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Neural correlates of the complexity of rhythmic finger tapping

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Abstract

Using functional magnetic resonance imaging (fMRI), we studied the neural correlates of the complexity of rhythmic finger tapping. Our experiments measured the brain activity of 13 subjects performing rhythmic tapping on a response box with multistable rhythms of 1 to 5 different interresponse intervals. From the button press response times, we constructed phase portraits where we identified the number of clusters of periodic points in a rhythm that corresponded to the number of different beats of the rhythm performed. We then constructed a statistical model for correlation analysis involving the following behavioral parameters: rate of tapping and number of beats in a rhythm. The tapping rate correlated with the brain activity in the ipsilateral pre/postcentral gyrus, and the number of beats (complexity) was correlated with activations in the primary motor cortex, supplementary motor area, basal ganglia, thalamus, and cerebellum. A region of interest (ROI) average analysis showed that the complexity of a rhythm had a differential correlation with the activity in these regions. The cerebellum and the thalamus showed increasing activity, and the basal ganglia showed decreasing activity with complexity of a rhythm. These results identify the areas involved in a rhythm generation and the modulation of brain activity with the complexity.
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Introduction

Rhythm refers to a patterned sequence of sensory or motor events, such as tones, drumrolls, flashes of lights, and steps in dances, which we commonly encounter in our everyday life. Rhythm is about the structure in time of event occurrences. Humans are able to generate and maintain self-paced rhythmic movements (e.g., finger tapping), and they can synchronize these movements with an external rhythmic cue. However, the study of the brain regions associated with these functions has only recently begun.

There have been pioneering theoretical and experimental studies in human sensory coordination and transitions in behavior (Haken, 1996; Kelso, 1995). The ability to both generate and maintain complex rhythms has been found to be closely dependent on the frequency of movement. For example, phase transitions have been observed in multifrequency coordination when the system is driven through different coordination states by an external metronome (DeGuzman, et al., 1991; Haken et al., 1996). These studies on the temporal organization of hand movements have shown that the rhythms with low-order ratios of interresponse time intervals are easier to perform and easier to maintain. Complex rhythm patterns, however, may involve transitions in coordination between different frequency states, usually between states of lower order frequency ratios (e.g., 1/1, 1/2) and rarely between lower to higher order frequency ratios (e.g., 1/3, 2/3). Other studies have reported brain areas associated with irregular versus regular movement patterns (Lutz et al., 2000), integer versus noninteger frequency ratio rhythms (Sakai et. al., 1999), and rhythm learning (Ramnani and Passingham, 2001). However, both the neural mechanism involved and the effect of the complexity of a self-paced rhythm in the brain have not been well understood.

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In the present study, we propose that both the rate of tapping and the number of different inter response intervals (beats) define the behavioral complexity of rhythms. We used functional magnetic resonance imaging (fMRI) to identify the brain regions of relative activations correlated with the complexity of self-paced multistable rhythms and the modulation of brain activity with complexity. This study differentiates the brain areas involved in the initiation and execution of motor and perceptual processes from the more coordinative movements requiring a precise timing mechanism.

Materials and methods

Subjects

Eighteen subjects participated in this study, but, because of either poor performance or excessive head movement, only 13 subjects (6 males and 7 females), aged between 23 to 37, were included in the analysis. All the subjects were right handed and neurologically normal. Informed consent was collected from each subject prior to the experiment, and the study was approved by the Emory University Institutional Review Board.

Experimental task

Experimental tasks consisted of two functional sessions of rhythmic finger tapping. Each session was 320 s long with 20 s of rest at the beginning and at the end of each session. Before the actual experiment, each subject was asked to think of rhythms of one to five beats and to try those rhythms in our computer setup. While in the scanner, subjects tapped their right index finger on a response box with stable rhythms of one to five beats. They were told to start tapping with a simple rhythm of one beat initially and then with more complex rhythms using higher numbers of beats up to a maximum of five. As feedback, a blue box was displayed briefly each time the subject pressed the button. After 20 consecutive trials of a stable rhythm, subjects were prompted with a visual cue to change the pattern of tapping. Subjects could perform any rhythm, but they had to keep it stable for 20 taps. Stability was defined as a repetition of the previous cycle of taps accurate to within 20 ms. An online computer algorithm measured the beat-to-beat fluctuations of tapping rate as well as the complexity (see below). When the rhythm was determined to be stable within 20 ms for 20 taps, the computer prompted the subject to change to a different rhythm. Subjects did not need to keep track of the already produced rhythms. In this way, we minimized the possible time-dependent load on memory resources in keeping track of rhythms. Response times (times for button press) were recorded.

