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# The temporal dynamics of reading: a PET study

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## SUMMARY

The temporal dynamics of evoked brain responses are normally characterized using electrophysiological techniques but the positron emission tomography study presented here revealed a temporal aspect of reading by correlating the duration a word remained in the visual field with evoked haemodynamic response. Three distinct types of effects were observed: in visual processing areas, there were linear increases in activity with duration suggesting that visual processing endures throughout the time the stimulus remains in the visual field. In right hemisphere areas, there were monotonic decreases in activity with increased duration which we relate to decreased attention for longer stimulus durations. In left hemisphere word processing areas there were inverted U-shaped dependencies between activity and word duration indicating that, after 400–600 ms, activity in word processing areas is progressively reduced if the word remains in the visual field. We conclude that these inverted U effects in left hemisphere language areas reflect the temporal dynamics of visual word processing and we highlight the implication of these effects for the design of activation studies involving reading.

## 1. INTRODUCTION

The aim of this work was to characterize the haemodynamic responses evoked by visually presented words as a function of the duration they remain in the visual field. These effects of stimulus duration are distinct from those of presentation rate (frequency) where the number of words presented per unit time is changed but the duration of each word is held constant. Previous studies manipulating stimulus duration on words and false fonts (Price *et al.* 1994, 1996a) have demonstrated that when stimuli remain in the visual field for 1000 ms relative to 150 ms, there is enhanced activation in visual processing areas and, for words only, there is decreased activation in temporal and frontal word processing areas. The contrasting effects of stimulus duration suggest functional specialization in the differing cortical regions. Further, the counter-intuitive observation that responses in temporal and frontal word processing regions are greater when word presentation is brief (150 ms) relative to when the same words remain in the visual field for longer periods of time (1000 ms), may be indicative of the time course of word processing. This hypothesis motivated a more detailed investigation of the relationship between evoked activity and the length of time a word remains in the visual field.

Three different explanations for the decreased activity in word processing regions with longer word durations have been considered. One specious argument is that there are additional effects with short durations which reflect cognitive processes other than those related to word processing. Such 'irrelevant

processing' would occur during the longer interstimulus intervals associated with short relative to long durations (the rate of presentation being constant). This explanation can be discounted because it predicts similar effects when the interstimulus interval is lengthened with slow relative to fast presentation rates (the duration of the stimuli being constant) and a previous study has shown this not to be the case (Price *et al.* 1996a). There are two more likely explanations for decreased activation with long durations and these are illustrated in figure 1. The first is that increased attention to short-lived stimuli enhances activity in word processing areas. In this case, the effects are attributable to the processing demands defined by the task (i.e. the attentional set) and represent a modulation of evoked responses that have a fixed form. The second possible explanation is that the effects are attributable to the stimulus itself and that the magnitude of the initial response remains the same but the form of the response changes with increased stimulus duration. This would be the case if increased activation in the word processing areas is followed by deactivation when (and only when) a word remains in the visual field after processing is complete. The deactivating component of these biphasic word responses will reduce the total activation when integrated over the entire 90 s scanning period.

These two contrasting explanations lead to different predications. If the decreased activation with longer duration stimuli reflects the attentional set of the task, then we might expect to see activity decrease monotonically as attentional demands decrease with longer stimulus durations. Alternatively, if decreased activation

