Interactions between auditory and dorsal premotor cortex during synchronization to musical rhythms

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When listening to music, we often spontaneously synchronize our body movements to a rhythm's beat (e.g. tapping our feet). The goals of this study were to determine how features of a rhythm such as metric structure, can facilitate motor responses, and to elucidate the neural correlates of these auditory–motor interactions using fMRI. Five variants of an isochronous rhythm were created by increasing the contrast in sound amplitude between accented and unaccented tones, progressively highlighting the rhythm's metric structure. Subjects tapped in synchrony to these rhythms, and as metric saliency increased across the five levels, louder tones evoked longer tap durations with concomitant increases in the BOLD response at auditory and dorsal premotor cortices. The functional connectivity between these regions was also modulated by the stimulus manipulation. These results show that metric organization, as manipulated via intensity accentuation, modulates motor behavior and neural responses in auditory and dorsal premotor cortex. Auditory–motor interactions may take place at these regions with the dorsal premotor cortex interfacing sensory cues with temporally organized movement.
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Introduction

Music can be a potent catalyst in stimulating timely movements. This phenomenon is commonly observed when we tap our feet or nod our heads to the beat of music. The ability to synchronize body movements to both familiar and novel music often occurs spontaneously and intuitively, even for those with no musical training (Drake et al., 2000; Large et al., 2002; Snyder and Krumhansl, 2001). More specifically, the phenomenon of tapping to the beat appears to be unique to auditory–motor interactions; visual cues are not as effective in facilitating accurate movement (Patel et al., 2005; Repp and Penel, 2004). Furthermore, the important role of auditory cues in influencing timed behavior is illustrated by studies involving subjects with movement disorders such as Parkinson's disease and stroke. Walking ability, as indexed by the speed and co-ordination of gait, and upper extremity arm function improve with training using auditory cues, as compared to rehabilitation protocols without auditory facilitation (McIntosh et al., 1997; Thaut et al., 1997; Whitall et al., 2000). These data lend support to the hypothesis that rhythmic auditory cues can influence motor behavior; however, little is known about the basic rhythmic features and neural mechanisms underlying this phenomenon. Thus, the purpose of this study is to examine specific rhythmic features that drive auditory–motor interactions, and to elucidate the neural basis of this behavior.

When we tap, dance, or march along with music, we are usually moving in time with the beat. A beat is the basic unit of measure indicating musical time, and is a perceived pulse inferred from a rhythm that occurs in equal temporal units (Lerdahl and Jackendoff, 1983). The regular occurrence of alternating strong and weak beats can be grouped together to form the percept of a meter (e.g. waltz or march time) (Handel, 1989). Meter can help organize a rhythm by parsing it into equal subdivisions or "measures" of temporal duration (Palmer and Krumhansl, 1990). Within a meter, a hierarchy of multiple beat levels can also be perceived (Drake et al., 2000; Parncutt, 1994) but the most perceptually salient level of beat sensation, the tactus, is the level at which most people choose to tap to the beat (Parncutt, 1994). We propose that perception of the metric structure and tactus facilitates movement synchronization to a rhythm and thus auditory–motor interactions.

Behavioral studies have suggested that there are several features of a rhythm that can contribute to metric and beat saliency. Melodic cues such as pitch can highlight important events in a rhythm, though not as effectively as a rhythm's temporal structure (Hannon et al., 2004; Pfordresher, 2003; Snyder and Krumhansl, 2001). Temporal structure, defined by the pattern of time intervals between notes, is an important feature that aids detection of the tactus by organizing musical events into equal time units (Essens and Povel, 1985; Povel, 1984; Povel and Essens, 1985). The ability to perceive the tactus

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from a musical rhythm is also aided by the fact that it is a regularly occurring cue. Such predictability can create an expectation for the likelihood of future temporal events even if the actual stimulus ceases (Cooper and Meyer, 1960; Large and Jones, 1999; Parncutt, 1994). Therefore, the recurring pattern of temporal expectations aids in solidifying the percept of meter and allows a listener to accurately anticipate and tap to the beat.

While pitch, temporal structure, and predictability are useful cues that highlight the meter and tactus, in this study we are interested in how a rhythm's accent structure can be an effective cue in facilitating movement synchronization. An accent is a point of beat intensification highlighted by the manipulation of physical properties of sound, such as intensity or duration (Lerdahl and Jackendoff, 1983). Intensity accents can bring attention to a rhythm's meter by emphasizing the relationship between individual beats (Drake, 1993). The presence of intensity accents at the level of the tactus improves rhythm reproduction. For example, Drake (1993) asked children, adult musicians and non-musicians to tap out simple and complex rhythms on a drum after hearing them once. Rhythms that had accents on important beats (i.e. the tactus) were reproduced correctly more often than those without accents, suggesting that accentuation enables a more accurate perception and encoding of rhythms. Accents may represent a perceptual cue to emphasize important events which aid the listener in organizing other rhythmic elements into their appropriate places.

The neural basis of entraining movement to a musical beat is little understood. Human lesion studies have shed some light on the neural correlates of auditory–motor interactions involved in both perception and production of auditory rhythms. These studies show that the temporal lobes play an important role in the discrimination of meter (Kester et al., 1991; Liegeois-Chauvel et al., 1998), tapping to the beat (Fries and Swihart, 1990; Wilson et al., 2002), and reproducing simple auditory rhythms from memory (Di Pietro et al., 2004; Penhune et al., 1999; Wilson et al., 2002). However, these studies have not converged on the same findings regarding the specific localization and function of the left versus right, and anterior versus posterior, temporal lobe. These discrepancies can in part be attributed to the fact that the type and extent of lesions were variable across studies, some encompassing cortical regions outside the temporal lobe.

