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Brain activity correlates differentially with increasing temporal complexity of rhythms during initialisation, synchronisation, and continuation phases of paced finger tapping

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Abstract

Activity in parts of the human motor system has been shown to correlate with the complexity of performed motor sequences in terms of the number of limbs moved, number of movements, and number of trajectories. Here, we searched for activity correlating with *temporal complexity*, in terms of the number of different intervals produced in the sequence, using an overlearned tapping task. Our task was divided into three phases: movement selection and initiation (*initiate*), synchronisation of finger tapping with an external auditory cue (*synchronise*), and continued tapping in absence of the auditory pacer (*continue*). Comparisons between synchronisation and continuation showed a pattern in keeping with prior neuroimaging studies of paced finger tapping. Thus, activation of bilateral SMA and basal ganglia was greater in continuation tapping than in synchronisation tapping. Parametric analysis revealed activity correlating with temporal complexity during *initiate* in bilateral supplementary and pre-supplementary motor cortex (SMA and preSMA), rostral dorsal premotor cortex (PMC), basal ganglia, and dorsolateral prefrontal cortex (DLPFC), among other areas. During *synchronise*, correlated activity was observed in bilateral SMA, more caudal dorsal and ventral PMC, right DLPFC and right primary motor cortex. No correlated activity was observed during *continue* at $P < 0.01$ (corrected, cluster level), though left angular gyrus was active at $P < 0.05$. We suggest that the preSMA and rostral dorsal PMC activities during *initiate* may be associated with selection of timing parameters, while activation in centromedial prefrontal cortex during both *initiate* and *synchronise* may be associated with temporal error monitoring or correction. The absence of activity significantly correlated with temporal complexity during *continue* suggests that, once an overlearned timed movement sequence has been selected and initiated, there is no further adjustment of the timing control processes related to its continued production in absence of external cues.

Keywords: Timing; Time perception; Movement complexity; fMRI; Paced finger tapping; Movement selection; PreSMA

1. Introduction

The human motor system has the potential to orchestrate an almost infinite number of different movement sequences. These may encompass a wide range of complexities, including the number of limbs used, number of trajectories, sequence length, and relative timing of movement. Neuroimaging work has shown that the involvement of some brain regions in movement varies with some of these aspects of complexity (reviewed in Harrington et al., 2000). One important aspect which has been little investigated in terms of these variations is the temporal structure of the sequence. Rhythmic finger tapping (Wing, 2002) provides a convenient task in which to study this by varying the number of intervals in a sequence while keeping all other parameters (number of movements, mean movement frequency, number of external stimuli) the same. Previous imaging studies of externally paced rhythmic tapping, at a fixed complexity level, have shown a fairly consistent pattern of activity in the motor system. Thus, contralateral sensorimotor cortex and ipsilateral cerebellum are normally involved, with additional activation of areas such as the basal ganglia, thalamus, and sensory cortices, depending upon task specifics such as the nature of the pacing stimuli (Jancke, Loose, Lutz, Specht, & Shah, 2000a; Lutz, Specht, Shah, & Jancke, 2000; Rao et al., 1997; Rubia et al., 2000).

After repeated practice, even very complex movement sequences can be executed without overt attention and are

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therefore sometimes referred to as 'automatic' (Passingham, 1996). Because brain activity observed during overlearned movements differs from that observed during less fully learned movements (Jenkins, Brooks, Nixon, Frackowiak, & Passingham, 1994; Penhune & Doyon, 2002), it is important to avoid learning-related confounds when investigating movement related brain activity. Several studies of movement complexity have achieved this by using overlearned movement sequences (Boecker et al., 1998; Catalan, Honda, Weeks, Cohen, & Hallett, 1998; Harrington et al., 2000; Haslinger et al., 2002; Sadato et al., 1995). These authors varied different aspects of complexity and observed slightly different activity patterns for each. Dorsal premotor cortex (dPMC) and cerebellum were the most commonly reported areas, with activity in the former correlating with most types of complexity (Catalan et al., 1998; Harrington et al., 2000; Haslinger et al., 2002; Sadato, Campbell, Ibanez, Deiber, & Hallett, 1996), and in the latter specifically with the number of digits used (Harrington et al., 2000; Haslinger et al., 2002).

Our goal here was to determine how brain activity during an overlearned movement sequence varies with the temporal complexity of the sequence. We defined temporal complexity as the number of different intervals included in a measure of fixed overall duration and fixed number of elements. We used a variant (Vorberg & Hambuch, 1978) of the *synchronise*/*continue* task (Wing & Kristofferson, 1973) with auditory cues (Rao et al., 1997) in which subjects first synchronised finger tapping responses with an auditory rhythm and then continued to tap the rhythm in the absence of cues. For comparison with previous work we also included a simple contrast between activation in synchronisation and continuation phases. The synchronisation phase was preceded by a brief initiate phase, in which the subjects selected the rhythm and initiated tapping. Recent work has shown that movement selection and initiation elicits activity in areas not directly involved in movement performance (Picard & Strick, 2001; Rowe & Passingham, 2001). Thus, our analysis examined whether activity differed in the initiate and synchronise phases.

Error detection and correction processes in rhythm tracking have been shown to vary with sequence temporal complexity (Large, Fink, & Kelso, 2002). Moreover, the demand placed on movement selection mechanisms might also be expected to vary with temporal complexity. We therefore used a parametric approach to evaluate the effect of a number of rhythms varying in temporal complexity. We expected that brain activity associated with these processes should correlate with temporal complexity during selection and initiation. Once a sequence has been selected and initiated, however, it is unclear whether execution in the absence of pacing stimuli requires complexity dependent processing. Thus, it has been suggested that timing of a hierarchical rhythmic sequence, that would otherwise require several levels of embedded timekeeping, might be simplified by a process of linearization (e.g. during initiation) that allows use of a single timekeeper in execution (Vorberg & Wing, 1996). Based upon these studies (Large et al., 2002; Picard & Strick, 2001; Rowe & Passingham, 2001; Vorberg & Wing, 1996) we hypothesised that different brain regions would be activated during *synchronise* and *continue* phases of the task, and that activation correlating with difficulty might be limited to *initiate* and *synchronise* phases of the task.