Image acquisition

All imaging was done on a 1.5 T Philips Intera scanner. After acquisition of a high-resolution T1-weighted anatomical image, two whole-brain functional runs were performed with 180 scans in each run (echo-planar imaging, gradient recalled echo; TR = 2000 ms; TE = 40 ms; flip angle = 90°; 64 × 64 matrix, 24 axial slices each of thickness 5 mm acquired parallel to anterior-posterior commissural line) for the measurement of the blood oxygenation level-dependent (BOLD) effect (Kong et al., 1992; Ogawa et al., 1992). Head movement was minimized by padding and restraints.

Behavioral parameters: Covariates for statistical model

A rhythm, in general, refers to a patterned sequence of events, which can be completely characterized by the number of events in sequence and the time intervals between those events. We used the instantaneous rate (inverse of time intervals), $f(t)$, and the number of different time intervals, $D(t)$ as the characteristic quantities defining a tapping rhythm. From the response times, we calculated the time intervals Δt between button presses. The reciprocal of the inter response intervals represented the number of taps per second, or the instantaneous frequency (f). The complexity of a rhythm was determined by plotting successive tapping intervals against each other in a phase portrait. Phase portraits, in which Δt_{i+1} was plotted against Δt_i, distinguish different rhythms by how points cluster around a line of slope 1. For example, clusters that lie on the diagonal, represent simple rhythms of one frequency. The next level of complexity contains two time intervals before repeating, and is therefore visualized as two clusters on either side of the diagonal. Formally, we determined the number of interresponse intervals or beats (D) in a rhythm where $\Delta t_{n+1} = g^D (\Delta t_n) \cong \Delta t_n$, meaning that D number of iterations will bring the system to the same cluster of points. The complexity, D, can be expressed as a time-varying function by factoring it into rest plus five different levels:

$$D(t) = \sum_{j=0}^{5} j D_j(t),$$

where $D_0(t)$, $D_1(t)$, $D_2(t)$, $D_3(t)$, $D_4(t)$, and $D_5(t)$ represent the presence (1) or absence (0) of the number of beats (0–5) performed at time t. Here, the level of complexity or the number of beats performed for rest period is 0. In this manner, both the instantaneous frequency, $f(t)$, and the complexity, $D(t)$, fully defined the behavioral complexity of rhythmic finger tapping as a function of time.

