
Chapter 5

Detection of Perceptual, Semantic and Emotional Deviance

Part I Non-Adapting Responses

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5.1 Introduction

The previous experiments demonstrated anterior hippocampal responses to novelty. Chapter 1 introduced the orienting response as the behavioural correlate of novelty detection, a response evoked by both novel and salient stimuli (O'Keefe and Nadel, 1978). An item can be salient because it violates the prevailing context in which it is encountered. The brain mechanisms for detecting such violations have been studied extensively in 'oddball' paradigms, where the oddball stimulus deviates in some dimension from the prevailing context (Rugg, 1995). The observation that we note, and remember, the exceptional over the mundane has motivated the extensive psychological and electrophysiological analysis in oddball paradigms. In fact, the majority of neuropsychological studies of cognitive event-related potentials (ERPs) have focused on the electrophysiological correlate of oddball detection, the P300 complex (Rugg, 1995).

Despite intensive investigation, the functional significance and neural origin of oddball-evoked electrical activity remain controversial. Hypotheses range from a single cognitive operation arising from activity in a single generator (Donchin and Coles, 1988) to the P300 reflecting summation of activity from multiple functionally independent generators, each sensitive to a different stimulus attribute (Johnson, 1993). To examine neuronal responses to oddball stimuli, I designed an event-related fMRI study which tested these hypotheses by presenting 3 types of oddballs, perceptual, semantic and emotional, all of which evoke a P300 (Williamson *et al.*, 1991; Fabiani and Donchin, 1995). Specifically, attribute-specific neuronal responses were examined, as well as responses common to all 3 oddball types.

During fMRI scanning, 11 subjects viewed lists of 19 nouns, serially presented, where all nouns within a given list belonged to the same category except for one, the semantic oddball. In these lists a further noun was presented in a novel font (perceptual oddball) and a further noun was emotionally aversive (emotional oddball). The three oddball types were randomly positioned within the lists with the constraints that the first 5 nouns were control nouns (i.e. non-oddballs), to set the context, and that each oddball was followed by at least one control noun. Figure 5.1 gives examples of the stimuli. Lists were studied under one of two tasks: deep (requiring a living/non-living judgement) and shallow processing (determining whether the first letter had an enclosed space) (Fraik and Lockhart, 1972). It was hypothesised that neuronal responses to the perceptual and emotional oddball would be task-independent, whereas neuronal responses to the semantic oddball would be enhanced by attending to meaning in the deep encoding condition. The P300 evoked by semantic oddballs is larger when subjects process stimuli according to semantic attributes than when attending to physical features (Fabiani and Donchin, 1995). Neuronal responses to semantic oddballs also address the origin of the N400 event-related potential, a component sensitive to semantic deviance that is also enhanced in semantic processing (Kutas and Van Petten, 1994).

In chapters 3 and 4, it was concluded that mismatch between expectation and experience is a critical variable for eliciting anterior hippocampal responses. As oddball stimuli are, by definition, unexpected, it was hypothesised that oddballs would engage anterior hippocampus. Stimuli that deviate from their prevailing context along some dimension are also better remembered than the remaining stimuli

that determine a context. This well-known memory enhancement, referred to as the von Restorff effect (von Restorff, 1933), suggests that deviant stimuli have preferential access to episodic memory, lending inferential support to a hypothesis that oddballs engage the hippocampus. Thus oddball-evoked neuronal responses measured in the current paradigm also speak to mechanisms mediating enhanced memory for P300-evoking oddball stimuli.

Figure 5.1. Examples of presented nouns. Abbreviations: P: perceptual oddball; S: semantic oddball; E: emotional oddball.

				P		S		E
..gathering	..meeting	.. conference	.. group	.. people	.. carrot	..assembly	..massacre..	
				E		P		S
..bucket	.. cloth	.. maid	.. poison	.. varnish	.. soap	.. housekeeper	.. clarinet ...	
				P		E		S
..attic	.. storage	.. container	.. <i>cabinet</i>	.. warehouse	.. morgue	.. locker	.. penguin ...	

5.2 Materials and Methods

5.21 Subjects

Informed consent was obtained from 12 right-handed, native English speaking subjects (6 male, 6 female; age range 18 - 30 yrs; mean age 23.3). Data from one subject were discarded due to technical failure. A further 10 subjects (3 male, 7 female; age range 22 – 32 yrs; mean age 26.3) completed the psychological task outside of MRI scanning.

