

RESEARCH ARTICLE

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The supplementary motor area in motor and sensory timing: evidence from slow brain potential changes

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Abstract The present study investigated the processing of durations on the order of seconds with slow cortical potential changes. The question is whether trial-to-trial fluctuations in temporal productions or judgments correspond to variations in the amplitude of surface Laplacians computed over particular scalp regions. Topographical analyses were done using the source derivation method. Subjects performed three successive tasks: (1) time production, in which they produced a 2.5-s interval separated by two brief trigger presses; (2) time discrimination, in which they detected small differences in intervals delimited by two brief clicks in comparison with a memorized standard interval; and (3) intensity discrimination (control task, devoid of time judgments), in which they detected small differences between the intensity of clicks, in comparison with standard clicks initially memorized. In order to focus on subjective differences, in the two discrimination tasks most comparison stimuli were identical to the standard, without the subjects being aware of it. At FCz, reflecting activity from the mesial frontocentral cortex that mainly includes the supplementary motor area (SMA), larger negativities were found during the longer target intervals, whether these were produced (task 1) or judged so (task 2). Those performance-dependent trends were restricted to the target intervals of the temporal tasks; they appeared neither during the 2 s preceding the target, nor during the control task. The data therefore suggest that the SMA subserves important functions in timing both sensory and motor tasks. We propose that the SMA either provides the “pulse accumulation” process commonly postulated in models of time processing or that it receives output from this process through striatal efferent pathways.

Key words Time processing · Supplementary motor area (SMA) · Slow brain potential changes · Laplacians

Introduction

Studies of time processing on the order of seconds or minutes have established that variations in temporal judgments may depend on changes in the level of attention or of activation. When a person allocates more attention to the target duration, he or she judges this duration as being longer (see for instance Block and Zakay 1996; Brown 1997; Casini and Macar 1997; Hicks et al. 1977; Macar et al. 1994). Increased activation level produces similar results, as is particularly obvious under the influence of stimulants (review in Doob 1971; Macar 1980), and, more specifically, of dopaminergic agonists (Meck 1996). One interpretation of these effects, whether induced by attention or activation, is that internal pulses are stored during the to-be-estimated interval, and that pulse accumulation is sensitive to various factors. The total amount of pulses accumulated at the end of the interval would determine the temporal judgment. These hypotheses are based on models of an “internal timer” which are prominent in the study of time processing (Church 1984; Gibbon et al. 1984; Thomas and Weaver 1975).

The following experiments originated in the idea that any variation in temporal performance deriving from attention or activation factors should be reflected in slow brain potential changes, given the “threshold regulation theory” proposed by Birbaumer et al. 1990 and Rockstroh et al. 1993. This theory states that cortical excitability is continuously regulated via feedback loops and that this regulation is reflected by changes in brain potential. Birbaumer and collaborators argued that increased negativity recorded over the scalp indicates increased activation, reflecting depolarization in the apical dendrites of pyramidal neurons: Thresholds of neuronal assemblies are adjusted through thalamocortical circuits (Skinner and Yingling 1977) to ensure appropriate levels

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of excitability, with lower thresholds inducing larger negative or smaller positive slow waves.

These changes should appear only over the cerebral regions concerned with the particular type of processing being performed. Hence, they can indicate which region is concerned, on the condition that an appropriate topographical analysis is achieved. Because of volume conduction, simple monopolar recordings are inadequate to disentangle the activity of close brain regions (Nuñez 1981). One of the methods that have been designed to separate a limited active locus from surrounding activation consists of computing Laplacian derivations (review in Law et al. 1993; Vidal et al. 1992). Laplacians mostly reflect radial sources from superficial layers and are relatively insensitive to deep sources. Hjörth's source derivation method (1975), based on an approximation of the surface Laplacian computed over selected scalp loci, was chosen in the present study to address the question of which brain areas are involved in temporal performance.

Our choice of electrode locations is guided by recent evidence concerning the involvement of striatocortical pathways in the timing of durations on the order of seconds (Gibbon et al. 1997; Macar 1998; Meck 1996). The nigrostriatal dopaminergic system is impaired in Parkinson's disease, which includes sensory and motor timing deficits (Malapani et al. 1998; Pastor et al. 1992). Data obtained with functional magnetic resonance imaging (fMRI) show that the striatum, the thalamus, and the frontal cortex are prominently activated in healthy subjects engaged in a timing task (Hinton et al. 1996). Activation of the prefrontal cortex is also observed with other methods, such as positron emission tomography (PET) (Lejeune et al. 1997; Maquet et al. 1996) and the recording of brain potential changes (Casini and Macar 1996a, 1996b; Elbert et al. 1991). Given its acknowledged involvement in attentional processes (review in Fuster 1989), this region is thought to account for the influence of attention on temporal performance (Gibbon et al. 1997; Casini and Macar 1996a).

One major component of the striatocortical loops implicated in basic timing processes is the supplementary motor area (SMA), which forms the main part of the mesial frontocentral cortex, rostral to the primary motor cortex (M1). Recent evidence promotes the view that the SMA, in the scope of its motor programming functions (reviews in Goldberg 1985; Tanji 1994), is concerned with temporal regulation. Systematic changes in Laplacians were observed over this area as a function of the particular response duration for which a subject was preparing (Vidal et al. 1995). Further, the SMA is activated during the production of a memorized rhythm (Rao et al. 1997), a task impaired in the case of SMA lesions (Halsband et al. 1993). The mesial central cortex is also involved in musicians while they tap different rhythms with each hand (Lang et al. 1990).