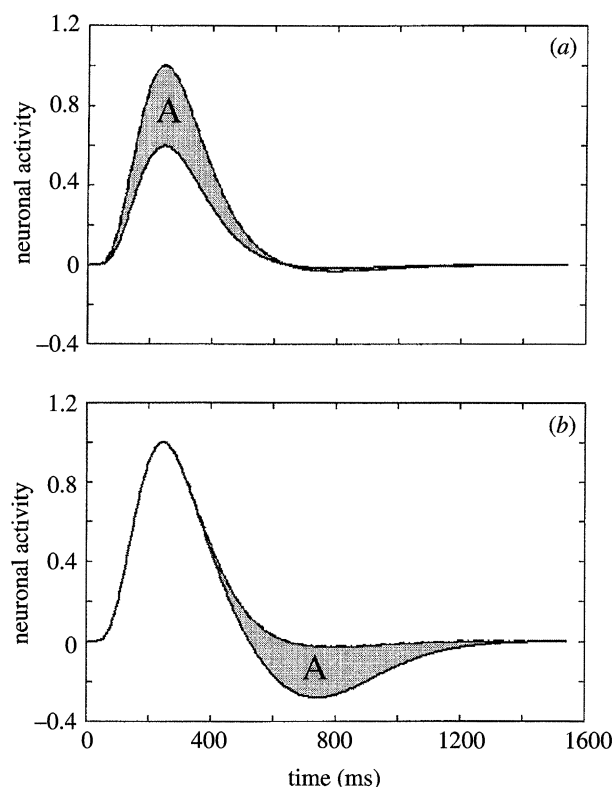


Figure 1. Explanations for the decreased activation with longer durations. Upper lines are hypothesized responses to 150 ms durations, lower lines are hypothesized responses to 1000 ms durations. (a) Attentional modulation: the shape of the response remains constant but the magnitude of the response is modulated by the attentional set with enhancement for short-lived stimuli. The enhancement for short-lived stimuli increases the total activation integrated over the 90 s scan. (b) Differential adaptation: the magnitude of the initial response remains constant, but with longer durations the shape of the response changes showing deactivation where there was initially an activation. The deactivating component with prolonged stimuli reduces the total activation integrated over the 90 s scan.

reflects deactivation following completion of word processing then we might expect to see a range of more complicated nonlinear responses depending on the time course of the neuronal dynamics associated with this processing.

In summary, differential activation with stimulus duration could reflect (i) attentional modulation of a fixed type of processing, or (ii) a qualitatively different processing elicited by long relative to short word durations. The first predicts monotonic relationships and the second more complicated nonlinear relationships. In order to distinguish between these, we have used a parametric design and functional neuroimaging with positron emission tomography (PET) to study the differential responses evoked by changing the duration of word presentation. This aim was achieved by manipulating, over scans, the duration with which a word remained in the visual field and then modelling the

average evoked response per scan as a continuous function of stimulus duration. Although this PET study measures activity averaged over a 90 s time frame, the temporal dynamics of word processing are revealed on a scale of hundreds of milliseconds by virtue of the relationship between the duration of the stimulus and the differential activation. This compliments the usual approach of measuring temporal dynamics directly using electrophysiological techniques.

## 2. METHODS

Fifteen right handed (Edinburgh Handedness Inventory) volunteers with English as their first language and no history of neurological disorder gave informed consent to participate in the study. There were seven female and eight male volunteers with a mean age of 60 years 6 months (range 30–75). Each subject contributed ten or eight PET scans that used bolus infusion of  $\text{H}_2^{15}\text{O}$ . None of these subjects participated in our previous studies of word duration (Price *et al.* 1994, 1996a). The effective dose equivalent was  $<6.6$  mSv (approved by the Administration of Radioactive Substances Advisory Committee of the Department of Health, UK). The protocol was approved by the research ethics committee of Hammersmith Hospital, London, UK.

### (a) Experimental design

The study was conducted as two separate PET experiments. In each, subjects were scanned whilst viewing 40 serially presented unrelated words (concrete nouns) per minute displayed on an Apple Mac VDU at a rate of 1 every 1.5 s. In experiment 1, seven subjects each contributed ten PET scans. One variable was word duration (150 ms, 300 ms, 450 ms, 600 ms and 750 ms), the other was reading aloud or reading silently. In experiment 2, eight subjects each contributed eight PET scans with replication of four different word durations (150 ms, 750 ms, 1000 ms and 1250 ms) and two scans for each duration. In both experiments the order of conditions was counterbalanced within and between subjects. After each scan the subjects were asked if they had read all the words. The results of our previous studies (Price *et al.* 1996b) have shown that as long as subjects look at the stimuli, there is robust activation in word processing areas. The neurophysiological responses observed in the current study were extremely consistent with these previous studies of word reading.

