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Orienting attention in time: behavioural and neuroanatomical distinction between exogenous and endogenous shifts

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Abstract

Temporal orienting of attention is the ability to focus resources at a particular moment in time in order to optimise behaviour, and is associated with activation of left parietal and premotor cortex [Coull, J. T., Nobre, A. C. Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. Journal of Neuroscience, 1998, 18, 7426–7435]. In the present experiment, we explored the behavioural and anatomical correlates of temporal orienting to *foveal* visual stimuli, in order to eliminate any spatial attention confounds. We implemented a two-way factorial design in an event-related fMRI study to examine the factors of trial validity (predictability of target by cue), length of delay (cue-target interval), and their interaction. There were two distinct types of invalid trial: those where attention was automatically drawn to a premature target and those where attention was voluntarily shifted to a delayed time-point. Reaction times for valid trials were shorter than those for invalid trials, demonstrating appropriate allocation of attention to temporal cues. All trial-types activated a shared system, including frontoparietal areas bilaterally, showing that this network is consistently associated with attentional orienting and is not specific to spatial tasks. Distinct brain areas were sensitive to cue-target delays and to trial validity. Long cue-target intervals activated areas involved in motor preparation: supplementary motor cortex, basal ganglia and thalamus. Invalid trials, where temporal expectancies were breached, showed enhanced activation of left parietal and frontal areas, and engagement of orbitofrontal cortex bilaterally. Finally, trial validity interacted with length of delay. Appearance of targets prematurely selectively activated visual extrastriate cortex; while postponement of target appearance selectively activated right prefrontal cortex. These findings suggest that distinct brain areas are involved in redirecting attention based upon sensory events (bottom-up, exogenous shifts) and based upon cognitive expectations (top-down, endogenous shifts).

Keywords: fMRI; Temporal orienting; Selective attention; Invalid; Parietal; Frontal; Motor preparation

1. Introduction

We have recently begun to investigate the ability to orient attention selectively towards particular moments in time [7,39,40]. Expectancies about *when* an event will occur can be used to optimise behavioural responding, in an analogous fashion to expectancies about where the event will occur [7]. In a previous neuroimaging study using both positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) [7], we compared and contrasted the neural systems involved in temporal and spatial orienting of attention, with adaptations of the classic attentional cueing paradigm [46]. These visual tasks required detection of peripheral targets, guided by informative cues regarding when and/or where they would occur. Both spatial and temporal orienting activated a common network of frontoparietal regions with most consistent foci in lateral and medial premotor areas and intraparietal sulcus. However, the overlap between spatial and temporal orienting net-

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works was not complete, and the two showed opposite hemispheric lateralisation. The right posterior parietal cortex was associated with spatial orienting, while the left posterior parietal cortex was associated with orienting attention in time. We suggested that the common premotor and parietal areas represent sensorimotor circuits which support attentional functions generally (see [50]). The right hemispheric lateralisation for spatial orienting was consistent with neuropsychological evidence for the right-hemisphere dominance for spatial attention in humans [17,23,38,62]. The left hemispheric lateralisation for temporal orienting was hypothesised to reflect a left-hemisphere dominance for a critically involved cognitive function such as motor intention or preparation [33,54] or fine temporal discriminations [37,57].

One of the main purposes of the present experiment was to verify whether the pattern of brain activations for temporal orienting would remain consistent in the absence of any spatial information in the task. It could be argued that the appearance of peripheral targets in the previous experiment introduced an element of reflexive spatial orienting. The common activation of frontoparietal areas might therefore have been a consequence of spatial orienting in all task conditions. This consideration is especially important in light of the hypothesised role of posterior parietal areas in spatial representations (see [1] and [6] for reviews). To address this possibility, all stimuli in the present task were presented foveally.

The second objective of the experiment was to identify the brain areas activated by some of the multiple factors involved in temporal orienting. We used event-related fMRI to examine brain activations linked to specific types of trials, in which length of the cue-target delay and the validity of the cue-target contingency were varied. In a previous experiment, we identified brain areas preferentially activated by being invalidly-cued to a target location or temporal interval [40]. Violations of spatial or temporal expectancies were accompanied by selective engagement of the orbitofrontal cortex bilaterally. In addition, increased activation occurred in the lateral premotor and posterior parietal foci of attentional orienting network. The orbitofrontal cortex may be engaged during invalid trials either because of the switch in stimulus contingencies that drive responses [12,13,16,25] or because of changes in emotional states linked to interference with expectancies or levels of task performance ([4,10,52]; see also [14]). Enhancement of activity in premotor and parietal areas during invalid trials suggested increased levels of cognitive functions linked to attentional orienting generally, such as sensorimotor preparation [50] or disengaging and shifting the attentional focus [17,47].

The present experiment builds upon these findings, within the context of a purely foveal temporal orienting task. The cues were foveal concentric circles that predicted the appearance of a foveal target at the prespecified interval (80% validity). A factorial design was used to test the effects of trial validity (valid, invalid cues) and cue-target interval (600, 1400 ms). Fig. 1 shows a schematic of the experimental design and task parameters. Furthermore, the event-related fMRI methodology provides a means to define the brain areas differentially engaged in single trials (events). Therefore, a more detailed analysis of invalid trials is possible than in our previous blocked design PET experiment [40] in which invalid trials were intermixed with valid trials during a scan. Using event-related fMRI, we can measure not only invalid trials in isolation from valid trials, but also distinct types of invalid trial.

