Effects of caffeine on visual attention
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The influence of caffeine on spatial-selective attention: an ERP study

Abstract

Following the indications of previous studies that caffeine might have a specific effect on the processing of spatial information as compared to other types of information, the present study investigated the influence of caffeine on an often used spatial-selective attention task. Event-related potentials (ERPs) were recorded from 11 participants under conditions of caffeine (250 mg) and placebo. They were instructed to attend selectively to stimuli with a specified location in order to react to the occurrence of a target stimulus. Spatial selective attention effects were reflected in the ERPs as more positive going occipital P1 and broadly distributed P2 components, and more negative going occipital-temporal N1 and broadly distributed N2 components. A treatment effect was found as a more positive going frontal P2 component in the caffeine condition, whereas interactions between treatment and attention were observed for P2 and N2 components, but not for P1 and N1 components. This pattern of results suggests that caffeine has no specific influence on spatial selective attention, but rather has a more general facilitating effect on perceptual processing, as well as a possible effect on the frontal control mechanisms, that is, focusing attention and increasing selectivity.
Introduction

Researchers have been studying the effects of caffeine on human performance for decades now. Although the results seem to depend, among other things, on the amount of caffeine administered and the participant's state, the general results indicate shorter reaction times and improved absolute alertness and vigilance measures with moderate amounts of caffeine (Lieberman, Wurtman, Emde, Roberts & Coviella, 1987; Loke, 1990; Frewer & Lader, 1991). Therefore, caffeine is seen as a mild stimulant that acts on the central nervous system.

To gain more insight into the ongoing cognitive operations that are influenced by caffeine intake, Lorist (1995) used a parametric experimental design to study which specific stage(s) of information processing are influenced by caffeine. In addition to performance measures, event-related brain potential (ERP) measures were used to allow a more precise analysis of the timing and organisation of the cognitive processes in the brain during task performance. For example, ERPs can be recorded to physically identical stimuli in both an "attend" and an "ignore" condition, with any differences between the ERPs revealing the effect of attention. Combining behavioural and physiological measures may enhance the insight in the influence of caffeine on cognitive performance.

Examining the effects of caffeine on different aspects of information processing, Lorist (1995) concluded that especially the input and output stages of information processing were influenced by caffeine. For example, when using a visual spatial-selective attention task (diagonal selection) Lorist, Snel, Kok and Mulder (1994) found effects of caffeine on ERPs around 150 ms poststimulus, taking the form of an increased negativity (N1) at posterior sites and an increased positivity for irrelevant stimuli (P2) at anterior sites. Lorist, Snel and Kok (1994) using a stimulus degradation task found similar results. These results showed that caffeine increased the amplitude of the posterior N1 peak while the amplitude of the anterior P2 peak decreased. In the same study, a stimulus-response compatibility task and a time-uncertainty task were used. Results from these tasks showed a caffeine-induced increase in N1 amplitude as well as a shorter latency of this component. This pattern of results could point to a modulation of the activity of the set of sensory neurons that generate the N1 component under the influence of caffeine. However, it could also point to the activation of a different or additional set of sensory neurons. Apart from which alternative might be true, the authors concluded that these results could probably be attributed to an increased receptivity of neurons to external stimuli under the influence of caffeine. In general, the early ERP components (before 200 ms post stimulus), such as the N1, are thought to mainly reflect the early perceptual processes of determining stimulus characteristics (Csisra, Czigler & Ambrò, 1994), although the N1 can be modulated by spatial selective attention (Harter, Aine & Schroeder, 1982; Hillyard & Münte, 1984;
Mangun & Hillyard, 1988). These findings would support the interpretation that caffeine benefits the early perceptual processes or the input stages of information processing. However, no effects of caffeine on input-related processes were found in a study by Kenemans and Lorist (1995), where participants had to select centrally-presented stimuli on the basis of spatial frequency, orientation or a conjunction of these stimulus features. In addition, studying the effects of caffeine on reaction times to different types of nonspatial selectivity, for example using a Stroop task (Hasenfratz & Bättig, 1992; Kenemans & Verbaten, 1998), no consistent support for improved perceptual selectivity by caffeine was found.

