The Effect of Task Relevance on the Cortical Response to Changes in Visual and Auditory Stimuli: An Event-Related fMRI Study

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Attention is, in part, a mechanism for identifying features of the sensory environment of potential relevance to behavior. The network of brain areas sensitive to the behavioral relevance of multimodal sensory events has not been fully characterized. We used event-related fMRI to identify brain regions responsive to changes in both visual and auditory stimuli when those changes were either behaviorally relevant or behaviorally irrelevant. A widespread network of "context-dependent" activations responded to both task-irrelevant and task-relevant events but responded more strongly to task-relevant events. The most extensive activations in this network were located in right and left temporoparietal junction (TPJ), with smaller activations in left precuneus, left anterior insula, left anterior cingulate cortex, and right thalamus. Another network of "context-independent" activations responded similarly to all events, regardless of task relevance. This network featured a large activation encompassing left supplementary and cingulate motor areas (SMA/CMA) as well as right IFG, right/left precuneus, and right anterior insula, with smaller activations in right/left inferior temporal gyrus and left posterior cingulate cortex. Distinct context-dependent and context-independent subregions of activation were also found within the left and right TPJ, left anterior insula, and left SMA/CMA. In the right TPJ, a subregion in the supramarginal gyrus showed sensitivity to the behavioral context (i.e., relevance) of stimulus changes, while two subregions in the superior temporal gyrus did not. The results indicate a role for the TPJ in detecting behaviorally relevant events in the sensory environment. The TPJ may serve to identify salient events in the sensory environment both within and independent of the current behavioral context. © 2001 Academic Press

INTRODUCTION

The sensory environment consists of a vast number of stimuli, any one of which is a potential focus for attention. However, only a small fraction of these stimuli are of direct relevance to behavior at any given moment. Attention is, in part, a mechanism for selecting the features of the sensory environment which are most salient—i.e., of greatest potential relevance to current or planned behavior (Coull, 1998; Parasuraman, 1998). Lesion data, in conjunction with neuroimaging and electrophysiological studies, suggest a large-scale distributed network for attention, with frontal, parietal, and cingulate components (Mesulam, 1981; Corbetta *et al.,* 1993; Nobre *et al.,* 1997; Kim *et al.,* 1999). In a previous study, we identified a similar but more ventrally located network of cortical regions responsive to sudden changes in visual, auditory, or tactile stimuli in the sensory environment in the absence of any task (Downar *et al.,* 2000). This multimodal network included a prominent activation in the right temporoparietal junction (TPJ), as well as activations in the inferior frontal gyrus (IFG), and cingulate and supplementary motor areas (CMA/SMA). This network closely corresponds to the areas most frequently damaged in stroke patients suffering from hemineglect (Vallar, 1998). It has been proposed that the regions damaged in hemineglect are responsible for detecting salient features of the sensory environment. The loss of these areas consequently reduces the salience of stimuli in the neglected space, thereby giving rise to deficits in attention and awareness (Aglioti *et al.,* 1997; Mesulam, 1999). If so, one would expect the TPJ and the other multimodal cortical regions responsive to sensory changes to show sensitivity to the salience of a given sensory event.

In the present study, we sought to test whether the regions of the cortical network responsive to sudden changes in sensory stimuli across multiple sensory modalities (Downar *et al.,* 2000) respond more strongly to stimuli of increased salience. One of the factors affecting the salience of a given stimulus is its relevance to current behavior. To manipulate salience, we therefore made the stimuli relevant or irrelevant to the performance of a simple task. We used event-related functional magnetic resonance imaging (fMRI) to compare cortical responses to changes in task-relevant and

task-irrelevant visual and auditory stimuli. Our experimental design involved the simultaneous presentation of a visual and an auditory stimulus. Subjects were cued to attend to just one of the two stimuli at a time and to report any changes in that stimulus. The experimental design allowed us to identify brain areas responding to both visual and auditory stimulus changes and to assess the effect of stimulus task relevance in modulating their responsiveness.

## METHODS AND MATERIALS

Subjects

Subjects were 10 individuals, 5 male and 5 female, 21–32 years of age (mean $\pm$ SD 26.6 $\pm$ 3.7), with no prior history of neurological injury, all right-handed by self-report. All subjects gave written informed consent for the experimental procedures, approved by the University of Toronto Human Subjects Review Committee.

Task Design

Visual and auditory stimuli were presented simultaneously during functional imaging. Visual stimuli were displayed on an LCD projector and back-projected onto a screen viewed by the subjects through an angled mirror incorporated into the head coil. Auditory stimuli were delivered via a piezoelectric speaker connected to a custom-built set of pneumatic headphones placed over the subjects' ears. Visual and auditory stimuli were generated using Adobe Premiere 4.2 software and presented using a Pentium PC connected to the LCD projector and speaker.

The visual stimulus was a square box containing a diagonal cross. The auditory stimulus was a steady buzzing sound (Fig. 1). Both stimuli were presented simultaneously. At pseudo-random intervals of 10, 12, or 14 s, *either* the visual *or* the auditory stimulus underwent a change. For visual changes, the box rotated 10° clockwise or counterclockwise. For auditory changes, the pitch of the buzzing sound increased or decreased by 5%. Subjects were required to attend to either the visual or the auditory stimulus and to report changes in the attended stimulus by briefly raising their right index finger. The subjects' right hands were positioned out of their view so that they could not receive visual feedback from their responses.

