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Disruption of the prefrontal cortex function by rTMS produces a category-specific enhancement of the reaction times during visual object identification

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ABSTRACT

Object identification is enabled through a distributed neural network but the relative contribution of the single components of this network is largely unknown. In the present study, we used online interference by repetitive transcranial magnetic stimulation (rTMS) to investigate the role of the dorso-lateral prefrontal cortex (DLPFC) in identifying semantically different stimuli presented as to make the decision process easy or difficult, according to the amount of sensory information available. Nineteen healthy volunteers performed an object identification task. Stimuli belonging to living and non-living categories were presented at different levels of spatial filtering following a coarse-to-fine order that gradually integrated spatial information. Six-pulse trains of 10-Hz rTMS were delivered at an intensity of 90% resting motor threshold simultaneously to the picture presentation. rTMS of either the left or right DLPFC produced a significant lengthening in the identification process of spatially filtered living stimuli, as shown by the increase in the reaction time, but not of non-filtered living stimuli or of non-living objects. rTMS over the vertex did not interfere with the identification task. These data indicate that DLPFC role in the network underlying object recognition is more crucial when this neural process is challenged by the level of sensory information available to the observer. Specificity of this effect for living objects is discussed taking into account the crucial role of DLPFC in recruitment of cognitive resources for accomplishing perceptual decision-making.

1. Introduction

How do we identify the objects we are looking at? The question of how the identification of semantically different stimuli is achieved in the human brain is still an open question. Neuropsychological, neuroimaging and electrophysiological studies have shown that the representation of visual stimuli belonging to different semantic categories relies on different neural substrates (Martin, 2007). The main dissociation between identification of natural objects or artefact has been accounted for referring to two main theories. The sensory/functional theory postulates that functional/action-related semantic features are relatively more relevant for representing artifacts whereas visual features are relatively more important for representing natural objects (Warrington & Shallice, 1984). The domain-specific theory (Caramazza & Shelton, 1998) assumes that evolutionary pressure resulted in the emergence of neuroanatomically and functionally specialized neural circuits dedicated to process specific semantic categories. According to this theory, object identification is the result of a dynamic interplay between perception and memory.

Recently, it has been demonstrated that such dynamic processes might be modulated by the semantic nature of the stimulus. By using filtered images and a presentation paradigm involving the sequential presentation of images with a progressively increasing content of high spatial frequencies, it has been shown that stimuli belonging to different semantic categories were identified at different levels of filtering (Vannucci, Viggiano, & Argenti, 2001; Viggiano, Costantini, Vannucci, & Righi, 2004; Viggiano, Righi, & Galli, 2006; Viggiano et al., 2007). The identification process uses a number of different and complex processes occuring in parallel at multiple levels of visual hierarchy. These processes are quickly activated during recognition, mediating the effortless identifica-

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tion of objects in just fractions of seconds typical of humans (Ishai, Ungerleider, Martin, Schouten, & Haxby, 1999). Theories over the last decades posit that the object recognition processes would begin with the extraction of sensory visual attributes in a coarse-to-fine processing scheme. Low spatial frequencies (LFs) representing the global information about the shape and orientation of the stimulus would be processed first. The analysis of high spatial frequencies (HFs) relevant for the local information (detection of visual details) (Bar, 2003; Braje, Tjan, & Legge, 1995; Hayes, Morrone, & Burr, 1986; Hughes, Nozawa, & Kitterle, 1996; Olds & Engel, 1998; Parker, Lishman, & Hughes, 1996) would follow. Even at coarsest information (at very low spatial frequencies), the visual system would generate hypotheses about object identity that might be confirmed or rejected at successive levels analysis involving higher spatial frequencies. Mismatches would lead to an extinction of the signal coding the current hypothesis alerting the system that a new pattern has to be generated (Grossberg, 1980). If additional physical information is revealed to the subject, a new hypothesis with higher recognition probability is generated and tested via attentional mechanism (Deco & Schürmann, 2000). As the sequence progresses, the "candidate" hypothesis finally match successfully with the representation stored in memory and recognition occurs. This iteractive and quick recursive process might be modulated by several variables such as the prior knowledge of the stimulus, which might determine the pre-allocation of resources (Carlson, Grol, & Verstraten, 2006), the context (Bar, 2004) or the orientation (Vannucci & Viggiano, 2000). Importantly, also the semantic nature of the stimulus affects the level of filtering at which the identification occurs: the category of animals is identified at a higher level of filtering (lower amount of physical information) with respect to the category of artefacts (Vannucci et al., 2001; Viggiano et al., 2004, 2006, 2007).

Given the complexity of such a process, it is challenging to draw an exhaustive sketch of the interconnections between the neuroanatomical structures underlying object identification. Neuroimaging studies have highlighted that a network of cortical areas involved in object recognition is coarsely localized in the ventral visual stream, which includes the temporal cortex (Logothetis & Sheinberg, 1996), the fusiform gyrus, the lateral occipital cortex, the inferotemporal cortex (Martin, Wiggs, Ungerleider, & Haxby, 1996; Malach, Levy, & Hasson, 2002; Carlson et al., 2006). However, the limited temporal resolution of neuroimaging makes it difficult to draw conclusions about the temporal sequence of activation in a network (Carlson et al., 2006). Therefore, neuroimaging studies are nicely complemented by studies employing techniques with higher temporal resolution such as transcranial magnetic stimulation (TMS). Our study specifically addresses this issue analysing the role of the prefrontal cortex (PFC) in category-specific visual object recognition.