Based on an overview of the results of all her studies and the contradictory results concerning the effects of caffeine on the input-related processes of information processing, Lorist (1995) concluded that the influence of caffeine seemed to depend on the experimental manipulations that were used. To better understand the nature of this statement, a closer look into some of the processes of perception and identification of incoming visual information seems relevant. Based on neuroanatomical data, a distinction is often made between two separate and parallel pathways used by the visual system to process incoming visual information (e.g. Goodale & Milner, 1993; Ungerleider & Mishkin, 1982). The ventral system is an anatomically lower pathway, mediated by the geniculo-striate pathway, involving pathways that go from the retina via the lateral geniculate nucleus to the occipital lobes and onto the inferior temporal lobes. The dorsal system depends on the tecto-pulvinar pathway, projecting from the retina to the superior colliculus, which in turn projects to the pulvinar and ends from there in the posterior parietal cortex. Apart from the anatomical differences between the systems, researchers have been interested in the possible differences in function. While the ventral system seems to be specialised for functions such as object segregation and object recognition by shape (Ungerleider & Haxby, 1994), the dorsal system seems to be specialised for functions such as spatial representation and attention (Mishkin, Ungerleider & Macko, 1983) and with the spatial control of action (Goodale & Milner, 1993). However, evidence of recent studies suggested some modifications to this rigid dichotomy. For example, anatomical connections might exist between the two pathways (Felleman & Van Essen, 1991; Van Essen, Anderson & Felleman, 1992; Zeki, 1993), as well as direct projections to areas of the cortex that are concerned with motion (Zeki, 1993).

Considering the observed effects of caffeine on the input-related processes, Lorist (1995), came to the cautious conclusion that the effects of caffeine might be somewhat more pronounced for spatial information-processing, compared to the processing of nonspatial information (such as colour, orientation, or frequency). Supporting this hypothesis is the idea that the occipital N1 peak is assumed to reflect activity in the dorsal projection pathway, which mainly encodes spatial stimulus information (Mangun, 1995; Mangun, Hillyard & Luck, 1993). The effects of caffeine on the N1 might therefore be interpreted as an effect on the dorsal system, confirming that the effects of
Effects of caffeine on visual attention

caffeine might be more pronounced in the processing of spatial information as compared to nonspatial information.

The present study investigated the influence of caffeine on spatial selective attention, using a task chosen for its suitability to reveal clear effects of selective attention on behavioural results, ERPs and dipole localisation (e.g., Mangun & Hillyard, 1988, 1990; Mangun et al., 1993). In general, ERPs from this kind of spatial selective attention tasks have shown a more positive going occipital P1 component (peaking between 90 and 140 ms) and a more negative going occipital N1 component (peaking between 140 and 220 ms) for the attended condition as compared to the unattended condition, whereas the latencies of these components are not influenced. The early ERP peaks can first be seen contralateral to the visual field of stimulus presentation and somewhat later ipsilateral as well. Both components have been localised at scalp sites overlying lateral extrastriate cortex (e.g., Gomez Gonzales, Clark, Fan, Luck & Hillyard, 1994). The possible effects of caffeine on spatial attention are expected to be observed as an interaction between treatment and the attention-modulated P1 and N1 ERP components.

Method

Participants

Eleven healthy participants, four men and seven women, aged 20-25 ($M = 22.4$, $SD = 2.0$) contributed to this study as a requirement of their psychology course. All participants were self-reported right-handed nonsmokers, had normal or corrected-to-normal vision, and were habitual coffee drinkers accustomed to a daily caffeine ingestion ranging from 3 to 6 cups of coffee a day ($M = 4.9$, $SD = 1.3$). Participants did not work night shifts, did not use prescription medication except for birth control, and reported no history of brain damage. Before the first experimental sessions started, participants filled out a consent form to agree to the administration of caffeine. In this study participants were treated according to APA ethical standards and were told that they could withdraw their participation at all times.

Treatment manipulation

A repeated measurements design was applied in order to use each participant as his/her own control, thereby minimising the impact of interindividual differences in performance. All participants were asked to maintain a 12-hour abstinence period prior to the experiment, of all caffeine containing foods and beverages and to refrain from drinking alcoholic beverages. Furthermore, participants were instructed to have a good night’s rest. The order of treatment conditions was balanced across participants (due to
equipment failure, the data of the twelfth participant were rejected for further analysis, resulting in five participants receiving placebo in the first session and six participants receiving caffeine). Treatment conditions consisted of 250 mg caffeine or lactose dissolved in a cup of normally brewed decaffeinated coffee. To suit their own taste participants could add milk powder and sugar to the coffee. Treatments were double-blind and deceptive, that is, participants thought that they were consuming normal caffeine-containing coffee during both experimental sessions.

