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Instruction-specific brain activations during episodic encoding: a generalized level of processing effect

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Abstract

In a within-subject design we investigated the levels-of-processing (LOP) effect using visual material in a behavioral and a corresponding PET study. In the behavioral study we characterize a generalized LOP effect, using pleasantness and graphical quality judgments in the encoding situation, with two types of visual material, figurative and nonfigurative line drawings. In the PET study we investigate the related pattern of brain activations along these two dimensions. The behavioral results indicate that instruction and material contribute independently to the level of recognition performance. Therefore the LOP effect appears to stem both from the relative relevance of the stimuli (encoding opportunity) and an altered processing of stimuli brought about by the explicit instruction (encoding mode). In the PET study, encoding of visual material under the pleasantness (deep) instruction yielded left lateralized frontoparietal and anterior temporal activations while surface-based perceptually oriented processing (shallow instruction) yielded right lateralized frontoparietal, posterior temporal, and occipitotemporal activations. The result that deep encoding was related to the left prefrontal cortex while shallow encoding was related to the right prefrontal cortex, holding the material constant, is not consistent with the HERA model. In addition, we suggest that the anterior medial superior frontal region is related to aspects of self-referential semantic processing and that the inferior parts of the anterior cingulate as well as the medial orbitofrontal cortex is related to affective processing, in this case pleasantness evaluation of the stimuli regardless of explicit semantic content. Finally, the left medial temporal lobe appears more actively engaged by elaborate meaning-based processing and the complex response pattern observed in different subregions of the MTL lends support to the suggestion that this region is functionally segregated.

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Introduction

Long-term memory formation in everyday life often occurs incidentally without explicit intention to remember the information processed and episodic memory formation represents a dynamic consequence of system plasticity and processing attended information (Petersson et al., 1997). Memory research indicates that several factors and specific

modes of information processing contribute to long-term memory formation, including meaning-based, context, and relational processing as well as emotional significance and the allocation of attention (Buckner et al., 1999; Wagner et al., 1999). The levels-of-processing (LOP) effect is a well-known and robust encoding effect observed in human memory research (Craik and Lockhart, 1972). When stimulus material is processed in an elaborate meaning-based or conceptual manner, so-called deep processing, the material will be better remembered or more effectively retrieved than when the same material is processed with an emphasis on superficial or perceptual features, so-called shallow processing. In the framework formulated by Craik and Lockhart (1972), it is suggested that a deeper more elaborate and

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semantically based processing of the information yields more extensive associations with previously acquired general knowledge of the subject (Anderson and Reder, 1979; Craik and Tulving, 1975). It is hypothesized that the richness and number of the associations that results from the processing of the stimulus determine the stability (durability) of the memory trace. Consequently, encouraging a processing strategy that leads to the formation of relatively more associations will prolong the lifetime of the memory trace and generate more associative access pathways for later retrieval (Anderson and Reder, 1979; Craik and Lockhardt, 1972; Craik and Tulving, 1975). Another related hypothesis regarding the foundation for the LOP effect suggests that the effect depends on the discriminability or distinctiveness of the memory trace compared to other memory traces (Baddeley, 1998; Moscovitch and Craik, 1976). This reasoning suggests that recognition depends on the selection from any number of memory traces to match the stimulus. Hence, the likelihood of a memory trace being correctly selected is a function of its distinctiveness or discriminability. Whether encoding is incidental or intentional appears to be of little consequence for the occurrence of the LOP effect (Craik and Tulving, 1975). Craik and Tulving (1975) also provided data indicating that the LOP effect could not be explained in terms of task demand, that is, that the meaningful semantic encoding was simply more demanding (task difficulty) or time-consuming (time on task) compared to shallow processing. A similar conclusion was reached in a recent event-related fMRI study (Otten et al., 2001). In addition, experimental evidence indicated that the effects do not simply spring from the fact that semantic contexts are more accessible at retrieval by demonstrating the LOP effect also in cued recall (Moscovitch and Craik, 1976).

A number of previous functional neuroimaging studies have investigated episodic encoding and retrieval of word material under levels of processing manipulations (Kapur et al., 1994; Otten et al., 2001; Rugg et al., 1997). It has been suggested that the neuroimaging studies of the LOP phenomena have provided a link between the functional role of the prefrontal cortex and encoding processes (Buckner et al., 2000). Direct evidence for a link between prefrontal activity and behavioral performance in episodic memory performance has been established by showing that the level of activity in the left prefrontal (BA 44/6 and 45/47) on average predicts whether information later will be retrievable or forgotten (Petersson et al., 1999; Wagner et al., 1998). Similar observations have been made concerning the medial temporal lobe (Brewer et al., 1998; Fernandez et al., 1998; Petersson et al., 1999; Wagner et al., 1998). In the deep versus shallow incidental encoding, Kapur et al. (1994) observed left middle-inferior prefrontal (PFC) activations [Brodmann's areas (BA) 45/46 and 47]. In addition to left middle-inferior PFC activations (BA 9, 44), Rugg et al. (1997) observed activations including left anterior cingulate (ACC BA 32), left medial superior PFC (BA 8), left

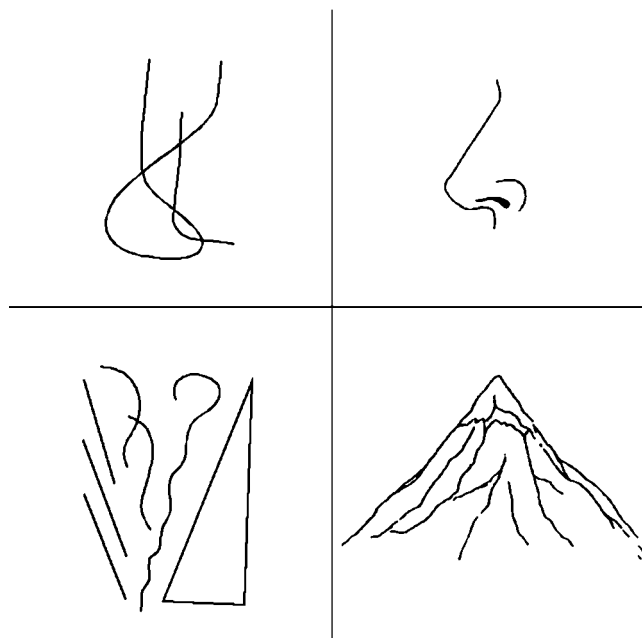


Fig. 1. Examples of the figurative and nonfigurative drawings used as stimuli in the behavioral and PET experiment.

superior temporal (BA 22), and medial temporal lobe (MTL) activations. These findings were essentially replicated in the study of Otten et al. (2001).

In the present study we investigated the LOP effect using two visual materials, that is, figurative and nonfigurative line drawings (Fig. 1), in two experiments. First, we characterized the LOP effect in a behavioral study, and then, in a second study, we investigated the network of brain regions related to incidental episodic encoding of visual material under a levels of processing manipulation contrasting judgments of pleasantness with judgments of graphical quality using positron emission tomography (PET). The former aspect may be thought of as a means to bias the processing of the stimuli toward an inherently meaningful encoding mode, in which the stimuli were associated in a meaningful way with an inner subjective state, while the latter provides richer encoding opportunity. In a 2×2 factorial design with the type of encoding instruction (i.e., deep versus shallow) and type of visual material (figurative versus nonfigurative line drawings) as the experimental factors, we investigated whether the LOP effect at the behavioral level generalized to our particular experimental setting.

By using pleasantness and perceptual quality judgments in figurative as well as nonfigurative drawings in the encoding situation, we investigated whether the semantic content of the encoded material interacted with the LOP effect. In the PET study we characterized the activation patterns in the brain along two dimensions: semantic content in the stimulus material as well as meaningful processing, here in the general sense of pleasantness judgment, through an explicit instruction. The first objective with the PET study was to investigate to what extent the LOP-related brain activations

found with word stimuli under standard LOP manipulations (Kapur et al., 1994; Rugg et al., 1997) generalized to our situation. In addition, the type of material manipulation may be viewed as a complementary way of manipulating meaning-based processing triggered by the semantic content of the stimulus material. The second objective was thus to investigate to what extent the encoding-related activations were similar when using line drawings with or without apparent semantic content, which hitherto remains an open question (Buckner et al., 2000). The primary anatomical foci of interest, given previously reported results (Kapur et al., 1994; Otten et al., 2001; Rugg et al., 1997), were several relevant regions of the PFC and the MTL (Buckner et al., 1999; Buckner and Koutstaal, 1998; Desgranges et al., 1998; Fletcher et al., 1997; Mayes and Montaldi, 2000; Nyberg, 1998; Nyberg et al., 1996; Tulving and Markowitsch, 1997a).

