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Neural Modulation by Regularity and Passage of Time

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Correa A, Nobre AC. Neural modulation by regularity and passage of time. *J Neurophysiol* 100: 1649–1655, 2008. First published July 16, 2008; doi:10.1152/jn.90656.2008. The current study tested whether multiple rhythms could flexibly induce temporal expectations (temporal orienting) and whether these expectations interact with temporal expectations associated with the passage of time (foreperiod effects). A visual stimulus that moved following a regular rhythm was temporarily occluded for a variable duration (occlusion foreperiod). The task involved making a speeded perceptual discrimination about the target stimulus that reappeared after the occlusion. Temporal-orienting effects were measured by comparing performance and event-related potentials on conditions in which the timing for target reappearance was predictable (valid) versus unpredictable (invalid) according to the rhythm. Foreperiod effects were measured by comparing conditions in which the target was occluded for progressively longer periods of time (short, medium, and long foreperiods) and hence were increasingly predictable. The results showed strong interactions between temporal orienting and foreperiod effects during the facilitation of behavior and neural activity associated with late perceptual and response selection processes. Temporal orienting attenuated the N2 amplitude and decreased the P3 latency only at short foreperiods. Temporal preparation related to foreperiod effects abolished temporal orienting effects at medium and long foreperiods. Likewise, foreperiod effects attenuated the N1 and N2 amplitudes and decreased the P3 latency only in the invalid orienting condition as preparation related to temporal orienting abolished foreperiod effects in the valid condition. This high degree of neural overlap between the effects of temporal orienting driven by rhythms and foreperiod effects associated with the passage of time suggests the involvement of a common mechanism for temporal preparation.

INTRODUCTION

Temporal expectation can rely on different types of predictive information, such as explicit messages regarding the onset or duration of events (e.g., traffic lights), periodic changes (rhythms) or the passage of time itself. Only recently the study of the interrelations between different temporal expectations has received increasing consideration (see Nobre et al. 2007 for a review). The present study compared neural modulations induced by temporal expectations based on *regular rhythms* versus the *passage of time*.

Regular auditory rhythms can orient attention toward a particular point in time (Jones et al. 2002). For example, Jones and colleagues found that pitch judgments were most accurate for a tone appearing in synchrony after a regular sequence of 600-ms intervals even when the delivery of the tone skipped one cycle of the rhythm. Analogous observations have been reported in the visual modality (Doherty et al. 2005). In this event-related potential (ERP) study, visual stimuli had to be discriminated on their reappearance from "under" a peripherally located occluding band. Temporal orienting was manipulated by the regularity of the rhythm with which the stimulus traversed the monitor screen until its occlusion. In "valid" conditions, the visual stimulus moved in regular steps of 550-ms intervals, and the stimulus reappeared after two steps under the occluder. In "neutral" conditions, the stimulus moved in irregular steps between 200 and 900 ms, providing no rhythmic information about the specific time at which the stimulus would reappear. Temporal orienting induced by regular rhythms facilitated reaction times (RTs) and modulated response-related potentials—attenuating N2 amplitude and decreasing P3 latency. This result replicated the findings from temporal-orienting research using explicit cuing to induce temporal expectations (Correa et al. 2006a; Griffin et al. 2002; Miniussi et al. 1999), showing that rhythmic predictability of stimuli can effectively drive temporal orienting even in the absence of explicit cues.

However, because only one regular interval was used in the previous studies, it is problematic to generalize the effects and conclude that temporal expectations can be flexibly and dynamically shaped by multiple rhythms. The present study tested the flexibility of rhythmically induced temporal orienting by modifying the previous visual task (Doherty et al. 2005) to include several regular intervals selected from a broad range of paces. The neural consequences of temporal orienting guided by multiple rhythms were studied by comparing ERPs to targets appearing at the expected (valid condition) versus unexpected (invalid condition) times following such regular rhythms.

The present study also explored how temporal expectations driven by the rhythmic regularity of stimuli interacted with another important and ubiquitous source of temporal expectations—the passage of time. The predictive value of the passage of time has traditionally been considered by the literature about temporal preparation and *foreperiod effects* (see Niemi and Näätänen 1981 for a review). The foreperiod is the time interval between a warning signal and an impending stimulus. RTs are shorter after longer foreperiods. The effect is typically interpreted according to the fact that the conditional probability about the occurrence of an event grows over time (Elithorn and Lawrence 1955; but see Los and Van den Heuvel 2001 for an account based on trace conditioning). This temporal certainty then allows optimal preparation for event onsets at long foreperiods.