5.22 Psychological task

During scanning subjects viewed nouns presented visually in lower case at a rate of one every 3 seconds. During each of the 4 sessions, subjects were presented with 8 lists of 19 nouns with the words “New List” presented between lists. For each list, 16 nouns were of the same semantic category, emotionally neutral and all presented in the same font. These are referred to as control nouns. The perceptual oddball was presented in a novel font but was emotionally neutral and of the same semantic category as the control words. The semantic oddball was of a different category but emotionally neutral and presented in the same font as the 16 control nouns. The emotional oddball was emotionally aversive but of the same category and perceptually identical to the control nouns. The semantically-related nouns were constructed using the Edinburgh associative thesaurus (www.itd.clrc.ac.uk/Activity/Psych). Nouns were presented in Times font (48 point;

4-10 degrees of horizontal visual angle) except for the perceptual oddballs, which appeared in 16 different fonts (same fonts as in chapter 3).

Subjects engaged in two distinct encoding tasks. During two of the sessions, subjects were required to indicate with a push-button whether or not the first letter in the noun had an enclosed space (the shallow encoding task) (Craik and Lockhart, 1972). During the other two sessions, subjects indicated whether the noun described a living or non-living entity (the deep encoding task). Encoding instructions were provided visually at the start of each session and half of the subjects followed the order: shallow, deep, deep, shallow, and the other half: deep, shallow, shallow, deep. Due to constraints of fMRI scanning, it was not possible to assess recall after each list presentation for the subjects who were scanned. 10 subjects completed the psychological task outside of scanning. In these subjects, memory for presented nouns was assessed by verbal recall following the presentation of each list of 19 nouns.

The P300 complex has been divided on the basis of scalp topography and task correlates into the fronto-central P3a, evoked by novel distractor stimuli and a component of the characteristic response to orienting stimuli, and a later parietal P3b, evoked by infrequent target stimuli (Rugg, 1995). This experiment was not designed to dissociate these two components. Furthermore, the P300 evoked by an oddball stimulus is often preceded by a negative component (N1 and/or N2) and often followed by slow potential shifts (Alexander *et al.*, 1997). These effects may contribute to the slow haemodynamic responses observed.

5.23 Data acquisition

For each subject, data were acquired in four scanning sessions. A total of 540 volumes were acquired per subject plus 20 ‘dummy’ volumes (5 at the start of each session), subsequently discarded, to allow for T1 equilibration effects. Volumes were acquired continuously every 3740 ms. Each volume comprised forty-two 3mm axial slices, with an in-plane resolution of 3x3mm, positioned to cover the whole brain. The imaging time series was realigned to correct for interscan movement and normalised into a defined space (Talairach and Tournoux, 1988) to allow group analyses. The data were then smoothed with a Gaussian kernel of 8 mm full width half-maximum to account for residual intersubject differences (Friston *et al.*, 1995a).

5.24 Data analysis

Imaging data were analysed using Statistical Parametric Mapping (SPM98) employing an event-related model (Josephs *et al.*, 1997; see chapter 2 part II and chapter 4). As mentioned previously, event-related analyses can identify changes in the BOLD response evoked by single stimuli by modeling responses with basis functions of peri-stimulus time. The basis functions used here were a synthetic, canonical haemodynamic response function and its temporal derivative. The inclusion of a derivative allowed for differential response latencies (Friston *et al.*, 1998b).

The event-related analysis was a random effects analysis implemented with a two stage procedure. To test for the effects of each oddball type vs control, 6 effects of interest were specified: the events corresponding to the presentation of the 3 oddball types and 3 randomly-selected control nouns (one for each oddball type).

The chosen control nouns, like the oddballs, could not occur within the first 5 nouns of each list and could not immediately follow an oddball or another chosen control noun. Trial-specific responses were modeled by convolving a delta function (or ‘stick’ function) that indicated each event-type onset with the haemodynamic response function, and its temporal derivative, to create regressors of interest. The events corresponding to the presentation of the ‘New List’ marker were modeled as regressors of no interest, as were low frequency drifts in signal (cut-off 120 secs). The data were normalised for global effects by proportional scaling. The fact that each oddball was always followed by a control word could have enabled subjects to predict when oddballs would and would not occur within a given list. This constraint was imposed, however, to minimise the correlation between haemodynamic responses evoked by different oddball types within each list.

The random effects analysis involved two stages. Firstly, session-specific parameter estimates pertaining to the height of the haemodynamic response for each effect of interest were calculated for each voxel. An appropriate contrast of parameter estimates across sessions was calculated in a voxel-wise manner to produce, for each subject, one contrast image for that particular comparison. Secondly, six contrast images for each subject (one image for each oddball type and one for each control noun type, all six collapsed across deep and shallow encoding) were entered into a repeated measures ANOVA (with pooled error term) across the 11 subjects. Although this analysis collapsed across encoding task, the parameter estimates for reported activations are plotted for deep and shallow encoding tasks separately. The error bars in these plots depict the standard error of the mean of the parameter estimate differences.