Behavioral study

Material and methods

Subjects

Twelve volunteers were included in the behavioral study (7 women, 5 men; mean age 26 years, range 22–29 years; mean educational level corresponded to 2, range 1–4, years of university level education).

Stimulus material

The stimulus material included 180 figurative line drawings of common everyday objects from the Snodgrass-Vanderwart collection (Snodgrass and Vanderwart, 1980) and 180 nonfigurative line drawings created by the authors, approximately matched for visual complexity by inspection (Fig. 1). Half the drawings of each kind were randomly designated targets and the others distractors. The target drawings were divided into six lists of each kind, containing 15 drawings each, making 12 lists of target drawings in all. Additionally, two lists for recognition with 90 drawings each were created for each type of drawings to account for the time from encoding to recognition as well as counterbalancing over subjects. In each list the numbers of distractors and targets were equal. Drawings were presented and responses were recorded using the MacStim software on Macintosh computers.

Experimental procedures

In the shallow conditions the participants were instructed to carefully evaluate the line drawings with regard to their graphical quality, that is, how clear and well drawn each line drawing is in its details with respect to whether the edges are jagged or whether too much ink makes the picture blurred. The line drawings were rated at three levels: good, medium, or poor quality, with a corresponding keyboard press. Each picture was presented for approximately 4 s and

Table 1

Means of hit rates, false alarm rates, and d' for all subject in the different conditions, and uncorrected P values from paired t tests between d' in the groups

	Deep	Shallow	P
Figurative			
Hit rate	0.94	0.80	<0.001
False alarm rate	0.05	0.05	
d'	3.58	2.94	
Non-figurative			
Hit rate	0.66	0.46	<0.001
False alarm rate	0.16	0.16	
d'	1.52	0.94	
P	0.002	0.01	

the participants were instructed to make their decision during this time by pressing the appropriate key. In the deep conditions the subjects were instructed to carefully evaluate the line drawings with respect to the level of pleasantness as determined from associations evoked by the pictures. The participants rated the pleasantness at three levels: pleasant, neutral, or unpleasant, with a corresponding keyboard press. In the subsequent recognition test the participants were instructed to make old/new judgments.

The order of presentation was balanced across material, instruction, and order of lists. Subjects were seated in front of a computer where the procedure was explained to them. The subjects performed a short practice list to get acquainted with all aspects of the experimental procedure. The first list then commenced where each drawing was presented for 4 s and the subjects made their response by pressing the appropriate key on the keyboard. The interval between drawings was 1 s. Immediately after the 12 encoding lists followed 4 recognition lists. All responses were recorded on the computer.

Results

Hit rates (H) were calculated in each category as $H = \text{hits}/\text{targets}$ and false alarm rates (FA) were calculated as false positive/distractors. From these d' was calculated as $d' = Z_{FA} - Z_H$ to obtain a composite measure that contains both types of information. The results were analyzed as a repeated-measures two-factor analysis of variance.

As can be seen in Table 1 and Fig. 2A there was a significant main effect of materials [figurative or nonfigurative; $F(1,11) = 102$, $P < 0.005$]. There was also a significant main effect of instruction [deep or shallow; $F(1,11) = 26$, $P < 0.005$]. The simple main effects of instruction in both types of materials were also significant. The interaction of materials and instruction was not significant [$F(1,11) = 0.6$, $P = 0.450$], which can be seen from the boxplot.

We also stratified the subject responses in terms of subject ratings (i.e., positive, neutral, negative) and analyzed the data as a repeated-measures three-factor analysis of variance with Greenhouse-Geisser sphericity correction in-

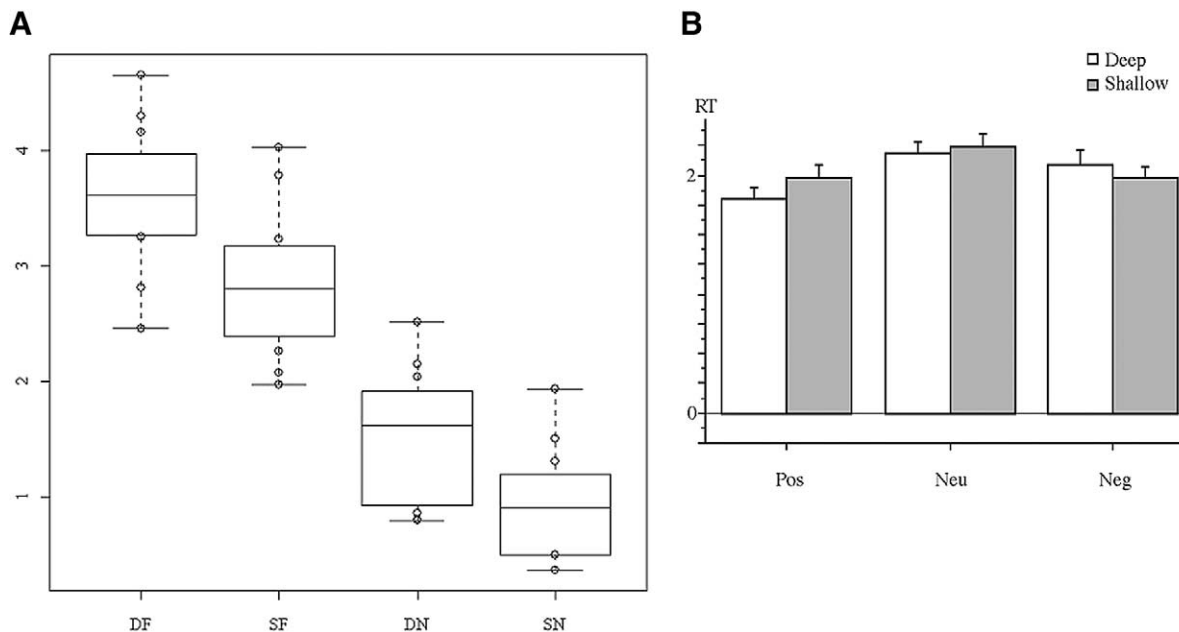


Fig. 2. (A) Boxplot of d' against condition. Deep and shallow encoding of figurative and nonfigurative drawings. Center line represents the median, box boundaries the 25th and 75th percentile, respectively, and whiskers indicate the range. (B) Reaction times during encoding. There was a significant effect of rating with longer times for neutral ratings than for positive/negative; $F(1,6) = 23.0$, $P < 0.002$ (G-G corrected).

cluding the factors instruction, material, and subject rating. The results showed similar significant main effects of materials and instruction [$F(1,8) = 110$, $P < 0.001$; $F(1,8) = 19.0$, $P < 0.01$]. The effect of subject ratings of the stimulus material was not significant [$F(2,16) = 5.4$, $P = 0.26$]. With regard to the reaction times during encoding, neither the instruction nor material factors were significant. However, the subject ratings of the pictures made a significant difference [$F(2,16) = 9.18$, $P = 0.003$] with longer reaction times for neutral than for negative/positive responses [$F(1,6) = 23.0$, $P < 0.002$, G-G corrected; Fig. 2B].

Discussion

In previous behavioral studies, the LOP effect has commonly been investigated using language-based material, and in particular, Vochatzer and Blick (1989) investigated the LOP effect using words and pseudo-words. Their results indicated that the LOP effect in the pseudo-word condition was comparable to the effect observed in the word condition (Vochatzer and Blick, 1989). The primary objective of the behavioral study was to establish the LOP effect in our experimental setting using two visual materials (Fig. 1).