On these grounds, the prefrontal and the mesial frontocentral regions were our primary target loci for Laplacian computations. We chose the M1 as another relevant

locus because a motor temporal task was part of the design. All these sites were expected to reveal differences in activity depending on temporal performance. A parietal locus was chosen in order to obtain control data, as previous investigations showed no temporal performance-related changes in this region (Vidal et al. 1995).

The Laplacians were analyzed during temporal performance in two situations. Among the numerous timing procedures that exist, a distinction is usually made between production and estimation tasks. The former concerns temporal regulation of motor responses, whereas motor aspects are restricted in the latter, in which a person judges the duration of external cues. Whether motor and sensory timing tasks involve identical mechanisms is an unanswered question, although some data suggest that they do. Correlations have been found between individual performance of both types of task (Keele et al. 1985), and lesions of the lateral cerebellum (Ivry and Keele 1989) or of striatal nuclei (Malapani et al. 1998; Pastor et al. 1992) produce deficits in both sensory and motor timing. In order to determine whether common cerebral areas are sensitive to both motor and sensory temporal performance, we used a production task and a task involving the discrimination of externally driven intervals; both used with a target of 2.5 s. In the former task, the analysis was conducted on the basis of the variable intervals that the subjects emitted. In the discrimination task, no measurable differences were introduced between most target durations, without the subjects being aware of this fact, so that the analysis could be focused entirely on subjective differences. As a control, we also used a comparable discrimination task with intensity rather than duration as the target feature.

Another important question is whether the relation we expected between Laplacians and temporal performance, if it showed up, would reflect sustained attention specifically devoted to time processing, or, rather, only global and nonspecific fluctuations of the level of activation during the session. This question was addressed in all tasks by analyzing the Laplacians not only during, but also before, the target intervals.

Subjects were selected on the basis of practice trials provided a few hours to a few days in advance; sufficient accuracy in the three tasks was the inclusion criterion (as described thereafter). The experimental tasks were presented individually in a between-subject semibalanced order: The two discrimination tasks were balanced; the production task, that implied extended training with knowledge of results, was always presented last in order to avoid the possibility that this training would counteract the subjective effects searched in the temporal discrimination procedure (devoid of feedback). For the sake of clarity, hereafter we describe each paradigm separately.

Experiment 1: time production

Materials and methods

Subjects and procedure

Ten 22- to 30-year-old subjects gave their informed consent to participate in this experiment. Male right-handed subjects were chosen exclusively to reduce interindividual variability. The subject was seated in a faradized room, in front of a 50×34-cm white panel provided with five diodes. The task was to produce a 2.5-s interval separated by two brief presses (R1 and R2, both less than 0.3 s) on a trigger handled with the left thumb. Feedback was delivered on the panel 0.5 s after R2. It consisted of the illumination, in the center of the panel, of one of three green diodes aligned horizontally, indicating whether the interval produced was too short (left diode), correct (middle diode), or too long (right diode). The duration of the feedback was 1 s. The “too short,” “correct,” and “too long” ranges were, respectively, 1.8–2.4 s, 2.4–2.6 s, and 2.6–3.2 s. A larger red diode (located above the green ones) was illuminated in addition to the left or the right green diode when the interval produced was less than 1.8 s or greater than 3.2 s, in which case the trial was rejected and replaced. A total of 252 successful trials were required. The fifth (yellow) diode was placed just below the green ones and was used for visual fixation during scalp recordings. This diode was lit from 0.5 s after the end of the feedback until R2.

No model for the target interval was presented. In the preliminary practice trials, the subject learned the target by observing the feedback diodes. The practice session ended when at least three correct intervals were produced in succession. This was obtained after 16–55 trials depending on the subject. (In addition to the ten subjects retained for recordings, three others were eliminated because they could not fulfill the accuracy requirements.)

Scalp recordings

During the recording session, the subject was required to produce intervals when he or she felt ready, provided that a few seconds had elapsed since the last trial. The scalp recordings were obtained both during a 2-s period preceding the R1–R2 interval, with a 100-ms baseline measured at the beginning (backward analysis time-locked to R1), and during the standard interval, with a 100-ms baseline measured before R1 (backward analysis time-locked to R2). Sampling frequency was 250 Hz. The amplifier bandpass was 0.01–100 Hz (6 dB/octave). Electrode impedance was kept below 5 kohms. Trials with eye movements or other visible artifacts were rejected. The most anterior electrodes, placed close to the eyes, detected ocular artifacts.

Thirteen Ag/AgCl electrodes were located symmetrically over the scalp (Fig. 1). The approximation of the surface Laplacian was computed at seven “nodal” electrodes by using the source derivation method (Hjörth 1975) to evaluate local activation. Each nodal electrode was placed at the center of an equilateral triangle formed by three other electrodes (MacKay 1983) at a distance=1/10 (inion-nasion + tragus-tragus). The nodal electrodes were located over three prefrontal sites (one midline and two lateral), a fronto-central site corresponding to the SMA (FCz location in the international 10–20 system; Jasper 1958), the left and right M1 (C3 and C4), and a centroparietal site (CPz). Among these seven selected sites, we expected the first six to be involved in some aspects of the temporal performance, whereas the last one was used as control. Two additional electrodes placed over the right and left mastoids served as reference and ground, respectively.

