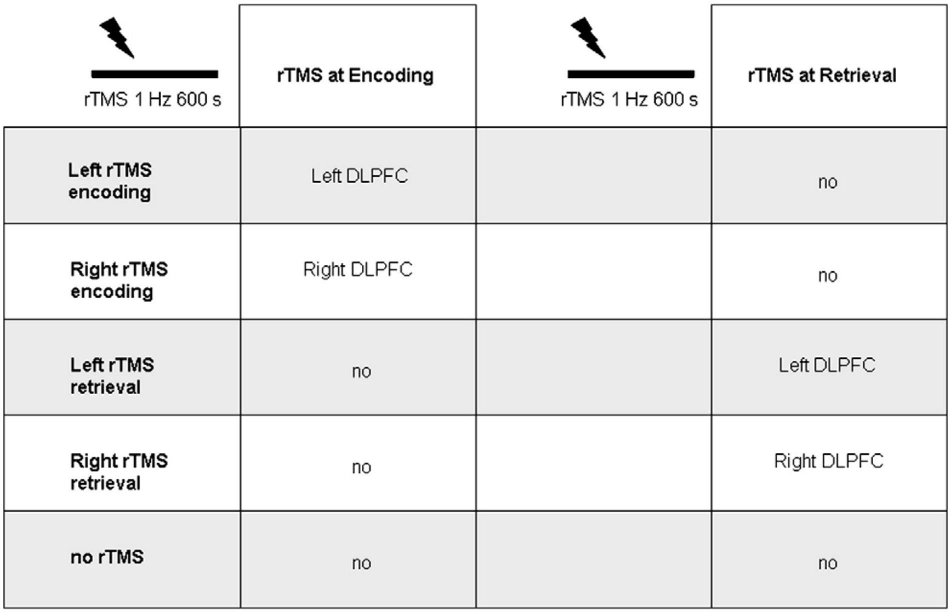
Results

Analysis 1. *DPSD model: recollection and familiarity*

The first analysis examined the involvement of recollection and familiarity in recognition judgments. The confidence ratings for each participant were used to plot ROC curves. The ROC function relates the proportion of correct recognitions (i.e. hit rate) to the proportion of incorrect recognitions (i.e. false alarm rate). Yonelinas et al. (1998) have developed a procedure for fitting ROC data, which is based on the assumption that performance on recognition tasks relies on two independent processes (recollection and familiarity).

In our ROC curves, the proportion of distractor (new) items rated as targets (old) was plotted on the x-axis and the proportion of targets (old) correctly identified as targets (old) was plotted on the y-axis. The first point on the function represents the proportion of hits and false alarms receiving only the most confident response (6), and each successive point represents progressively more relaxed response criteria (e.g. items receiving confidence responses 5 or 6, followed by items receiving confidence responses 4, 5 or 6, and so on).

The original Yonelinas et al. (1998) procedure was used to quantify recollection and familiarity. Recollection was estimated from the intersection of the regression line with the ordinate, whilst familiarity was estimated by constraining the intercept with the y-axis in relation to the estimated probability that an item was recollected. A nonlinear equation was then fitted to the observed points of the ROC curve using a least-squares method through the solver in Excel (Yonelinas et al., 1998). Thus, the estimate of recollection was taken as the intersection of the regression line with the ordinate for the most conservative response criteria, the degree of curvature was taken as an estimate of familiarity.



rTMS 1 Hz 600 s	**rTMS at Encoding**	rTMS 1 Hz 600 s	**rTMS at Retrieval**
Left rTMS encoding	Left DLPFC		no
Right rTMS encoding	Right DLPFC		no
Left rTMS retrieval	no		Left DLPFC
Right rTMS retrieval	no		Right DLPFC
no rTMS	no		no

Fig. 2. It depicts the 5 experimental conditions. (1) Left rTMS at encoding, no stimulation at retrieval; (2) right rTMS at encoding, no stimulation at retrieval; (3) left rTMS at retrieval, no stimulation at encoding; (4) right rTMS at retrieval, no stimulation at encoding; (5) no rTMS, absence of stimulation.

In line with previous studies, we carried out a ROC analysis of the confidence judgments made for old and new stimuli (e.g. Aggleton et al., 2005; Carlesimo et al., 2007; Cipolotti et al., 2006, 2008; Bird et al., 2007; Yonelinas et al., 2002).

Fig. 2 shows the ROC curves for recollection and familiarity in the five experimental conditions. According to DPSD model, recollection is a threshold-based retrieval process whilst familiarity is best described by a standard equal–variance signal detection model. For this reason, recollection and familiarity were analyzed separately in our study. One-way ANOVAs were used to compare the estimates of recollection and familiarity for each of the five experimental conditions: no rTMS; left rTMS encoding; right rTMS encoding; left rTMS retrieval; right rTMS retrieval. We found that recollection estimates were significantly affected by rTMS [F (4,55) = 5.80; $p < 0.001$]. Post hoc analysis using Scheffe's test showed that the application of right rTMS before encoding significantly worsened recollection performance ($p < 0.01$). In contrast left rTMS before encoding did not significantly affect recollection performance ($p = 0.12$). Similarly rTMS before retrieval had no effect on recollection left ($p = 0.39$) and right ($p = 0.99$). Thus, recollection is disrupted only when rTMS is applied over the right DLPFC at the encoding phase.

Familiarity estimates were significantly affected by r TMS as demonstrated by a separate ANOVA [F (4,55) = 4.79; $p < 0.01$]. Post hoc analysis showed that right rTMS before encoding led to a significant worsening in familiarity performance ($p < 0.01$). In contrast, left rTMS before encoding ($p = 0.27$) had no effect. Similarly, left ($p = 0.48$) and right ($p = 0.99$) rTMS before retrieval did not affect familiarity performance. Fig. 3 shows the means and standard errors for recollection and familiarity estimates.

Qualitatively, we noted that following rTMS at encoding the number of incorrect responses rated “1” (never seen before) increased whilst the number of correct responses rated “6” (previous seen) decreased. No such noticeable change was observable for the other confidence ratings.