The behavioral results indicate that recognition was better in both types of material and to a similar degree when the encoding instruction referred to the content of the drawing instead of the graphical appearance (Table 1 and Fig. 2A). There was no interaction between the two experimental factors of material and instruction. Thus, it seems that the instruction in itself is sufficient to produce the effect regard-

less of whether the material carried any explicit semantic content consistent with the findings of Vochatzer and Blick (1989). Our findings indicate that the explicit instruction promotes a mode of processing that favors retention regardless of whether there is explicit semantic content to associate with preexistent knowledge or experience. Even if it is possible that subjects may have instilled some of the nonfigurative drawings with some degree of semantic content the majority of subjects reported that this phenomenon was uncommon. It thus appears that the nonfigurative drawings were not prone to or relatively ineffective in eliciting semantic associations. In addition, and also consistent with this suggestion, is the fact that shallowly encoded figurative drawings produced higher performance than deeply encoded nonfigurative drawings. However, these suggestions have to be taken with some caution since it is difficult to determine more precisely what type of processing subjects engage in and subjective ratings are potentially unreliable indicators of the actual type of cognitive processing taking place. Thus, it is not possible to entirely rule out that there may be a tendency for semantic processing with nonfigurative material induced by the deep instructions. However, the following PET experiment allows us to address this issue directly by comparing the overlap between the contrasts deep nonfigurative versus shallow nonfigurative, as an indicator of deep encoding and the brain regions engaged by this instruction, and shallow figurative versus shallow nonfigurative, as an indicator of semantic content in the material and the brain regions engaged by the material. To the extent that there is little or no overlap, this would be consistent

with the suggested interpretation above (see the PET results).

For the material factor, the detrimental effect on encoding/retrieval by the lack of explicit semantic content can be assumed to make the number of possible associations at encoding fewer or less effective (Baddeley, 1998; Ellis and Hunt, 1993; Reisberg, 1997). This indicates that subjects cannot make as efficient use of an already acquired and well-developed conceptual infrastructure at encoding of the nonfigurative as with the figurative drawings. An alternative interpretation is that multiple (dual) codes are available for the figurative drawings such that they are processed in a linguistic-semantic manner as well as in a visuossemantic manner while this is not possible to the same degree for nonfigurative drawings. In addition, it is possible that the main effect of material in part is due to a retrieval effect, meaning that the nonfigurative material constitutes less distinctive retrieval cues compared to the figurative drawings. In short, as noted by Fischer and Craik (1977), no factor alone, whether type of encoding, cue characteristics, or encoding-cue compatibility, is sufficient to explain behavioral performance.

In conclusion, it appears that the encoding instruction biases the system toward different encoding modes whereas the semantic content of the drawings independently provides different encoding opportunities. Compliance with the instruction thus controls the manner in which stimuli are processed, so that in the one case effective encoding is enhanced, and in the other, reduced, as measured by recognition performance. Possibly this is the result of the formation of meaningful associative connections between the stimulus at hand, the subjective experience and previously acquired knowledge. Independently from this mechanism, the semantic content of the stimulus, its interpretability, provide different levels of encoding opportunities. We also note that previous behavioral studies have suggested little levels-of-processing effects for pictures. In the context of our results, one possible explanation is that the line drawings used here may be inherently less memorable than pictures used in previous levels of processing studies, thus avoiding a potential ceiling effect.

Pet study

Material and methods

Subjects

Fifteen right-handed (Edinburgh handedness inventory, Oldfield, 1971) healthy male subjects (mean age 25 years; range 18–40 years) were included in the study. The subjects were prescreened and none used any medication, had a history of drug use (including nicotine), head trauma, neurological or psychiatric illness, or family history of neurological or psychiatric illness that was considered relevant to the study. The local Ethics and Radiation Safety Commit-

tees at the Karolinska Hospital approved this study. All subjects gave written informed consent.

PET scanning

Each subject underwent 12 measurements of regional cerebral blood flow with a 3D ECAT EXACT HR PET scanner (Wienhard et al., 1994) and bolus injections of [O^{15}]water. The PET scanner was used in 3D sampling mode producing 60-s tracer uptake images. The different tasks were started at the time of tracer injection and the scanning was automatically initiated when the brain radioactivity exceeded a predetermined level above background. Scatter correction was made and a 2D transmission scan was used for attenuation correction. If the subject temporarily had to leave the scanner, a second transmission scan was acquired after the last activation scan.

Experimental procedures

The same stimulus material described above was used, including 180 figurative and 180 nonfigurative line drawings. Twenty line drawings of each type were used in the training protocols and the remaining 160 of the two kinds were randomly assigned to be targets or distracters in the subsequent forced choice old-new recognition paradigm, as described above. The target drawings were, individually for each subject, randomly assigned to four different types of encoding lists of 20 drawings each. Recognition lists (divided into two lists for technical reasons) were the same for all subjects with all targets mixed with an equal number of distractors in random order. Stimuli were presented for 4 s with an interstimulus interval of 1 s on a computer screen comfortably suspended in the visual field of the subjects.

The subjects practiced all aspects of the experimental paradigm (with sham injections) for approximately 20 min in the PET scanner before the experiment started. The experimental paradigm consisted of two blocks (6 conditions/block randomized within block). Within each block, the subjects were scanned in six different conditions: two low-level reference or baseline conditions [visual fixation (*VF*) and viewing (*VI*)] and four high-level activation conditions in a 2×2 factorial design (deep/shallow \times figurative/nonfigurative). The participants were instructed as described above in the four high-level activation conditions including deep encoding of figurative (*DF*) and nonfigurative pictures (*DN*), as well as shallow encoding of figurative (*SF*) and nonfigurative pictures (*SN*). In the visual fixation (*VF*) conditions the subjects were presented with a cross hair and asked to fixate their gaze on the cross hair. In the viewing (*VI*) condition the subjects passively viewed a simple geometrical figure (a piece of a regular lattice that can be considered an extended cross hair). In both *VF* and *VI* the subjects were asked to press the left button in response to each stimulus presentation. Responses were recorded on the computer that presented the pictures. Each block consisted of six scans in random order with at least 10 min between successive scans. Immediately following scanning subjects

were presented with a forced choice recognition test and their performance was recorded in terms of accuracy. However, due to an unfortunate computer failure behavioral data were lost for all but two of the subjects included in the PET study. On the other hand, and not surprisingly given the robustness of the effect, these performance data were fully consistent with the results from the behavioral study for both subjects (mean d' in $DF = 1.51$, $SF = 1.20$, $DN = 0.84$, $SN = 0.38$).

Preprocessing and statistical analysis of PET data

The PET images were realigned, anatomically normalized, and transformed into a common stereotactic space as defined by the SPM99 template, an approximate Talairach space (Talairach and Tournoux, 1988), 3D isotropic Gaussian filtered (14 mm FWHM), proportionally scaled to account for global confounders, and analyzed with statistical parametric mapping (Friston et al., 1995) using the SPM99 software (<http://www.fil.ion.ucl.ac.uk>). The general linear model was used to model the regional cerebral blood flow response data in a fixed effects model and relevant contrasts corresponding to null hypotheses were used to generate statistic images (Frackowiak et al., 1997). The resulting set of voxel values for each contrast, a t statistic image $SPM[t]$, was thresholded at $t = 3.35$ (or a voxelwise false positive rate of $P < 0.0005$; $df = [1,160]$), reducing the number of false positive voxels of activated clusters.

A hierarchical approach to hypothesis testing was used. The activated networks were first characterized at the set level. A network of clusters were considered significantly activated if $P < 0.05$ (corrected). The activated networks were resolved into their regional structure. The activated regions were characterized in terms of the spatial extent statistic. Only clusters of a significantly activated network with spatial extents that were significant at $P < 0.1$ (corrected for multiple nonindependent comparisons) are described. The activated clusters were further resolved into peak height of local maxima. Likewise, only local maxima of significantly activated clusters are reported if the local maxima are significant at $P < 0.1$ (corrected for multiple nonindependent comparisons). All reported P values are corrected for multiple nonindependent comparisons (except where explicitly indicated) based on the theory of differentiable 3D stationary Gaussian random fields (Adler, 1981; Worsley et al., 1992, 1996). The terms of activation and deactivation are used as synonyms for relative increased and decreased RCBF, respectively. For reasons of portability of data the tables of local maxima use approximate Talairach designations (Talairach and Tournoux, 1988). When a region is described to include a Brodmann's area (BA), this is not in an inclusive sense but only implies that parts of that BA are included in the activated cluster.

Given the central importance of the medial temporal lobe (MTL) in episodic memory (Squire and Zola-Morgan, 1991; Tulving and Markowitsch, 1997b) we also explored our PET results in this region at a low threshold ($Z > 1.68$)

in combination with a small volume correction ($P \leq 0.05$; sphere of radius 30 mm) based on the false discovery rate (Genovese et al., 2002).

