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Caffeine and Selective Visual Processing

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KENEMANS, J. L. AND M. M. LORIST. *Caffeine and selective visual processing.* PHARMACOL BIOCHEM BEHAV 52(3) 461–471, 1995.—This work addressed five issues: a) Does caffeine modulate electroencephalogram (EEG) background activity in a manner consistent with the idea of cortical "arousal"? b) Is performance in a simple speeded task improved under caffeine? c) Is visual processing more selective under caffeine? d) Does caffeine affect sensory discrimination? and e) Does it affect motor processes? We presented 16 subjects with a visual selection task under conditions of either caffeine or placebo. Background EEG data, gathered before administration of the task, revealed that caffeine resulted in lower slow-α power, relative to placebo, which is consistent with the idea of increased cortical "arousal." During the selection task, subjects had to respond manually to a given target conjunction of spatial frequency and orientation. Other conjunctions shared spatial frequency, orientation, or neither with the target. The four conjunctions were presented in a random sequence, with SOAs ranging between 750 and 950 ms. Event-related potentials (ERPs) to the conjunctions were recorded at standard scalp locations Fz, Cz, Pz, and Oz. Under caffeine, subjects made faster responses to target conjunctions (382.9 vs. 404.5 ms) and more hits, whereas the false-alarm rate was equal across conditions. Caffeine did not affect the selection potentials normally obtained in this task by subtracting, from ERPs to nontargets with the target spatial frequency, those to nontargets with the other frequency. However, an early differential positivity (50–160 ms) was found specifically under caffeine, indicative of increased selectivity. Difference ERPs as a function of physical parameters were not affected by caffeine, indicating no effect on sensory discrimination. Onsets of response-related lateralizations above the motor cortex were not affected by caffeine, suggesting that the shorter reaction times under caffeine were due to faster central or peripheral motor processes.

Visual selective attention Event-related potentials Spatial frequency Caffeine Arousal Background EEG

STIMULATING effects of caffeine on behavior are well documented (4,23). When behavior is constrained as in simple laboratory tasks, stimulants improve speed and/or accuracy in selective processing or signal detection kinds of tasks (16). Especially in the case of caffeine, improved accuracy concerns the hit rate, with no changes in the false-alarm rate, in the great majority of cases. The changes in brain state brought about by caffeine are generally described in terms of increases in excitatory processes, reduced inhibitory processes, and/or increased availability of "energy." There seems to be consensus that these stimulating effects on brain activity are mediated by adenosinergic antagonism, which modulates the activity of a variety of neurotransmitter systems (3,23,29). The global picture of excitatory effects has correlates at the global-physiologic level manifest in the spontaneous background electroencephalogram (EEG). The one robust result that has been obtained in a number of studies seems to be a reduction under caffeine of power in the lower α or θ band (6–9 Hz) (6,24,27). Changes in higher bands (β), as well as increases in the dominant α frequency are less consistent, and a change in δ power (0–4 Hz) was not found in the three studies mentioned.

Together, then, the effect of caffeine can be seen as central, and as increasing the efficiency and intensity of behavior; it seems reasonable to view the observed effect on compound scalp-recorded neural activity (as reflected in the EEG) as a reflection of heightened cortical "arousal" under caffeine. The beneficial effects of caffeine seem to be confined to simple tasks, whereas tasks requiring more extensive short-term memory operations, or the division of attention across multiple inputs or domains, result in less beneficial or even adverse effects of caffeine administration (1,2). A by now classic theory [(5); see also (8)] asserts that arousal and selectivity of information processing are positively related. For tasks in which relatively few sources of information have to be monitored (among distracting sources), this is beneficial to perfor-

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mance, the more so when the need for selectivity is stressed (e.g., by increasing time pressure). On the other hand, when multiple sources of information in sensory space or working memory have to be used, performance does not benefit from increasing selectivity, and hence may deteriorate with increasing arousal. A similar view has been expressed by Loke (17,18), who contended that in tasks requiring "controlled" processing (as opposed to "automatic"), increasing task difficulty would cause arousing substances to result in performance costs rather than benefits.

It can thus be predicted that a putative arousal-enhancing substance such as caffeine a) reduces EEG power in the lower α band; b) results in improved performance in terms of both speed and accuracy in a simple task stressing selective attention; and c) results in greater selectivity of processing. This work sought to verify these predictions. To this end, subjects were presented a rapid pseudorandom series of visual stimuli, consisting of both target stimuli, which had to be behaviorally responded to, and nontargets, which had to be ignored. Nontargets either shared (relevant nontargets) or did not share (irrelevant nontargets) an elementary attribute with the targets. Hit rate and reaction time to targets, and correct-rejection rate with respect to nontargets were determined. To evaluate the selectivity of processing, event-related potentials (ERPs) recorded to relevant nontargets were compared to those recorded to irrelevant nontargets. In addition, spontaneous resting EEG was recorded before administration of the task. All subjects participated in two sessions: once under caffeine and once under placebo.

A related procedure to assess selectivity of visual processing under caffeine was used by Lorist et al. (20). These authors had subjects search for prespecified targets among letters presented on one diagonal in a visual display; letters presented on the other diagonal had to be ignored. On each trial, letters were presented on either diagonal, with relevant and irrelevant diagonals alternating pseudorandomly. Compared with placebo subjects exhibited faster reaction times (RTs) to targets under caffeine, whereas there was no treatment effect on accuracy parameters. As to the difference in ERPs to relevant- and irrelevant-diagonal stimuli, respectively, its early phase (frontal positivity) was not affected, whereas as a later phase (frontocentral negativity) was increased under caffeine.

The present study differed from that by Lorist et al. (20) by using a task with a lower memory load. Furthermore, a stimulus-selection criterion, spatial frequency, was used that is known to have an ERP signature different from the one associated with visual diagonal (9,11,13). Specifically, the difference between ERPs to relevant and irrelevant spatial frequencies contains an occipital component in addition to the frontal positivity and central negativity, with the former slightly lagging in time. This means that selective attention to spatial frequency (as well as to color, which has a similar ERP signature) (10,30) involves brain processes different from those involved in diagonal selection. Thus, this work extended the previous study to different aspects of visual selectivity.

