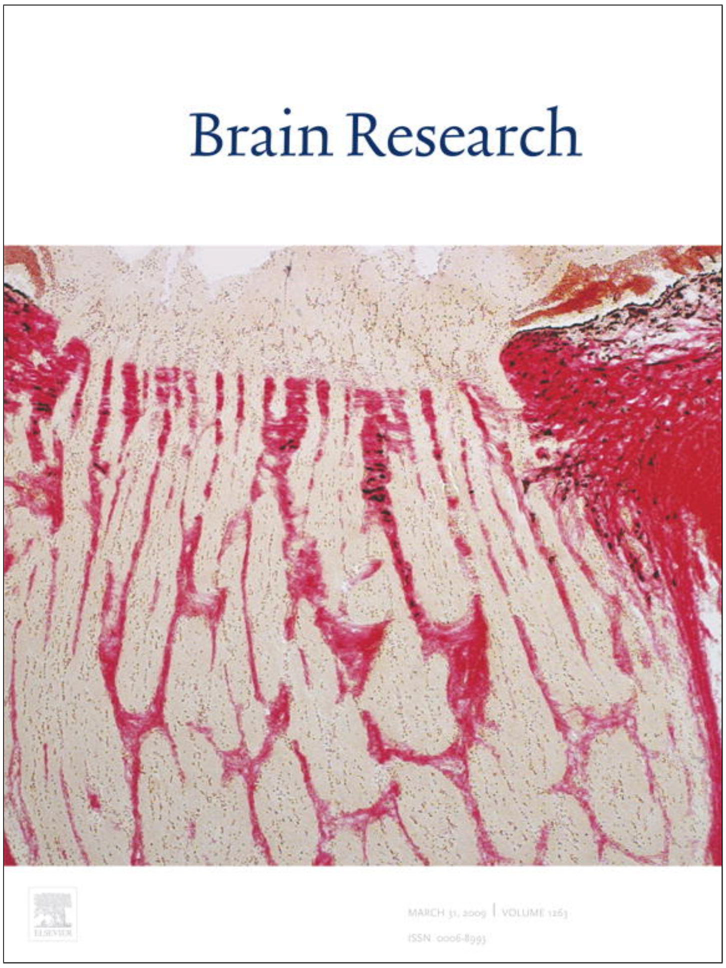

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Research Report

The lexical processing of abstract and concrete nouns

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ABSTRACT

Recent activation studies have suggested different neural correlates for processing concrete and abstract words. However, the precise localization is far from being defined. One reason for the heterogeneity of these results could lie in the extreme variability of experimental paradigms, ranging from explicit semantic judgments to lexical decision tasks (auditory and/or visual). The present study explored the processing of abstract/concrete nouns by using repetitive Transcranial Magnetic Stimulation (rTMS) and a lexical decision paradigm in neurologically-unimpaired subjects. Four sites were investigated: left inferior frontal, bilaterally posterior-superior temporal and left posterior-inferior parietal. An interference on accuracy was found for abstract words when rTMS was applied over the left temporal site, while for concrete words accuracy decreased when rTMS was applied over the right temporal site. Accuracy for abstract words, but not for concrete words, decreased after frontal stimulation as compared to the sham condition. These results suggest that abstract lexical entries are stored in the posterior part of the left temporal superior gyrus and possibly in the left frontal inferior gyrus, while the regions involved in storing concrete items include the right temporal cortex. It cannot be excluded, however, that additional areas, not tested in this experiment, are involved in processing both, concrete and abstract nouns.

1. Introduction

A better performance with concrete as compared to abstract nouns (e.g., lexical decision is faster and recall is superior for concrete terms than abstract items) has been demonstrated in a number of psycholinguistic studies (for a review see Paivio, 1991), and is the rule in aphasia (e.g., Coltheart et al., 1980), although neuropsychological patients with a reversal of concreteness effect have been reported (Breedin et al., 1994; Macoir, 2008; Papagno et al., in press; Sirigu et al., 1991; Warrington, 1975, 1981).

Two main models have been proposed to explain the concreteness effect. The dual-coding theory claims that the processing of abstract nouns relies on verbal code representations of the left cerebral hemisphere only, whereas concrete nouns additionally access a second image-based processing system eventually located in the right hemisphere (Paivio, 1991). The alternative model, the context availability theory (Schwanenflugel and Shoben, 1983), argues that the faster recognition of concrete vs. abstract nouns results from a larger contextual support of concrete words and not from a distinct non verbal system; this theory does not explicitly rule out a

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Table 1 – Neuropsychological cases with reversal of concreteness effect

Authors	Patient	Aetiology	Lesion site
Warrington (1975)	AB	Atrophy	Bilateral
Warrington (1981)	CAV	Glioma	Left T-P-O
Warrington and Shallice (1984)	SBY	HSE	Bilateral T
Sirigu et al. (1991)	FB	HSE	Bilateral medial T
Breedin et al. (1994)	DM	SD	Bilateral ITG, >left ant
Marshall et al. (1996)	RG	CVA	Left (? no details)
Bachoud-Lévi and Dupoux (2003)	DPI	CVA	Left T
Papagno et al. (in press)	MC	SD	Bilateral T, >left ant
Macoir (2008)	SC	SD	Bilateral T, >left

HSE = herpes simplex encephalitis, CVA = cerebrovascular accident, SD = semantic dementia, T = temporal, P = parietal, O = occipital, ITG = inferior temporal gyrus, ant = anterior.

right hemisphere involvement, but attributes the concreteness effect purely to the access of more verbal information, which implies a predominantly left-hemisphere-based processing system. These theories assume a quantitative distinction between concrete and abstract concepts, but none of them can explain the presence of brain-damaged patients with a reversal of concreteness effect, i.e., a superiority of abstract concepts with respect to concrete ones. So far, a few single cases have been reported in the literature with poorer concrete than abstract concept knowledge (Breedin et al. 1994; Macoir, 2008; Marshall et al., 1996; Papagno et al., in press; Sirigu et al., 1991; Warrington, 1975, 1981; Warrington and Shallice, 1984) (see Table 1), supporting however the view that concrete and abstract words are represented in a different qualitative way in the brain.