Analysis 2. *UVSD model*

It has been suggested that although both the DPSD model and the UVSD model fit the old-new recognition data well, the latter model fits it better (Wixted, 2007). Therefore, we analyzed our data also from the perspective of the UVSD model (Parks and Yonelinas, 2007; Wixted, 2007). This procedure does not make any assumptions about the relative contributions of recollection and familiarity to recognition performance. From z-ROC curves, the intercept provides a measure of sensitivity closely related to d' and the slope provides a measure of the variance ratio between the strength of “old” items and “new” items (MacMillan and Creelman, 1991).

To fit the data to the UVSD model, the ROC data for all experimental conditions were z-transformed in order to calculate slope and intercept values. In a small number of cases, the hit rate or false alarm rate was 0 or 1, which are values that cannot be z-transformed. In these cases, the number of correct items was adjusted so that it was mid-way between 0 and 1. Thus, a proportion of 0/60 (i.e. no false alarms when confidently recognizing old items) was converted into a proportion of 0.5/60, and a proportion of 60/60 (i.e. no misses when confidently rejecting new items) was converted into a proportion of 59.5/60.

Performance was characterized by two parameters: the slope of the z-ROC and a measure of sensitivity (Da), which was calculated using the slope of the z-ROC and its intercept with the y-axis (see MacMillan and Creelman, 1991). The slope of the z-ROC corresponds to the variance ratio of the noise distributions of studied and unstudied items. The sensitivity (Da) provides a measure of overall accuracy. We used this latter parameter, rather than d', as a measure of accuracy in this analysis since it is more appropriate when the slope of the z-ROC does not equal 1 (MacMillan and Creelman, 1991).

Table 1 shows the slopes and sensitivity (Da) parameters for the z-transformed ROC data in the five experimental conditions. An ANOVA showed that the slopes of the z-ROCs did not differ significantly between conditions [F (4,55) = 0.98; $p > 0.43$]. By contrast, there was a significant difference in accuracy (Da) across conditions [F (4,55) = 5,28; $p < 0.001$]. Post-hoc tests revealed that the application of right rTMS at encoding led to a decrease in memory strength [$p < 0.005$]. In contrast, left rTMS at encoding ($p = 0.23$), left ($p = 0.54$) and right ($p = 0.99$) rTMS at retrieval did not significantly affect accuracy.

Experiment 2. Verbal recognition memory test

Experiment 2 was identical to Experiment 1, with the exception of the participants and the materials used.

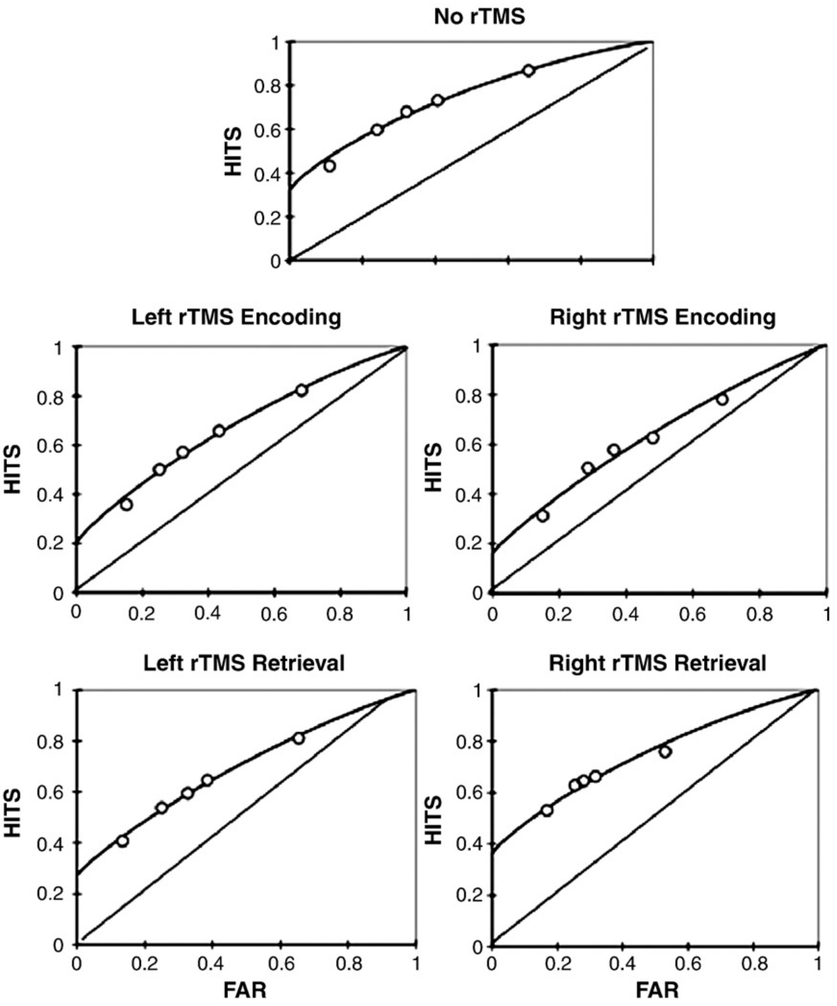


Fig. 3. ROC curves of recollection and familiarity in the five experimental conditions on the non-verbal recognition test.

Materials and methods

Subjects

We enrolled sixty-two right-handed, healthy Italian psychology students (26 males; 36 females; mean age = 22.8 ± 1.9 years) with no previous history of psychiatric and/or neurological disorders, from the University of Palermo.

Materials

The stimuli were 120 Italian concrete and abstract words adapted from Laudanna et al. (1995). The words were presented in black upper-case letters on a white background in the centre of a computer screen. The 120 words were randomly divided into two sets: a set of 60 study items to be presented at the encoding phase, and a set of 60 "lure" items. All 120 words were used in the retrieval phase.

Table 1
The slopes and sensitivity (Da) parameters for the *z*-transformed ROC data of subjects in the five experimental conditions on the nonverbal recognition memory test.

	Slope		Sensitivity (Da)	
	Mean	S.D.	Mean	S.D.
no rTMS	0.79	0.20	0.82	0.29
L rTMS encoding	0.87	0.34	0.56	0.26
R rTMS encoding	0.81	0.37	0.45**	0.33
L rTMS retrieval	0.69	0.21	0.63	0.40
R rTMS retrieval	0.67	0.20	0.88	0.28

$^{**}p<0.01$.
$^{*}p<0.05/^{**}p<0.01$.

Procedure

There was a study and a test phase. As in previous studies, in the study phase, participants were required to decide whether the presented word was concrete or abstract (Cipolotti et al., 2006). In the test phase, they were asked to make recognition judgments following the presentation of each item, according to the six-point confidence scale described in Experiment 1.

