Abstract

Two previous studies in which we recorded slow brain potential shifts over the scalp revealed performance-dependent effects that sustained one prominent model of timing mechanisms. These effects seemed to be derived from the supplementary motor area (SMA). Event-related functional magnetic resonance imagery (fMRI) was used to check this hypothesis. Brain activations were contrasted in Time production and (control) Force production tasks involving left-hand responding. These tasks, presented in mixed order, were designed to be of equivalent difficulty and involve comparable levels of attention. Several brain areas were activated in both tasks relative to baseline: the SMA, the putamen, and the lateral cerebellum. Contrasts between tasks gave clear-cut differences. Activations specific to the Time task were found in the SMA proper and the left primary motor cortex. The Force task activated the right sensorimotor cortex and the left cerebellum, and, bilaterally, the infero-parietal cortex and the insula. The main result, i.e. prominent activation of the SMA proper in relation to temporal production, corroborates our previous studies based on slow cortical potentials. The data are referred to current evidence suggesting that timing processes are subtended by a striato-thalamo-cortical pathway including the SMA.

1. Introduction

Every action takes time, but does not necessarily imply accurate timing. When this is the case, evidence from multidisciplinary sources indicates that specific timing control takes place, which involves dedicated mechanisms and structures. The neural bases of time processing in the tenth of second-to-minute range are being progressively elucidated, in part due to advances in brain imaging. A recent survey of brain imaging literature [35] concluded that a common set of brain areas is activated in relation to timing, irrespective of differences in task features.

To begin with, systematic activations are found in attentional areas such as the right parietal and dorsolateral prefrontal cortex, which are linked to selective and sustained attention, and the anterior cingulate cortex, which is viewed as a supervisory attentional system [16]. This activation pattern is consistent with the great number of behavioural studies showing that attention is mandatory for accurate timing. Indeed, the data from dual-task paradigms consistently establish that time estimates shorten whenever attention is shifted from a temporal task toward a concurrent one (Ref. [7] for review). In the frame of the prominent “internal timer” models [8,19], this bias is explained in relation to the “accumulator” metaphor: during a target interval, an internal clock emits (regular or irregular) pulses, such that the amount of pulses accumulated when the target comes to an end determines perceived duration. Attention shifting is assumed to cause partial pulse loss, hence shortening temporal estimates [5,56]. Note that due to the nature of the accumulation process, decreased or increased activation levels could also produce biases in estimates by acting on...
The duration of an auditory stimulus [24]. This study, (PET) revealed cerebellar activation when subjects judged others, one study using Positron Emission Tomography (PET) revealed cerebellar activation when subjects judged the duration of an auditory stimulus [24]. This study, however, did not establish that the contribution of the cerebellum, in the context of the task used, was specific to timing. In another PET work [38], though the cerebellum was activated in a similar task, the authors concluded that this effect was not time-specific as it also showed up when the subjects had to judge the intensity rather than the duration of the stimulus. The cerebellar activation vanished when the two tasks were contrasted (duration vs. intensity judgment). Rao et al. [48] reached the same conclusion on the basis of functional magnetic resonance imagery (fMRI). Although they found that the cerebellum was activated in a timing task, this activation did not seem to be due specifically to timing processes.

The role of the basal ganglia, in relation with the dopaminergic nigro-striatal pathway, has been extensively studied in timing mechanisms. It has been proposed that the basal ganglia play a crucial role in the encoding of temporal targets, whereas other structures, such as the cerebellum, are involved in the decisional or memory processes which, although required for time judgments, are not specific to duration encoding [17]. The first indices in favour of such basal ganglia functions came from pharmacological studies in animals. Dopaminergic agonists or antagonists induced either under- or overestimates in rats submitted to temporal conditioning schedules, as if their timekeeping mechanisms slowed down or speeded up [39]. These results are consistent with the fact that Parkinsonian patients are impaired in motor [42, 43] and sensory timing [36] but improve their performance under dopaminergic treatment. Event-related fMRI data also revealed specific activation of the striatum in a timing task (e.g. Ref. [48]); the authors considered this activation as closely related to the duration encoding phase. Taken together, these different methodological approaches strongly support the idea that the basal ganglia have a major implication in temporal encoding.