### (b) Data acquisition and preprocessing

The scans were obtained using a Siemens 953B (CTI, Knoxville, USA) dedicated head scanner (Spinks *et al.* 1992) and radiolabelled water ( $\text{H}_2^{15}\text{O}$ ) according to standard protocols (Silbersweig *et al.* 1993). Correction for attenuation was made using a transmission scan with an exposed 68 Ge/68 Ga external source at the beginning of each study. Images were reconstructed by filtered back projection (Hanning filter, cut-off frequency 0.5 Hz), giving a transaxial resolution of 8.5 mm full width at half maximum. The reconstructed images contained  $128 \times 128$  pixels, each  $2.05 \times 2.05 \times 2.00$  mm in size. The data were analysed with statistical parametric mapping (SPM: Wellcome Department of Cognitive Neurology, London, UK; <http://www.fil.ion.ucl.ac.uk/spm>), implemented in Matlab (Mathworks Inc., Sherborn, MA, USA). Prior to statistical analysis the images from each subject were realigned using the first as a reference to correct for any interscan head movements and transformed into standard

space (Friston *et al.* 1995). When stereotactically normalized, one voxel in the transformed image represents 2 mm in the *x* and *y* dimensions and 4 mm in the *z* dimension, corresponding to the atlas of Talairach & Tournoux (1988). Images were smoothed using an isotropic Gaussian kernel (16 mm full width at half maximum) to account for variations in gyral anatomy, individual variability in structurefunction relationships, and to improve the signal-to-noise ratio.

(c) Statistical analysis

The data were analysed using SPM97. In order to characterize the nonlinear relationship between neuronal activity and stimulus duration, we employed a nonlinear regression as described in Buechel *et al.* (1996). This analysis models the effects of exposure duration as a polynomial expansion of stimulus duration up to second order (in other words, the mean corrected duration and the mean corrected duration squared). Subject specific effects (including the effects of reading aloud or silently) and global effects were treated as confounding variables. This instance of the general linear model corresponds to a multiple linear regression. The regressors of interest constitute exposure duration to second order. By virtue of the fact that the duration was mean corrected these two regressors are approximately orthogonal. This allowed us to make separate inferences about the linear (first order) and nonlinear (second order) effects using the appropriate *t*-statistic while modelling both effects in the same regression analysis.

To characterize, and make inferences about, the exact form of the regression, we tested separately the significance of the first and second order terms (polynomial coefficients). This procedure generated four SPMs of the ensuing *t*-statistic reflecting (i) monotonic increases, (ii) monotonic decreases, (iii) U-shaped dependencies, and (iv) inverted U-shaped dependencies. This approach was preferred to the alternative approach (i.e. SPM of the *F*-statistic) because it parses significant regressions into the four basic forms ((i) to (iv) above).

The data from both experiments were pooled in order to generate the full range of durations from 150 ms to 1250 ms, and statistical inferences about significant effects are reported at *p* < 0.001 (uncorrected).

3. RESULTS

Four classes of response were identified: (1) monotonic increases, (2) monotonic decreases, (3) inverted U-shaped dependencies, and (4) U-shaped dependencies. See table 1 and figure 2.

(1) Monotonic increases in activity with exposure duration were characterized using the parameter estimates. On inspection, the shape of the regressions fell into two types. In bilateral posterior fusiform gyri, left premotor cortex (BA6), the junction of the posterior cingulate with the precuneus (BA31/7) and the left superior frontal cortex (BA8), there were linear (proportional) relationships between activity and duration suggesting that evoked neural activity endures for the duration of the presentation and protracted early sensory processing engenders more activity. By contrast, in the left intraparietal sulcus (BA 19/39) and the left medial anterior temporal lobe (in the vicinity of the amygdala) there was a nonlinear monotonic relationship with activity reaching a peak around 750 ms, with no further increases between the 750 ms and 1250 ms durations. These nonlinear monotonic increases suggest

Table 1. Results of nonlinear regression analysis

(The anatomical location and coordinates from the stereotactic atlas of Talairach & Tournoux (1988) are reported with the *Z* scores (printed in brackets) for areas where there was a significant first or second order regression with stimulus duration. The coordinates are in the order *x* (–is left, + is right), *y* (–is posterior to the anterior commissure line, + is anterior to the anterior commissure line), *z* (–is inferior to the intercommissural line, + is superior to the AC–PC line).)

