Time Perception and Motor Timing: A Common Cortical and Subcortical Basis Revealed by fMRI

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Though it is well known that humans perceive the temporal features of the environment incessantly, the brain mechanisms underlying temporal processing are relatively unexplored. Functional magnetic resonance imaging was used in this study to identify brain activations during sustained perceptual analysis of auditorally and visually presented temporal patterns (rhythms). Our findings show that the neural network supporting time perception involves the same brain areas that are responsible for the temporal planning and coordination of movements. These results indicate that time perception and motor timing rely on similar cerebral structures. © 2000 Academic Press

INTRODUCTION

Orientation and adequate behavior in an environment shaped by continuously changing conditions requires adaptation and adjustment to its spatial and temporal characteristics. In the temporal domain this adaptation is not limited to the precisely timed perceptual and motor skills revealed by musicians, dancers, and athletes, but also applies to common actions, such as crossing the street or catching a falling object. On the one hand, preparation of motor output requires the temporal order and duration of component movements in complex sequential behavior to be specified. On the other hand, the temporal structures and characteristics of events that we experience and react to have to be stored in long-term memory independent of motoric implementations. In everyday life both kinds of temporal processing, motor timing and time perception, have to interact for successful action. This leads to the hypothesis that both the analysis of environmental temporal features and the coordination of one's motor output possibly rely on similar mechanisms and brain structures (Keele *et al.,* 1985; Treisman *et al.,* 1992). However, the question of whether the mnemonic or preparatory representation of temporal structure in the cortical areas that contribute to movement organization is necessarily motor related or if it can be better

described as a representation that is independent of motoric output implementation remains unresolved.

The cortical structures that are involved in motor timing functions such as the scaling of amplitude and velocity of movement are organized in a combined open and closed loop with subcortical structures, the so-called *motor circuit* (Alexander *et al.,* 1986, 1990; Picard and Strick, 1996; Joel and Weiner, 1997; Kischka *et al.,* 1997; Kitano *et al.,* 1998; Strick *et al.,* 1998). It comprises the premotor cortex (PMC), primary motor cortex (MI), primary somatosensory cortex (SI), and medial wall motor areas in the cingulate cortex as well as parts of the basal ganglia and the thalamus. Within this circuit, a small premotor sector around the most medial and superior part of the parasagittal region, the supplementary motor area (SMA) (Penfield and Welch, 1949), holds an exceptional functional status. Like the PMC, MI, and SI, the SMA sends input projections to the putamen, a part of the basal ganglia (Takada *et al.,* 1998; Saint-Cyr *et al.,* 1995); however, of these structures the SMA is the only one which receives projections from the thalamus (Schell and Strick, 1984), thereby closing the motor circuit. Additionally, the cerebellum has reciprocal connections with several motor circuit structures (Middleton and Strick, 1997) and is also regarded as involved in the control of movement. Motor timing or response timing functions have been attributed to several structures of the motor circuit including, for example, the cerebellum (Buonomano and Mauk, 1994; Ivry, 1996, 1997; Raymond *et al.,* 1996; Penhune *et al.,* 1998; Casini and Ivry, 1999), the basal ganglia (Jueptner *et al.,* 1995; Hinton *et al.,* 1996; Harrington and Haaland, 1998; Harrington *et al.,* 1998; Turner *et al.,* 1998), and the PMC (Kubota and Hamada, 1978; Weinrich *et al.,* 1984; Halsband *et al.,* 1993; Rao *et al.,* 1997; Rubia *et al.,* 1998).

The present study set out to investigate the hypothesis that if motor timing and time perception rely on similar brain processes, i.e., if the mechanisms that control the timing of motor performance and those that underlie the perception of time are realized by the same brain structures, then the brain areas that contribute

to the temporal organization of movement, such as the PMC, the cerebellum, and the basal ganglia, should also be involved in time *perception*. To test this hypothesis we investigated the perceptual analysis of temporal structures using a duration monitoring task.

Investigations of timing and sequencing functions are often restricted to motor rehearsal and motor planning tasks and thereby do not allow examination of the nature of temporal structure representations in the cerebral cortex independent of overt or imagined, planned, or remembered movements. Although studies of motor timing can use tapping tasks with long activation phases that are very well suited to imaging techniques, the main problem with time perception studies using functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) to date is that they employ exclusively paradigms that require timing only for a very short duration. Subjects most frequently have to perform in delay tasks such as temporal generalization, i.e., a task which requires a comparison between two durations. Other studies make use of a temporal orienting task in which subjects have to react after certain target durations (Jueptner *et al.,* 1995; Maquet *et al.,* 1996; Lejeune *et al.,* 1997; Coull and Nobre, 1998). These tasks activate time processing only for the target duration used, in these studies never more than 1500 ms, and therefore might not lead to a BOLD response that reflects the timing system working to full capacity.

In contrast, the present study is the first to utilize a go/no-go oddball paradigm that takes advantage of continuous timing requirements in the absence of task-related motor requirements. We tested the hypothesis that cortical structures involved in motor timing providing input to the MI are also activated in time perception and memory. To control for influences of stimulus presentation modality, both visual and auditory stimuli were used in separate conditions. We used fMRI to scan subjects while they monitored a stimulus stream for rhythmically deviant items.