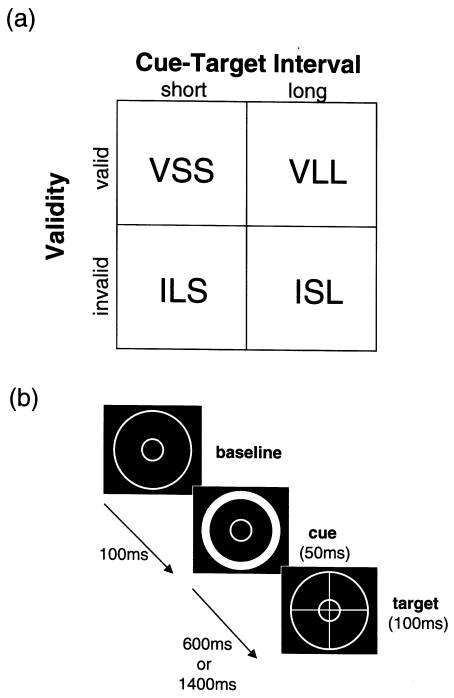

Fig. 1. (a) The 2 × 2 factorial design used in the event-related fMRI study. The two factors of interest were cue validity and length of cue-target interval. These were crossed to produce four distinct trial (event) types. (b) Schematic of the task parameters used in the foveal temporal orienting task. The trial began with a brief brightening (100 ms) of the inner or outer circle of the compound cue, which indicated that the target would appear in either 600 ms (short SOA) or 1400 ms (long SOA). The contingency between inner/outer circle and short/long time interval was varied between subjects. Subjects signalled detection of a briefly-presented (50 ms) target ('+') superimposed over the background cue by pressing a response button with their right index finger.

Different types of invalid trials during temporal orienting may involve different mechanisms of breaking and redirecting expectations. The bimodal nature of the cue-target intervals (short, long) guarantees that if a target does not appear at the short interval it must appear at the long interval. Omission of an expected

target at the short interval signals a breach in the cue-target contingency and permits subjects to re-orient attention voluntarily to the later time-point. Analysis of the behavioural data during temporal orienting in our previous experiments [7,39,40] supported the presence of additional shifts of attention during such invalid trials. The disadvantage of being invalidly cued was significantly smaller for trials in which the target occurred later than expected compared to those in which the target appeared sooner than expected. Trials in which targets appear later than predicted afford time for subjects to re-orient attention, and may therefore involve top-down, voluntary control of attentional shifts. In contrast, the appearance of an unexpected premature target interrupts the active attentional focus and draws attention reflexively. Trials in which targets appear sooner than predicted may therefore emphasise bottom-up, automatic grabbing of attention. Voluntary and automatic orienting of attention have been hypothesised to have distinct neural bases and have usually been measured using central and peripheral cues respectively [45]. We distinguish between being validly cued to *orient* attention towards a particular time point, and being invalidly cued which necessitates a *shift* of attention to a different time point. In our foveal task, we differentially measured voluntary and automatic shifting of attention through the use of unexpectedly short or long invalid trials. Though this approach is novel, we believe that it captures exogenous and endogenous attentional mechanisms at work, analogous to the way in which they may operate during spatial orienting of attention.

The length of the interval between a cue and a target in an attentional orienting task is also a critical variable. In the context of temporal orienting, different cue-target intervals may involve different degrees of motor preparation and anticipation. The event-related fMRI methodology allowed us to examine the contribution of cue-target interval to brain activations associated with temporal orienting. We were interested in distinguishing the effects of cue-target interval from those of trial validity, and in examining how these two factors may interact.

2. Methods

2.1. Subjects

Six healthy, right handed volunteers (mean age = 26.8, four male) took part in the experiment. Subjects were physically fit, and none were taking medication. The experimental protocol was approved by the local hospital ethics committee, and written informed consent was obtained prior to the study.

2.2. Cognitive tasks

The task required detection of a visual target presented after an informative cueing stimulus. All stimuli were presented at the centre of gaze (foveally). Fig. 1(b) shows a schematic of the task. Visual cues predicted a cue-target stimulus-onset asynchrony (SOA), which informed subjects (Ss) *when* the ensuing visual target would appear. Subjects detected the target stimuli and responded as rapidly as possible, while avoiding mistakes.