As the SMA is one of the major projection sites of the striatum to the cortex via the globus pallidus and the thalamus [50, 55], it is reasonable to assume that this cortical region may be involved in situations requiring explicit timing. This hypothesis has been documented in neuropsychological studies dealing with patients whose lesions include the SMA (Ref. [19] for review), and in numerous brain imaging studies using PET, fMRI, or event-related potentials (ERP) (Ref. [35] for review). However, these studies did not attempt to specify, in the frame of the “internal timer” models, the exact nature of the processes performed by the SMA in motor and perceptual timing.

In this line of reasoning, we examined whether the SMA might exhibit an accumulator-like activity in different timing tasks [33, 34]. We indirectly estimated the level of activity of the SMA and other cortical areas by the amplitude of a scalp-recorded slow brain potential: the Contingent Negative Variation [54]. Increased negativity in slow brain potentials is assumed to reveal increased depolarisation of apical dendrites in the underlying cortical pyramidal cells [4]. In a temporal production task, we asked subjects to produce a 2.5-s interval between two brief button presses with optimal accuracy. After each trial, the subjects received a feedback cue indicating whether the interval they had produced was accurate, too short or too long. We found that intervals longer than 2.5 s evoked larger CNVs, compared to intervals shorter than 2.5 s; correct estimates evoked intermediate amplitudes. This relationship between CNV amplitude and timing accuracy was strictly confined to the delay separating the two presses that delimited the produced interval. To improve the poor spatial resolution of EEG recordings, we estimated surface Laplacians over different cortical areas. This allowed us to establish that the relationship between CNV amplitude and timing performance appeared only over the median fronto-central region (overlying the SMA) in contrast with other frontal, central and parietal sites [34]. Since surface Laplacians are sensitive to local sources [3], we argued that the SMA was the source of these effects. A following study [33] revealed that the performance-dependent activation showed up after memory consolidation rather than in the early learning step which involved feedback control.

Given the motor functions attributed to the SMA, these data might have been restricted to motor timing. However, another task was used to indicate that they could be extended to perceptual timing [34]. When subjects had to judge whether the duration of an interval delimited by two “clicks” was longer than, shorter than, or equal to a 2.5-s target duration, CNV amplitude was larger when the interval was judged “longer”, smaller when the interval was judged “equal”, and even smaller when the interval was judged “shorter” than the target interval. Importantly, in this study, subjects were neither informed, nor aware that most probe intervals were, in fact, equal to the target. Hence, the differences observed in CNV amplitude were related to purely subjective timing. We concluded that if, as argued above, the amplitude of slow brain potentials is related to the level of activation of the sources which generate them, the relationship between CNV amplitude and timing perfor-
mance may uncover the accumulation process. Computer simulations of this process [11] are compatible with our CNV data. In sum, if the source of the performance-dependent effects is the SMA, then this structure behaves as an accumulator in timing tasks.

However, our arguments concerning the cortical source of the above-mentioned effects were only indirect. Considering that the sensitivity of surface Laplacian to a source decreases sharply with its depth [37,45], we proposed that the SMA was the most likely candidate. Nevertheless, just beneath the SMA lies the anterior part of the cingulate areas, which is also tightly connected to the basal ganglia [1]. Therefore one important question was whether the structure activated in our ERP studies was the SMA or the underlying cingulate cortex. Furthermore, the SMA is composed of two functionally different substructures (Ref. [46] for review). The pre-SMA, lying rostral to the level of the anterior commissure (VCA line), seems to be involved prominently in complex tasks and/or during learning phases, whereas the SMA proper, lying caudal to the VCA line, may rather be concerned with simple or overlearned performance. Even after Laplacian transformation, the spatial resolution of ERP data is not sufficient to separate the two SMA substructures.

In order to examine these issues, we conducted an event-related fMRI study in which we asked subjects to produce a 2.5-s target interval, using a procedure similar to that we chose for ERP recordings [33,34]. To control that the activation of the structures involved in this task was not purely related to motor, attentional or effortful processes, a task of force production was designed for comparison, and subjects were trained to produce an equivalent performance in both conditions. Thus, motor programming, attention and memory aspects were comparable between tasks. In contrast with blocked-based designs, event-related fMRI rules out possible confounds linked to subject’s differential preparatory state between tasks [14,22].