Physiological and subjective measures

An automatic blood pressure device was used for blood pressure and heart rate measurements (oscillometric method, boso-Oscillomat). Physiological and subjective measures were used to examine changes in mood and state anxiety within participants as a result of caffeine intake. In addition, the questionnaires were used to examine changes in subjective feelings between the two sessions of the same participant.

From a general health checklist it was assessed to what extent participants were morning or evening types (Kerkhof, 1984). Four questionnaires were used to measure subjective feelings: (a) The short version of the Profile of Mood States (POMS, Wald & Mellenbergh, 1990). Participants indicated how they felt at that moment for each of 32 adjectives on a 5-point scale. The five clusters of adjectives represented specific mood states: depression, anger, fatigue, vigour and tension. (b) The state part of the Dutch version of the State-Trait Anxiety Inventory (STAI; Van der Ploeg, Defares & Spielberger, 1980). Participants reported on 20 items on a 4-point scale. (c) A subjective workload inventory based on the NASA-TLX inventory (Damos, 1987; Hart & Staveland, 1988). The inventory items represented overall amount of workload, task difficulty, time pressure, mental effort, physical effort, frustration, stress, fatigue and type of activity. Participants could indicate on a 5-point scale how they felt. (d) A sleep quality inventory (Mulder-Hajonides van der Meulen, Wijnberg, Hollander & Van de Hoofdakker, 1980) was used to measure participants' sleep duration and quality of the nights before the experimental sessions. Participants could indicate whether they agreed or disagreed with each of 14 statements concerning their sleep quality.

Task

All participants performed three tasks: (1) a colour selection task (Ruijter, de Ruiter, & Snel, in press), (2) a spatial selection task, and (3) a concentration task (Ruijter, Lorist, Snel & de Ruiter, in press). In this article only the spatial selection task will be discussed. The order in which the participants had to perform these tasks varied according to a rolling Latin square paradigm. All participants were tested individually in a dimly lit, sound-attenuated room, comfortably seated in an easy chair. A response button was positioned on a table to the right of the chair.
Effects of caffeine on visual attention

Stimuli were presented with a Zenith Z-Select 100 PC by the CSSP program of the Psychonomics Department on a Nec Multisync 3FG monitor positioned at 80 cm from the participant's eyes. All stimuli were vertically oriented white bars presented against a black background. Nontarget (standard) stimuli consisted of 2.7° x 0.3° bars while target stimuli were slightly shorter at the top, and measured 2.2° x 0.3°. Stimuli were flashed in random order to one of two visual field locations: in each of the lateral visual fields the centre of the white bar was located 5.3° to the left or right from the centre of the of the screen and 2.2° above the centre of the screen, which was defined by a fixation cross that was continuously present. Stimulus duration was 100 ms and the interval between successive stimulus onsets varied randomly between 350 and 650 ms (rectangular distribution). Participants were instructed to focus attention on stimuli with a specified, task-relevant location (left or right), while ignoring the other, irrelevant stimuli. In addition, they were instructed to maintain constant fixation on the fixation cross on the centre of the screen and to press the response button with the right index finger as quickly as possible, while maintaining a high level of accuracy, each time a target stimulus occurred among the relevant-location stimuli. The spatial selection task consisted of 12 blocks of trials, each containing 96 stimuli, and the location selection cue (left or right) was alternated at each block. Consequently, during the task, both the left and right locations served as selection criterion six times. Targets were presented among both relevant (attended) and irrelevant (unattended) stimuli. Accordingly, participants were presented four types of stimuli (relevant target, probability .08, relevant nontarget, probability .42, irrelevant target, probability .08 and irrelevant nontarget, probability .42). The stimuli were presented successively and in a random order except that relevant target stimuli did not occur in succession. All participants were presented with two practice runs in each session, consisting of 96 stimuli of which both the left and the right location served as relevant location once.