Selective visual cues were derived from the compound central stimulus involving two concentric circles. For half of the Ss the brightening of the inner circle indicated that the target would appear at the short time interval (600 ms) while brightening of the outer circle indicated the longer time interval (1400 ms). In the remaining Ss, these contingencies were reversed. The trial began with a brief brightening (100 ms) of the inner or outer circle of the compound cue, which indicated that the target would appear in either 600 ms (short SOA) or 1400 ms (long SOA). Subjects signalled detection of a briefly-presented (50 ms) target ('+') superimposed over the background cue by pressing a response button with their right index finger. The computer recorded reaction times to target stimuli. In 80% of trials, the SOA was correctly predicted by the cue (valid trials), while in 20% of trials it was incorrectly predicted (invalid trials). There were four trial-types: *valid* trials in which the cue predicted the *short* interval and the target appeared as expected at the *short* interval (VSS); *valid* trials in which the cue predicted the *long* interval and the target appeared as expected at the *long* interval (VLL); *invalid* trials in which the cue predicted the *short* interval and the target appeared unexpectedly at the *long* interval (ISL); *invalid* trials in which the cue predicted the *long* interval and the target appeared unexpectedly at the *short* interval (ILS). Trials lasted either 750 ms (VSS, ILS) or 1550 ms (VLL, ISL) (plus the subjects' response times), and were presented in a pseudo-random order. The baseline visual display (first frame of Fig. 1(b)) remained visible during the interval between trials (ITI).

Subjects performed two behavioural experimental sessions, one before and one during the brain-imaging session. The behavioural session preceding scanning familiarised the subjects with the task, trained them on the contingency between inner/outer circle and short/long SOA, and confirmed they showed an attentional validity effect. 800 trials were performed (80:20% valid:invalid cues, 50:50% long:short SOA) prior to scanning. The ITI during this behavioural session varied between 1.0–1.6 s. During fMRI scanning, three blocks of 60 trials were performed (48:12 valid:invalid cues 30:30 long:short SOA, per block). The ITI during

scanning varied randomly between 10–12 s. Trial types were presented in a pseudo-random counterbalanced manner.

2.3. fMRI scanning

Scans were acquired using a 2-Tesla Magnetom VISION (Siemens, Erlangen, Germany) whole body MRI system, equipped with a head coil. Echo-planar imaging (EPI) was used to obtain T2*-weighted fMRI images in the axial plane. Twenty-two 5-mm thick slices (voxel size of $3 \times 3 \times 5$ mm) were obtained and covered the entire cortex, except for the most ventral parts of the occipital and temporal lobes. The inter-scan interval (TR) was 2.0 s. Three blocks of images (294–296 images per block) were acquired for each subject,[1] during which subjects performed 60 experimental trials. The randomised 10–12 s ITI ensured random sub-sampling of the brain volume relative to the experimental trials. A structural MRI was also acquired (using a standard T1-weighted scanning sequence, 1.5 mm^3 resolution) to allow anatomically specific localisation of significant areas of brain activation.

2.4. Data analysis

2.4.1. Behavioural data

Data from both behavioural sessions, before and during fMRI scanning, were pooled together for all subjects. Reaction-times were analysed using repeated measures ANOVAs to test for the effects of cue-target interval (short, long) and trial validity (valid, invalid cues). Reaction times faster than 50 ms and slower than 600 ms were counted as errors, and were not considered in the statistical analyses.

2.4.2. fMRI data

Image processing and analysis of fMRI data were conducted with SPM97 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). All functional images for each subject were realigned to the first image, in order to correct for head movement between scans. The structural MRI was then co-registered to the functional images, in order to put both functional and structural images into the same space. All images were then spatially normalised into a standard spatial reference frame [56], by matching each image to a standardised template from the MNI (Montreal Neurological Institute) using both linear and non-linear 3-dimensional transformations [18]. Functional images were spatially smoothed to accommodate inter-subject differences in anatomy, using isotropic Gaussian kernels of 8 mm.

The haemodynamic responses evoked by the behavioural trials were modelled as single events convolved with a synthetic haemodynamic response function [21,28], in the context of the general linear model as employed by SPM. Modelling of the four trial-types (VSS, VLL, ILS, ISL) was time-locked to the presentation of the cue. The resulting data were analysed for regionally specific changes in amplitude of the haemodynamic response.

Condition (trial-type) and subject effects were estimated according to the general linear model at each voxel in brain space [19]. Images were adjusted for both global intensity, using proportional scaling; and for low-frequency physiological drifts, using a highpass filter of 300 s. A Gaussian temporal smoothing kernel of 4 s (at full-width half maximum) was applied to the data during statistical analysis.

Regionally specific effects of trial conditions were tested using linear contrasts, which produced a statistical parametric map of the t statistic generated for each voxel (SPM{t}). The SPM{t} was transformed to a map of corresponding Z values, thresholded at a Z value of 3.09 ($p = 0.001$ uncorrected for multiple comparisons), and the resulting foci were characterised in terms of both spatial extent and peak height.

Statistical analyses were aimed at identifying both the common regions activated by temporal orienting in all trial conditions, and the brain areas that were sensitive to the factors of cue-target duration and trial validity. Brain regions commonly activated by all types of trials during temporal orienting were defined by the statistical conjunction [48] of the activations obtained for each trial type. In addition to areas sensitive to temporal orienting, this comparison also revealed brain areas involved in the basic perceptual and motor demands of the task. Brain regions selectively associated with length of cue-target interval were obtained by contrasting valid trials with long (VLL) vs short (VSS) SOAs. Invalid trials were not included in this analysis to avoid confounding effects of duration and validity of the expected delays. We predicted that long and short trials would differentially engage structures associated with motor preparation, such as supplementary motor area (SMA) and basal ganglia (see [42] for a review).