PFC is strongly interconnected with the temporal lobe structures and seems to play an important role in multiple operations related to object recognition. In fact, it has been shown that it exerts a top-down control, as reported by several studies on humans and animals (Freedman, Riesenhuber, Poggio, & Miller, 2001; Ganis, Schendan, & Kosslyn, 2007). The PFC is thought to be engaged in the manipulation and monitoring of information and in the selection of processes specially when shreds of information are simultaneously active in memory and a decision has to be made taking into consideration the relevance of the stimuli (Petrides, 2000). The dorso-lateral prefrontal cortex (DLPFC) role in object recognition (Hofer et al., 2007) is commonly associated with the recruitment of cognitive resources. It maintains cognitive activities, aimed at achieving specific goals and provides the means for achieving those goals especially in presence of novel sensory information. DLPFC seems particularly active when cerebral resources are challenged (Hillary, Genova, Chiaravalloti, Rypma, & De Luca, 2006). When the task is particularly difficult because, e.g. of insufficient physical information, greater cognitive control may be required. In this respect, the activation of the DLPFC might be modulated by the sensory evidence available to the observer and its role might be particularly important when perceptual decision-making is made difficult by the reduction in sensory information available.

Heekeren, Marrett, Bandettini, & Ungerleider (2004) used an fMRI approach to investigate DLPFC involvement in visual decision-making when healthy humans were requested to choose whether a given image was a face or a house. To increase the difficulty of this categorization task, sensory information was arbitrarily modulated by adding noise to visual stimuli (Heekeren et al., 2004; Heekeren, Marrett, Ruff, Bandettini, & Ungerleider, 2006). The authors found that the amount of DLPFC activation predicted the accuracy of task performance. Their results paralleled previous animal data obtained by single-unit recordings, showing that neural activity in posterior DLPFC of monkeys performing a motion discrimination task increased proportionally to the strength of the motion signal in the stimulus (Kim & Shadlen, 1999; Heekeren et al., 2004).

A second question is whether or not the DLPFC is sensitive to the semantic nature of the stimuli. The existence of neurons selective for living subcategories has been demonstrated in primate PFC (Freedman et al., 2001). In humans, repetitive transcranial magnetic stimulation (rTMS) data show that the role of DLPFC in cognitive tasks is material specific/task dependent (Rossi et al., 2001). However, we are unaware of any causative studies to date on the involvement of human DLPFC in identification of visual stimuli as a function of their semantic nature.

On the bases of these findings, one may expect an involvement of DLPFC especially when physical information (e.g. only LFs) is scanty, stimulus presentation is short, and/or the stimulus is uncertain. In addition, decision-making could be modulated as function of the relevance of the stimuli in terms of their adaptive value.

The aim of the present study was to investigate the role of the DLPFC in processing semantically different stimuli presented as to make the decision process easy or difficult by manipulating the sensory evidence available to the observer. An on-line interference approach using focal rTMS was used. This technique can be employed to disrupt transiently the function of the stimulated cortical area and, therefore, may produce a temporary "virtual brain lesion" (Walsh & Rushworth, 1999; Pascual-Leone, Walsh, & Rothwell, 2000). rTMS was applied over the DLPFC while subjects participated in an identification task which involved pictures which were displayed at different levels of spatial filtering in an ascending sequence of frames following a coarse-to-fine order. This paradigm was inspired by the information processing approach to study how the brain captures the evolving of the representation of visual information and the relative identification time course.

2. Methods

2.1. Participants

We recruited 39 right-handed healthy volunteers (25 women; mean age 28.1 years, range 21–52 years) with normal or corrected-to-normal vision and no history of implanted metal devices or neurological disease. The study was performed according to the Declaration of Helsinki and the local ethics committee approved the use of rTMS. All subjects gave their written informed consent before participation. During the experiments, the subjects were asked to report adverse effects experienced during or after rTMS.

2.2. Visual stimuli and object identification task

Stimuli were 112 spatially filtered versions of gray-level photographs of real-life objects, belonging to animals ($n = 56$) and non-living objects (tools, clothing, furniture, kitchen utensils, musical instruments, and vehicles; $n = 56$), taken from a standardized set (Viggiano, Vannucci, & Righi, 2004) (Fig. 1). Four blocks of 28 stim-