General procedure

Each participant participated in two sessions with an interval of approximately one week. Both experimental sessions were identical except for the treatment manipulation and the completion of an informed consent form and a general health questionnaire in the first session. Participants arrived at the laboratory at 9.30 a.m. where blood pressure and heart rate were measured and participants were asked to fill out the POMS, STAI and sleep quality questionnaires. After that they consumed their coffee. Subsequently, the electrodes were applied and participants were seated in the experimental room. On average 40 minutes after the coffee consumption participants started to perform the experimental tasks. The tasks lasted for about 1 hour, after which participants filled out the POMS, STAI and the subjective task load inventory again. Blood pressure and heart rate were measured a second time. Thereafter, the electrodes were removed and the participants were thanked for their participation.
Chapter 4: Influence of caffeine on spatial selective attention

Recordings

The EEG was recorded from 30 tin electrodes attached to an electrocap according to the 10/20 system (American Electroencephalographic Society, 1991). The following electrode locations were used: Fp1, Fpz, Fp2, AFz, F7, F3, Fz, F4, F8, FC5, FC6, T7, C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, PO3, PO4, O1, Oz and O2. To monitor vertical and horizontal EOG activity electrodes were attached above and below the right eye and at the outer canthi of both eyes. The right mastoid was used as a reference electrode and an electrode placed on the right side of the nose was used as ground. The signals were amplified by a Nihon-Kohden Neurotop amplifier (MME-3100 series) with a low-pass filter set at 35 Hz and a time constant of 2.5 s and continuously digitally sampled and stored at 250 Hz on a Compaq Pro Linea PC with the CMSP program developed at the Psychonomics Department.

Data reduction and statistical analysis

Behavioural measurements

Button presses were classified as hits if they occurred in a 200-1000 ms window after the onset of the relevant target stimulus. Reaction times also had to fall within a range of 2.5 SD from each participant's average. Button presses to the other three categories of stimuli were classified as false alarms, while failures to respond to relevant targets were classified as misses. The first two trials within each block were excluded from analysis. Overall comparison between reaction times and number of hits for both conditions was done with an ANOVA with a repeated measurements design: Treatment (2: placebo/caffeine) x Visual field of stimulus presentation (2: left/right). In addition, behavioural measures were analysed using the following signal detection parameters (Pollack & Norman, 1964): the proportion of hits (PH), the sensitivity of the visual system (d') and A' (a nonparametric equivalent of d'). A' is in fact the proportion of correctly recognised targets, corrected for the participant's response tendency and described as a measure of sensitivity (e.g. Boice & Gardner, 1988). Statistical testing was done with a univariate ANOVA with a repeated measurements design, with the factor Treatment (2: placebo/caffeine).

EEG measurements

The first two trials within each block and trials with incorrect behavioural responses (defined above) were excluded from analysis. Trials containing amplifier blocking or in which the EEG showed flat lines (no voltage fluctuation for a period of more than 40 ms) were detected automatically and omitted from further analysis. Ocular artefact in the EEG was controlled using regression analysis in the frequency domain (Woestenberg, Verbaten & Slangen, 1983). After EOG correction all intervals containing movement artefacts (change in amplitude of more than 40 μV between two additional samples) or electrical drifts (difference between lowest and highest
Effects of caffeine on visual attention

amplitude more than 100 μV within one trial, 256 samples) were excluded from further analyses. For each participant average stimulus-locked ERPs were computed separately for each scalp location and for each of the four stimulus types, as well as for both treatment conditions. The averaging epochs lasted for 880 ms poststimulus, using the last 100 ms of the 144 ms prestimulus period as a baseline. After averaging across trials, the ERPs were digitally low-pass filtered at 20.5 Hz prior to subsequent processing and analysis.

To compare peak latency measures from both treatment conditions, ERP waveforms were averaged over relevant nontargets, irrelevant nontargets, both sites of presentation, and all leads from a particular region (see below). Subsequently, a computerised peak-picking method was used to estimate the peak latencies of NP80, P1, N1, P2 and N2 on averaged ERPs for frontal (F3, F4, FC5, FC6), central (C3, C4, T7, T8), parietal (P3, P4, CP1, CP2,) and occipital (O1, O2, PO3, PO4) scalp regions. These peaks were then all checked visually to determine their accuracy. In cases where the computer yielded inaccurate peaks, which resulted mainly from the presence of multiple peaks in the latency range, the search epoch was restricted and the onset estimate again determined. Repeated-measures univariate analyses of variance (ANOVAs) in a Treatment (2: placebo/caffeine) design were performed on the peak latency measures separately for the most prominent ERP peaks for separate regions.