2. Methods

2.1. Subjects

Ten right handed subjects, who gave informed consent, participated. The mean age was 27 years and five subjects were female. The experiment was approved by the Central Oxfordshire Research Ethics Committee.

2.2. Task

The task involved the production of temporal rhythms by tapping with the right index finger on a force sensor (response detection threshold set at 1.5 N). Each 42 s trial consisted of three phases: in the 6 s *initiate* phase a sequence of auditory cues (100 Hz tones of 50 ms duration, at an intensity audible over the background scanner noise) was used to define a rhythm. Subjects were instructed to attempt to tap in time with the rhythm as soon as they felt they had identified it. This was immediately followed by the 18 s *synchronise* phase in which subjects were to maintain their tapping accurately in phase with the auditory rhythm. This was immediately followed by the 18 s *continue* phase in which auditory cues ceased and subjects continued to reproduce the rhythm on their own (Fig. 1). There was a brief (∼700 ms) interval between trials, allowing subjects to cease tapping before the next trial. A pseudo-random order of trials was employed to ensure that there was no consistent relation between the rhythm sequences used in successive trials, allowing dissociation of brain activity between different sequences despite the short inter-trial interval.

The stimulus set comprised one isochronous pattern of repeating 500 ms intervals and three sets of multi-interval rhythms. Each multi-interval rhythm was composed of a 'measure' or repeating set of intervals that lasted 3 s and

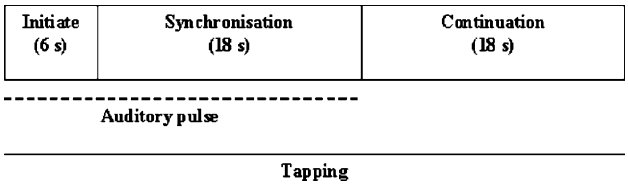

Fig. 1. Timeline of the three experimental conditions (i.e. *initiate*, *synchronisation* and *continuation*) and presentation of stimulus (i.e. auditory tone). Subjects began to tap during the *initiate* condition, synchronise with the tone during the *synchronisation* condition, and maintain tapping without the benefit of the auditory tone during the *continuation* condition.

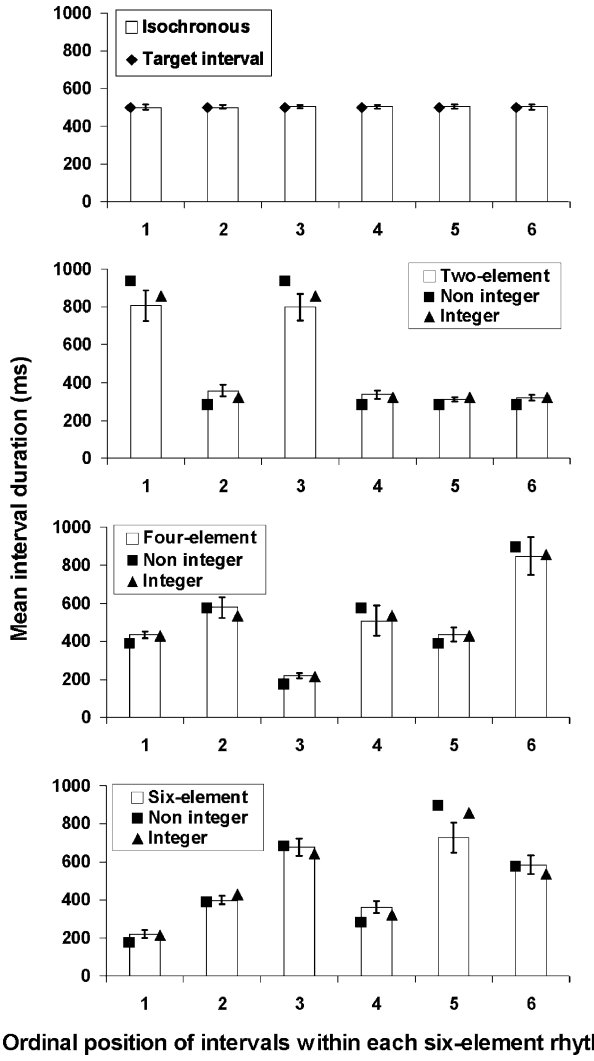

Fig. 2. Mean produced interval durations for group data as a function of ordinal position in each condition averaged across the two slightly different duration ratios, and synchronise and continue phases. Square and triangle symbols show the target intervals for the two rhythm conditions with slightly differing ratios (a, b). Diamond symbols indicate the target interval for the isochronous condition. Error bars indicate the within group standard deviation for producing each interval.

involved six intervals. The three sets of rhythms contained a linearly increasing number of intervals: 2, 4, and 6, respectively. To maintain attention by making the task more challenging, each level of complexity was presented in two variants, differing slightly in the ratios of their durations (Fig. 2). The two 2-element rhythms had intervals of (a) 321 and 858 ms (in ratio 1:2.7) or (b) 282 and 936 ms (1:3.3). The four-element rhythms had intervals of (a) 214, 428, 536 and 857 ms (1:2:2.5:4) or (b) 174, 389, 576 and 896 ms (1:2.2:3.3:5.1). The six-element rhythm intervals were (a) 214, 321, 429, 536, 643 and 857 ms (1:1.5:2:2.5:3:4) or (b) 174, 282, 389, 576, 683 and 896 ms (1:1.6:2.2:3.3:3.9:5.1). In each case small corrections of up to ±0.25 ms were made as required to add up to a measure of 3000 ms total duration. This measure was repeated two times (6 s) to define the *initiate* phase and six times (18 s) to define the *synchronise* phase.