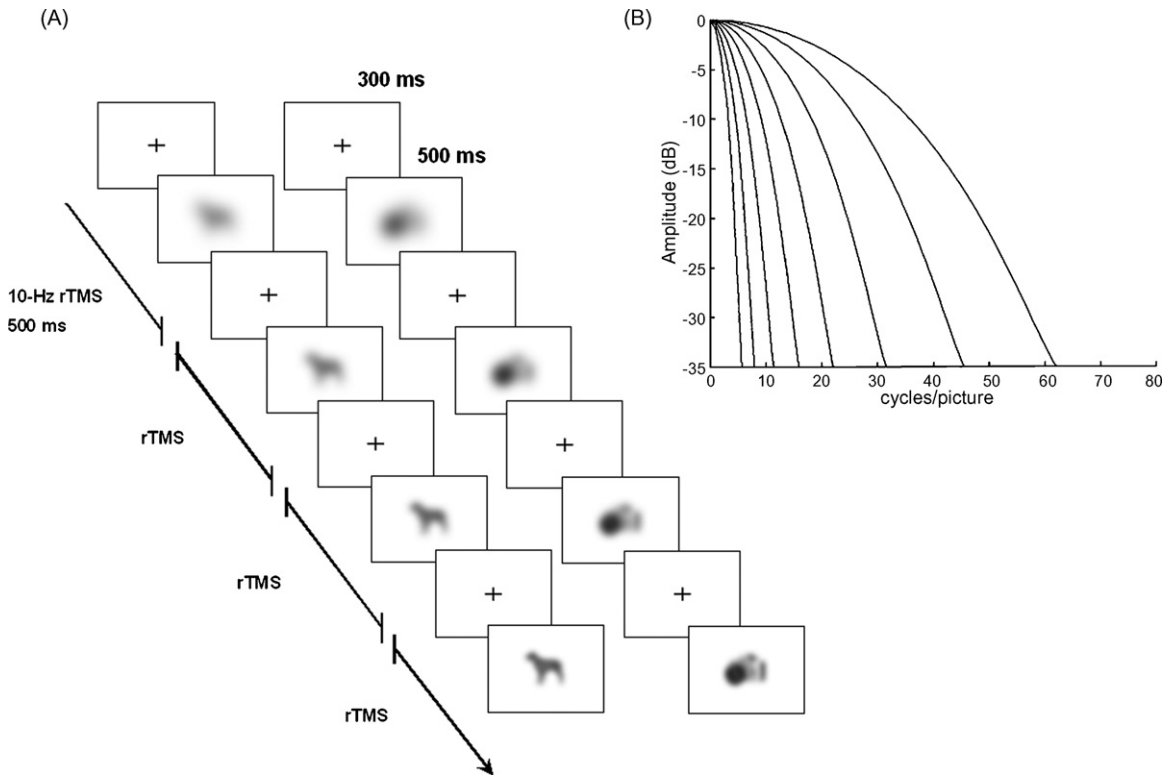

Fig. 1. (A) Time course of the experimental protocol with respect to object identification task and repetitive transcranial magnetic stimulation (rTMS). Stimuli were presented by an ascending sequence of nine filtering levels following a coarse-to-fine order. At each resolution level, the stimulus was displayed for 500 ms and was preceded by a fixation point for 300 ms. Trains of 10-Hz rTMS were delivered simultaneously with the picture presentation. The subjects were instructed to press a button as quickly as possible and to name the picture. If object naming was wrong, the subsequent version of the same image was shown. A representative sample in which subject identifies the stimuli ('dog' and 'camera') at the fourth level of filtering is reported. (B) Amplitude frequency responses (in logarithmic scale) of the low-pass digital filters used to obtain the different resolutions of stimuli.

uli (14 living and 14 non-living) were created. In each block, stimuli belonging to the living and non-living category were matched for visual complexity rates according to the normative data (Viggiano et al., 2004). Namely, visual complexity was evaluated according to a semiquantitative scale ranging from 1 ('visually simple') to 5 ('very visually complex') (Viggiano et al., 2004). In each block, unpaired *t*-test revealed no difference in visual complexity rates between the two groups of stimuli (*P* values: 0.12, 0.09, 0.47, and 0.34). Subjects were seated in a comfortable chair and the images were displayed on a computer screen and subtended a visual angle of 7.5° by 7.5°, on average. The stimuli were blurred by removing ranges of spatial frequencies from the spectrum of the image (Fig. 1). This filtering process creates a multiresolution representation of the scanned images. The different resolutions were obtained by means of a digital filter applied to the bidimensional array representing the original image scanned at the resolution of 300 dpi. The multiresolution filter selected was the Gaussian mask that performs a lowpass filtering. This function is related to Marr's model of human vision (Marr, 1982). The width of the filtering window was the key parameter that determined the bandwidth of the filter (Fig. 1). Unless stated otherwise (see Control 2 experiment), nine different filtering levels were used and each image was presented in an ascending way, starting from the most blurred (level 1) and adding high spatial frequencies until the original resolution version (level 9) (Fig. 1). At each resolution level, the stimulus was displayed for 500 ms (Viggiano & Kutas, 1998, 2000). The subjects were requested to press a button with the right index finger as soon as possible after presumed object identification. Afterward, they were asked to name the stimulus. If the object identification had actually occurred, then the following image was presented. In contrast, if object naming was wrong, the subsequent, less filtered version of the same image was shown (Fig. 1). The presentation order of the stimuli was randomized for each participant. The experimental phase was preceded by a training phase in which different pictures were used.

2.3. Transcranial magnetic stimulation

rTMS was delivered using a Magstim Rapid stimulator with a biphasic current waveform (Magstim Co., UK), connected to an eight-shaped coil (external diameter of each loop, 9 cm) placed tangentially to the scalp, with the handle pointing backwards and 45° away from the midline. Prior to object identification experiments, single magnetic pulses were delivered to the hand area of each primary motor cortex to establish the resting motor threshold (RMT) in either first dorsal interosseous (FDI) muscle. RMT was measured with the coil placed at the optimal position (hot spot) to elicit motor evoked potentials in the contralateral FDI, and was defined as the minimum stimulus intensity that produced MEP > 50 μV in at least 5 of 10 consecutive trials during muscle relaxation (Rossini et al., 1994). During the object identification task, focal 10-Hz rTMS was used to disrupt the activity of different cortical areas. The 10-Hz rTMS trains consisted of 6 pulses (train duration 500 ms) delivered simultaneously to the picture presentation (Fig. 1) at an intensity of 90% RMT of the contralateral FDI. The 6 pulses of the rTMS train were delivered at 0, 100, 200, 300, 400, and 500 ms from the onset of the picture presentation. This timing of stimulation was chosen in order to ensure an interference during all the perceptual processing. These rTMS parameters were in accordance with published international safety recommendations (Wassermann, 1998). A specially designed eight-shaped coil that produces no magnetic field but mimics the acoustic artefact of real stimulation (Magstim Co.) was used to deliver 500-ms long trains of sham rTMS at 10-Hz during image presentation.

2.4. Experimental protocols

The study consisted of one main target experiment and two control experiments (Controls 1 and 2). Participants differed across the three experiments to avoid repetition of picture presentation in the same subject.

In the Main experiment (19 subjects), the object identification task was performed in four different experimental conditions: no rTMS (baseline), real rTMS of the left DLPFC, real rTMS of the right DLPFC, and sham rTMS of the left DLPFC during image presentation (Fig. 2A). For stimulation of the left and right DLPFC, the centre of the junction of the coil was placed over F3 and F4 positions of the 10–20 EEG International System, respectively, which correspond to the Brodmann area 9 (Rossi et al., 2001). Twenty-eight pictures (14 living and 14 non-living) were presented in each condition. Pictures differed across the different experimental conditions.