In another study by Lorist and colleagues (19), the shortening of RT under caffeine was found to depend on stimulus quality. The authors interpreted this finding as indicating that caffeine affects an "input stage" of information processing; this conclusion was also supported by the discovery of a larger occipital early negativity in the ERP (N1) under caffeine. The present study used low (0.8 cycles per degree) and high (3.2 c/d) spatial frequencies, which are known to differ profoundly with respect to the early phases (50–200 ms poststimulus) of the ERPs which they elicit above the occipital scalp (11,13). We used this difference as an index of the extent to which subjects discriminate between high and low spatial frequencies, independently of task requirements. As such, it can be viewed as an additional operationalization of the concept of "input stage."

A further, seemingly specific index of input-related processing is the latency of the P3, a parietally distributed positivity, peaking between 300 and 600 ms poststimulus, which has been repeatedly found to vary with factors though to affect input processes, and to be relatively insensitive to response-related variables (22). In the present task, P3 latency was known to be selectively lengthened by the detection of a relevant spatial frequency. This lengthening can be seen as reflecting the extended processing of such stimuli with respect to other attributes relevant for performance (e.g., orientation). Thus far, the effects of caffeine on P3 latency have been equivocal (19,20).

Lorist et al. (19) found that the shortening of RT under caffeine also depended on temporal uncertainty about stimulus occurrence. They interpreted this to indicate that caffeine speeded up central motor processes ("output stage"). However, the validity of their specific operationalization of temporal uncertainty (i.e., variability of the interstimulus interval) is questionable (28). In the present study we used a direct ERP index for central motor processes, viz., the lateralization of brain potentials recorded above the motor cortex as a function of responding hand (7,30). By comparing the effects of caffeine on the latency of this lateralization and on RT, we obtained a measure for its effect on motor processes.

This article addresses five possible effects of caffeine: a change in brain state as indexed by background EEG; improved performance in a simple selective attention task; increased selectivity of processing; improved task-independent discrimination of stimuli; and accelerated central motor processes.

METHODS

Subjects

Subjects were 16 righthanded, healthy undergraduate students (eight women), between the ages of 19 and 29 (mean 21.5, SD 2.9). All were reported to be nonsmokers with an average regular consumption of 5.9 cups (SD 2.6) of caffeinated coffee a day. All subjects had normal or corrected-to-normal vision, did not work night shifts, had no sleep problems, and had average scores on a morning–evening-type scale (14). They received course credits for their participation.

Treatment Manipulation

Each subject participated in two sessions, separated by 2 weeks. Subjects were asked to abstain from substances containing caffeine for at least the 12 h preceding each experimental session. An additional analysis of the behavioral data was conducted to evaluate the possible contribution of withdrawal effects (see Data Recording and Analysis: Performance). In one session subjects were given 3 mg/kg body wt. of caffeine; in the other, they were given 3 mg/kg lactose dissolved in a cup of decaffeinated coffee. The order of treatment conditions was balanced across subjects. In addition, assignments to treatment conditions were double-blind and deceptive—that is, subjects were made to believe that normal coffee was served in both sessions (15). Milk powder and sugar were added to the coffee to suit the taste of the subject. Saliva

samples were taken before substance administration, 45 min after substance administration and at the end of the session. After the second saliva sample had been taken, subjects first performed a memory-search task, which is reported elsewhere (21). Subsequently, subjects performed the selective attention task. At the end of the session, the saliva samples were centrifuged for 10 min at 3000 rpm. About 2 ml of the supernatant was taken and stored at −20°C. Saliva caffeine concentrations were determined using high-performance liquid chromatography (courtesy of Dr. Van der Stegen, Douwe Egberts, Utrecht, The Netherlands).

Stimuli and Procedure

Stimuli consisted of square, square-wave gratings, subtending 4° of arc. The stimulus duration was 50 ms, and stimulus onset asynchrony varied between 750 and 950 ms. Stimuli were presented in the centre of the visual field on a Zenith/VGA monitor positioned at 80 cm from the subject's eyes. The grating contrast was about 0.14; the decrease in illumination associated with stimulus presentation, as measured on the screen, amounted to 42 lx, and ambient illumination was 35 lx. Stimuli differed in spatial frequency (3.2 and 0.8 c/≤) and orientation (vertical and horizontal), resulting in four different feature combinations. These four stimuli were randomly mixed within four blocks of 256 trials (4 × 64).

Subjects were seated in a dentist's chair that had response buttons attached to the right and left armrests. They were instructed to focus on a cross that was presented in the centre of the visual field throughout each block. Before each block, the subject was instructed to respond to one particular feature combination (the target) by pressing the button with the right or the left hand (varied between blocks). We emphasized that responses were to be made as quickly as possible. After instruction, the block started, which consisted of a pseudorandom sequence in which the four different stimuli were repeatedly presented, one at a time. Subjects had been instructed specifically to press the button in response to one of the four stimuli (the target) and ignore the others. Each block was followed by three further pseudorandom sequences of the same four stimuli, but with a different target instruction. In this way each of the four stimuli was the target in one block. Note that the circulation of targets also implied the circulation of other stimulus categories (e.g., the stimulus that had the same spatial frequency as the target). Each subject responded with the right hand in two blocks and with the left hand in the other two. The use of lefthand together with righthand blocks was necessary to derive lateralized readiness potentials (see Data Recording and Analysis). Response hands were combined with target instructions in such way that each combination occurred equally often across subjects. For a given subject the same combinations were used in both treatment conditions.

Just before the first block, subjects were asked to sit quietly and focus on the fixation cross for 1 min, during which time the background EEG was recorded.