According to the conditional-probability explanation, foreperiod effects and temporal orienting would be expected to

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show a large degree of neural overlap. A common mechanism for temporal preparation is supported by the observation that foreperiod effects influence temporal orienting. Temporal orienting effects are typically much larger at (or restricted to) targets appearing after short rather than long foreperiods (Correa et al. 2004, 2006b; see Nobre 2001 for a review). However, neural modulations related to temporal orienting versus foreperiod effects remain to be compared directly. Here we manipulated, on a trial-by-trial basis, the duration of the expectation interval (occlusion foreperiod) and temporal orienting driven by rhythms, to determine whether these effects interact and how they influence neural processing of events framed in time. If temporal orienting and foreperiod effects engage a common mechanism, they should interact and modulate similar stages of stimulus processing, for example, related to the N2 and P3 potentials (Doherty et al. 2005).

METHODS

Participants

Sixteen participants (aged 20–31, 11 females) gave informed consent to take part in the experiment. The experimental methods were noninvasive and had ethical approval from the University of Oxford.

Stimuli and task

Participants viewed displays in which a small circle moved across the screen from left to right, in discrete steps, and passed "behind" a vertical occluding band. The task was to track the movement of the circle covertly, without eye movements, and to detect whether a black dot was present in the circle at the moment it reappeared to the right of the occluding band.

Figure 1 (*top*) shows a schematic of the task. The display consisted of a light gray background with a dark green fixation point (diameter: 0.23°) at the center of the screen and a dark gray vertical occluding band (width: 2.55°) on the right (11.7–14.25° eccentricity). The moving stimulus was a yellow circle (diameter: 0.7°) that always appeared on the left-hand side of the screen and moved from left to right in 15 steps of equal horizontal distance (1.3°). Its location along the vertical axis on each step was random, so that whereas there was a general left-to-right movement of the circle, its precise spatial trajectory could not be predicted. Nine steps occurred before the circle reached the occluding band ("rhythmic temporal cuing").Two steps occurred behind the occluding band and were therefore invisible ("occlusion foreperiod"). One step occurred adjacent to the right-hand side of the occluding band ("target" or nontarget event). To provide a continuous sense of motion, three additional steps occurred until the circle reached the edge of the display. The next trial began after a random intertrial interval that ranged from 700 to 1,000 ms.

Temporal orienting was induced by presenting the circle moving across the display at a regular and predictable rhythm with every step occurring at a constant interval. This constant interval varied between trials, with a 200- to 900-ms range. The circle was present for the entire duration of each step. Therefore on a trial-by-trial basis, the movement of the circle afforded specific temporal predictions about when the circle would re-emerge after the occlusion foreperiod. Across trials, the time at which the circle appeared either conformed (valid trials) or violated (invalid trials) these temporal predictions. Trials were equally divided into valid and invalid trials. In invalid trials, the occlusion foreperiod was either shortened or lengthened by ≥200 ms. The occlusion foreperiod for invalid trials could take any value between 400 and 1,800 ms, which was ≥200 ms earlier than or later than the foreperiod predicted by the preceding regular step