Several neuroimaging studies have examined the neural correlates of auditory rhythm processing, including rhythm perception (Sakai et al., 1999), discrimination (Platel et al., 1997), and reproduction (Lewis et al., 2004; Penhune et al., 1998; Stephan et al., 2002). These studies, however, were not designed to specifically address the auditory–motor interactions involved in movement synchronization. Studies that ask subjects to synchronize finger tapping to a simple auditory rhythm commonly show activation of the primary sensorimotor area, ipsilateral cerebellum, premotor cortex, supplementary motor area, and superior temporal gyrus (Jancke et al., 2000; Mayville et al., 2002; Rao et al., 1997; Thaut, 2003). The cerebellum has been implicated in tasks requiring motor timing (Penhune et al., 1998; Spencer et al., 2003; Theoret et al., 2001). It has been suggested that both the premotor and supplementary motor areas are involved in sensorimotor integration, with the premotor cortex involved in the selection and/or production of the response, and the supplementary motor area involved in the organization of relevant sensory information (Kurata et al., 2000; Picard and Strick, 2001), such as the initiation of a sequence or sequence chunk during motor action (Kennerley et al., 2004). Muller et al.

(2000) has also suggested that the inferior somatosensory region could mediate a time evaluation process involved in the synchronization of a tap with a click. However recent studies have suggested that this region is more likely involved in tactile and kinaesthetic feedback processing during movement execution rather than timing feedback to the auditory cue (Pollok et al., 2003, 2004). Thus far, studies on rhythm processing have informed us that regions such as the cerebellum, premotor cortex, and supplementary motor area are involved in tapping in time to a salient auditory temporal pattern. However, one cannot distinguish the specific contributions of each region from one another nor can one conclude that these regions facilitate, or drive the auditory–motor interactions.

Two major goals of the present study are to answer the following questions: 1) How does manipulation of a rhythm's accent structure influence the ability to synchronize finger tapping movements? 2) What is the pattern of brain activity associated with the integration of an auditory cue that facilitates an appropriate motor response? We hypothesized that movement entrainment would be most affected when a rhythm's meter is most salient, and the least affected when listeners are unable to formulate a clear percept of meter. Furthermore, we predicted that as subjects synchronized their tapping to rhythms with an increasingly salient metric structure, brain regions driven by these auditory–motor interactions would also be modulated. To address this hypothesis, five parametric levels of metric saliency were created via progressively increasing the contrast in sound intensity between accented and unaccented notes. Critically, since temporal information (duration) about the stimulus is kept constant, our paradigm will allow us to draw specific conclusions about how a higher-order cognitive process, metric structure, can modulate motor responses.

Materials and methods

Subjects

Twelve healthy right-handed volunteers (6 females) with normal hearing participated in the study after giving informed written consent for a protocol approved by the Montreal Neurological Institute Research Ethics Review Board. One subject was subsequently excluded as a result of incomplete data. Subjects had no musical and/or voice training and ranged from 19 to 39 years of age ($M = 27$ years).

Stimuli and conditions

In this experiment, subjects imitated a series of six different auditory rhythms by tapping in synchrony on a computer mouse key with the index finger of the right hand. All rhythms were isochronous, that is, made up of twelve complex tones (440 Hz fundamental with 9 harmonics, 50 ms onset/offset ramp) of equal duration (300 ms) with a constant interstimulus interval (300 ms). This resulted in an intertap interval of 600 ms which is in the range of the most common rate of spontaneous tapping (Fraisse, 1982). Each trial contained the following events in sequential order: 750 ms of silence, 500 ms white noise warning sound, 1000 ms of silence, 7200 ms of stimulus presentation (where subjects listened and tapped in synchrony to all rhythms), and 90 ms of silence (Fig. 1). The isochronous rhythm was manipulated

parametrically for five levels such that the metric organization became increasingly salient. Intensity accents were placed on the first of every group of three tones, resulting in a triple or waltz time meter. Five levels were created, consisting of 0, 1, 2, 6, or 10 decibel (dB) attenuation between unaccented and accented tones. Pilot testing was conducted to select these levels; ranging from a level at which subjects could detect no difference between the accented and unaccented tones, to a level where there was a very noticeable difference. The sixth control condition contained the same number of accented and unaccented tones (10 dB attenuation) as in the parametric rhythms, but these accents were placed in an unpredictable or quasi-random manner. In this way, no schema of meter could be created to aid entrainment and therefore subjects would have no expectation of when the next beat would take place. All stimuli were presented at a weighted average sound intensity of 85 dB at sound pressure level (SPL) (as measured using a sound pressure meter in each left and right earphone), such that the total sound energy was equivalent for all six rhythm conditions. Thus all tones in the 0 dB condition were calibrated to and presented at 85 dB and the range of decibel levels for the other conditions was from 76.7 to 86.7 dB. These rhythms were presented binaurally through Siemens MR-compatible pneumatic sound transmission headphones using the software Media Control Functions (MCF Digivox, Montreal, Canada) on a PC computer.