Data Recording and Analysis

EEG was recorded from Oz, Pz, Cz, and Fz, referenced to linked earlobe electrodes and from a bipolar C3-C4 derivation (10/20 system), using tin electrodes attached to an electrocap. Tin electrodes were also used to record the vertical (above and below the pupil of the right eye) and horizontal (at outer canthi of both eyes) electrooculogram (EOG). The ground electrode was attached to the middle of the forehead. All signals were fed through a Nihon Koden polygraph with low-pass filters at 35 Hz and a time constant of 5 s. Signals were monitored on-line by a paper readout. Background EEG was sampled in 25 2-s segments, with 500-ms intervals. During the task, sampling of EEG, EOG, and button presses started 50 ms before stimulus onset and lasted for 600 ms. In both cases, the sample rate was 100 Hz. Prestimulus samples served as a baseline. Segments (background EEG) and trials (task EEG) with amplifier blocking were detected off-line and omitted from further analysis. Ocular artifact was controlled according to Woestenburg et al. [(31); see also (12)].

Performance was analyzed in terms of speed and accuracy. RT was measured as the time between stimulus onset and the button press. Mean RT was based on button presses to target stimuli. Accuracy was computed as the proportion of target trials in which a button press was emitted (hits), and the proportion of nontarget trials in which the button press was withheld (correct rejections). If treatment affected a behavioral parameter, the mean values in the two treatment conditions were compared to the mean value for a group of normal young subjects from a previous study (13). In this comparison only data from the first of the two sessions were used, in which half of the subjects received placebo and the other half caffeine. In this way the two studies were completely identical except for the caffeine/placebo manipulation. A difference between the present placebo values and the corresponding values from the previous study would indicate withdrawal effects.

We analyzed background EEG by computing the periodogram for each 200-sample segment, for each midline lead, after tapering (19-point cosine bell at both sides) and padding with 56 zero values. Subsequently, each periodogram was subjected to three-point smoothing and ln-transformed. Finally, a power spectrum estimate was obtained by averaging across segments.

Average stimulus-locked ERPs were computed across correct-response trials, separately for each lead, in two ways. For the first averaging procedure, trials within each block were sorted according to their physical characteristics, yielding four different exogenous ERPs: one for low spatial frequency/vertically oriented gratings, one for low/horizontal, one for high/vertical, and one for high/horizontal. Each of these four time series was then averaged across blocks. For the second averaging procedure, trials were sorted according to their relevance level. This yielded four different endogenous ERPs: one for targets, one for frequency-relevant stimuli (sharing only the frequency with the target), one for orientation-relevant stimuli (sharing only the orientation with the target), and one for irrelevant stimuli (sharing neither). Averages were computed separately for each block, and after sorting with respect to the preceding stimulus (32). Subsequently, the subaverages within each of the four endogenous ERP classes were averaged.

Derivation of the lateralized readiness potential proceeded in the following way. For lefthand blocks, average ERPs from the C3-C4 lead were polarity-inverted. Then, each of the four time series was averaged across blocks (two righthand and two lefthand blocks). The resulting average difference waveform thus reflected activity recorded above the motor cortex specific to the hand that was to be used for responding.

P3 latency was scored for each subject, task condition, and treatment condition as the maximum value in the average waveform recorded from Pz between 300 and 600 ms poststimulus.

Statistical Analysis

For the exogenous ERPs, analyses were carried out for Oz only. The independent variables were Treatment (spatial), Frequency (low vs. high), and Orientation (vertical vs. horizontal). For the endogenous ERPs, the independent variables were Treatment, Frequency Relevance, Orientation Relevance, and midline electrode Site. Note that Frequency Relevance refers to a main effect in the statistical design (i.e., the difference between targets and frequency-relevant stimuli on the one hand, and the orientation-relevant and irrelevant stimuli on the other). The former two stimuli have the relevant frequency; the latter do not. As the primary measure of selectivity, we used the difference between ERPs to relevant spatial frequencies and those to irrelevant ones. In previous studies (11,13,25) both behavioral and electrophysiologic results showed that in this setup, spatial frequency is selected faster than orientation, and hence can be considered the primary selection dimension.

RESULTS

Unless stated otherwise, degrees of freedom for reported F values are 1, 15.

Saliva Caffeine Levels

Differences in saliva caffeine levels between caffeine and placebo conditions were not significant for the pretreatment samples; they were, however, for the posttreatment samples. For the former, mean levels amounted to 1.28 (caffeine) and 0.42 (placebo; $F = 1.7$, $p > 0.2$). For the second sample, levels were 10.99 for caffeine and 0.64 for placebo ($F = 33.0$, $p < 0.001$). For the third sample, levels were 3.09 for caffeine and 0.35 for placebo ($F = 22.0$, $p < 0.001$). Thus, saliva caffeine levels differed between caffeine and placebo conditions only after substance administration, both before and after the selective attention task.

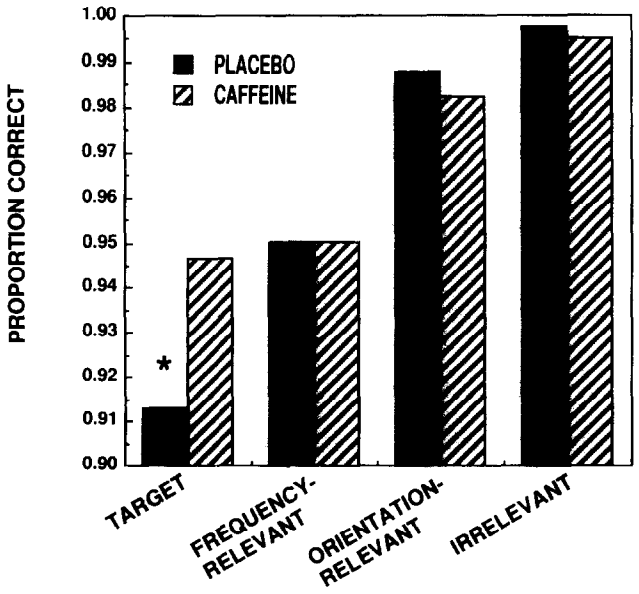

FIG. 1. Proportions of hits (targets) and correct rejections (other three categories) under placebo and caffeine conditions.