Analysis of fMRI images

The data were analyzed using Statistical Parametric Mapping (SPM99; Wellcome Department of Cognitive
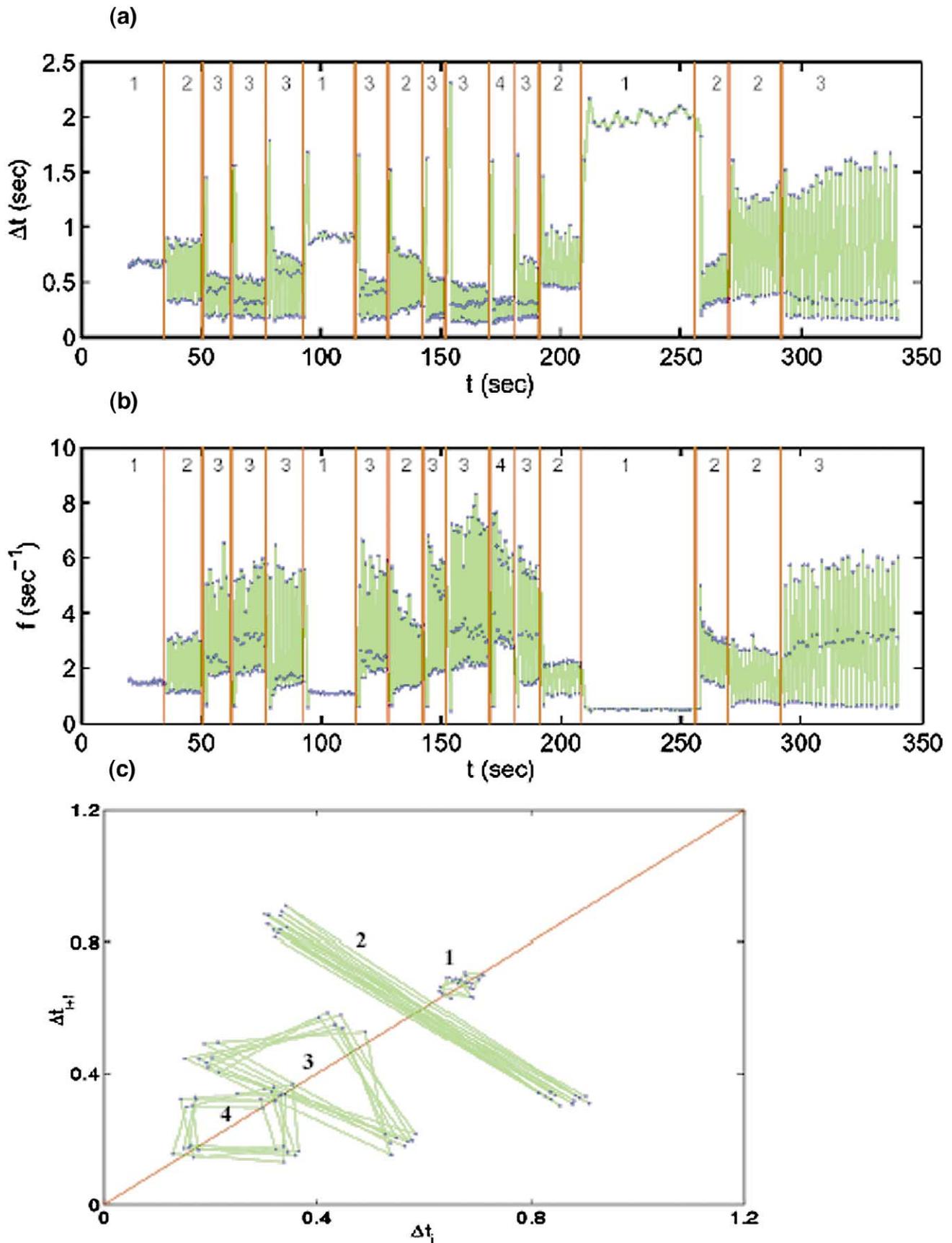
Fig. 1. Behavioral response to rhythmic finger tapping. (a) The interresponse interval (Δt) versus the reference time (t). (b) The instantaneous frequency of tapping (f) versus time (t). The vertical red lines in (a) and (b) represent the times at which visual cues were presented to change the patterns. The numbers 1, 2, 3, etc. marked for different blocks in (a) and (b) represent D, the number of beats performed. (c) Phase portrait of Δt for the first three blocks marked 1, 2, 3, and the block marked 4 in (a) and (b).
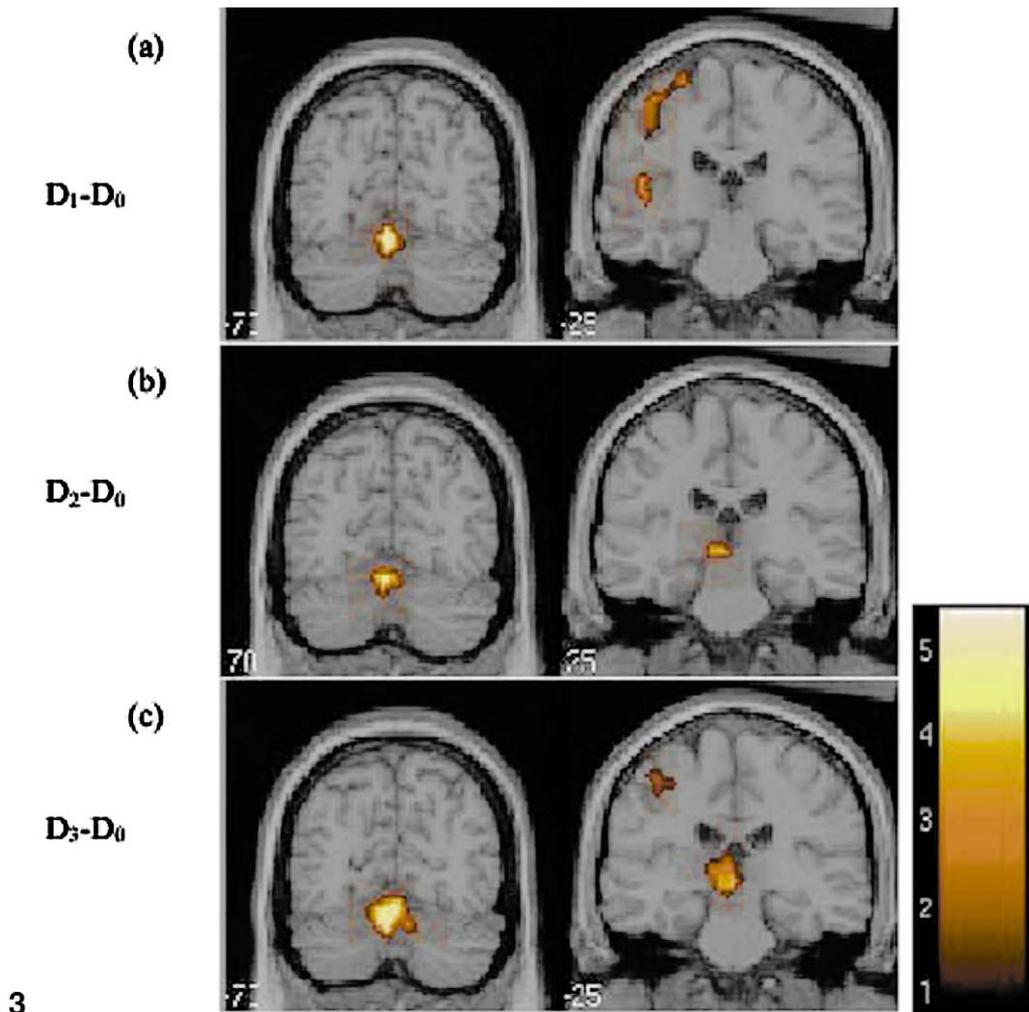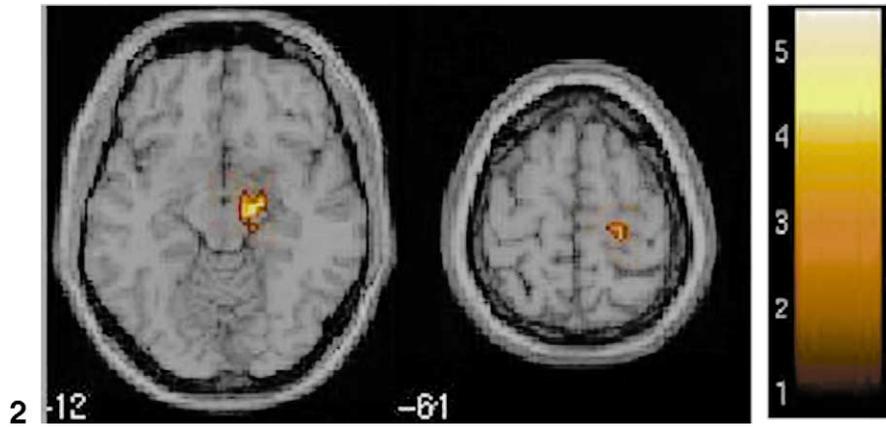
Fig. 2. Brain activity correlated with increased rate of finger tapping. After the main effect of tap-versus-rest is accounted for, activations in the right midbrain and ipsilateral pre/postcentral gyrus scaled with tapping rate. The color scale indicates the *t* score with 12 degrees of freedom.