The experimental procedure was identical to that of Experiment 1. The stimulus exposure time was reduced to 250 ms in order to match the difficulty of the verbal and non-verbal recognition tasks (Sweet et al., 2000). The duration of the fixation point and the ISI were identical to those in Experiment 1.

rTMS

Before the encoding phase, ten participants received right DLPFC rTMS and ten received left DLPFC rTMS. Before the retrieval phase, ten participants received right DLPFC rTMS and ten received left DLPFC rTMS; 22 subjects performed the experiment without receiving rTMS (Fig. 1).

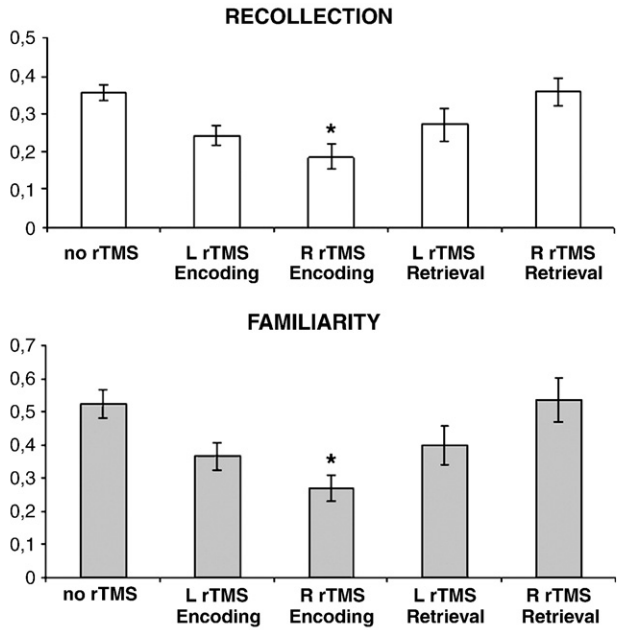


Fig. 4. Estimates of recollection and familiarity derived using the DPSD procedure for the 5 experimental conditions on the non-verbal recognition test (error bar: ±1 S.E.; $^*p<0.05$).

Results

The results were analyzed using the same statistical tests as in Experiment 1.

Analysis 1. *DPSD model: recollection and familiarity*

Fig. 4 shows the ROC curves for recollection and familiarity in the five experimental conditions.

Recollection and familiarity were analyzed separately. Statistical analysis was performed using one-way analysis of variance (ANOVA) to compare the estimates of recollection and familiarity for each of the five experimental conditions: no rTMS; left rTMS encoding; right rTMS encoding; left rTMS retrieval; right rTMS retrieval.

ANOVA revealed a significant effect of rTMS on recollection estimates [$F(4, 57) = 6.86$; $p<0.001$]. Post hoc analysis using Scheffe's Test showed that recollection was selectively impaired when rTMS was applied over left DLPFC at the encoding phase ($p<0.05$). Right rTMS before encoding ($p = 0.18$), left ($p = 0.50$) and right ($p = 0.42$) rTMS before retrieval did not significantly affect recollection performance.

An analysis of familiarity revealed a significant effect of rTMS [$F(4, 57) = 4.89$; $p<0.002$]. Post hoc analysis showed that the application of left rTMS at the encoding phase significantly disrupted familiarity performance ($p<0.02$). However, right rTMS at encoding ($p = 0.78$) and left ($p = 0.97$) and right ($p = 0.71$) rTMS at retrieval did not affect familiarity performance. Fig. 5 shows the means and standard errors for recollection and familiarity estimates.

Qualitatively, similar to what was noted in Experiment 1, following rTMS at encoding the number of incorrect responses rated “1” (never seen) increased whilst the number of correct responses rated “6” (previous seen) decreased. No such noticeable change was present for the other confidence ratings.

Analysis 2. *UVSD model*

Table 2 shows the slopes and sensitivity (Da) parameters for the z-transformed ROC data of the participants in the five experimental conditions (no rTMS, left rTMS encoding, right rTMS encoding, left rTMS retrieval, right rTMS retrieval).

The slopes of z-ROCs did not differ significantly [$F(4,57) = 0.57$; $p = 0.68$]. By contrast, there was a significant difference in accuracy (Da) [$F(4,57) = 7,60$; $p<0.001$]. Post hoc tests revealed that administration of left rTMS at the encoding phase led to a decrease in memory strength ($p<0.001$). In contrast, right rTMS before encoding ($p = 0.40$), left ($p = 0.74$) and right ($p = 0.37$) rTMS before retrieval did not significantly affect memory strength (Fig. 6).

Comparing the fit indices to the DPSD model and the UVSD model

It has been reported that both DPSD and UVCD models provide a good description of curvilinear probability of ROCs. Both models are commonly used to fit ROC data. We separately fitted the rTMS data from the different experimental conditions to the DPSD model, using the solver in Excel (see http://psychology.ucdavis.edu/labs/Yonelinas/), and to the UVSD model, using curve fitting software from www.unifr.ch/psycho/site/units/allpsy/team/Macho. Both techniques calculate predicted ROC points that can be compared with the actual data. This allows calculating the error between the model and the data. Goodness of fit for both models was assessed by the chi-squared statistic. The total sum of squared errors for the two models is: UVSD (average = 0.000660395; s.d. 0.000521172), DPSD (average = 0.001030734; s.d. 0.000675578). Thus, both the DPSD model and the UVSD model fit the data well. Interestingly, a paired t-test to directly compare the fits for all the 10 experimental conditions (*Non-verbal:* no rTMS, left rTMS encoding, right rTMS encoding, left rTMS retrieval, right rTMS retrieval. *Verbal*: no rTMS, left rTMS encoding, right rTMS encoding, left rTMS retrieval, right rTMS retrieval) revealed that the UVSD model provide a significantly better fit to the data [$t(9) = -4.885$, $p<0.005$]. To take it to account inter-subject variability, we ran a $2\times2\times3$ ANOVA with Model (DPSD, UVCD) as the within-subjects factor whilst Material (non-verbal, verbal) and Condition (no rTMS, rTMS encoding, rTMS retrieval) were between-subjects factors. The ANOVA did not revealed significant effects, in particular, there was no significant interaction between Model type and Condition.