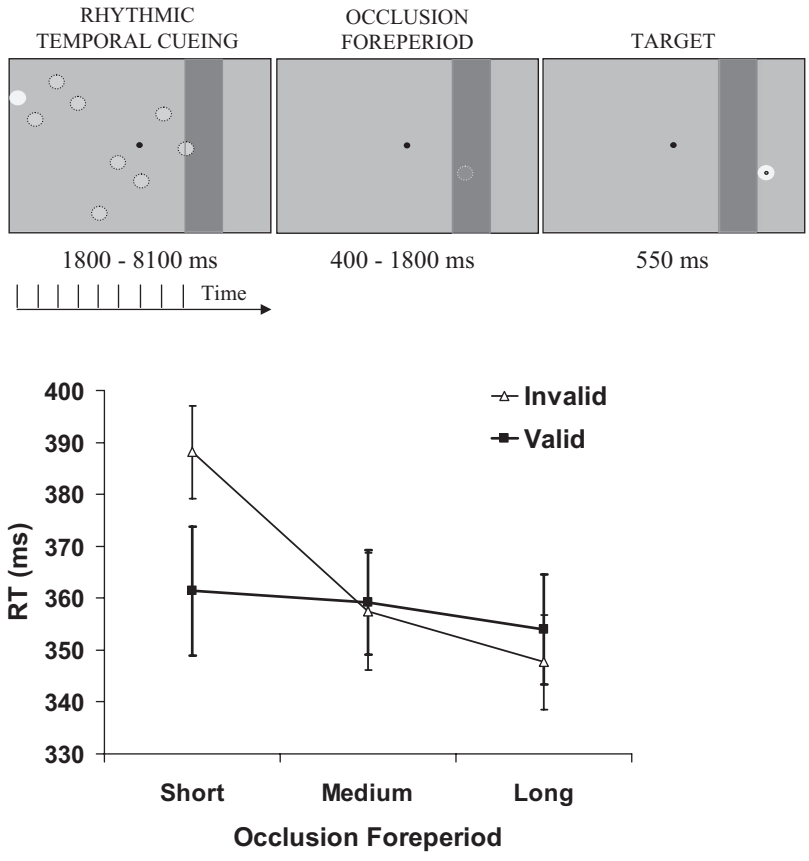

FIG. 1. *Top*: example of a trial. First the stimulus moved from left to right at a regular and predictable rhythm, acting as temporal cue (rhythmic temporal cueing). During the occlusion foreperiod, the stimulus disappeared under the occluding band. After the occlusion, the target appeared at the right hand-side of the occluding band. *Bottom*: temporal orienting and foreperiod effects on behavior. Mean reaction times (RTs) as a function of temporal orienting (valid, invalid) and occlusion foreperiod (short: 400–867 ms, medium: 868–1,333 ms, long: 1,334–1,800 ms). Vertical bars represent SEs.

duration. Values were randomly selected from these ranges, leading to targets appearing earlier than expected on ~25% of total trials and later than expected on ~25% of trials. Because of the influence of the passage of time, however, the distribution of early invalid and late-invalid trials differed over the range of foreperiod occlusions. For short occlusion foreperiods, most invalid targets occur early; for medium occlusion foreperiods, early and late invalid trials are equally distributed; for long occlusion foreperiods, most invalid targets occur early. The full distribution of occlusion foreperiods for each step duration is shown in the supplementary material.[1]

Only the first step after occlusion was selected for the possible appearance of the target. The target consisted of the same yellow circle with a black dot in its center (diameter: 0.17°), and occurred on 80% of trials. On the remaining 20% of trials, the yellow circle contained no black dot in the center. The target or nontarget event was presented for 550 ms in all trials. Participants were instructed to press the space bar if the black dot was present (target trials) and to withhold responding if the yellow circle appeared without the black dot (nontarget trials). Making this discrimination required a high level of attention and required participants to identify and discriminate the stimulus before responding, thus avoiding automatic responding in anticipation of the stimulus. The three final steps after the target or nontarget event had a similar duration to the preceding rhythm.

Participants completed 320 trials presented in blocks of 40 trials.[2] Each experimental block included 32 targets and 8 nontargets, which were divided into 20 valid and 20 invalid trials (50% validity) and presented in random and unpredictable order within blocks. Repeated-measures ANOVAs compared accuracy or RT for detecting target stimuli across the experimental factors: temporal orienting (valid, invalid) and occlusion foreperiod (short, medium, long). Occlusion foreperiod referred to the amount of time during which the stimulus was occluded, and was divided into three levels: 400–867 ms (short), 868–1,333 ms (medium), and 1,334–1,800 ms (long).[3] Follow-up subsidiary analyses were used, when necessary, to clarify the nature of the main effects and interactions.

Procedure

The stimuli were presented on a 21-in CRT monitor (CTX ultra screen) connected to a PC, which controlled the presentation of stimuli and data collection using the E-prime software (Schneider et al. 2002). The participants were seated in a dimly illuminated room at ~100 cm from the screen. Task instructions emphasized the use of information inherent in the way the stimulus moved to anticipate the moment of the stimulus reappearance from behind the occluding band. The participants were also encouraged to respond as quickly and accurately as possible and were reminded to hold their gaze at the center throughout the experiment and to avoid excessive blinking during the trial.

EEG recording

The EEG recording was performed in an electrically shielded room, using Ag/AgCl electrodes mounted on an elastic cap and distributed along 34 scalp sites according to the 10–20 International system (AEEGS 1991). The montage included 6 midline sites (FZ, FCZ, CZ, CPZ, PZ, and OZ) and 14 sites over each hemisphere (FP1/FP2, F7/F8, F3/F4, FT7/FT8, FC3/FC4, T7/T8, C3/C4, TP7/TP8, CP3/CP4, P7/P8, P3/P4, PO7/PO8, PO3/PO4, and O1/O2). Additional electrodes were used as ground and reference sites and for recording the electrooculogram (EOG). Data were acquired at a sampling rate of 500 Hz using a low-pass filter of 200 Hz and a DC high-pass setting. All electrodes were referenced to the right mastoid during the recording and were algebraically re-referenced off-line to calculate the average of the right and left mastoids. Horizontal and vertical eye movements were monitored by horizontal and vertical EOG bipolar recordings with electrodes placed around the eyes. Eye movements were also monitored using a remote, video-based infrared eye tracker (IView X, SMI). On-line monitoring of eye-gaze position was used to ensure participants maintained central fixation and performed the task covertly.