Results

Encoding compared to the low-level reference conditions (visual fixation and viewing) yielded a significant network of 8 regions (set level inference $P = 0.002$; thresholding at $Z = 3.29$, corresponding to a voxelwise false positive rate of $P < 0.0005$ and cluster size = 150 voxels). Prefrontal (PFC) activations included the right middle-inferior PFC ($P < 0.001$; BA 45, 46, 47 extending into BA 11), the left middle-inferior PFC ($P < 0.001$; BA 6, 44, 45, 46, 47 extending into BA 11), the anterior cingulate ($P < 0.001$; BA 24, 32) extending into the medial superior PFC (BA 6, 8). Posterior activations included both the occipitoparietal pathway (right superior parietal BA 7, $P = 0.008$; left superior-inferior parietal BA 7/40, $P < 0.001$) and the occipitotemporal pathway. The left PFC activations were clearly more pronounced compared to the right.

Activations in deep compared to shallow encoding

In the deep vs. shallow encoding (Fig. 3 and Table 2) comparison a significant network of 8 regions ($P = 0.008$; expected number < 3) was activated. The network encompassed several regions that were significant at the cluster level, including medial-left prefrontal, bilateral inferior parietal, and anterior temporal clusters: the prefrontal cluster ($P < 0.001$) consisted of medial and bilateral superior (BA 6, 8, 9, 10) as well as left lateralized middle and inferior frontal regions (BA 44, 45, 46, 47), extending into medial orbitofrontal (BA 11) and anterior inferior cingulate regions (BA 24, 25, 32). The inferior parietal clusters consisted of a right angular-superior temporal ($P = 0.075$; BA 22, 39) and a left angular-supramarginal region ($P < 0.001$; BA 39, 40).

The temporal clusters (right $P < 0.001$; left $P < 0.001$) included bilateral middle-inferior temporal regions (BA 20, 21) extending into the temporal polar region (BA 38).

Activations in shallow compared to deep encoding

In the shallow vs. deep encoding (see also Fig. 4 and Table 3) comparison a significant network of 11 regions ($P < 0.001$; expected number < 3) was activated. This network included several regions that also were significant at the cluster level, including right middle-inferior prefrontal, bilateral superior, and left-inferior parietal as well as inferior temporal, bilateral occipital, and cerebellar clusters: the prefrontal clusters consisted of a right middle frontal ($P < 0.001$; BA 9, 10, 46) and a right inferior frontal region ($P = 0.003$; BA 6, 44). The superior parietal cluster ($P < 0.001$) included precuneus and superior parietal lobe bilaterally

D vs S

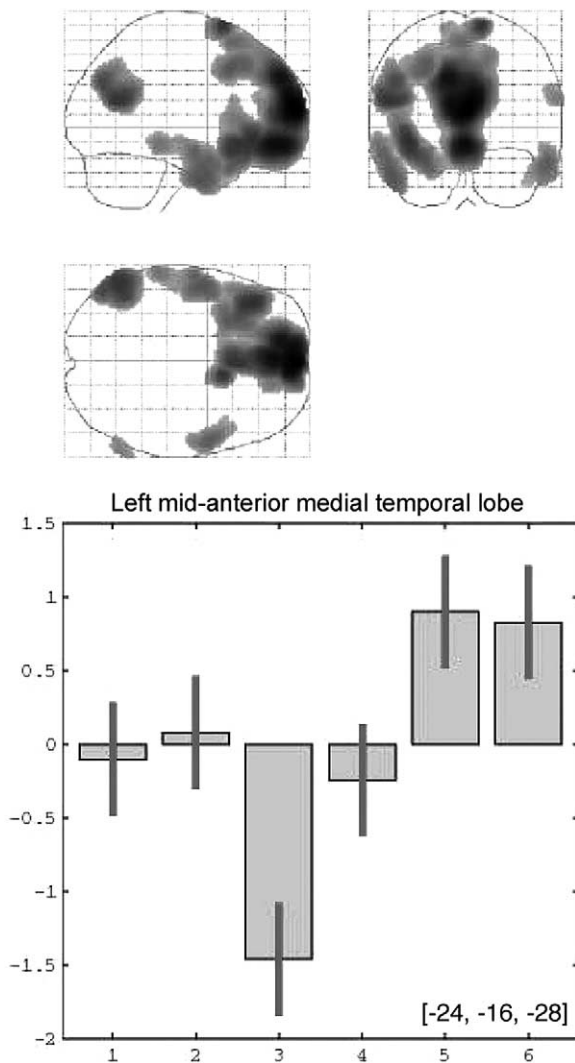


Fig. 3. (Upper panel) Maximum intensity projections of the main effect of instruction deep (D) vs. shallow (S), thresholding at $Z = 3.29$ ($P < 0.0005$) and cluster size = 150 voxels. (Lower panel) Parameter estimates of effects of interest in the left midanterior medial temporal lobe $[-24 -16 -28]$. 1 = visual fixation, 2 = viewing, 3 = shallow nonfigurative (SN), 4 = deep nonfigurative (DN), 5 = shallow figurative (SF), and 6 = deep figurative (DF).

(BA 7) extending into the superior parts of supramarginal gyrus (BA 40) and the right inferior parietal-superior occipital region (BA 7, 19). In addition, a left right inferior parietal cluster was observed ($P = 0.018$; BA 40). The temporal and occipital clusters consisted of a right inferior temporal ($P < 0.001$; BA 37) and a right middle-inferior occipital region ($P = 0.002$; BA 18, 19), both regions extending into the right fusiform gyrus. Cerebellar activations (right $P = 0.046$; left $P < 0.001$) included a right anterior medial and a more posterior left mediolateral region.

Activations in encoding of figurative compared to nonfigurative pictures

When encoding of figurative was compared with encoding of nonfigurative pictures (see also Fig. 5 and Table 4) a significant network of 16 regions ($P < 0.001$; expected number < 3) was activated. The activated network included prefrontal, left inferior parietal, left anterior temporal, right posterior inferior temporal, and medial temporal clusters that were significant at the cluster level: the prefrontal clusters included a left lateralized medial superior frontal ($P < 0.001$; BA 6, 8, 9, 10) and a left middle frontal region ($P = 0.095$; BA 6, 8). The inferior parietal cluster was localized to the posterior angular gyrus ($P = 0.034$; BA 39). The left anterior temporal and right posterior inferior temporal clusters included an anterior middle-inferior temporal region extending into the temporal pole ($P < 0.001$; BA 20, 21, 38) and a posterior inferior temporal ($P = 0.091$; BA 20). The left medial temporal activation included the left parahippocampal cortex ($P = 0.002$; BA 28, 36) extending posteriorly and laterally into the anterior fusiform gyrus (BA 36, 20).

Activations in encoding of nonfigurative compared to figurative pictures

Comparing encoding of figurative with encoding of nonfigurative pictures (see also Fig. 6 and Table 5) yielded a significant network of 12 regions ($P < 0.001$; expected number < 3) was activated. Three regions in the network were significant at the cluster level: the bilateral parieto-occipital clusters (right $P < 0.001$; left $P < 0.001$) encompassed parts of superior parietal (BA 7) and superior-middle-inferior occipital (BA 18, 19) areas bilaterally (right $>$ left). The left cerebellar activation ($P = 0.034$) included a medial-mediolateral region.

Interaction effects

A significant interaction in the contrast [(deep versus shallow) in figurative] versus [(deep versus shallow) in nonfigurative] was observed in the left anterior medial superior frontal gyrus ($P < 0.001$; BA 9, 10). In the reverse interaction contrast, [(deep versus shallow) in nonfigurative] versus [(deep versus shallow) in figurative], significant interactions was observed in the right posterior parietal ($P = 0.001$; on the border between BA 7, 40), the inferior temporal ($P = 0.005$; BA 37), and bilateral fusiform/posterior medial temporal (right $P = 0.009$; left $P = 0.094$) regions. For further details see Fig. 7 and Table 6.