Each set of five changes (visual or auditory) was preceded by an instruction stimulus event, which cued the subject to attend to one of the stimuli, visual or auditory, and commence reporting changes in that stimulus. The cue to commence reporting changes in the auditory stimulus was a 1-s buzzing sound rapidly changing in pitch. The cue to commence reporting changes in the visual stimulus was a 1-s rapidly rotating box and cross. When subjects were reporting changes in the auditory stimulus, the auditory changes
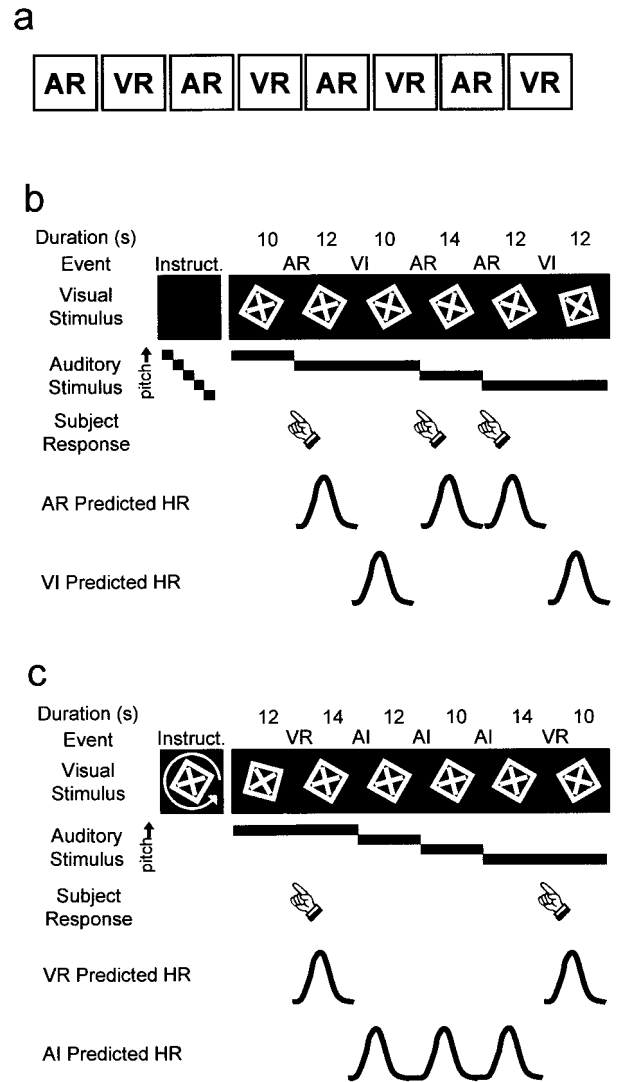
FIG. 1. Task design schematic. (a) The experimental protocol consisted of eight blocks: four visually relevant and four auditorily relevant. A total of 10 visual-relevant (VR), 10 visual-irrelevant (VI), 10 auditory-relevant (AR), and 10 auditory-irrelevant (AI) stimulus changes took place during the experiment. (b) Example of an AR block. (c) Example of a VR block. Visual and auditory stimuli were presented simultaneously during the experiment. The visual stimulus was a centrally presented square box containing a diagonal cross. The auditory stimulus was a continuous buzzing sound. At the beginning of each block, a nonverbal instruction stimulus cued the subject to attend to either the visual or the auditory stimulus and report changes in the attended stimulus by raising the right index finger briefly. A total of five changes took place in each block, in a pseudo-random order, at intervals of 10, 12, or 14 s. Changes in the visual stimulus were 10° rotations to the left or right. Changes in the auditory stimulus were 5% increases or decreases in overall pitch.

were considered to be task relevant and the visual changes were considered to be task irrelevant and vice versa when subjects were reporting changes in the visual stimulus. A total of 10 visual-task-relevant (VR), 10 visual-task-irrelevant (VI), 10 auditory-task-relevant (AR), and 10 auditory-task-irrelevant (AI) stimulus changes took place during the experiment. It

should be noted that the task design in the present study involves both event-related components (the transient responses to the stimulus changes) and blocked components (the prolonged periods of maintained attention to either the visual or the auditory stimulus). The activations associated with maintained attention would in themselves present an interesting topic for study. However, in this study, we were primarily interested in assessing the effect of behavioral context on the transient, event-related activations we previously observed in response to stimulus changes in a neutral behavioral context. Hence, we focused our design and analysis on the transient aspects of the task by using correlation analyses designed to reveal transient rather than tonic responses, as described below. It is for this reason that we emphasize the event-related design of the present study.

Imaging

A 1.5-T Echospeed MRI system (GE Medical Systems, Milwaukee, WI) and a standard quadrature head coil were used to obtain all images. For anatomical images, a T1-weighted 3D SPGR sequence (flip angle 45°, TE = 5 ms, TR = 25 ms) was used to generate 124 1.5-mm-thick sagittal slices with a 256 × 256 matrix size and 24 × 24-cm field of view. The resulting anatomical images covered the whole head at a resolution of 1.5 × 1.17 × 1.17 mm. For functional imaging, 25 contiguous 4-mm-thick axial slices were chosen to provide whole-brain coverage. T2*-weighted images were acquired with a gradient echo sequence using a single-shot spiral trajectory through k space (Glover and Lee, 1995), flip angle 85°, TE = 40 ms, TR = 2000 ms, a 64 × 64 matrix size, and a 20 × 20-cm field of view. The resulting functional images covered the whole cortex, thalamus, and superior cerebellum at a resolution of 3.125 × 3.125 × 4 mm every 2 s. Two hundred eighty-nine functional volumes (i.e., frames) were acquired from each subject in a single scanning run, and the first 3 volumes were discarded to allow for signal equilibration.

Data Processing

Preprocessing, volumetry, statistics, and event-related averaging were performed using Brain Voyager 4.0 (Brain Innovation, Frankfurt, Germany). Anatomical images were resampled to 1 × 1 × 1 mm using sinc interpolation, then aligned with the AC-PC plane and transformed into standard stereotactic space (Talairach and Tournoux, 1988).

Functional data were corrected for interslice differences in time of acquisition. The time course of each voxel was high-pass filtered to remove slow drifts in signal intensity (period >1 min). Finally, the 2D functional slices were coregistered with the 3D anatomical images, transformed into standard stereotactic space, and resampled at a resolution of 3 × 3 × 3 mm. Data

were then smoothed using a 6-mm full-width at half-maximum isotropic Gaussian filter to accommodate anatomical and functional–anatomical variation between subjects. Individual subjects' data were averaged together for group analysis. During the visualization of statistical maps, data were interpolated to 1 × 1 × 1-mm resolution.

Statistical Analysis

We used a two-stage approach in analyzing the data: (1) We identified the common set of regions responding to all events (VR AND VI AND AR AND AI). (2) We assessed the effect of relevance both region by region and voxel by voxel in the set of regions identified in Stage 1.

In Stage 1, regions responsive to each type of event were identified in four separate analyses, each using voxel-wise temporal correlation to an empirically derived hemodynamic response waveform based on the average response in the regions of the multimodal cortical network we sought to replicate (Downar *et al.,* 2000). A schematic of the predicted response waveforms is shown in Fig. 1. Only data points 0–6 frames (0–12 s) after the appropriate type of event were included in each correlation analysis. The result was a map of areas showing the predicted response to VR events, regardless of their response to VI, AR, or AI events, and similar maps for the other three types of events. A conjunction analysis (Price and Friston, 1997; Friston *et al.,* 1999) of the four resulting maps was then used to identify the common set of regions responding to all events. We used voxel-wise Boolean AND operations on the VR, VI, AR, and AI maps to construct a conjunction map of voxels responding to VR AND VI AND AR AND AI events at a conjoint $P < 0.0001$ ($P < 0.1$ in each of the four maps). The total volume of the conjunction map was 1,519,216 mm^3; hence, at a threshold of $P < 0.0001$, ~150 of the 1-mm^3 voxels in each conjunction map would be expected to show activation due to type 1 errors. These voxels would also be expected to display a certain degree of clustering due to spatial autocorrelation following spatial smoothing of the data. As a conservative measure to minimize false-positive activations, we therefore required a minimum cluster size of 150 contiguous interpolated 1-mm^3 voxels for all reported activations.