Discussion

The aim of the current rTMS study was to investigate the role of the DLPFC in verbal and non-verbal recognition memory tasks and its contribution to recollection and familiarity processes.

The following methodological key points should be taken into account, before discussing the possible implications of the present results. The accuracy of TMS coil positioning (SofTax system) can be estimated of the order of less than 1 cm (Herwig et al., 2001). The spatial selectivity and the intimate mechanisms by which rTMS works are still not wholly understood. Moreover increasing the stimulation intensity may lead to spreading of TMS effects towards adjacent brain areas (Walsh and Pascual-Leone, 2003; Rossi and Rossini, 2004). However, intensities of stimulation similar to the one we adopted in this study have been previously used by studies applying either on-line (e.g. Oliveri et al., 2001; Koch et al., 2005; Hamidi et al., 2009) or off-line (e.g., Mottaghy et al., 2002; Sole-Padulles et al., 2006) rTMS to the DLPFC to interfere with memory functions using intensities of stimulation similar to the one adopted in the present study. Moreover, a recent study (Mottaghy et al., 2002) used off-line rTMS over the prefrontal cortex to differentiate the contribution of dorsal (DLPFC) and ventral (VLPFC) in the domain-specific segregation of working memory. Therefore, we are fairly confident that stimulation over the DLPFC specifically interferes with information processing of the stimulated region without significantly disrupting other frontal areas, such as VLPFC, known to be involved in recognition memory.

Our results showed that the frontal lobes are critically involved in recognition memory. We found that the application of rTMS over DLPFC modulates subjects' performance on verbal and non-verbal

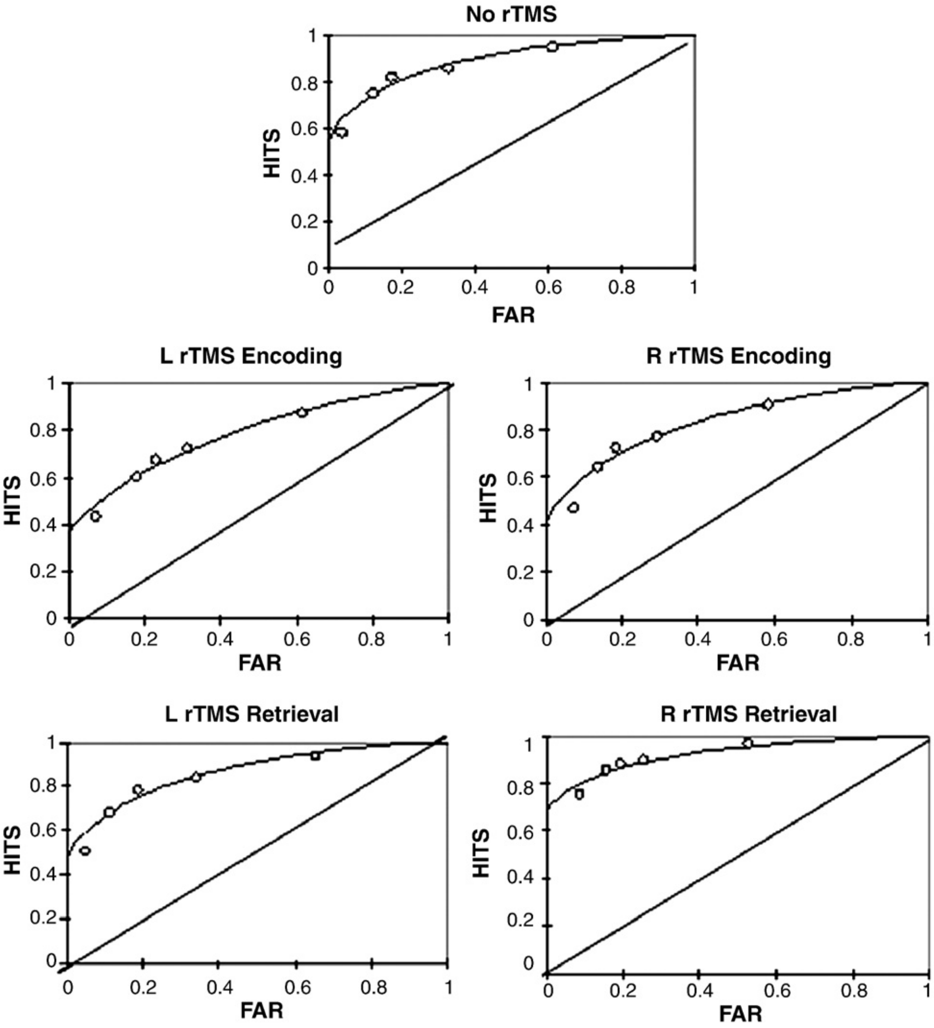


Fig. 5. ROC curves of recollection and familiarity in the five experimental conditions on the verbal recognition test.

recognition memory tasks. This is in good accord with lesion studies suggesting a critical role for these regions in memory tasks. Indeed patients with frontal lesions have been shown to have impaired recognition memory (e.g., Alexander et al., 2003; Delbecq-Derouesne et al., 1990; Dimitrov et al., 1999; Rapcsak et al., 1996, 1998; Schacter et al., 1996; Swick and Knight, 1999; Turner et al., 2007).

Moreover, our findings suggest that there is a degree of lateralisation in the contribution of frontal lobes to recognition memory. Specifically, rTMS over left and right DLPFC disrupted recollection and familiarity for verbal (Experiment 2) and non-verbal-buildings-(Experiment 1) stimuli, respectively. This is in accord with some findings from neuropsychological and neuroimaging studies. Left laterality effects for verbal memoranda have been reported in the

Table 2
The slopes and sensitivity (Da) parameters for the *z*-transformed ROC data of subjects in the five experimental conditions on the verbal recognition memory test.