TABLE 1

MEAN VALUES FOR RT, WITHIN-SUBJECT RT SD AND PROPORTION OF HITS FOR A CONTROL GROUP FROM A PREVIOUS STUDY (13; $n = 13$), AND FOR THE FIRST SESSION FROM THE PRESENT EXPERIMENT IN WHICH SUBJECTS RECEIVED EITHER PLACEBO OR CAFFEINE ($n = 8$ IN BOTH CASES)

Condition	RT (ms)	SD	Proportion Hits
Previous study	402.9	61.8	.92
Placebo	408.7	62.0	.89
Caffeine	385.2	53.9	.95

Performance

Figure 1 depicts the proportions of hits (target stimuli) and correct rejections (other three categories) for both treatment conditions. The number of hits to target stimuli was larger for caffeine than for placebo ($F = 12.1$, $p < 0.005$); the numbers of correct rejections did not differ significantly between the two conditions. Note that false-positive responses were predominantly elicited by frequency-relevant stimuli. This is consistent with the notion that spatial frequency is selected faster than orientation. RTs to target gratings were shorter for caffeine (382.9 ms, SD 33.2) than for placebo (404.6 ms, SD 29.7; $F = 34.6$, $p < 0.0001$). In addition, within-subject RT standard deviations, computed per block and averaged across blocks, were smaller for caffeine (56.2, SD 6.5; 60.0, SD 5.6 for placebo; $F = 14.9$, $p < 0.005$).

Table 1 compares the data from a previous study, which had used an identical procedure, and mean values for the first session of the present experiment. The comparison was limited to RT, the within-subject RT standard deviation, and the proportion hits, because these variables were significantly affected by treatment. As can be seen, the difference between the previous values and the present placebo values, compared with the difference between the previous values and the present caffeine values, were either negligible (RT SD) or very modest (RT), or of similar size (hits). Thus, if there were any, withdrawal effects could only partially explain the present behavioral data.

Background EEG

Figure 2 shows the mean power spectrum for Pz for both treatment conditions. It can be seen that power was lower under caffeine in various frequency regions. Spectral values were averaged across eight succesive frequency components (3.125-Hz bands) and subjected to multivariate analysis of variance (MANOVA; BMDP 4V) with the factors Treatment and midline electrode Site. Treatment effects were significant for the 0-3.1 Hz band (δ: $F = 10.4$), for the 6.3-15.6 band (including low α; $7.4 < F < 9.0$), and for the β range (15.7-25 Hz; $5.7 < F < 12.5$). For the 3.2-6.2 band (θ) the treatment effect was not significant ($F = 0.6$). Mean significant-effect sizes were largest for the lower α band (6.3-9.4 Hz), and smallest for the β range. There was no interaction between Treatment and electrode Site.

For each subject, electrode site, and treatment condition α-peak frequency was scored as the frequency number having the largest power value between 7.8 and 13.6 Hz. A MANOVA of these data did not reveal any significant effects of treatment.

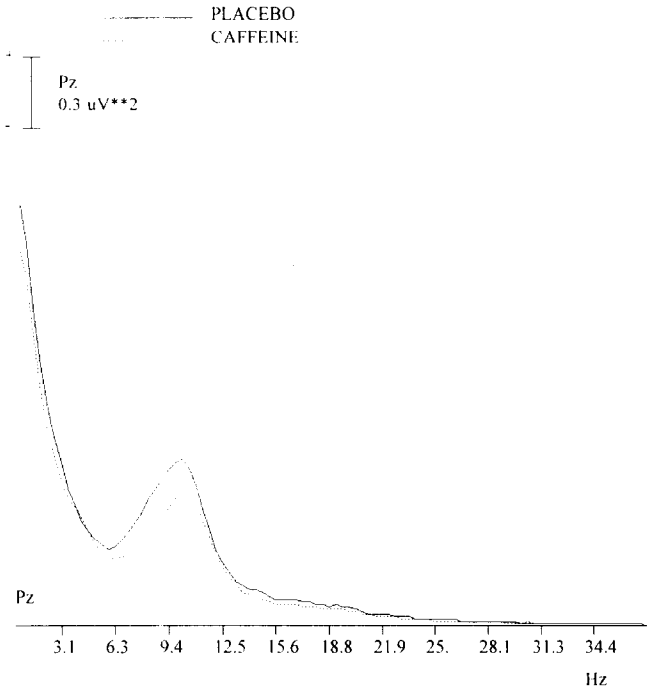

FIG. 2. Grand average ln-transformed power spectra, as recorded from Pz, under placebo and caffeine.

Exogenous Potentials

Figure 3 shows grand average difference waveforms recorded from Oz under placebo and caffeine. These difference waveforms were obtained by subtracting ERPs to high from those to low spatial frequencies for both orientations, and by subtracting ERPs to horizontal from those to vertical orientations, for both frequencies. As found previously (11,13), the difference associated with spatial frequency consisted of a positivity around 100 ms poststimulus followed by negativity after 150 ms; the difference associated with orientation was marked mainly by a prolonged positivity. An ANOVA on the raw waveforms was conducted for each sample between 0 and 300 ms to test the effects of Frequency, Orientation, and their interaction with Treatment. Frequency effects were significant from 70–120 ms ($11.1 < F < 29.7$), and from 170–210 ms ($4.6 < F < 17.2$). Orientation effects were significant from 80–100 ($6.3 < F < 17.3$) and from 270–300 ($5.7 < F < 7.7$) ms. There were no significant interactions with Treatment.

Endogenous Potentials

Figure 4 shows the ERPs to frequency-relevant stimuli, with those to irrelevant stimuli subtracted, as derived from midline and C3-C4 recordings (LRP), under placebo and caffeine. As before (11,13), we found the well-known sequence of frontal positivity (Fz, 150–200 ms poststimulus), occiptal negativity (Oz, about 200 ms), central negativity (Cz, after 200 ms), and late parietocentral positivity (Pz, 300 ms). Neither of these components seemed to be clearly affected by treatment. This was confirmed in a MANOVA conducted for 10 successive averages across four samples (40-ms stretches, extending from 0–400 ms), with independent variables Frequency Relevance, Orientation Relevance, midline electrode Site (Fz, Cz, Pz, and Oz), and Treatment. The sequence of components described above was reflected in a Frequency Relevance × Site effect from 170–400 ms [$6.2 < F(3, 13) < 45.6$]. In addition, this interaction was significant from 50–80 ms [$F(3, 13) = 3.8$, $p < 0.05$], and the main effect of Frequency Relevance was from 90–160 ms [$F(3, 13) = 5.1$ and 4.8].