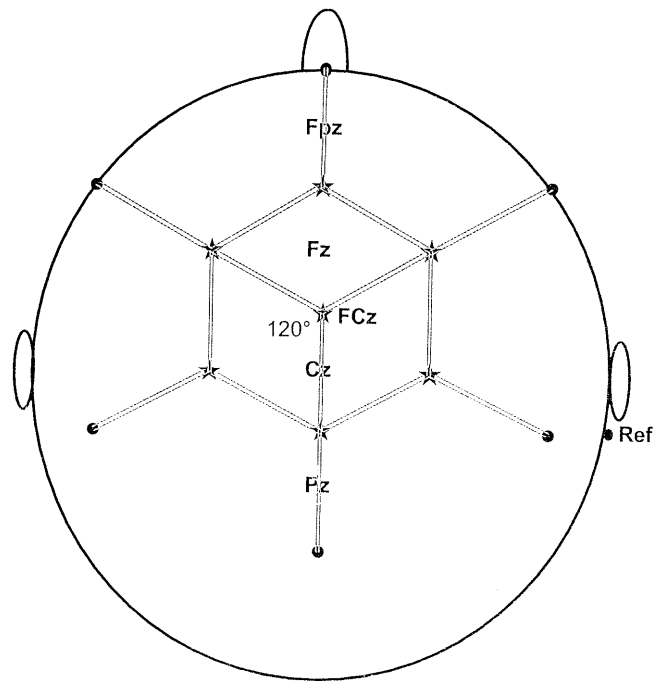


Fig. 1 Electrode configuration designed to calculate Laplacians at the seven nodal leads (tagged by stars). Three electrodes forming an equilateral triangle are placed around each nodal electrode

Results

The intervals produced were sorted into 0.2-s categories. Three categories designated as “short” (2.2–2.4 s), “correct” (2.4–2.6 s), and “long” (2.6–2.8 s) were compared. Overall, 77% of the trials were included within these ranges: 33% “correct,” 22% “short,” and 22% “long.” The records obtained during the target intervals were sorted as a function of these categories. After Laplacian computations at each nodal site, a relation between amplitude and response category was observed at FCz: with respect to negativity, “long” > “correct” > “short.” The left part of Fig. 2 illustrates the Laplacians obtained at FCz during the target interval. An analysis of variance (10 subjects × 3 categories) was done at each nodal electrode with area measures based on the integral under the Laplacian waveforms in the 1.5 s preceding R2. Significant differences between categories were obtained at FCz ($F_{2,18}=4.99$, $P<0.05$) but not at the other sites ($F_{2,18}=2.02$ and 2.59 at C3 and C4, respectively; $F_{2,18}<1$ in all other cases). Paired comparisons within the 1.5-s period at FCz showed significant differences between the “long” and “short” categories ($F_{1,9}=7.43$, $P<0.05$), but “correct” was not different from “long” ($F_{1,9}=2.15$) or from “short” ($F_{1,9}=4.07$). The right part of Fig. 2 illustrates the Laplacian data during the 2-s period preceding R1. It may suggest that the amplitude differences began to develop just prior to R1; however, no significant differences were obtained during the pre-R1 100- or 500-ms periods ($F_{2,18}<1$). In all sites, the traces overlapped in the pre-R1 interval and were close to baseline, except for the

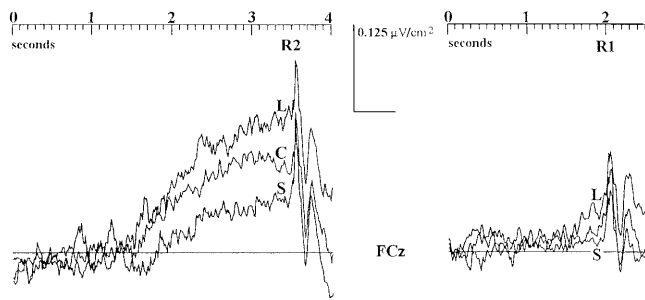


Fig. 2 Laplacians obtained at FCz during the target interval of the time production task (experiment 1), as a function of subject's performance (L "too long," C "correct," S "too short"). *Left traces* backward recording time-locked to the second trigger press (R2), *right traces* backward recording from the beginning of the 2-s interval, time-locked to the first trigger press (R1). Amplitude (negative up) on ordinates, time on abscissas. Mean of ten subjects

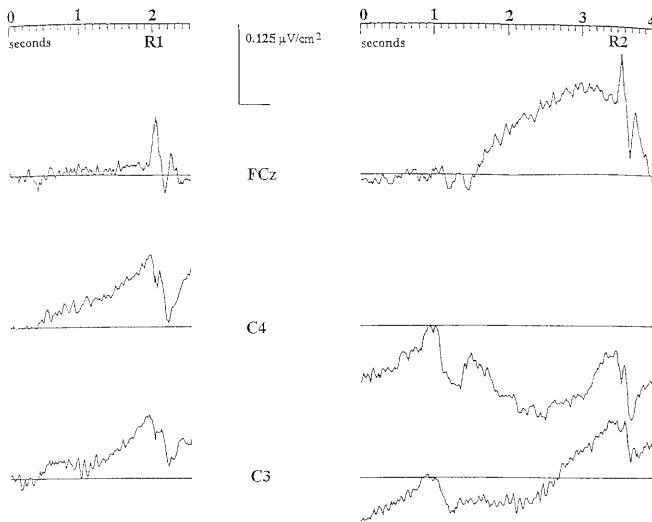


Fig. 3 Laplacians obtained at FCz (*upper traces*), C4 (*middle traces*), and C3 (*lower traces*), time-locked backward to the first (R1) and second (R2) trigger presses (respectively, *left and right part of the figure*) in the "correct" responses of the time production task (experiment 1). Amplitude (negative up) on ordinates, time elapsed before R1 or R2 on abscissas. Mean of ten subjects