	Slope		Sensitivity (Da)	
	Mean	S.D.	Mean	S.D.
no rTMS	0.65	0.20	1.80	0.44
L rTMS encoding	0.73	0.22	1.10**	0.35
R rTMS encoding	0.74	0.24	1.43	0.54
L rTMS retrieval	0.71	0.17	1.55	0.43
R rTMS retrieval	0.76	0.36	2.17	0.60

**$p<0.01$.

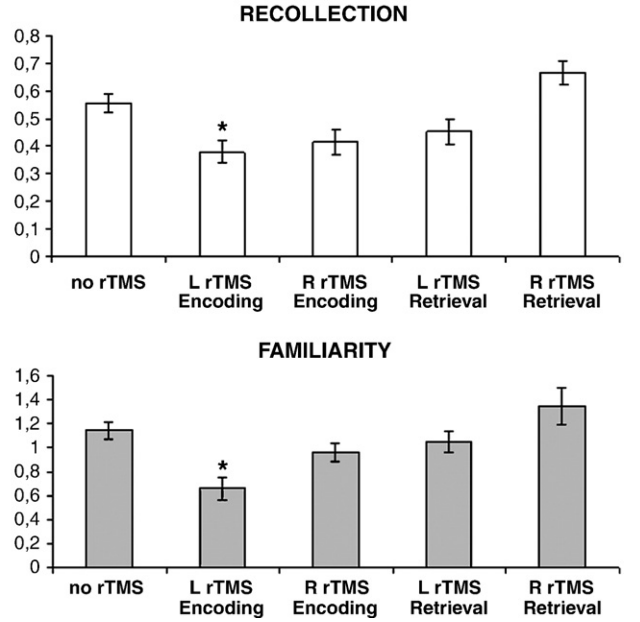


Fig. 6. Estimates of recollection and familiarity derived using the DPSD procedure for the 5 experimental conditions on the verbal recognition test (error bar: ±1 S.E.; *$p<0.05$).

lesion (e.g., Milner et al., 1991; Warrington, 1984) and neuroimaging literature (e.g., McDermott et al., 1999; Wagner et al., 1998). This evidence, taken together with our findings, suggests that the left DLPFC has a degree of functional specialization for verbal memoranda. However, it remains possible that our left laterality effect may be due to the nature of our encoding task (concrete/abstract decision) or an interaction between the verbal stimuli and the task. Our right laterality effect for buildings is also in keeping with findings suggesting functional specialisation within the prefrontal cortex for the processing of non-verbal-abstract drawing (e.g. Milner et al., 1991; Kelley et al., 1998; McDermott et al., 1999; Wagner et al., 1998). However, Turriziani et al. (2008) reported an rTMS study showing no clear cut familiarity lateralization effects for faces. It may well be that there are material specific laterality effects for different types of non-verbal memoranda. Certainly lesion studies have repeatedly reported double dissociation between topographical memoranda such as buildings and non-topographical memoranda, such as faces (for a review, Cipolotti and Bird, 2006). Future research will be necessary to establish which aspects of nonverbal memory rely upon DLPFC.

To the best of our knowledge, this is the first study examining the effect of rTMS on recollection and familiarity using both non-verbal and verbal memoranda. Adopting DPSD analysis, we found that rTMS application over DLPFC at encoding modulates both familiarity and recollection processes. In particular, rTMS over left and right DLPC at encoding modulated familiarity and recollection for verbal and non-verbal memoranda, respectively. Qualitatively it was noticeable that, following rTMS at encoding, the subjects became less certain of their responses to targets as they reduced the selection of rating “1” (never seen before) and “6” (previous seen) to targets. Interestingly, rTMS application over DLPFC at retrieval had no significant effect on either familiarity or recollection processes. The previous study of Turriziani and colleagues (2008) using a different rTMS methodology also did not find any significant effect of rTMS at retrieval for R/K processes. In this context, we noted that functional neuroimaging studies have reported different results from ours. Thus, some studies have documented that familiarity and recollection dissociate at retrieval but not at encoding (e.g., Davachi et al., 2003; Kahn et al., 2004). Others have suggested that they dissociate both at retrieval and encoding (e.g., Ranganath et al., 2004; Otten, 2007). This is in line with some event-related brain potential (ERPs) studies reporting that familiarity and recollection dissociate both at encoding and retrieval (e.g., Duarte et al., 2004). The reasons behind these important differences between our rTMS study and the neuroimaging literature and within the neuroimaging results remain unclear. It may well be that crucial differences in task methodology, results analysis and localisation of the relevant frontal areas may underlie this contrasting pattern of results.

Adopting UVSD analysis, we fitted our ROC data to the UVCD model. This analysis showed that rTMS at encoding affected the accuracy for non-verbal and verbal material respectively. Interestingly, rTMS in this condition did not affect the variance, since the slope of z-ROC remained unchanged. At retrieval, rTMS did affect neither the accuracy nor the slope of z-ROC. Thus, our DPSD and UVCD analyses demonstrated that rTMS affect recollection and familiarity processes only at encoding and in a material specific manner. In the literature it is hotly debated whether the DPSD or the UVCD models provide a better fit for the data (e.g., Wixted, 2007). Our study was not set up to differentiate between these two contrasting models. However, our analysis using SSE average estimate to compare the fits of the UVCD and DSPD models revealed that the fits of our encoding group average data was good for both models, although the UVCD analysis fitted our encoding data significantly better than the DPSD analysis. This result agrees with the finding of a recent study that analysed recollection familiarity in hippocampal patients reporting that the fit of the signal detection model was better than that of the dual process model patients (Wais et al., 2006). Unfortunately, we did not find any significant result when we analysed subjects' individual SSE estimate with an ANOVA.

We would argue that the rTMS application at encoding results in a weakening of memory traces which behaviourally manifests itself in a change of the decision criterion for the most extreme confidence ratings for the target items. Mickes and colleagues (2009) suggested that continuous recollection and familiarity signals are combined into a memory strength variable. In our view, the application of rTMS over DLPC at encoding interferes with the contributions of familiarity and recollection to the strength of the memory traces. Alternatively it may well be that rTMS over DLPC disrupt the implementation of high level attentional- processes necessary to enhance memory strength at encoding (see Ranganath and Knight, 2003 for a detailed review of the role of prefrontal cortex in encoding and retrieval).

Our findings suggest that DLPFC has a degree of functional specialisation and plays an important role in the encoding of memory traces. Further research using rTMS paradigms is necessary in order to clarify the contribution of DLPFC to recognition memory processes.

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References

Aggleton, J.P., Brown, M., 1999. Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. Behav. Brain Sci. 22, 425–489.

Aggleton, J.P., Brown, M.W., 2006. Interleaving brain systems for episodic and recognition memory. Trends Cog. Sci. 10, 455–463.