The interaction between Treatment and Frequency Relevance was significant only before 170 ms. As such, it was significant between 50 and 80 ms ($F = 4.6$, $p < 0.05$), and tended to be from 90–120 ms ($p < 0.09$). In the latter range, the interaction between Treatment, Frequency Relevance, and Orientation Relevance was significant ($F = 5.2$, $p < 0.05$). From 130–160 ms, this interaction tended to significance ($p < 0.09$), whereas the four-way interaction involving Treatment, Frequency Relevance, Orientation Relevance, and Site was significant [$F(3, 13) = 3.8$, $p < 0.05$]. Separate tests for placebo and caffeine conditions, in the time range from 50–160 ms, revealed significant effects of Frequency Relevance only under caffeine, throughout this whole time range ($8.8 < F < 11.2$). In Fig. 4, this effect is seen as a protracted positivity between 50 and 200 ms poststimulus, especially at Cz and Pz, and only under caffeine. The dependence on the electrode site of this effect was reflected in a significant interaction between Frequency Relevance and Site (under caffeine) from 50–80 ms [$F(3, 13) = 6.9$, $p < 0.005$; $p < 0.1$ from 90–120 ms].

LRP and P3 Latency

As can be seen in Fig. 4, there were no significant differences in LRP as a function of frequency relevance. Figure 5 shows grand average raw ERPs to target and frequency-relevant stimuli. Tested sample by sample, LRPs to targets started to deviate from zero at 230 ms poststimulus. For the 230–300 ms range, F values ranged from 4.8–20.1. Treatment effects on target LRPs were not significant for any of the samples between 0 and 300 ms; indeed, Fig. 5 does not reveal a clear difference between treatment conditions. The lack of a treatment effect was confirmed in an ANOVA using 40-ms windows instead of single samples.

Figure 5 (left panel, Pz) suggests that for target stimuli P3 latency was shorter under caffeine. Statistical analyses with independent variables Treatment, Frequency Relevance, and Orientation Relevance revealed two significant effects on P3 latency: A main effect of Frequency Relevance ($F = 23.1$, $p < 0.0005$) and an interaction between Frequency Relevance and Treatment ($F = 6.6$, $p < 0.05$). Figure 6 illustrates these effects by comparing ERPs to targets with those to orientation-relevant stimuli in both treatment conditions. P3 latencies to targets were longer than those to orientation-relevant stimuli (as reflected in the Frequency Relevance main effect), but this difference was clearly smaller under caffeine (as reflected in the interaction between Frequency Relevance and Treatment). Further analyses revealed that caffeine significantly shortened P3 latencies for targets and frequency-relevant stimuli ($F = 6.4$, $p < 0.05$), but had no effect for the other two categories ($F < 0.01$). It is puzzling, however, that the treatment effect did not clearly show in the grand average waveforms for frequency-relevant stimuli (Fig. 5, right panel, Pz); in contrast, mean single-subject values were 433.8 (placebo) and 408.8 (caffeine).

Figure 6 also shows an amplitude affect in that there was more late positivity to target stimuli, relative to orientation-relevant stimuli. This difference partly reflects the effect of frequency relevance already shown in Fig. 4 (late positivity,