Procedure

Prior to scanning, a baseline condition consisting of five trials of the 0 dB rhythm condition was performed as a warm-up. Baseline data from each participant helped establish the criterion for outlier or invalid responses for each individual's test conditions. During scanning subjects completed two runs, each of which included six test conditions and a silent baseline, for a total of seven conditions. Subjects were told that some tones would be louder/softer than others but that the task was to focus on synchronizing their tap responses to the tones as accurately as possible. With the exception of the silent baseline, each test condition was presented in blocks of 12 trials,

ensuring enough time for subjects to be fully entrained to the stimuli. Two silent trials of the same duration as the rhythm trials were interspersed between each test block. Test conditions were presented in a pseudo-random order within each run across all subjects and all conditions were performed with eyes closed. For all conditions, tap responses (key onset and offset times) were collected online.

fMRI acquisition

Scanning was performed on a 1.5 T Siemens Sonata imager. High resolution T1-weighted anatomical scans were collected for each subject (voxel size: $1 \times 1 \times 1$ mm^3, matrix size: 256×256). A total of 85 frames were obtained for each of two runs in the functional T2*-weighted gradient echo planar scans (12 frames per condition per run). Whole head interleaved scans ($n = 25$) were taken, oriented in a direction orthogonal to that of the Sylvian Fissure (TE = 50 ms, TR = 11790 ms, voxel size: $5 \times 5 \times 5$ mm^3, matrix size: $64 \times 64 \times 25$, FOV: 320 mm^2) (Fig. 1). A single-trial sparse-sampling design was used whereby scan acquisition occurred after each trial presentation, when the subject ceased to perform the task. Since the hemodynamic response is delayed, scan acquisition would thus coincide with neural activity associated with rhythm entrainment and not with the initial portion of the task when the entrainment process has yet to commence. Moreover, a long TR was used so that subjects would be able to hear the stimuli without the loud, rhythmical scanner noise that could interfere with the task, a potential confound present in some studies that have examined auditory rhythm processing using fMRI (Jancke et al., 2000; Lewis et al., 2004; Mayville et al., 2002; Rao et al., 1997). Furthermore, a single trial design avoids contamination of the blood-oxygenation level dependent (BOLD) response to the auditory stimuli with the BOLD response to the acquisition noise (Belin et al., 1999; Hall et al., 1999).

fMRI analyses

The first volume of each functional run was discarded. Images from each scan were then realigned with the third frame
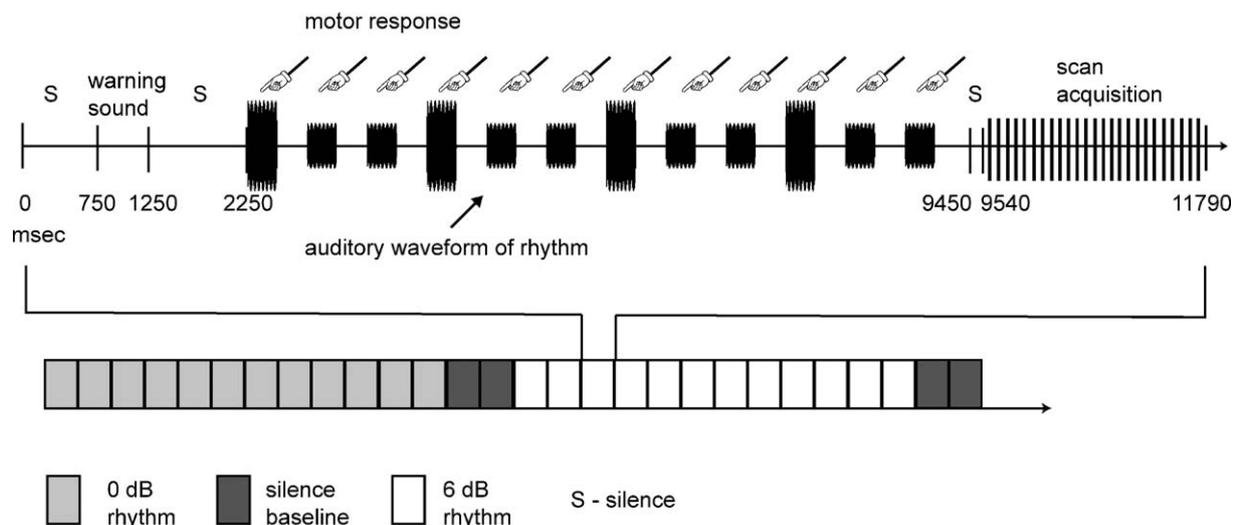

Fig. 1. Representation of the sparse sampling fMRI protocol. Pseudo-randomization of each blocked test condition, with two trials of silence interspersed between blocks. Subjects tapped in synchrony to each tone of the rhythm.

as reference, motion corrected using the AFNI software (Cox, 1996), and smoothed using a 12 mm full-width half-maximum (fwhm) isotropic Gaussian kernel. For each subject, the anatomical and functional volumes were transformed into standard stereotaxic space (Talairach and Tournoux, 1988) based on the MNI 305 template (Collins et al., 1994). Statistical analysis of fMRI data was based on a linear model performed using an in-house tool called fMRISTAT that involves a set of four MATLAB functions (Worsley et al., 2002; available at www.math.mcgill.ca/keith/fmristat). The general linear model $Y = X\beta + \varepsilon$ is an equation that expresses the response variable (BOLD signal) Y, in terms of a linear combination of the explanatory variable (stimulus) X, the parameter estimates (effects of interest) β, and the error term ε. Temporal drift is modeled as cubic splines and then removed since it can be confounded with the BOLD response. The first matlab function 'fmridesign' sets up the design matrix, where each column contains the explanatory variables and each row represents a scan. The next step 'fmrilm' fits the linear model with the fMRI time series, solving the parameter estimates β, in the least squares sense and yielding estimates of effects, standard errors, and t statistics for each contrast, for each run. An effect of interest is specified by a vector of contrast weights that give a weighted sum or compound of parameter estimates referred to as a contrast. To determine the basic neural network associated with simple finger tapping to an unaccented auditory cue, we performed the 0 dB minus silence contrast. To directly address changes in neural activity related to the five levels of accentuation, we performed a covariation analysis. This analysis examines the relationship between BOLD response and increasing accentuation across the five parametric conditions (0, 1, 2, 6, 10 dB), where each condition is assigned a value from 1 to 5, assuming a linear response in this variable. In this case the parameter estimates represent the covariation of the BOLD response with the linear measures 1 to 5. The t statistical map obtained for this analysis thus assesses whether the slope of the regression line at each voxel is significantly different from zero. The third MATLAB program 'multistat' combines runs together within subjects (using a fixed-effects model), and then results from each subject are combined to generate group statistical maps for each contrast of interest. A mixed effects model is used in averaging data across subjects; the data are smoothed with a fwhm Gaussian filter so that the ratio of the random-effects variance divided by the fixed-effects variance results in 100 degrees of freedom. Lastly, the program 'stat_summary' assesses the threshold for significance using the minimum given by a Bonferroni correction, random field theory, and the discrete local maximum to account for multiple comparisons (Worsley, 2005). The threshold for a significant peak was $t = 4.47$ at $P < 0.05$, using a whole brain search volume. Peaks below this threshold, but contralateral to significant regions are also reported since they have a high likelihood of representing real effects as opposed to false positives.