Two further conditions, intended as controls, were included. An 18 s *rest* condition, which merely required subjects to maintain fixation, and a 24 s *random* condition (with *initiate* and *synchronise* but no continuation phase). In *random*, subjects pressed a button in response to tones heard at two unpredictable intervals (either 282 or 936 ms, pseudo-randomly presented with a 2:1 presentation frequency). The results from the *random* condition were not analysed since the shorter, more frequent, interval (282 ms) did not allow sufficient time for a response to the first of the two tones before the second tone sounded, and thus lead to response repetition and omission errors.

During scanning, all of the conditions were presented as a randomly ordered series of 10 blocks (three levels of rhythm difficulty × two variants + two isochronous sequences + *rest* + *random*). This series was repeated four times, with a different random order on each repetition. This process gave four repetitions of every condition (and eight of the isochronous sequence), with one repetition occurring in each quarter of the entire scanning period.

Subjects were pre-trained at least one day prior to scanning (range 1–5 days), performing all conditions of the task at least six times and until the rhythms were overlearned and performance accuracy ceased to improve over the last four training sessions (mean regression slope of −0.8% per session). The last formal training session never occurred more than 24 h prior to scanning, and every subject was given a final 10-min practice just before the scanning session, while in the scanner and in the presence of the scanner background noise. Accuracy was measured as (1 − (expected − produced)/expected) × 100, and collapsed across synchronisation and continuation conditions. The minimum accuracy reached in this manner was 84%, however all subjects except one attained a level above 90% accuracy during training.

2.3. fMRI data acquisition

Four hundred and forty-eight whole brain EPI data volumes were acquired on a 3 T Siemens-Varian scanner, using a T2 weighted GE modulated BEST sequence (TE 30 ms, flip angle 90°), 256 mm × 256 mm FOV, 64 × 64 × 21 matrix size, and a TR of 3 s. Twenty-one contiguous 7 mm thick slices were acquired in each volume. The experiment lasted 22.4 min. T1 weighted structural images were also acquired using a 3D FLASH sequence with inversion pulse 500 ms, 64 contiguous slices, 1 mm × 1 mm × 3 mm each.

2.4. fMRI data analysis

Data were analysed using the Oxford Functional MRI of the Brain (fMRIB)'s in-house analysis tool 'FEAT', on a MEDx platform (http://www.fmrib.ox.ac.uk/fsl). Pre-statistics processing included motion correction using MCFLIRT (Jenkinson & Smith, 2001) to realign images

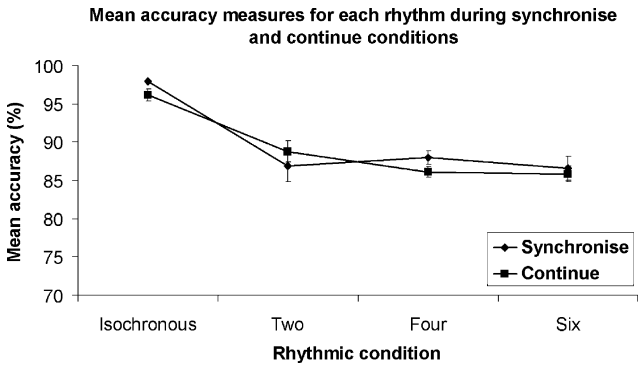

Fig. 3. Measures for accuracy for group data averaged across integer and non-integer, for both synchronise and continue phases of the task. Error bars indicate the within group standard error of the mean for each condition.

on the central volume, spatial smoothing with a Gaussian kernel of FWHM = 5 mm, mean-based intensity normalisation of all volumes; non-linear band-pass temporal filtering (low-frequency rejection by Gaussian-weighted LSF straight line fitting, with $\sigma = 35$ s; high-frequency filtering above 2.8 Hz).

Statistics were computed using a general linear model convolved with a gaussian kernel to simulate haemodynamics. In the GLM model we first fitted the main conditions (separate explanatory variables for isochronous, two-, four- and six-element rhythms). We then made pair-wise comparisons between the various phases of the task (*synchronise* > *continue*, *continue* > *synchronise*, and *initiate* > *synchronise*). We also performed a separate parametric analysis for the *initiate*, *synchronise* and *continue* phases. These models used linear contrast weights (−1, 0, +1) to reflect the increase of temporal complexity across two-, four- and six-element rhythms. The isochronous rhythm was not included in this parametric analysis as its one-element rhythm would have created an unequal step size compared to the other three conditions, and also because performance was significantly better in this condition than in the other three conditions (Figs. 3 and 4). Previous work has shown that sequence complexity effects are adequately modelled by such

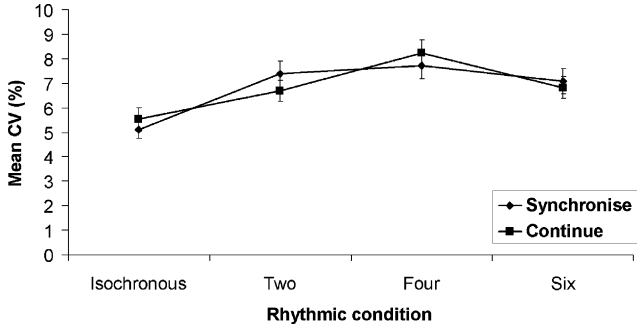

Fig. 4. The mean coefficient of variation (CV) for group data averaged across integer and non-integer, for both synchronise and continue phases of the task. Error bars indicate the within group standard error of the mean for each condition.

a first-order linear approach (Haslinger et al., 2002). Rest was the un-modelled baseline in all cases. The random condition was modelled as a covariate of no interest.