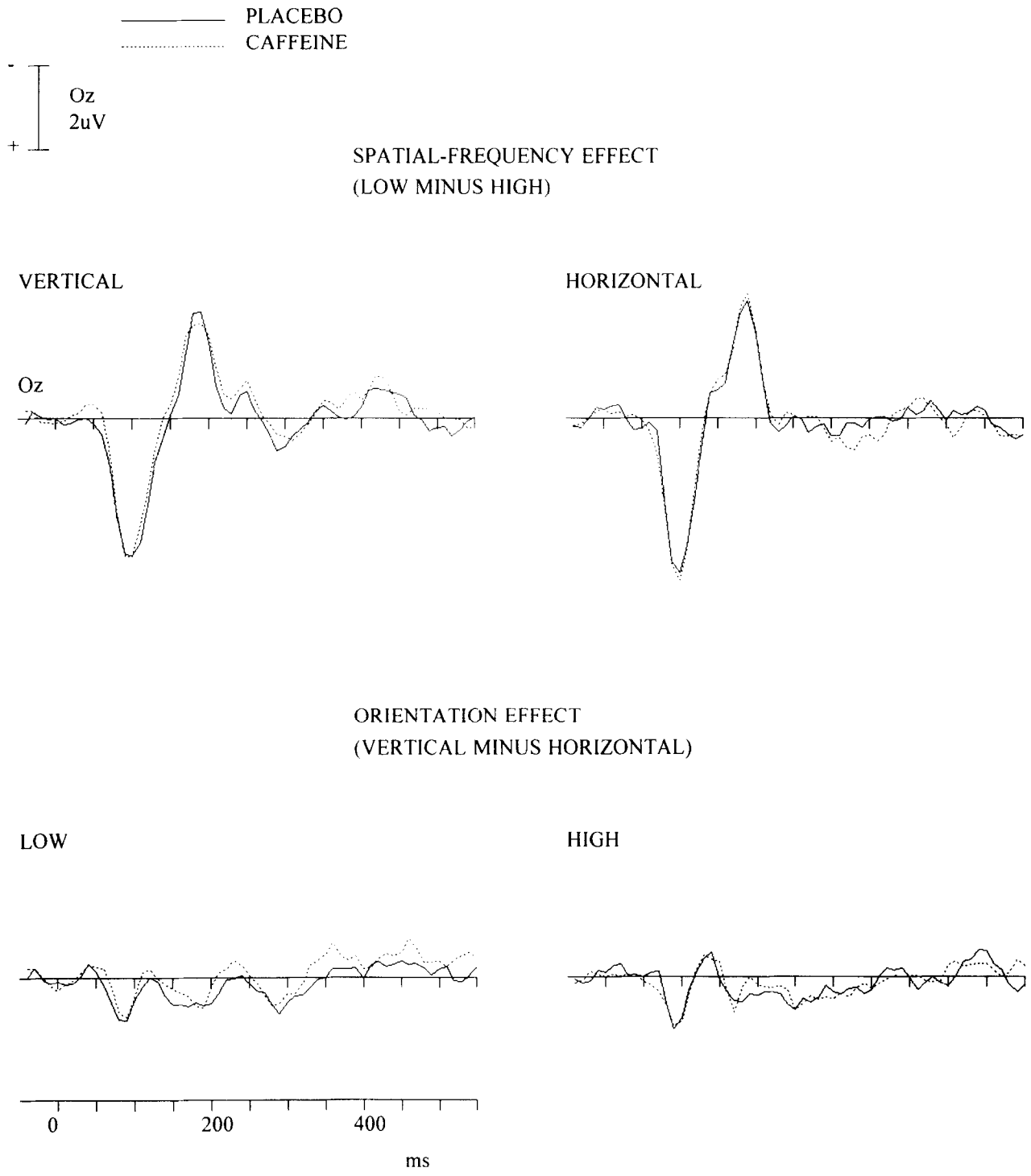

FIG. 3. Grand average exogenous difference waves, recorded from Oz, under placebo and caffeine. ERPs to high spatial frequencies were subtracted from those to low ones (LOW-HIGH), for both vertical and horizontal orientations. ERPs to horizontal orientations were subtracted from those to vertical ones for both spatial frequencies.

Pz). Furthermore, relative to frequency-relevant stimuli, target stimuli elicited additional late positivity. This can be derived from Fig. 5 (Pz) and is a normal finding in this paradigm (11,13).

Main Effects of Caffeine

An amplitude-modulating effect of treatment that was independent of task conditions was found from 290–400 ms. Figure

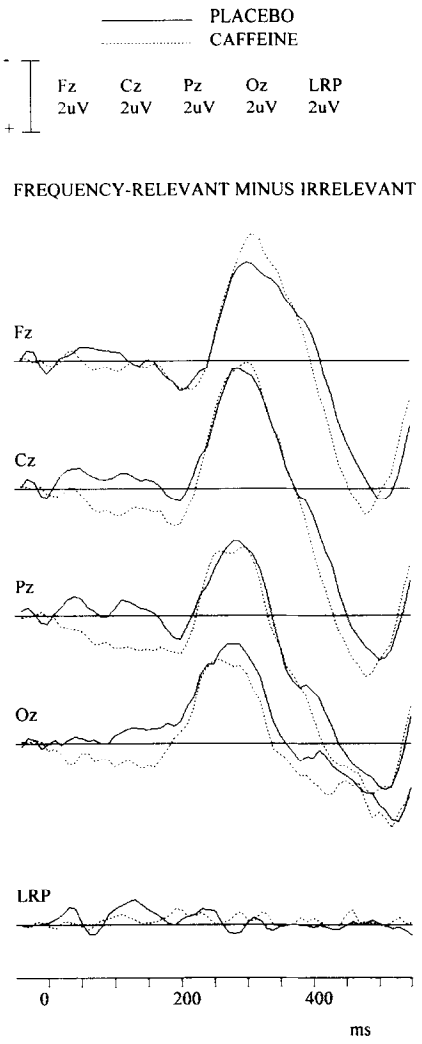

FIG. 4. Grand average endogenous difference waves, under placebo and caffeine. ERPs to irrelevant stimuli were subtracted from those to frequency-relevant ones.

5 shows this effect for targets and frequency-relevant stimuli: under caffeine, more late positivity was elicited, especially so at Cz. This was confirmed by significant Treatment × Site effects [$4.3 < F(3, 13) < 5.1$] between 290 and 400 ms.

DISCUSSION

This research was directed at five possible effects of the administration of 3 mg/kg caffeine (compared with placebo): a change in brain state as indexed by background EEG; improved performance in a simple selective attention task; increased selectivity of processing; improved task-independent discrimination of stimuli; and accelerated central motor processes.

As to the change in brain state, clear differences as a function of treatment were found in the background-EEG power spectrum. The largest reduction under caffeine was found in the lower α range (6.3–9.4 Hz); a somewhat smaller reduction was found for the higher α range (9.4–12.5 Hz) and for the δ range (0–3.1 Hz), and very small changes were found between 12.5 and 25 Hz (σ and low β). There were no differences in θ (3.1–6.3 Hz) or α peak frequency. These effects are partly consistent with other recent reports. Etevenon et al. (6) reported decreased power under caffeine between 3.9 and 14.0 Hz, and no effects on lower or higher frequency ranges. In addition, they found a higher α peak frequency under caffeine. Newman et al. (24) reported reductions in power under caffeine between 6.3 and 10 Hz, and between 12.5 and 30 Hz, as well as an increase in dominant α frequency. Saletu et al. (27) reported decreased power under caffeine between 7.5 and 10.5 Hz, and in two small β ranges, but no effect on dominant α frequency. Thus, power reduction in the lower α range under caffeine seems to be consistent across studies, including the present one. Other effects, e.g., on dominant α frequency or β power, are less consistent and perhaps more dependent on differences in experimental variables (e.g., dose, or time or method of EEG recording).

The reduction in α power is consistent with the notion that caffeine increases cortical "activation," "excitability," and/or "arousal," as are the effects of caffeine on behavioral activity [see (23) for a review]. In the introduction we hypothesized that increased cortical arousal would augment performance in simple speeded tasks like the one presently used, and that this might be related to increased selectivity in processing of incoming information.

Indeed, our behavioral results indicate improvements under caffeine in both speed and accuracy: RTs were faster and hit rate increased, with no alteration in the number of false positives. The accuracy effects are entirely consistent with other reports [see review in (16)]. The combination of increased hit rate with an equal number of false positives can be explained by assuming that caffeine increases both the rate at which information about the stimulus accumulates in the processing system ("sensitivity"), and the tendency to respond to it with a button press (i.e., as if it were a target). Had only the former been influenced, there should have been both more hits and fewer false positives under caffeine; and the exclusive contribution of the latter would have resulted in more hits and more false alarms.