ERP analysis

The continuous EEG was filtered off-line with a 40-Hz low-pass filter. The data were segmented off-line into epochs starting 100 ms before and ending 600 ms after target presentation. A strict baseline from 0 to 50 ms was used to minimize misalignments of the waveforms based on anticipatory neural activity (CNV) as recommended by previous research (Correa et al. 2006a; Griffin et al. 2002; Woldorff 1993). Epochs in which an eye blink or eye movement occurred were rejected on the basis of large deflections (± 50 μV) in the horizontal electrooculogram or vertical electrooculogram electrodes. Epochs with large signal drift in the EEG were also removed on the basis of large deflections (± 100 μV) in any channel. The ERP analysis compared the effects of temporal orienting and foreperiod on target processing. The epochs were averaged according to the six conditions defined by temporal orienting (valid, invalid) and occlusion foreperiod (short: 400–867 ms, medium: 868–1,333 ms, long: 1,334–1,800 ms). Repeated-measures ANOVAs compared the mean amplitude of the identifiable potentials across the experimental factors: temporal orienting, occlusion foreperiod, electrode position, and electrode side. Significant effects of electrode position and electrode side were not reported unless they involved interactions with either temporal orienting or occlusion foreperiod. Time windows and electrode locations for the analyses were based on a previous study (Doherty et al. 2005) and on visual inspection of the grand-average waveforms. The P1 occurred between 140 and 180 ms over parietal and occipital electrodes and was therefore analyzed during 140–180 ms at lateral posterior electrodes (O1/2, PO3/4, PO7/8). The N1 was analyzed between 180 and 220 ms at the same electrodes as P1. The N2 was analyzed during 240–280 ms at frontal and central electrodes over the midline and flanking positions (F3/Z/4, FC3/Z/4, C3/Z/4, and CP3/Z/4).

[1] The online version of this article contains supplemental data.

[2] To test whether the behavioral effects induced by temporal predictions represented validity benefits, invalidity costs, or a combination of both, two blocks of "neutral" 80 trials were also presented at either the beginning or end of the experiment, in counterbalanced order across participants. Here the duration of each step within a trial was unpredictable and varied randomly between 200 and 900 ms (as in Doherty et al. 2005). The purpose of the neutral condition was only to help interpret the nature of the behavioral effects because the smaller number of trials in this condition and possible state-related differences between blocks with and without regular temporal rhythm precluded the use of the neutral condition in the ERP analysis. An ANOVA with temporal orienting (valid, neutral, invalid) and occlusion foreperiod (short, medium, long) as factors replicated the main effect of foreperiod [$F(2,30) = 38.54$, $P < 0.001$] and the interaction between temporal orienting and foreperiod [$F(4,60) = 8.18$, $P < 0.001$]. At the short foreperiod, temporal orienting effects were due to benefits [$F(1,15) = 21.06$, $P < 0.001$] rather than costs ($F < 1$). Typically, temporal orienting effects were not observed at longer foreperiods ($F < 1$). Analyses of the neutral condition hence mirrored the invalid condition.

[3] Most invalid-target trials occurring after short occlusion foreperiods appeared earlier than the time predicted by the regular step duration (47% of total trials). Only a small proportion (3% of total trials) appeared later than predicted (see Supplementary Materials 1 showing the distribution of trials across conditions). Although early- and late-invalid targets were indeed processed differently (see Supplementary Materials 2), further analyses comparing valid vs. invalid-early conditions led to similar behavioral and ERP effects as the valid vs. invalid comparison at the short foreperiod condition that was described in the main text. The convergence between these two analyses suggests that the effect of including such a small proportion of invalid-late trials within the short foreperiod condition was negligible.

The P3 was analyzed during 350–450 ms over midline and flanking parietal electrodes (CP3/Z/4, P3/Z/4, and PO3/Z/4). The latency of the largest peak was also analyzed for the P3 potential at the same temporal window and electrodes. Where appropriate, only effects that survived the Greenhouse-Geisser epsilon correction for nonsphericity (Jennings and Wood 1976) were considered.

RESULTS

Behavioral results

RTs from correct responses were submitted to a repeated-measures ANOVA with temporal orienting (valid, invalid) and occlusion foreperiod (short, medium, long) as factors. Errors were very infrequent (2.5% overall), and their variance was too small to be analyzed. The RT analysis excluded errors as well as excessively fast (<100 ms) or slow (>1,000 ms) responses (0.2% rejected). The main effect of temporal orienting was significant, $F(1,15) = 5.69$; $P = 0.03$, leading to the typical validity effect: faster RTs for valid compared with invalid trials. The effect of occlusion foreperiod was also significant, $F(2,30) = 28.24$; $P < 0.001$, showing the classical foreperiod effect: decreasing RTs as the foreperiod increased. Furthermore, the effects of temporal orienting and foreperiod interacted significantly, $F(2,30) = 11.71$; $P < 0.001$ (Fig. 1, *bottom*). Subsidiary analyses revealed that the foreperiod effect was only significant in the invalid condition, $F(1,15) = 81.71$, $P < 0.001$, and was abolished by temporal orienting in the valid condition, $F(1,15) = 1.88$, $P = 0.19$. This interaction also replicated the common finding of temporal orienting effects exclusively at short foreperiods. RTs were faster for valid versus invalid conditions at the short occlusion foreperiod only, $F(1,15) = 21.06$, $P < 0.001$ (at medium and long foreperiods: $F < 1$ and $F(1,15) = 2.51$, $P = 0.13$, respectively).