Functional connectivity allows us to determine how neural activity at a pre-chosen reference (or seed) voxel correlates with all other voxels in the brain across time. To determine how functional connectivity is modulated by the parametric stimulus manipulation, a variant of the psychophysiological interactions method proposed by Friston et al. (1997) (see www.math.mcgill.ca/keith/fmristat) was performed for regions identified from the covariation analysis. In modeling the stimulus modulated changes

in temporal coherence, the effects of the stimulus are accounted for such that correlations are between the voxels of interest and not with those of the stimulus already identified from the covariation analysis. Thus in the general linear model, an interaction product between the stimulus (X) and reference voxel value (R) is added as a regressor variable at each time point for every voxel and is solved for: $Y_{ij} = X_i\beta_{1j} + R_i\beta_{2j} + X_iR_i\beta_{3j} + \varepsilon$, where Y_{ij} is the voxel value at each frame i, for each voxel j. Slice timing correction is also implemented and the voxel values at each frame are extracted from native space. The effect, standard error, and t statistic are then estimated using fMRISTAT as described previously. Positive t statistics show voxels whose temporal correlation with the reference voxel is increased as a function of stimulus salience and vice versa for the negative t statistics. Since we had an *a priori* hypothesis concerning the regions that would demonstrate stimulus-modulated functional connectivity, other regions that were also identified from this analysis are not reported, and the significance threshold of $t = 2.64$ at $P < 0.005$ uncorrected was used.

Results

Behavioral data

To assess subjects' response to the different levels of rhythmic accentuation, the dependent variable used was the tap duration, the reproduction of the interval between tone onset to tone offset. Tap duration was calculated for each tap subjects made, and averaged across the accented and unaccented elements for each condition. Individual subjects' data were filtered to exclude outliers or invalid responses based on each person's baseline performance data, following the procedure described by Penhune et al. (1998). Fig. 2 shows six graphs representing the six conditions, and in each graph, the tap durations corresponding to each tone of the rhythm, averaged across all subjects. Inspection of these raw data showed that subjects appear to entrain to the rhythms from tone 4 onwards. Thus behavioral performance was analyzed using the valid responses excluding the first three tap responses. The percentage of valid responses did not differ (approx. 98%) across conditions (One-way repeated measures ANOVA, $F(5, 50) = 0.83$, $P > 0.5$). Tap duration was used to assess the relationship of the averaged accented and unaccented tones across the parametric conditions. A significant linear correlation was demonstrated, such that as saliency of the metric structure increased across the five parametric conditions, tap durations of accented tones also increased ($r = 0.99$, $t = 12.12$, $P < 0.005$); this trend was not present for the tap durations of unaccented tones ($r = -0.73$, $t = -1.84$, $P = 0.16$) (Fig. 3). Planned comparisons verified that the accented and unaccented tones in the 10 dB condition differ from each other ($F(1,10) = 14.91$, $P < 0.005$) where as those in the random condition did not ($F(1,10) = 0.70$, $P = 0.42$).