Activations in the medial temporal lobe

The most robust effect was observed in the left midanterior MTL related to the figurative versus nonfigurative main effect ($P = 0.002$; BA 28, 36; see above). This effect

Table 2

Local activation maxima in the deep vs. shallow encoding (see also Fig. 3)^a

Region/cluster <i>P</i> value	BA	[x y z] ^b	<i>Z</i>	<i>P</i> value
Prefrontal cortex <i>P</i> < 0.001				
Superior frontal gyrus	6 R	10 12 72	6.10	<0.001
	6/8 L/R	-4 20 60	4.73	0.018
	10 R/L	2 62 14	>10	<0.001
	8/9 R	14 48 46	4.54	0.038
	10/11 L/R	-2 50 -12	7.55	<0.001
	9/10 L	-12 52 34	7.32	<0.001
Middle frontal gyrus	6/8 L	-28 16 40	5.09	0.004
	6/8 L	-26 26 44	5.03	0.005
Inferior frontal gyrus	47 L	-40 32 -10	6.24	<0.001
Medial orbitofrontal/cingulate gyrus	11/25 L	0 20 -14	6.08	<0.001
Inferior parietal cortex				
Right <i>P</i> = 0.075; left <i>P</i> < 0.001				
Angular/superior temporal gyrus	39/22 R	62 -62 22	6.08	<0.001
Angular/supramarginal gyrus	39/40 L	-54 -62 20	6.08	<0.001
	39/40 L	-50 -72 30	5.55	<0.001
Anterior temporal cortex				
Right <i>P</i> < 0.001; left <i>P</i> < 0.001				
Middle temporal gyrus	21 L	62 -24 4	4.89	0.009
Inferior/middle temporal gyrus	20/21 R	58 0 -26	4.99	0.006
Inferior temporal gyrus	20 L	-62 -30 6	5.20	0.002
Inferior temporal gyrus	20 L	-62 -34 -12	4.64	0.049

^a g, gyrus; l, lobule; R, right; L, left. All *P* values are corrected for multiple nonindependent comparisons.

^b The [x, y, z] coordinates refer to an approximate Talairach space (Talairach and Tournoux, 1988).

reflected an activation in the figurative condition relative to baseline, while the deep nonfigurative condition was at and the shallow nonfigurative condition appeared to be rela-

tively deactivated compared to baseline (Fig. 3, lower panel).

Further detailed analysis of the MTL responses using small volume correction (see above) showed in the deep versus shallow comparison regional increases along most of the axis of the left MTL, including the hippocampus and the parahippocampal cortex (BA 28/35/36; local maxima at [x y z] = [-24 -20 -8], *Z* = 1.92; [-24 -30 -14], *Z* = 2.05; [-34 -22 -32], *Z* = 2.81; [-14 -44 6], *Z* = 4.21). This left MTL region included or was in the vicinity of the local maxima reported by Rugg et al. (1997; [-26 -24 -8], [-32 -38 4]). Otten et al. (2001) also reported LOP-related activations in the MTL, including a left MTL region that also showed subsequent memory effects [-27 -12 -12], which are in or in the vicinity of the left MTL region reported here. In the figurative versus nonfigurative main effect, bilateral (left > right) midanterior MTL activations were observed (right BA 36, [30 -4 -40], *Z* = 3.91; left BA 28/35/36, [-24 -16 -28], *Z* = 3.99; [-38 -30 -26], *Z* = 3.90; [-28 -6 -34], *Z* = 3.90). Given the interactions observed in this MTL region bilaterally (see above), we investigated the main effect of deep versus shallow in more detail. This indicated that the deep versus shallow effect was greatest for the nonfigurative material in the anterior parts of right MTL (BA 36; [28 -12 -22], *Z* = 1.99) and the midposterior parts of the left MTL ([-32, -22 -32], *Z* = 3.69; [-28 -36 -16], *Z* = 3.30; [-14 -42 6], *Z* = 3.56). Again, the figurative versus nonfigurative effect appeared to be more pronounced in the shallow condition in the poste-

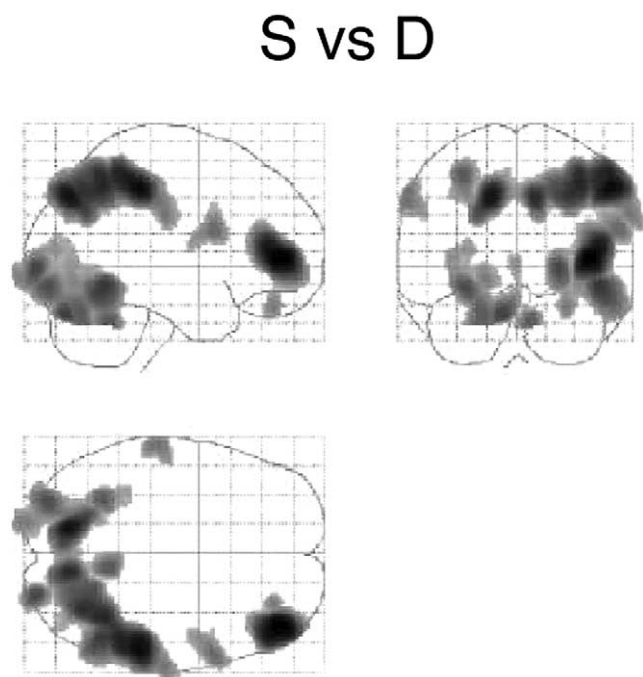


Fig. 4. Maximum intensity projections of the main effect of instruction shallow (S) vs. deep (D), thresholding at *Z* = 3.29 (*P* < 0.0005) and cluster size = 150 voxels.

Table 3

Local activation maxima in the shallow vs. deep encoding (see also Fig. 4)^a

Region/cluster <i>P</i> value	BA	[x y z]	<i>Z</i>	<i>P</i> value
Middle prefrontal cortex <i>P</i> < 0.001				
Middle Frontal gyrus	10 R	42 46 6	6.41	<0.001
Inferior prefrontal cortex <i>P</i> = 0.003				
Inferior Frontal gyrus	44/6 R	58 8 22	4.43	0.059
Parietal cortex <i>P</i> < 0.001				
Precuneus	7 R	10 -74 40	5.48	0.001
	7 L	-14 -74 40	5.97	<0.001
Superior parietal lobule	7 R	36 -54 48	5.84	<0.001
	7 L	-30 -54 54	4.67	0.023
Supramarginal gyrus	40 R	54 -34 46	6.13	<0.001
Inferior parietal/superior occipital gyrus	7/19 R	32 -66 44	5.38	0.001
Inferior parietal cortex <i>P</i> = 0.018				
Supramarginal gyrus	40 L	-62 -24 40	4.30	0.099
Temporal cortex <i>P</i> < 0.001				
Inferior temporal/fusiform gyrus	37 R	48 -54 -10	5.24	0.002
Occipital cortex <i>P</i> = 0.002				
Middle/inferior occipital gyrus	18 R	24 -94 -2	5.00	0.005
Inferior occipital/fusiform gyrus	18/19 L	-30 -86 -12	4.84	0.011
Cerebellum right <i>P</i> = 0.046; left <i>P</i> < 0.001				
Medial cerebellum	R	8 -52 -30	4.71	0.019
	L	-8 -76 -28	5.07	0.004
Mediolateral cerebellum	L			

^a g, gyrus; l, lobule; R, right; L, left. All *P* values are corrected for multiple nonindependent comparisons.

rior MTL (right BA 36; [33 -40 -10], *Z* = 4.65; left BA 28/36 [x y z] = [-30 -40 -14], *Z* = 4.15) as well as the left midanterior MTL ([-36 -26 -28], *Z* = 3.74; [-26 -18 -34], *Z* = 4.48).

Overlap between *DN - SN* and *SF - SN*

One way to investigate the degree or tendency for semantic processing during deep processing of nonfigurative material is to compare the overlap between the contrasts *DN - SN*, as an indicator of deep encoding of nonfigurative material and the brain regions engaged by the deep instruction, and *SF - SN*, as an indicator of semantic content in the material and the brain regions engaged by the figurative material. If the depth of processing effect noted for nonfigurative drawings arises because the deep processing task (pleasantness judgment) encourages them to attribute meaning to these drawings then one would predict an overlap in the localization of activations for the deep nonfigurative versus shallow nonfigurative contrast and the shallow figurative versus shallow nonfigurative contrast. To the extent that there is little or no overlap, this would be consistent with the suggested interpretation above and the observation that it was relatively uncommon, judge by the self-report, that subjects instilled some of the nonfigurative drawings with some degree of semantic content. The results of a minimum *T*-field conjunction yielded limited indications of any significant overlap between these contrasts (*P* > 0.15) except in the left MTL (parahippocampal region, BA 28/35/26 [-28 -20 -32], *Z* = 5.01, *P* = 0.009; extending posteriorly into the anterior parts of the fusiform gyrus BA

36/37 [-30 -40 -14], *Z* = 4.73, *P* = 0.030). We suggest that the common overlap in the left MTL between *DN - SN* and *SF - SN* reflects the common cognitive component of episodic encoding, induced by the deep instruction in *DN - SN* and the explicit semantic content in *SF - SN*.