The association of a poorer performance with concrete than abstract concept with semantic dementia or herpes simplex encephalitis is striking. Both these pathological conditions systematically affect anterior temporal regions. Therefore, the anatomoclinical correlates of the reverse concreteness effect prompt considerations on the role of these regions in processing abstract and concrete terms.

Neuroimaging studies have produced inconsistent results on this topic, possibly because of the use of different experimental paradigms. Concrete, relative to abstract word

Table 2 – Neural correlates of concrete vs. abstract words: activation studies (results of direct comparisons are reported)

Authors	Technique	Task	Presentation	Concrete	Abstract
D'Esposito et al. (1997)	fMRI	Mental image generation (conc), passive listening (abs)	Auditory	L area 37 and 19	Right area 10 and 7
Mellet et al. (1998)	PET	Mental image generation (conc), passive listening (abs)	Auditory	Bilateral IT, L premotor and preF	Bilateral ST, ant. RMTG
Kiehl et al. (1999)	fMRI	Lexical decision	Visual		Ant RSTG, RIFG
Perani et al. (1999)	PET	Lexical decision	Visual	–	RT pole, amygdala, bilateral IFG
Jessen et al. (2000)	fMRI	Encoding for later recognition	Visual	Bilateral lower P, ant. LIFG, precuneus	LIFG (Broca's area)
Wise et al. (2000)	PET	Exp 1: effect of implicit perception of words of different imageability	Auditory Auditory	L fusiform low frequency: rostral medial T bilat for high imageability	LSTG (slower to understand single abstract words)
		Exp 2: semantic decision on triplets	Visual and auditory	Time-on-task effect	
		Exp 3: as Exp 1, but effect of sensory modality		No differences due to input	
Grossman et al. (2002)	fMRI	Pleasantness decision	Visual	L ventral-medial occipital	R post-lat. T, R preF
Fiebach and Friederici (2003)	fMRI	Lexical decision	Visual	L basal T	LIFG
Whatmough et al. (2004)	PET	Semantic judgment: reading	Visual	L ventral T (fusiform gyrus)	R ventral T (fusiform gyrus)
Noppeney and Price (2004)	fMRI	Synonym judgments	Visual	–	LIFG, LMTG, LSTS, L ant T pole
Binder et al. (2005)	fMRI	Lexical decision	Visual	Bilateral: angular gyrus, posterior cingulate, precuneus. L preF	LIFG, L premotor cortex, L dorsal T pole
Sabsevitz et al. (2005)	fMRI	Semantic similarity judgment	Visual	Bilateral: medial SFG, post MFG, orbital; RIFG, LIFS, fusiform gyrus.	LIFG, ant. LSTG, LSTS, post. MTG; RSTS, L medial SFG
Pexman et al. (2007)	fMRI	Semantic categorization	Visual	No areas activated strongly than for abstract	Bilateral T, P, F

conc = concrete, abs = abstract, IT = inferior temporal, L = left, F = frontal, ST = superior temporal, RMTG = right middle temporal gyrus, RSTG = right superior temporal gyrus, RIFG = right inferior frontal gyrus, RT = right temporal, IFG = inferior frontal gyrus, P = parietal, LIFG = left inferior frontal gyrus, T = temporal, LSTG = left superior temporal gyrus, R = right, LMTG = left middle temporal gyrus, LSTS = left superior temporal sulcus, LIFS = left inferior frontal sulcus, MTG = middle temporal gyrus, RSTS = right superior temporal sulcus, SFG = superior frontal gyrus, MFG = middle frontal gyrus.

processing produced greater activation in a bilateral network of associative areas, including temporal, parietal and prefrontal cortex, while processing of abstract words produced greater activation almost exclusively in the left superior temporal and inferior frontal cortex, using a semantic similarity judgment task on concrete and abstract noun triads (Sabsevitz et al., 2005), or synonymy judgments (Noppeney and Price, 2004). But semantic similarity judgment tasks also produced an area of greater activation on the left medial fusiform gyrus for concrete words, and a greater activation on the *right* medial fusiform gyrus for abstract words (e.g., Whatmough et al., 2004).

In the case of lexical decision, three studies, among others, report (i) a selective activation of the temporal pole and amygdala on the right, and of the inferior frontal cortex bilaterally for abstract word processing, while no brain areas were more active in response to concrete words (Perani et al., 1999), (ii) a significant area of activation in the right anterior temporal cortex for abstract words as compared to concrete stimuli, and a right posterior temporal lobe engagement during lexical decision for both abstract and concrete words, the statistical significance of the activation being greater for the abstract words (Kiehl et al., 1999); (iii) a bilateral activation of the angular gyrus and dorsal prefrontal cortex for auditory-presented concrete words and a left lateral temporal lobe activation for both types of words (Binder et al., 2005) (see Table 2).