Electrophysiological results

The target-locked analysis tested the generality of the patterns of modulation during temporal orienting induced by moving stimuli when multiple visual rhythms are employed and tested whether the effects of temporal orienting interacted with foreperiod effects. Figure 2 shows the standard pattern of modulation by temporal orienting (e.g., Doherty et al. 2005) and a strong interaction between temporal orienting and foreperiod effects, which mirrored the RT data. As can be observed, temporal orienting attenuated the amplitude of the N2 and reduced the latency of the P3, but this modulation was confined to targets appearing after short occlusion foreperiods only.

Likewise, Fig. 3 depicts this interaction by showing that the modulation of the N1, N2, and P3 potentials by foreperiod occlusion was specific to the invalid condition. The figure also shows a graded effect of foreperiod duration on late potentials. Specifically, the N2 amplitude and the P3 latency were progressively attenuated as the foreperiod occlusion became longer.

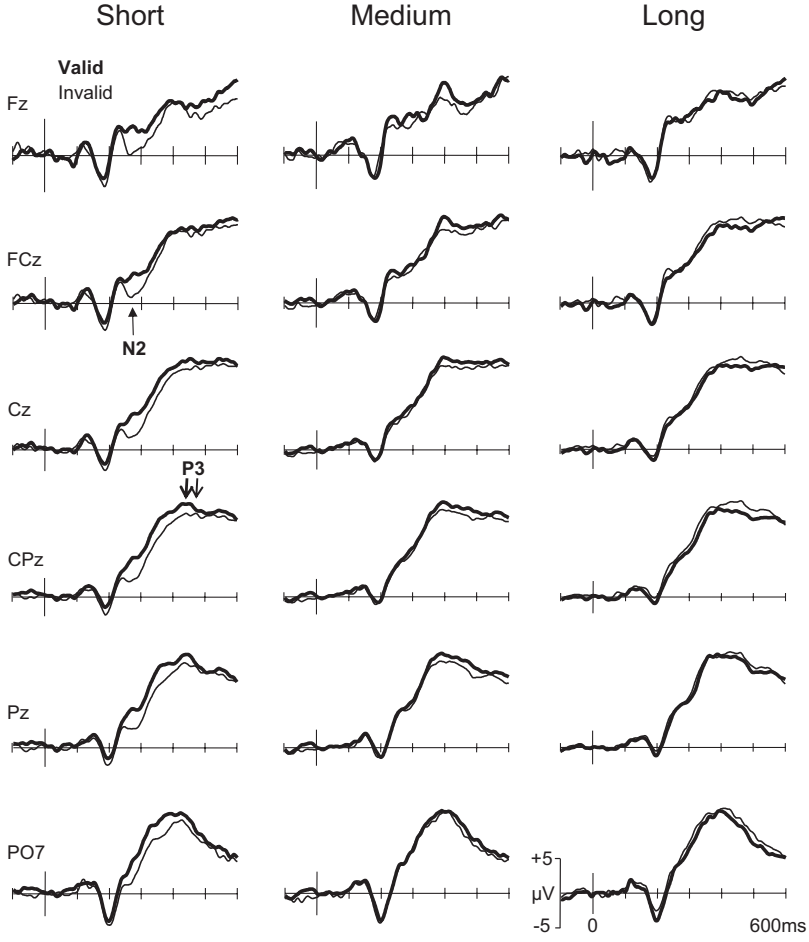

FIG. 2. The effects of temporal orienting as a function of foreperiod duration. Target-locked event-related potential (ERP) waveforms averaged across 16 participants for valid (solid line) and invalid (soft line) conditions, after short, medium, and long foreperiod occlusion. The figure shows 5 electrodes from the midline (Fz, frontal; FCz, frontocentral; Cz, central; CPz, centroparietal; Pz, parietal) and a posterior electrode contralateral to the target appearance (PO7, parieto-occipital). The single arrow pointing the N2 potential marks a significant temporal-orienting effect on the mean amplitude. The pair of arrows marks a significant effect on the P3 latency.