To examine responses commonly evoked by all oddballs, a conjunction analysis was performed on the three oddballs versus their respective controls. A conjunction is defined as a significant main effect in the absence of any interactions among the simple effects (Price and Friston, 1997) and requires an independent baseline for each effect being tested. This is why 3 control words were randomly assigned as the control for each oddball type. In both reported conjunctions, the interactions were removed at a threshold of $p < 0.001$. The conjunction therefore tests for the activating effects of oddballs relative to controls that are common to three different contexts. A psycho-physiological interaction analysis (Friston *et al.*, 1997), testing for the modulatory effects of the right prefrontal cortex on novelty responses, followed the same 2 level procedure except that, for each subject, the effects of interest were the convolved oddball and control noun regressors multiplied by that subject's session-specific adjusted activity at, or nearest to, voxel (48, 21, 21). The regressors themselves and the right prefrontal adjusted activity were modeled as effects of no interest.

To test for oddball x encoding task interactions, a further six contrast images for each subject (one image for each oddball type minus its respective control in the deep and in the shallow encoding conditions) were entered into a repeated measures ANOVA (with pooled error term) across the 11 subjects. This analysis also provided a test for an interaction with encoding task in regions that previously demonstrated a main effect of oddball. The absence of a significant interaction ($p < 0.05$ uncorrected) in these regions was taken to suggest that oddball-evoked activation in these regions was independent of encoding task.

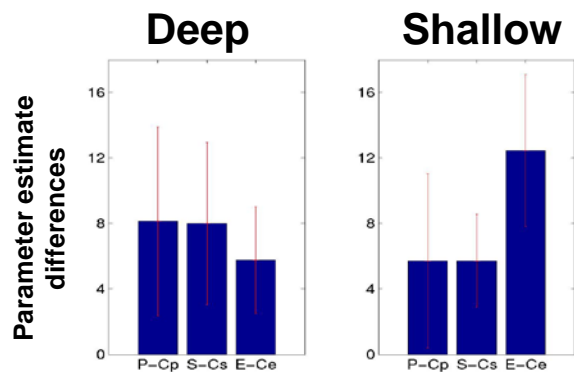
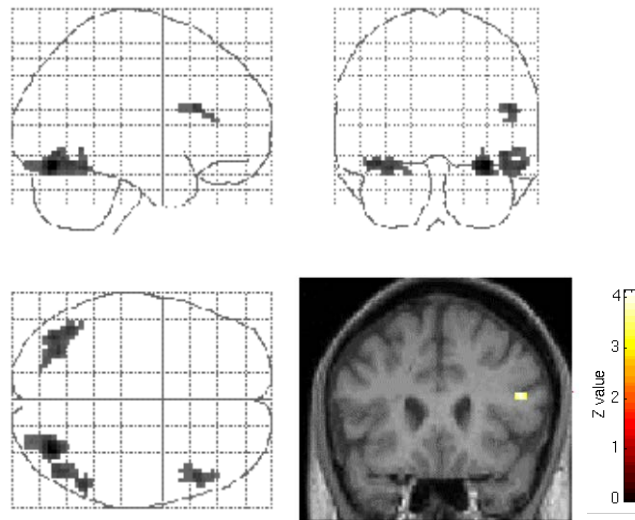
All regions which survived correction for multiple comparisons at $p < 0.05$ are reported plus those regions surviving an uncorrected threshold of $p < 0.001$ for which there was an *a priori* hypothesis for activation (namely left and right prefrontal and inferior parietal cortices and amygdala). In all random effects ANOVAs it was assumed that the within-subject between-contrast variability was at the same level for all contrasts (i.e. sphericity).

5.3 Results

5.3.1 fMRI data

For each oddball type, the neuronal response evoked by an oddball was compared with that evoked by a randomly chosen control noun in the same list, yielding an independent control for each oddball. To determine activation commonly evoked by all oddball types, a conjunction analysis was conducted for the 3 oddball types versus their respective controls. Activation, independent of encoding task, was evoked in right inferior frontal sulcus and bilateral posterior fusiform cortex (figure. 5.2). The graph in figure 5.2 demonstrates the parameter estimates for the height of the haemodynamic response for the 3 oddballs minus their respective control nouns in right prefrontal cortex for both deep and shallow encoding.