Statistical images were produced for each subject by contrasting the parameters associated with each condition. Statistical maps were fit to the Montreal Neurological Institute (MNI) canonical brain using fMRIB's linear image registration tool (FLIRT), and then combined across subjects using a fixed effects model. *Z* (Gaussianised *T*) statistic images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.01$ (Forman et al., 1995; Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1996; Worsley, Evans, Marrett, & Neelin, 1992). The statistical images resulting from direct subtraction contrasts (test versus control, e.g. *synchronise* > *continue*) were masked to guard against significant differences in activation due to negative activity in the control condition. This was accomplished by multiplying each statistical map by binarised maps of significant activity resulting from contrast of the appropriate test versus rest baseline condition. Masked probability maps were rendered onto the MNI canonical brain. Cluster maxima were localised using anatomical landmarks (Duvernoy, 1999). DLPFC and VLPFC were determined as defined in Rushworth & Owen (1998), SMA and preSMA, were determined according to the description in Picard & Strick (2001). The dividing line between dPMC and vPMC was set at 48 mm above the anterior commisure as described in Jancke, Shah, & Peters (2000b). The frontal eye fields were determined according to Paus (1996).

2.5. Task presentation

Behavioural tasks were presented and controlled by a DOS program running on a PC laptop. During fMRI sessions, visual stimuli specifying task phases were projected by an InFocus LP1000 LCD projector onto a back-projection screen (image subtending approximately 14° at the eye, VGA resolution) viewed from inside the magnet bore using 90° prism glasses. A fixation point was always present at the centre of the display. Responses were recorded using a force sensor made from resistive plastic (Interlink Electronics Europe). This was calibrated outside the scanner and sampled at 1000 Hz using a 12-bit analogue to digital converter. The time of each press was determined by the time when applied force crossed a minimum threshold, set above baseline noise levels at approx. 10% of peak force.

Auditory cues were presented monaurally using an electrostatic headphone system designed and built by the Medical Research Council Institute of Hearing Research in Nottingham, UK.

Statistical tests on the behavioural data were performed in SPSS. Because of variation in the force of subject responses during the scanning session, occasional press responses were not detected. Trials in which at least two complete repetitions of the rhythm could not be determined from the recorded re-

sponses were excluded from the behavioural analysis. In total, 38 of the 640 blocks were excluded in this manner, constituting 5.9% of all behavioural data, approximately evenly distributed across rhythms and task phases. Despite these missing data, we have no evidence that subjects failed to perform the tasks; in fact, the detected responses show good compliance (Fig. 2). Since subjects failed to tap hard enough to trigger our force sensitive response detector during this small percentage of blocks, but appear to have performed all other aspects of the task normally, we have chosen to analyse all of the associated fMRI data rather than excluding the parts relating to the low-force key presses. This is a conservative approach since post hoc exclusion of conditions in a random design may upset the experimental balance.

3. Results

3.1. Behaviour

All results are for group data averaged across the two slightly different duration ratios for each rhythm. Fig. 2 shows the mean intervals (and target intervals) in each rhythm produced by each subject during the fMRI session. The mean accuracy, averaged across intervals produced, was 89.8% during *synchronise*, and 89.2% during *continue*. A two (*synchronise*/*continue*) × four (isochronous, two-, four- and six-element rhythm) repeated measures ANOVA, performed on the mean accuracy measures showed a significant main effect of rhythm type, $F(3, 7) = 70.759$, $P < 0.001$. Bonferroni corrected paired *t*-tests showed that mean performance about target intervals was significantly better ($P < 0.05$) for isochronous sequences than for the three rhythmic conditions (Fig. 3). There was no significant main effect of *synchronise* versus *continue* conditions, nor did this factor interact with rhythm.

A second repeated measures ANOVA, following the same 2×4 format but examining the average of the coefficient of variation (CV (multiplied by 100)) for each interval, also showed a main effect of rhythm type, $F(3, 7) = 10.057$, $P < 0.01$. Bonferroni corrected paired *t*-tests showed that the CV was lower for isochronous sequences than for the three rhythmic conditions, where the CVs were similar. This result also demonstrates that variability about the mean was constant across the three rhythmic conditions (Fig. 4).

3.2. Functional imaging

All imaging results are based on the group data combined across the two slightly differing duration ratios in each rhythm condition.

3.3. Task phase

Clusters of fMRI activity which were significant at $P < 0.01$ for comparisons between task phases are rendered onto the MNI canonical brain in Fig. 5. The (*initiate* > *synchronise*) comparison showed no activity with significance at this threshold. The (*synchronise* > *continue*) (Fig. 5 (blue) and Table 1A) contrast showed bilateral activity in the temporal cortex (Fig. 5A) with local peaks in the bilateral superior temporal gyrus, and right transverse temporal gyrus. A separate peak was observed in right inferior parietal gyrus; in the left superior temporal gyrus activation ex-