According to our initial hypothesis as regards the role of the basal ganglia and of the SMA in timing, we predicted stronger activation of these structures in the Time compared to Force task. In the inverse contrast, activation of the primary motor cortex on the hemisphere contralateral to the response should provide proper control, considering the overwhelming evidence for its involvement in response force rating (Ref. [2] for review).

2. Materials and methods

2.1. Subjects

Thirteen right-handed subjects (seven males and six females, age range 23–56 years old) took part in the experiment. This study was approved by the Ethical Committee for Biomedical Research (Marseilles). The subjects underwent two sessions in different days, one for training and one for fMRI recording.

2.2. Tasks

A Time production and a Force production task were used. The subjects held a push-button, equipped with a force transducer, with their left hand. They responded by exerting an isometric force on the button with the tip of their left thumb. The trials in each task began with the presentation of a different letter at the centre of a video screen.

2.2.1. Training session

The two targets (interval and force) were memorized in separate preliminary trial blocks which included accuracy constraints. The order of the Time and Force tasks was balanced between subjects.

2.2.1.1. Time task. The first letter appearing on the screen was a “T”, which remained visible for 1 to 1.6 s. After this variable foreperiod, the “T” was replaced by the letter “X”. Subjects had to press the button 2.5 s after the presentation of the “X”, with optimal temporal accuracy. After responding, they received an auditory feedback indicating whether the delay between the presentation of the “X” and the button press was “correct” (2.4–2.6 s), “too short” (2.2–2.4 s), “too long” (2.6–2.8 s), “much too short” (<2.2), or “much too long” (>2.8 s). The feedback consisted of recorded words emitted through a loudspeaker.

2.2.1.2. Force task. The first letter appearing on the screen was an “F”, which remained visible for 1 to 1.6 s. After this foreperiod, the “F” was replaced by an “X”. Subjects had to press the push-button with a force of 8 N, without any speed constraint. After responding, they received auditory feedback through the loudspeaker, indicating whether the force they produced was “correct” (6.5–9.5 N), “too weak” (5–6.5 N), “too strong” (9.5–11 N), “much too weak” (<5 N), or “much too strong” (>11 N).

Training in each task was continued until eight “correct” responses were obtained in a set of 10 trials. The extent of the “correct” class in each task was chosen such that this criterion could be reached after a comparable number of trials, thus implying equivalent difficulty. Next the subjects performed another block of trials in which the Time and Force tasks were randomly mixed, until the same performance criterion was reached.

2.2.2. Recording session

Three short warm-up blocks (Time, Force, with order balanced between subjects, plus a mixed Time and Force block) were given just before the subjects entered the scanner. The trials were comparable to those delivered in the training session and were meant for target rehearsal.

In the scanner the subjects rested in a supine position, with the left arm oriented parallel to the trunk, and grasped a
nonmagnetic force transducer with their left hand during the entire session. Earplugs and headphones were used to reduce scanner noise. Through a mirror system, the subjects watched a screen placed inside the scanner behind their head. The Time and Force tasks were randomly mixed between trials. Each trial began with either the letter “T” or “F” appearing for 1 to 1.6 s at the centre of the screen, which indicated which task was to be performed. This letter was then replaced by the letter “X”, after which responding took place. Contrary to the training session, no feedback was delivered after the response, and the letter “X” remained visible until the beginning of the next trial, delimiting a variable intertrial interval of 5–8 s. Hence a letter was continually displayed at the centre of the screen. It was used as a fixation point that the subjects were instructed to gaze, and ensured identical visual perception during the tasks and the intertrial intervals.

“Null” trials were inserted so as to serve as baseline for analyzing the fMRI data. They consisted of adding a 1.5–3.5 s delay to 30% intertrial intervals, thus prolonging the X period without any additional signal being visible to the subject. In total, 600 mixed trials were presented in four EPI acquisition runs of 150 trials separated by short breaks.