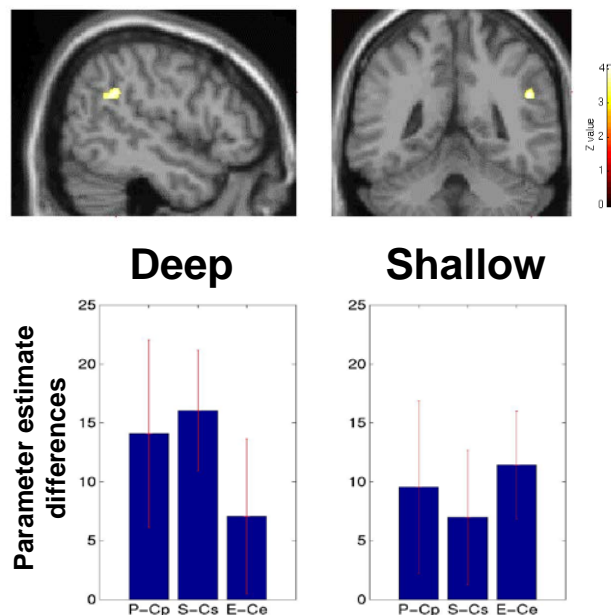
Figure 5.2. Areas commonly activated by all oddball types. The SPM (threshold $p < 0.001$, extent threshold $p < 0.05$) of the conjunction is superimposed on a glass brain and demonstrates activation in the right prefrontal cortex (dorsal BA45; x, y, z coordinates 48, 21, 21; $Z = 4.15$) and bilateral posterior fusiform (33, -75, -18; $Z = 5.51$, $p < 0.05$ corrected and -39, -72, -15; $Z = 4.42$, both in BA19) extending into the inferior temporal gyrus on the right. Also shown is the SPM superimposed on a coronal section of the Montreal Neurological Institute (MNI) reference T1 image (Cocosco *et al.*, 1997) at $y = 21$, demonstrating activation in right inferior frontal sulcus. The plot shows the parameter estimates for the height of the haemodynamic response in right prefrontal cortex for the 3 oddballs minus their respective control words during both deep and shallow encoding. The units are adimensional and correspond to responses per unit increase in the explanatory variables scaled arbitrarily. Here and in all subsequent figures, error bars represent ± 1 standard error and abbreviations are: P: perceptual oddball; S: semantic oddball; E: emotional oddball; Cp: control noun for perceptual oddball; Cs: control noun for semantic oddball; Ce: control noun for emotional oddball.



It is thought that oddball detection involves recruitment of an attentional orienting system (Ritter *et al.*, 1968). Right prefrontal activation evoked by oddballs is consistent with a role for this region in monitoring discrepancies between expectation and experience (Fink *et al.*, 1999). A monitoring role for right prefrontal cortex suggests its involvement in engaging attention during oddball presentation. Consequently, a statistical parametric map was created to identify areas where activity can be explained in terms of oddball-specific interactions with right prefrontal activity. The analysis used a statistical model that included an effect of each oddball type, an effect of each corresponding control noun and a term that represents the interaction between each of these effects and the adjusted activity in

right prefrontal cortex. A conjunction analysis of these interactions for all 3 oddball types revealed significant modulatory effects in inferior parietal lobule (IPL) bilaterally (figure 5.3). This prefrontal-parietal coupling was not significantly modulated by depth of processing.

Figure 5.3. The right prefrontal cortex exerts significant modulatory effects on activity in the right inferior parietal lobule during presentation of all oddball types relative to control nouns. The SPM (threshold $p < 0.001$) is superimposed on a sagittal ($x = 51$) and coronal ($y = -45$) section of the T1 image and demonstrates activation of right inferior parietal lobule (BA 40; 51, -45, 30; $Z = 4.11$). Activation was also observed in left inferior parietal lobule (BA 40; -48, -57, 36; $Z = 3.79$). The plot below demonstrates the parameter estimates for the degree to which the height of the right inferior parietal haemodynamic response is modulated by right prefrontal cortex during presentation of each oddball relative to respective control nouns during both deep and shallow encoding.