The Boolean conjunction-based approach used in our study was necessary for two reasons. First, it was necessary to ensure that identified regions showed a response to visual as well as auditory events, rather than simply a significant average response across both modalities (in which case the response might be strong in one modality but absent or even slightly negative in the other). Second, it was necessary to distinguish areas responding to both irrelevant and relevant events from areas that merely showed a strong response to relevant events but no response to irrelevant events.

The former response profile would be expected of the multimodal network we previously identified, given that it responded to changes in the absence of a task; the latter response profile would be expected of areas purely involved in response execution, such as primary motor cortex. Hence, we used the conjunction of relevant and irrelevant events to ensure that identified regions showed a response to irrelevant as well as relevant events, rather than simply a significant average response across relevant and irrelevant events. Conjunction analysis has been used successfully elsewhere to identify common regions responding across multiple sensory modalities (Bremmer *et al.,* 2001) and across multiple tasks (Critchley *et al.,* 2001).

In Stage 2, we assessed the effect of task relevance in the set of common regions identified in Stage 1. A region-by-region analysis was used to distinguish relevance-sensitive from relevance-insensitive regions of interest (ROIs). In addition, to test for the possibility of relevance-sensitive and -insensitive subregions within the common set of regions responsive to all events, we also performed a voxel-by-voxel analysis within the ROIs defined in Stage 1. The effect of task relevance was assessed by correlation of the time course in each region or voxel to the predicted hemodynamic response waveform for task-relevant events minus the waveform for task-irrelevant events, as in a linear contrast of two predictor waveforms in a general linear model (for an illustration of the predicted waveforms, see Fig. 1). A conjunction analysis was again used to ensure an effect of relevance in both the visual and the auditory modalities: VR minus VI AND AR minus AI. Regions or voxels showing a greater response to relevant than to irrelevant events (or vice versa) in visual and auditory modalities at a conjoint $P < 0.01$ were considered relevance sensitive. For consistency with the first stage of analysis, a minimum size of 150 mm^3 was required of all subregions within larger regions of activation.

We also identified the set of regions responsive to task-relevant but not task-irrelevant events. To identify these regions, we first used conjunction analysis to identify the common set of regions responding to VR and AR events at a voxel-wise conjoint $P < 0.0001$. We then excluded any voxels showing responses to either VI or AI events at $P < 0.1$. The lower statistical threshold is more conservative in this case since the criterion was used for the exclusion rather than the inclusion of voxels in the map of activated regions. We used an analogous approach to identify regions responsive to task-irrelevant but not task-relevant stimulus changes.

RESULTS

Task Performance

All subjects reliably detected the stimulus changes. Seven of the 10 subjects reported all 20 of the changes

in the task-relevant stimulus. Two subjects reported 19 of the 20 changes, and 1 subject reported 17 of the 20 changes. No subject made any false-alarm responses.

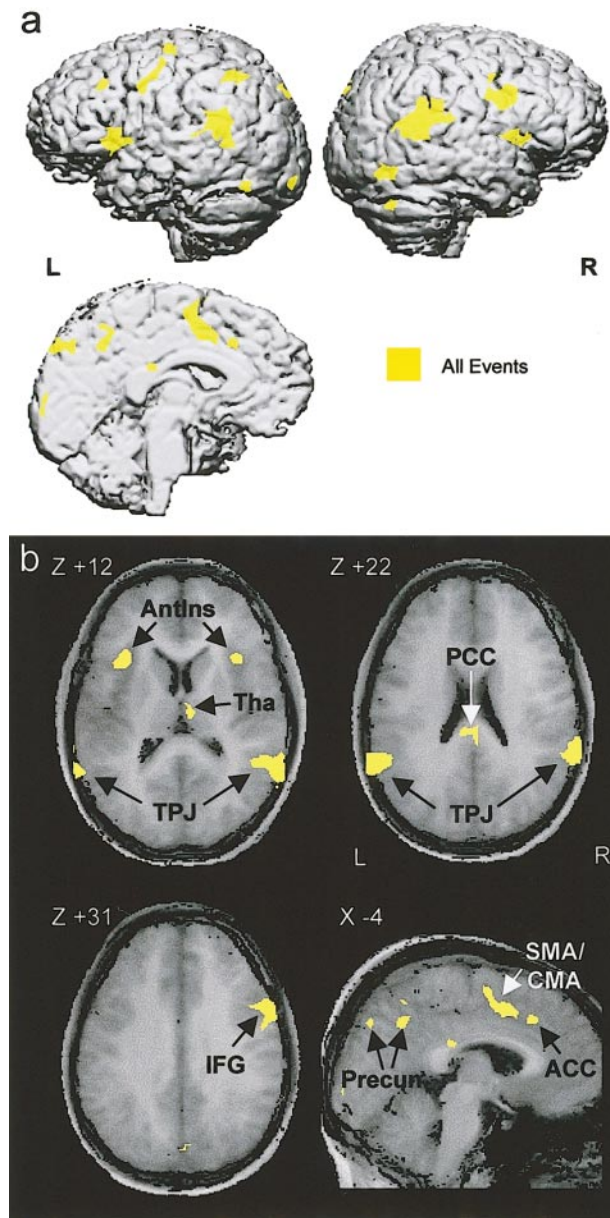### Regions Responsive to All Events

The common set of regions responsive to VR, VI, AR, and AI events included large activations in right and left TPJ. In both hemispheres, these large TPJ activations encompassed inferior regions of the supramarginal gyrus (SMG) as well as the neighboring, posterior extremity of the superior temporal gyrus (STG), corresponding to the intersection of Brodmann areas 22, 39, and 40 (Fig. 2). A distinct hemispheric asymmetry was observed in the TPJ activations, with the total volume of activation approximately twice as large in the right TPJ (4902 mm^3) compared to the left TPJ (2392 mm^3). Other regions showing responses to all four event types included right and left anterior insula, right IFG, and left SMA/CMA. Smaller activations were seen in left middle frontal gyrus (MFG), left anterior cingulate cortex (ACC), left posterior cingulate cortex (PCC), left intraparietal sulcus (IPS), right/left precuneus, and dorsomedial nucleus of the right thalamus. In addition, small activations were seen in right and left inferior temporal gyrus (ITG), left fusiform gyrus, right/left curieus, left precentral gyrus, and right cerebellum (Table 1, Fig. 2).