Fig. 3. Brain activity correlated with increasing rhythm complexity. (a) D_1-D_0 contrast, activations in the cerebellar vermis, left pre/postcentral gyrus and left transverse temporal gyrus. (b) D_2-D_0, activations in the cerebellar vermis and left thalamus. (c) D_3-D_0, activations in the cerebellar vermis, left thalamus, and left precentral gyrus. There was an increasing cerebellar and thalamic activity with level of rthythm complexity.

Neurology, London, UK) (Friston et al., 1995). Motion correction to the first functional scan was performed within subject using a six-parameter rigid-body transformation. All the 13 subjects included in this analysis had less than 4 mm of translation in all directions and less than 1.5° of rotation about the three axes. The mean of the motion-corrected images was then coregistered to the individual's 24-slice structural image using a 12-parameter affine transformation. The images were then spatially normalized to the Montreal Neurological Institute (MNI) template (Talairach and Tournoux, 1988) by applying a 12-parameter affine transformation, followed by a nonlinear warping using basis functions (Ashburner and Friston, 1999). Images were subsequently smoothed with an 8-mm isotropic Gaussian kernel and band-pass-filtered in the temporal domain. A random-effects, model-based, statistical analysis was performed with SPM99 (Friston et al., 1995, 1999).

First, the correlation analysis was performed with two general linear models, tap-versus-rest and the model involving f and D covariates for each subject. Here f and D were resampled from $f(t)$ and $D(t)$ according to the scan repetition times at 0, TR, 2TR and so on. With f and D, we constructed the following statistical model:

$$\mathbf{Y} = \mathbf{X}\beta + \varepsilon,$$

where $\mathbf{X} = [a \, f \, D_0 \, D_1 \, D_2 \, D_3 \, D_4 \, D_5, \, D_5]$, $\beta = [I \, \beta_f \, \beta_0 \, \beta_1 \, \beta_2 \, \beta_3 \, \beta_4 \, \beta_5]^T$, $\varepsilon = N(0, \sigma^2)$, and a was a constant and was equivalent to the implicit baseline of activity. Thus,

$$\beta = (\mathbf{X}^{*T}\mathbf{X}^*)^{-1}\mathbf{X}^{*T}K\mathbf{Y},$$

where $\mathbf{X}^* = K\mathbf{X}$, and K was a matrix for the hemodynamic response function, which was constructed with a gamma function:

$$\gamma(t) = t^b exp(-t/c),$$

where $b = 8.6$ and $c = 0.547$ (Cohen, 1997).

Individual contrast images were created by correlating the brain response with the aforementioned covariates for each subject. Global differences among subjects were controlled by proportional scaling, and high-frequency noise was removed by temporal filtering the data with a low-pass filter. The individual contrast images were then entered into a second-level analysis, using a separate one-sample t test for each term in those two general linear models (a total of 8 contrasts, including tap-versus-rest contrast). We then thresholded these summary statistical maps at $P < 0.01$ (uncorrected for multiple comparisons). These maps were overlaid on a high-resolution structural image in MNI orientation. We used the summary map of the tap-versus-rest contrast (thresholded at $P < 0.001$, uncorrected) to perform a region of interest (ROI) analysis for the effects of rhythmic tapping. This procedure restricted the analysis of both frequency and complexity to those regions identified in the tap vs rest contrast, i.e., only regions involved in the production of

movement. We used Analysis of Functional Neural Images (AFNI) software (Cox, 1996) for this analysis. We then used a one-sample t test to test the null hypothesis about the correlation slopes of the lines connecting β_1 to β_5 across all the subjects.

Results

Behavioral response

All 13 subjects were able to perform and stabilize self-paced rhythms of various beats. As an example, Fig. 1A shows a plot of the variation of inter-response intervals (Δt), in one subject. The vertical lines represent the times at which visual cues were presented to change the stable patterns of tapping. The inverse of the interresponse interval is the number of taps per second, which is the rate of tapping, or the instantaneous frequency (f), including the short transients after the change of rhythm pattern. From the time course of interresponse intervals, one can see that this subject was able to perform different rhythms and hold these rhythms stable for at least 20 cycles. To determine the measure of periodicity (D) in a rhythm (which corresponded to the number of beats performed), we considered the phase portraits of Δt. Fig. 1B is a plot of Δt_{i+1} versus Δt_i for the rhythms of 1–4 beats, corresponding to the intervals marked 1–4 in Fig. 1A. Here, using concepts from the dynamical systems theory, one can assume that a complex rhythm is one that has a higher D and whose cluster of points are away from the diagonal line. We extracted D for the whole time course of interresponse intervals. Thus, we have both f and D as the behavioral parameters defining the complexity of a rhythm.

To check the independence of f and D, we performed a repeated-measures ANOVA. We grouped $f(t)$ according to $D(t)$ for instance, $f_1(t)$, $f_2(t)$, $f_3(t)$ corresponding to $D_1(t)$, $D_2(t)$, $D_3(t)$, respectively. We then calculated the averages of $f_1(t)$, $f_2(t)$, and $f_3(t)$ for each subject and tested the null hypothesis, H_0: $<f_1(t)> = <f_2(t)> = <f_3(t)>$. With repeated-measures ANOVA, the null hypothesis could not be rejected ($P < 0.28$). This suggests that the distribution of $f_i(t)$'s was not significantly different regardless of $D(t)$. The Spearman's correlation of $f(t)$ and $D(t)$ was also less than 0.15 for every subject included in the analysis.