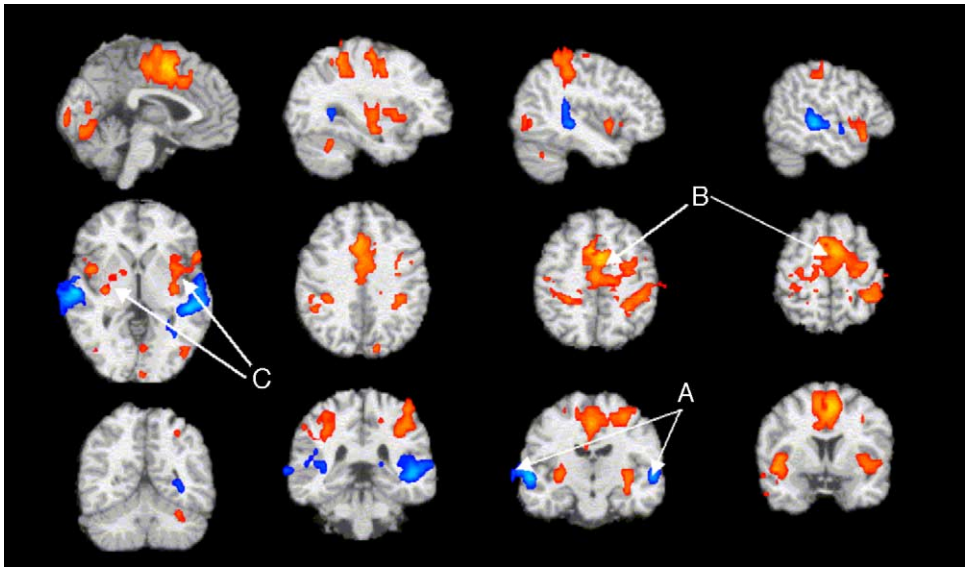

Fig. 5. Shows functional activity in response to the *synchronise* > *continue* (blue), and *continue* > *synchronise* (red) contrasts at the threshold of $P < 0.01$. The slices shown were taken at sagittal: −1, −31, −41, −51 mm; axial: −53, −33, −13, 7 mm; coronal: 1, 41, 51, 61 mm. The figure is in radiological convention such that the L side corresponds to R and vice versa. Letters refer to specific structures: (A) primary auditory cortex; (B) SMA; (C) basal ganglia.

Table 1
MNI coordinates for the highest local maxima of BOLD activity found in each functional area associated with the synchronise > continue (A); continue > sychronise (B) contrasts

x	*y*	*z*	Value	Laterality	Anatomical locus
(A) Synchronise > continue					
Temporal lobe					
−48	−30	0	7.2	L	STG
−59	−27	6	6.8	L	STG
−56	−15	0	5.4	L	STG
59	−15	0	7.0	R	STG
68	−21	6	7.0	R	STG
62	−3	0	5.7	R	STG
39	−30	12	3.1	R	TTG
Other					
45	−30	24	2.9	R	Inferior parietal gyrus
(B) Continue > synchronise					
Prefrontal lobe					
−48	6	48	3.4	L	Anterior precentral gyrus
−6	6	54	6.0	L	Medial wall SFG
−36	0	48	3.6	L	Anterior precentral gyrus
−6	−6	72	4.7	L	Medial precentral gyrus
−15	−18	54	3.6	L	Posterior MFG
−30	−12	60	4.0	L	Anterior precentral gyrus
42	27	−12	4.4	R	IFG
53	21	30	2.8	R	IFG anterior to VVPCS
3	15	48	5.6	R	Medial SFG
9	3	60	5.4	R	Medial SFG
0	−12	54	4.6	R/L	SFG
Insula					
−36	18	−6	3.5	L	Insula
−39	9	0	3.6	L	Insula
Limbic lobe					
−33	−9	−12	4.2	L	Parahippocampal gyrus
15	−24	36	2.7	R	Cingulate
3	−18	36	3.1	R	Cingulate gyrus
Temporal lobe					
−53	21	−12	4.5	L	STG
−56	21	0	4.1	L	STG
53	18	−18	4.8	R	STG
48	9	−6	5.0	R	STG
Parietal lobe					
−12	−80	42	3.6	L	Intraparietal sulcus
−42	−33	48	4.0	L	Supramarginal gyrus
−33	−45	54	4.4	L	Supramarginal gyrus
30	−36	48	4.1	R	Supramarginal gyrus
45	−45	42	3.4	R	Supramarginal/angular gyrus
56	−30	48	2.9	R	Supramarginal gyrus
21	−48	60	3.1	R	Superior parietal lobe
45	−30	36	3.6	R	Supramarginal gyrus
Occipital lobe					
−9	−80	−6	4.0	L	Cuneus
−9	−71	12	2.9	L	Cuneus
−48	−74	−6	3.5	L	MOG
−24	−89	−18	3.8	L	SOG
−15	−95	−18	3.4	L	IOG
−3	−95	6	3.4	L	Cuneus/SOG
3	−71	18	3.1	R	Cuneus
42	−71	6	3.1	R	MOG
Basal ganglia					
−36	−12	0	3.7	L	Putamen/capsule
30	−12	6	3.7	R	Putamen
24	0	6	3.4	R	Putamen

Table 1 (*Continued*)

x	*y*	*z*	Value	Laterality	Anatomical locus
Cerebellum					
−39	−56	−24	4.7	L	Cerebellar hemisphere
36	−65	−24	2.8	R	Cerebellar hemisphere
24	−71	−24	2.4	R	Cerebellar hemisphere

Columns show the coordinates in millimetres from the anterior commisure, the *z*-score value of each local max, laterality, and an anatomical description of the point's location on the SPM canonnical brain. SFG: superior frontal gyrus, SFS: superior frontal sulcus, MFG: middle frontal gyrus, MFS: middle frontal sulcus, IFG: inferior frontal gyrus, IFS: inferior frontal sulcus, STG: superior temporal gyrus, TTG: transverse temporal gyrus, IIPCS: inferior portion of inferior precentral sulcus, SSPCS: superior portion of superior precentral sulcus, ISPCS: inferior portion of superior precentral sulcus, VVPCS ventral portion of ventral precentral sulcus, SOG: superior occipital gyrus, MOG: middle occipital gyrus, IOG: inferior occipital gyrus.

tended into the same region of inferior parietal gyrus, but no local maximum was observed there. The opposite contrast (*continue>synchronise*) (Fig. 5 (red) and Table 1B) showed local peaks of activity bilaterally in SMA (Fig. 5B), and VLPFC. More caudally, peaks were also observed in post-central gyrus, inferior parietal, and in the occipital lobe. The cerebellar hemispheres and putamen (Fig. 5C) also showed bilateral peaks of activity. Right hemisphere specific peaks were observed in preSMA, DLPFC, and primary motor cortex, and in the superior parietal lobe, superior temporal gyrus, and cingulate cortex. Left hemisphere specific peaks were observed in the dPMC, vPMC, intraparietal sulcus, insula, and parahippocampal gyrus.