Control 1 experiment (10 subjects) was designed to test whether the change in object identification observed with real rTMS of the DLPFC in the Main experiment (see Section 3) were topographically specific. The object identification task was performed in two experimental conditions: no rTMS (baseline) and real rTMS delivered

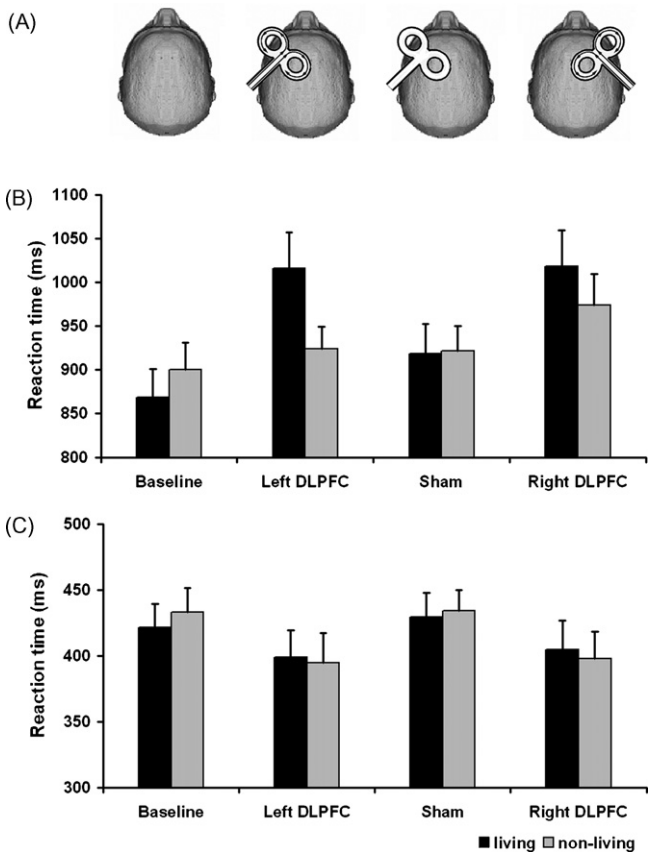

Fig. 2. (A) Coil placements in the different experimental conditions in the Main and in Control 2 experiments. From the left to the right of the figure: no rTMS (baseline), real rTMS of the left DLPFC, sham rTMS of the left DLPFC, and real rTMS of the right DLPFC. (B) Mean values and standard errors of reaction times in the Main experiment. Interference by rTMS of either the left or right DLPFC induced a significant prolongation of the reaction times compared to baseline and sham stimulation conditions, specifically for stimuli belonging to the living category. (C) Mean values and standard errors of reaction times in Control 2 experiment (object identification of non-filtered pictures). No significant difference in reaction times was seen between experimental conditions.

2 cm behind the vertex (Cz' of the 10–20 EEG International System). Otherwise, the experimental setup was identical to the Main experiment.

In Control 2 experiment (10 subjects), only the original resolution versions (level 9) of the images were displayed to test whether the effect produced by real rTMS of the DLPFC during identification of filtered pictures (see Section 3 of the Main experiment) also occurred during recognition of the spatially non-filtered images. Real pictures and 10 scrambled stimuli (distractors) were intermingled to avoid an automatic response. Each stimulus was displayed for 200 ms. Participants were instructed to press the button only when a real image was displayed. Afterward, they were asked to name the stimulus. Otherwise, the experimental setup was identical to the Main experiment.

In all experiments, the order of experimental conditions and coupling between blocks of visual stimuli and experimental conditions were randomized and counterbalanced across subjects.

2.5. Measures and statistical analysis

The primary measures used to quantify object identification were the level of filtering at which the visual stimulus was correctly identified (accuracy) and the reaction time between the beginning of identified stimulus presentation and motor responses (RTs). In each participant, mean accuracy and RT were separately calculated in each experimental condition and semantic category (living and non-living).

For each experiment (Main and Controls), the dependent variables (accuracy and RT) were entered in separate two-way repeated-measures analyses of variance (ANOVA) with experimental condition (4, 2, and 4 levels in Main, Control 1, and Control 2 experiments, respectively) and semantic category (two levels: living and non-living) as within-subject factors. Post hoc tests were performed using Tukey's test. Significance was set at $P < 0.05$.

3. Results

None of the participants reported adverse effects during or after the experimental procedures.

In the Main experiment (see Section 2, Fig. 2A), repeated-measures ANOVA showed a significant main effect of experimental condition on RTs ($F = 5.835$, $P = 0.002$), whereas the main effect of semantic category was not significant ($F = 1.552$, $P = 0.229$). There was a significant interaction between these two factors ($F = 3.070$, $P = 0.035$). Post hoc comparisons revealed that real rTMS of both the left and the right DLPFC significantly prolonged RTs with respect to baseline ($P < 0.001$ for both left and right DLPFC) and sham stimulation ($P = 0.044$ and $P = 0.037$ for left and right DLPFC, respectively) specifically for stimuli belonging to the living category (Fig. 2B). In contrast, for stimuli belonging to the non-living category no significant effect emerged on the RTs (left DLPFC vs. baseline: $P = 0.916$; left DLPFC vs. sham: $P = 1.00$; right DLPFC vs. baseline: $P = 0.185$; right DLPFC vs. sham: $P = 0.478$). Post hoc tests also showed a significant difference between living and non-living category when rTMS was applied over the left DLPFC ($P = 0.008$) but not when was applied over the right DLPFC ($P = 0.195$). The stronger category-effect after interference with left DLPFC depended on a moderate, non-significant prolongation of the RTs with respect to the baseline for non-living stimuli with real rTMS of the right DLPFC.