Therefore, results differ even when the same type of task is used, possibly depending on the stimuli features, such as the degree of imageability: although concrete material is mostly imageable, abstract words present a high degree of variability within this dimension (Paivio, 1971). Response type can also have a relevant effect in semantic memory tasks with a significant interaction between response type and brain regional activation (Jennings et al., 1997).

To summarize, most (*but not all*) neuroimaging studies suggest a bilateral representation for concrete items, essentially involving several structures almost invariably including the fusiform gyrus, while abstract word representation is less defined, resulting either in a left, right, or bilateral activation.

Therefore, neither neuropsychological nor neuroimaging studies can prove the case conclusively: concerning anatomical lesions, one cannot exclude reorganization processes and compensatory strategies. In the case of neuroimaging studies, only correlations between brain and behaviour are indicated, but we do not know for sure that those areas are essential to normal task performance. In 2003, Fiebach and Friederici reviewed the literature on functional neuroimaging studies of abstract and concrete nouns and concluded that there is no evidence for a right hemispheric system specifically associated with concrete nouns, since there are more often right-lateralized peaks of activation associated with the processing of abstract than concrete words.

Given these premises, we sought to further explore and verify previous results by means of repetitive Transcranial Magnetic Stimulation (rTMS). Since it is an interventional technique to investigate causality in the brain–behaviour relationship, it has the advantage that it can be used to demonstrate not only that a brain region is active while a given task is performed, but also that the area is actually essential for task performance. In addition, it allows studying healthy subjects, eliminating the confounding effects of the diffuse impairment and compensatory cortical plasticity associated with brain lesions, and thus complementing neuropsychological studies. Finally, in studying healthy subjects we can use them as their own controls, thus increasing experimental power and retest reliability.

2. Results

2.1. *Accuracy*

The Kolmogorov–Smirnov test showed that error rate had a Gaussian distribution, therefore data were analyzed using a repeated-measures ANOVAs, with Stimulus type (abstract vs. concrete) and Stimulation site (left BA 22, right BA 22, left BA 40 and sham), as factors. Stimulus type significantly affected performance [$F\ (1, 11)=10.8$; $p=0.007$, partial $\eta^2=0.495$], with an increased number of errors for abstract with respect to concrete words. Stimulation site was also significant [$F\ (3, 27)=6.16$; $p=0.002$, partial $\eta^2=0.36$], with a reduced accuracy for all sites as compared to the vertex (sham condition). Finally, the interaction between Stimulus type and Stimulation site was also significant [$F\ (3, 27)=9.014$; $p=0.001$, partial $\eta^2=0.45$].

In the case of abstract words, a significantly higher number of errors was found with left BA 22 stimulation as compared to right BA 22 rTMS ($p=0.001$), left BA 40 rTMS ($p=0.009$) and sham ($p=0.002$); on the contrary, there was no significant difference between right BA 22 and sham ($p=0.39$). Finally left BA 40 was not significantly different from sham ($p=0.42$) (see Fig. 1, Experiment 1).

In the case of concrete words, accuracy was significantly lower after rTMS applied over the right BA 22 and left BA 40 as

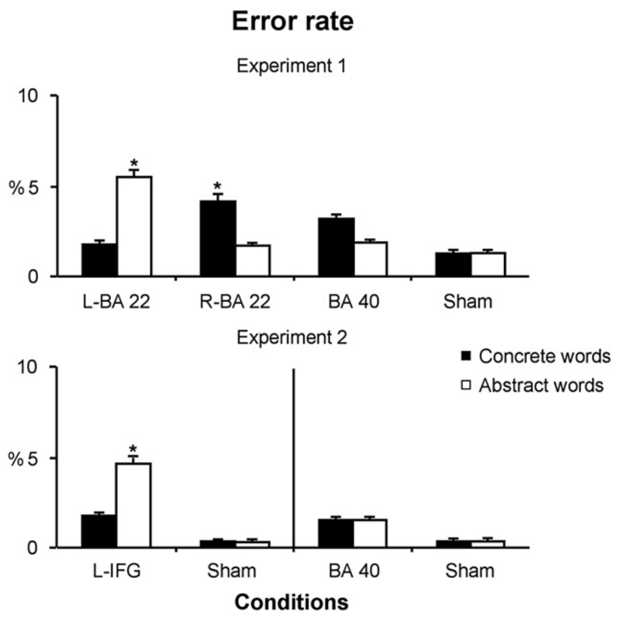

Fig. 1 – Average error rate in the four conditions (sham and three stimulation sites) for the two experiments. *rTMS significantly reduced accuracy as compared to sham in Cz; L = left; R = right; IFG = inferior frontal gyrus.

compared to sham ($p=0.002$ and $p=0.023$, respectively), while no significant difference was evident after left BA 22 ($p=0.42$) stimulation as compared to sham.

Since the level of accuracy was very high (about 95% in all conditions) and multiple testing was performed, the analysis of accuracy was repeated using a non-parametric test (Wilcoxon test) with Bonferroni correction. We found a significant effect of rTMS over left BA 22 for abstract words as compared to sham ($Z=-3.088$, $p=0.002$), but not after stimulation of left BA 40 ($p=0.372$) and right BA 22 ($Z=-0.905$, $p=0.366$) as compared to sham; the effect was significant for concrete words when rTMS was applied over the right BA 22 as compared to sham ($Z=-2.791$, $p=0.005$), but not when rTMS was applied over left BA 22 ($Z=-0.791$, $p=0.429$) or left BA 40 ($Z=-2.122$, $p=0.034$) as compared to sham.