response profiles	<i>x</i>	<i>y</i>	<i>z</i>	<i>Z</i>
<i>monotonic increases</i>				
left posterior fusiform	–26	–98	–8	(7.7)
right posterior fusiform	30	–92	–8	(7.5)
left premotor cortex (BA6)	–52	0	36	(3.9)
posterior cingulate/ precuneus (BA31/7)	–16	–42	44	(3.8)
left superior frontal cortex (BA8)	–26	32	44	(3.8)
left intraparietal sulcus (BA 19.39)	–34	–66	36	(3.3)
left amygdala	–16	–4	–20	(3.3)
<i>monotonic decreases</i>				
right posterior inferior temporal cortex (BA37)	48	–50	–16	(4.4)
right posterior middle temporal cortex (BA37)	46	–52	4	(3.8)
right posterior inferior parietal cortex (BA39)	44	–56	24	(3.7)
right frontal operculum (BA47)	40	18	0	(4.1)
right putamen	18	–18	0	(3.7)
right precentral sulcus (BA44/6)	42	0	28	(3.8)
medial lingual gyrus	–2	–70	–12	(3.4)
anterior cingulate	–6	16	36	(3.2)
<i>inverted U-shaped dependencies</i>				
left middle and inferior frontal cortex (B46)	–48	28	24	(4.7)
left middle temporal cortex (BA21)	–60	–32	–4	(3.5)
left posterior superior temporal sulcus	–28	–54	24	(3.2)
<i>U-shaped dependencies</i>				
right medial superior frontal cortex (BA10)	18	62	8	(4.4)

physiological adaptation, or saturation, with prolonged exposure duration. When we refer to these nonlinear monotonic increases, we are simply referring to the shape of the curves as opposed to making a statistical inference about the second order component.

(2) Monotonic decreases in activity with exposure duration were identified in the medial lingual gyrus, the anterior cingulate and the right hemisphere homologues to the language areas: posterior inferior and middle temporal cortex (BA37) extending to the junction with the posterior inferior parietal cortex (BA39), the frontal operculum (BA47) spreading medially into the putamen and the right precentral sulcus (BA44/6). In all these areas activity decreased linearly with