For living category, the mean values ± S.D. of the level of filtering at which the visual stimulus was correctly identified (accuracy) in the different experimental conditions were 4.3 ± 0.7 (baseline), 4.7 ± 0.6 (rTMS of the left DLPFC), 4.7 ± 0.5 (sham stimulation), and 4.6 ± 0.4 (rTMS of the right DLPFC). For non-living stimuli, mean accuracy values ± S.D. were 4.5 ± 0.4 (baseline); 4.4 ± 0.4 (rTMS of the left DLPFC); 4.5 ± 0.5 (sham stimulation), and 4.6 ± 0.6 (rTMS of the right DLPFC). The repeated-measures ANOVA showed no significant effect on the accuracy (experimental condition: $F = 1.887$, $P = 0.143$; semantic category: $F = 3.826$, $P = 0.066$; interaction: $F = 1.566$, $P = 0.208$).

In Control 1 experiment, repeated-measures ANOVA did not reveal significant differences in accuracy (experimental condition: $F = 1.255$, $P = 0.310$; semantic category: $F = 1.020$, $P = 0.339$; interaction: $F = 2.112$, $P = 0.122$) and RTs (experimental condition: $F = 0.281$, $P = 0.609$; semantic category: $F = 0.925$, $P = 0.361$; interaction: $F = 0.029$, $P = 0.868$) when baseline and real rTMS over Cz' where compared.

In Control 2 experiment, repeated-measures ANOVA did not show significant differences in accuracy (experimental condition: $F = 2.139$, $P = 0.119$; semantic category: $F = 4.571$, $P = 0.061$; interaction: $F = 0.615$, $P = 0.611$) and RTs (experimental condition: $F = 2.511$, $P = 0.080$; semantic category: $F = 0.833$, $P = 0.385$; interaction: $F = 1.508$, $P = 0.235$) when non-filtered pictures were used (Fig. 2C).

4. Discussion

Recent studies indicate that the PFC with its strong connections to the inferior temporal cortex (Bar, 2003; Ganis et al., 2007) might play an active role in the cortical network that mediates visual object identification. Although the advent of sophisticated techniques has gradually enabled clarification of the functional contributions of the prefrontal region, the specific roles of subregions within the prefrontal cortex are still unclear. The DLPFC is thought to be involved in many tasks especially in relation to verbal working memory (Smith, Jonides, & Koeppe, 1996; Hillary et al., 2006); but less is known about its role in object identification.

The present study aimed at determining whether – and to what extent – the prefrontal area is involved when subjects are actively

involved in the identification process of stimuli progressively easier to identify due to the progressive addition of higher spatial frequencies. rTMS represents a useful method to interfere transiently with the ongoing task subserved by neural networks implicated in specific cognitive processes; in addition it can be used as a direct test of the causal role of a given task to assess what areas are relevant for a specific task (Pascual-Leone et al., 2000).

The main new finding of the present study is that rTMS produced an increase of RTs when it was applied over the DLPFC compared to the baseline condition during the identification task. This effect significantly exceeds the non-significant, slight increase that was found in the sham condition. The effect of rTMS over the DLPFC seems to be category-specific. Indeed, RT increase was observed for stimuli belonging to the living but not to the non-living category. In addition, subjects were significantly slower in identifying living images when rTMS was applied over both the left and right DLPFC, supporting the hypothesis of bilaterally activation for animals (Grabowski, Damasco, & Damasco, 1998; Kim & Shadlen, 1999; Martin & Chao, 2001; Tranel, Damasio, & Damasio, 1997).

A significant semantic difference in RTs has been observed when the rTMS was applied over the left DLPFC. In contrast, after right DLPFC stimulation, the difference between living vs. non-living was not significant, probably because of a moderate, and statistically non-significant, prolongation of the reaction times also for non-living stimuli. This finding cannot be accounted for by the non-specific effect of TMS because the interference over the vertex did not produce a delay in time response. Therefore, this result supports the hypothesis of a prefrontal bilateral activation for living category. On the other hand, a potential hemispheric-effect could be suggested for stimuli belonging to non-living semantic category even if further studies are needed to support this hypothesis.

Our results show that RT prolongation produced by rTMS of each DLPFC occurs without significant changes in the amount of visual information needed to object identification (as instead observed in previous behavioural studies). The lack of focal rTMS effects on accuracy may merely reflect the fact that the neural network underlying visual object identification is distributed and involves several cortical areas in addition to the DLPFC. However, the alternative hypothesis that dissociation between accuracy and RT may be more specifically related to the role of DLPFC in object recognition should be taken in account. DLPFC seems less related to the process of sensory analysis and more to that of perceptual decision. Several authors have shown that, during a simple RT, execution of the movement is delayed by focal TMS of the M1 contralateral to the motor task (Day et al., 1989; Rossini, Zarola, Stalberg, & Caramia, 1988; Ziemann, Tergau, Netz, & Hmberg, 1997). However, this delay occurs without changes in the pattern of the agonist and antagonist electromyographic bursts in the target muscles, suggesting that TMS transiently interferes with the execution of a motor program already stored in the motor cortex (Day et al., 1989). Similarly, in the present experiment, rTMS of the DLPFC could prolong the RT by transient inhibition of group of neurons whose activation in the process of visual recognition at a given level of sensory information is already programmed. Nevertheless, when rTMS is applied to the DLPFC during other cognitive tasks, the interference pattern may differ from that we have observed during visual recognition. Namely, using an episodic memory paradigm, Rossi et al. (2001) found that high-frequency rTMS of the right DLPFC specifically worsened the accuracy of retrieval of encoded picture information. In contrast, reaction times were shortened by either real or sham rTMS, suggesting a nonspecific arousal effect on this variable (Rossi et al., 2001). Furthermore, it has been reported that during action naming, high-frequency rTMS of the DLPFC speeded up task performance in young healthy volunteers (Cappa, Sandrini, Rossini, Sosta, & Miniussi, 2002) and even improved performance accuracy in patients with Alzheimer's disease (Cotelli et al., 2006). These differences may support the view that disrupting effects of focal rTMS do not merely depend on the stimulated cortical area and more likely reflect the engagement of distinct neuronal subsets in different tasks.