2.2. *Reaction times (RTs)*

RTs were excluded from the analyses if the subject responded incorrectly or when they fell outside ± 2 SD from the mean for each condition and type of sentence.

The main effect of Stimulus type was significant [$F(1,11)=10.66$; $p<0.008$, partial $\eta^2=0.492$], with faster RTs to concrete (mean RT: 595 ms) than abstract (593 ms) words, even though lexical decision times did not differ in the control condition (653 and 664 ms for concrete and abstract words, respectively). The main effect of Stimulation site was also significant [$F(3, 27)=5.38$; $p=0.021$, partial $\eta^2=0.328$], since RT significantly decreased in all stimulation conditions as compared to sham for both, concrete and abstract words. Mean RT after left BA 22 stimulation was 576 ms for concrete and 570 ms for abstract words, after right BA 22 stimulation was 595 ms for concrete and 571 ms for abstract words, while in the case of BA 40 stimulation it was 558 and 567 ms for concrete and abstract words, respectively. The interaction between Stimulus type and Stimulation site was significant [$F(3, 27)=8.12$; $p=0.001$, partial $\eta^2=0.425$]. Post-hoc analyses showed that while there was no significant difference between concrete and abstract words for all conditions ($p=0.73$, $p=0.065$, $p=0.60$, $p=0.53$ for left BA 22, right BA 22, left BA 40 and sham, respectively), stimulation significantly reduced RTs as compared to sham for concrete words ($p=0.04$, $p=0.02$, $p=0.01$ for left BA 22, right BA 22 and left BA 40, respectively), as well as for abstract words ($p=0.001$, $p=0.000$, $p=0.002$ for left BA 22, right BA 22 and left BA 40, respectively) (see Fig. 2).

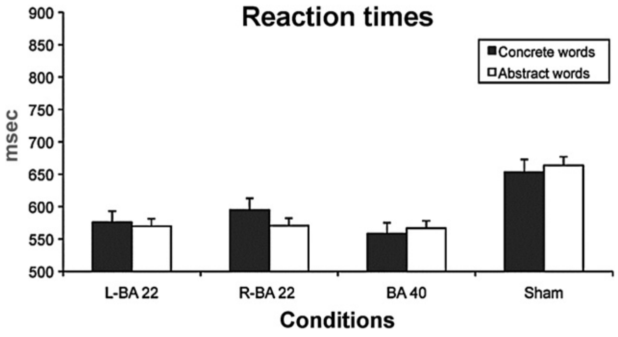

Fig. 2 – Average RTs in the four conditions (sham and three stimulation sites).

2.3. *Discomfort of stimulation*

The level of discomfort reported by participants was very low (on a scale from 0 "not at all" to 4 "very intense", the mean range of response varied from 0 to 0.83). A repeated measures ANOVA was performed on the mean score on discomfort given by the subjects, with condition (4 levels: left BA 22, right BA 22, left BA 40 and sham) as within subjects factor. The main effect of the site of stimulation was significant [$F(3, 33)=87.44$, $p=0.000$]. The mean discomfort score was 0.69 for left BA 22, 0.68 for right BA 22, 0.61 for left BA 40 and 0.03 for the control condition. Post-hoc analyses showed that real rTMS produced significant discomfort as compared to sham ($p=0.000$), but no significant difference was found between sites of stimulation ($p=0.785$ for left BA 22 vs. right BA 22, $p=0.102$ for right BA 22 vs. left BA 40, and $p=0.116$ for left BA 22 vs. left BA 40).

3. Discussion

An rTMS experiment was run on 12 healthy subjects using a lexical decision task in order to test the neural correlates of concrete/abstract word processing. RTs significantly decreased in all stimulation sites, as compared to sham, probably due to an unspecific factor like a general arousal due to rTMS. This effect has been observed before with TMS (see for example Marzi et al., 1998; Fogliata et al., 2007) and can be explained by a non-specific inter-sensory facilitation phenomenon (Hershenson, 1962). A non-specific arousal effect might mask *specific* effects. Dräger et al. (2004) have overcome this problem by including trials without any stimulation in an *offline* paradigm. We have used sham stimulation, as a baseline condition, and two types of stimuli for the same site in an *online* paradigm. The lack of an arousal effect with sham can be attributed to the distance from the ear of the acoustic stimulus, which was placed at the vertex in the case of the sham stimulation, as compared with the parietal and temporal sites. However, an alternative possibility could be a generalized facilitation of stimulation resulting in a speed accuracy trade-off. Since accuracy for abstract and concrete words decreased specifically for certain sites and not for others, while RTs were reduced for each type of stimulus and all stimulation sites, this explanation seems unlikely.

Therefore, the main result concerns accuracy and seems to suggest different sites for concrete (right BA 22) and abstract (left BA 22) words.

However, two questions are still left. The first concerns the role of the left inferior frontal gyrus, which seems to be critical for the representation of abstract concepts, according to neuroimaging studies and neuropsychological reports. In neurological cases with a strong concreteness effect, lesions typically involve left prefrontal structures (e.g., Coltheart et al., 1980; Bub and Kertesz, 1982). Conversely, in subjects with reverse concreteness effects following unilateral left hemisphere lesions (Warrington, 1981; Marshall et al., 1996; Bachoud-Lévy and Dupoux, 2003) damage spared both the right temporal pole and the left inferior prefrontal cortex. Left inferior prefrontal regions were intact in reported cases with reversed concreteness effects following semantic dementia, herpes simplex encephalitis or stroke. Additional evidence for the involvement of the left prefrontal regions in processing abstract terms is provided by neuroimaging studies (Sabsevitz et al., 2005; Noppeney and Price, 2004; Fiebach and Friederici, 2003; Jessen et al., 2000).