Mean amplitude values were determined by computing the mean voltage of windows of 36 or 52 ms intervals (depending on visual inspection of the broadness of the peak) in the latency range of the ERP component of interest for each electrode site separately. Four separate repeated-measures univariate analyses of variance (ANOVAs) were performed, one for each of the scalp regions (defined above, each consisting of 4 leads), in the following design: Visual field of presentation (2: left/right) x Treatment (2: placebo/caffeine) x Attention (2: relevant/irrelevant location) x Electrode location (2: lateral medial or anterior/posterior, depending on the scalp region) x Hemisphere location of the electrodes (2: left/right). When interactions between factors emerged, follow-up simple tests were used to determine which factor levels were responsible for the differences in amplitude. In addition, significant two or three way interactions of Treatment with Electrode Location or Hemisphere when present in the analyses, were followed by a second ANOVA with normalised data (according to the vector length scaling method proposed by McCarthy & Wood, 1985) to assess scalp topographic differences. Interactions with Location are only reported if the interactions remained significant after normalisation. For all analyses, an alpha of .05 was used as the accepted level of significance.

Two methods were available to obtain information about the generator locations of the ERP components, namely topographic mapping (CSD distributions) and dipole source localisation. Topographic mapping of the scalp potentials and corresponding CSD distributions were calculated with the Brain Electric Source Analysis program (BESA, NeuroScan, Inc., Herndon VA; Scherg, 1990), for each Treatment and each Attention condition, as well as for the difference waves. Attentional difference waves
were obtained separately for both fields of attention by subtracting ERP to irrelevant nontargets from ERPs to relevant nontargets. CSD maps provide meaningful information about the location of effects because they are relatively insensitive to activity arising from distant sources and favour relatively more local (cortical) brain activity (Gomez Gonzales et al., 1994; Johannes, Münte, Heinze & Mangun, 1995). In BESA, the waveforms were re-referenced to the average reference, and interpolated for mapping by means of a spherical surface spline method. The corresponding CSD values were estimated by taking the second order spatial derivatives of the spherical spline interpolated surface data (Perrin, Pernier, Bertrand & Echallier, 1989).

To enable a comparison between our results and those of Lorist (1995) an additional statistical analysis was performed including all stimulus categories on lead Pz from 152-252 ms, to reveal possible differences between placebo and caffeine conditions.

Results

Subjective and physiological measurements

Participants reported no differences in quality of sleep on the night before the experimental sessions. All items from the task load inventory were analysed separately, revealing no effects of Treatment on subjective effort needed to perform the set of tasks. There were neither any differences in mood (measured with the POMS and the STAI) between the treatment conditions as measured upon the arrival of the participants, nor as measured at the end of the experimental sessions. Averaged over conditions participants felt more fatigued, $F(1,10) = 7.87, p = .019$, and less vigorous, $F(1,10) = 11.31, p = .007$, at the end of the session compared to the start of the session. There were no differences in systole and diastole blood pressure or heart rate as a result of caffeine intake.

Performance

No significant effects of order of treatment were observed in reaction time and proportion of hits, $F(1,20) = 0.04-0.09$, all ps n.s. Hence, treatment order was omitted as a variable in further analysis. No differences in reaction time and number of hits due to the Field of presentation (left or right) the participants had to attend to were observed, $F(1,20) = 0.32-0.83$, all ps n.s. Furthermore, no interactions between Treatment and Field of presentation were revealed, $F(1,20) = 0.93-1.10$, all ps n.s.

Overall, a significant main effect of Treatment was found on the number of hits, $F(1,10) = 6.47, p = .029$, with more correct reactions for the caffeine condition ($M = 5.9$, $SD = 1.1$) as compared to the placebo condition ($M = 5.4$, $SD = 1.1$). No main effect of
**Effects of caffeine on visual attention**

Treatment on reaction times could be observed. However, signal detection parameters revealed an effect of Treatment on $A'$, $F(1,10) = 6.43, p = .030$, indicating a higher perceptual sensitivity in the caffeine condition ($M = 0.93, SD = 0.04$) as compared to the placebo condition ($M = 0.91, SD = 0.04$).