Brain regions associated with breaches in temporal expectations were obtained by subtracting the two conditions with valid cues (VSS and VLL) from the two conditions with invalid cues (ISL and ILS). This comparison is more likely to isolate areas sensitive to the attentional orienting specifically, and to exclude areas contributing to more basic sensory and motor functions. It also eliminates factors associated with the length of the cue-target interval. According to our pre-

[1] In two of the subjects, only two blocks of data were successfully collected.

Table 1
Mean reaction times and standard errors (ms) for all four event types[a]

Condition	Reaction time (ms) ±SE
VSS	243.3 ± 5.8
VLL	237.9 ± 7.6
ISL	255.5 ± 8.7
ILS	292.26 ± 13.5

[a] VSS = Valid, expect short, get short; VLL = Valid, expect long, get long; ISL = Invalid, expect short, get long; ILS = Invalid, expect long, get short.

vious findings, we predicted enhanced activation of premotor and posterior parietal areas with left-hemisphere lateralisation [7], and selective activation of the orbitofrontal cortex [40].

Differential regional brain activation produced selectively by the two types of invalid trials (ISL and ILS) was revealed by two interaction terms in the factorial design. The interactions isolate the neural correlates of each of the invalid trial-types while controlling for the possible confounds of both length of delay and cue validity. Brain regions associated with trials including a premature target ('exogenous' shifting) were identified by testing for areas more sensitive to invalid trials with short vs long SOAs [i.e. (ILS−VSS)–(ISL−VLL)]. This comparison highlights areas that are more sensitive to the differences between unexpected and expected early targets (ILS−VSS) than unexpected and expected late targets (ISL−VLL). We predicted that sensory visual areas may be more sensitive to the interruption of an attentional focus by an unexpected sensory event and the consequent *exogenous* summoning of attention. While this subset of areas may also be revealed in the simple main effect of e.g. ILS−VSS, this comparison is confounded by the main effect of invalid vs valid trials.[2] Therefore the ILS condition must be contrasted to both VSS trials (to control for length of interval) and to ISL trials (to control for validity of the cue). Therefore, the interaction term assesses the brain areas recruited during ILS trials more accurately, and more conservatively, than the simple main effect. The benefits of using factorial designs and interactions in order to isolate cognitive components of a task more accurately have been discussed by Friston et al. [20].

The converse interaction tested for brain regions associated with trials in which omission of an expected early target signalled that the target would appear at the later time interval, triggering re-orienting of attention to the later time point ('endogenous' shifting) [i.e. (ISL−VLL)–(ILS−VSS)]. We predicted that additional activation of premotor and parietal areas would be engaged by voluntary re-orienting of temporal attention [7], in addition to selective activation of prefrontal areas associated with voluntary control of behaviour.

3. Results

3.1. Behavioural data

Subjects performed the task with a high degree of accuracy. Anticipation errors, where subjects responded prior to target appearance accounted for less than 2% of the responses. Subjects failed to respond to targets on less than 1% of the trials. Reaction times for valid trials were shorter than those for invalid trials [$F(1,10) = 25.04$, $p < 0.001$] (Table 1) demonstrating appropriate allocation of attention to temporal cues. A significant interaction between validity and SOA indicated that the cost of being invalidly cued was larger for ILS trials than ISL trials [$F(1,10) = 8.07$, $p < 0.02$] (Fig. 2).

3.2. Brain activations

3.2.1. Common network for temporal orienting

The general network activated by orienting attention to time intervals was defined by the conjunction of activations obtained in all four types of trials. An extensive bilateral network of areas was activated. Frontal areas included inferior premotor/prefrontal cortex (BA

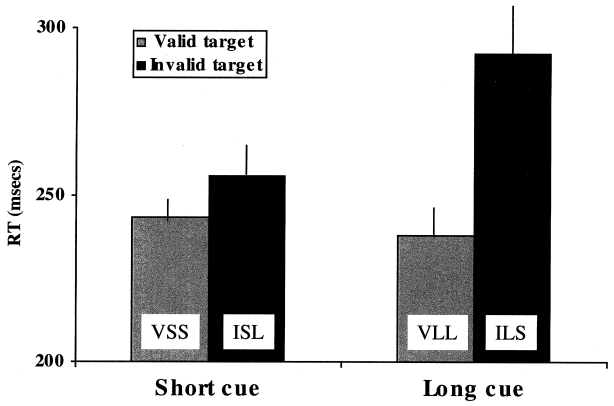

Fig. 2. Reaction times and standard errors (ms) for all four trial types. Foveal cues either correctly (valid) or incorrectly (invalid) predicted whether an ensuing target would appear at a short or long time-interval. *Valid* cues could predict either a *short* (VSS) or *long* interval (VLL). *Invalid* cues could predict the *short* interval but the target appeared unexpectedly at the *long* interval (ISL) or could predict the *long* interval but the target appeared unexpectedly at the *short* interval (ILS).

[2] The simple main effects comparisons included the areas revealed by the interaction but also showed areas activated by the main effect of cue validity. We do not present the simple main effect results because of this confound.