The values of behavioral variables that were influenced by caffeine were compared to those from a previous study (13). The two studies were identical in all respects except for the caffeine manipulation. The comparison revealed that the present effects of caffeine cannot be fully explained on the basis of withdrawal effects in the placebo condition. This is consistent with the prevailing estimates of the withdrawal period after which caffeine withdrawal symptoms start to develop, which range from 12–24 h [see (23) for review]. Subjects in the present study were regular coffee drinkers who had refrained from ingesting caffeine-containing substances for 12 h before the experimental session.

With respect to the shorter RTs under caffeine, in principle these could have been caused anywhere in the chain of processes between stimulus and response. However, recording LRPs provided us with a measure of the time at which, at the level of central motor processes, preparation of the overt response began. It seems reasonable to assume that this preparation starts after the final decision whether to respond has been made; this view is supported by the lack of significant LRPs to nontarget stimuli. There was no difference in the onset latency of the LRP to targets between treatment conditions; hence, we conclude that, first, decision times were not affected by caffeine, and second, faster overt reactions under

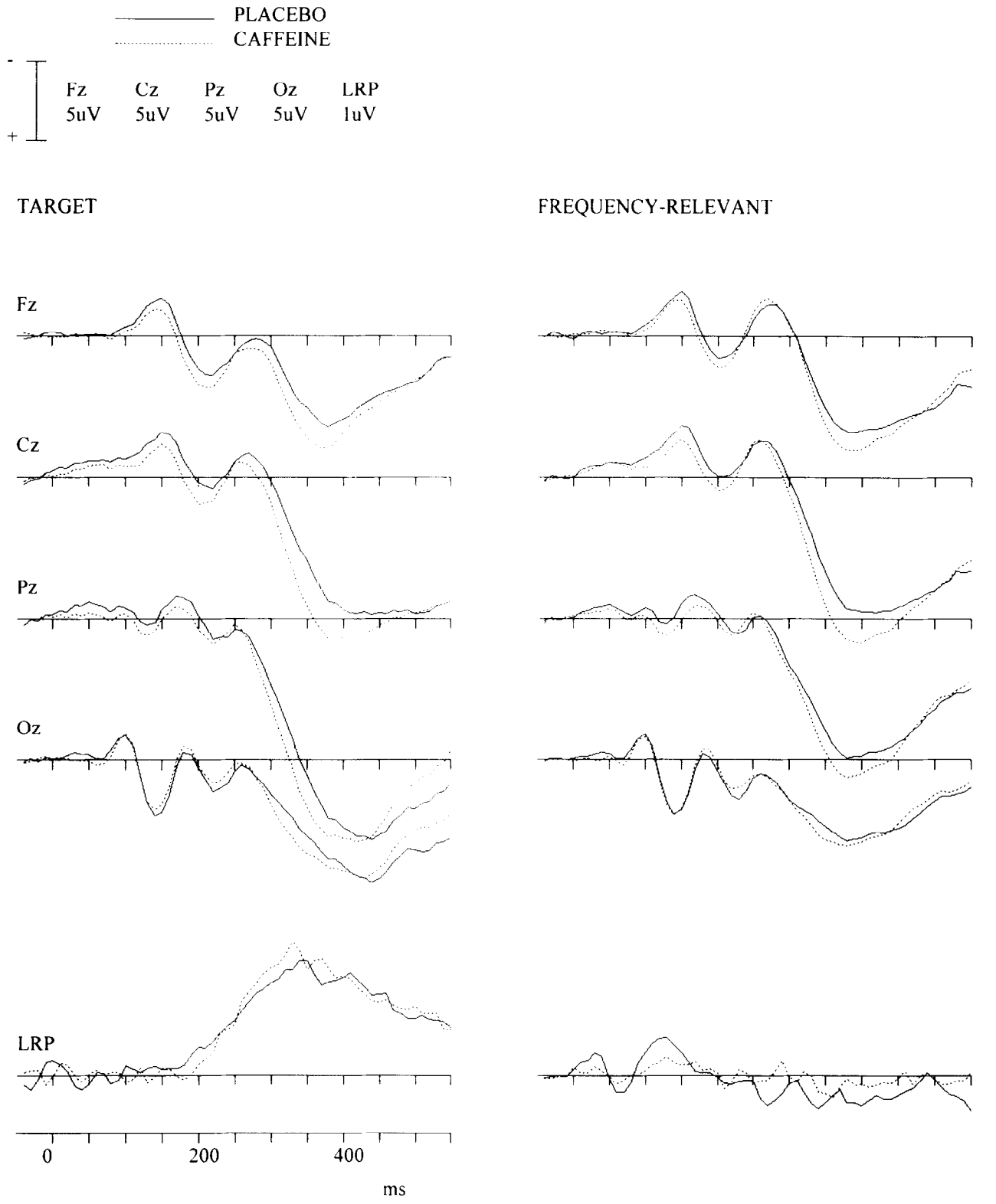

FIG. 5. Grand average (raw) ERPs to target stimuli (left panel), and to frequency-relevant non-targets (right), under placebo and caffeine.

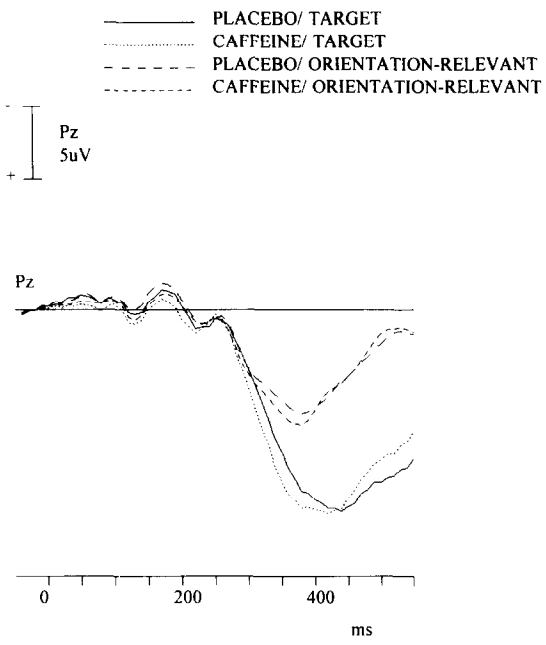

FIG. 6. Grand average (raw) ERPs to target stimuli and orientation-relevant nontargets, under placebo and caffeine, as recorded from Pz.

caffeine were due to faster processing taking place after response preparation had begun, which is probably at the level of central or peripheral motor execution. This is consistent with the conclusion of Lorist et al. (19), that caffeine affects "output stages."