The second question arises from the significant effect on accuracy when rTMS was applied over the left BA 40, which disappeared after Bonferroni correction. This site is known to be involved in processing tools (see for example Chao and Martin, 2000). Therefore, we thought that using only living items as concrete stimuli would eliminate any doubtful effect.

For this reason an additional group of 12 subjects, comparable to the first group for age ($p=0.38$) and educational level ($p=1$), was submitted to a second experiment. Experiment 2 was performed in two different sessions: during the first session the same stimuli as in Experiment 1 were used and a frontal site was stimulated (Session A); our expectation was that stimulation of the left inferior frontal gyrus (IFG) would have selectively impaired lexical decision for abstract words. In the second session, concrete stimuli were represented by living items only and the previous parietal site (left BA 40) was stimulated (Session B); our expectation was that, using this material, no interference had to be found and consequently no difference between concrete and abstract words.

4. Experiment 2

4.1. Session A

4.1.1. Results

4.1.1.1. Accuracy. The Kolmogorov–Smirnov test showed that error rate had a Gaussian distribution.

An ANOVA 2×2 (Stimulation site: IFG vs. sham; Stimulus type: abstract vs. concrete; as factors) showed that Stimulation site significantly affected performance [F (1, 11)=12.439, $p=0.005$, partial $\eta^2=0.531$], while neither Stimulus type nor the interaction were significant ($p=0.339$ and $p=0.105$, respectively). However, when accuracy for abstract words in the control site was directly compared with accuracy for the same type of words during frontal stimulation, a significant effect was found [t (11)=2.945, $p=0.013$], while in the case of concrete words accuracy did not change after frontal stimulation as compared to the control site [t (11)=1.864, $p=0.089$].

Despite the normal distribution of errors, since the level of accuracy was very high, error rate was also analyzed by means of a non-parametric test (Wilcoxon test, Bonferroni correction) and it was found that while frontal stimulation did not produce any effect in the case of concrete words ($Z=-1.58$, $p=0.114$), accuracy decreased as compared to sham in the case of abstract words ($Z=-2.456$, $p=0.014$).

4.1.1.2. Reaction times. RTs were excluded from the analyses if the subject responded incorrectly or when they fell outside ± 2 SD from the mean for each condition and type of sentence.

The ANOVA showed a significant effect of Stimulation site [F (1, 11)=7.055, $p=0.022$, partial $\eta^2=0.391$], since RTs decreased after stimulation as found in the previous experiment: the difference was significant in the case of concrete words (839 and 634 ms during sham and frontal stimulation, respectively, $p=0.007$) while it did not reach significance in the case of abstract stimuli ($p=0.080$). Stimulus type was also significant [F (1, 11)=5.138, $p=0.045$, partial $\eta^2=0.318$], since RTs were faster for concrete than abstract words. In addition, while RTs did not differ ($p=0.766$) in the sham condition (839 and 849 ms for concrete and abstract words, respectively), the difference was significant after frontal stimulation ($p=0.01$; RTs 634 and 707 ms for concrete and abstract words, respectively). The interaction was not significant [F (1, 11)=2.722, $p=0.127$].

4.2. Session B

4.2.1. Results

4.2.1.1. Accuracy. An ANOVA 2×2 (Stimulation site: parietal BA 40 vs. sham stimulation; Stimulus type: abstract vs. concrete) showed a significant effect of Stimulation site [F (1, 11)=11, $p=0.007$], but Stimulus type ($p=1.00$) and the interaction were not significant ($p=1.00$). The same number of errors was produced for abstract and concrete words during stimulation. The Wilcoxon test was not significant ($Z=-1.225$, $p=0.221$).

4.2.1.2. Reaction times. RTs were excluded from the analyses if the subject responded incorrectly or when they fell outside ± 2 SD from the mean for each condition and type of sentence. Mean RTs were 664 ms for concrete and 667 ms for abstract words in the sham condition.

An ANOVA 2×2 (Stimulation site: parietal BA 40 vs. sham stimulation; Stimulus type: abstract vs. concrete) showed no significant effect of Stimulation site ($p=0.086$), Stimulus type ($p=0.198$) and interaction ($p=0.085$).

4.2.1.3. Discomfort of stimulation. Also in this experiment the level of discomfort reported by participants was very low (on a scale from 0 “not at all” to 4 “very intense” the mean range of response varied from 0 to 0.83). A repeated measures ANOVA was performed on the mean score given by the subjects, with condition (3 levels: left frontal, left BA 40 and sham) as within subjects factor. The main effect of the site of stimulation was significant [F (2, 22)=70.8, $p=0.000$]. The mean discomfort score was 0.69 for the left IFG, 0.58 for left BA 40, and 0.06 for the control condition. Post-hoc analyses showed that real rTMS produced significant discomfort as compared with sham ($p=0.000$), but no difference was found between the two stimulated sites ($p=0.068$).

5. General discussion

Two rTMS experiments were run in order to verify the neural correlates of lexical representation of abstract and concrete nouns. In Experiment 1 a significant effect on accuracy was found for abstract words when rTMS was applied over left BA 22, while stimulation of the right corresponding area reduced accuracy in the case of concrete words. In Experiment 2, a further site was tested, namely the left frontal inferior gyrus. Accuracy during frontal stimulation decreased as compared to the control stimulation site with a significant effect in the case of abstract words, but not in the case of concrete ones. It has to be noted that, during frontal stimulation, while we observed significantly faster RTs but not reduced accuracy in the case of concrete words, the opposite was true for abstract words: there was a significant increase in error rate, but no faster RTs. This result supports the view that speed accuracy trade-off is not likely.