It is important to note that no effect of rTMS of the DLPFC was observed when non-filtered living stimuli were presented. This strongly suggests that DLPFC role in the neural network underlying object recognition is particularly crucial when this neural process is challenged by the low level of sensory information available to the observer.

The tendency for a faster response observed for animal images in baseline condition are in line with previous studies where an advantage for animals – in terms of speed of response and/or amount of physical information required – has been observed. (New, Cosmides, & Tooby, 2007; Vannucci et al., 2001; Viggiano et al., 2004, 2006, 2007). It has been hypothesized the existence of a mechanism in the PFC which acts as a cortical source of a top-down facilitation in visual object recognition. Such a mechanism generates prediction on stimulus identity by analysing coarse visual information of the image resulting in early top-down facilitation (Bar, 2003; Bar et al., 2006; Frith & Dolan, 1997; Petrides, 2000). Bar, however localized the source of the top-down facilitation in the orbitofrontal cortex. The fact that this top-down mechanism seems to be more active in presence of exemplars belonging to ancestrally important categories, such as animals, suggests a domain-specific subsystem as an adaptive mechanism designed for detecting the presence of human and non-human animals (Caramazza & Mahon, 2003; Caramazza & Shelton, 1998) and monitoring them in their state and location changes (New et al., 2007).

This top-down mechanism should be particularly active and effective in situation of insufficient physical information where a fuzzy input-representation activates the mnemonic network to obtain the most likely interpretation of the input. It is likely that in this context the DLPFC might play its most relevant role. A fast perceptual decision-making under these critical conditions requires massive recruitment of cognitive resources. Recent fMRI studies have suggested that the DLPFC is crucial in the recruitment of cognitive resources for accomplishing perceptual decision-making, especially when poor sensory evidence is available to the observer (Heekeren et al., 2004, 2006). More cognitive resources may be necessary for stimuli identification when physical information is revealed gradually.

Therefore, on one hand the differential results associated with DLPFC stimulation as a function of semantic category might be due by the fact that animals, as vital features of the visual environment, represent salient stimuli. Converging evidence comes from study of León-Carrión et al. (2007), where activation in DLPFC has been found to depend on the affective salience of the stimuli: persists after stimulus cessation and this does not occur with non-arousing stimuli: in particular, the activation persists after stimulus cessation for more salient stimuli, but not for non-arousing stimuli.

On the other hand it is worth to note that animals have a more complex intrinsic physical structure compared to artefacts and share several visual-perceptual features (i.e., legs, head, ears, tail), it could be more difficult to recognise them as a single exemplar. In this respect, a larger number of "candidate" hypotheses are generated until a successful match is made with the representation stored in the memory. Hadland, Rushworth, Passingham, Jahanshahi, & Rothwell (2001) showed with TMS that the DLPFC is important in decision-making processes implying the selection from multiple hypotheses arising from the amount of available physical information. It is likely that our task, given its nature (sequential presentation of progressively less filtered images), also engages working memory processes requiring DLPFC. Indeed,

Mottaghy, Gangitano, Sparing, Krause, & Pascual-Leone (2002) found that TMS of the DLPFC affected visuospatial working memory. Recent neuropsychological studies support the hypothesis that DLPFC could be important in identification tasks requiring selection from multiple hypothesis. In an identification task of filtered stimuli, the animal recognition impairment observed in Parkinson disease (Righi, Viggiano, Paganini, Ramat, & Marini, 2007) was attributed to the presence of multiple competing implicit hypotheses for this semantic category. This hypothesis is consistent with several other recent studies using multi-priming paradigms with verbal stimuli (Angwin, Chenery, Copland, Murdoch, & Silburn, 2005; Arnott, Chenery, Murdoch, & Silburn, 2001), where it has been reported that the semantic deficits of Parkinson patients are specifically linked to the presence of semantic competitors. Specifically, the dopaminergic neurons of the DLPFC and the dorsal striatum seem to be the substrates that are most involved in set shifting (Cools, 2006; Ravizza & Ciranni, 2002) and active manipulation of information within working memory (Owen, 2004) as well as in top-down representation stability during the categorization tasks (Kéri, 2003).

In conclusion, the DLPFC of both hemispheres seems to be involved in the network for object recognition and its contribution is modulated by the salience of the stimulus especially when the perceptual decision-making is challenged by the sensory information available to the observer.

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References

Angwin, A. J., Chenery, H. J., Copland, D. A., Murdoch, B. E., & Silburn, P. A. (2005). Summation of semantic priming and complex sentence comprehension in Parkinson's disease. *Cognitive Brain Research*, *25*, 78–89.

Arnott, W. L., Chenery, H. J., Murdoch, B. E., & Silburn, P. A. (2001). Semantic priming in Parkinson's disease: Evidence for delayed spreading activation. *Journal of Clinical Experimental Neuropsychology*, *23*, 502–519.

Bar, M. (2003). A cortical mechanism for triggering top-down facilitation in visual object recognition. *Journal of Cognitive Neuroscience*, *154*, 600–609.

Bar, M. (2004). Visual objects in context. *Nature Reviews Neuroscience*, *5*, 617–629.