MATERIALS AND METHODS

For technical reasons, the upper limit on the number of slices required for one MRI image was 16. Given that slice thickness and slice spacing should not exceed a certain limit in order to maintain a high resolution of MRI data, 16 slices cannot cover the whole brain either in axial or in coronal orientation. Therefore, the experiment was run two times. In the first run of the experiment (referred to as *Experiment 1*), the whole brain, with the exception of the cerebellum, was imaged using axial slices (Fig. 1, Experiment 1). To examine cerebellar activation, the experiment was run a second time (referred to as *Experiment 2*) using coronal slices that covered the entire cerebellar cortex (Fig. 1, Experiment 2). Note that the only difference between Experiments 1 and 2 was the mode of acquisition (axial versus coronal slices and different ranges of brain tissue imaged).

Subjects, Design, and Materials

All experiments complied with German legal requirements. Participants signed consent forms that indicated the nature and the risks of the experimental procedures. Twenty right-handed, healthy subjects (Ex-
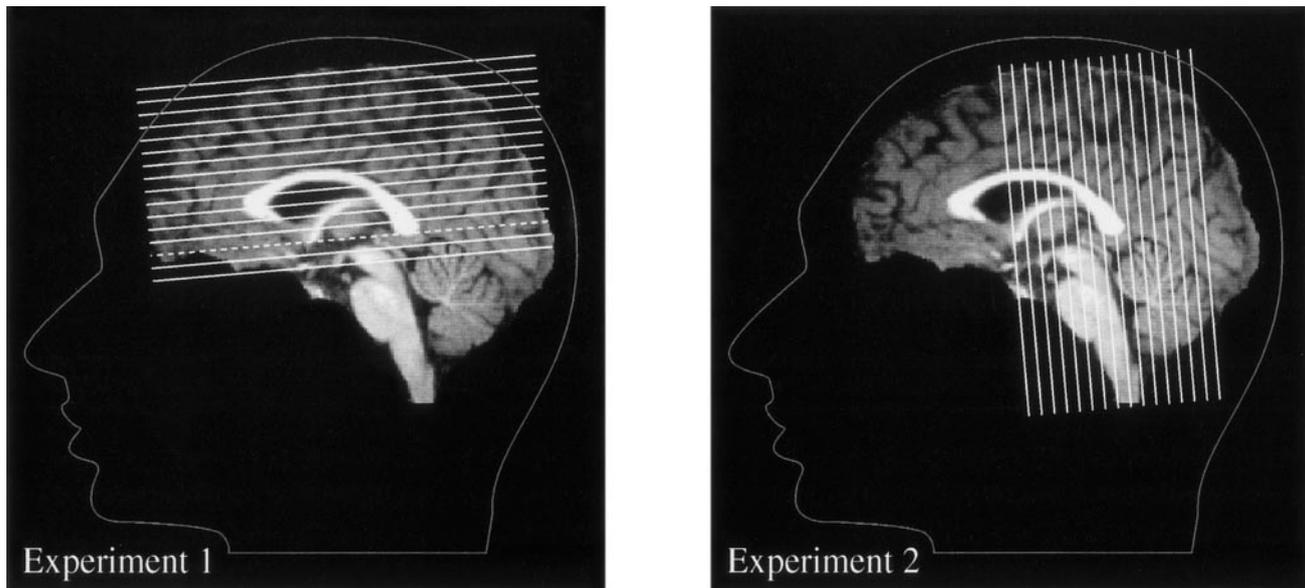

FIG. 1. Midline sagittal section illustrating the locations of the 16 slices acquired during Experiment 1 (axial, parallel to the bicommissural plane (AC-PC, broken line)) and Experiment 2 (coronal, perpendicular to AC-PC).

TABLE 1

Experimental Conditions (Experiments 1 and 2)

	Experimental condition: Attention to rhythm	Baseline condition: Attention to stimulus properties
Visual block	Condition *Rv* (rhythm, visual) Task: report visual rhythm deviation	Condition *Bv* (baseline, visual) Task: report color deviation
Auditory block	Condition *Ra* (rhythm, auditory) Task: report auditory rhythm deviation	Condition *Ba* (baseline, auditory) Task: report pitch deviation

periment 1, 4 male, 6 female, mean age 24; Experiment 2, 3 male, 7 female, mean age 23) were presented with two visual and two auditory tasks (Table 1). In each task, three-element sequences of stimuli were presented repeatedly and subjects monitored for deviants in a go/no-go response mode (Fig. 2).

Condition Rv

In the *visual rhythm task,* a sequence of pictures was presented successively for different durations. Each display contained two small blue squares in opposing symmetrical locations on a virtual circle. Over three successive frames, the location of the stimuli moved along six possible circle locations, remaining at each location for a designated interval and thus forming one visual "rhythm." One trial consisted of four repetitions of one rhythm. The order of the pictures differed between trials. The presentation durations were 300, 600, 900, 1200, 1500 or 1800 ms, and the sum duration was always 2400 ms for each rhythm (e.g., 600–1500–300 ms). Subjects monitored for rhythmical deviants, which were 900 ms longer or shorter than the first presentation duration.

Condition Ra

In the *auditory rhythm task,* three different tones (396, 440, or 495 Hz) were presented successively for different durations. The order of the tones differed between trials. The task instructions and presentation durations were the same as in the visual rhythm task.

Condition Bv

In the *visual baseline task* (color monitoring), the same type of sequence as in the visual rhythm task was monitored for color deviants, which were pictures showing red instead of blue colored squares.