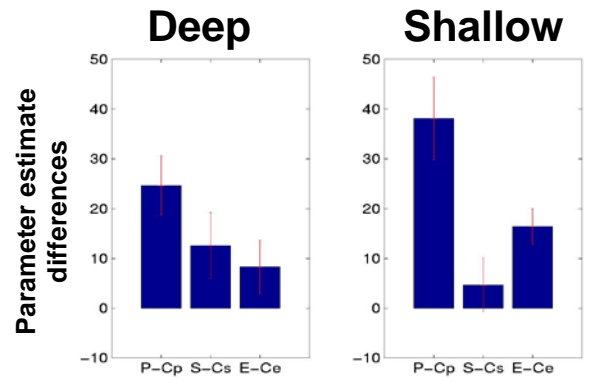
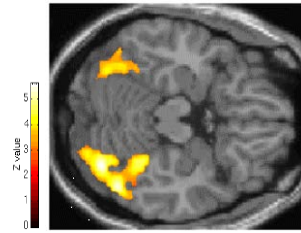
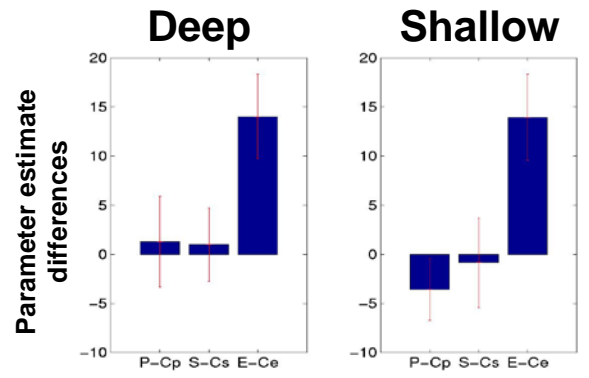
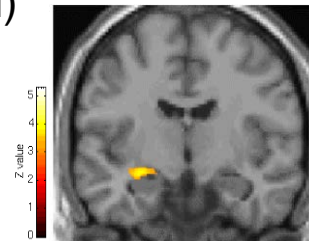
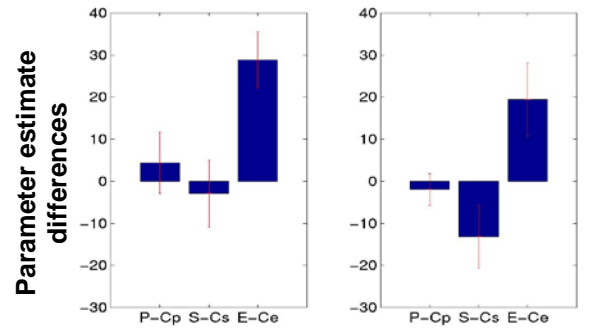
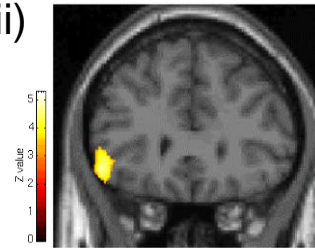
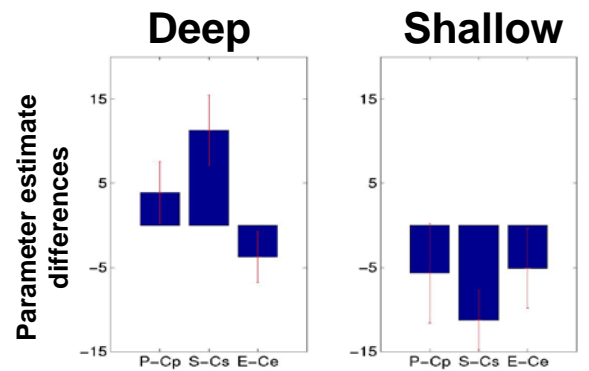
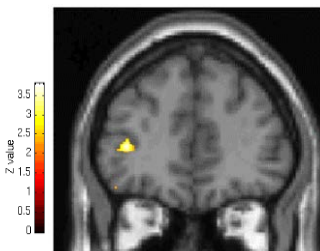


In addition to a right prefrontal-fusiform generic deviance detection network, attribute-specific responses were evoked in neuroanatomical regions known to be sensitive to either the perceptual, semantic or emotional content of stimuli. The neuronal response to perceptual oddballs, relative to their controls, is shown in figure 5.4a which demonstrates activation in posterior fusiform cortices bilaterally ($p < 0.05$ corrected) extending into inferior temporal gyrus. The response to perceptual oddballs was not significant modulated by depth of encoding, despite the shallow task directing attention to the perceptual attributes of the nouns, suggesting that the fusiform response to perceptual novelty is automatic and independent of the aspect of the stimulus being processed. The plots also demonstrate that the posterior fusiform was sensitive to semantic and emotional oddballs, as indicated by the conjunction analysis of all oddball types versus control.

Figure 5.4b illustrates the neuronal responses to emotional oddballs relative to controls. Activation was observed in left amygdala ($p < 0.001$, figure 5.4bi) and in left inferior prefrontal cortex ($p < 0.05$ corrected, figure 5.4bii). Importantly, as for perceptual oddballs, the responses in left amygdala and inferior frontal cortex appear automatic and obligatory in so far as they were not modulated by depth of processing.

Although the above responses were task-independent, it was predicted that semantic oddballs would show enhanced responses only when subjects attended to the semantic characteristics of stimuli. This interaction of deep versus shallow encoding and semantic oddballs versus controls was evident in left ventral prefrontal cortex, on the inferior bank of the inferior frontal sulcus (figure 5.4c).