Bar, M., Tootell, R. B., Schacter, D. L., Greve, D. N., Fischl, B., Mendola, J. D., et al. (2001). Cortical mechanisms specific to explicit visual object recognition. *Neuron*, *29*, 529–535.

Bar, M., Kassam, K. S., Ghuman, A. S., Boshyan, J., Schmid, A. M., Dale, A. M., et al. (2006). Top-down facilitation of visual recognition. In *Proceedings of the National Academy of Sciences of the United States of America, Vol. 103* (pp. 449–454).

Braje, W. L., Tjan, B. S., & Legge, G. E. (1995). Human efficiency for recognizing and detecting low-pass filtered objects. *Vision Research*, *35*, 2955–2966.

Cappa, S. F., Sandrini, M., Rossini, P. M., Sosta, K., & Miniussi, C. (2002). The role of the left frontal lobe in action naming: rTMS evidence. *Neurology*, *59*, 720–723.

Caramazza, A., & Mahon, B. Z. (2003). The organization of conceptual knowledge: The evidence from category-specific semantic deficits. *Trends in Cognitive Science*, *7*, 354–361.

Caramazza, A., & Shelton, J. R. (1998). Domain-specific knowledge systems in the brain the animate–inanimate distinction. *Journal of Cognitive Neuroscience*, *10*, 1–34.

Carlson, T., Grol, M. J., & Verstraten, F. A. (2006). Dynamics of visual recognition revealed by fMRI. *Neuroimage*, *32*, 892–905.

Cools, R. (2006). Dopaminergic modulation of cognitive function-implications for L-DOPA treatment in Parkinson's disease. *Neuroscience & Biobehavioral Reviews*, *30*, 1–23.

Cotelli, M., Manenti, R., Cappa, S. F., Geroldi, C., Zanetti, O., Rossini, P. M., et al. (2006). Effect of transcranial magnetic stimulation on action naming in patients with Alzheimer disease. *Archives of Neurology*, *63*, 1602–1604.

Day, B. L., Rothwell, J. C., Thompson, P. D., Maertens de Noordhout, A., Nakashima, K., Shannon, K., et al. (1989). Delay in the execution of voluntary movement by electrical or magnetic brain stimulation in intact man. Evidence for the storage of motor programs in the brain. *Brain*, *112*, 649–663.

Deco, G., & Schürmann, B. (2000). A hierarchical neural system with attentional top-down enhancement of the spatial resolution for object recognition. *Vision Research*, *40*, 2845–2859.

Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2001). Categorical representation of visual stimuli in the primate prefrontal cortex. *Science*, *12*, 312–316.

Frith, C., & Dolan, R. J. (1997). Brain mechanisms associated with top-down processes in perception. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *352*, 1221–1230.

Ganis, G., Schendan, H. E., & Kosslyn, S. M. (2007). Neuroimaging evidence for object model verification theory: Role of prefrontal control in visual object categorization. *Neuroimage*, *34*, 384–398.

Grabowski, T. J., Damasco, H., & Damasco, A. R. (1998). Premotor and prefrontal correlates of category-related lexical retrieval. *Neuroimage*, *7*, 232–243.

Grossberg, S. (1980). How does a brain build a cognitive code? *Psychological Review*, *87*, 1–51.

Hadland, K. A., Rushworth, M. F., Passingham, R. E., Jahanshahi, M., & Rothwell, J. C. (2001). Interference with performance of a response selection task that has no working memory component: An rTMS comparison of the dorsolateral prefrontal and medial frontal cortex. *Journal of Cognitive Neuroscience*, *13*, 1097–1108.

Hayes, A., Morrone, M. C., & Burr, D. C. (1986). Recognition of positive and negative band-pass filtered images. *Perception*, *15*, 595–602.

Heekeren, H. R., Marrett, S., Bandettini, P. A., & Ungerleider, L. G. (2004). A general mechanism for perceptual decision-making in the human brain. *Nature*, *14*, 859–862.

Heekeren, H. R., Marrett, S., Ruff, D. A., Bandettini, P. A., & Ungerleider, L. G. (2006). Involvement of human left dorsolateral prefrontal cortex in perceptual decision making is independent of response modality. In *Proceedings of the National Academy of Sciences of the United States of America, Vol. 103* (pp. 10023–10028).

Hillary, F. G., Genova, H. M., Chiaravalloti, N. D., Rypma, B., & De Luca, J. (2006). Prefrontal modulation of Working Memory performance in brain injury and disease. *Human Brain Mapping*, *27*, 837–847.

Hofer, A., Siedentopf, C. M., Ischebeck, A., Rettenbacher, M. A., Widschwendter, C. G., Verius, M., et al. (2007). The neural regions sustaining episodic encoding and recognition of objects. *Brain and Cognition*, *63*, 159–166.

Hughes, H. C., Nozawa, G., & Kitterle, F. (1996). Global precedence, spatial frequency channels, and the statistics of natural images. *Journal of Cognitive Neuroscience*, *8*, 197–230.

Ishai, A., Ungerleider, L. G., Martin, A., Schouten, J. L., & Haxby, J. (1999). Distributed representation of objects in the human ventral visual pathway. In *Proceedings of the National Academy of Sciences of the United States of America, Vol. 96* (pp. 9379–9384).

Kéri, S. (2003). The cognitive neuroscience of category learning. *Brain Research Reviews*, *43*, 85–109.

Kim, J. N., & Shadlen, M. N. (1999). Neural correlates of a decision in the dorsolateral prefrontal cortex of macaque. *Nature Neuroscience*, *2*, 176–185.

León-Carrión, J., Martín-Rodríguez, J. F., Damas-López, J., Pourrezai, K., Izzetoglu, K., Barroso y Martin, J. M., et al. (2007). A lasting post-stimulus activation on dorsolateral prefrontal cortex is produced when processing valence and arousal in visual affective stimuli. *Neuroscience Letters*, *422*, 147–152.