3.4. Parametric variation in rhythm complexity

The areas where fMRI signal correlated parametrically with temporal complexity (number of intervals) of rhythmic sequences during *initiate* (red) and *synchronise* (blue) phases have been rendered onto the MNI canonical brain in Fig. 6. The same region of right hemispheric SMA proper activated in both phases (area of green overlap, Fig. 6A), however activity in the preSMA occurred only during *initiate* (Fig. 6B) with a larger area of activity and stronger peak intensity in the left hemisphere. Large areas of PMC were active in both *initiate* and *synchronise*, with dPMC activity occurring more anteriorly during *initiate*, and only small regions of overlap (Fig. 6C). Because from necessity each *initiate* condition was immediately followed by the corresponding *synchronize* condition, some activity in the former might spread into the latter. However, the *synchronize* condition was 3 times longer (18 s versus 6 s); moreover, there are clear differences in the pattern of activity (Fig. 6). Hence we do not expect that the overlap in activation patterns is an artefact of our design. In both hemispheres, *synchronise* related activity extended into vPMC, with additional local maxima in that region. Although some *initiate* related activity also extended into vPMC, no local maxima were observed there. In the right hemisphere, *initiate* and *synchronise* associated activity overlapped at the junction of the inferior frontal sul-

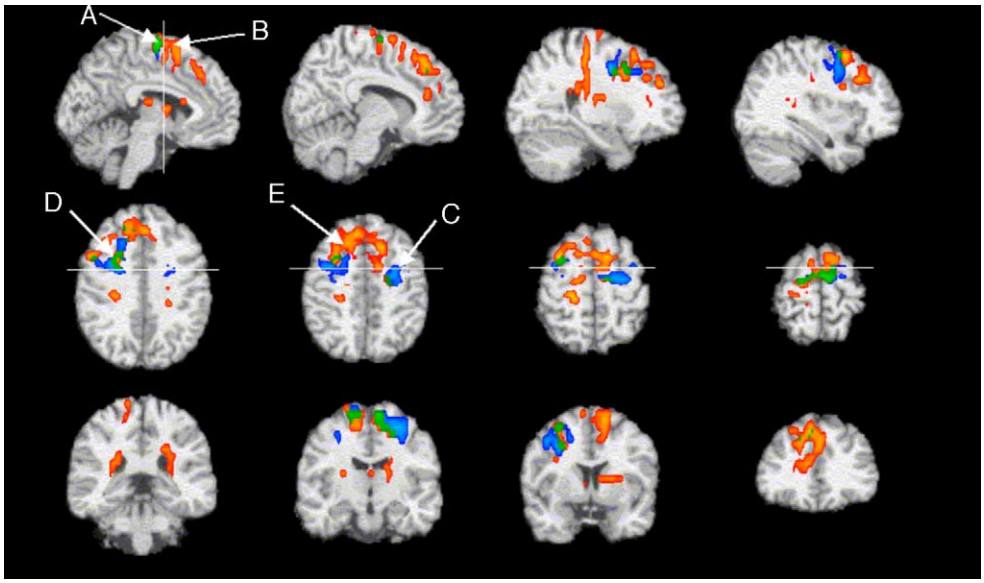

Fig. 6. Functional activity in response to parametric modelling of initiate (red) and synchronise (blue) phases with areas of overlap shown in green. Data was thresholded at $P < 0.01$. The slices shown were taken at sagittal: −5, 10, 26, 34 mm; axial: 40, 50, 60, 70 mm; coronal: −33, −10, 7, 37 mm. The figure is in radiological convention such that the L side corresponds to R and vice versa, the white dividing lines show the location of the anterior commisure in some views, letters refer to specific structures: (A) SMA; (B) preSMA; (C) dPMC; (D) DLPFC/dPMC; (E) DLPFC.

cus and inferior branch of the inferior precentral sulcus, in a region which may correspond to either dPMC or DLPFC, as the boundary between these is not clearly defined (see area of green overlap, Fig. 6D). Note that this region is near the FEF, but peaks do not fall within it. *Initiate* associated activity extended anteriorly from here and covered a large portion of DLPFC (Fig. 6E). A smaller region of *initiate* related DLPFC activity was also observed in the left hemisphere. Only very small areas of DLPFC activity were observed during *synchronise*, and these were limited to the right hemisphere (see Table 2B for coordinates).

Initiate was also associated with bilateral activity in the right hemispheric primary sensorimotor cortex, basal ganglia (left head and tail of caudate, right tail of caudate, and bilateral putamen), right hemispheric anterior cingulate, and left hemispheric thalamus.

No parametrically varying activity was found during the *continue* phase when data were thresholded at cluster-level probability threshold of $P < 0.01$. When the threshold was lowered to $P < 0.05$, however, an area of left hemispheric inferior parietal activity emerged (angular gyrus, peak coordinates (x:y:z): −42, −33, 34). This area was also active at the $P < 0.05$ threshold during *synchronise*, peak coordinates at (x:y:z −50, −30, 48), but not *initiate*.

4. Discussion

The purpose of this study was to describe the brain activity involved in production of movement sequences of varied temporal complexity, and to determine how that activity correlates with temporal complexity. We took as our measure of complexity the number of different intervals in each six-element measure. Our design allowed examination of three task phases: *initiate* (listening to a presented sequence and attempting to tap in time with it when ready, presumably by selecting a prelearned movement sequence for these overlearned rhythms), *synchronise* (tapping in time with auditory cues), and *continue* (continuing to tap, in absence of auditory cues). We used rhythms which varied in temporal complexity from isochronous to six intervals per measure.

Because we were interested in movement complexity effects, we attempted to control learning. Therefore, we used well-practiced subjects. The efficacy of the practice was demonstrated by behavioural measures consisting of mean accuracy and of CV across conditions (Figs. 3 and 4). We assume that if subjects were still learning the more complex sequences, their mean accuracy would have been lower, and their mean CV would have been higher than the easier conditions. Since there was no significant difference between CVs for the two-, four- and six-element rhythms, we assume learning was adequately controlled. We did find that mean accuracy was higher and CV lower for the isochronous condition, but this condition was not included in the parametric analysis.