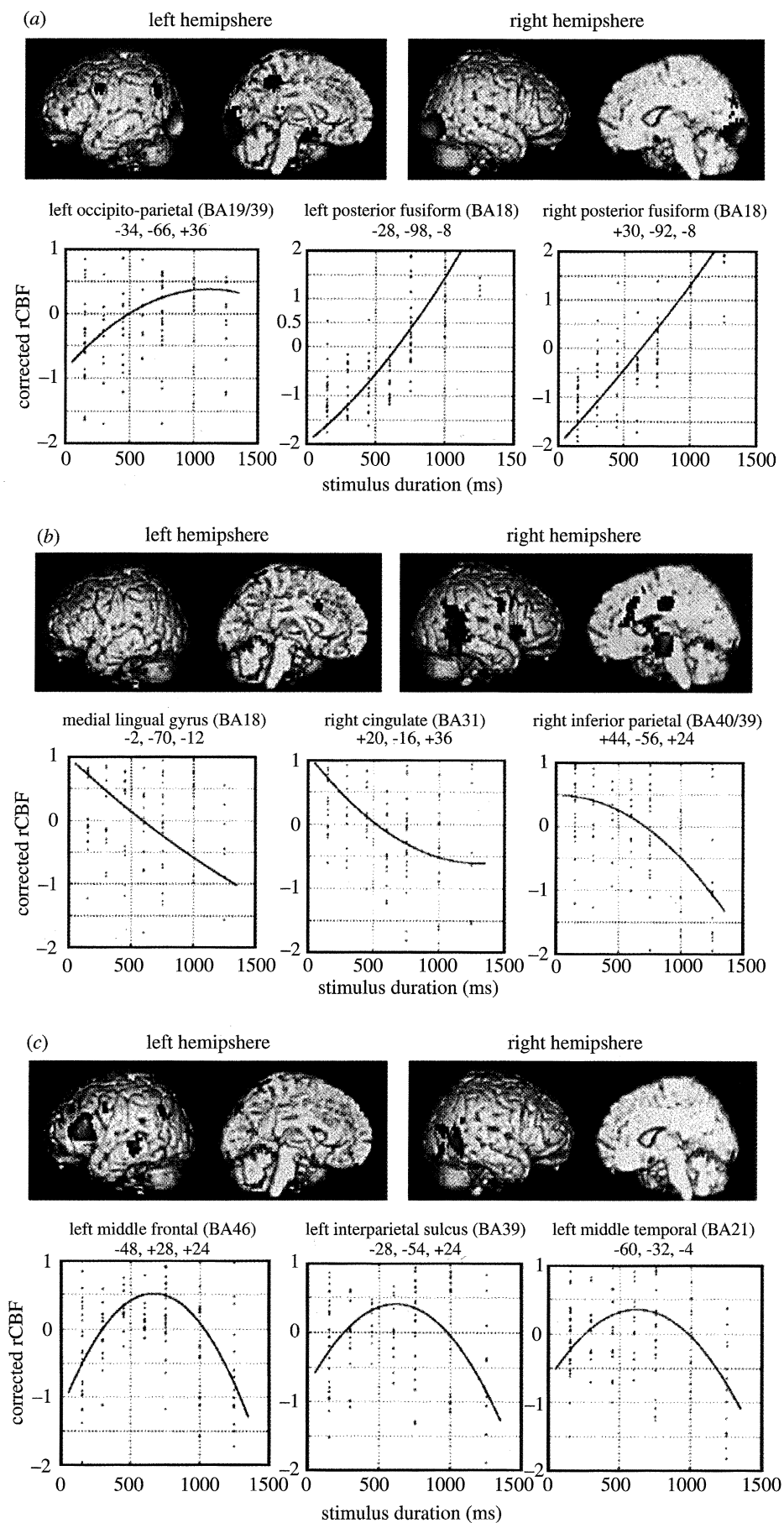


Figure 2. Examples of the different types of duration effects. Regions where the regression coefficients reached significance for each of the three different effects of duration ((a) monotonic increases, (b) monotonic decreases and (c) inverted U-shaped dependencies) are highlighted in red and yellow on MRI models of the brain. Beneath, examples of the relationship between regional cerebral blood flow (corrected rCBF) and stimulus duration are displayed for selected regions from table 1.

duration. These effects are consistent with the explanation that shorter durations elicit enhanced responses because of increased attention to briefly presented stimuli.

(3) Inverted U-shaped dependencies of activity with exposure duration were identified in the left hemisphere only; in the middle and inferior frontal cortices (BA46), the middle temporal cortex (BA21) and deep in the posterior superior temporal sulcus. These areas are classically associated with word processing from lesion studies (Mesulam 1990) and neuroimaging studies (Wise *et al.* 1991). Activity reached a maximum at 400–600 ms and then fell if the word remained in the visual field for longer. Such nonlinear effects are consistent with the second explanation proposed in §1, i.e. increased activation in word processing areas is followed by deactivation when a word remains in the visual field after processing is complete.

(4) Finally, a U-shaped dependency of activity with exposure duration was identified in the right medial superior frontal cortex (BA10). We have no clear explanation at present for the response in this area but one possibility is that the inverse relationship to that observed in word processing areas reflects proportional deactivation in the right medial superior frontal cortex.

In order to ensure validity of our assessment of the effect of exposure duration we tested for interactions between duration and task in those subjects that read both aloud and silently. No significant interactions were found in the areas reported above.

#### 4. DISCUSSION

In this paper we have characterized the temporal dynamics of evoked responses to visually presented words using PET. We did this by parametrically varying the duration of the stimuli (at a fixed presentation rate) and measuring the integrated response over 90 s scans. The response profiles fell into three distinct classes: monotonic increases, monotonic decreases and inverted U-shaped dependencies. We will discuss each of these qualitatively different response patterns in turn.

##### (a) *Monotonic increases with duration*

Monotonic increases with duration can be divided into those that are linear and those that are nonlinear. Linear (proportional) relationships were identified in bilateral posterior fusiform gyri, left premotor cortex, the left superior frontal cortex and the posterior cingulate. The bilateral posterior fusiform gyri are associated with the processing of a number of types of visual stimuli. Left premotor activation probably relates to increased involvement of the frontal eye fields (Paus 1996). The left superior frontal cortex (BA8) and the posterior cingulate gyrus have been found, by Démonet *et al.* (1992), to be more active during semantic than phonological processing of auditory words (although their precise role during these tasks is unclear). These linear monotonic increases in activity with stimulus duration can be explained most parsimoniously in terms of processing differences elicited by factors intrinsic to the stimulus itself—the longer a

stimulus remains in the visual field the more activity it evokes.