As to "input stages," this work considered the possibility that caffeine might affect sensory discrimination on task-relevant visual dimensions. This was done by analyzing the differential ERP as a function of spatial frequency and orientation as such. In neither case was there any sign of an interaction between treatment and physical stimulus parameters. We therefore conclude that caffeine did not affect sensory discrimination, as far as discrimination is reflected in our ERPs. This may be contrasted with results reported by Lorist et al. (19,20), which were interpreted as indicating an effect of caffeine on "input stages" of information processing. A relevant behavioral result concerned the interaction between caffeine and stimulus degradation in a choice RT task (19). It would seem, however, that a translation of the present operationalization of "sensory discrimination" to a choice RT context would concern a manipulation of stimulus discriminability (rather than degradation), which may be seen as affecting yet another input stage (26). A second relevant result concerned the larger N1 amplitude under caffeine, reported in both studies by Lorist et al. As this N1 result was found independently of any task manipulation, it can in principle signify anything, for example "generalized increased responsibility" (see above). The question remains, however, why there was no such effect in the present study. One possible answer lies in the sensitivity of such early deflections to physical stimulus parameters; the stimuli used here were quite different from the letters and digits in the studies by Lorist et al.

Selectivity of processing was indexed by the brain responses to relevant spatial frequencies, relative to those to irrelevant ones. As before (11,13), the resulting selection potentials started at about 170 ms poststimulus and consisted of frontal positivity, occipital negativity, central negativity, and late parietocentral positivity. An increase in amplitude of the selection potential would have been indicative for more selectivity. However, none of these components of the selection potential was influenced by caffeine. The only interaction between treatment and frequency relevance concerned a very early positivity (60–150 ms poststimulus, mainly at parietal and central electrodes), which was significant under caffeine, not under placebo. Such an early effect is anomalous for nonspatial visual selection. It may be related to the early positive selection potential described by Kenemans et al. (11), which, however, was reported to occur at Oz. It is possible that caffeine causes early selectivity to occur across and within subjects more systematically, and therefore significantly, relative to placebo conditions.

The present lack of effect of caffeine on components of the selection potential that were specified in advance contrasts with the results of Lorist et al. (20). These authors reported an increased central negativity under caffeine. In their raw grand average waveforms this effect appeared to be caused by ERPs to irrelevant stimuli being less negative (more positive) under caffeine, whereas there was no difference between treatment conditions in the ERPs to relevant stimuli. In the present study, increased positivity with a central focus in the same latency range (290–400 ms) was found to all stimuli alike, rather than to irrelevant stimuli in particular. The pattern of effects reported by Lorist et al. was explained most parsimoniously by assuming reduced responsivity to irrelevant events (and therefore more selectivity). The late central positivity in our data, however, cannot be explained in terms of task-directed selectivity. Rather, it only added to the late positivity specifically elicited by target and frequency-relevant stimuli as reported before (11,13). As an alternative, and speculating, one might conceive of the task-independent central positivity as a reflection of generalized increased responsibility under caffeine. A more specific test of this idea could for, example, involve a manipulation of the intrinsic salience of stimuli. A possible reason for the difference in results between the two studies might be that both the selection process proper and the task demands for relevant (selected) stimuli were probably more difficult in the study by Lorist et al.; this could have prompted more need for selectivity which was realized better under caffeine.

Provided that the early positive selection potential observed under caffeine turns out to be a reliable phenomenon, what can be said about its functional meaning? First, it seems to reflect a process that is independent of those reflected in the later selection components, as these were not influenced by caffeine. Second, rejection of irrelevant spatial frequencies on the behavioral output level in this task is virtually perfect (see Fig. 1), whereas rejection of irrelevant orientations is not. Thus, the improvement in accuracy in the caffeine condition is not likely to be caused by improved spatial frequency analysis, but could very well reflect improved orientation analysis. The selection potential associated with spatial frequency is a direct reflection of "further processing" of stimuli having the relevant frequency; and this further processing might well be related, either directly or indirectly, to processing of the orientation. With this viewpoint then, the early selection positivity may be related to improved analysis of the orientation of relevant spatial frequencies.

A further result supports this interpretation. As before, P3 latency was selectively affected by frequency relevance. That is, targets and frequency-relevant stimuli (both having the relevant frequency) elicited P3s with longer latencies than did the

other categories. The simplest interpretation of this difference in P3 latency is that it reflects "further processing" of frequency-relevant stimuli, which might very well concern their orientation. In turn, caffeine specifically shortened this difference in latency. If we assume that in both treatment conditions P3 latency signals the moment in time at which a fixed amount of stimulus evaluation has been conducted, then it must be concluded that the same level of stimulus evaluation is reached earlier in time under caffeine. This faster stimulus evaluation is due to faster processes after frequency selection (which may concern orientation selection) and increases the possibility of a correct response, especially when decision times are equal across treatment conditions. As discussed earlier, both larger hit rates and smaller false-positive rates would be predicted from this scenario. The lack of a treatment effect on the latter suggests the contribution of yet another factor, for example an increased tendency under caffeine to respond behaviorally to both target and nontarget spatial frequencies.

In conclusion, our data are consistent with the following: a) caffeine increases cortical activation; b) caffeine increases sensitivity, or the rate at which information on the stimulus accumulates; c) caffeine increases selectivity, in particular with respect to further processing of stimuli once selected on the basis of the primary attribute; however, the electrophysiologic reflection of selectivity as such must be considered somewhat anomolous and especially in need of replication; d) caffeine speeds up central or peripheral motor processes. These conclusions accord well with theories postulating benefits of "arousal" in simple speeded tasks as a result of stronger selectivity with higher arousal. Our results do not suggest an influence of caffeine on sensory discrimination, but then, other data point to an effect on other input processes.

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