Table 2
Areas activated in common by all four types of trials. The coordinates in this and following tables are given within the framework of the standardised stereotactic atlas of Talairach and Tournoux [56]. All areas were significant at $p < 0.05$ (corrected for multiple comparisons) (L = Left; R = Right)

Brain area	*x, y, z* co-ordinates (mm)	*Z* score
Frontal cortex		
L inferior frontal gyrus/frontal operculum (BA 45)	−51, 12, 18	7.06
R inferior frontal gyrus/frontal operculum (BA 45)	57, 18, 21	6.61
L supplementary motor area (BA 6)	−6, 6, 57	7.44
R supplementary motor area (BA 6)	9, 18, 54	5.63
L insula	−33, 21, 12	7.65
R insula	33, 27, −3	7.61
Parietal cortex		
L intraparietal sulcus	−24, −54, 48	4.82
R intraparietal sulcus	27, −75, 42	5.10
Temporal cortex		
L middle temporal gyrus (BA 21/37)	−45, −57, 9	7.52
R middle temporal gyrus(BA 21/37)	45, −60, 0	7.52
L superior temporal gyrus (BA 22)	−48, −42, 21	6.88
R superior temporal gyrus (BA 22)	54, −39, 9	6.23
Visual cortex		
L extrastriate cortex (BA 19)	−30, −84, 15	8.00
	−30, −63, −3	5.72
R extrastriate cortex (BA 19)	39, −72, −3	8.26
	36, −84, 15	7.28
Subcortical		
L thalamus	−6, −18, 0	7.98
R thalamus	6, −18, −3	8.18

44/45), medial premotor/prefrontal cortex (BA 6), and the anterior insula. Posterior parietal cortex was activated in the region of the intraparietal sulcus. Temporal foci were observed in the posterior middle and superior temporal gyri/sulci. Activation of visual cortex was centred over lateral extrastriate regions. Subcortical activations were obtained in the thalamus bilaterally. More inferior brain regions, such as the cerebellum, were not imaged (Table 2).

3.2.2. Trial validity

Comparison of trials in which the target did *not* appear at the expected SOA to those in which it did [(ILS + ISL)–(VSS + VLL)] showed significantly greater activation in inferior premotor/prefrontal and orbitofrontal cortex bilaterally, in the left insula and in left inferior parietal cortex (BA40) (Table 3). The reverse contrast did not show any significant areas of activation preferentially activated by valid trials.

3.2.3. Length of cue-target interval

Comparison of valid trials in which the target appeared at the *long* SOA to those in which it appeared in the *short* SOA (VLL−VSS) produced significantly greater activation of the left anterior pu-

Table 3
Areas of significant regional activation during all invalid trials compared to all valid trials. All areas in this and subsequent tables are significant to at least a value of $p < 0.001$ (uncorrected for multiple comparisons)

Brain area	*x, y, z* co-ordinates (mm)	*Z* score
Frontal cortex		
L insula	−45, 3, −3	4.03
L orbitofrontal cortex (BA 11)	−30, 30, −18	3.51
R orbitofrontal cortex (BA 47)	33, 21, −15	3.17
L inferior prefrontal cortex (BA 45)	−54, 30, 3	3.39
R inferior prefrontal cortex (BA 45)	45, 24, 6	3.46
Parietal cortex		
L inferior parietal cortex (BA 40)	−57, −51, 30	5.67

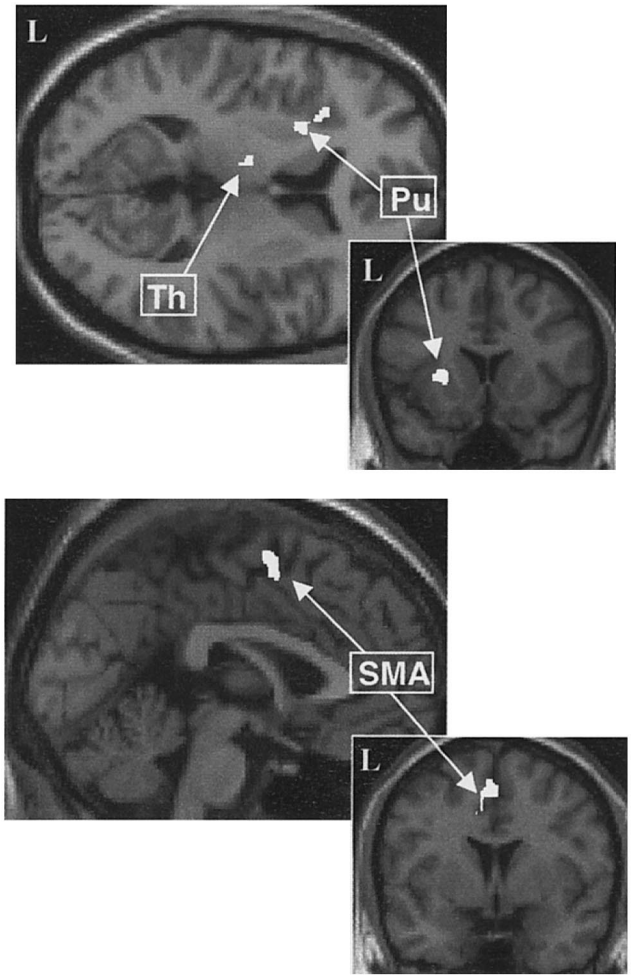

Fig. 3. Brain regions significantly more activated during long delay trials (VLL) than short delay trials (VSS), presented on a standardised high-resolution MRI image (L = left).
Pu = putamen; Th = thalamus; SMA = Supplementary Motor Area.

tamen, bilateral thalamus and supplementary motor area (SMA) (Fig. 3 and Table 4). No areas were preferentially activated by trials in which the target appeared at the *short* SOA (VSS−VLL).