**ERP Measurements**

Figures 1 and 2 depict the grand average ERPs for the placebo and caffeine conditions, respectively, elicited during the spatial selection task from all scalp locations for the left visual field of stimulus presentation from 100 ms prestimulus till 320 ms poststimulus. Superimposed are ERPs elicited by relevant nontarget and irrelevant nontarget stimuli. In Table 1, results of statistical analyses on mean ERP amplitudes are reported. Main effects of Attention and Treatment are presented as well 2 and 3-way interactions with Treatment. For reasons of clarity, only significant results are reported. NP80 and P1 peaks were not clearly identifiable for frontal and central scalp regions and both amplitude and latency measurements for these particular cases will be discarded from further analysis. Statistical analysis revealed no significant differences in peak latencies for the different peaks and the separate regions as an effect of Treatment.

Results of the statistical test concerning the mean amplitudes on the Pz lead from 152-252 ms including all stimulus categories, revealed no effects of caffeine on either the P1 or the N1 peak. This indicates that responses to relevant targets and irrelevant targets were not differentially influenced by caffeine as compared to responses to relevant nontargets and irrelevant nontargets.
Table 1 F and p-values for the main effects of Attention and the effects involving Treatment, for different scalp regions and for different peaks of the ERP. Only p-values of < .05 are mentioned. All degrees of freedom are F (1,10). Treatm. = Treatment, Hemi. = Hemisphere location of the electrodes, VF = Visual field of stimulus presentation, Elec Loc. = Electrode Location, other than hemisphere differences (lateral/medial or anterior/posterior).

<table>
<thead>
<tr>
<th>Scalp region:</th>
<th>Peak</th>
<th>Attention</th>
<th>Treatm.</th>
<th>Treatm. x Attention</th>
<th>Treatm. x Hemi.</th>
<th>Treatm. x VF</th>
<th>Treatm. x Attention x Elec Loc.</th>
<th>Treatm. x Attention x Hemi.</th>
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<tr>
<td>Occipital:</td>
<td>NP96</td>
<td>-</td>
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<td>PO3, PO4</td>
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<td>F =17.76</td>
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<td>p=.008</td>
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<td>P236</td>
<td>-</td>
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<td>-</td>
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<td>p=.007</td>
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<td>-</td>
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<td>F =15.55</td>
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<td>p=.001</td>
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<td>p=.001</td>
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<tr>
<td></td>
<td>F3, F4,</td>
<td>P204</td>
<td>F =5.58</td>
<td>F =7.45</td>
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<td>-</td>
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<td>FC5, FC6</td>
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<td>N296</td>
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<td>-</td>
<td>-</td>
<td>F =9.62</td>
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<td>p=.003</td>
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81
Effects of caffeine on visual attention

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**Figure 1** Grand average ERPs for the placebo condition, for all scalp locations, for the left visual field of stimulus presentation from 100 ms prestimulus till 320 ms poststimulus. Superimposed are ERPs elicited by relevant nontarget and irrelevant nontarget stimuli.
**Figure 2** Grand average ERPs for the caffeine condition, for all scalp locations, for the left visual field of stimulus presentation from 100 ms prestimulus till 320 ms poststimulus. Superimposed are ERPs elicited by relevant nontarget and irrelevant nontarget stimuli.
Effects of caffeine on visual attention

Effects of Attention
As can be seen in Table 1, significant main effects of Attention were found for occipital P136, N196 and N284; parietal N164, P236 and N284; central N148, P204 and N296; and frontal N148, P204 and N296 peaks. The amplitudes of these peaks were larger in response to stimuli at the attended location compared to stimuli at the unattended location. In other words, the attended condition yielded more positive going waveforms for the positive peaks and more negative going waveforms for the negative peaks. No main effects of Attention could be observed for the occipital NP96 and P236 peaks and parietal NP96 and P120 peaks. However, a trend towards an Attention effect on the parietal P120 was observed, $F(1,10) = 3.91, p = .076$. P120 effects were maximal at occipital leads and were initially larger contralaterally to the field of stimulus presentation but with time became larger over ipsilateral sites. The same pattern holds for the N196 peak that was found to be maximal at occipital-temporal sites.

![Figure 3](image-url)

**Figure 3** Exogenous effect (irrespective of attention condition and visual field of stimulus presentation) for the frontal P204 component for leads F3, F4, FC5, and FC6. Superimposed are ERPs elicited by the placebo and the caffeine condition.
Effect of Treatment
Caffeine intake yielded a more positive going exogenous frontal P204 component irrespective of the attention condition, which can be seen in Figure 3. On the basis of visual inspection of the ERP waveforms the question was raised whether it was only the P204 peak that showed this difference between treatment conditions or whether the effects of caffeine possibly had a longer lasting and broader effect on the ERP. This observation was confirmed in an additional analysis, showing that a significant main effect for Treatment was also observable for the F3 and F4 leads in the 220-240 ms interval, $F(1,10) = 7.80, p = .019$, with the caffeine condition showing a more positive amplitude than the placebo condition.