In Experiment 2 we also controlled for the effect of stimulus type and we found that, when concrete stimuli were represented only by living items, stimulation over left BA 40 clearly did not reduce the level of accuracy.

Let us consider first the results concerning abstract nouns. Published lesion data show that in cases of reversed concreteness effects damage was either bilateral, but more extensive in the anterior left temporal lobe (Warrington and Shallice, 1984; Sirigu et al., 1991; Breedin et al., 1994; Macoir, 2008; Papagno et al., in press), or restricted to the left hemisphere (Warrington, 1981; Marshall et al., 1996); therefore, the left temporal pole seems more crucial for the representation of concrete than abstract concepts, which were relatively spared. Our results are compatible with these findings, since the interference effect on abstract words was found in the posterior part of the left temporal lobe, a region that usually is not damaged in patients with reversal of concreteness effect. Neuroimaging investigations are also in accordance with this suggestion. Overall, several studies show left-sided activations to abstract words, often in regions that are not affected in semantic dementia until later stages [e.g., the left posterolateral temporal and prefrontal regions in Grossman et al. (2002) and the left superior temporal and inferior frontal in Sabsevitz et al. (2005)]. In particular, our results on abstract nouns are completely in line with Sabsevitz et al.'s (2005) findings, since both, a posterolateral superior temporal and inferior frontal involvement, were detected.

However, some further studies demonstrate significantly greater activation to abstract than to concrete words in the right temporal pole (e.g., Kiehl et al., 1999; Perani et al., 1999) or, more generally, in the right than in the left temporal lobe (Whatmough et al., 2004). In addition, at least one study shows greater activation for concrete than abstract words in left temporal regions (Mellet et al., 1998). Finally, a recent rTMS experiment (Romero Lauro et al., 2007) has shown that stimulation in the right (but not the left) temporal lobe interfered with abstract (but not concrete) semantic judgments. In that study a more antero-inferior site on the right temporal lobe was stimulated. From a careful inspection of the literature, it does not seem that, in general, differences in lateralization are due to the type of task used, being it a lexical decision or a semantic judgment. Therefore, taking together data from the present experiments and the review of the neuroimaging literature, as well as neuropsychological reports, it can be suggested that not only concrete, but also abstract words are represented bilaterally, in a diffuse network, involving the inferior frontal and posterior superior temporal gyrus on the left and more anterior parts of the temporal cortex on the right.

Concerning concrete nouns, the negative result on left BA 40 (particularly when using only living items) and on BA 22 (no interference for concrete items) is entirely in agreement with a previous rTMS study (Romero Lauro et al., 2007) and with the reported patients with reversal of concreteness effect: in those cases, the concrete items impairment, in general, was more severe for animate entities as compared to man-made objects (see for example Breedin et al., 1994; Papagno et al., in press). As already mentioned, patients with reversal of concreteness effect frequently suffered from herpes simplex encephalitis or semantic dementia: both diseases tend to spare the most posterior regions of the temporal lobes and the parietal cortex. Finally, rTMS does not allow testing for the most inferior parts of the temporal lobes, which are presumably involved in living item processing, as suggested by the literature on this topic.

To sum up, converging evidence suggests that both, abstract and concrete words, are processed by a bilateral network, but the involved regions differ from each other. Our data do not support Fiebach and Friederici's (2003) conclusion that there is no evidence for a right hemispheric system associated with concrete nouns. This result of diffuse networks to process words of different types is entirely in line with more recent studies using intraoperative direct cortical stimulation during surgical removal of tumours in eloquent regions. For example, in the case of face naming, specific sites were detected in the left superior, middle and inferior frontal gyri, but also in the anterior part of the superior and middle temporal gyri (Giussani et al., 2008). These neurosurgical studies integrate the localizationist and holistic views of the organization of association cortex (Ojemann, 1990), since they show a behavioural specificity of neurons in an individual subject, but also a wide dispersion of these behaviourally specific neurons across the association cortex of individuals.

6. Experimental procedures

6.1. *Experiment 1*

6.1.1. *Materials*

Stimuli were selected from an Italian database (Della Rosa et al., 2008) that includes 420 words equally divided between abstract and concrete items (210 concrete words, 210 abstract words). Norms were collected by asking 250 participants to rate the set of 420 Italian words on 7 dimensions: age of acquisition, concreteness, familiarity, context availability, imageability, abstractness and modality of acquisition. For each word a corresponding nonword was created by using the program Random Word Generator (http://www.download.com/Random-Word-Generator/3000-2279_4-10034698.html), following the criteria outlined by Fiebach and Friederici (2003). This program creates lists of random, artificial words for a given word. Nonwords were created by changing two or three letters. We used some restrictions: letters such as y, j, k and oddball components, such as cv, bd etc., that are not legal strings in Italian, were excluded. In addition we prevented 'illegal' word components from occurring at the beginning or ending of a word. This avoids generating unusable words, such as "mpopa" for "scopa" (broom). A first pilot experiment was run on 30 subjects, not involved in any of the following rTMS experiments, using the 420 words and the corresponding nonwords. This was done in order to select those words that evoked a correct response in all subjects. Subjects were healthy Italian right-handed undergraduate students, who were naive to the purpose of the study. This procedure allowed selecting 120 abstract and 120 concrete words, matched for length and for the above mentioned dimensions. These 240 words were used in two further pilot experiments on 30 subjects each, together with the corresponding nonwords. From this pool, items with the following characteristics were selected: 100% accuracy in the pilot experiment; a response time for all stimuli between 400 and 600 ms, a matched number of letters within words and nonwords. The 80 concrete and the 80 abstract words that were finally selected did not differ either in length ($p=0.112$) or in frequency of use ($p=0.543$). In addition, the 80 nonwords were selected among those obtained by replacing 2 letters, and only legal strings that did not resemble the real word: for example, the item that we accepted for the word "tavolo" (table) was "favogo" (see Supplementary material for the complete list of stimuli).