2.3. fMRI scanning

Scans were acquired using a 3-T MEDSPEC 30/80 AVANCE whole-body imager (Bruker, Ettlingen, Germany), equipped with a circular polarized head coil. Echo-planar imaging (EPI) was used to collect T2*-weighted volumes in the axial plane, parallel to the AC-PC line, with blood oxygenation level-dependent (BOLD) contrast. The parameters were: echo time (TE) = 35 ms; matrix size = 64 × 64; voxel size = 3 × 3 × 3 mm; 36 axial slices of 3 mm thickness were collected in each volume to cover the whole brain (TR = 3 s; flip angle 90°). Functional images were obtained in 4 runs, each of which included the task trials in randomized order. For each run, a total of 207 volumes was collected.

2.4. Data analysis

Image processing and analysis were conducted with SPM-99 [15]. The first functional volumes of each session were removed to eliminate non-equilibrium effects of magnetization. The remaining images were corrected for differences in slice acquisition time, and after this step the last two volumes were also discarded to prevent invalid temporal interpolation. All functional images were realigned to the first so as to correct for head movements between scans. They were normalized into a standard spatial reference frame [51], by matching each image to a standardised template from the MNI (Montreal Neurological Institute). Functional images were spatially smoothed to accommodate interindividual differences in anatomy, using isotropic Gaussian kernels of 6 mm. Haemodynamic responses time-locked to presentation of the preparatory cue (T or F) were modelled as single events (impulse responses) convolved with a synthetic haemodynamic response function (HRF) [15,23] in the context of the general linear model as used by SPM. The resulting data were analysed for regionally specific changes in amplitude of the haemodynamic response. In addition, a control analysis in which we took into account the duration of the common foreperiod (1–1.6 s) was used to account for possible response time breaks.

### Table 1

<table>
<thead>
<tr>
<th>Brain area</th>
<th>Voxels</th>
<th>Z score</th>
<th>p corrected</th>
<th>Number of voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(A) Time task</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMA (BA 6)</td>
<td>0 – 6</td>
<td>5.24</td>
<td>&lt; 0.001</td>
<td>401</td>
</tr>
<tr>
<td>R. Putamen</td>
<td>21 12</td>
<td>4.50</td>
<td>&lt; 0.001</td>
<td>78</td>
</tr>
<tr>
<td>L. Putamen</td>
<td>21 9</td>
<td>4.27</td>
<td>&lt; 0.001</td>
<td>80</td>
</tr>
<tr>
<td>R. Cerebellum</td>
<td>30 – 96</td>
<td>4.38</td>
<td>&lt; 0.001</td>
<td>328</td>
</tr>
<tr>
<td>L. Cerebellum</td>
<td>– 21</td>
<td>4.62</td>
<td>0.008</td>
<td>44</td>
</tr>
</tbody>
</table>

| **(B) Force task**    |          |         |             |                  |
| SMA (BA 6)            | 0 – 12   | 5.53    | < 0.001     | 433              |
| R. Premotor cortex    | – 57     | 4.09    | 0.004       | 42               |
| R. Primary motor cortex (BA 6) | 48 – 18 | 60 4.66 | < 0.001 | 193              |
| R. Middle temporal gyrus (BA 12/21) | 48 9 | – 9 4.59 | < 0.001 | 98               |
| L. Insula             | – 39     | 4.16    | 0.003       | 44               |
| R. Putamen            | 24 6     | 4.62    | < 0.001     | 132              |
| L. Putamen            | – 24 3   | 4.78    | < 0.001     | 199              |
| R. Thalamus           | 18 – 18  | 5.06    | 0.002       | 49               |
| L. Thalamus           | – 15 – 18 | 4.81 | 0.004       | 43               |
| R. Cerebellum         | 27 – 66  | 5.60    | < 0.001     | 279              |
| L. Cerebellum         | – 21     | 4.96    | < 0.001     | 235              |

| **(C) Contrast Time vs. Force** |          |         |             |                  |
| SMA (BA 6)             | 6 – 3    | 4.36    | < 0.001     | 73               |
| L. Primary motor cortex (BA 4) |– 51     | 48 4.32 | 0.018       | 42               |