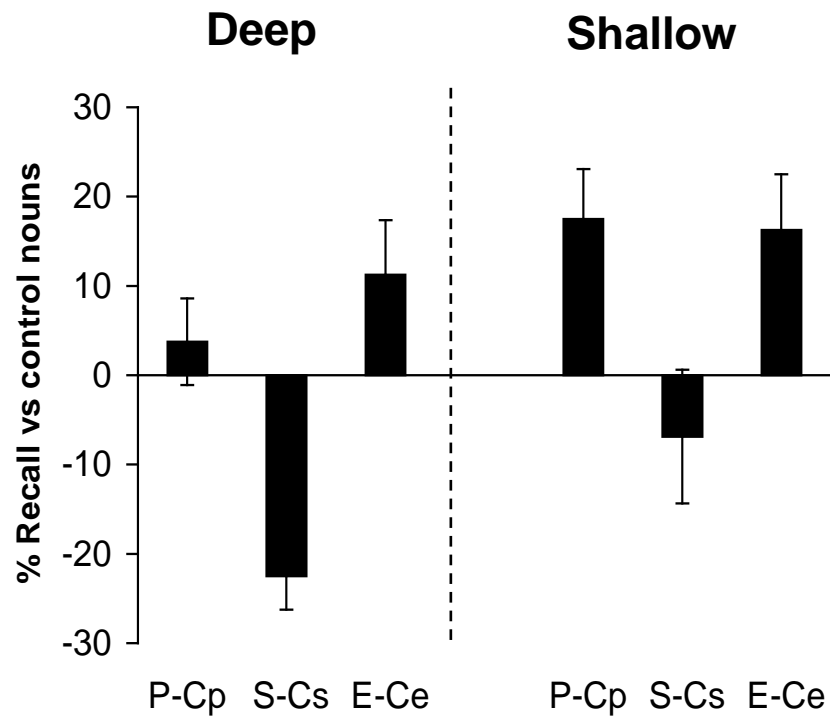
Figure 5.4. Attribute-specific activations. (a) Perceptual oddballs, regardless of encoding task, activate the posterior fusiform cortices bilaterally (33, -75, -18; $Z=5.66$ and -45, -63, -15; $Z=4.95$ both in BA19 and both $p<0.05$ corrected for multiple comparisons) extending into inferior temporal cortex. The SPM, thresholded at $p<0.001$, superimposed on a transverse section of the canonical T1 image ($z = -18$), demonstrates this activation. The parameter estimates for the height of the response in right posterior fusiform during both deep and shallow encoding are shown to the right of the section. (b) Emotionally aversive oddballs activate the left amygdala and left inferior frontal cortex, regardless of encoding task. (i) the SPM (threshold $p<0.001$) is superimposed on a coronal section of the T1 image at $y = -9$ and demonstrates activation of the left amygdala (-27, -9, -12; $Z=4.14$). (ii) the same SPM is superimposed on a coronal section ($y = 36$) and shows activation of the left inferior prefrontal cortex (BA47; -51, 36, -12; $Z=5.38$, $p<0.05$ corrected). (c) The response to semantic oddballs is modulated by depth of processing. Left, the SPM (threshold $p<0.01$), superimposed on a coronal section of the T1 image at $y = 42$, demonstrates the interaction of deep vs shallow encoding of the semantic oddballs relative to control in left ventral prefrontal cortex, on the inferior bank of the inferior frontal sulcus (BA46; -36, 42, 9; $Z=3.88$).

a**b****(i)****(ii)****c**

5.32 Behavioural data

Figure 5.5 illustrates free recall for oddballs versus control nouns which was assessed in a separate group of 10 subjects. Recall was tested immediately after each 19 noun list under both deep and shallow encoding conditions. The results demonstrate that the von Restorff effect is influenced by both attribute deviancy and the encoding task. Emotional oddballs were remembered better than controls regardless of encoding task. Perceptual oddballs, however, only showed a von Restorff effect for shallow-encoded nouns. Semantic oddballs show no von Restorff effect following shallow encoding and are in fact recalled worse than controls following deep encoding. The mean percentage of recalled control nouns following deep encoding was 60.8 % and following shallow encoding was 50 %.

Figure 5.5. Recall performance for the 10 subjects who completed the psychological task outside of scanning, recalling nouns freely after each 19 noun list presentation. The difference between recall of each oddball type and its respective control noun is plotted following both deep and shallow encoding. Subjects demonstrated enhanced recall for perceptual oddballs relative to controls (i.e. a von Restorff effect) following shallow encoding (one-tailed t-test; $p < 0.01$) but not following deep encoding ($p > 0.2$). Recall of semantic oddballs was not significantly different from controls following shallow encoding ($p > 0.15$) but deep encoding resulted in significantly less semantic oddballs being recalled than controls ($p < 0.005$). A von Restorff effect was evident for emotional oddballs following both deep ($p < 0.05$) and shallow ($p < 0.05$) encoding. Error bars represent ± 1 standard error.