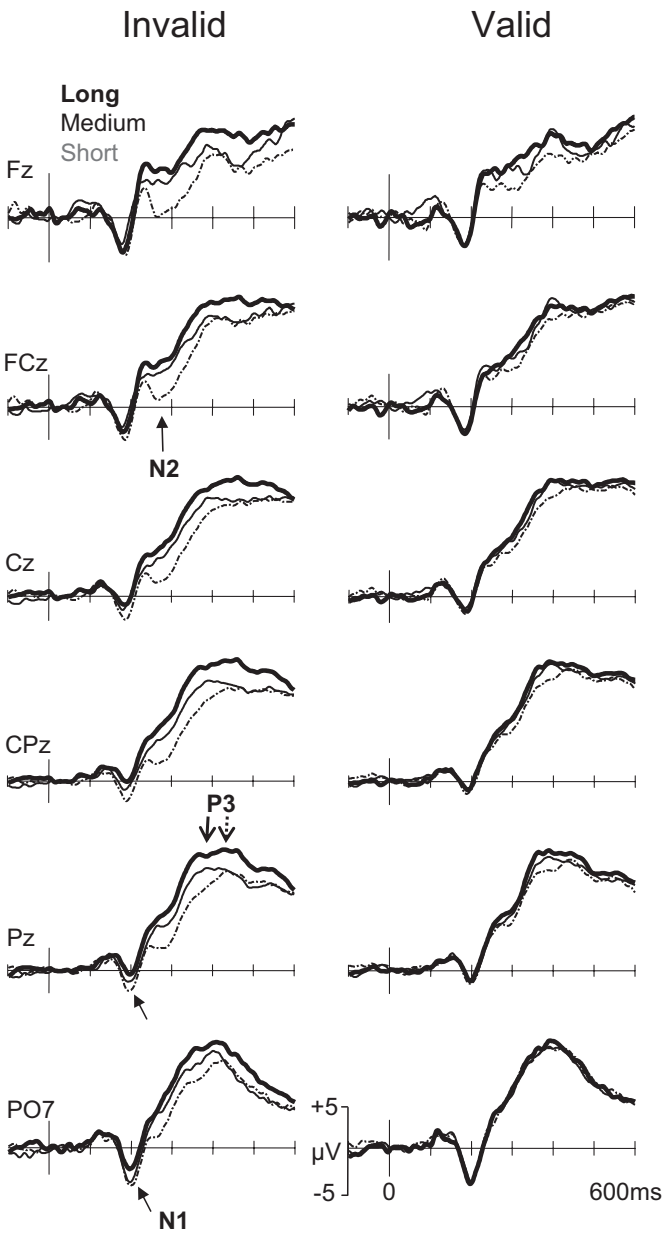

FIG. 3. Foreperiod effects as a function of temporal orienting. Target-locked ERP waveforms averaged across 16 participants after long (solid line), medium (soft line), and short (dashed line) foreperiods for valid and invalid conditions. The figure shows 5 electrodes from the midline and a posterior electrode contralateral to the target appearance (PO7: parieto-occipital). The single arrows pointing the N1, N2, and P3 potentials mark significant foreperiod effects on the mean amplitude. The pair of arrows marks a significant effect of short vs. medium foreperiods on the P3 latency.

Statistical analyses of the mean amplitudes of the P1 showed no significant effects or interactions (all $P > 0.2$). In contrast, the N1 was modulated by occlusion foreperiod, $F(2,30) = 5.89$, $P = 0.007$, such that the amplitude of the N1 was attenuated (i.e., became less negative) as the occlusion foreperiod increased [short vs. medium foreperiods: $F(1,15) = 2.89$, $P = 0.1$; medium vs. long: $F(1,15) = 3.15$, $P = 0.09$; short vs. long: $F(1,15) = 13.75$, $P = 0.002$]. The interaction between temporal orienting and foreperiod was also significant, $F(2,30) = 3.81$, $P = 0.03$. As shown in Fig. 3, the N1 attenuation by the foreperiod effect was only significant in the invalid condition, $F(1,15) = 13.75$, $P = 0.002$, and was abolished by temporal orienting in the valid condition, $F < 1$.

Analyses of the N2 amplitude showed a main effect of temporal orienting, $F(1,15) = 5.59$, $P = 0.03$, leading to attenuated N2 on valid versus invalid trials; and a main effect of occlusion foreperiod, $F(2,30) = 12.52$, $P < 0.001$, which led to attenuated N2 along the foreperiod [short vs. medium: $F(1,15) = 19.03$, $P < 0.001$; medium vs. long: $F(1,15) = 2.97$, $P = 0.1$]. Critically, the interaction between temporal orienting and foreperiod was significant, $F(2,30) = 3.88$, $P = 0.03$. Subsidiary analyses closely replicated the RT findings, as the N2 was attenuated by temporal orienting only at short foreperiods [valid vs. invalid: $F(1,15) = 6.90$, $P = 0.02$] but not at medium or long foreperiods, $F < 1$ (Fig. 2). Likewise, foreperiod effects were modulated by temporal orienting, as they were significant only on invalid trials [short vs. long: $F(1,15) = 36.04$, $P < 0.001$], but not on valid trials, $F(1,15) = 2.66$, $P = 0.12$ (Fig. 3).