pre-R1 Bereitschaftspotential (BP) visible over M1. Figure 3 illustrates the Laplacians obtained in the "correct" response category before R1 (left) and before R2 (right) at FCz (top), C4 (middle), and C3 (bottom). It shows that the BP preceding both trigger presses at C4 and C3 is entirely different from the large negativity that appears at FCz before R2, but not before R1. Figure 4 provides the corresponding monopolar data, in which a negative shift resembling a BP appears before R1 and R2 at those three sites, including FCz.¹

¹ Note that in Figs. 3 and 4, at C4, the negative shift corresponding to the BP preceding R2 is detectable despite the slow positive shift observed in the DC level

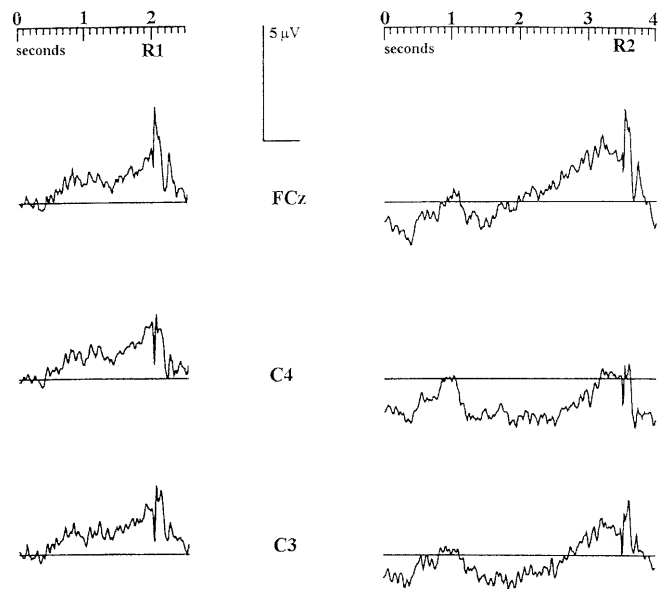


Fig. 4 Monopolar data obtained at FCz (*upper traces*), C4 (*middle traces*), and C3 (*lower traces*), time-locked backward to the first (R1) and second (R2) trigger presses (respectively, *left and right part of the figure*) in the "correct" responses of the time production task (experiment 1). Amplitude (negative up) on ordinates, time elapsed before R1 or R2 on abscissas. Mean of ten subjects

Discussion

The first question to consider here concerns the origin of the effects recorded at FCz, the only location that yielded significant differences as a function of response categories. Because the Laplacian operator acts as a high-pass spatial filter, Laplacian derivations are supposed to be sensitive to local sources only (Nuñez 1981). Hence, the effects we observed at FCz very likely come from the mesial frontocentral cortex, mainly including the SMA. With monopolar recordings, activities originating from the lateral sensorimotor or premotor cortices may add up and produce an artifactual maximal activity over mesial central sites because of volume conduction effects (as modeled by Bötzel et al. 1993), but this risk is reduced with the Laplacian method. If our Laplacian data at FCz were sensitive to sensorimotor sources, before R1 they should as well reveal summed activities from the left and right M1s. Figure 3 shows that this is not the case: after source derivation, C3 and C4 reveal underlying activity before R1 whereas FCz does not, in contrast with what appears on monopolar records (see Fig. 4). Anterior and posterior sources can also be ruled out, as the analysis of variance showed that the nodal electrodes placed over the three prefrontal and the centroparietal sites were insensitive to the temporal performance. Performance-related activities do not seem to originate in premotor sources either: if so, they should be detectable at C3 and C4 as well as at FCz. Finally, it should be noted that the anterior cingulum (which includes a motor area) is situated beneath the SMA and, hence, is a plausible source of activation at FCz. However, as Laplacians are almost blind to activities from

deep sources (Pernier et al. 1988), cingulate sources should not be visible unless they are extremely intense.

We therefore favor the interpretation that, in the present experiment, the mesial frontocentral cortex, and in particular the SMA, is the locus where significant differences in activation appeared as a function of response categories. Larger negativities corresponded to longer produced durations and smaller negativities to shorter ones. Secondly, no effect of response category was seen during the 2 s preceding R1; in fact, mostly overlapping traces close to baseline were observed. Thirdly, there was no activation at FCz prior to R1 (despite what the monopolar data suggested), whereas a BP appeared on the M1 before both R1 and R2. These trends suggest that producing brief durations under accuracy constraints involves the mesial frontocentral cortex and in particular the SMA, and that this involvement is restricted to the to-be-estimated interval, even if this interval starts with a motor response.