Table 4
Areas of significant regional activation during valid trials in which the target appeared at the long SOA (VLL) compared to those in which it appeared at the short SOA (VSS)

Brain area	*x, y, z* co-ordinates (mm)	*Z* score
Frontal cortex		
Supplementary motor area	0, 3, 51	4.23
Subcortical		
L anterior putamen	−24, 15, 6	4.44
L thalamus	−9, −12, 9	4.03
R thalamus	12, −12, 6	3.47

3.2.4. Interaction between trial validity and cue-target interval

The contrast testing the interaction weighted to reveal brain regions preferentially associated with trials containing unexpected premature targets [(ILS−VSS)–(ISL−VLL)] yielded activation of right posterior extrastriate visual cortex only (Table 5(a) and Fig. 4(a)). The opposite contrast was weighted to reveal brain regions preferentially associated with trials in which the target appeared later than expected [(ISL−VLL)–(ILS−VSS)]. Omission of expected early targets and re-orienting toward the later time interval was associated with activation of left superior parietal lobule and right frontal areas in ventrolateral and dorsolateral prefrontal regions and in lateral motor/premotor regions (Table 5(b) and Fig. 4(b)).

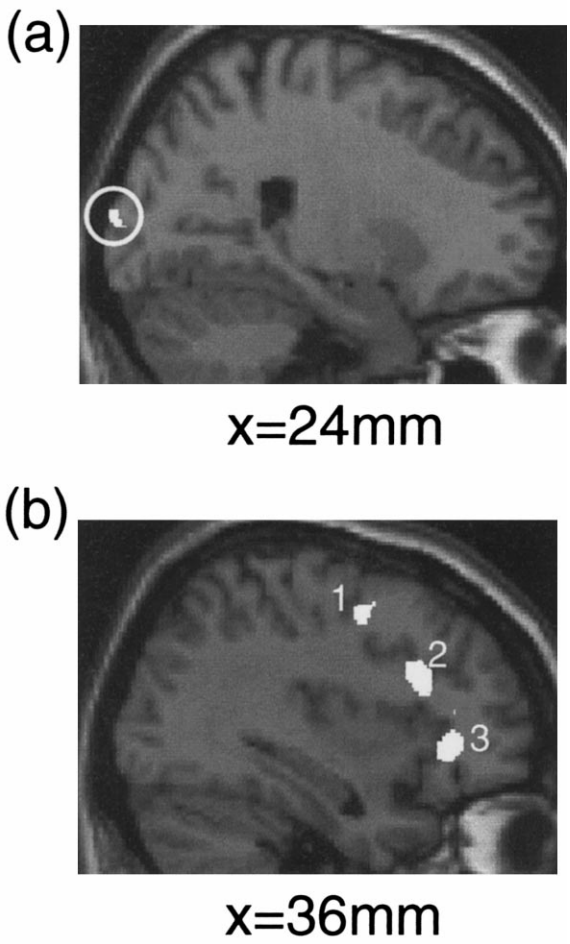

Fig. 4. (a) Right extrastriate visual cortex (circled) was preferentially activated by invalid trials in which the target appeared earlier then expected [(ILS−VSS)–(ISL−VLL)]. We suggest that 'exogenous' shifting of attention occurred during these trials. (b) Right frontal cortex (including premotor cortex[1], and dorsolateral[2] and ventrolateral[3] prefrontal cortex) was preferentially activated by invalid trials in which the target appeared later than expected [(ISL−VLL)–(ILS−VSS)]. We suggest that 'endogenous' shifting of attention occurred during these trials.

Table 5
Areas preferentially activated during (a) invalid trials in which the target appeared at the short SOA, *before* expected [(ILS−VSS)–(ISL−VLL)], (b) invalid trials in which the target appeared at the long SOA, *after* expected [(ISL−VLL)–(ILS−VSS)]

Brain area	*x, y, z* co-ordinates (mm)	*Z* score
(a) ILS trials		
R occipital pole (BA 18)	24, −96, 9	3.32
(b) ISL trials		
Frontal cortex		
R premotor cortex (BA 6)	54, −15, 36	4.33
	39, −3, 51	4.16
R dorsolateral prefrontal cortex (BA 46)	36, 21, 24	4.00
R ventrolateral prefrontal cortex (BA 47)	36, 30, −3	3.65
Parietal cortex		
L superior parietal cortex (BA 7)	−36, −39, 63	3.38

4. Discussion

This study complements and extends previous research indicating a role for left frontoparietal areas in temporal orienting of attention [7]. Specifically, the present study used foveal (non-spatial) presentation of both cue and targets to disambiguate the role of spatial processing in temporal orienting of attention. Furthermore, the use of event-related fMRI allowed us to model the neural substrates of different types of trials separately. It was possible to identify brain regions sensitive to two critical factors involved in temporal orienting: length of cue-target interval and validity of the cue prediction. The methodology further allowed us to observe how the two factors interacted. We identified the neural substrates of two different types of invalid trials: those that predict a target will be presented sooner than it actually is (ISL trials), compared to those that predict a target will be presented later than it actually is (ILS trials).