ROI-Based Assessment of the Effect of Task Relevance

Each of the regions responsive to all events was further characterized according to its response to the task relevance of visual and auditory events. Regions showing a greater response to VR than to VI events, and to AR than to AI events, included the right and left TPJ, left anterior insula, left precuneus, left ACC, and right thalamus, as well as the left precentral gyrus and right cerebellum (Table 1, Fig. 3). Regions showing a similar response to all events, regardless of task relevance, included right IFG, left MFG, right anterior insula, left SMA/CMA, left and right precuneus, left PCC, and left IPS, as well as the small activations in right and left ITG, left fusiform gyrus, left/right cuneus, and right cerebellum. (Table 1, Fig. 3). No region showed a greater response to irrelevant than to relevant events.

### Voxel-wise Assessment of the Effect of Task Relevance

To test for the possibility of relevance-sensitive and -insensitive subregions within the regions responsive to all events, we also assessed the effect of task relevance on a voxel-wise rather than a region-wise basis. A number of the brain regions responsive to all events contained distinct subregions with sensitivity or insensitivity to task relevance (Table 2, Fig. 4). Subregions with a preference for task-relevant events were found bordering relevance-insensitive subregions in the right
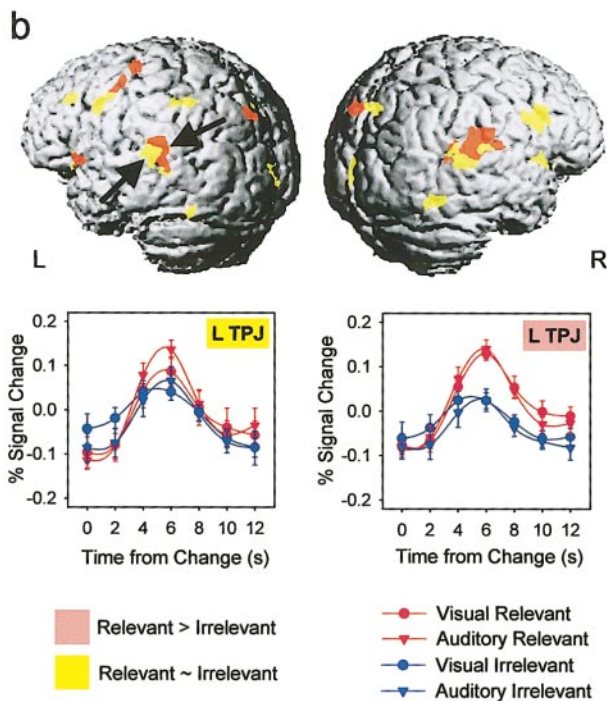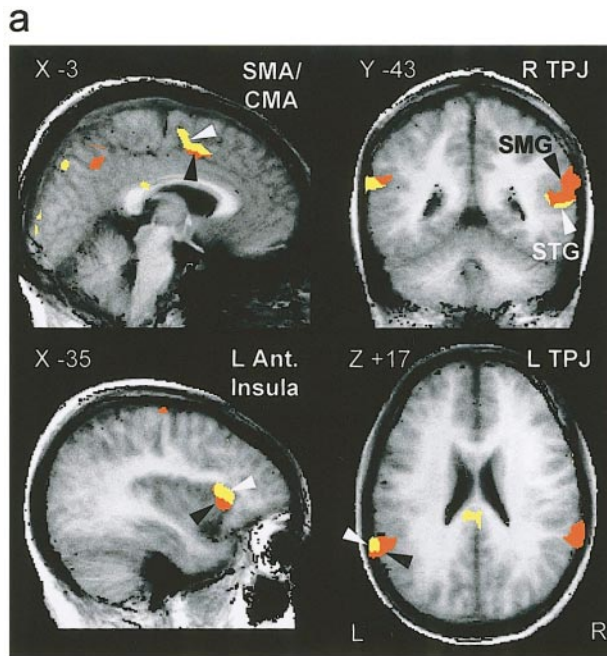
FIG. 2. Brain regions responding to all changes. (a) Surface rendering of the common set of regions responsive to VR, VI, AR, and AI events, superimposed on the standardized brain of one subject. Conjoint $P < 0.0001$, minimum 150 mm^3. (b) Slice views of the common set of regions responsive to VR, VI, AR, and AI events. The plane coordinate of each slice is indicated at upper left. Regions responding to all events included right and left TPJ, right IFG, left SMA/CMA, right and left anterior insula, PCC, precuneus right IFG, and right thalamus. This network corresponds closely to the set of regions we previously identified as responsive to changes in the sensory environment across multiple modalities in the absence of a task (Downar *et al.*, 2000).