Nonlinear monotonic responses were identified in the left intraparietal sulcus (BA39/19) and the left medial anterior temporal cortex where activity reached a peak at 750–1000 ms durations. Both areas have been associated with semantic processing. For instance, activation in the left intraparietal sulcus (BA39/19) has been reported during semantic decisions on visually presented words and pictures relative to visual decisions on the same stimuli (Vandenberghe *et al.* 1996), and electrophysiological studies have demonstrated that the response in the left medial anterior temporal region is specific to the semantic attributes of words (Nobre & McCarthy 1995). The nonlinear monotonic relationship between activity and word duration suggests that output from these regions reaches a maximum when words remain in the visual field for approximately 750 ms. Two possible explanations are: (i) there is neuronal adaptation or saturation with prolonged stimuli; and (ii) briefer stimuli enhance proportionally more activity because there is attentional modulation in these regions for short durations. See below for further discussion of these effects.

##### (b) *Monotonic decreases with duration*

Monotonic decreases in activity with word duration were identified in the medial lingual gyrus, the anterior cingulate and the right hemisphere homologues of the language system (temporal, frontal and parietal cortices). We can discount an explanation of these responses purely in terms of increased deactivations with prolonged word durations because we know that these regions are activated relative to low level non-word baselines such as rest (Price *et al.* 1996a) and false-font (Price *et al.* 1994). An alternative explanation is that activity is a direct correlate of attention in the sense that short durations may instantiate mechanisms of directed attention and the degree to which these mechanisms are engaged falls as exposure duration increases. The monotonic decreases observed may reflect brain activity associated with the attentional mechanisms themselves or they may reflect attentional modulation of stimulus dependent activity.

In this PET experiment the stimuli were blocked in terms of duration thereby confounding the effects of attentional set (or expectation of a particular duration) with those that are attributable to word duration itself. Our latest experiments are employing event-related functional magnetic resonance imaging (fMRI) which enables us to randomize the stimuli thereby preventing subjects from engaging in a particular set. The haemodynamic responses to words as a function of stimulus duration can then be examined with and without the expectation of a particular duration. In this way it should be possible to dissociate the effects of attentional modulation from those that are intrinsic to the stimulus parameters themselves.

##### (c) *Inverted U-shaped dependencies*

The most interesting responses were observed in the left middle/inferior frontal cortex (BA46), the left

middle temporal cortex (BA21), and the left posterior superior temporal sulcus, areas classically associated with word processing by both lesion studies (Mesulam 1990) and imaging studies (Vandenberghe *et al.* 1996). Activity in these regions rose progressively as exposure durations increased from 150 to 450–600 ms and then fell progressively as durations increased from 600 to 1250 ms. This inverted U behaviour points to the interesting possibility that the neuronal dynamics elicited by words are self-limiting or self-terminating when visual input remains 'on' for too long. This may be necessary for the cessation of redundant processing when stimuli remain in the visual field after processing is complete.

We suggest two possible mechanisms that could induce self-terminating responses. The first is that increasing, saturating responses to stimulus duration are modulated by attentional set and at longer stimulus durations, this modulation reduces the overall response. This explanation posits an attentional set that is constant over a scan and governed by the subjects' expectation of the stimulus duration (rapidly acquired after the first few stimuli). An alternative and more plausible explanation is that irrespective of expectation, responses are inhibited if they remain in the visual field after 600 ms thereby eliciting a reduction in activity with longer durations. Mechanisms that might account for this are either intrinsic to the word processing system itself or reflect modulatory inputs from other systems. The intrinsic mechanisms correspond to an emergent property of the neural dynamics that mediate the competition between different word representations. In this framework, prolonged sensory drive to the correct representation results in suppression of competing representations to render the overall neuronal activity less (Plaut *et al.* 1996). This would be equivalent to a change in the effective connectivity between sensory and word processing regions wherein the effects of input initially activates multiple competing representations and then, when the correct representation has been established (at around 600 ms), activity is inhibited. The other possibility is that this disengagement is mediated by modulatory mechanisms wherein the responses of word processing regions are actively suppressed if the word remains in the visual field for too long. This dynamic attentional-like modulation is very different from that which is constant across the scan and associated with expectation and set (as mentioned above). In summary, if we can discount the effects of attentional set (using the event-related fMRI study proposed above), our results suggest that neuronal activity is 'switched off' when a word remains in the visual field after processing is complete. This 'switching off' can only occur with durations above 400–600 ms because up to this point the brain cannot know how long a stimulus will be on for.