To summarize, reproduction of the tap duration was relatively lengthened for those tones that were accented. This effect of intensity accentuation became more pronounced as the intensity cues signaling the metric structure became more salient across the 0 to dB conditions. The linearity of the response validated our choice of   dB differences as corresponding roughly to perceptually equal increments. In
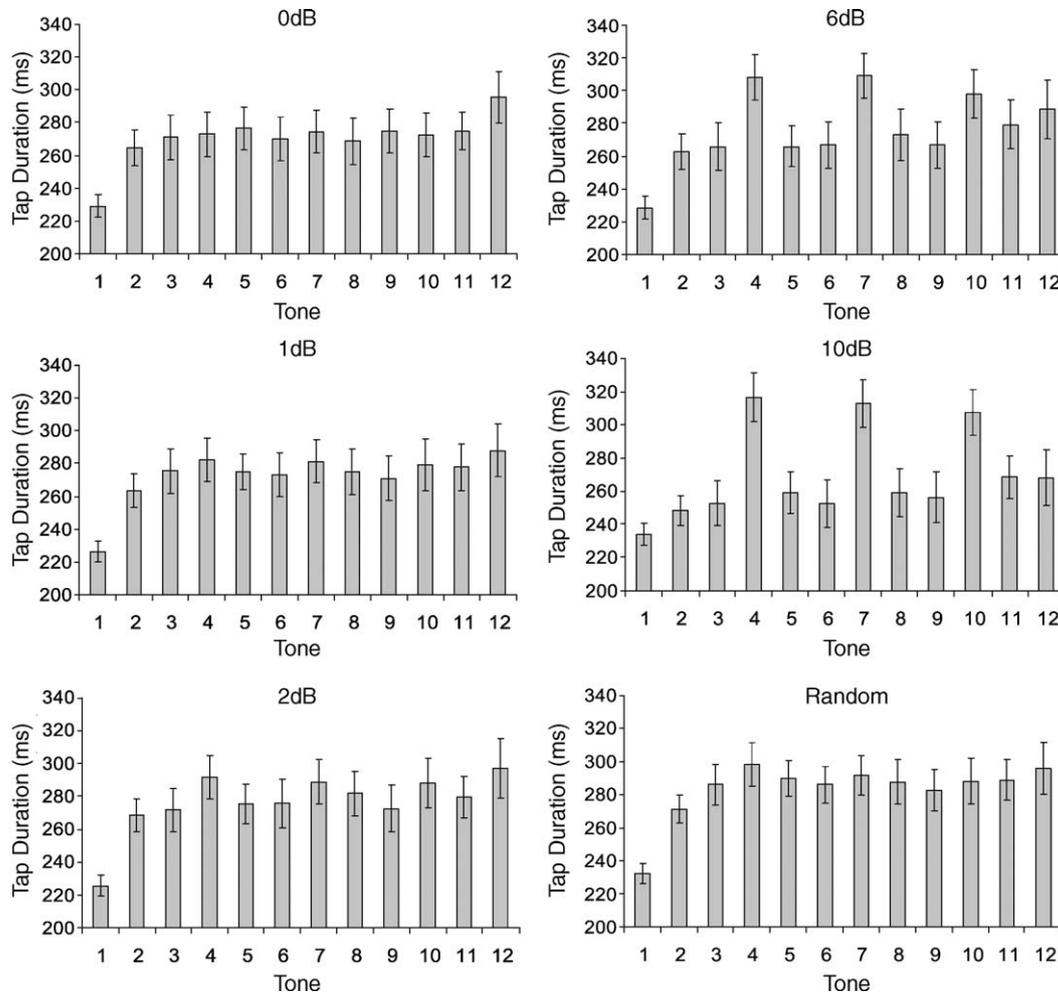
Fig. 2. Raw data for tap duration, for each tone in the rhythm, averaged across subjects. Data reported as means ± SE. The effect of accentuation on metric saliency becomes more pronounced in going from the 0 to 10 dB conditions; louder tones are reproduced as longer in duration. No effect of accentuation is present in the random condition. Steady entrainment to the rhythms also appears to take place only after the first three taps.

addition, metric structure appeared to influence cue saliency because accented elements in the random condition were not lengthened compared to the unaccented elements.
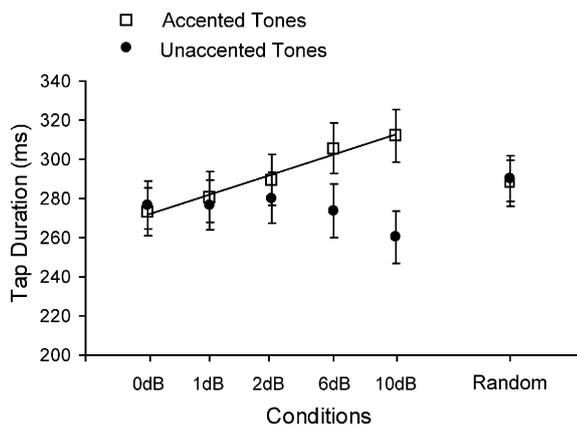

Fig. 3. Effect of accent structure across rhythm conditions. Data are reported as means ± SE. A significant linear trend exists ($P < 0.005$) for tap duration of accented tones across parametric conditions. Louder tones are lengthened in reproduction as a function of increasing metric saliency.

fMRI data

Subtraction analysis

A subtraction of the 0 dB versus the silent condition showed brain regions involved in the synchronization of a simple tapping response to isochronous rhythms without effects of accentuation. These regions are bilateral posterior superior temporal gyrus (STG), left primary motor cortex, left thalamus, and right cerebellum lobule V (as determined from the atlas of Schmahmann et al. (2000)) (Table 1).

Covariation analysis

The results of the behavioral data showed a significant linear correlation between increasing metric saliency and tap duration; thus to reveal brain regions that covaried as a function of metric saliency we performed a parametric analysis with 5 levels, corresponding to 0 dB, 1 dB, 2 dB, 6 dB, and 10 dB. The only regions found to covary with metric saliency were the left planum temporale, as determined by anatomical probability maps (Westbury et al., 1999), the right posterior STG, and bilateral dorsal premotor cortex (dPMC) as defined by the criterion of Picard and Strick (2001) (Table 2; Fig. 4). The percent BOLD signal change across the five levels relative to the silent baseline was then

Table 1
0 dB−silence: basic network for finger tapping

Region of peak	BA	x	y	z	t
R STG	22/42	58	−16	8	6.69
L STG	22/42	−62	−24	10	5.37
L STG	22/42	−68	−24	12	5.23
L STG	22	−56	−8	2	4.90
L thalamus		−18	−6	20	6.59
R cerebellum (lobule V)		20	−50	−24	5.79
L primary motor cortex	4	−52	−8	50	4.97

Peaks of increased activity when tapping in synchrony with an isochronous auditory rhythm (no accents present). The stereotaxic coordinates of peak activations are given according to Talairach space (Talairach and Tournoux, 1988), along with peak t values ($P < 0.05$, corrected). L, left; R, right; STG, superior temporal gyrus; BA, Brodmann area.

extracted in each of these regions. BOLD signal in these bilateral secondary auditory and dorsal premotor areas was found to respond in a significant positive linear manner to the parametric variation in the behavioral stimulus.