The level of negativity observed with scalp recordings is thought to reflect the amount of simultaneously depolarized apical dendrites in pyramidal neurons, with larger negativity corresponding to a larger amount of depolarization (Birbaumer et al. 1990). This suggests that greater activity occurred in the mesial frontocentral cortex when long compared to short durations were produced. These data are congruent with the pulse accumulator process postulated in prominent models of timing (Block and Zakay 1996; Church 1984; Thomas and Weaver 1975; Zakay 1989). Computer simulations of such an accumulator are based on groups of neurons needing no complex properties (see, e.g., Desmond 1990; Miall 1993). In Desmond's (1990) two-dimensional planar array of units, activation spreads from one initial element triggered by the onset of the target interval towards some other units in a contiguous column, which in turn activate adjacent ones (in Desmond's example, each unit activates three other ones). Spreading activation results from temporal/spatial summation of inputs; in contrast, propagation decays in all units that receive only one input, so that after the initial rise, activation finally comes to an end. The amount of activation in the net of units follows an inverted-U-shaped function, and the strength of the behavioral timing response is maximal at its peak. In Miall's (1993) version of the temporal accumulator, the input comes from an internal clock that periodically triggers a group of neurons as the target interval elapses. Those neurons have a low probability of being switched on at each clock beat, and thereafter a lower probability of switching off, as Miall assumes that neurons may not be capable of reliable activity over long periods. Here no spreading activation from one unit to another is postulated, but additional units are recruited at each clock beat, so that the total amount of activity increases with time.

It is reasonable to assume that activation and attention factors can modify the excitation threshold of the units involved in such types of accumulators, and, hence, influence either the number of units involved or the inten-

sity of their responses (in Miall's version, activation and attention factors may also influence the rate of clock beats; however, ultimately, this may have similar consequences on pulse accumulation). If we imagine, as in Desmond's model, that in our temporal production task R2 is emitted when activation peaks, then threshold reduction should provoke larger activation during the target interval; furthermore, it should delay R2, because activation is prolonged as the number of units increases. This pattern is congruent with the trends revealed by our Laplacian data as a function of response category.

Along these lines, we propose that the mesial frontocentral cortex, and perhaps the SMA itself, contains neuronal assemblies in which the level of activity increases during a to-be-estimated interval on the order of seconds. The SMA might be the neural substrate of the temporal accumulator postulated in popular models of time processing. Alternatively, because it receives major efferent connections from striatal structures via the ventrolateral part of the thalamus, it might reflect the output of a temporal accumulator located in the striatum, in line with current hypotheses promoted on the basis of data from brain lesions and brain imaging, among others (Gibbon et al. 1997; Meck 1996). In this case, the role of the SMA in connecting this central temporal device with motor activity should be prominent.

The temporal accumulator is supposed to store a certain number of units for a brief period at each trial, thereby acting as a working memory for temporal information. Neuropsychological data suggest that the SMA plays a role in memory for temporal parameters and acts as a buffer in which response specifications are held. In particular, patients suffering from lesions in this area can produce rhythmic finger tapping in synchronization with an auditory model but are unable to continue tapping at the same rhythm once the model is no longer present (Halsband et al. 1993). fMRI shows that the caudal SMA is activated, together with the putamen and the ventrolateral thalamus, in healthy subjects performing such a "continuation" tapping task (Rao et al. 1997). Activation of the mesial central cortex is also observed after analysis of radial current density in musicians while they are bimanually tapping distinct rhythms (with a 2:3 ratio defined beforehand), and this activation precedes the performance by several seconds (Lang et al. 1990).

The data obtained prior to each trigger press support the hypothesis that the mesial frontocentral cortex, and in particular the SMA, is involved in timing processes. They also suggest that the SMA is not systematically activated prior to the M1 in spontaneous unimanual movements. In contrast with monopolar recordings, the Laplacians revealed underlying activity at FCz before R2 but not before R1. At C3 and C4, BPs appeared before both trigger presses. An important factor to consider is that only R2 indexed temporal accuracy, as it ended the estimated interval. Thus, it seems likely that activation of the SMA may depend on the specific constraints of a task, and in particular on whether time processing is or is

not involved. Previous Laplacian data obtained by Vidal et al. (1995) in a choice reaction-time task also pointed to this hypothesis; further, they suggested that, because the R1–R2 sequence was to be produced as soon as possible after a signal, the target duration was programmed in advance, which resulted in activating the SMA before R1 rather than before R2.

Absence of SMA activation prior to simple movements was previously reported on the basis of neuromagnetic recordings but was attributed to the cancellation of two equivalent dipoles of opposite orientations (Kristeva et al. 1991). With monopolar recordings, similarly to what we observed at FCz, Deecke and Kornhuber (1978) detected a BP over the vertex before it appeared over the M1. However, dipole modeling suggested that this type of activity can result from symmetrical activations of the ipsilateral and contralateral M1 which summate over the vertex (Bötzel et al. 1993).

Finally, it should be noted that the occurrence of a BP over the left M1, ipsilateral to the motor responses in the present task, is consistent with the ipsilateral activation of the M1 reported after dipole analysis of neuromagnetic fields preceding finger movements (Cheyne et al. 1995). Further, the left M1 seems to be especially concerned with the execution of motor sequences that require accurate timing (Chen et al. 1997). It is possible, however, that mirror activity could take place in the right hand while the left hand executes the sequence of trigger presses, as was shown by EMG records in the case of simple ipsilateral movements (Kristeva et al. 1991).