It is also possible that the nonlinear monotonic increases in activity with duration detected in the left intraparietal sulcus (BA39/19) and the left medial anterior temporal cortex (where activity reached a plateau between 750 and 1250 ms durations) may decrease with durations above 1250 ms. Further experiments extending the duration range are required to confirm this prediction. The present results suggest, nevertheless, that

activity in the left intraparietal sulcus (BA39/19) and the left medial anterior temporal cortex is maintained for longer than activity in the other word processing areas reported with inverted U-shaped responses. This may have some similarity to the work reported by Synder *et al.* (1995), who recorded evoked potentials during word generation and reading aloud. Task-specific signals during word generation were recorded in the left frontal cortex 200 ms after word presentation, but not until 700 ms in the left temporoparietal region. These data confirm that the time course of temporoparietal activity is delayed relative to frontal activity.

The role of inhibitory processes in cognitive functions has recently received considerable attention (see, for example, Anderson & Spellman 1995; Arbuthnott 1995). Relevant to the present study are the findings that activation-reducing mechanisms are involved in language comprehension and production (e.g. Gernsbacher 1990, 1991; Gernsbacher & Faust 1991). Further, priming studies have shown that the inter-trial interval (ITI) between the prime and the target has implications for the processing time of the target. With short ITIs—up to 500 ms—the prime has a facilitatory effect but with longer intervals there is inhibition (Brown 1981; Blaxton & Neely 1983; Vitkovitch *et al.* 1996). For example, Brown (1981) demonstrated that naming times increased as subjects named a series of pictures from the same category, although little interference was seen in the first few trials. In this study we show that inhibition is greatest when items remain in the visual field for more than 400–600 ms. Relative to the many priming studies manipulating ITIs, there are few that address exposure duration and it would be very interesting to see if there is a convergence between our neurophysiological results and priming effects.

The notion that the neuronal dynamics of word processing have a self-limiting component can also be related to negative priming of unattended stimuli (Neill 1977; May *et al.* 1995) and spatially directed attention paradigms (e.g. Posner & Snyder 1975). These studies suggest that (i) unattended distractors are processed to a certain depth, and (ii) in some situations an active disengagement from these distractors is required. In our instance however, the domain over which stimuli are selected is temporal rather than spatial: if a stimulus remains in the visual field after processing is completed, it may become an unattended distractor as subjects wait for the next stimulus. It would be extremely interesting to explore such inhibition further by correlating evoked potentials to visually presented words as a function of exposure duration. There is also the potential for fMRI studies to explore individual differences in the time course of word processing and likewise differences associated with a particular pathology.

#### **(d) Conclusions and implications for the design of functional imaging experiments**

This study highlights the point that varying a stimulus parameter, in this instance exposure duration, can substantially alter the pattern of detected neuronal

activation. At least three distinct patterns of effect have been observed. First, in regions associated with visual processing, activity increased linearly with duration. In higher order right hemisphere regions, the anterior cingulate and the medial lingual gyrus activity decreased linearly with duration and these effects can be attributed to changes in attentional set. In some left hemisphere word processing areas (BA46, 21, 39) activation reached a maximum between 400 and 600 ms and then decreased with longer durations. In other left hemisphere areas associated with word processing (BA39/19; BA28/38), activation reached a plateau between 750 and 1250 ms durations. It is possible that activation in the latter regions may decrease with durations above 1250 ms. These effects suggest that maximum activation in word processing areas is detected when the stimulus duration is approximately 600 ms and neuroimaging studies of reading may fail to show activation in word processing areas if stimuli are presented for more than 1000 ms.

In conclusion, we have used PET to address the temporal dynamics of visual word processing on a hundred millisecond time scale and this has led to some important insights and new questions pertaining to which factors determine evoked responses in the word processing system.

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