| **(D) Contrast Force vs. Time** |          |         |             |                  |
| R. Primary sensorimotor cortex (BA 4/3,1,2) | 42 21 | 60 4.53 | < 0.001 | 115              |
| R. Inferior parietal cortex (BA 40) | 60 – 27 | 27 5.03 | < 0.001 | 135              |
| L. Inferior parietal cortex (BA 40) |– 60 30 | 30 3.96 | 0.005 | 55               |
| R. Insula              | 36 – 15  | 4.46    | < 0.001     | 90               |
| L. Insula              | – 39 – 3 | 4.36    | 0.011       | 47               |
| L. Cerebellum          | – 15 – 57 | 30 4.81 | 0.018       | 42               |

The coordinates are given within the framework of the standardized stereotactic atlas of Talairach and Tournois [51]. The significant increases in the BOLD contrast signal are thresholded at p < 0.001 uncorrected for multiple comparisons. We also report, at the cluster level, the number of activated voxels and the p corrected values (R. = Right, L. = Left).
s) and the average response latency of each task (2.9 s for Time vs. 1.4 s for Force) was also carried out; it yielded the same patterns of activation as the synthetic analysis we report.

Task effects were estimated according to the general linear model at each voxel in brain space. Images were adjusted using a high-pass filter of 60 s and a Gaussian temporal smoothing kernel of 4 s. Data were subject to a random-effects analysis, which points out selectively the brain regions activated in common in all subjects, and allows generalization from this subject sample to the population. Regionally specific effects of tasks were tested using linear contrasts, which produced a statistical parametric map of the t statistic generated for each voxel (SPM \( t \)). The SPM \( t \) was transformed to a map of corresponding Z values. An activation was considered significant at a thresh-

Fig. 1. Activation maps showing significant increases in the BOLD signal in the Time and Force tasks as compared to baseline \( (p<0.001 \text{ uncorrected for multiple comparisons}) \). Group analysis (13 subjects).

Fig. 2. Activation maps showing significant increases in the BOLD contrast signal in the Time task as compared to Force \( (p<0.001 \text{ uncorrected for multiple comparisons}) \). Group analysis (13 subjects).
old of \( p < 0.001 \) uncorrected for multiple comparisons for both peak value and cluster size.

3. Results

3.1. Behavioural data

Average response latency was 2.9 s (S.D. 0.34) in the Time task and 1.4 s (S.D. 0.34) in the Force task. Smaller intra-individual variability in the Time task was attested by the coefficient of variation (in average, 0.11 for Time vs. 0.25 for Force). This pattern of results indicates that subjects adequately focused on response latency in the Time task, and did not care for this parameter in the Force task, in accordance with the instructions. Note that the average latency for Time was slightly longer than the “correct” criterion (2.4–2.6 s): due to the suppression of feedback cues in the scanning session, drifts towards overestimation in the Time task as the session unfolded were noted in several subjects (cf. the intra-individual drifts in Ref. [33]).

Average force was 6.9 N (S.D. 0.89) in the Force task (target: 8 N), and 9.9 N (S.D. 1.28) in the Time task. The intra-individual coefficient of variation was comparable (0.10 for Force vs. 0.11 for Time). Absence of feedback cues also caused some force drifts in the Force task, but overall the force produced was within the “correct” criterion (6.5–9.5 N), indicating that subjects focused on the force parameter as required. In the Time task, between subjects the range of forces produced was larger, but the force chosen by each subject (without the constraints of the Force task) remained relatively constant. This suggests that self-selected response force is naturally stable.

3.2. fMRI data

Activations were first tested in each task compared to baseline (“null” trials). In the Time task, activations were found in the caudal part of the SMA (SMA proper), and bilaterally in the putamen and the lateral cerebellum (Table 1A, Fig. 1). In addition to these areas (Fig. 1), the Force task elicited activation of the left premotor cortex, the right primary motor cortex, the right middle temporal gyrus, the left insula, and the thalamus (Table 1B).

Secondly, the two tasks were directly compared. Activations specific to the Time task were found in the SMA proper and the left primary motor cortex (Table 1C, Fig. 2). The Force task yielded specific activations in the right primary sensorimotor cortex and the left cerebellum (near vermis), and, bilaterally, the infero-parietal cortex and the insula (Table 1D, Fig. 3).