The analysis of the P3 latency showed a significant effect of occlusion foreperiod, $F(2,30) = 12.7$, $P < 0.001$. The P3 peaked earlier as the occlusion foreperiod increased [short foreperiod: 414 ms vs. medium foreperiod: 399 ms, $F(1,15) = 18.64$, $P < 0.001$], reaching the asymptote at the medium foreperiod [medium vs. long foreperiod: 396 ms, $F(1,15) = 1.23$, $P > 0.28$]. Most relevant was the significant interaction between temporal orienting and foreperiod, $F(2,30) = 3.78$, $P = 0.03$. Subsidiary analyses showed that temporal orienting reduced the P3 latency only at the short foreperiod [valid: 406 ms vs. invalid: 422 ms, $F(1,15) = 8.62$, $P = 0.01$] but not at medium or long foreperiods ($F < 1$; Fig. 2). Likewise, the foreperiod effect was clearly significant in the invalid condition, $F(1,15) = 16.23$, $P < 0.001$, while it was weakened by temporal orienting in the valid condition, $F(1,15) = 3.46$, $P = 0.08$ (Fig. 3).

Analyses of the P3 amplitude showed a main effect of occlusion foreperiod, $F(2,30) = 14.23$, $P < 0.001$. The P3 potential became progressively larger as the occlusion foreperiod increased [short vs. medium foreperiods: $F(1,15) = 3.87$, $P = 0.068$; medium vs. long foreperiods: $F(1,15) = 16.09$, $P < 0.001$]. The interaction between occlusion foreperiod and electrode position, $F(4,60) = 6.07$, $P < 0.001$, involved the most evident foreperiod effects over parietal electrodes. The interaction between temporal orienting and foreperiod was marginally significant, $F(2,30) = 2.88$, $P = 0.07$, such that temporal orienting tended to enhance the P3 amplitude at short [$F(1,15) = 3.83$, $P = 0.07$] rather than medium or long foreperiods ($P > 0.14$).

DISCUSSION

Previous research has emphasized the role of regularity and rhythm for the framing of behavior in time (Barnes and Jones 2000; Doherty et al. 2005; Jones et al. 2002; Large and Jones 1999; see also Schubotz and von Cramon 2001). Such studies have generally reported that task performance is enhanced for targets appearing after a single regular rhythm as compared with after an irregular rhythm. This enhancement agrees with the classic temporal-orienting findings using explicit symbolic cues (Nobre 2001) and is also interpreted as a consequence of temporal expectation induced by the single regular rhythm.

The current study further tested the flexibility of temporal expectation by presenting multiple rather than single regular rhythms. Visual targets were detected most rapidly when their onset coincided with moments previously marked by the rhythms. This result suggests that temporal orienting can be tuned flexibly to different intervals on the basis of multiple rhythms; this adds to previous behavioral research showing temporal-orienting effects for multiple symbolic and predictive cues (Correa et al. 2004; Griffin et al. 2001). Furthermore, temporal-orienting effects survived to our "strict" validity manipulation, which minimized the predictive value of the rhythm by including equivalent proportions of valid and invalid trials ($P = 0.5$). This finding is consistent with previous research showing that attentional orienting in time can also be driven exogenously—just by presenting nonpredictive regular rhythms (Jones et al. 2002).

Once the temporal-orienting manipulation was validated, its effect was compared with the effect of the passage of time along the foreperiod (foreperiod effect).[4] The RT data revealed a strong interaction between temporal orienting and foreperiod effects. RT facilitation by temporal orienting was only observed in the absence of foreperiod effects (at short foreperiods), and facilitation by foreperiod effects was only observed in the absence of temporal orienting (on invalid conditions). The interaction between these two factors suggests that a common mechanism for temporal preparation is involved in both types of effects. The analyses of target-locked ERPs further specified that temporal orienting and foreperiod effects converged during the modulation of processing mainly located at postperceptual stages. The interactive effects observed in RTs were clearly supported by significant interactions between temporal orienting and foreperiod during the modulation of the N1 and N2 amplitudes and the P3 latency.