Brain response

The main effect of tap-versus-rest showed widespread activations in the primary motor cortex, premotor cortex, auditory cortex, basal ganglia, thalamus, and the cerebellum (not shown). Table 1 summarizes the results of relative brain activations associated with the increasing complexity of a rhythm, after being masked by the main effect of tap-versus-rest. The correlation with rate of tapping (f) (Fig. 2) revealed ipsilateral activity in pre/postcentral gyrus and

Table 1
Brain regions correlated with complexity of rhythms (see also Figs. 2 and 3)

Contrast	Brain region	Cluster size	Voxel t (z equivalent)	MNI coordinates
f	Right midbrain	23	4.99 (3.60)	16, −16, −12
	Right precentral gyrus	10	3.84 (3.04)	24, −28, 64
D_1–D_0	Cerebellar vermis	35	6.62 (4.22)	−4, −72, −20
	Left superior temporal gyrus	28	4.09 (3.17)	−56, −72, −8
	Left pre/post central gyrus	35	3.57 (2.89)	−36, −28, 64
D_2–D_0	Cerebellar vermis	36	5.96 (3.90)	−4, −72, −20
	Left thalamus	13	5.29 (3.66)	−8.3, −28, −4
D_3–D_0	Cerebellar vermis	69	6.45 (4.07)	−4, −72, −24
	Left precentral gyrus	19	4.49 (3.76)	44, −20, 56
	Left thalamus	40	3.22 (3.19)	−4, −20, 12

The table displays the anatomical location, cluster size, t values of peak voxels (equivalent z scores), MNI coordinates (x, y, z) (thresholded at $P < 0.01$ uncorrected, voxel extent, $k \geq 10$).

in the right midbrain. The correlation with complexity (D_1, D_2, D_3, D_4, and D_5) showed trends of either increasing or decreasing brain activity depending on the specific brain region (Fig. 3). The D_1–D_0 contrast showed correlated activity in both the cerebellum and the superior temporal gyrus along with the primary motor cortex. The D_2–D_0 contrast showed activity in the cerebellar vermis and left thalamus. The D_3–D_0 contrast revealed correlated activity in the cerebellar vermis, left thalamus, and left precentral gyrus.

An ROI average analysis (using the masks created by the images of tap-versus-rest contrast at $P < 0.001$) showed increasing activity in the cerebellum and thalamus, and decreasing activity in the basal ganglia (Fig. 4). For all the subjects, the regressed slopes from β_1 to β_5 for cerebellar vermis and thalamus were significantly greater than zero ($P < 0.01$ and $P < 0.05$ respectively), whereas the slope was negative for the basal ganglia, trending toward significance ($P < 0.1$). Because the relationship of activation to complexity appeared nonlinear in the basal ganglia, we tested an alternate model that included a quadratic term. This model did not fit the data significantly better than a linear model, nor was the quadratic term significant ($P < 0.21$). Taken together, these results suggest greater involvement of the cerebellum and thalamus, and less involvement of basal ganglia as the complexity of rhythms increases.

Discussion

Internally, generation of a self-paced rhythm requires (1) a flow of temporal sequence of events, perceived or imagined, (2) motor preparation, (3) actual execution of rhythmic tapping with precise timing mechanism. Previous studies on coordinative movements and rhythms have shown that a complex movement involves a higher degree of central internal effort (Rao et al., 1993, Mayville et al., 1999; Kelso et al., 1990; Luria, 1980; Sakai et al., 1999). The cortical areas involved may depend on the specific timing relationship required between motor and perceptual or imagery

processes. Our results identified the main areas involved in rhythm generation and are consistent with previous findings. Additionally, we identified a subset of brain areas associated with the complexity of the rhythms.

The main effect of finger movements, that is, the activity in the premotor, motor, and supplementary motor areas, was observed by the tap-versus-rest contrast. In addition to these areas, this contrast showed activations in the basal ganglia, thalamus, and cerebellum. The supplementary motor and premotor regions are generally responsible for planning of motor tasks, whereas the primary motor area is responsible for the execution of the task (Rao et al., 1993; Roland et al., 1980; Samuel et al., 1998). The frontomesial motor areas (supplementary motor areas and anterior cingulated cortex) are associated with movement initiation, in both self-initiated and externally triggered movements (Deiber et al., 1999). The contralateral activations extended to the part of the postcentral gyrus, which is primary somatosensory cortex and is concerned with the initial cortical processing of tactile and proprioceptive information. These areas are believed to contribute to the temporal organization of motor behavior (Halsband et al., 1993; Truelle et al., 1995). Similar results were obtained in several other studies (Bressler et al., 1996; Gerloff et al., 1998; Lang et al., 1990), and these areas were found to show pronounced activity with complexity of coordinative movements. These previous results indicate that the magnitude of premotor and supplementary motor activity relates directly to the degree to which a movement pattern must be planned.