4. Discussion

4.1. Timing and the SMA

The main question which motivated this study can be given a positive answer: the Time task did yield prominent activation of the SMA. This result confirms the hypothesis we based on CNV recordings [33,34]. Due to the exquisite spatial resolution of the fMRI technique, we now have

![Force - Time](image_url)

Fig. 3. Activation maps showing significant increases in the BOLD contrast signal in the Force task as compared to Time (\( p < 0.001 \) uncorrected for multiple comparisons). Group analysis (13 subjects).
stronger evidence that the performance-dependent changes in brain activation we had observed over the median fronto-
central cortex were issued from the SMA, and not from the 
 anterior cingulate cortex which is located beneath. None of 
 the analyses carried out here revealed any cingulate activa-
tion. Furthermore, the present study enables us to distin-
guish between SMA substructures: it selectively points out 
the involvement of the SMA proper.

Our fMRI data were time-locked to the trial onset, with 
the response signal occurring after a 1–1.66 s foreperiod. 
No distinction between the brain activation linked to the
foreperiod and the execution period is therefore possible;
this necessitates much greater foreperiod variability [52], 
which was incompatible with our design meant for favour-
ing efficient programming. Data from Dale and Buckner 
[10], who compared the haemodynamic response produced 
by single events and by a series of two or three events 
occurring closely in time, show that the initial slope of the
BOLD response behaves in a quite perfect linear fashion, 
and that non-linearities appear only in the later, descending
slope. In the typical HRF, the initial, sharply ascending slope
best accounts for the activation data. Considering all this, we 
amsume that our model best described the processes involved
in the foreperiod and the earlier part of the execution period.
This means that the brain regions devoted to the program-
ming of the specific task parameters (time or force) were
activated as soon as the relevant information was available
(T or F cues), as was also indicated by ERP data showing
activation differences in foreperiods as a function of advance
(T or F cues), as was also indicated by ERP data showing
activation differences in foreperiods as a function of advance
information on the upcoming timed responses [53].

However, it cannot be excluded that the later portion of 
the execution period may also contribute, even to a lesser
extent, to the measured signal. This does not imply that the
differences in SMA activation between tasks are merely due
to different trial lengths. It is assumed that a sustained
neuronal activity elicits a BOLD response that reaches a
plateau after the peak of the HRF [52]. Because the general
linear model used in the present analysis is a linear regres-
sion analysis, and because we considered in our model an
impulse response convolved with an HRF response, a long-
lasting BOLD response should not yield a larger regression
coefficient as compared to a short-lasting one. At best, the
 correlation would be stronger for short-lasting responses
than for long-lasting ones. Therefore the greater SMA
activation obtained in the Time compared to the Force Task
cannot be explained by a difference in the length of the
execution period between these two tasks.

One might consider that an impulse function is not the
most appropriate to be sensitive to the sustained activity
that is supposed to occur in a time estimation task. However, if we had used a rectangular function, the model
could have been more sensitive to the Time than the Force
task (as force production probably does not evoke sus-
tained activity), and in this case the differences in SMA
activation could have been attributed to differences in the
fit of the model to each task. Another possibility was to
use different models between tasks, hence risking that
activation could be due to differences in the modelling
functions. Everything considered, we therefore adopted the
crude (impulse) function in our model to compare the two
tasks in the same, straightforward way at the risk of
loosing sensitivity in our analysis. It appears that sensitiv-
ity was sufficient to evidence a stronger activation of the
SMA in the Time compared to the Force task, and that
controls using time varying rectangular functions yielded
similar data, as specified in Section 2.