Stimulus-modulated functional connectivity analysis

Since the covariation analysis established that both posterior STG and dPMC covaried with the parametric stimulus manipulation, a functional connectivity analysis was performed to assess how temporal correlations between these two regions might be modulated by the stimulus. The voxels of the left and right dPMC identified from the covariation analysis were each taken as reference seed voxels to look for stimulus-modulated correlations with any of the pre-identified posterior STG voxels. An interaction between the stimulus and connectivity in the left dPMC was found in bilateral dPMC and left Heschl's gyrus as determined by anatomical probability maps (Penhune et al., 1996) (Fig. 5; Table 3). Similarly, stimulus modulated connectivity in the right dPMC was found to occur with bilateral dPMC and right posterior STG (Fig. 5; Table 3).

Discussion

Summary of findings

In this study we parametrically manipulated saliency of accentuation, keeping duration of the elements constant, thus allowing us to identify brain regions that are specifically modulated by metric structure. We show that the metric structure of a rhythm is an effective cue in driving motor behavior. As the metric saliency of the rhythms increased, beats that were louder were reproduced as longer in tap duration, an effect not seen when the pattern of accentuation had no metric structure. Activity in posterior STG and dPMC covaried with the stimulus variation, and the functional connectivity between these two regions was also modulated by it. These findings suggest the involvement of posterior STG and dPMC in auditory–motor interactions.

Behavioral results

Our results showed that tapping with an isochronous auditory cue was modulated as a function of a rhythm's accent structure. Previous studies have also shown that louder sounds (Fraisse,

1982) and force-accentuated taps (Billon et al., 1996; Semjen and Garcia-Colera, 1986) are perceived and reproduced as relatively lengthened. Importantly, the results of this study also show that tap duration for all elements did not change in the random condition despite the presence of accentuation. In a closed system, if input stimulus timing information is the same, then the output should be no different; the effect of sound intensity should have no influence on the timing of executed taps. Instead, these findings suggest the importance of top-down processes; the perception of a waltz or triple meter as highlighted by accentuation modifies the timing of taps. Performance (percent correct) was the same for all rhythm conditions, indicating that any differences in the pattern of brain activity are not due to the level of sequence difficulty but attributable to changes in the metric structure of the stimuli. These behavioral findings therefore validate the task and permit us to interpret the imaging findings in relation to metric processing.

Basic network for finger tapping

Tapping in synchrony with an isochronous auditory rhythm elicited neural activity in posterior STG, primary motor cortex, thalamus, and cerebellum lobule V. These regions are consistent with those observed in previous studies of isochronous finger tapping with an auditory cue (Jancke et al., 2000; Rao et al., 1997; Thaut, 2003). However, we did not find dPMC activity related to this task, nor was this area recruited in the studies by Jancke et al. (2000) and Rao et al. (1997); this is likely due to the comparable nature of the stimuli across these studies. The result of this basic subtraction suggests that tapping to a simple isochronous rhythm with auditory cues does not tease out activity in dPMC. Interestingly, Lutz et al. (2000) have also demonstrated for the visual domain, that the dPMC is only recruited when tapping to irregular as opposed to isochronous cues, suggesting that activity in this region can be elicited when the neural system mediating sensorimotor timing is taxed.

Effect of accentuation on basic network for finger tapping

Though the conventional subtraction approach may be adequate in identifying regions of interest pertaining to a cognitive task, some fundamental disadvantages are that it assumes linearity of all brain–behavior relationships, discounting possible interactions, and requires the selection of an appropriate baseline condition (Friston et al., 1996; Jennings et al., 1997; Newman et al., 2001;

Table 2
Covariation results

Region of peak	BA	x	y	z	t	r	t_r
L posterior STG	42	−58	−34	18	4.5	0.86	2.92*
R posterior STG	22	64	−36	8	3.8	0.89	3.45*
R dPMC	6	18	10	68	4.6	0.88	3.25*
R dPMC	6	24	10	58	4.0	0.45	0.87
L dPMC	6	−24	10	58	3.4	0.99	17.15*