Experiment 2 was designed to further evaluate the activation of the mesial frontocentral cortex with regard to the temporal accumulator mechanism. We wanted to determine whether this region is also involved in temporal performances that are not mediated by motor sequences. A positive answer to this question might suggest that the SMA, beyond its acknowledged motor functions, plays a ubiquitous role in time processing whatever the particular task parameters. A discrimination task focused on the duration of an interval delimited by two auditory clicks was chosen as the test procedure. Knowledge of results was not provided; further, without the subjects being aware of it, in most trials no actual difference existed between the target durations to be discriminated. The idea was that spontaneous fluctuations of temporal judgments would appear, and that they would be revealed by different amplitudes of the Laplacians at FCz. Spontaneous fluctuations in subjective duration during constant intervals may be interpreted as due to variations in the excitation threshold of units involved in the temporal accumulator, in the same line as our preceding suggestions.

Finally, an important control of those suggestions was to check whether the level of activation at FCz would still be sensitive to performance if temporal parameters were not involved. With this aim, Laplacians were also analyzed in an equivalent discrimination task focused on stimulus intensity instead of stimulus duration.

Experiment 2: time discrimination

Materials and methods

The same subjects as in experiment 1 were used. In addition to the white panel containing five diodes, a loudspeaker was located about 1.50 m in front of the subject. The task was to detect small differences in the duration of a target interval delimited by two clicks (100 ms, 1000 Hz, 45 dB). The recording session was preceded by practice trials. First, the standard (2.5 s) was presented 10 times. Next were 30 trials in which three different durations occurred with equal probability in a random order: the 2.5-s standard, one slightly shorter duration, and one slightly longer duration. All durations consisted of intervals delimited by the same two clicks. The shorter and longer durations were adjusted individually in order to obtain at least 80% correct responses: They differed from the standard by 200–280 ms depending on the subject.

The subject's left hand rested on a metal plate provided with five digital disks. After each presentation of an interval, the subject decided whether it was shorter than, equal to, or longer than the memorized standard. The response was given with the index finger, the middle finger, or the ring finger. Response latencies less than 1 s were required, longer latencies being considered "no responses" (the idea was that responses having too long latencies would not reflect subjects' spontaneous feelings). Immediately after response execution, the thumb and the little finger were used to indicate the person's confidence in each judgment, "sure" or "not sure." (Unfortunately, this index enabled no consistent analysis because of large intersubject variability.) One second after the second click, feedback was delivered on the panel. One of the three green diodes indicated the actual duration of the target interval: shorter than (left diode), equal to (middle diode), or longer than (right diode) the standard. The diodes were illuminated for 1 s.

The practice session was repeated, if necessary, until the required level of performance was reached. Next, the recording session took place, including 162 trials. The procedure was similar with one key exception: without the subject's knowing it, now most intervals were identical. There were 80% standard intervals of 2.5 s, plus 10% shorter and 10% longer. No feedback was given.

Another discrimination task, focused on signal intensity rather than duration, was used for comparison. Each trial unfolded in a comparable way. Two auditory clicks delimited a 2.5-s interval. Their intensity (identical for the two paired clicks) was manipulated between trials. The standard intensity was 45 dB. In practice trials, after ten presentations, the standard was mixed with one slightly weaker and one slightly stronger intensity, adjusted individually in order to obtain at least 80% correct responses. Maximal intensity ranges were 40–50 dB. In the recording session, without the subject's knowing it, there were 80% clicks of standard intensity, 10% weaker and 10% stronger. The subjects decided whether the clicks were weaker than, equal to, or stronger than the standard (three fingers), and then indicated their confidence level (two fingers).

In both discrimination tasks, during the recording session the subject was required to fixate the yellow diode placed at the center of the panel. It was lit from 2.5 s preceding the first click until the subject's response. The intertrial interval, from the second click to the next lighting of the diode, was 3 s. Electrode configuration and technical details were as in experiment 1. Laplacians were computed both during the between-clicks interval and during the 2 s preceding the first click. Here forward rather than backward analyses could be done because S1 and S2 took place at predetermined times.

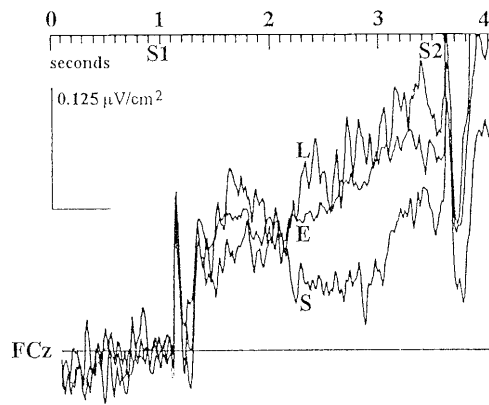


Fig. 5 Laplacians obtained at FCz during the target 2.5-s interval of the temporal discrimination task (experiment 2), as a function of subject's judgment (*L* "too long," *E* "equal," *S* "too short"). Amplitude (negative up) on ordinate, time on abscissa (the two clicks are marked as S1 and S2). Mean of ten subjects