Numerous data using ERP, MEG, PET or fMRI strongly
suggest that the SMA is involved in programming opera-
tions [16]. In particular, ERP data suggested that this
structure is involved from the beginning of the foreperiod,
as soon as prior information concerning the upcoming
response is available [53]. The common activation of the
SMA in the Force and the Time tasks relative to baseline is
likely to be due to these programming operations taking
place during the foreperiod. In addition, in the Time task,
duration encoding began when the letter X showed up on
the screen. We assume that this additional operation is
responsible for the greater activation of the SMA in the
Time vs. Force contrast. Prominent “internal timer” models
[8,17] depict duration encoding in terms of pulse accumu-
lation throughout the target interval, which might corre-
spond to spreading activation in neuronal networks. Our
ERP studies [33,34] provided arguments for such accumu-
lation mechanisms as, in motor and perceptual timing tasks,
avtivation of the median fronto-central region increased as
subjective duration lengthened. If some neuronal popula-
tions in the SMA subtend the temporal accumulator, this
implies that in the present conditions, these neurons were
necessarily activated from the occurrence of the letter X
until the final response. This sustained involvement can
account for the prominent SMA activation in the Timing
task. We suggest that the programming operations in this
context consisted of directing attention to time, that is,
selecting the neuronal populations to be involved in the
forthcoming timing period. This process might involve
moderate pre-activation of the selected neurons.

4.2. Response force

The effect of response force must be considered as one
possibly confounding factor with respect to SMA involve-
ment. According to the behavioral data, stronger response
forces were produced in the Time compared to Force task,
suggesting that motor features can be responsible for prom-
inent SMA activation. Individual controls were carried out
on this question. Response force was found to be greater in
the Time task in all subjects but one. Although an opposite
force pattern was observed in this subject, SMA activation
was visible in the Time vs. Force contrast but not in the
inverse contrast; this is consistent with the group data. In
fact, current literature provides evidence that the SMA (in
particular its caudal part) is less active in relation to self-
selected or increased grip force than during skillful force reduction, even though the latter condition induces weaker contractions of the hand muscles [28]. In our study, self-selected force corresponded to the Time task and skillful reduction to the Force task, which means that the prominent SMA activation we observed in the Time vs. Force contrast was independent of force aspects. Much higher force levels appear to be necessary to induce force-dependent increases in SMA activation [13]. Furthermore, Dettmers et al. [12] did not find any correlation between force level and activation of the dorsal part of the posterior SMA, which fits with the focus found here.

4.3. SMA proper vs. pre-SMA

The question of the relative contribution of each SMA substructure to timing can be first examined beyond the context of temporal tasks. The SMA proper, caudal to the level of the anterior commissure (Vca line), is thought to subserve simple or overlearned performance. The pre-SMA, more rostrally located, would subserve complex tasks, and is also particularly involved in the first steps of learning, when a new task is presented ([46,49] for review). These views are compatible with the fact that the SMA proper was activated in the present study. The Time task was indeed relatively simple, and relatively overlearned, as preliminary training ensuring optimal performance was given prior to the fMRI session. Nonetheless, current literature on temporal tasks indicates activation of either the pre-SMA [26,27,30,47] or the SMA proper [48], and which of these substructures is really concerned with timing is an open question. A current argument in favour of the pre-SMA is that this area may be related to internally triggered behaviour, whereas the SMA proper would rather be linked to signal-cued responses [27]. This distinction may not hold in our study, however, since responses in the two tasks were both internally and externally triggered: they were based on memorized targets but were initiated after onset of the X-cue (following an internally controlled delay in the Time task).

Contrary to the present data, activation of the pre-SMA rather than the SMA proper was observed in another recent event-related fMRI study, in which a task of temporal discrimination was used [9]. In this study, the level of activation in the pre-SMA was correlated with the subjects’ level of attention to time, which was manipulated in a dual-task context (duration + colour judgments), implying greater difficulty than the present design. Thus, taken together, all available data suggest that distinct components of the SMA may subtend time processing as a function of particular task features or of the extent of learning. As concerns task features, distinguishing between motor (cf. the present study) and perceptual paradigms (cf. Ref. [9]) is irrelevant: indeed the pre-SMA can be activated in motor timing (e.g. Ref. [27]) as well as in temporal discrimination (e.g. Ref. [48]); and the SMA proper can also be activated in both procedures (e.g. Ref. [47,48]).