We observed increasing brain activation with increased rate of tapping in the ipsilateral pre and postcentral gyrus and midbrain. The ipsilateral activity in the pre/postcentral gyrus might have been due to an additional internal effort for the increased rate of tapping. The ipsilateral activation for rhythms has also been observed previously (Ronald et al., 1981; Rao et al., 1993; Sakai et al., 1999). The present results support the idea that the neural processing of rhythm is not confined to one cerebral hemisphere (Peretz, 1990). In a previous fMRI study, higher movement frequency was seen to increase the extent of activated area in the intrapa-
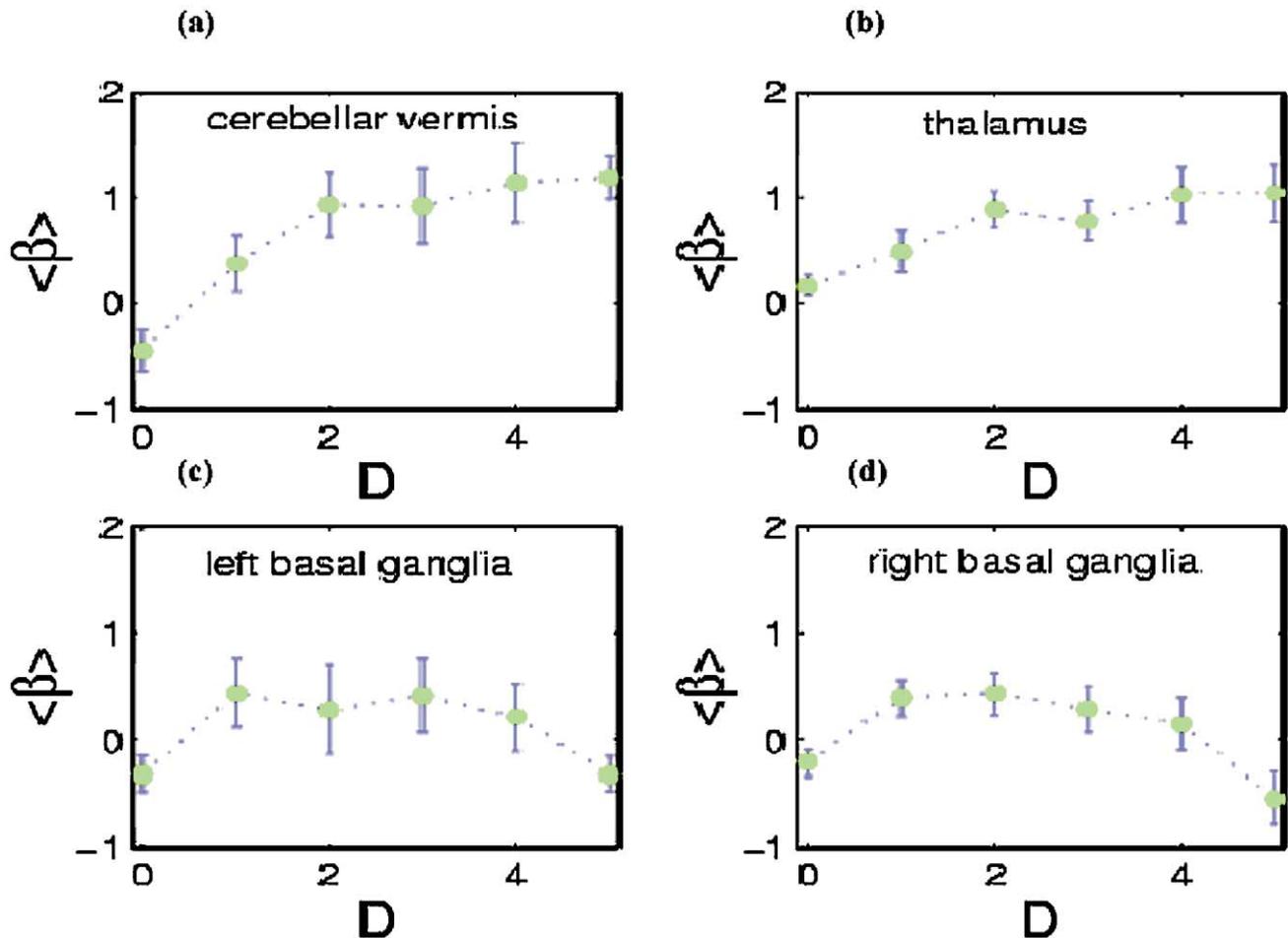
Fig. 4. Relationship of the average regressed activation parameters, $<\beta_i>$, to complexity (D_i), where $i = 1, 2, 3, 4,$ and 5. The greater the complexity of a rhythm, the greater the activations in the cerebellum and thalamus, shown in panels (a) and (b), whereas the opposite was true for the basal ganglia, shown in panels (c) and (d). Error bars are standard errors of the mean.