Discussion

The level at which a stimulus is ultimately processed depends on factors such as meaningfulness, affective quality, attention allocation, relevance, self-reference, and the subjective purpose and intention with respect to the stimulus. In the present PET study, we investigated to what extent the levels-of-processing (LOP)-related brain activations found with verbal stimuli under standard LOP manipulations (Kapur et al., 1994; Otten et al., 2001; Rugg et al., 1997) generalize to visuospatial stimuli using our version of the LOP manipulation (i.e., pleasantness vs. perceptual quality judgments during encoding). In addition, we investigated the differences in the pattern of brain activations related to encoding of figurative and nonfigurative line drawings, that is, the changes induced by manipulation of the explicit semantic content. The behavioral results indicate that recognition was better in both types of material and to a similar degree when the encoding instruction referred to the content of the drawing instead of the graphical appearance. There was no interaction between the two manipulated experimental factors. Stratifying recognition based on the response alternatives revealed better recognition performance when the observer gave either a positive or a nega-

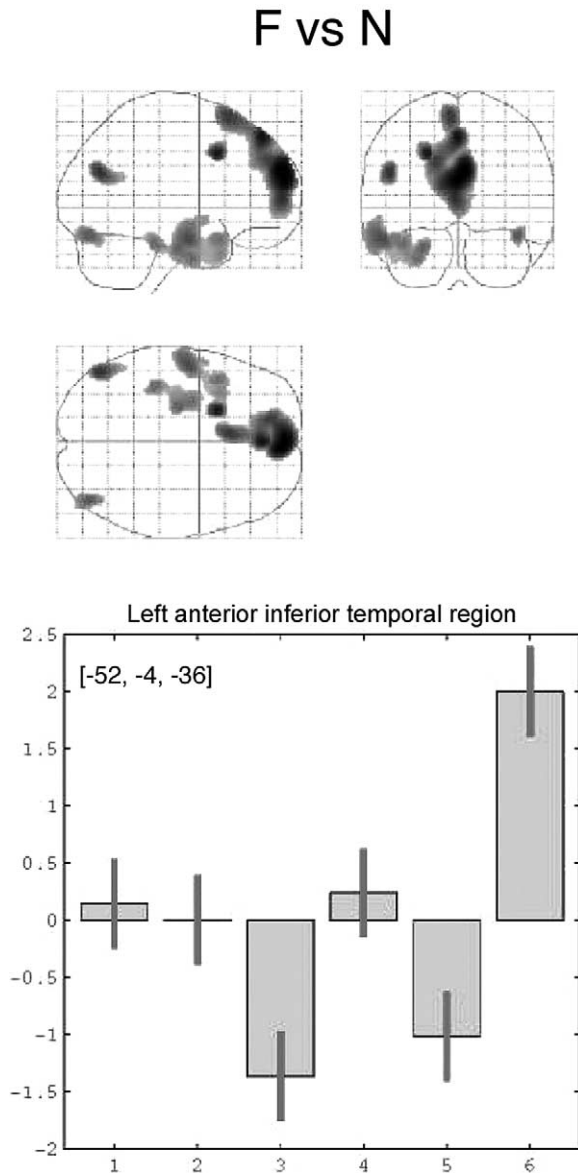


Fig. 5. (Upper panel) Maximum intensity projections of the main effect of material figurative (F) vs. nonfigurative (N), thresholding at $Z = 3.29$ ($P < 0.0005$) and cluster size = 150 voxels. (Lower panel) Parameter estimates of effects of interest in the left anterior inferior temporal region (BA 20/38) $[-52 -4 -36]$. 1 = visual fixation, 2 = viewing, 3 = shallow nonfigurative (SN), 4 = deep nonfigurative (DN), 5 = shallow figurative (SF), and 6 = deep figurative (DF).

tive response during encoding compared to neutral. There was no difference in the response times between the deep and shallow encoding tasks (see Otten et al., 2001).

Levels-of-processing effects in fronto-parietal networks

Previous functional neuroimaging studies have investigated episodic encoding and retrieval of verbal material under LOP manipulations (Kapur et al., 1994; Otten et al., 2001; Rugg et al., 1997). In the deep versus shallow incidental encoding, Kapur et al. (1994) observed left middle

and inferior PFC activations (BA 45/46, 47) and Rugg et al. (1997) observed a left inferior PFC activations (BA 45/46). Otten et al. (2001) described LOP-related prefrontal activations within which the left inferior frontal (BA 47) also showed a subsequent memory effect. We observed, in relation to the perceptually oriented encoding instruction condition, elaborate meaning-based activations in the left middle-inferior region (BA 44, 45, 46, 47).

Our results also demonstrate an extensive medial and bilateral superior (BA 6, 8, 9, 10) cluster extending into the very anterior and inferior parts of the anterior cingulate (ACC; BA 24, 32) and medial orbitofrontal cortex (BA 11, 25). These latter activations were not observed in the study of Kapur et al. (1994). Rugg et al. (1997) observed a medial superior frontal activation (BA 8) and the results of Otten et al. (2001; Fig. 1A) indicate an anterior medial superior frontal activation similar to the one observed in this study. It has been suggested that a precise characterization of the functions of prefrontal cortex has been elusive (Kimberg et al., 1997) and often couched in general terms (Fletcher and Henson, 2001). In particular, the detailed functional role of the medial PFC territory is largely unknown. However, the more posterior parts of the observed medial PFC territory has been related to generative aspects of semantic memory and working memory (object, spatial, and problem solving), and more anterior, to episodic memory encoding, both for verbal material and objects/faces (Cabeza and Nyberg, 2000). That the medial superior frontal region was activated in the figurative versus nonfigurative contrast, together with a left middle frontal region (BA 6, 8), suggests that this region is related to some aspects of semantic processing, perhaps reflecting semantic information being loaded and manipulated in on-line working memory (Fletcher and Henson, 2001). We note that a subregion of the medial superior frontal cluster showed an interaction effect; that is, the deep versus shallow effect was greater in the figurative compared to the nonfigurative condition (Fig. 7, left panel). Several studies have reported changes in activity of the medial frontal region as a result of identifying internal states (Frith, 1999; Gusnard et al., 2001). Our LOP manipulation invoked a difference in the degree of self-reference. Specifically, the deep task required the subjects to reference the picture to an inner subjective state. The interaction $[(DF - SF) - (DN - SN)]$ in the frontal lobe was most clearly expressed in the superior parts of the medial aspect of the left hemisphere (BA 9,10) and it seems probable that the opportunity for self-reference is greater in the figurative compared to the nonfigurative drawings contributing to this effect.

In shallow encoding there was a marked right middle/inferior frontal activation (Table 3) in line with a feature-based, i.e., nonsemantically dominated, on-line processing of visuospatial material (Jonides et al., 1993). In parallel with the observed prefrontal lateralization, there was a corresponding posterior parietal side difference when comparing pleasantness based with perceptually based processing. Parallel neuroanatomical frontoparietal networks have been

Table 4

Local activation maxima in encoding of figurative vs. nonfigurative pictures (see also Fig. 5)^a

Region/cluster <i>P</i> value	BA	[<i>x y z</i>]	<i>Z</i>	<i>P</i> value
Superior prefrontal cortex <i>P</i> < 0.001				
Superior frontal gyrus	6 L	−6 20 66	4.39	0.070
	8 R/L	0 44 50	4.88	0.009
	9 L	−16 50 32	4.38	0.073
	9/10 R/L	4 58 26	5.26	0.002
Middle prefrontal cortex <i>P</i> = 0.095				
Middle frontal gyrus	6/8 R	−22 12 38	4.80	0.013
Inferior parietal cortex <i>P</i> = 0.034				
Angular gyrus	39 L	−48 −70 26	4.45	0.056
Anterior temporal cortex <i>P</i> < 0.001	20/21/38 L			
Lateral occipitotemporal cortex <i>P</i> = 0.091	20 R			
Medial temporal cortex <i>P</i> = 0.002	28/36 L			

^a All *P* values are corrected for multiple nonindependent comparisons.