Results

Duration discrimination

Overall, 43% of the 2.5-s intervals were judged equal to the standard, 29% shorter and 19% longer; 9% yielded no response. The small proportion of nonstandard intervals induced a high proportion of correct responses (67%), indicating that the subjects were attentive. The records corresponding to the target interval were sorted as a function of judgment category. After Laplacian computations at each nodal site, a relation between amplitude and judgment category was observed at FCz: with respect to negativity, the pattern was "longer">"equal">"shorter". Figure 5 illustrates the Laplacians obtained at FCz during the target interval. The analysis of variance (10 subjects \times 3 categories) was done in the second half of the interval (1.25–2.5 s), where the pattern was clearer. It was applied to area measures based on the integral under the Laplacian waveforms computed at each nodal site. Only FCz revealed a significant effect of judgment category ($F_{2,18}=4.12$, $P<0.05$; $F_{2,18}<1$ in all other cases). Paired comparisons at FCz showed that the "shorter" category significantly differed from "longer" ($F_{1,9}=5.25$, $P<0.05$) and "equal" categories ($F_{1,9}=5.81$, $P<0.05$), the two latter categories showing no significant differences ($F_{1,9}=0.83$).

During the 2 s preceding the target interval, the Laplacian waveforms corresponding to the three judgment categories overlapped and were close to baseline (see Fig. 5).

Intensity discrimination

In the standard trials, 44% of the clicks were judged to be equally intense as the target, 15% weaker and 31% stronger; 10% yielded no response. Most nonstandard trials induced correct responses (80.5%). As in the dura-

tion discrimination task, the records corresponding to the target interval were sorted by judgment category. Laplacian waveforms were computed at each nodal site and were submitted to analysis of variance with area measures taken in the second half of the interval. There was no significant effect of judgment category at any location (FCz, C3, and C4, left prefrontal cortex: $F_{2,18}<1$ in each case; right prefrontal cortex: $F_{2,18}=1.51$; medial prefrontal cortex: $F_{2,18}=3.50$; CPz: $F_{2,18}=2.81$). The Laplacian waveforms corresponding to the three judgment categories overlapped and were close to baseline during the 2 s preceding the first click.

Discussion

The Laplacians obtained in the duration discrimination task were comparable to those found in the time production task of experiment 1. At FCz, larger negativity appeared when the target duration was judged to be "long" rather than "short" (with intermediate amplitudes for "equal" judgments) in comparison with the standard. This relation was obtained in the absence of objective differences between the durations tested. Hence, it depended only on subjective sources. Furthermore, no performance-dependent trend appeared either during the 2 s preceding the target interval or during another discrimination task that had exactly the same structure but involved no temporal estimation. This task provided a necessary control: had any mechanism common to the duration and the intensity discrimination tasks (for instance, working memory processes, or motor preparation of the relevant finger) been responsible for performance-dependent Laplacians over the SMA, similar trends should have been observed in both tasks. Everything considered, our data indicate that the observed pattern reflects the specific activation of timing mechanisms involved within the target duration.

These data suggest that if, as we argued when discussing experiment 1, the Laplacian derivations at FCz actually reflect the activity of the SMA, then this region may contain neural networks involved in the temporal accumulator mechanism. Larger Laplacian negativity would reveal increased activation of the relevant neurons as proposed by the threshold regulation theory (Birbaumer et al. 1990; Rockstroh et al. 1993). Changes in the contents of the accumulator were likely to derive from spontaneous fluctuations of the level of activation or of attention from one trial to another. In the present discrimination task, the subject memorized a standard interval during the practice trials; thereafter this temporal reference was to be compared with the interval elapsing at each trial. Following the lines described above, if the subject's level of activation increased on one trial, the units forming the temporal accumulator might yield increased excitation due to threshold reduction. Hence, when S2 occurred (after a constant delay following S1), the level of activation within the group of units was relatively high as compared to the level predefined in refer-

ence memory. In this case the subject should judge the actual interval to be longer than the memorized standard. The opposite outcome should elicit "short" responses. This pattern is in agreement with our data.

A number of studies concerned with time processing in humans and animals have shown that stimulus duration is judged longer when the level of activation or attention increases. The available evidence comes from pharmacological studies, research on cerebral lesions, and performance of healthy subjects in dual-task paradigms (Block and Zakay 1996; Brown 1997; Doob 1971; Gibbon et al. 1997; Macar et al. 1994; Meck 1996). For example, if a person is given stimulants such as amphetamines and asked to estimate a target duration on the order of seconds, he or she will tend to judge it longer than before drug intake; opposite effects are induced by sedatives. Studies contrasting the effects of dopaminergic agonists and antagonists on rats submitted to temporal conditioning schedules suggest that the dopaminergic system is concerned with temporal processing in the second-to-minute range (review in Meck 1996). The prevailing interpretation is in terms of an "internal timer": internal pulses accumulate at various speeds (depending on activation) during the to-be-estimated interval (Church 1984; Treisman et al. 1992). Subjective duration, which is positively correlated with pulse number, therefore varies. The exact nature of the pulses is unclear; notwithstanding, the "internal timer" model also accounts for the fact that, in dual-task paradigms including temporal and nontemporal components, subjective duration shortens as a person allocates more attention to nontemporal and, hence, less attention to temporal components (review in Brown 1997). Here again the accumulation process may be concerned; for instance, duration shortening might result from the fact that the relevant units have higher thresholds when attention is diverted from the target interval, therefore reducing the amount of activation reached at its end.