Condition Ba

In the *auditory baseline task* (pitch monitoring), the same type of sequences as in the auditory rhythm task had to be monitored for pitch deviants (526-Hz tones).
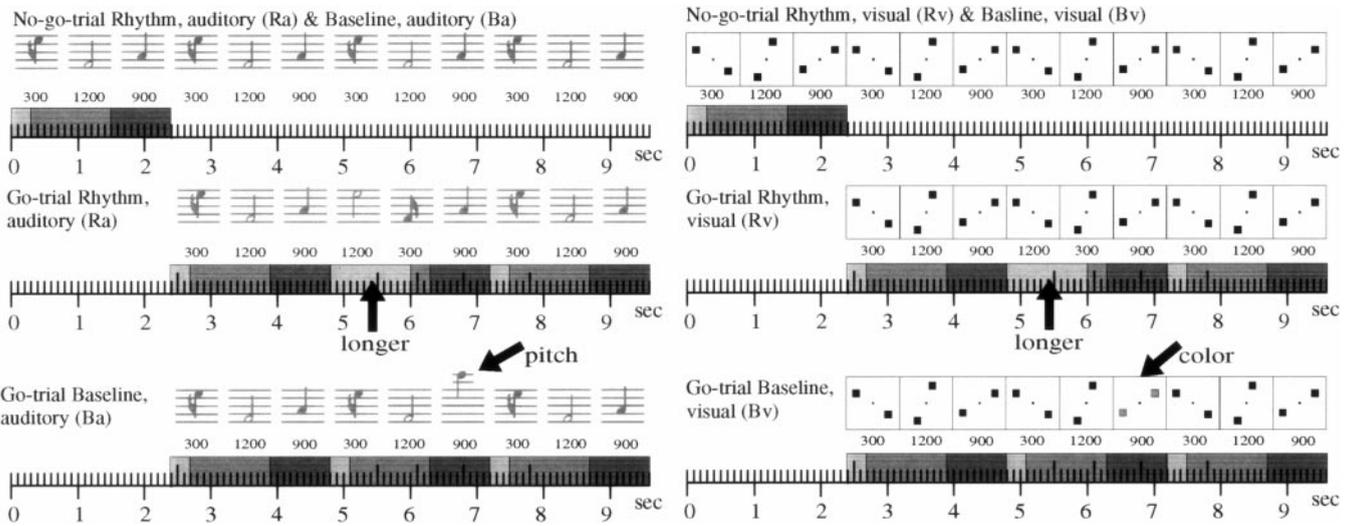

FIG. 2. Examples of stimulus sequences presented in the auditory (left) and the visual (right) conditions (the task cue preceding the stimulus sequence in each trial is omitted here). The specific presentation time of each picture or tone constituting three-element rhythms is indicated by different gray rectangles on the time scale (the example shows a rhythm of 300–1200–900 ms). The auditory presentation is displayed here as note symbols. The upper row shows a no-go trial, e.g., a trial with four presentations of a rhythm without deviants. The middle row shows a go-trial in the auditory (left, *Ra*) and the visual (right, *Rv*) rhythm task. In the example displayed, the first item of the third rhythm presentation is longer than the first item of the first rhythm presentation and therefore has to be indicated as rhythmical deviant by button press. The lower row shows a go-trial in the auditory (left, *Ba*) and the visual (right, *Bv*) baseline task. In this example, the subject has to indicate the item that is deviant in pitch (third item of third presentation) in the auditory task and the item that is deviant in color (third item of third presentation) in the visual task. Note that there were no color or pitch deviants during the rhythm conditions (*Rv, Ra*) and no rhythm deviants during the baseline conditions (*Bv, Ba*).

All trials were presented in two blocks, one visual presentation block (42 trials of condition *Rv* and 42 trials of condition *Bv,* in randomized order) and one auditory presentation block (42 trials of condition *Ra* and 42 trials of condition *Ba,* in randomized order). Visually presented trial cues indicated the subsequent task for each trial. The order of block presentation was counterbalanced across subjects. A cue was presented at the onset of each trial. In the visual presentation block, subjects were instructed to indicate either rhythm deviants (cue "rhythm") or color deviants (cue "color") as quickly as possible by button press immediately upon deviant detection. In the auditory presentation block, subjects had to indicate either rhythm deviants (cue "rhythm") or pitch deviants (cue "tone") by button press. There were no color or pitch deviants during the rhythm conditions (*Rv, Ra*) and no rhythm deviants during the baseline conditions (*Bv, Ba*). Subjects were required to respond to deviant stimuli, meaning that no responses were emitted in no-go trials because no deviant stimuli were presented.

In each trial, the monitoring phase lasted 10 s, with 5 s of rest between successive trials to allow the fMRI signal to return to baseline. To rule out any motor response contribution only no-go trials were used for signal analysis (70% of all trials).

Data Acquisition

Imaging was performed at 3 T on a Bruker Medspec 30/100 system equipped with a standard "bird cage" head coil. High-resolution whole-brain images were recorded from each subject to improve the localization of brain activation foci using a T1-weighted 3D segmented MDEFT sequence (128 sagital slices, 1.5 mm thick, 256×256-pixel matrix). To align the echo planar functional images to the 3D images, conventional 2D anatomical images in plane with the functional images were acquired immediately before the functional scan using an IR-RARE sequence (TE = 20 ms, TR = 3750 ms, 512×512 matrix). Finally, functional images were acquired as follows.

Experiment 1

During each trial six images were obtained from 16 axial slices (6 mm thick, 2 mm spacing) using a single-trial fMRI design. A single-shot gradient EPI sequence (matrix 64×64, TE = 40 ms, flip angle 40°, field of view 192 mm) with 2.5 s for completing one image (volume), i.e., 16 slices, was used. Two slices were positioned ventrally to the bicommissural plane (AC-PC), the entire range of remaining slices covered the whole brain dorsally (see Fig. 1, Experiment 1).

Experiment 2

During each trial eight images were obtained from 16 coronal slices (6 mm thick, 2 mm spacing). The same EPI sequence was used, but with only 2 s for completing one image. Slices were positioned perpendicularly to AC-PC, covering the brain from the cerebellum to the motor cortex (see Fig. 1, Experiment 2).