Regions of BOLD signal covariation with the parametric rhythm conditions. The stereotaxic coordinates of peak activations are given according to Talairach space (Talairach and Tournoux, 1988), along with peak t values ($P < 0.05$, corrected). Correlations (r) are also reported along with the significance of the correlation (t_r), *$P < 0.05$. L, left; R, right; STG, superior temporal gyrus; dPMC, dorsal premotor cortex; BA, Brodmann area.
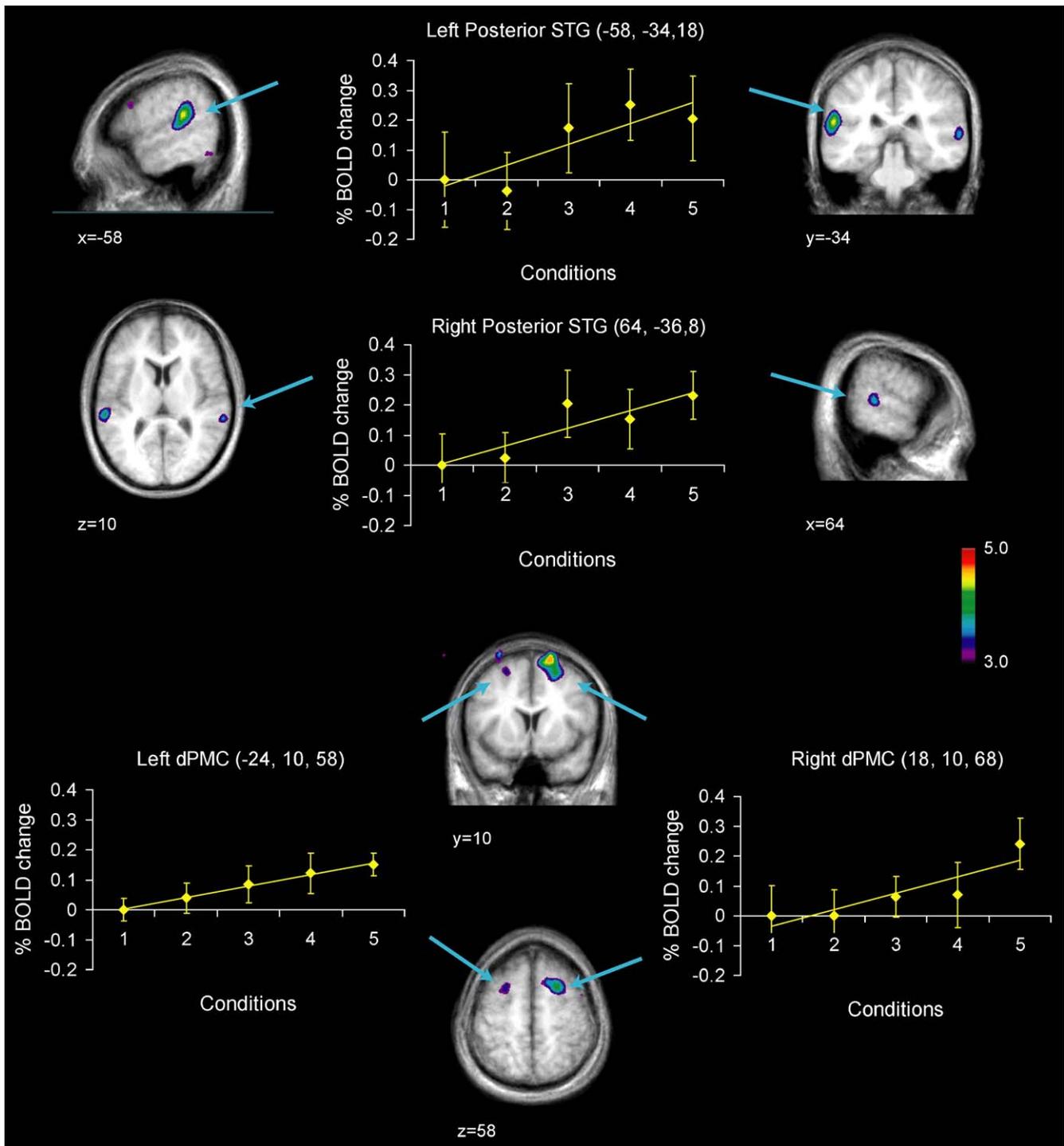
Fig. 4. fMRI covariation results. Conditions 1 through 5 on the x axis of graphs represent stimuli conditions 0 dB through 10 dB respectively. The percent BOLD signal changes (plotted relative to condition 1) in posterior STG and dPMC demonstrate a positive linear modulation of activity across the parametric variation in metric saliency. Colour bar represents t values.

Sidtis et al., 1999). Thus, the method we took in identifying regions specific for auditory–motor interactions was to look for areas whose activity covaried with the stimulus manipulation. This approach allows one to directly couple variations in the BOLD response to the manipulation in question. In this experiment, only the posterior STG and dPMC were responsive to the parametric manipulation; the subtraction method being insensitive in detecting

these subtle, yet important changes in brain activity (see Paus et al. (1996) for discussion concerning subtraction versus covariation approaches).

The stimulus covariation and voxel of interest analyses revealed greater involvement of bilateral secondary auditory regions as saliency of the metric structure increased. Both peaks were situated in posterior STG with the left auditory peak localized to the region
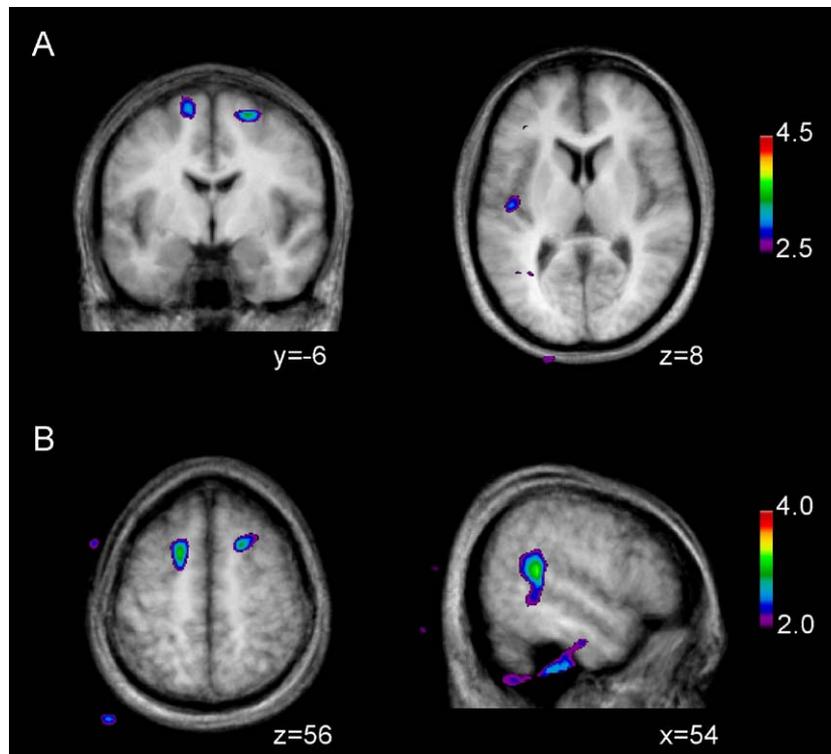
Fig. 5. Functional connectivity results. (A) Brain regions whose functionally connectivity with the left dPMC seed voxel are modulated by the stimulus; these are bilateral dPMC (in coronal view) and left Heschl's gyrus (in horizontal view). (B) Brain regions whose functionally connectivity with the right dPMC seed voxel are modulated by the stimulus; these are bilateral dPMC (in horizontal view) and right posterior STG (in sagittal view). Colour bar represents t values.