events, were located in the right STG rather than the SMG (Table 2). The left TPJ contained one subregion with a strong sensitivity to relevance and a similar-sized subregion insensitive to relevance (Table 2, Fig. 4b). The left TPJ subregions, however, did not correspond as clearly to SMG and STG as those in the right TPJ. The left anterior insula contained an inferior rel-
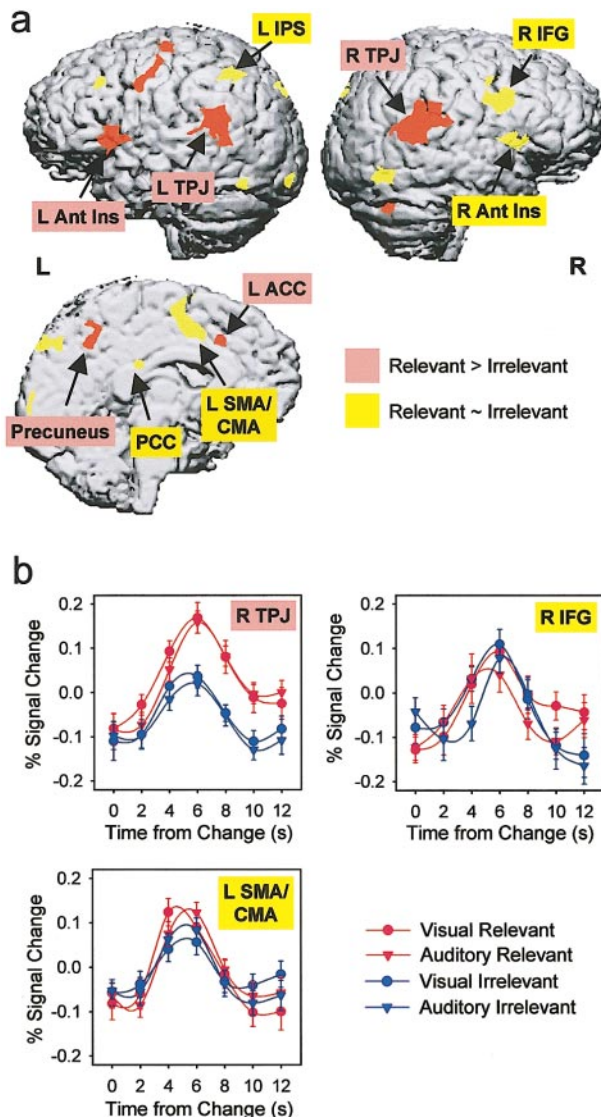
FIG. 3. ROI-based analysis of the effect of task relevance. (a) The effect of task relevance on the response to a given sensory event was assessed on a region-by-region basis (ROI analysis). All regions responded significantly to all events, but context-dependent regions also responded significantly more strongly to VR versus VI and to AR versus AI events. Regions showing context-dependent responses included right and left TPJ, left anterior insula, left precuneus, left ACC, and right thalamus. Context-independent regions responded similarly to all events, regardless of task relevance. Large regions with context-independent responses included right IFG, left CMA/SMA, right anterior insula, left IPS, and precuneus. Smaller context-independent regions included right and left ITG, left MFG, and PCC. (b) Average BOLD responses to task-relevant and task-irrelevant events in right TPJ, right IFG, and left SMA/CMA, indicated by arrows in (a).

and left TPJ, left anterior insula, and left medial wall. The right TPJ contained a large subregion with a greater amplitude of response to relevant events, with a location mostly confined to the right SMG. In contrast, two smaller subregions, with a similar amplitude of response for both task-relevant and -irrelevant

FIG. 4. Voxel-wise analysis of the effect of task relevance. The effect of task relevance on the response to a given sensory event was assessed on a voxel-wise basis to identify context-dependent and -independent subregions within the ROIs responsive to all events. (a) Distinct context-dependent (black arrowheads) and context-independent (white arrowheads) subregions >150 mm³ were found in four ROIs: left SMA/CMA, left anterior insula, right TPJ, and left TPJ. The context-dependent and -independent subregions of the SMA/CMA region correspond to CMA and SMA, respectively. The context-dependent and -independent subregions of the right TPJ correspond to the supramarginal gyrus and superior temporal gyrus, respectively. The plane coordinate of each slice is indicated at upper left. (b) Surface-rendered view of both context-dependent and context-independent subregions in left and right TPJ. Average BOLD responses to task-relevant and task-irrelevant events in subregions of the left TPJ, indicated with arrows on the surface rendering.
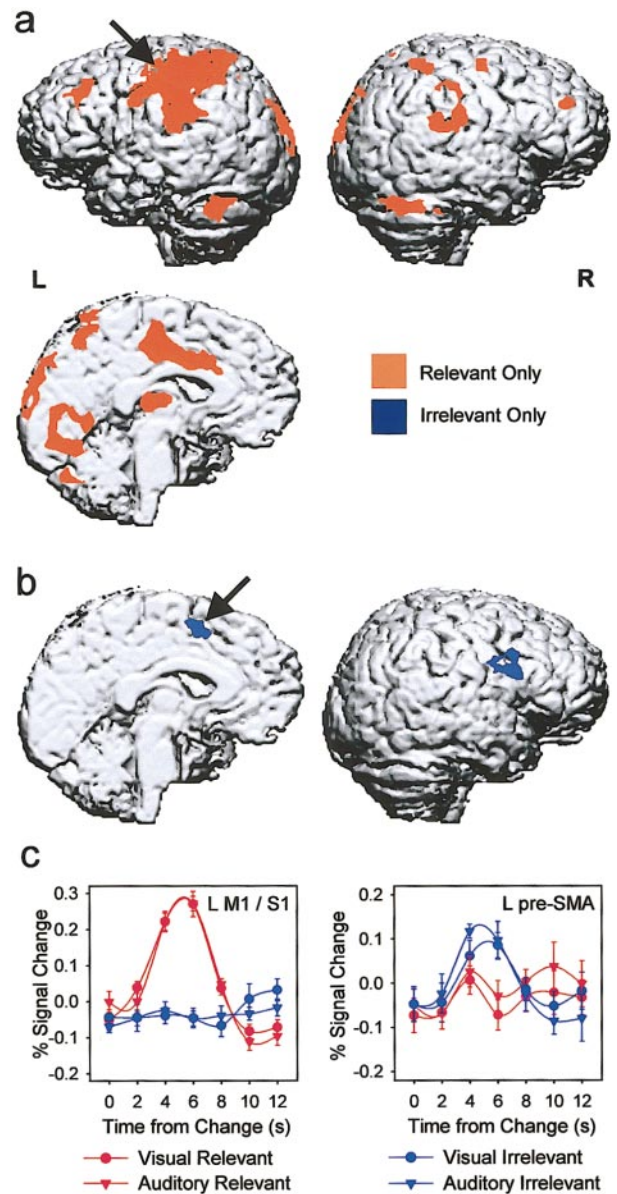
FIG. 5. Brain regions responding exclusively to task-relevant or task-irrelevant events. (a) Regions responding exclusively during task-relevant stimulus changes included a wide array of sensory and motor areas, including left M1 and S1, bilateral S2 and cerebellum, left thalamus, and a large medial region encompassing left SMA and ACC. Some occipital regions, including superior occipital gyrus and left lingual gyrus, also showed responses only to task-relevant changes. Additional activations were found bilaterally in SPL and MFG and in right IPL. (b) Regions responding exclusively during task-irrelevant stimulus changes included only right IFG and left pre-SMA. (c) Average BOLD response of the exclusively task-relevant activation encompassing M1/S1 (shown at left) and of the exclusively task-irrelevant activation in right pre-SMA (shown at right). The former area shows a strong response to task-relevant events but a minimal response to task-irrelevant events, while the latter shows the opposite response profile. Arrows in (a) and (b) indicate the regions whose average time courses are plotted in (c).

evance-sensitive subregion and a superior relevance-insensitive subregion. The large left SMA/CMA activation contained a large superior relevance-insensitive

TABLE 1

Region-Based Classification of Brain Regions Activated during All Stimulus Changes