The N1 potential recorded over posterior electrodes showed a main effect of foreperiod duration qualified by an interaction with temporal orienting. Temporal orienting alone did not modulate the N1, but the potential was significantly attenuated for target stimuli appearing at the longest foreperiods in the absence of temporal expectations generated by regular motion steps. The results show that temporal expectations can affect this later stage of perceptual processing, and suggest that the effect of foreperiod was stronger than that of temporal orienting in the present experiment. In the previous experiment using visual apparent motion and occlusion (Doherty et al. 2005), the N1 was attenuated by temporal orienting, but the use of multiple regular temporal intervals across trials in the present experiment may have weakened the effect. Recently, Praamstra and colleagues (2006) reported attenuation of the visual N1 for targets occurring later than expected based on a regular temporal rhythm, which fits with our finding of attenuated N1 at long foreperiods.

It remains difficult to pinpoint the functional roles or neuroanatomical substrates of the visual N1 potential. Several putative roles have been suggested, including fine perceptual discriminations required by task goals (Vogel and Luck 2000) and object recognition (Doniger et al. 2002). Multiple visual and multisensory areas may be involved in its generation (Di Russo et al. 2002), and the specific sources may further depend on the specific task requirements. Whatever the precise functional and neural bases for the N1, the current and previous findings indicate that this stage of processing can be significantly influenced by temporal expectations. However, there is also some indication that the nature of N1 modulation may depend on whether temporal expectations develop exogenously, based on the regularity or passage of time or are triggered endogenously, based on explicit temporally predictive cues. In experiments using explicit temporal orienting cues, the visual N1 is either unaffected or enhanced by temporal expectations (Griffin et al. 2002; Miniussi et al. 1999). To address this intriguing issue, research comparing directly these two modes of attentional orienting in time will be critical.

The N2 potential also reflected temporal orienting, foreperiod effects and their interaction. Several studies had already reported attenuation of the N2 by temporal orienting (Correa et al. 2006a; Doherty et al. 2005; Griffin et al. 2002). However, the functional significance of this modulation is not completely understood to date. The N2 has been associated with temporally deviant stimuli in oddball tasks (Loveless 1986), controlled S-R selection in conflict tasks (Kopp et al. 1996), and response inhibition in go-nogo tasks (Kok 1986). In fact, our task included some of these features, as it involved the controlled release of a prespecified response at the appropriate time (i.e., response execution *when* the stimulus appears only in target/go trials). It is possible, therefore that the N2 reflected the temporal maintenance of response inhibition to prevent responding at inappropriate times. Hence the N2 attenuation by temporal expectation could be related to a more efficient "releasing of the brake" for temporally anticipated targets, which was also reflected as faster responses. Our hypothesis about the role of the N2 in temporal preparation is based on recent lesion studies suggesting that the prefrontal cortex mediates this inhibitory control during temporal preparation (Davranche et al. 2007; Narayanan et al. 2006; Vallesi et al. 2007a,b). We suggest that the N2 modulation is a key feature of temporal preparation, which adds to the well-documented modulations of the P3 latency by temporal expectations (Correa et al. 2006a; Doherty et al. 2005; Griffin et al. 2002; Miniussi et al. 1999; see also Müller-Gethmann et al. 2003).

To summarize, the present study showed that temporal expectations can be flexibly driven by multiple regular rhythms and that they interact with expectations based on the passage of time (foreperiod effects) during the facilitation of behavior and brain potentials following the initial stages of visual processing. This interaction reveals a strong neural overlap between temporal preparation mechanisms triggered by these two sources. Temporal orienting and foreperiod effects may use a shared neural network that controls the attentional biasing of task-relevant neural resources over time. At the functional level, the distribution of resources may rely on dynamic computations of conditional probabilities associated with the temporal occurrence of relevant events at a given moment given that it has not yet occurred (hazard function). At the neural

[4] When comparing ERPs across foreperiods, it is important to rule out the possible contributions of the differential pattern of potential overlap from preceding events. To overcome this necessary limitation, we included a large range of intervals in each of the foreperiod conditions (~470 ms in range), used a strict baseline correction approach centered around the presentation of the target time, and ensured that the baseline periods of the waveforms were well aligned and free from any drift. We were reassured that there was no contamination of the measurements by the lack of any statistical effects on the first identifiable (P1) potential, and by the replication of previous findings in which different interval ranges were used.

level, hazard functions have been shown to influence significantly the dynamics of transient activity within a large number of brain areas, involved in perceptual, motor, and reward processing (Ghose and Maunsell 2002; Janssen and Shadlen 2005; see Nobre et al. 2007; for a review; Riehle et al. 1997; Tsujimoto and Sawaguchi 2005). The future challenge will be to determine where and how temporal hazard functions are computed and how these predictive signals come to bias ongoing information processing based on expectations and task goals related to nontemporal stimulus dimensions. In particular, it will be interesting to investigate if the computation of hazard functions is a distributed property of neural systems or if centralized timing networks are involved in generating temporal predictions.

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