5.4 Discussion

Right prefrontal activation evoked by oddballs, irrespective of the attribute conferring deviance, is consistent with a role for this region in monitoring discrepancies between expectation and experience. The activation in right inferior frontal sulcus lies between the right ventral prefrontal region that has previously been found responsive to sensory conflict between vision and proprioception and the right dorsal prefrontal region found responsive when maintaining action in the face of conflict between intention and sensory outcome (Fink *et al.*, 1999). Furthermore, a previous neuroimaging study of visual oddballs (McCarthy *et al.*, 1997) reported bilateral activation of middle frontal gyrus, with more extensive activation on the right. A role for the right prefrontal-bilateral fusiform network in processing generic deviance is supported by a similar network being engaged by viewing abnormally coloured objects compared to viewing their black and white counterparts (Zeki and Marini, 1998).

Two previous functional imaging studies of visual (McCarthy *et al.*, 1997) and auditory (Higashima *et al.*, 1996) oddball detection have demonstrated oddball-evoked activation of IPL. The former study suggested that bilateral IPL activation reflected the engagement of working memory whereas the latter suggested that right IPL mediates auditory discrimination. An alternative explanation for IPL activation in the current experiment, which was most significant on the right, is that it reflects increased attention to oddballs relative to control nouns. Note that the right hemisphere, particularly the IPL, is thought to be critical for human attention (Heilman *et al.*, 1985; Mesulam, 1990; Driver and Mattingley, 1998). The current

data suggest that a discrepancy detector located in the right prefrontal cortex mediates this attentional engagement.

It has been suggested that activity in the inferior frontal sulcus and IPL mediate a ‘preparation-to-process’ function of the orienting response (Baudena *et al.*, 1995; Halgren *et al.*, 1995; Halgren and Marinkovik, 1995), a component of which is manifest electrophysiologically as the P300 evoked by novel stimuli (Halgren and Marinkovik, 1995). Although the IPL makes a major contribution to the P300 (Smith *et al.*, 1990; Halgren *et al.*, 1998), the P300 evoked by novel stimuli has a shorter latency in prefrontal than in parietal cortex (Baudena *et al.*, 1995; Halgren *et al.*, 1995) and prefrontal lesions attenuate this P300 component over both anterior and posterior cortex (Knight, 1984). This supports the current observation of prefrontal modulation of IPL activity as well as the suggestion that prefrontal cortex plays a leading role in organising the human orienting response (Halgren and Marinkovik, 1995). Furthermore, the observed prefrontal-IPL response to oddballs might explain why lesion studies report attenuation of the oddball-evoked P300 following either lesions to temporoparietal junction (TPJ, which includes the inferior parietal lobule) or prefrontal cortex (Knight *et al.*, 1989; Yamaguchi and Knight, 1991). In further support of a right prefrontal role in engaging attention, patients with frontal damage exhibit diminished visual attention to novel events (Daffner *et al.*, 2000) leading to the suggestion that frontal damage prevents the generation of a signal indicating that a novel stimulus requires additional attention.

The posterior fusiform region activated by all oddball types has been shown to be equally sensitive to words and letter strings but insensitive to word meaning

(Nobre *et al.*, 1994). This suggests that posterior fusiform mediates a prelexical stage in word processing prior to semantic or emotional evaluation. This is consistent with the current observation that perceptual oddballs evoke activation in bilateral posterior fusiform, indicating sensitivity to perceptual attributes of stimuli (Desimone and Ungerleider, 1989). Functional imaging data have shown that posterior fusiform mediates early preferential selection of attended visual stimuli (Heinze *et al.*, 1994) with selective responses to infrequent targets (Coull *et al.*, 1998). Furthermore, intracranial ERPs demonstrate that focusing attention on words evokes focal field potentials in posterior fusiform (Nobre *et al.*, 1998). I propose, therefore, that activation in posterior fusiform reflects attentional modulation of this prelexical stage, yielding all 3 types of oddball nouns preferential access to higher stages of the word recognition process. In addition to the specific fusiform role in processing perceptual features, the data demonstrate modulation of a perceptual region by the semantic and emotional content of stimuli. Activation in posterior fusiform may, however, also reflect longer time spent attending to oddballs. It has been demonstrated that activity in bilateral posterior fusiform increases with increasing presentation duration of words (Price *et al.*, 1996) and reaction times showed that subjects took longer to respond to oddballs than they did to controls (main effect of oddball significant at $p < 0.05$, with no interactions reaching significance).