Bilateral parietal, premotor/prefrontal and visual cortices were activated in common by all event types, consistent with our previous findings during spatial or temporal orienting to *peripheral* visual targets [7]. Activation of the frontoparietal network in our previous study could have resulted from reflexive visual spatial orienting to the appearance of peripheral targets. However, this cannot explain the bilateral activation of frontoparietal areas in the present experiment, where there was no spatial information to guide attention. This supports the notion that frontoparietal networks form ubiquitous systems for allocating attentional resources, independent of stimulus dimension (spatial or temporal). On the other hand, one cannot rule out the existence of right posterior parietal areas in the human brain with a critical role in constructing or using spatial representations to guide behaviour. Indeed, a right parietal lateralisation for visual spatial orienting was shown in our previous study [7].

We previously demonstrated a preferential engagement of right parietal cortex for spatial orienting and left parietal cortex for temporal orienting [7]. In order to isolate the areas sensitive to attentional rather than sensory and motor aspects of temporal orienting, we contrasted activations obtained during invalid and valid trials. When expected cue-target contingencies are breached, attention must be disengaged from the expected focus and redirected (see [46]). Invalid trials thus preferentially tax disengagement and shifting of the attentional focus from one time interval to the other. The direct comparison between invalid and valid trials yielded activation of frontoparietal areas, predominantly in the left hemisphere, and selective engagement of bilateral orbitofrontal cortex for invalid trials, consistent with our previous report [40]. This comparison supports a reliable role for the inferior premotor/prefrontal areas in temporal orienting, a result which was significant in our previous PET, but not fMRI, experiment [7].

Activation of the left inferior parietal cortex and of inferior premotor/prefrontal areas is consistent with the pattern of activations obtained during studies of motor preparation [11,33,54]. Humans with lesions to the left parietal cortex often have apraxic deficits. More specifically, patients with left, but not right parietal lesions have attention-related deficits in a version of the cued orienting task in which the cue guides preparation of the type of movement to be executed to an impending stimulus instead of alerting the likely location of the stimulus [54]. These observations strengthen the interpretation that orienting attention in time engages nodes in sensorimotor systems related to motor control [50]. Areas involved in controlling hand movements may be particularly involved in the current task, such as ventral premotor areas [51], and parietal areas AIP [55] and MIP [27,34]. This view is not incompatible with the alternative explanation previously suggested [7], that temporal orienting may rely on areas involved in fine temporal discrimination. Ac-

tivations in the inferior premotor/prefrontal areas, for instance in Broca's area, have been found not only during tasks requiring movement or articulation, but also in tasks requiring perceptual discriminations or manipulations of sound-sequences in linguistic (e.g. [63]) or non-linguistic [15,44] stimuli. Such findings emphasise the strong relationship between certain (temporal) perceptual and motor functions; and suggest that their neural representations may be highly overlapping.

Given that temporal orienting of attention may be closely associated with motor preparation, we were interested to test the effect that the length of cue-target intervals had upon brain activations. The question was whether areas involved in orienting attention in time were the same as those involved with additional movement preparation, anticipation, or withholding during the longer cue-target intervals. The brain areas preferentially activated during valid long cue-target intervals involved medial premotor cortex in the region of the supplementary motor area (SMA), the left putamen and bilateral thalamus. These areas have been traditionally associated with motor preparation and selection ([11,29]; see [42] for a review). Furthermore, the medial premotor activation is just anterior to the anterior commissure, and so may correspond to a 'pre-SMA' area which is associated more with preparation than execution of a motor act [24,35,36]. In addition, the SMA, left putamen and thalamus were recently shown to be activated by internal generation of precisely timed movements [49]. This raises the possibility that long valid trials may not just place additional demands on motor preparation or holding processes, but also on those associated with self-generated fine timing. However, it is difficult to imagine how long-interval trials could place additional demands on fine-timing operations compared to those required during short-interval trials.

We have recently employed the complementary methodology of event-related potentials (ERPs) to a foveal temporal orienting task similar to the one used here with fMRI [39]. One of the main differences between long and short cue-target intervals involved modulation of CNV potentials that have been linked to motor preparation and anticipation [60,61]. The results across methodologies have proven mutually informative. The ERP experiments suggest a time-window of 340–500 ms for differential activity linked to motor preparation, while the fMRI data supports the involvement of SMA in the generation of such activity. There were also some interesting differences between the findings across the two methodologies. The high temporal resolution of ERPs enabled the detection of transient effects linked to the temporal orienting that could not be measured using fMRI. We observed [39] left-lateralised differences (280–340 ms) between long and short intervals predicted by cues, over parietal and central electrodes. These differences may have reflected differential *transient* activity in parietal and/or frontal regions, related to the setting up of cue-target contingencies.