General discussion

The present temporal tasks led the subjects to allocate sustained attention to a target interval on the order of seconds. Therefore the spontaneous fluctuations of subjective duration from one trial to another can be the result of small changes in the level of activation or in the level of attention; both were closely entangled. Sustained attention has been considered equivalent to vigilance (Posner and Petersen 1990). It is also known, in particular from dual-task experiments, that attending to time entails a cost in attentional resources. The variations observed in subjective duration can be expected to be caused, for instance, by factors modifying the speed of metabolic changes or thresholds for synaptic transmission, and hence acting on the amount of cumulative activation during the target interval.

The two temporal paradigms used in the present study elicited activation of the mesial frontocentral cortex, as

revealed by the finding that computed Laplacians at FCz were sensitive to performance. These data suggest that, among its other functions, this region, which mainly includes the SMA, contains the temporal accumulator described in prominent models of time processing (Block and Zakay 1996; Church 1984; Thomas and Weaver 1975; Zakay 1989). Alternatively, through thalamic relays, it may receive output from a temporal accumulator located in striatal structures (Gibbon et al. 1997; Meck 1996) and translate this output into sensorimotor activities.

A prevalent opinion is that the SMA is involved in motor, but not sensory, processing. For example, patients with lesions in the SMA show deficits on tasks requiring smooth motor coordination and have difficulties in reproducing a rhythm from memory, but are able to discriminate auditory rhythm patterns (Halsband et al. 1993). However, Lim and collaborators (1994) found that, in a few cases, electrical stimulation of the SMA and of the upper part of the cingulum evoked somatosensory sensations, such as numbness, tingling, or pressure sensations. They concluded that the SMA is a mixed sensorimotor area with prominent motor representation. Besides, the SMA concerns internally driven behavior (Goldberg 1985). Single cell recordings in animals (Mushiake et al. 1991) and PET studies in humans (Deiber et al. 1991) indicate that the SMA is activated when particular motor sequences are produced spontaneously rather than cued by external signals. Time estimation is an internally driven behavior; this was especially true in our discrimination task, which involved no objective differences in the target stimulus duration. Thus, our data strongly support the hypothesis that the mesial frontocentral cortex, and perhaps the SMA, plays a key role in the internal representation of time (Halsband et al. 1993; Rao et al. 1997; Vidal et al. 1995) by showing that this hypothesis holds not only for motor but also for sensory timing tasks, when durations on the order of seconds are used.

This conclusion may be explained in one of three ways. First, as suggested above, the SMA may perform other than motor functions, and the present data add to the available evidence (Ivry and Keele 1989; Keele et al. 1985; Pastor et al. 1992) indicating that some common mechanisms subserve motor and sensory temporal tasks. Second, time processing may rely on motor representation whatever the particular task parameters. Motor preparation processes are intimately linked to time processing (Macar and Bonnet 1997; Requin et al. 1991). Motor inhibition, which is likely to involve the SMA (Tanji 1985; Vidal et al. 1995), is of major importance in timing, as shown by data from animals (review in Richelle and Lejeune 1980) and children (review in Pouthas et al. 1986). Indeed, a number of errors in temporal tasks simply reflect difficulties in inhibiting motor responses. Further, from a developmental point of view, time processing is thought to originate from waiting behavior (Fraisse 1957). Finally, a much more restricted possibility is that in our study a motor representation of the target

delay was induced in the discrimination task because time production was required in another block of trials. Although the latter task was achieved after the discrimination procedure in all subjects, this possibility cannot be entirely ruled out as practice trials for all tasks were provided in a preliminary session taking place a few hours or days before recordings.

In addition to the SMA, the prefrontal cortex receives afferences from the striatum via pallidothalamic relays. These pathways are considered essential to time processing with respect to the postulated process of pulse accumulation (Meck 1996). In the present study, the prefrontal sites did not exhibit any significant relation between Laplacian amplitude and subjective duration. Our previous Laplacian (Casini and Macar 1996a, 1996b) and PET data (Lejeune et al. 1997; Maquet et al. 1996) suggest that the prefrontal cortex is more concerned with attention mechanisms in general than with basic timing processes, because the processing of both nontemporal and temporal parameters induced its activation in similarly attention-demanding tasks. The PET data contrasted activation levels between tasks, whereas the Laplacians, in addition to between-task comparisons, were also used to contrast levels of performance within a task (as was the case here). Such a parametric analysis is likely to offer a better index of how much a given brain region is sensitive to the type of processing studied. The records obtained over the prefrontal cortex by Casini and Macar (1996a) did reveal performance-dependent changes in a duration reproduction task involving no feedback,² whereas no such trends were found in a linguistic task of similar structure. However, in that study, the target interval during the temporal task corresponded to the presentation of visual stimuli (four identical letters); therefore, sustained attention was directed to the visual modality for relatively long durations (on average 6–8 s, as target intervals of 3 or 4 s were to be reproduced). This factor, more than time processing in itself, was probably responsible for the observed prefrontal involvement (Pardo et al. 1991; Posner and Petersen 1990). Further research is needed to test this hypothesis and reveal the precise conditions under which the prefrontal cortex is sensitive to temporal performance.

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² However, due to the fact that the electrodes in Casini and Macar's study (1996a) were placed over close prefrontal sites, polarity shifts were so frequent that only absolute Laplacian values could be used. This difference in the analysis makes difficult a straightforward comparison of those data with the present ones. Nevertheless, the present performance-dependent trends were suggested by the monopolar data of that experiment (reported in Macar and Bonnet 1997), in which the "long" response category tended to correspond to larger negative ERPs

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