Data Analysis

Prior to statistical analysis, individual subjects' data were preprocessed (Kruggel *et al.,* 1998) by (1) 2D-motion correction (Friston *et al.,* 1994), (2) correction for baseline fluctuations using a voxel-wise low-pass filter in the temporal domain (cut-off frequency of 1.5 times the trial length), and (3) a Gaussian filter in the spatial domain to reduce noise ($\sigma = 1$, FWHM = 8.9 mm). Standard procedures to detect functional activity were performed as follows. Because the BOLD response typically reaches its peak level about 5 s after event onset (Vazquez and Noll, 1998), (1) we computed a voxel-wise t test of the preprocessed data using a 5.1-s delayed box car function relative to the beginning of the stimulus presentation. (2) The t values were then converted into Z scores. (3) A transformation matrix was calculated by mapping the 2D anatomical slices onto the individual 3D anatomical data set. The Statistical Parametric Maps (SPM[Z]) were then transformed by this matrix. (4) The resulting SPM[Z] were transformed into Talairach space (Talairach and Tournoux, 1988) by a linear affine transformation. (5) Finally, individual SPM[Z] were averaged. Regions with a Z score higher than 4 were considered significantly activated ($P < 0.0001$) without corrections for multiple comparisons.

RESULTS

Behavioral Results

A repeated-measures ANOVA conducted on error rates with the two-level factors Task (rhythm, pitch/color monitoring) and Modality (visual, auditory) indicated no Task × Modality interaction and no performance differences in terms of sensory modalities in Experiment 1 and Experiment 2 (Fig. 3). There was a main effect of Task in Experiment 1 ($F_{(1,9)} = 27.89$, $P < 0.0005$) and Experiment 2 ($F_{(1,9)} = 36.0$, $P < 0.0002$), suggesting that task performance was better in the pitch/color monitoring tasks (i.e., the baseline conditions) than in the rhythm monitoring tasks. The error rates were 11.7% in *Rv,* 10.7% in *Ra,* 2.4% in *Bv,* and 1.9% in *Ba* (Experiment 1) and 7.9% in *Rv,* 5.7% in *Ra,* 1.4% in *Bv,* and 3.6% in *Ba* (Experiment 2).

As only no-go trials entered the MRI signal analysis, a second ANOVA restricted to the performance data of the no-go-trials was conducted. Again, there was a main effect of Task in Experiment 1 ($F_{(1,9)} = 5.76$, $P < 0.03$) and Experiment 2 ($F_{(1,9)} = 15.78$, $P < 0.003$), but no main effect of Modality in Experiment 1. In
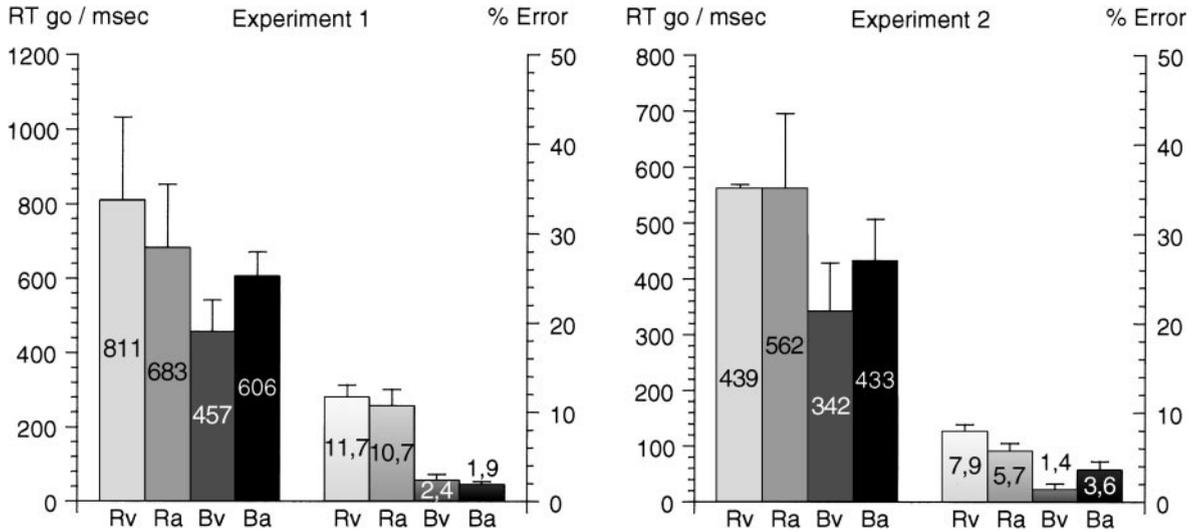
FIG. 3. Behavioral performance in Experiment 1 (left) and Experiment 2 (right). The reaction times of deviant detection (i.e., go trials only) and the overall error rate (go and no-go trials) of the four conditions visual rhythm task (*Rv*), auditory rhythm task (*Ra*), visual baseline task (*Bv*), and auditory baseline task (*Ba*) are shown.

Experiment 2 there was a main effect of Modality ($F_{(1,9)} = 7.23, P < 0.025$) and a significant Task × Modality interaction ($F_{(1,9)} = 15.06, P < 0.004$), indicating that the performance level on no-go trials in Experiment 2 was better in the auditory domain than in the visual domain. However, because the overall error rate on the no-go trials was very low in Experiment 1 (5% in *Rv,* 2.5% in *Ra,* 0.6% in *Bv,* and 0.3% in *Ba*) and in Experiment 2 (3.8% in *Rv,* 0.6% in *Ra,* 0% in *Bv,* and 0.9% in *Ba*), these sensory modality-related performance differences on no-go trials in Experiment 2 are not considered further.