Structure	Brodmann area	Talairach			Volume (mm³)	Z score	
		x	y	z		All events	Rel − Irrel
Relevant > irrelevant							
R temporoparietal junction	22/39/40	58	−44	16	4902	8.48	5.21
L temporoparietal junction	22/39/40	−61	−48	17	2392	9.85	3.08
L anterior cingulate cortex	32	−3	22	38	200	4.77	3.69
L anterior insula	—	−36	19	8	1267	7.07	2.57
L precuneus	7	−2	−57	39	477	5.07	4.38
R thalamus (MD)	—	6	−15	10	325	5.57	3.23
L precentral gyrus	4	−47	−7	46	588	9.30	3.80
L precentral gyrus	4	−32	−17	63	343	9.10	6.26
R cerebellum	—	34	−61	−35	175	4.14	3.04
Relevant ~ irrelevant							
R inferior frontal gyrus	9/44	52	7	32	1392	7.53	0.01
R inferior frontal gyrus	44	48	11	3	1565	6.74	0.05
L middle frontal gyrus	8	−41	24	41	251	5.06	1.14
L SMA/CMA	6/24	−2	2	50	1794	9.04	1.27
L posterior cingulate cortex	23	−2	−29	23	376	6.22	1.02
R anterior insula	—	34	19	9	556	6.77	0.06
L intraparietal sulcus	7/40	−44	−57	46	561	5.55	1.17
R/L precuneus	7	−4	−80	36	836	5.18	2.46
R inferior temporal gyrus	37	50	−65	−16	420	5.15	1.20
L inferior temporal gyrus	37	−47	−64	−22	192	5.97	0.15
L fusiform gyrus	19	−30	−69	−22	172	5.95	3.01
R/L cuneus	18	0	−95	−2	236	5.36	1.27
R cerebellum	—	25	−52	−35	211	4.51	1.82

Note. Activations shown are based on a voxel-wise conjoint $P < 0.0001$ for VR AND VI AND AR AND AI events and a minimum cluster volume of 150 mm³ (see Methods and Materials). Classifications are based on a region-by-region contrast of VR > VI events AND AR > AI events at a conjoint $P < 0.01$. Z scores are calculated using the average time course of all voxels in each region and indicate the average response to VR + AR + VI − AI events (All events) and the average response to VR + AR − VI − AI events (Rel − Irrel). Coordinates indicate the center of mass of each activation with respect to the anterior commissure in the standardized stereotaxic space of Talairach and Tournoux (1988). SMA/CMA, supplementary motor area/cingulate motor area; MD, dorsomedial nucleus.

subregion confined to SMA and a smaller, inferior relevance-sensitive region confined to CMA (Picard and Strick, 1996). No subregions with a greater response to irrelevant than to relevant events met the minimum volume criterion.

Exclusively Task-Relevant or Task-Irrelevant Regions

Areas responding only to task-relevant stimulus changes (Table 3, Fig. 5a) comprised mostly sensory and motor areas. The largest exclusively task-relevant activations were found in the left precentral and post-central gyri, corresponding to primary sensory and motor cortex (S1, M1) for the right hand. Bilateral activations in secondary somatosensory cortex (S2) and a large medial activation encompassing the left ACC and SMA were also noted. Large subcortical activations were found bilaterally in the cerebellum and unilaterally in the left thalamus. Responses to task-relevant but not task-irrelevant visual and auditory changes were also noted in visual cortical areas, including left lingual gyrus and bilateral superior occipital gyrus.

A small set of frontal and parietal regions not readily corresponding to sensory, motor, or unimodal visual areas also activated exclusively for task-relevant stimulus changes. These included bilateral activations in the anterior MFG and superior parietal lobule (SPL) as well as unilateral activations in the left anterior insula and right IPL. These regions generally showed a weaker response to task-relevant events than did the sensory, motor, or occipital activations (Table 3).

Areas responding exclusively to task-irrelevant stimulus changes (Table 3, Fig. 5b) included only the right IFG and left pre-SMA.

DISCUSSION

Use of the Term "Task Relevance"

It should be noted that the term "task relevance" is used here in a specialized sense. "Task relevant" and "task irrelevant" here denote the behavioral context in which the visual and auditory stimulus changes are presented. When the task is to report changes in the visual stimulus, the auditory stimulus need not be monitored in order to perform the task correctly, and so changes in the auditory stimulus are irrelevant to the task being performed. It is in this sense that changes in the nonreported stimulus are referred to as changes in the task-irrelevant stimulus. However, it should be

TABLE 2

Voxel-wise Analysis Reveals Relevance-Sensitive and Relevance-Insensitive Subregions
within Areas Activated during All Stimulus Changes

Structure	Brodmann area	Talairach			Volume (mm³)	Z score	
		x	y	z		All events	Rel − Irrel
Relevant > irrelevant							
R temporoparietal junction (SMG)	22/39/40	58	−43	17	3933	8.16	5.82
L temporoparietal junction	22/39/40	−59	−50	18	1056	9.07	4.77
L CMA	24	−2	4	43	335	8.52	3.82
L anterior insula	—	−37	18	5	477	5.79	3.71
Relevant ∼ irrelevant							
R temporoparietal junction (STG)	22/39/40	57	−48	10	723	8.41	1.63
R temporoparietal junction (STG)	22/39/40	58	−34	16	215	5.59	1.64
L temporoparietal junction	22/39/40	−62	−48	16	1265	9.10	1.56
L anterior insula	—	−36	19	10	789	7.31	1.38
L SMA	6/24	−2	1	51	1434	8.58	0.42

Note. Subregions shown are based on a voxel-wise conjoint $P < 0.0001$ for VR AND VI AND AR AND AI events and a minimum cluster volume of 150 mm³ (see Methods and Materials). Classifications are based on a voxel-wise contrast of VR > VI events AND AR > AI events at a conjoint $P < 0.01$. Z scores are calculated using the average time course of all voxels in each subregion and indicate the average response to VR + AR + VI + AI events (All events) and the average response to VR + AR − VI − AI events (Rel − Irrel). Coordinates indicate the center of mass of each subregion with respect to the anterior commissure in the standardized stereotaxic space of Talairach and Tournoux (1988). SMG, supramarginal gyrus; STG, superior temporal gyrus; SMA, supplementary motor area; CMA, cingulate motor area.

noted that changes in the nonreported stimulus may also involve an element of response suppression, similar to that found in a go/no-go task. One key difference is that a go/no-go task typically involves two different types of change in a single stimulus (e.g., light turns green = go and light turns red = no-go), so that the nature of the change must be evaluated on each trial in order to make the go/no-go decision. By contrast, in the present task, two entirely different stimuli in different sensory modalities are used, and the task-irrelevant stimulus need not be monitored at all in order to perform the task correctly. Nonetheless, given the low attentional demands of the present task, the response-suppression elements of changes in the irrelevant stimulus should be recognized.