4.1. Task phase

Two prior studies (Jancke et al., 2000a; Rao et al., 1997) have described brain activity associated with auditory synchronization and continuation tapping; our observations are in keeping with their findings. Our *synchronise* > *continue* contrast showed activity in the bilateral auditory cortex, as expected when comparing an auditory cued task to an un-cued task (Jancke et al., 2000b). Our *continue* > *synchronise* contrast showed activity in the bilateral SMA and basal ganglia, regions previously reported as more active during continuation (Jancke et al., 2000a). We also observed activity in a number of areas not reported by prior studies of synchronisation and continuation tapping, this may be due in part to our novel requirement that subjects produce temporally complex as well as simple sequences, and in part to the large volume of data collected: 192 volumes in *synchronise* and in *continue* for each of ten subjects, allowing a very sensitive contrast.

4.2. Movement complexity

The most interesting aspect of our result relates to the way brain activity varies with the temporal complexity of a movement sequence. Prior studies varying the complexity of overlearned movements have shown that dPMC activation relates to the number of limbs used, the number of limb transitions and the sequence length (Catalan et al., 1998; Harrington et al., 2000; Haslinger et al., 2002; Sadato et al., 1996). Our observation of temporal complexity related dPMC activity in both *initiate* and *synchronise* phases suggests that this region responds to increased movement complexity in general since it shows that involvement of this structure also varies in parallel with the degree of temporal complexity of a motor sequence. To our knowledge, only one prior imaging study (Boecker et al., 1998) of overlearned movements has reported complexity related activity in the SMA. Our observation of SMA activity in both *initiate* and *continue* may therefore be specifically associated with our manipulation of *time* rather than other aspects of the movement complexity, as it has recently been suggested that SMA plays a critical role in temporal processing (Macar et al., 2002). This is also true for bimanual rhythmic tapping movements, as well as for unimanual finger tapping, in which the dPMC and SMA form part of a network for controlling the temporal complexity of movements (Ullen, Forssberg, & Ehrsson, 2003).

4.3. Initiation of a rhythm

Studies of movement selection have shown that preSMA and rostral dPMC are involved in higher hierarchical roles in motor control (Luppino, Matelli, & Rizzolatti, 1990; Picard & Strick, 2001; Rizzolatti et al., 1990), while SMA proper and caudal dPMC are more involved in motor execution (Dum & Strick, 1991a, 1991b; Hummelsheim, Bianchetti,

Table 2
MNI coordinates for the highest local maxima of BOLD activity found in each anatomical region in response to parametric modelling of the initiate (A); synchronise (B) phases when thresholded at $P < 0.01$, cluster level

x	*y*	*z*	Value	Laterality	Anatomical locus
(A) Parametric analysis, initiate phase					
Prefrontal cortex					
−15	24	48	3.7	L	SFG
9	33	54	3.5	R	Anterior SFG
27	36	48	3.1	R	Anterior SFS
24	48	30	3.6	R	Anterior SFS
39	27	36	3.7	R	MFG
18	27	54	3.6	R	SFG
27	24	54	3.4	R	Superior bank SFS
18	33	36	4.0	R	Anterior SFG
Premotor/supplementary motor cortex					
−12	−9	54	2.8	L	Posterior SFG
	3	54	3.5	L	SFG
−15	12	66	3.7	L	SFG
−3	36	42	3.4	L	Anterior medial SFG
−3	15	60	3.5	L	SFG
−6	−6	72	3.9	L	Posterior SFG
50	15	42	3.4	R	Junction IFS/IIPCS
33	12	60	4.4	R	SFS just anterior to ISPCS
33	12	30	2.7	R	IFS just anterior to ISPCS
15	15	60	3.3	R	SSPCS
9	6	72	3.2	R	SFG
18	−12	72	3.4	R	Anterior precentral gyrus
Primary sensorimotor cortex					
12	−30	78	3.1	R	Central sulcus, posterior bank
21	−24	60	3.9	R	Posterior precentral gyrus
Anterior cingulate					
9	39	18	3.2	R	Anterior cingulate gyrus
Basal ganglia					
−18	21	6	3.1	L	Head of caudate/internal capsule
−18	−3	18	2.8	L	Caudate/putamen
−21	−18	24	3.3	L	Caudate
−33	−36	12	2.6	L	Tail of caudate/white matter
−30	−33	24	2.7	L	Tail of caudate
−21	9	12	3.3	L	Internal capsule/insula
27	−6	18	3.4	R	Putamen
27	−15	18	3.1	R	Putamen
30	−39	18	3.0	R	Tail of caudate
Thalamus					
−6	3	12	3.1	L	Anterior thalamus
−6	−15	18	3.0	L	Thalamus
Other					
−9	21	18	3.0	L	Anterior cingulate
−24	−30	36	3.4	L	Cingulate gyrus
18	−24	36	3.2	R	Cingulate gyrus
18	−15	30	3.1	R	Caudate nucleus
18	−6	36	2.8	R	Cingulate gyrus
(B) Parametric analysis, synchronise phase					
Prefrontal cortex					
−27	0	48	3.6	L	IFS/IIPCS
42	12	30	2.6	R	Superior bank, IFS
9	39	42	2.5	R	Anterior SFG
21	27	42	3.1	R	Middle SFG
33	−3	66	3.0	R	Dorsal posterior MFG
Premotor/supplementary motor cortex					
−30	−9	60	3.6	L	Posterior SFS
−39	3	60	2.7	L	Precentral gyrus

Table 2 (*Continued*)

x	*y*	*z*	Value	Laterality	Anatomical locus
−24	3	72	2.5	L	SFG
−6	−6	72	4.6	L	SFG
18	−12	72	2.9	R	Precentral gyrus
42	9	48	3.5	R	MFS
6	−6	72	3.0	R	SFG
30	−9	48	2.6	R	SFG
24	0	48	3.6	R	SFG
21	12	66	2.6	R	Anterior inferior bank SFS

Columns and abbreviations are as in Table 1. The MNI coordinates for anatomical regions listed under 'other' in Table 2A, strictly correspond to corpus callosum, but on pragmatic grounds these have been identified with nearest grey matter structures.