rietal sulcus, and this area was suggested to be associated with finger movements (Schubert et al., 1998). In our study, subjects may have started moving their left hand, or they might have imagined moving the left hand in a syncopated fashion as either rhythm complexity or speed increased (Stephan et al., 1995). Either of these behaviors might have contributed to the ipsilateral activation changes. Ipsilateral motor activity has been previously observed with increased motor complexity (Rao et al., 1993); however, in that study, movement frequency was not modeled independently of complexity. In contrast, we found activity in ipsilateral motor cortex correlating not with complexity, but with tapping frequency (after controlling for the complexity). The small ipsilateral representation of motor function has been known for decades. The contralateral activity may have saturated with movement complexity, and the small contribution from the ipsilateral cortex picked up the remaining function as movement speed increased.

In contrast to movement frequency, rhythm complexity was correlated with a different network of brain activation. The basal ganglia and cerebellum have long been known to

have recurrent connections with the cerebral cortex via the thalamus and are generally believed to be involved in some aspect of motor control. We observed activations in the cerebellum and the basal ganglia that were directly related to coordination of rhythmic movements. There is considerable support for the view that the cerebellum has a specific role in the timing of movements (Casini and Ivry, 1999), whereas the basal ganglia may be involved in action sequencing (Brown and Marsden, 1990). Cerebellar activation has been shown to be differentially sensitive to subdominant and dominant hand movements (Jancke et al., 1999), and the cerebellum, thalamus, and basal ganglia have all been implicated in controlling some aspect of the complexity of sequential finger movements (Sadato et al., 1996; Turner et al., 1998). Recent neuroimaging experiments have also suggested that the cerebellum is involved in executing coordinated movements (Ramnani et al., 2001) and in rhythm learning (Ramnani and Passingham, 2001). The cerebellum has also been found to be involved in response reassignment rather than attention (Bischoff-Grethe et al., 2002). In addition, several lesion studies have provided evidence that

the cerebellum is essential for coordinated movement (Ivry and Keele, 1989; Thach et al., 1992), but the role of the basal ganglia has remained elusive.

The correlation of brain activity with rhythm complexity in the ROI analysis (Fig. 4) showed increasing brain activity in the cerebellum and thalamus, but decreasing activity in the basal ganglia. These results suggest that the cerebellum is associated with the increasing complexity of rhythms and has a role in the timing mechanism of higher coordinative movements. The increasing activity in the thalamus with complexity could relate to its greater involvement in the pathways between the cerebral cortex and the cerebellum. Some thalamic nuclei receive inputs and project to discrete functional areas of the cerebral cortex and association cortex and others have no projections to the cortex at all (Nolte, 2000). The decreased activity in the basal ganglia suggests lesser involvement in sequencing complex movements.

In summary, the network of brain regions that we have identified and their relative activations with movement complexity begin to elucidate the roles that these different structures play in complex movements. While the cerebellum has been known to play a critical role in movement timing, the respective contribution of the basal ganglia has been relatively unclear. Although Marsden proposed that the basal ganglia assisted with the automatization of movement sequences (Brown and Marsden, 1990), evidence for this function has been scant. Although not quite reaching statistical significance, our findings are consistent with the proposed automatization function of the basal ganglia, but only of rhythmic movement sequences of moderate length. As the complexity increases, the basal ganglia contribution appears to become less significant.

Conclusion

Rhythmic finger tapping involves brain activations in the primary motor cortex, premotor cortex, auditory cortex, basal ganglia, thalamus, and cerebellum. The ipsilateral brain activations in the motor cortex can be related to the additional internal effort to increase the rate of tapping above and beyond the initiation of motor execution. Increased cerebellar activation was associated with greater timing demands for more complex rhythms. Increased thalamic activity with greater rhythm complexity could relate to its greater involvement in the pathways between the cerebral cortex and the cerebellum. Relatively decreased basal ganglia activity with complexity can be associated with diminished involvement in automatic movement sequencing, with perhaps a maximal level of involvement with rhythms of two to three beats.

Acknowledgments

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