described by Goldman-Rakic (1988) and the hypothetical functional correlate of this seems to be represented as co-occurring activations in defined parietal and frontal regions (Cabeza and Nyberg, 2000; Fletcher et al., 1997). In the deep versus shallow comparison, the left inferior parietal region (angular-supramarginal BA 39, 40) was dominating although a small right angular—superior temporal activation was also observed (Fig. 3). It has been suggested that the left parieto-temporal-occipital region is part of a unitary semantic network (Vandenberghe et al., 1996). Consistent with this suggestion is the observation of a left inferior parietal (angular gyrus BA 39) activation in the figurative versus nonfigurative. In the reverse comparison of shallow

versus deep, the posterior parietal activations were clearly dominating on the right side (Fig. 4). These included the precuneus, the superior parietal (BA 7; right > left) extending into the right inferior parietal and superior occipital regions (BA 19). This is in line with the emphasis on visuo-perceptual feature-based processing and stimulus-controlled visuospatial attention (Corbetta and Shulman, 2002; Gitelman et al., 1999; Mesulam, 1998) and that we observed greater parietal activations on the right compared to the left in the nonfigurative versus figurative contrast. Furthermore, the interaction effect observed on the border of right BA 7 and BA 40 can also be interpreted along these lines (Fig. 7, right panel). In summary, these results indicate clear instruction-specific lateralization in parallel frontoparietal networks reflecting the encoding instruction manipulation. The bilaterally distributed, frontal cortical activations in both encoding levels, when compared to the low-level reference conditions, complement the HERA model (Tulving et al., 1994) as well as the observation of a material-specific PFC activation in encoding that was recently reported (Kelley et al., 1998). However, holding the material constant, the left prefrontal activation in deep versus shallow and the right prefrontal activation in shallow versus deep is difficult to reconcile with the HERA model. Our findings indicate that the prefrontal pattern of activation is processing sensitive and depends on task instructions (Petersson et al., 2001), in this case a LOP manipulation.

Our generalization to visual material of the left middle-inferior PFC results reported by Kapur et al. (1994) and Rugg et al. (1997) independent of whether the material was figurative or nonfigurative lends support to the suggestion by Kapur et al. (1994) that these activations are related to elaborate meaning-based processing. However, in our experimental setting this conceptualization may need to be given a broader interpretation since we used pleasantness judgments in the deep encoding condition, meaning that the subjects were associating the stimuli in a meaningful way with an inner subjective state (Craik and Tulving, 1975). The human orbitofrontal cortex has been related to affective

N vs F

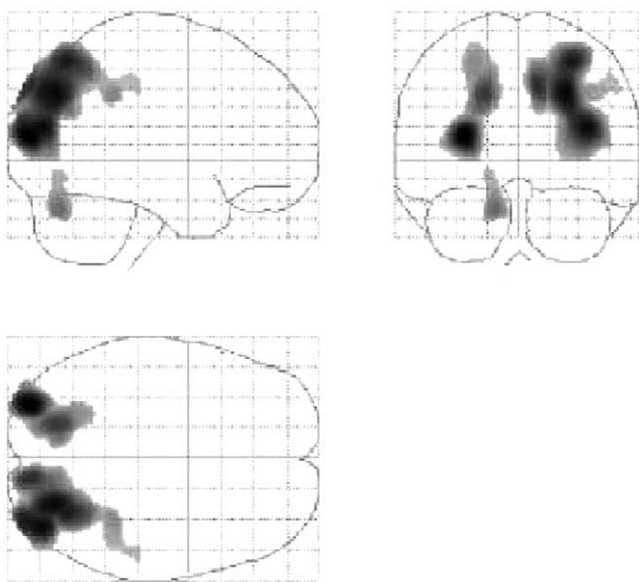


Fig. 6. Maximum intensity projections of the main effect of instruction nonfigurative (N) vs. figurative (F), thresholding at $Z = 3.29$ ($P < 0.0005$) and cluster size = 150 voxels.

Table 5
Local activation maxima in encoding of nonfigurative vs. figurative pictures (see also Fig. 6)^a

Region/cluster <i>P</i> value	BA	[x y z]	Z	<i>P</i> value
Parieto-occipital cortex				
Right <i>P</i> < 0.001; left <i>P</i> < 0.001				
Superior parietal lobule	7 R	30 -68 56	5.78	<0.001
Superior parietal lobule/occipital gyrus	7/19 R	26 -74 38	6.08	<0.001
	7/19 L	-18 -72 38	5.29	0.001
Superior occipital gyrus	19 R	38 -80 18	6.08	<0.001
	19 R	12 -88 40	5.46	0.001
Middle occipital gyrus	18 R	34 -90 20	6.09	<0.001
Middle/inferior occipital gyrus	19/18 L	-30 -88 14	6.38	<0.001
Cerebellum <i>P</i> = 0.034	L	-12 -72 -26	4.56	0.036

^a All *P* values are corrected for multiple nonindependent comparisons.

processing in both lesion and functional neuroimaging studies (Elliot et al., 2000), including pleasant touch (Francis et al., 1999) as well as abstract reward and punishment (O'Doherty et al., 2001). We therefore suggest that the observation of activations during deep encoding in the inferior parts of the ACC and the medial orbitofrontal cortex, with both figurative and nonfigurative line drawings, indicates that the subjects meaningfully engaged in the pleasantness evaluation of the stimuli regardless of whether the stimuli contained any explicit semantic content or not (see Frey et al., 2002).

In the reverse comparison, shallow versus deep, a right lateralization of the prefrontal activation independent of whether the material was figurative or nonfigurative was expected given the emphasis on visuo-perceptual feature-based processing during the shallow encoding of the stimulus material (Golby et al., 2001; Kelley et al., 1998). Two regions of the PFC were significantly activated, the right middle frontal (BA 9, 10, 46) and more posterior, the right inferior frontal region (BA 6, 44). Altogether, this indicates instruction-specific left middle-inferior and medial PFC regions associated with meaning-based as well as right middle and inferior frontal PFC regions associated with perceptual feature-based processing independent of whether the material was figurative or nonfigurative; that is, the simple main effect, deep versus shallow, and its reverse with nonfigurative line drawings, yielded almost identical results as the main effect, deep versus shallow; that is, activations were observed in the left middle and inferior frontal region (*P* = 0.057 BA 9, 10, 46; *P* = 0.001, BA 47), medial superior frontal (*P* < 0.001; BA 9, 10), inferior parts of the left ACC/medial orbitofrontal cortex (*P* = 0.020, BA 32, 11), as well as the right middle-inferior frontal gyrus (*P* = 0.017; BA 9, 10, 46), respectively.

Levels-of-processing effects in temporal regions

Lesion and PET data indicate that the left middle-inferior temporal and the left anterior temporal regions are related to the interaction of semantic processing and lexical retrieval (Damasio et al., 1996) and Vandenberghe et al. (1996) also

include the left middle-inferior temporal region in their suggested semantic network. In the present study we observed left middle-inferior temporal and temporal pole activations (BA 20, 21, 38). In addition there was a smaller right anterior temporal activation. The left anterior middle-inferior temporal region was also activated in the figurative versus nonfigurative comparison. Consistent with the suggested functional interpretation of this region, the anterior temporal activations were mainly related to the deep figurative condition (Fig. 5, lower panel; this was the case for both the left and right activation). In contrast, in the reverse comparison, the right posterior inferior temporal (BA 37) and occipitotemporal (BA 18, 19) regions extending into the right fusiform gyrus were activated instead, presumably reflecting aspects of visuo-perceptual processing relating to the judgment of graphical quality.

The medial temporal lobe

It appears that the different MTL structures are crucially involved in associative binding of distributed information representations processed on-line and stored as a long-term declarative memory at the time of encoding (Squire, 1992; Squire and Zola-Morgan, 1991). Rugg et al. (1997) reported greater activation in the left MTL in the deep versus shallow comparison. Otten et al. (2001) reported similar LOP manipulation effects in the MTL. This is consistent with the suggestion of Craik and Tulving (1975) that emphasizes that the intention to memorize information is not a critical determinant of subsequent retrieval. In other words, long-term memory formation often occurs incidentally without any explicit intention to remember the information processed and represents an automatic and dynamic consequence of processing attended information in combination with system plasticity. In the present study these MTL findings were replicated, using visuospatial stimuli instead of word stimuli, indicating a greater level of activation in the left MTL during incidental encoding in the deep versus shallow comparison. At closer examination, the deep versus shallow effect appeared to be greater in the encoding of the non-figurative compared to figurative material. This may indi-