In the present study, there was no anatomical overlap between brain areas sensitive to motor preparation or timing (indexed by long cue-target intervals) and brain areas sensitive to *attentional* aspects of temporal orienting (indexed by invalid trials) which we speculated might involve motor control mechanisms. Therefore, although motor preparation or timing may be intimately linked to temporal attentional orienting from a conceptual viewpoint, anatomically they can be dissociated. This suggests that orienting attention in time engages processes other than those required simply for preparing or holding of a motor response, or for judging precise temporal intervals. Activation of left parietal cortex by invalid trials is consistent with the results of Rushworth et al. [54] who demonstrated that left parietal cortex is necessary for shifting the focus of motor attention from one *type* of movement to another, but not for simply selecting or preparing an appropriate movement. We suggest that we are measuring a similar type of attentional shift with the invalid trials in our temporal orienting task. Therefore our task requires allocation of attentional resources towards a selected time-point and the ability to shift this focus of attention, if required. Indeed, the behavioural data support the notion that attentional processes are involved since subjects effectively utilise the cues to guide attention accurately, and so optimise responding.

The analysis of brain activations linked to the two types of invalid trials, probed the neural areas involved when shifts of temporal attention are driven exogenously, by the appearance of an unexpected premature stimulus, or endogenously, by the omission of an expected early target. Behavioural data from this as well as from previous experiments [7,39] suggested that these two trial types were distinct and that subjects did redirect attention endogenously after omission of the early target to enhance responding to the later time interval. The brain activations showed that different brain regions were sensitive to exogenous and endogenous shifts of temporal attention. Exogenous shifts were accompanied by increased activation in visual cortex, suggesting the involvement of a sensory perceptual mechanism. Preferential activation of posterior visual cortex during ILS trials may represent ventral visual processing of non-spatial (object) attributes [59] following unexpected presentation of the visual target. It is possible that visual areas more ventral than the one we observed could have been activated by this task, but unfortunately scanning parameters restricted brain coverage.

Endogenous shifts were accompanied by activations in right frontal cortex, including ventrolateral and dorsolateral prefrontal areas, and left superior parietal lobule. The prefrontal activations are generally compatible with the view that endogenous shifts engage areas involved in higher order controlled cognitive processes. The precise functional contributions of the specific areas, however, remain a matter for speculation. Activation in right ventrolateral and dorsolateral prefrontal cortex may represent inhibition of responses to the early (cued) time interval when the target does not appear when expected. Activation of both of these areas has been reported in Go/No-go tasks, which require a similar response inhibition [5,30,32,58]. Ventrolateral and dorsolateral prefrontal areas have also been differentially implicated in holding and updating representations in working memory (see [43,53]). Both of these functions may have been engaged preferentially during ISL trials: as soon as omission of the expected early target is detected, the response plan must be updated and held in working memory until the later target eventually appears. Holding items online in working memory has been likened to the process of sustained attention [2,3,8], which itself has been linked to functioning of right prefrontal cortex [9,41]. Activation of this brain area during ISL trials may therefore simply reflect short-term sustained attention over the delay period. However, the lack of right prefrontal cortex activity in the complementary comparison of long to short valid trials suggests otherwise. It is likely that the delay period is not long enough to activate sustained attention mechanisms, and that the right prefrontal cortex activation represents some other higher-order cognitive process. Right dorsolateral prefrontal cortex has also been associated with voluntary, rather than automatic, responding (see [26] for a review). Reduced reaction-time costs during ISL, compared to ILS, trials may represent the behavioural manifestation of additional voluntary control of attentional shifts which underlies the ability to re-orient attention to the later time point. Explanations linked to inhibition, working memory or voluntary control of behaviour are not mutually exclusive, and may combine to account for the constellation of activations in right frontal cortex.

Preferential activation of premotor cortex during ISL trials is consistent with enhanced motor planning and execution. The right lateralisation of the activation, however, is not compatible with left sided dominance for motor function [22,31,54], especially given that subjects responded using their right hand. Activation of the left *superior* parietal lobule is also difficult to explain since invalid trials (and associated shifts of temporal attention) have been associated with more inferior parts of the parietal lobe. The finding is nevertheless instructive in emphasising that large areas of heteromodal cortex, such as the posterior parietal region, contain multiple functional areas some of whose specialisations remain to be elucidated.

In conclusion, we have demonstrated both behaviourally and anatomically the existence of two distinct forms of attentional shifting: endogenous shifts, which are initiated by the subject in order to meet the cognitive demands of the task, and exogenous shifts, which are stimulated by unexpected events in the periphery. The former represents a 'top-down' attentional mechanism and is subserved by frontal cortex, while the latter represents a 'bottom-up' mechanism and is subserved by sensory association cortex. Of course we recognise that alternative interpretations of our results are possible. For example, the two invalid trial-types may differentially measure 'surprise' to absence or premature appearance of an expected stimulus. However, the processes of endogenous or exogenous orienting may themselves be implicit in these 'surprise' reactions or, conversely, surprise may be implicit in either of these reorienting mechanisms. Further experiments are required in order to disambiguate these interpretations. Finally, the use of a factorial design has allowed us to image the neural correlates of motor preparation (indexed by length of SOA) separately from those of temporal orienting (indexed by validity of cue-target association). The dissociation of areas recruited by these two process refutes the possibility that temporal orienting is simply analogous to motor preparation.

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