Aggleton, J.P., Vann, S.D., Denby, C., Dix, S., Mayes, A.R., Roberts, N., Yonelinas, A.P., 2005. Sparing of the familiarity component of recognition memory in a patient with hippocampal pathology. Neuropsychologia 43, 1810–1823.

Alexander, M.P., Stuss, D.T., Fansabedian, N., 2003. California Verbal Learning Test: performance by patients with focal frontal and non-frontal lesions. Brain 126, 1493–1503.

Bird, C.M., Shallice, T., Cipolotti, L., 2007. Fractionation of memory in medial temporal lobe amnesia. Neuropsychologia 45, 1160–1171.

Brown, M.W., Aggleton, J.P., 2001. Recognition memory: what are the roles of the perirhinal cortex and hippocampus? Nat. Rev. Neurosci. 2, 51–61.

Carlesimo, G.A., Serra, L., Fadda, L., Cherubini, A., Bozzali, M., Caltagirone, C., 2007. Bilateral damage to the mammillo-thalamic tract impairs recollection but not familiarity in the recognition process: a single case investigation. Neuropsychologia 45, 2467–2479.

Cipolotti, L., Bird, C.M., 2006. Amnesia and the hippocampus. Curr. Opin. Neurol. 19, 593–598.

Cipolotti, L., Bird, C., Good, T., Macmanus, D., Rudge, P., Shallice, T., 2006. Recollection and familiarity in dense hippocampal amnesia: a case study. Neuropsychologia 39, 151–172.

Cipolotti, L., Husain, M., Crinion, J., Bird, C.M., Khan, S.S., Losseff, N., Howard, R.S., Leff, A.P., 2008. The role of the thalamus in amnesia: a tractography, high-resolution MRI and neuropsychological study. Neuropsychologia 46, 2745–2758.

Curran, T., Schacter, D.L., Norman, K.A., Galluccio, L., 1997. False recognition after a right frontal lobe infarction: memory for general and specific information. Neuropsychologia 35, 1035–1049.

Davachi, L., Mitchell, J.P., Wagner, A.D., 2003. Multiple routes to memory: distinct medial temporal lobe processes build item and source memories. Proc. Natl. Acad. Sci. USA 100, 2157–2162.

Davidson, P.S.R., Glisky, E.L., 2002. Neuropsychological correlates of recollection and familiarity in normal aging. Cog. Aff. Behav. Neurosci. 2, 174–186.

Davidson, P.S., Anaki, D., Saint-Cyr, J.A., Chow, T.W., Moscovitch, M., 2006. Exploring the recognition memory deficit in Parkinson's disease: estimates of recollection versus familiarity. Brain 129, 1768–1779.

Delbecq-Derouesne, J., Beauvois, M.F., Shallice, T., 1990. Preserved recall versus impaired recognition. A case study. Brain 113, 1045–1074.

Dimitrov, M., Granetz, J., Peterson, M., Hollnagel, C., Alexander, G., Grafman, J., 1999. Associative learning impairments in patients with frontal lobe damage. Brain Cogn. 41, 213–230.

Donaldson, W., 1996. The role of decision processes in remembering and knowing. Mem. Cog. 18, 23–30.

Duarte, A., Ranganath, C., Winward, L., Hayward, D., Knight, R.T., 2004. Dissociable neural correlates for familiarity and recollection during the encoding and retrieval of pictures. Cog. Brain Res. 18, 255–272.

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

Dunn, J.C., 2004. Remember–know: a matter of confidence. Psychol. Rev. 111, 524–542.

Eichenbaum, H., 2000. A cortical–hippocampal system for declarative memory. Nat. Rev. Neurosci. 1, 41–50.

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, 1149–1152.

Floel, A., Poeppel, D., Buffalo, E.A., Braun, A., Wu, C.W., Seo, H.J., Stefan, K., Knecht, S., Cohen, L.G., 2004. Prefrontal cortex asymmetry for memory encoding of words and abstract shapes. Cereb. Cortex. 14, 404–409.

Gonsalves, B.D., Kahn, I., Curran, T., Norman, K.A., Wagner, A.D., 2005. Memory strength and repetition suppression: multimodal imaging of medial temporal cortical contributions to recognition. Neuron 47 (5), 751–761.

Habib, R., Nyberg, L., Tulving, E., 2003. Hemispheric asymmetries of memory: the HERA model revisited. Trends Cogn. Sci. 7, 241–245.

Hamidi, M., Tononi, G., Postle, B.R., 2009. Evaluating the role of prefrontal and parietal cortices in memory-guided response with repetitive transcranial magnetic stimulation. Neuropsychologia 47 (2), 295–302.

Herwig, U., Schönfeldt-Lecuona, C., Wunderlich, A.P., von Tiesenhausen, C., Thielscher, A., Walter, H., Spitzer, M., 2001. The navigation of transcranial magnetic stimulation. Psychiatry Res. 108 (2), 123–131.

Jacoby, L.L., 1991. A process dissociation framework: separating automatic from intentional uses of memory. J. Mem. Lang. 30, 513–541.

Jacoby, L.L., Dallas, M., 1981. On the relationship between autobiographical memory and perceptual learning. J. Exp. Psychol. Gen. 110, 306–340.

Kahn, I., Davachi, L., Wagner, A.D., 2004. Functional–neuroanatomic correlates of recollection: implications for models of recognition memory. J. Neurosci. 24, 4172–4180.

Kelley, W.M., Miezin, F.M., McDermott, K.B., Buckner, R.L., Raichle, M.E., Cohen, N.J., Ollinger, J.M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Petersen, S.E., 1998. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. Neuron 20, 927–936.

Kirwan, C.B., Wixted, J.T., Squire, L.R., 2008. Activity in the medial temporal lobe predicts memory strength, whereas activity in the prefrontal cortex predicts recollection. J. Neurosci. 28, 10541–10548.

Knowlton, B.J., Squire, L.R., 1995. Remembering and knowing: two different expressions of declarative memory. J. Exp. Psychol. Learn. Mem. Cogn. 21, 699–710.

Koch, G., Oliveri, M., Torriero, S., Carlesimo, G.A., Turriziani, P., Caltagirone, C., 2005. rTMS evidence of different delay and decision processes in a fronto-parietal neuronal network activated during spatial working memory. Neuroimage 24 (1), 34–39.

Kohler, S., Paus, T., Buckner, R.L., Milner, B., 2004. Effects of left inferior prefrontal stimulation on episodic memory formation: a two-stage fMRI- rTMS study. J. Cogn. Neurosci. 16, 178–188.