A repeated-measures ANOVA conducted on reaction times with the two-level factors Task (rhythm, pitch/color monitoring) and Modality (visual, auditory) indicated no Task × Modality interaction and no main effects of Modality or Task in Experiment 1 and Experiment 2. The absence of any reaction time differences between tasks or modalities in both experiments indicated no attentional effects.

fMRI Results

Several brain regions revealed significant activation during temporal processing relative to the perceptual baseline condition (Table 2 and Fig. 4).

Bilaterally, a broad stripe of activation extended from the medial PMC including the SMA and pre-SMA via the anterior and posterior banks of the superior and the inferior precentral sulcus to the frontal operculum (FO). Thus, the whole premotor area including Broca's area and its right side homologue were activated (Fig. 4, 1–5).
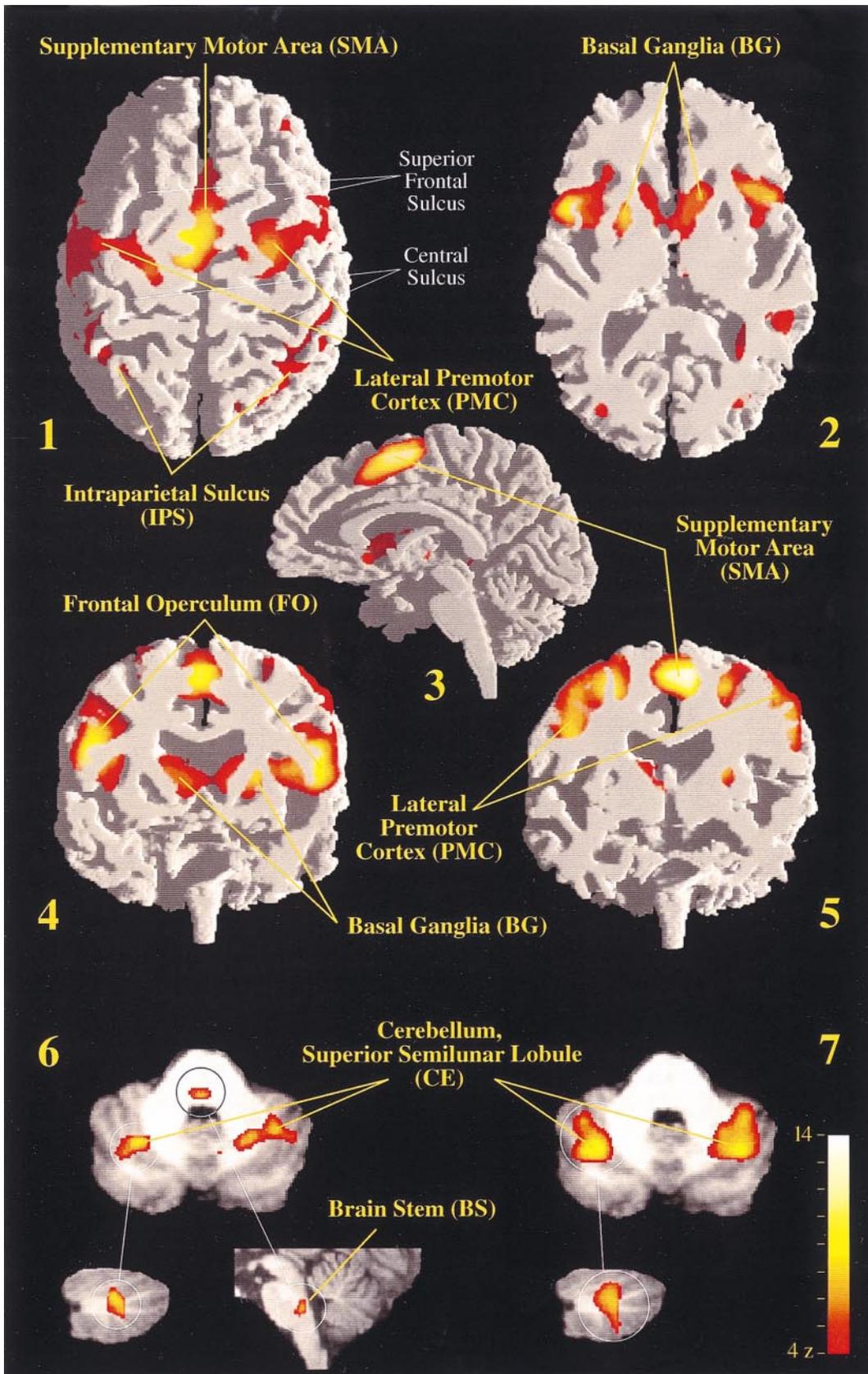
As expected, the basal ganglia (BG) showed a significant activation in the region of the striatum, with a

focus in the left putamen (Fig. 4, 2 and 4). As shown in 6 and 7 of Fig. 4, activation during rhythm monitoring was found in both lateral cerebellar hemispheres. Activation foci were located in the lateral hemispheres of the posterior cerebellar lobe (CE), in the superior semilunar lobule. In addition, the brain stem (BS) was

TABLE 2

Foci of Activations Obtained in the Visual (Vis) and Auditory (Aud) Rhythm Monitoring Tasks Relative to the Control Conditions