4.4. Left primary motor cortex

Apart from the SMA proper, the only other region that was activated in the Time vs. Force contrast was the primary motor cortex over the left hemisphere, i.e. ipsilateral to the involved hand. Accordingly, in our ERP study which involved a timing task comparable to that used here as well as left hand responding, the response was preceded by Bereitschaftspotentials of similar amplitudes over the left and right primary motor areas [34]. These data suggest that the left hemisphere controls both hands when motor timing is involved. The fact that here the activation of the right motor cortex did not survive the Time vs. Force contrast is not surprising since left-hand responding was common to both tasks.

4.5. Activations related to force production

An entirely different pattern of activation was obtained in the Force vs. Time contrast. This pattern included the right sensorimotor cortex and the left cerebellum, and, bilaterally, the infero-parietal cortex and the insula. These data are consistent with those obtained in other studies that involved near-isometric force production [12,13,28].

The right cortical activations were located at the junction of BA 4 (primary motor area) and BA 3,1,2 (somatosensory area). Activation of the right primary motor cortex, as of the left cerebellum, obviously derived from the control on force that was exerted by the left hand. Compared to the pattern that was common to both tasks, the cerebellar activation specific to the Force task was closer to the vermis, which is consistent with Dettmers et al. [12]. Activation of the somatosensory area accounts for the core importance of proprioceptive feedback in modulating force delicately, the more as visual control was not available inside the scanner. Contralateral activation of this area was also related to skillful scaling of fingertip forces in the study by Kuhtz-Buschbeck et al. [28], together with activation of the infero-parietal cortex. In addition with motor control, this region, in particular on the right hemisphere, is also attributed attentional functions. Given that attentional demands were, as much as possible, equalized between tasks, based on the comparable task designs and on the equivalent performance levels obtained during the training session, the contribution of attention is nonetheless questionable; it should have shown up when comparing both tasks with baseline rather than in the Force vs. Time contrast. It is probable that the relatively fast presentation of mixed trials prevented decrease in sustained attention during the intertrial intervals. As to the activation specific to the Force task, it is more likely to result from the existence, in the inferior rostral parietal cortex, of a somatosensory area that has strong reciprocal connexions with the primary motor area and the spinal cord [31,41]. A similar explanation may be suggested to account for bilateral activation of the insula. This structure is typically related to emotional aspects, in interaction with limbic structures; nonetheless, it receives projections from the primary motor...
and somatosensory cortex [29] and seems to contribute to the representation of body schema [6].

4.6. Activations common to time and force production

Finally, comparing the common pattern of activation in the Time and Force tasks with the pattern specific to each of these tasks leads to one important conclusion. Although both the Time and Force tasks elicited activation of three structures, the SMA proper, the putamen, and the lateral cerebellum, the two latter structures did not survive the contrasts between tasks. This suggests that the putamen and the lateral cerebellum subtended processes that were common to both tasks, such as motor control, attention or working memory, but provided no specific contribution to the processing of either time or force.

Concerning the cerebellum, this conclusion is consistent with the PET study by Maquet et al. [38], and with the idea that this structure may be involved in memory and decision mechanisms rather than in duration encoding [18]. Comparing an on-going movement with an internal model is one of the cerebellar functions [44]. Both the Time and Force tasks implied such a comparison, which can explain why the bilateral cerebellar activation found in both tasks relative to baseline disappeared in the between-task contrasts.

The putamen, however, is generally allocated a prominent role in timing mechanisms, as a part of the striato-frontal dopaminergic pathways that modulate duration encoding (Ref. [39] for review). One prevailing view is that the timing functions of the SMA are secondary to its connections with the striatum. The present data suggest that the opposite may be true. The SMA might play the primary role in temporal encoding as it sends direct pathways to the putamen and the caudate nucleus [25]. Contribution of the basal ganglia has been related to automatic compared to more attention-demanding timing [32]. One possibility to consider is that, within the striato-frontal network, subcortical structures are devoted to automatic performance, following more or less extended training depending on the task, whereas cortical structures such as the SMA subend performance implying greater attention load. Nevertheless, the fact that bilateral activation of the putamen appeared in both tasks compared to baseline, but disappeared in the two contrasts, suggests, above all, that this activation was related to motor programming, which was common to time and force production, rather than specifically to motor timing, at least in the frame of the current paradigm.

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References

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