Laudanna, A., Thornton, A.M., Brown, G., Burani, C., Marconi, L., 1995. Un corpus dell'italiano scritto contemporaneo dalla parte del ricevente. In: Bolasco, S., Lebart, L., Salem, A. (Eds.), 23 *III* Giornate Internazionali di Analisi Statistica dei Dati Testuali, vol. 1. Lawrence Erlbaum Associates, pp. 103–109. Roma:Cisu.

Lavenex, P., Amaral, D.G., 2000. Hippocampal–neocortical interaction: a hierarchy of associativity. Hoppocampus 10, 420–430.

MacMillan, N.A., Creelman, C.D., 1991. Detection theory: A user's guide. New York, NY: Cambridge University Press.

MacPherson, S.E., Bozzali, M., Cipolotti, L., Dolan, R.J., Rees, J.H., Shallice, T., 2008. Effect of frontal lobe lesions on the recollection and familiarity components of recognition memory. Neuropsychologia 46, 3124–3132.

Mandler, G., 1980. Recognizing: the judgement of previous occurrence. Psychol. Rev. 87, 252–271.

Manns, J.R., Hopkins, R.O., Reed, J.M., Kitchener, E.G., Squire, L.R., 2003. Recognition memory and the human hippocampus. Neuron 37, 171–180.

McClelland, J.L., Chappell, M., 1998. Familiarity breeds differentiation: a subjective-likelihood approach to the effects of experience in recognition memory. Psychol. Rev. 105, 724–760.

McDermott, K.B., Buckner, R.L., Petersen, S.E., Kelley, W.M., Sanders, A.L., 1999. Set- and code-specific activation in frontal cortex: an fMRI study of encoding and retrieval of faces and words. J. Cogn. Neurosci. 11, 631–640.

Mickes, L., Wais, P.E., Wixted, J.T., 2009. Recollection is a continuous process: implications for dual-process theories of recognition memory. Psychol. Sci. 20, 509–515.

Milner, B., Corsi, P., Leonard, G., 1991. Frontal-lobe contribution to recency judgements. Neuropsychologia 29, 601–618.

Miniussi, C., Cappa, S.F., Sandrini, M., Rossigni, P.M., Rossi, S., 2003. The causal role of the prefrontal cortex in episodic memory as demonstrated with rTMS. Clin. Neurophysiol. 56, 312–320.

Mottaghy, F.M., Krause, B.J., Kemna, L.J., Töpper, R., Tellmann, L., Beu, M., Pascual-Leone, A., Müller-Gärtner, H.W., 2000. Modulation of the neuronal circuitry subserving working memory in healthy human subjects by repetitive transcranial magnetic stimulation. Neurosci. Lett. 280 (3), 167–170.

Mottaghy, F.M., Gangitano, M., Sparing, R., Krause, B.J., Pascual-Leone, A., 2002. Segregation of areas related to visual working memory in the prefrontal cortex revealed by rTMS. Cereb. Cortex 12, 369–375.

Oliveri, M., Turriziani, P., Carlesimo, G.A., Koch, G., Tomaiuolo, F., Panella, M., Caltagirone, C., 2001. Parieto-frontal interactions in visual-object and visual-spatial working memory: evidence from transcranial magnetic stimulation. Cereb. Cortex 11, 606–618.

Otten, L.J., 2007. Fragments of a larger whole: retrieval cues constrain observed neural correlates of memory encoding. Cereb. Cortex 17, 2030–2038.

Owen, A.M., 2004. Cognitive dysfunction in Parkinson's disease: the role of frontostriatal circuitry. Neuroscientist 10, 525–537.

Parks, C.M., Yonelinas, A.P., 2007. Moving beyond pure signal-detection models: comment on Wixted. Psychol. Rev. 114, 188–202.

Pascual-Leone, A., Hallett, M., 1994. Induction of errors in a delayed response task by repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex. NeuroReport 20 (5), 2517–2520.

Petrides, M., 2000. Frontal lobes and memory, In: Boller, F., Grafman, J. (Eds.), 2nd edition. Handbook of neuropsychology, vol. 2. Elsevier, Amsterdam, pp. 67–84.

Rami, L., Gironell, A., Kulisevsky, J., Garcia-Sanchez, C., Berthier, M., Estevez-Gonzalez, A., 2003. Effects of repetitive transcranial magnetic stimulation on memory subtypes: a controlled study. Neuropsychologia 41, 1877–1883.

Ranganath, C., Knight, R.T., 2003. Prefrontal cortex and episodic memory: integrating findings from neuropsychology and event-related functional neuroimaging. In: Parker, A., Wildng, E., Bussey, T. (Eds.), The cognitive neuroscience of memory encoding and retrieval. Psychology Press, Philadelphia, pp. 83–99.

Ranganath, C., Yonelinas, A.P., Cohen, M.X., Dy, C.J., Tom, S.M., D'Esposito, M., 2004. Dissociable correlates of recollection and familiarity within the medial temporal lobes. Neuropsychologia 42, 2–13.

Rapcsak, S.Z., Polster, M.R., Glisky, M.L., Comer, J.F., 1996. False recognition of unfamiliar faces following right hemisphere damage: neuropsychological and anatomical observations. Cortex 32, 593–611.

Rapcsak, S.Z., Kaszniak, A.W., Reminger, S.L., Glisky, M.L., Glisky, E.L., Comer, J.F., 1998. Dissociation between verbal and autonomic measures of memory following frontal lobe damage. Neurology 50, 1259–1265.

Rapcsak, S.Z., Reminger, S.L., Glisky, E.L., Kaszniak, A.W., Comer, J.F., 1999. Neuropsychological mechanisms of false facial recognition following frontal lobe damage. Cogn. Neuropsychol. 16, 267–292.

Rosene, D., Van Hoesen, G.W., 1977. Hippocampal efferents reach widespread areas of cerebral cortex and amygdale in rhesus monkey. Science 198, 315–317.

Rossi, S., Rossini, P.M., 2004. TMS in cognitive plasticity and the potential for rehabilitation. Trends Cogn. Sci. 8, 273–279.

Rossi, S., Cappa, S.F., Babiloni, C., Pasqualetti, P., Miniassi, C., Carducci, F., Babiloni, F., Rossigni, P.M., 2001. Prefrontal cortex in long-term memory: an 'interference' approach using magnetic stimulation. Nat. Neurosci. 4, 948–952.