Anatomical location	Talairach coordinates (mm)			Max. Z score	
	x	y	z	Aud	Vis
Supplementary motor area	−3	−3	53	13.8	14.6
Left premotor cortex	−24	−13	50	11.6	9.7
Right premotor cortex	24	−10	52	10.4	9.8
Left frontal opercular cortex	−46	9	12	10.9	10.8
Right frontal opercular cortex	44	9	18	10.7	10.2
Left posterior intraparietal sulcus	−18	−70	43	7.0	8.0
Right posterior intraparietal sulcus	22	−67	39	8.8	6.3
Left anterior intraparietal sulcus	−37	−44	48	7.7	8.0
Right anterior intraparietal sulcus	39	−44	38	9.7	7.4
Left putamen	−20	3	11	8.6	7.9
Right putamen/caudatum	13	8	9	7.0	7.2
Left cerebellum (superior semilunar lobule)	30	−54	−32	4.0	10.4
Right cerebellum (superior semilunar lobule)	−27	−61	−35	4.4	11.1
Brain stem	−1	−42	−20	3.5	—

Supplementary Motor Area (SMA)

Basal Ganglia (BG)

Superior Frontal Sulcus

Central Sulcus

Lateral Premotor Cortex (PMC)

1

2

Intraparietal Sulcus (IPS)

Supplementary Motor Area (SMA)

Frontal Operculum (FO)

3

Lateral Premotor Cortex (PMC)

4

5

Basal Ganglia (BG)

6

7

Cerebellum, Superior Semilunar Lobule (CE)

Brain Stem (BS)

14

4 z

activated in the auditory condition (Fig. 4, 6). Furthermore, there was significant activation in the anterior (aIPS) and the posterior (pIPS) branches of the intraparietal sulcus (for IPS, see Fig. 4, 1).

The local maxima of activity of the visual ($Rv–Bv$) and the auditory ($Ra–Ba$) rhythm tasks were computed. In each single case the activation peaks of the visual and the auditory tasks were localized within the same anatomical regions. Cortical and subcortical activation peaks of the visual and the auditory tasks did not differ spatially more than a Euclidean distance of 8 and 4 mm, respectively. Moreover, when averaged across the visual and the auditory tasks, the common activation map revealed the same total number of peaks within similar brain regions. This indicates that the common maximum activations were unimodal distributions and not bimodal distributions as one would expect if the averaged activation maps were spatially different. For this reason, the following analysis was based on the averaged values of the activation maps of both sensory domains. Note that all activation peaks reported here are from Experiment 1 with the exception of the cerebellar activations, which are from Experiment 2.

To quantify the distribution of activation in both the visual ($Rv–Bv$) and the auditory ($Ra–Ba$) tasks, spherical regions of interest (ROI) were defined for the SMA, BS, the left (l) and the right (r) PMC, FO, BG, aIPS, dIPS, and CE. These ROIs where defined as spheres with a radius of 5 mm, centered on the local maxima of the summed activity of the visual ($Rv–Bv$) and the auditory ($Ra–Ba$) tasks. To allow repeated-measure ANOVAs with the factors ROI and Modality, Z values were then averaged within each ROI for each modality and subject (Bosch, in press).

To control for hemispheric differences, Z values were averaged within each hemisphere for ROIs located bilaterally (PMC, FO, BG, aIPS, dIPS, and CE). A two-way ANOVA with the two-level factor Modality (auditory, visual) and the two-level factor Hemisphere (left, right) indicated the Modality × Hemisphere interaction, and the main effects of Modality and Hemisphere were nonsignificant.

A second two-way ANOVA with the 2-level factor Modality (auditory, visual) and the 14-level factor ROI (SMA, lPMC, rPMC, lFO, rFO, lBG, rBG, laIPS, raIPS, ldIPS, rdIPS, BS, lCE, and rCE) indicated the Modality × ROI interaction, and the main effects of Modality were nonsignificant, but the main effect of ROI ($F_{(13,117)} = 2.83, P < 0.002$) was significant.

To ensure there were no effects of task modality, separate one-way ANOVAs with the factor Modality (auditory, visual) were performed for each of the ROIs. There were no significant differences between the auditory and the visual conditions except in the left cerebellum ($F_{(1,9)} = 7.66, P < 0.02$), the right cerebellum ($F_{(1,9)} = 9.71, P < 0.01$), and the brain stem ($F_{(1,9)} = 8.03, P < 0.02$). However, these differences were not significant after applying a Bonferroni correction for multiple statistical comparisons.

Thus, the overall activation pattern was not statistically different as a function of presentation modalities, thus ruling out effects of sensory modality on the cortical and basal ganglia activation. Additionally, the data indicated that effects of effector recruitment (right index finger) can be excluded because there was no asymmetric hemispheric activation.

DISCUSSION

The extensive activation pattern that comprised the whole premotor area can be attributed neither to effector recruitment, because only no-go trials were analyzed, nor to motoric preparation, because the baseline condition controlled for those basic preparatory effects that are typically generated in a go/no-go oddball paradigm. Thus, continuously comparing a short-term mnemonic representation of a temporal structure and a current perceptual input of identical repetitions initiated activations in brain areas that are generally involved in motor preparation and motor coordination. Single-cell studies in monkeys reveal that certain types of premotor cells show anticipatory discharge before movement (Tanji *et al.,* 1980). Those studies have shown substantial differences between MI and PMC, the former containing much higher proportions of neurons with movement-related activity, the latter revealing a higher concentration of neurons with set-related or preparatory activity (Alexander and Crutcher, 1990; Riehle and Requin, 1989; Wise and Mauritz,