Human lesion data (Aggleton, 1992) and neuroimaging studies (Morris *et al.*, 1996) indicate that the amygdala has a critical role in detecting and responding to stimuli that represent threat. A recent functional imaging study (Isenberg *et al.*, 1999) also demonstrates an amygdala response to visually presented threatening words. These results support the current finding of amygdala engagement by emotionally

aversive oddballs. The left inferior frontal gyrus, also engaged by emotional oddballs, may also play a role in detecting threat as it has been shown to activate with increasing fearful intensity of faces (Morris *et al.*, 1998). Amygdala and left inferior frontal activations may, however, be attributed to simple aversiveness rather than to emotional deviance from the current context. One way to dissociate these effects would be to measure neuronal responses commonly evoked by an aversive word presented in a neutral context and by a neutral word that is presented in an aversive context.

There is strong evidence for greater episodic memory for emotionally aversive relative to neutral events (Cahill *et al.*, 1996) and words (Bower, 1992). Amygdala activation during encoding has been shown to correlate with subsequent retrieval of visual stimuli (Cahill *et al.*, 1996). The present imaging data demonstrate that, regardless of encoding task, left amygdala is activated by emotionally aversive nouns. The behavioural experiment demonstrated that, regardless of encoding task, these emotional nouns are recalled better than their neutral controls. Thus, together these findings suggest that amygdala activity during encoding of emotional words is the neurophysiological correlate of subsequent enhanced recall.

The responses evoked by perceptual and emotional oddballs were not significantly modulated by depth of processing suggesting automatic and obligatory responses. The left prefrontal response evoked by semantic oddballs was, however, significantly enhanced by attending to the semantic characteristics of nouns (deep encoding) relative to attending to their perceptual features (shallow encoding). This left prefrontal activation is commonly associated with memory encoding tasks,

particularly those that emphasise processing of study material in terms of semantic attributes (Tulving *et al.*, 1994; Dolan and Fletcher, 1997).

Perceptual oddballs were remembered better than controls following shallow but not deep encoding. This modulation of the von Restorff effect by depth of encoding could be due to the shallow task directing attention to the perceptual attributes of the nouns. Nonetheless, a previous study found a von Restorff effect for perceptual oddballs only following rote encoding, which does not direct attention towards perceptual attributes, and not following elaborative encoding (Fabiani *et al.*, 1990). As suggested by Fabiani *et al.* (1990), this observed modulation may also arise from differences in retrieval strategy following the two levels of processing. Although the perceptual oddball will be noted as deviant during both encoding tasks, only following shallow encoding might subjects use this perceptual attribute in their retrieval search. Deep encoding would encourage a category-cued retrieval strategy making subjects less reliant on perceptual characteristics during encoding. That emotional oddballs are recalled better than control nouns following both encoding tasks suggests that the mnemonic advantage given to emotionally aversive stimuli is not modulated by encoding task or subsequent retrieval strategy. Semantic oddballs are recalled worse than controls following deep encoding, most likely reflecting an effect of the category-cued retrieval strategy adopted following deep encoding of the semantically-related control nouns.

Contrary to prediction, the current analysis did not reveal oddball-evoked hippocampal activation. In the following section, chapter 5 part II, it is shown that hippocampal responses to oddballs adapt across the course of the experiment. The

current analysis was not sensitive to this response profile as activations were averaged across all 4 sessions. There was also no evidence of perirhinal activation in the current analysis, nor in the analysis presented in chapter 5 part II. It is noted that interactions between frontal and perirhinal cortices have been suggested as mediating the von Restorff effect in non-human primates (Parker *et al.*, 1998). The lack of perirhinal activation may be explained by the fact that the responses mediating the von Restorff effect could not be specifically tested for in the current paradigm. To test for the neuroanatomical correlates of the von Restorff effect, responses evoked by remembered vs forgotten oddballs need to be compared with responses to remembered vs forgotten control words. A further experiment is therefore required in which recall is assessed following a pause in scanning after each 19 word list. This approach (similar to that adopted in chapter 6) would produce free recall performance similar to that observed in subjects who completed the psychological task outside of scanning, which is sufficient to test for this interaction.

5.41 Summary

In conclusion, these data provide evidence in support of both hypotheses (Donchin and Coles, 1988; Johnson, 1993) concerning the origin and function of oddball-evoked neuronal activity. Oddball nouns engage a discrete attention orienting network as well as attribute-specific, functionally independent brain structures (for further discussion of these findings, see Strange *et al.*, 2000). The activation of an attention network coupled with enhanced activity in neuroanatomical regions known to be sensitive to either the perceptual, semantic or emotional content of stimuli, may influence the von Restorff effect for oddballs. Importantly, however, the behavioural data show that this memory effect is likely to depend on interactions

between the attribute conferring deviance, the encoding task and the subsequent retrieval strategy.