The stimuli (80 concrete words, 80 abstract words, 80 nonwords) were divided in four blocks. Each block consisted of 60 trials: 20 concrete words, 20 abstract words and 20 nonwords. No item was presented more than once in the whole experiment. We decided to use only 20 nonwords to reduce the amount of overall rTMS stimuli delivered to each subject. This line of reasoning was based on the aim to keep stimulation on a safe side as much as possible. Moreover even if the nonword condition was unbalanced, in terms of word vs. nonword responses, this was the same across stimulation sites. Therefore, for each site, 33% of stimuli were concrete words, 33% abstract and 33% nonwords. The distribution of stimuli within each block was chosen based on a pilot experiment performed with 20 participants (different from those recruited for the main study, but always recruited among undergraduate students at the University of Milano-Bicocca) to balance the mean response time across the blocks. The order of stimuli within each block and the order of blocks were randomised and counterbalanced across participants.

6.1.2. *Participants*

Twelve healthy volunteers (7 females), aged between 20 and 26 years (mean age 23.69), participated in the study. The study was approved by the local ethical committee and informed consent from participants was obtained prior to the beginning of the experiment. All the participants were right handed (mean score on the Edinburgh Handedness Inventory 99.19%) and had normal or corrected to normal visual acuity. They were all native Italian speakers and were undergraduate students. They were naive to the experimental procedure and to the purpose of the study.

6.1.2.1. *TMS procedure*. rTMS was applied using a Magstim Rapid with a figure-of-eight (double 70 mm) coil. Before the experiment, individual resting motor excitability thresholds of stimulation were determined by stimulating the left motor cortex and inducing a contraction evoked by a single TMS pulse in the contralateral first interosseus dorsalis muscle. The threshold was defined as the minimum intensity that induced a visible contraction in the tested muscle on at least 5 out of 10 trials. The stimulation intensity used during the experiment was set at 90% of each subject's threshold. The mean stimulation intensity (as a percentage of the maximum machine output) was 57.7 (SD 6.1, range 54–72). During the experiment, rTMS was delivered starting 50 ms after trial onset using a train of six pulses with a frequency of 15 Hz (i.e., lasting a total of 400 ms), which is within safety guidelines for rTMS (Wasserman, 1998). Participants tolerated rTMS well and did not report any adverse effects.

The stimulation sites were chosen referring to the neuroimaging literature. Since there is a high degree of variability depending on each study, we did not refer to the anatomical coordinates of specific peaks of activation, but to the regions (i.e., superior temporal gyrus) that were more frequently reported. In order to localize these sites, Talairach coordinates of cortical sites underlying coil locations were estimated for each participant by the SofTaxic Evolution Navigator system (E.M.S., Bologna, Italy). This frameless stereotaxic neuronavigational system consists of a graphic user interface and a 3D optical digitizer (NDI: Polaris Vicra) having 3 location items. One of these items was placed solidly on the subject's head, in order to rule out the inaccuracy due to head movements. The second item was accurately positioned on the TMS coil, in order to measure its position (X, Y, and Z Cartesian coordinates) and orientation. The third item is part of a stylus that was used to register craniometric landmarks on the subject's head. Furthermore, the SofTaxic Navigator system permits the computation of an estimated volume of MRIs of the subject's head, in order to guide the TMS coil positioning. The estimated MRI images are automatically calculated by means of a warping procedure, by operating on a generic MRI volume (template) on the basis of a set of points digitized from the subject's scalp. With respect to using the individual subject's MRs for the coil localization on the target area, the mean accuracy of the estimated MR images obtained with the above procedure is 4.06 (±1.54 SD) mm.

Based on these estimated MRIs, the location of the 3 sites was identified: the left and right temporal lobe (Superior Temporal Gyrus — BA 22) sites were on average centred on Talairach coordinates $X=\pm 49$, $Y=-48$, $Z=12$ (Talairach and Tournoux, 1988), while the left posterior parietal site corresponded to $X=-46$, $Y=-23$, $Z=24$ (left BA 40) (Talairach and Tournoux, 1988) (see Fig. 3). To stimulate these sites, we placed the anterior end of the junction of the two coil wings above these locations. The stimulation coil was supported and fixed in place by a mechanical arm. The site for the sham condition was on the vertex with the coil held perpendicular to the scalp, thus ensuring that no effective magnetic stimulation reached the brain during the sham condition.