FIG. 4. Brain activations during monitoring rhythms in Experiment 1 (1–5) and Experiment 2 (6 and 7). Multisubject average ($N = 10$) of significant activation during temporal processing relative to the perceptual baseline condition superimposed onto a T1-weighted individual brain. In all images voxels exceeding a threshold of $Z = 4$ are shown against a white matter segmentation. That means that the brain's white matter is separated from gray matter so that the cortical layers (the outermost 3 to 5 mm) are removed. Thus, for reasons of distinctness, the cortex is made "transparent," and cortical activations can be shown without anatomical distortion. Sagittal sections show the brain from the left side and coronal sections from the front. Activation was noted in both presentation modalities bilaterally in the medial premotor cortex (supplementary motor area, SMA), the lateral premotor cortex (PMC), the frontal operculum (FO), the anterior and the posterior intraparital sulcus (IPS), and the basal ganglia (striatum) (BG). Coronal (6 and 7, upper row) and sagittal (6 and 7, lower row) slices revealed cerebellar activation (CE) in the superior semilunar lobule. In the auditory condition, a small structure of the brain stem (BS) was activated too. Since the overall activation patterns in cortical and subcortical structures were not statistically different for auditory and visual rhythms, only the auditory condition is displayed in 1–5. 6 and 7 show cerebellar activity in the auditory and the visual condition, respectively.

1985). Although the separation of SMA and PMC proper is not clear-cut with regard to all cellular characteristics (Fuster, 1995), it can be distinguished by various criteria including their phylogenetic, cytoarchitectonic, and physiological features as well as their anatomical connections (Goldberg, 1985), thus predicting different functional roles in motor processing. As a premotor structure, the SMA is said to be involved in preparation for movement (*motor set*) (Alexander and Crutcher, 1990; Wise and Mauritz, 1985; Tanji and Shima, 1996; Lee *et al.,* 1999). In event-related brain potential studies, the so-called readiness potential (or *Bereitschaftspotential*) precedes deliberate actions and is believed to be of premotor origin (Praamstra *et al.,* 1996). However, single-cell studies showed that, during an instructed delay before movement, SMA units were activated if the movement was self-initiated but not if initiated in response to a visual stimulus, whereas the reverse was true for PMC units (Mushiake *et al.,* 1991). Lesions of SMA in the monkey induce deficits in self-initiation of limb movements, whereas lesions of PMC disrupt movements triggered by sensory cues (Passingham *et al.,* 1989; Thaler *et al.,* 1995; Halsband and Passingham, 1985). Behavioral deficits caused by premotor lesions in humans also support the idea that the SMA especially contributes to the organization and initiation of motor sequences based on internal, i.e., mnemonic representations (Laplane *et al.,* 1977). Imaging studies indicate that regional cerebral blood flow (rCBF) increases exclusively in premotor areas while subjects are programming a sequence of movements without actually executing it (Roland *et al.,* 1980). The combination of single-cell studies and lesion and imaging work supports the view that the SMA seems to be mainly involved in the internal generation of movement sequences, i.e., coordinated motor planning and initiation, whereas the lateral PMC or PMC proper seems to play a major role in externally referenced, sensory-guided motor behavior (Wise, 1985; Halsband *et al.,* 1994; Clower and Alexander, 1998). Early imaging studies led to the assumption that a queue of time-ordered motor commands is formed in the SMA before voluntary movements are executed by the MI (Tanji and Shima, 1996). Thus, altering the temporal complexity of movement preparation increases rCBF in the SMA significantly (Grafton *et al.,* 1992). These findings are in accordance with impairment in the ability to reproduce motoric rhythms from memory, i.e., to generate a motor sequence from memory that fits into a precise timing plan, following premotor lesions (Halsband *et al.,* 1993). Accordingly, tapping in synchrony with isosynchronous stimuli leads to an activation in the SMA relative to free tapping (Rao *et al.,* 1997). Against this background, the brain areas activated in the present study appear to reflect both the

mnemonic representation and the perceptually triggered timing function required by the rhythm-monitoring task. The medial premotor areas employed in the organization of motor sequences could reference current rhythmic input to a rhythm memory, whereas the lateral premotor activation might reflect a transformation process of the visual or auditory rhythm input into a motor sequence offering a reference structure for the mnemonic representation. Thus, both components of the rhythm comparison process might lead to the extensive premotor activations revealed by the present data.

As the PMC is important for motor action preparation (Evarts *et al.,* 1984), it is possible that the large premotor activation found in the present rhythm tasks is caused by the go/no-go oddball paradigm. This interpretation is consistent with the significant error rate differences between the rhythm tasks and the baseline tasks. However, performance was highly accurate in both the rhythm and the baseline conditions, and differences in the false alarm rate (errors in no-go trials) did not exceed 5%. Moreover, there were no reaction time differences between the rhythm tasks and the baseline tasks. This makes it very unlikely that the brain activations were caused by performance differences in the task. Moreover, premotor neurons contribute to differential go/no-go responses, as shown, for example, by a single-cell study in monkeys (Kalaska and Crammond, 1995) that examined the contribution of dorsal PMC to response selection. These results strongly suggest that the premotor correlate of the monkey's decision not to move, i.e., not to "go," is expressed by a *decrease* in mean premotor activity in no-go trials. As the probability of a no-go trial was 70% in the present study, it is unlikely that the *increase* in premotor activity was due to the paradigm employed.

Even though the tasks employed in the present study were designed to require the monitoring of temporal rhythms, one might claim that these tasks could also be performed by associating the stimulus location (in the visual rhythm task, Rv) or the stimulus pitch (in the auditory task, Ra) with the stimulus duration. A way to prevent this strategy would be to vary the other stimulus features while maintaining the temporal relationships constant. Further research is required to determine if such a stimulus feature association might have an effect on the brain activation pattern revealed in the present rhythm-monitoring tasks. However, if subjects memorized single durations by associating them with other stimulus features, they would not attend to the temporal order of the presented durations, but only to the single durations themselves. Thus, subjects would not be performing a *rhythm*-monitoring task, but a *duration*-monitoring task. Since the intention was to employ a task which requires the

perceptual analysis of temporal patterns, i.e., a timing task, this possibility does not have implications for the present results. It is important to point out that the mapping of stimulus location (in the visual rhythm task, Rv) or the stimulus pitch (in the auditory rhythm task, Ra) to duration never varied within a trial, so that a "go" was never indicated by changes in stimulus features other than the temporal duration itself.