of the planum temporale (Westbury et al., 1999). One model of auditory processing proposes that these regions may be sensitive to time-varying spectral changes, or auditory pattern processing (Griffiths and Warren, 2002; Zatorre and Belin, 2005). Though the total spectral energy was equivalent for each rhythm, the distribution of this energy was manipulated to create a specific auditory temporal pattern that progressively highlighted its metric structure. Activity in these posterior auditory regions may therefore be related to the detection of the emerging pattern of metric saliency. Moreover, Hickok et al. (2003) have shown that these areas demonstrate both motor and auditory response properties to speech and musical stimuli, supporting the hypothesis that this region is involved in auditory–motor interactions regardless of domain specificity (Hickok and Poeppel, 2004). This view has been incorporated into a similar model for auditory–motor interactions proposed by Warren et al. (2005) who suggest that

Table 3
Stimulus-modulated functional connectivity

Reference seed voxel	Correlated region	x	y	z	t
L dPMC (−24, 10, 58)	L dPMC	−16	0	68	4.11
	R dPMC	22	−6	64	3.44
	L HG	−46	−16	8	3.05
R dPMC (18, 10, 68)	L dPMC	−18	8	58	3.07
	R dPMC	20	12	58	3.00
	R posterior STG	54	−42	16	3.27

The stereotaxic coordinates of peak activations are given according to Talairach space (Talairach and Tournoux, 1988), along with peak t values ($P < 0.005$, uncorrected). L, left; R, right; dPMC, dorsal premotor cortex; HG, Heschl's gyrus; STG, superior temporal gyrus.

transformations of auditory information to motor programs may take place via the dorsal auditory pathway, connecting regions in the posterior superior temporal plane with prefrontal, premotor and motor cortices.

As metric saliency increased across the rhythms we hypothesized that the degree of interaction between auditory and motor regions would also increase, since more information about the stimulus could be influencing behavior. This behavioral change was associated with increased percent BOLD signal change in bilateral dPMC. We propose that dPMC has a role in auditory–motor interactions while under the influence of higher order top-down processes. Neurons in monkey dPMC are responsive to auditory tones signaling distal forelimb movements (Kurata and Tanji, 1986; Weinrich and Wise, 1982). Furthermore, literature in monkey and human subjects demonstrates the role of dPMC in the association of a sensory cue with a motor response, or conditional motor association. (Halsband and Freund, 1990; Kurata et al., 2000; Petrides, 1986; Sugiura et al., 2001). In these studies, the dPMC is involved in processing the association of one auditory cue with one motor action. Our study used a stream of auditory cues, and dPMC showed greater activity as the metric saliency of those cues increased. This suggests that dPMC may have a more general role in integrating auditory information with a motor response, and/or selecting movements in the appropriate context and timing (Davare et al., 2006).

The covariation analysis revealed the involvement of posterior STG and dPMC in auditory–motor interactions since activity in these two regions covaried with the stimulus manipulation. Evidence for their association was also demonstrated through the functional connectivity analysis which

showed that the stimulus manipulation modulated the voxel-based temporal correlations between these regions. The existence of direct anatomical connections between posterior STG and dPMC in non-human primates (Luppino et al., 2001; Petrides and Pandya, 1988; Seltzer and Pandya, 1989) could be a route supporting this type of auditory–motor interaction. From the functional connectivity results, both seed voxels in the left and right dPMC are coupled to their contralateral site, as well as to an ipsilateral auditory region. Thus, several possible mechanisms for auditory–motor associations could be posited and studied in future experiments. For example, information from posterior STG may be processed serially, feeding forward to (and feeding back from) dPMC. On the other hand, if dPMC possesses auditory response properties, analogous to the motor response properties of the posterior temporal plane (Hickok et al., 2003), then both regions could respond to auditory cues in a parallel manner.

Lastly, one cannot exclude the possibility that other brain regions could be involved in auditory–motor interactions. Non-human primate studies have shown that direct anatomical connections exist between posterior auditory regions and ventral premotor cortex (vPMC) (Seltzer and Pandya, 1989) and insula (Mesulam and Mufson, 1982, 1985; Mufson and Mesulam, 1982; Pandya, 1995). Since the insula, vPMC, and dPMC all share direct connections with each other (Barbas and Pandya, 1987; Dum and Strick, 2005; Mesulam and Mufson, 1982, 1985; Mufson and Mesulam, 1982), it is plausible that the vPMC and insula could also participate in auditory–motor interactions. The polymodal vPMC has been shown to respond to auditory stimuli (Bremmer et al., 2001; Graziano and Gandhi, 2000; Graziano et al., 1999; Schubotz et al., 2003) while the multimodal insula, known to be involved in the temporal integration of sensory stimuli (Bushara et al., 2001, 2003; Calvert, 2001) and the detection of stimulus onset synchrony (Lux et al., 2003), can also orchestrate auditory–motor interactions between posterior auditory regions and dPMC, either directly or via vPMC.

Conclusions

The results of this study demonstrate that as metric saliency increased, behavioral performance as measured by tap duration, and functionally coupled neural activity in posterior STG and dPMC, were modulated during these auditory–motor interactions. We suggest that the posterior STG may encode the pattern of the metric rhythms, while activity in the dPMC may represent the integration of this auditory information with temporally organized motor actions. These findings shed light on the phenomenon of how we tap to the beat of music and also point to a specific role of the dPMC in sensorimotor timing.

Acknowledgments

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