Rossi, S., Pasqualetti, P., Zito, G., Vecchio, F., Cappa, S.F., Miniassi, C., Babiloni, C., Rossigni, P.M., 2006. Prefrontal and parietal cortex in human episodic memory: an interference study by repetitive transcranial magnetic stimulation. Eur. J. Neurosci. 23, 793–800.

Sandrini, M., Cappa, S.F., Rossi, S., Rossigni, P.M., Miniassi, C., 2003. The role of prefrontal cortex in verbal episodic memory: rTMS evidence. J. Cogn. Neurosci. 15, 855–861.

Schacter, D.L., Curran, T., Galluccio, L., Milberg, W.P., Bates, J.F., 1996. False recognition and the right frontal lobe: a case study. Neuropsychologia 34, 793–808.

Shiffrin, R.M., Steyvers, M., 1997. A model for recognition memory: REM—retrieving effectively from memory. Psychon. Bull. Rev. 4, 145–166.

Simons, J.S., Spiers, H.J., 2003. Prefrontal and medial temporal lobe interactions in long-term memory. Nat. Rev. Neurosci. 4 (8), 637–648.

Skinner, E.I., Fernandes, M.A., 2007. Neural correlates of recollection and familiarity: a review of neuroimaging and patient data. Neuropsychologia 45, 2163–2179.

Sole-Padulles, C., Bartres-Faz, D., Junque, C., Clemente, I.C., Molinuevo, J.L., Bargallo, N., Sanchez-Aldeguer, J., Bosch, B., Falcon, C., Valls-Sole, J., 2006. Repetitive transcranial magnetic stimulation effects on brain function and cognition among elders with memory dysfunction. A randomized sham-controlled study. Cereb. Cortex 16, 1487–1493.

Spaniol, J., Davidson, P.S., Kim, A.S., Han, H., Moscovitch, M., Grady, C.L., 2009. Event-related fMRI studies of episodic encoding and retrieval: meta-analyses using activation likelihood estimation. Neuropsychologia 47, 1765–1779.

Squire, L.R., Zola, S., 1997. Amnesia, memory and brain systems. Phil. Trans. R. Soc. B 352, 1663–1673.

Sweet, J.J., Demakis, G.J., Ricker, J.H., Millis, S.R., 2000. Diagnostic efficiency and material specificity of the Warrington Recognition Memory Test: a collaborative multisite investigation. Arch. Clin. Neuropsychol. 15, 301–309.

Swick, D., Knight, R.T., 1999. Contributions of prefrontal cortex to recognition memory: electrophysiological and behavioral evidence. Neuropsychology 13, 155–170.

Talairach, J., Tournoux, P., 1988. Coplanar stereotaxic Atlas of the Human Brain. Thieme, Stuggart, Germany.

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

Tulving, E., 1989. Remembering and knowing the past. Am. Sci. 77, 361–367.

Tulving, E., Kapur, S., Craik, F.I.M., Moscovitch, M., Houle, S., 1994. Hemispheric encoding/retrieval asymmetry in episodic memory: positron emission tomography findings. Proc. Natl. Acad. Sci. USA 91, 2016–2020.

Turner, M.S., Cipolotti, L., Yousry, T., Shallice, T., 2007. Qualitatively different memory impairments across frontal lobe subgroups. Neuropsychologia 45, 1540–1552.

Turriziani, P., Oliveri, M., Salerno, S., Costanzo, F., Koch, G., Caltagirone, C., Carlesimo, G. A., 2008. Recognition memory and prefrontal cortex: dissociating recollection and familiarity processes using rTMS. Behav. Neurol. 19, 23–27.

Vann, S.D., Tsivilis, D., Denby, C.E., Quamme, J.R., Yonelinas, A.P., Aggleton, J.P., Montaldi, D., Mayes, A.R., 2009. Impaired recollection but spared familiarity in patients with extended hippocampal system damage revealed by 3 convergent methods. Proc. Natl. Acad. Sci. U S A 106, 5442–5447.

Verfaellie, M., Keane, M.M., 2002. Impaired and preserved memory processes in amnesia. In: Squire, L.R., Schacter, D. (Eds.), The neuropsychology of memory. Guilford Press, New York.

Wagner, A.D., Poldrack, R.A., Eldridge, L.L., Desmond, J.E., Glover, G.H., Gabrieli, J.D., 1998. Material-specific lateralization of prefrontal activation during episodic encoding and retrieval. Neuroreport 9, 3711–3717.

Wais, P.E., Wixted, J.T., Hopkins, R.O., Squire, L.R., 2006. The hippocampus supports both the recollection and the familiarity components of recognition memory. Neuron 49, 459–466.

Walsh, V., Cowey, A., 2000. Transcranial magnetic stimulation and cognitive neuroscience. Nat. Rev. Neurosci. 1, 73–79.

Warrington, E.K., 1984. The recognition memory tests. NFERNelson, Windsor, UK.

Wheeler, M.A., Stuss, D.T., 2003. Remembering and knowing in patients with frontal lobe injuries. Cortex 39, 827–846.

Wixted, J.T., 2007. Dual-process theory and signal-detection theory of recognition memory. Psychol. Rev. 114, 152–176.

Wixted, J.T., Squire, L.R., 2004. Recall and recognition are equally impaired in patients with selective hippocampal damage. Cog. Aff. Behav. Neurosci. 4, 58–66.

Yonelinas, A.P., 1994. Receiver-operating characteristics in recognition memory: evidence for a dual-process model. J. Exp. Psychol. Learn. Mem. Cog. 20, 1341–1354.

Yonelinas, A.P., 2002. The nature of recollection and familiarity: a review of 30 years of research. J. Mem. Lang. 46, 441–517.

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.

Yonelinas, A.P., Kroll, N.E., Quamme, J.R., Lazzara, M.M., Sauve, M.J., Widaman, K.F., Knight, R.T., 2002. Effects of extensive temporal lobe damage or mild hypoxia on recollection and familiarity. Nat. Neurosci. 5, 1236–1241.

Yonelinas, A.P., Otten, L.J., Shaw, K.N., Rugg, M.D., 2005. Separating the brain regions involved in recollection and familiarity in recognition memory. J. Neurosci. 25, 3002–3008.