As a second result, the frontal opercular cortex including Broca's area and its homologue was extensively activated by the rhythm analysis task. The functions ascribed to the frontal opercular cortex although traditionally restricted to speech and language are today supplemented by nonlinguistic functions, as indicated by patient studies (Grossman, 1980) as well as by imaging studies using PET. Thus, nonspeech tongue movements give a bilateral opercular response too, and actual and imagined finger movements activate the operculum contralateral to the corresponding hand (Fox *et al.,* 1988). The left frontal operculum is activated by perception of both linguistic and nonlinguistic rapid temporal patterns as revealed by PET studies using auditory presentation (Fiez *et al.,* 1995; Plathel *et al.,* 1997). These and other findings have led to the conclusion that syntagmatic disorders that sometimes follow Broca lesions might be a general sequencing deficit that can affect not only linguistic behavior, but each kind of motor output (Fuster, 1995). Thus, Broca's area has been described as a multifunctional organ adapted to the regulation of sequential activity in several different domains (Lieberman, 1991). Others have suggested that the left hemisphere dominance for language comes from the specialization of the left hemisphere for rapid temporal integration (Tallal *et al.,* 1993). Therefore, the activation of Broca's area and its homologue caused by rhythm monitoring in the present study might reflect sequencing processes, i.e., the analysis of units of specific durations ordered in time. This is in accordance with the finding that Broca's area is activated when subjects have to decide whether rhythms are isochronous or not (Plathel *et al.,* 1997).

The overall subcortical activation pattern revealed by the present data is in accordance with the notion that certain subcortical structures, such as the basal ganglia and the cerebellum, play an important role in time perception and motor timing (Jueptner *et al.,* 1995; Harrington *et al.,* 1998; Ivry, 1996, 1997). Interestingly, the more medial cerebellar areas that are assigned to movement coordination and planning (Allen *et al.,* 1997) were not activated by the present task, but rather the more lateral regions that are implicated in sensory integration and timing (Bower, 1996; Ivry *et al.,* 1988). These findings emphasize the timing functions of the cerebellum and are in accordance with our current findings that a rhythmic task causes activa-

tions not in the medial, but in the lateral regions of the cerebellum. Given that all subjects indicated that the visual condition was more difficult to perform, the finding that the visual task led to more activation in the cerebellum is consistent with earlier studies that found visual timing more difficult than auditory timing and that explained additional cerebellar activation by effortfulness of performance (Penhune *et al.,* 1998).

Finally, IPS activation has been reported in imaging studies involving functions related to visuospatial working memory such as mental imagery or mental transformation (Sugishita *et al.,* 1996; Bonda *et al.,* 1996). However, in the present study the IPS was activated during the auditory stimulation task, also, and even more extensively than in the visual condition. If the IPS is involved in the mnemonic retrieval of visuomotor sequences, as is the case when subjects have to press buttons in a particular order instead of randomly (Sakai *et al.,* 1998), then the IPS activation revealed by the present study using rhythm monitoring might indicate that this region processes sequential structure at a supramodal level. This interpretation is in line with the notion that this region of the inferior parietal cortex is involved in working memory and planning tasks irrespective of the sensory modality of the stimuli (Klingberg *et al.,* 1997).

Other imaging studies of timing using shorter intervals have shown that temporal orienting in relation to spatial orienting produces significantly more activation of the left IPS, the left ventral premotor cortex in the region of Broca's area (BA 6/44), and the left cerebellum (Coull and Nobre, 1998). The authors suggest that the preferential activation of the left hemisphere for temporal orienting may reflect fine discrimination of temporal intervals and attribute the lateralization effect to a specialization of the left hemisphere for rapid temporal integration (Merzenich *et al.,* 1996). A PET study investigating time estimation supplies further evidence for the cerebellum in time-critical perception (Jueptner *et al.,* 1995). The authors show that cerebellar timing functions are anatomically distinguished from a cerebellar activation elicited by motor execution, as indicated by increased rCBF in the superior cerebellar planes. In comparison to the areas activated in these imaging studies, our present results show the same brain structures to be active during timing. However, these tasks require timing processes only for short target durations and therefore might not lead to a brain response that reflects the cerebral timing network working to full capacity.

The present modulations indicate that the role of PMC extends beyond motor-related functions by supporting sequencing and timing activities independent of motor implementation. This finding is in accordance with the assumption that premotor areas are involved

in the representation of ordinal properties. Thus, single-cell studies in monkeys have found premotor cells firing just before and during the execution of a sequence of movements but not during execution of the component movements separately (Mushiake *et al.,* 1990), thus possibly reflecting a representation of abstracted sequential information (Fuster, 1995). Microstimulation in the SMA does not trigger brief single-muscle contractions, as is the case in the MI, but leads to complex (sequential) motor responses involving whole limbs, called *synergic movement* (Foerster, 1936; Fried *et al.,* 1991). SMA stimulation has also been reported to elicit rhythmical sequences of syllables (Penfield and Roberts, 1966). Together with these findings, our data suggest that tasks requiring rhythmic skills without any motoric implementation rely on those brain structures that normally serve motoric functions.

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