Logothetis, N. K., & Sheinberg, D. L. (1996). Visual object recognition. *Annual Review of Neuroscience*, *19*, 577–621.

Malach, R., Levy, I., & Hasson, U. (2002). The topography of high-order human object areas. *Trends in Cognitive Science*, *6*, 176–184.

Marr, D. (1982). *Vision: A computational investigation into the human representation and processing of visual information, eds*. San Francisco: Freeman WH.

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

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

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

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. *Cerebral Cortex*, *12*, 369–375.

New, J., Cosmides, L., & Tooby, J. (2007). Category-specific attention for animals reflects ancestral priorities, not expertise. In *Proceedings of the National Academy of Sciences of the United States of America, Vol. 104* (pp. 16598–16603).

Olds, E. S., & Engel, S. A. (1998). Linearity across spatial frequency in object recognition. *Vision Research*, *38*, 2109–2118.

Owen, A. M. (2004). Cognitive dysfunction in Parkinson's disease: The role of frontostriatal circuitry. *Neuroscientist*, *10*, 525–557.

Parker, D. M., Lishman, R., & Hughes, J. (1996). Role of coarse and fine spatial information in face and object processing. *Journal of Experimental Psychology: Human Perception and Performance*, *22*, 1448–1466.

Pascual-Leone, A., Walsh, V., & Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience–virtual lesion, chronometry, and functional connectivity. *Current Opinion in Neurobiology*, *10*, 232–237.

Petrides, M. (2000). Dissociable roles of mid-dorsolateral prefrontal and anterior inferotemporal cortex in visual working memory. *The Journal of Neuroscience*, *20*, 7496–7503.

Ravizza, S. M., & Ciranni, M. A. (2002). Contributions of the prefrontal cortex and basal ganglia to set shifting. *Journal of Cognitive Neuroscience*, *14*, 472–483.

Righi, S., Viggiano, M. P., Paganini, M., Ramat, S., & Marini, P. (2007). Recognition of category-related visual stimuli in Parkinson's disease: Before and after pharmacological treatment. *Neuropsychologia*, *45*, 2931–2941.

Rossi, S., Cappa, S. F., Babiloni, C., Pasqualetti, P., Miniussi, C., Carducci, F., et al. (2001). Prefontal cortex in long-term memory: An "interference" approach using magnetic stimulation. *Nature Neuroscience*, *4*, 948–952.

Rossini, P. M., Zarola, F., Stalberg, E., & Caramia, M. (1988). Pre-movement facilitation of motor-evoked potentials in man during transcranial stimulation of the central motor pathways. *Brain Research*, *458*, 20–30.

Rossini, P. M., Barker, A. T., Berardelli, A., Caramia, M. D., Caruso, G., Cracco, R. Q., et al. (1994). Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: Basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalography and Clinical Neurophysiology*, *91*, 79–92.

Smith, E. E., Jonides, J., & Koeppe, R. A. (1996). Dissociating verbal and spatial working memory using PET. *Cerebral Cortex*, *6*, 11–20.

Tanaka, K. (1996). Inferotemporal cortex and object vision. *Annual Review of Neuroscience*, *19*, 109–139.

Tranel, D., Damasio, H., & Damasio, A. R. (1997). A neural basis for the retrieval of conceptual knowledge. *Neuropsychologia*, *35*, 1319–1327.

Vannucci, M., & Viggiano, M. P. (2000). Category effects on the processing of plane-rotated objects. *Perception*, *29*, 287–302.

Vannucci, M., Viggiano, M. P., & Argenti, F. (2001). Identification of spatially filtered stimuli as function of the semantic category. *Cognitive Brain Research*, *12*, 475–478.

Viggiano, M. P., & Kutas, M. (1998). The covert interplay between perception and memory: Event-related potential evidence. *Electroencephalography and Clinical Neurophysiology*, *108*, 435–439.

Viggiano, M. P., & Kutas, M. (2000). Overt and covert identification of fragmented objects inferred from performance and electrophysiological measures. *Journal of Experimental Psychology: General*, *129*, 107–125.

Viggiano, M. P., Costantini, A., Vannucci, M., & Righi, S. (2004). Hemispheric asymmetry for spatially filtered stimuli belonging to different semantic categories. *Cognitive Brain Research*, *20*, 519–524.

Viggiano, M. P., Vannucci, M., & Righi, S. (2004). A new standardized set of ecological pictures for experimental and clinical research on visual object processing. *Cortex*, *40*, 491–509.

Viggiano, M. P., Righi, S., & Galli, G. (2006). Category-specificity visual recognition has affected by aging and profession. *Archives of Gerontology and Geriatrics*, *42*, 329–338.

Viggiano, M. P., Gori, G., Zaccara, G., Righi, S., Vannucci, M., & Giovannelli, F. (2007). Category-specific visual identification of filtered objects in Alzheimer's disease. *Archives of Gerontology and Geriatrics*, *44*, 125–139.

Walsh, V., & Rushworth, M. (1999). A primer of magnetic stimulation as a tool for neuropsychology. *Neuropsychologia*, *37*, 125–135.

Warrington, E. K., & Shallice, T. (1984). Category specific semantic impairments. *Brain*, *107*, 829–854.

Wassermann, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: Report and suggested guidelines from the international workshop on the safety of repetitive transcranial magnetic stimulation, June 5–7, 1996. *Electroencephalography and Clinical Neurophysiology*, *108*, 1–16.

Ziemann, U., Tergau, F., Netz, J., & Hmberg, V. (1997). Delay in simple reaction time after focal transcranial magnetic stimulation of the human brain occurs at the final motor output stage. *Brain Research*, *744*, 32–40.