Wiesendanger, & Wiesendanger, 1988; Picard & Strick, 2001; Wiesendanger, Hummelsheim, & Bianchetti, 1985). Specifically, preSMA has been associated with selection between movements (Deiber et al., 1991), while SMA proper has been associated with execution of cued motor commands (Deiber et al., 1991; Matelli et al., 1993; Sadato et al., 1995). It has recently been suggested that rostral dPMC is involved in cognitive processing associated with movement, while caudal dPMC is involved more directly in movement preparation (Picard & Strick, 2001).

We observed stronger correlation with temporal complexity in preSMA and rostral dPMC during *initiate* than during *synchronise* or *continue*, with the former active only during *initiate*, and the latter active more rostrally in that phase. Since selection and initiation of more complex rhythms likely requires more processing, initiation related activity can be expected to vary with sequence complexity. The pattern we observed suggests temporal complexity dependent involvement of preSMA and rostral dPMC in movement initiation (Rowe & Passingham, 2001).

We did not observe a correlation between cerebellar activity and temporal complexity. Although fMR studies of timing have implicated the cerebellum (Jancke et al., 2000a; Rao et al., 1997), a study of rhythm learning (Penhune & Doyon, 2002) showed cerebellar activity in rhythm versus isochronous conditions only during an early learning phase, with significant decreases in activity thereafter. Thus, our failure to find an effect of temporal complexity in the cerebellum is consistent with overlearned performance.

It must be remembered, however, that the goal of our *initiate* condition was not to isolate activity associated with initiation of a movement, but rather to ensure that selection and movement initiation related activity did not occur during *synchronise*. Subjects were therefore asked to begin tapping during *initiate*, and it is thus likely that the activity we observed in SMA proper and more caudal dPMC during that phase is associated with movement initiation and the synchronisation with pacing stimuli. In order to distinguish more fully between activity varying with temporal complexity during sequence initiation and production phases it will be necessary to perform a further experiment in which movement is prohibited during the *initiate* phase.

4.4. Synchronisation with auditory cues

A recent imaging study of synchronised tapping (Stephan et al., 2002) showed activity in DLPFC, and PMC in association with motor adjustments to perturbations in the pacing sequence. Our observation of activity in these areas during *synchronise* could be associated with the same type of error-related processing. We also observed activity ($P < 0.05$ cluster-level threshold) in the centromedial frontal cortex during this phase.

In order to synchronise responses, our subjects had not only to produce the remembered rhythm sequence, but also to attend to pacing stimuli, recognise errors, and correct them to remain in phase with the stimuli. Processing associated with sensorimotor transformation, error recognition, and error correction therefore occurred during this condition. The error-related negativity (ERN) is an event related potential elicited by error commission, and sensitive to temporal aspects of performance (Luu, Flaisch, & Tucker, 2000) relevant to synchronised tapping. This suggests that an ERN (i.e. medial frontal cortex activation) might be expected if subjects make synchronisation errors. Indeed, anterior cingulate and SMA activity can be observed when subjects become aware of (induced) asynchronies between their tapping and auditory pacing signals (Stephan et al., 2002).

In our design, any such effect should be more obvious during *synchronise*, when external cues indicate error magnitude, than during self-paced *continue* since error awareness and therefore monitoring is greater in the former. Despite this expectation, no medial frontal activity was observed in the *synchronise* > *continue* comparison, but parametrically related activity peaking in SMA and spreading into anterior cingulate, was observed during *initiate* and *synchronise* phases. Thus, medial frontal activity was only seen when task complexity was taken into account, an observation which still supports a performance monitoring account since more careful monitoring was likely required for the more complex tasks.

4.5. Continuation tapping without external cues

Unlike *synchronise*, the *continue* phase of our task required only execution of pre-selected overlearned motor

sequences which were already being performed when the phase started. The absence of temporal complexity related activity in the frontal cortex, even at the lenient $P < 0.05$ threshold, shows that, once they have been selected and initiated, the execution of overlearned movements in absence of external cues does not require temporal complexity dependent processing in that region. Further, the absence of temporal complexity dependent activity in the frontal and prefrontal areas which were active during *initiate* and *synchronise* phases from the activation map for *continue* strengthens our arguments, presented above, that these regions are involved in complexity dependent aspects of movement selection and error monitoring/detection rather than in motor execution. The only temporal complexity dependent activity we observed during *continue* was in inferior parietal (angular gyrus), which activated only at the lenient ($P < 0.05$, corrected) threshold.

4.6. Comparison of phases

The lack, during *continue*, of activity relating linearly to temporal complexity compared to the presence of such activity during *synchronise* and *initiate* is interesting at two levels. First, it suggests that once an overlearned movement sequence has been selected and initiated, the processing involved in continuing to perform it in absence of external cues does not depend strongly upon the temporal complexity of the sequence itself. This is consistent with the proposal of Vorberg & Wing (1996), in which hierarchical relations in a rhythm, relevant to its selection and preparation, are converted to a linear sequence of intervals in execution, thus suppressing the hierarchical complexity of the original. For the purposes of this interpretation, it would be interesting to know whether variation in other types of motor complexity also fail to elicit strongly correlated activity during the continuation phase. This would provide one possible future direction for research. The absence of strongly complexity related activity during *continue* is also interesting because it suggests that the parametrically related activity observed in other phases is due to something other than motor execution, thus supporting our suggestion that some of this activity is due to selection, error monitoring, and corrective action.

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