The Multimodal Network Responsive to All Changes

The common set of regions responsive to all events in the present study closely resembles the multimodal network we previously identified as responsive to changes in the sensory environment across multiple modalities in the absence of any task (Downar *et al.,* 2000). This network also included left and right TPJ, right IFG, right anterior insula, and a medial activation encompassing left SMA and CMA. As in the present study, the right TPJ activation in this network was considerably larger than the left TPJ activation. The similarity of these two networks is noteworthy given that the previously identified network responded during the passive observation of stimulus changes in a neutral behavioral context. Therefore, the results of the present study confirm the role of these areas in detecting changes in the sensory environment across multiple sensory modalities.

Context-Dependent and Context-Independent Regions

The present study identified a widespread network of brain regions with enhanced responses to task-relevant as opposed to task-irrelevant events. In all of these regions, the strength of response depended not on the modality of the event, but on the behavioral context of the event, with a given type of change producing a larger response when the stimulus was task relevant compared to when it was task irrelevant. The largest and most pronounced response within this set of context-dependent regions was found in the right TPJ, with smaller activations in left TPJ, left anterior insula, precuneus, ACC, and right thalamus. Again, this set of areas corresponds closely to the set of regions we previously identified as responsive to stimulus changes in a neutral behavioral context. As in our previous study, the right TPJ activation in the present study was considerably larger than the left TPJ activation. A similar right-hemisphere asymmetry has also been found in TPJ activation for visual target and nontarget stimuli (Perry and Zeki, 2000), particularly those appearing at unattended locations (Corbetta *et al.,* 2000). This right-hemisphere asymmetry in TPJ activation echoes the predominance of right rather than left TPJ lesions in patients with hemineglect. It has been suggested that the right TPJ may play a role in detecting the presence of potentially relevant sensory stimuli (Perry and Zeki, 2000), and that damage to this area therefore reduces the salience of stimuli in the neglected field, giving rise to hemineglect (Mesulam, 1999). The results of the present study support these hypotheses. The sensitivity of the right

TABLE 3

Brain Regions Activated Exclusively during Task-Relevant or Task-Irrelevant Stimulus Changes

| Structure | Brodmann area | Coordinates | | | Volume (mm³) | Z score | |
		x	y	z		Relevant	Irrelevant
Task relevant							
L precentral/postcentral gyrus	1/2/3/4	−44	−27	50	11,523	11.58	0.69
L precentral gyrus	6	−54	3	7	658	9.14	1.41
R precentral gyrus	4	38	−8	56	218	4.77	0.88
L anterior cingulate cortex/SMA	6/24	−3	−6	40	5,472	9.05	1.00
R secondary somatosensory cortex	43	54	−28	23	1,595	8.33	0.68
L secondary somatosensory cortex	43	−55	−30	25	2,576	8.08	0.68
R cerebellum	—	33	−55	−29	3,547	8.70	0.45
L cerebellum	—	−5	−72	−38	375	6.55	1.00
L cerebellum	—	−38	−52	−31	1,147	6.48	0.22
L thalamus	—	−3	−17	9	1,668	6.55	0.52
R anterior insula	—	31	10	13	221	5.50	0.22
R middle frontal gyrus	9/46	25	45	33	272	5.30	0.16
L middle frontal gyrus	9/46	−36	32	41	554	5.62	0.32
R superior parietal lobule	40	40	−45	56	614	5.07	0.47
L superior parietal lobule	40	−31	−49	58	3,498	5.83	0.17
R inferior parietal lobule	40	56	−28	43	244	8.05	0.38
R superior occipital gyrus	19	19	−84	40	223	4.62	0.64
R superior occipital gyrus	19	10	−95	14	480	5.77	0.13
L superior occipital gyrus	19	−9	−91	23	2,330	7.23	0.64
L lingual gyrus	18	−8	−74	−14	3,410	7.34	0.03
L lingual gyrus	18	−14	−68	0	195	5.92	0.79
Task irrelevant							
R inferior frontal gyrus	9/44	46	11	28	1,236	0.41	6.65
L presupplementary motor area	6	−4	8	51	363	0.05	5.34

Note. Exclusively task-relevant activations shown are based on a voxel-wise conjoint $P < 0.0001$ for VR AND AR events, excluding any voxels with $P < 0.1$ for VI or $P < 0.1$ for AI events. Exclusively task-irrelevant activations shown are based on a voxel-wise conjoint $P < 0.0001$ for VI AND AI events, excluding any voxels with $P < 0.1$ for VR or $P < 0.1$ for AR events. A minimum cluster volume of 150 mm³ is used for all reported regions (see Methods and Materials). Z scores are calculated using the average time course of all voxels in each region and indicate the average response to VR and AR events (Relevant) and to VI and AI events (Irrelevant). Coordinates indicate the center of mass of each activation with respect to the anterior commissure in the standardized stereotaxic space of Talairach and Tournoux (1988). SMA, supplementary motor area.

SMG, in particular, to the task relevance of the stimulus changes suggests it may constitute a neural substrate for the detection of sensory events within a particular behavioral context.

The dorsolateral prefrontal cortex (DLPFC) did not show sensitivity to task relevance in the present study. However, neurophysiological studies in awake, behaving monkeys have indicated that the behavioral significance of stimuli used in delayed-matching-to-sample tasks modulates the working-memory activity of neurons in this region (Yajeya *et al.,* 1988). The lack of a delay between stimulus changes and responses in our task likely explains the absence of relevance-sensitive DLPFC activation in the present study. However, the case of the DLPFC illustrates that relevance sensitivity may emerge in areas other than those noted in the present study, under the appropriate cognitive conditions.

In contrast, another widespread set of brain regions responded similarly to all stimulus changes regardless of task relevance. This set of context-independent regions included prefrontal activations in right IFG and left MFG; medial activations in left SMA/CMA, left and right precuneus, and PCC; and a parietal activation in left IPS. Two interpretations are possible for context-independent regions. First, they may be involved in detecting changes in the sensory environment regardless of behavioral context. Second, they may be involved in response execution at the level of planning or decision-making and therefore activate similarly whether or not a response is ultimately made. It should be noted that these two roles are not necessarily mutually exclusive and that there may be a substantial cognitive overlap between the mechanisms of stimulus evaluation and response planning.