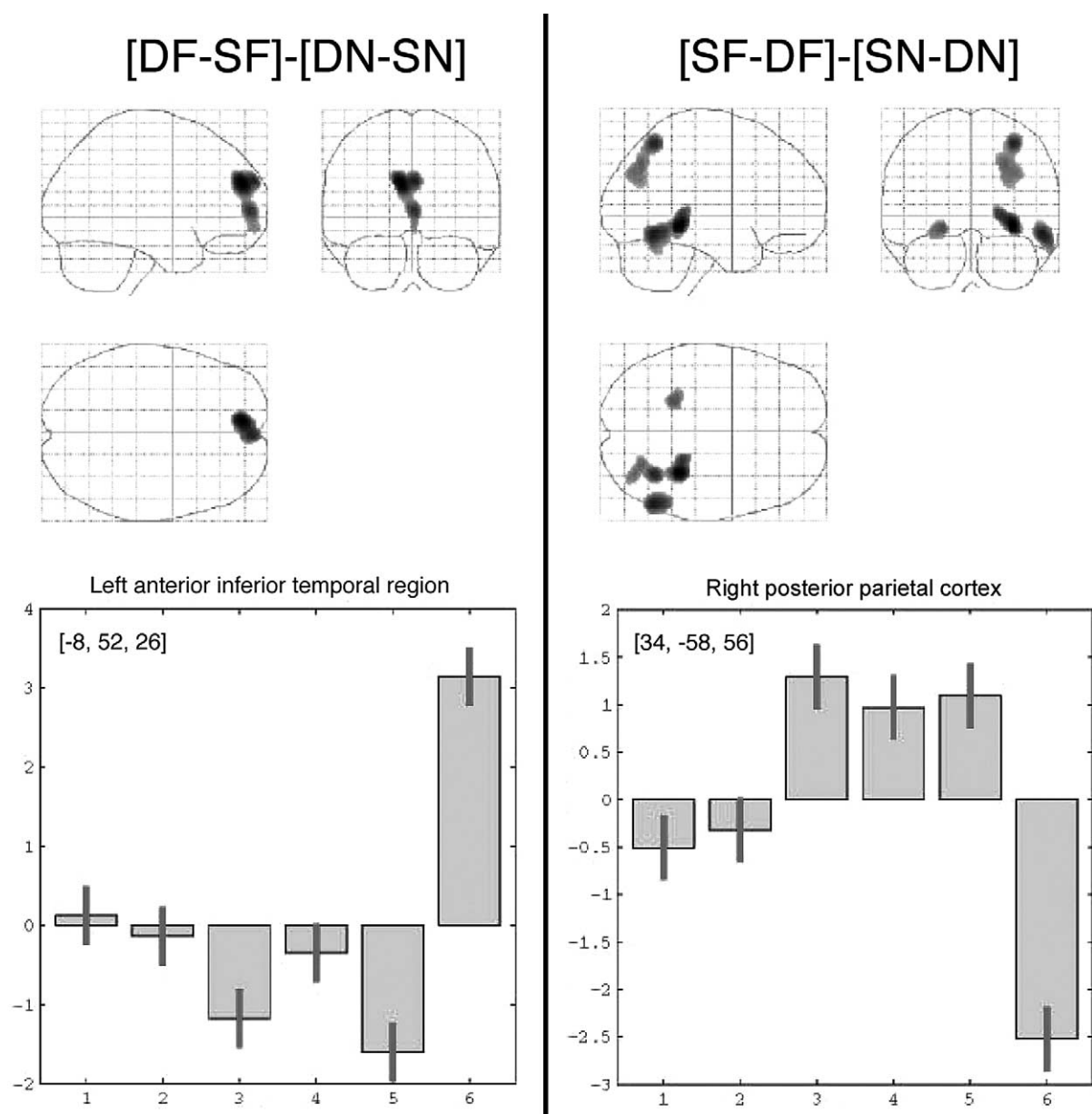


Fig. 7. (Left panel) Maximum intensity projections of the interaction effects, thresholding at $Z = 3.29$ ($P < 0.0005$) and cluster size = 150 voxels, $[DF - SF]$ vs. $[DN - SN]$. Parameter estimates of effects of interest in the left anterior medial superior frontal cortex $[-8\ 52\ 26]$. 1 = visual fixation, 2 = viewing, 3 = shallow non-figurative (SN), 4 = deep nonfigurative (DN), 5 = shallow figurative (SF), and 6 = deep figurative (DF). (Right panel) $[DN - SN]$ vs. $[DF - SF]$. Parameter estimates of effects of interest in the right posterior parietal cortex (BA 7/40) $[34 - 58\ 56]$. 1 = visual fixation, 2 = viewing, 3 = shallow nonfigurative (SN), 4 = deep nonfigurative (DN), 5 = shallow figurative (SF), and 6 = deep figurative (DF).

cate that more information is encoded into the memory trace in the nonfigurative condition when modulated by the deep instruction. Alternatively, this may be interpreted as indicating an interaction with novelty effects (Tulving et al., 1994), attentional, or familiarity processing factors (Petersson et al., 2001).

In addition, the MTL was more active when encoding figurative compared to the nonfigurative material. A closer examination indicated that this effect was more pronounced in the shallow encoding condition. In particular we found that the left midanterior parahippocampal cortex was more

activated in figurative compared to nonfigurative drawings, in particular during shallow encoding (BA 28/35, $[-26 -18 -34]$; $Z = 4.48$, $P = 0.048$, corrected), and a similar tendency was also noted in deep encoding. This may indicate a relatively greater automatic recruitment of meaning-based processing triggered by the figurative content and thus it appears that region is particularly related to encoding of meaningful visuospatial material.

Overall these results point to a complex pattern of responses in what appears to be different subregions of the MTL (Tulving and Markowitsch, 1997b; see also Otten et

Table 6

Interaction effects: local activation maxima observed in the contrast [(deep vs. shallow) in figurative] vs. [(deep vs. shallow) in nonfigurative] and the reverse, that is, [(deep vs. shallow) in nonfigurative] vs. [(deep vs. shallow) in figurative] (see also Fig. 7)^a

Region/Cluster P-value	BA	[x y z]	Z	P value
[DF – SF] vs. [DN – SN] Superior prefrontal cortex $P < 0.001$				
Superior frontal gyrus	9/10 L	–8 52 26	4.68	0.021
[DN – SN] vs. [DF – SF] Parieto-occipital cortex $P = 0.001$				
Superior/inferior parietal lobule	7/40 R	34 –58 56	4.30	0.097
Temporal cortex $P = 0.005$				
Inferior temporal/fusiform gyrus	37 R	54 –60 –14	4.42	0.062
Posterior medial temporal cortex Right $P = 0.009$; left $P = 0.094$				
Fusiform/parahippocampal gyrus	36 R	32 –40 –6	4.92	0.008
	36/37 L	–22 –44 –8	3.92	0.329

^a All P values are corrected for multiple nonindependent comparisons.

al., 2001; Strange et al., 2002). Strong evidence for a functional segregation of subregions in the human MTL was recently reported by Fernandez et al. (2002). It therefore appears that the MTL is more actively engaged by elaborate meaning-based processing indicated by the greater engagement of especially the left MTL in the main effects deep versus shallow and figurative versus nonfigurative processing.

Conclusions

In conclusion, the behavioral result indicates that the type of instruction and the type of material both contribute independently to the level of recognition performance. This, taken together with the assumption that the nonfigurative drawings contain less semantic information, indicates that the foundation of the LOP effect lies both in the relative relevance of the stimuli and in an altered processing mode brought about by the explicit instruction. Possibly this is the result of the formation of meaningful associative connections between the stimulus at hand, the subjective experience, and previously acquired knowledge. Independently from this mechanism, the semantic content of the stimulus, its interpretability, may provide different levels of encoding opportunity. It appears then that the encoding instruction biases the system toward different encoding modes, whereas the semantic content of the stimuli provides different encoding opportunities.

In the PET study, incidental encoding of visual material under a pleasantness judgment instruction yielded left lateralized frontoparietal and anterior temporal activations while surface-based perceptually oriented processing yielded right lateralized frontoparietal, posterior temporal, and occipitotemporal activations. Most of these effects were independent of whether the stimuli were figurative or nonfigurative. The result that deep encoding was related to the left prefrontal cortex while shallow encoding was related to

the right prefrontal cortex, holding the material constant, is not consistent with the HERA model. In addition, we suggest that anterior medial superior frontal region is related to aspects of semantic processing and that the activations in the inferior parts of the ACC and the medial orbitofrontal cortex are related to self-referential affective processing, regardless of whether the stimuli contained any explicit semantic content or not. Concerning the medial temporal lobe, it appears that it is more actively engaged by elaborate meaning-based processing. This is indicated by the greater engagement of especially the left MTL in the main effects deep versus shallow and figurative versus nonfigurative processing. However, the complex response pattern observed in different subregions of the MTL lends support to the suggestion that this region is functionally segregated, as suggested by others.

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