6.1.2.2. *Experimental task*. Participants sat in a dimly illuminated room at a distance of approximately 75 cm from a 19-inch computer screen. Stimulus presentation and rTMS delivery were controlled by E-Prime software (version 1.2, Psychological Tools, Inc). After establishing stimulation thresholds and before starting the experiment, subjects completed 8 practice trials using different stimuli from those

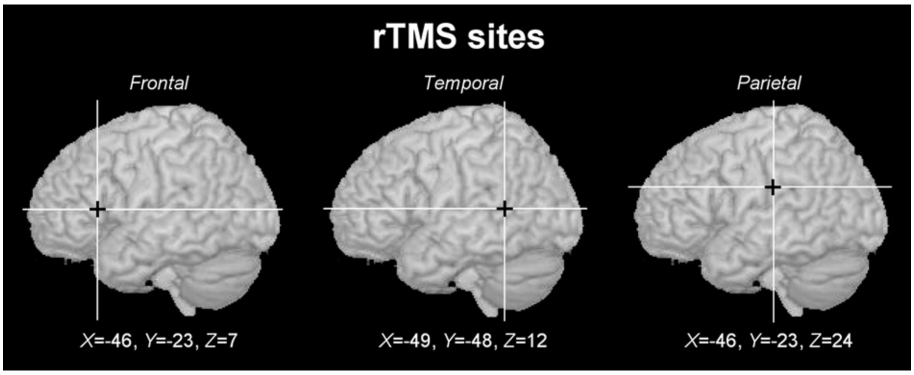

Fig. 3 – Lateral view of a 3D brain reconstruction showing the localization of the stimulation sites as identified using the SofTaxic system. Cz was defined as a point midway between the inion and the nasion and equidistant from the left and right inter-trachial notches. The location of the stimulation points was on average centred on the reported Talairach co-ordinates.

included in the experimental set. Following practice, the TMS coil was fixed in position at the relevant site and the subject completed four blocks, three with real rTMS (left and right BA 22 and left BA 40 sites), and one with sham rTMS applied on a vertex control site, with the order counterbalanced across participants.

Each trial began with a fixation cross appearing on the screen for 1000 ms, followed by a written string of letters, i.e., a concrete word or abstract word or nonword, which remained on the screen until the subject responded. The task was to decide whether the string was a real word, by pressing one of two keys on the keyboard with the index finger of the right or left hand. Half of the subjects used the left index for “yes” responses and the right for “no” responses, while for the other half of participants the response was reversed. Accuracy and RTs were measured. At the end of the experimental session, subjects were asked to fill a questionnaire in which they evaluated on a 5-level Likert scale (from 0 “not at all” to 4 “very intense”) any discomfort (noise, pain, touch, twitches, etc.) caused by the stimulation; they also evaluated how they rated that painful sensations had affected their level of attention during the task. Subjects giving a score >2 in at least one question were excluded from the experiment (two subjects not reported in the study).

6.1.2.3. Statistical methods. Both accuracy and RTs data were analyzed using 2×4 repeated-measures ANOVAs, with Stimulation site (left BA 22, right BA 22, left BA 40 and sham) and Stimulus type (abstract vs. concrete) as within subject factors, for the first experiment. In Experiment 2, data were analyzed using 2×2 repeated-measures ANOVAs, with Stimulus type (abstract vs. concrete) and Stimulation site (left IFG vs. sham, for session A, and parietal BA 40 vs. sham, for session B, respectively), as within subject factors. The effect size was computed as eta-square (η^2). To assess significant interactions, selected two-sample comparisons were performed by means of *t* tests. In the case of accuracy, we tested whether the dependent variable accuracy had a Gaussian distribution by means of the Kolmogorov–Smirnov test. Nevertheless, a non-parametric analysis (Wilcoxon test) with a correction (Bonferroni) for possible alpha inflation due to multiple testing was also run. Since we were not studying “word form” recognition but a specific dimension of words (concreteness vs. abstractness), nonwords were not included in the analyses.

6.2. *Experiment 2*

6.2.1. *Participants*

Twelve healthy volunteers (six female and six male) recruited among undergraduate students, but different from those of Experiment 1, aged between 24 and 27 years (mean age 25.33) participated in the study. The study was approved by the local ethical committee and informed consent from participants was obtained prior to the beginning of the experiment. All the participants were right handed (mean score on the Edinburgh Handedness Inventory 99.28 %) and had normal or corrected to normal visual acuity. They were all native Italian speakers and they were naive to the experimental procedure and purpose of the study.

6.2.1.1. *Session A*

6.2.1.1.1. Materials. As already mentioned, stimuli were selected from the previous experiment, matching 40 concrete and 40 abstract nouns for all the relevant variables ($p=0.118$ for length and $p=0.173$ for frequency of use). Two blocks were prepared following the same procedure described above. Each item was presented only once during the experiment.

The rTMS procedure was the same as in Experiment 1, but the stimulation site, based on Fiebach and Friederici’s (2003) study, was on average centred on Talairach coordinates $X=-46$, $Y=23$, $Z=7$ (Talairach and Tournoux, 1988), which correspond to the IFG. There were two conditions: one with rTMS and one sham condition. The order of conditions, blocks and stimuli within blocks was counterbalanced across subjects.

6.2.1.2. *Session B*

6.2.1.2.1. Materials. Stimuli were selected from the database used in the pilot experiment, matching 40 concrete (fruit and animals) and 40 abstract items (length: $p=0.094$; frequency $p=0.123$) for which subjects had shown 100% accuracy, and the corresponding nonwords (see Supplementary material for the list of stimuli used in this session). Two blocks were prepared following the previously described procedure.

The rTMS protocol was the same as in Experiment 1, but there were two stimulation sites only: one with rTMS on the parietal (BA 40) and one sham (vertex) site. The order of Stimulation sites, blocks and stimuli within blocks was counterbalanced across subjects.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.brainres.2009.01.037.

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