Interestingly, voxel-wise examination of the effect of task relevance revealed that the large activations in right and left TPJ contained distinct subregions with context-dependent and context-independent responses. In the right TPJ, the subregion in the SMG showed sensitivity to the behavioral context of stimulus changes, while the subregions in the STG did not. The presence of these subregions within the right TPJ, and

of similar subregions in the left TPJ, suggests that the region as a whole may play a role in identifying salient events both within and independent of the current behavioral context.

Context-dependent and independent regions may play complementary roles in identifying salient features of the sensory environment. Sensory events may be salient either due to their own intrinsic features (such as change, novelty, intensity) or due to the current behavioral context. To be effective in identifying salient stimuli, a complete attentional system therefore requires both context-dependent and context-independent mechanisms. In this sense, the concepts of context-dependent and context-independent salience are congruent with those of voluntary and involuntary attention. The results of the present study suggest that the neural substrates of these complementary mechanisms may involve not only distinct brain regions but also distinct subregions within particular brain areas.

The Role of Exclusively Task-Relevant and Task-Irrelevant Activations

As noted in the Introduction, it should be recognized that task relevance as referred to here also relates to the need to execute a response to relevant changes and inhibit it for irrelevant changes. Many of the activations observed exclusively for changes in the task-relevant stimuli likely reflected either response execution or sensory feedback from the finger movements required during task performance. In particular, strong activations were detected in sensorimotor regions such as the left M1, left S1, right and left S2, left thalamus, and right and left cerebellum during stimulus changes requiring a motor response but not during identical stimulus changes not requiring a response. It should be noted, however, that areas showing exclusively task-relevant activation may also perform premotor, planning, or cognitive functions. In particular, task-relevant activations in right and left SPL, left ACC, and right and left MFG are unlikely to reflect the mere execution of a particular motor response. For example, the exclusively task-relevant MFG regions activated in the present study have also been reported to activate for target but not nontarget stimuli in a visual oddball task, whether the required response was button-pressing or silent counting (Kirino et al., 2000). These anterior MFG regions may therefore be involved in identifying the presence of a stimulus requiring a response or in initiating the motor response to an identified target stimulus. Likewise, the exclusively task-relevant ACC activations identified in the present study lie within the dorsal or "cognitive division" of the ACC (Bush et al., 1999). This region has been reported to activate during a wide variety of cognitive tasks involving selection between conflicting stimuli and/or responses (Paus et al., 1998). Its activation in the present study is therefore unlikely to reflect simple response execution

(Picard and Strick, 1996; Bush et al., 2000). Distinguishing activations in areas such as MFG and ACC from activations specific to finger-raising was not one of the primary objectives of the present study and would require a modified experimental design. However, the identification of a set of response-general, exclusively task-relevant areas would constitute an interesting topic for future study.

Only left pre-SMA and right IFG showed exclusively task-irrelevant activation. Right IFG activation has been previously reported during no-go events on a go/no-go task (Konishi et al., 1998a, 1999) and during cognitive set shifting on the Wisconsin Card Sorting Task, both of which require inhibition of prepotent motor responses (Konishi et al., 1998b). Hence, it is possible that the exclusively task-irrelevant right IFG activation identified in the present study reflects inhibition of the finger-raise response following changes in the task-irrelevant stimulus. However, it should be noted that neighboring right IFG regions responded similarly to task-relevant and task-irrelevant changes (Table 1, Fig. 3). Right IFG therefore appears to play more than a purely inhibitory role in planning and directing behavior. The insensitivity of some right IFG regions to behavioral relevance is more consistent with an evaluative role in determining whether a given sensory event requires a response.

A Proposed Role for the TPJ in Identifying Behaviorally Relevant Events

The results of the present study confirm the hypothesis that the responsiveness of the TPJ to changes in a sensory stimulus increases when the stimulus is more salient due to its relevance to task performance. The TPJ has been implicated in a variety of processes, including the detection of visual stimuli appearing at unexpected locations (Corbetta et al., 2000) and the detection of visual oddball stimuli differing from the standard stimulus in form, location, or both (Marois et al., 2000). TPJ activations have also been reported for visual and auditory oddballs requiring silent counting or button-pressing responses (Linden et al., 1999) and for target but not distractor oddballs in a stream of visually presented letters (Clark et al., 2000). Unlike the present study, however, the aforementioned studies all involved the presentation of a single rather than a double sequence of stimuli and hence could not differentially manipulate the task relevance of the stimuli presented.

Few specific factors affecting the amplitude of the TPJ response have been identified to date. On the contrary, previous neuroimaging studies have shown the TPJ to respond nonspecifically to a wide variety of sensory events, regardless of type or sensory modality (Linden et al., 1999; Marois et al., 2000; Downar et al., 2000). The results of the present study provide evidence for a factor that strongly and reliably affects the

amplitude of TPJ response: task relevance. This finding may help to provide a framework for integrating the findings of earlier studies into a more general account of TPJ function. Specifically, we propose that the TPJ plays a key role in identifying sensory events of potential relevance to behavior.

A role for the TPJ in identifying salient sensory events is consistent with findings from EEG studies of patients with focal cortical lesions using single-train oddball paradigms. Lesions of the TPJ reduce the amplitude of the P3b event-related potential, elicited by target oddballs requiring a behavioral response such as counting or button-pressing. This reduction has been observed in auditory and tactile sensory modalities (Knight *et al.,* 1989; Yamaguchi and Knight, 1992; Verleger *et al.,* 1994). In contrast, lesions of prefrontal cortex or of parietal cortex superior to the TPJ do not affect the latency or amplitude of the P3b (Swick and Knight, 1998). Interestingly, lesions of the TPJ also reduce the amplitude of the P3a, elicited by novel or unexpected stimuli (Knight, 1997, 1984; Yamaguchi and Knight, 1991; Swick and Knight, 1998). These findings corroborate the findings of the present study in suggesting a general role for the TPJ in detecting salient (task-relevant or novel) events in the sensory environment.

In conclusion, the results of the present study illustrate a network of brain areas responsive to the task relevance of changes in visual and auditory stimuli. The TPJ is central to this network, which also includes the precuneus, anterior insula, ACC, CMA, and thalamus. The TPJ in particular plays a key role in detecting events of potential relevance to behavior across multiple sensory modalities. However, the TPJ is not functionally homogeneous but contains distinct subregions, some of which respond preferentially to task-relevant events while others respond similarly to all events. The TPJ may therefore play a crucial role in identifying and attending to task-relevant or otherwise salient features of the sensory environment.

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