![Figure 4](image_url)

**Figure 4** Grand average ERPs (averaged over visual field of stimulus presentation) on leads PO3, O1, O2 and PO4 to denote the interaction effect of Treatment x Attention on occipital P236 and N284 components. Superimposed are ERPs elicited by relevant and irrelevant nontargets in the placebo condition and relevant and irrelevant nontargets in the caffeine condition.
Effects of caffeine on visual attention

Interactions of Treatment and Attention
Interactions of Treatment and Attention were found for occipital scalp regions for P236 and N284 components and can be seen in Figure 4. However, simple tests concerning the P236 component revealed neither a significant main effects of Treatment in either Attention condition, nor a significant main effect of Attention in either Treatment condition. Visual inspection revealed that the placebo condition showed a larger amplitude for stimuli at the attended locations, while the caffeine condition showed an opposite effect with a larger amplitude for stimuli at the unattended locations. Simple tests for the N284 component revealed a significant effect of attention in the caffeine condition, \( F(1,10) = 8.10, p = .017 \), but not in the placebo condition. In addition, a significant effect of Treatment on relevant nontargets was found, \( F(1,10) = 5.76, p = .037 \), but not on irrelevant nontargets.

Interaction of Treatment and Hemisphere
A significant interaction of Treatment and Hemisphere was found for the parietal NP96 component. After normalisation of these data this interaction remained significant, \( F(1,10) = 9.29, p = .012 \). Simple tests revealed neither statistical significance for a main effect of Treatment on either Hemisphere, nor a main effect of Hemisphere in either Treatment condition. Visual inspection of the ERPs revealed that for the left hemisphere, this interaction consisted of a negative amplitude for the placebo condition and a positive amplitude for the caffeine condition, while for the right hemisphere the amplitudes were similarly negative for both conditions. Apparently, caffeine has a more pronounced effect on parietal regions of the left hemisphere at early time intervals (88-114 ms) as compared to the right hemisphere.

Interactions of Treatment, Attention and Electrode Location
Significant 3-way interactions of Treatment, Attention and Electrode Location were found for the parietal P236 and frontal P204 peaks. The ERP waveforms showed that for the parietal regions the attention effect was larger in the caffeine condition than in the placebo condition and also that the attention effect for the placebo condition was smaller on P3 and P4 leads than on CP1 and CP2 leads. For the frontal region this effect resulted from a different pattern: on F3 and F4 leads the attention effect was somewhat smaller in the caffeine condition than in the placebo condition, while on FC5 and FC6 leads the attention effect was smaller for the placebo condition.

Interactions of Treatment, Electrode Location and Hemisphere
Significant 3-way interactions of Treatment, Electrode Location and Hemisphere were found for the occipital NP96 peak and for the parietal N164 peak, indicating that the effect of Treatment is differential for all leads in the particular region. However, none of the leads analysed independently, in either the occipital or parietal region revealed a main effect of Treatment. Close inspection of the ERP waveforms for the parietal
region revealed a more negative going amplitude for the caffeine condition as compared to the placebo condition for the P3 lead, while for the P4 lead this pattern was reversed. CP1 and CP2 leads showed virtually no differences in amplitude between the Treatment conditions. For the occipital region this 3-way interaction can be explained by a more negative going amplitude in the placebo condition for the PO3, O1 and O2 leads as compared to the caffeine condition, while for the PO4 lead this pattern was reversed.

CSD maps and dipole source localisation.
CSD maps of attention modulated P1 and N1 peaks looked similar for stimuli presented in the left and right visual field and were comparable to those of earlier spatial-selective attention studies (e.g., Mangun & Hillyard, 1988, 1990; Mangun et al., 1993). The P1, mostly prominent over occipital scalp areas, peaked between 120-140 ms. The N1, having a very broad scalp distribution over occipital, temporal and parietal scalp areas, as well as more anterior scalp regions, peaked between 140-200 ms. There was no apparent difference in CSD maps on these attention-related components due to caffeine.

As far as the effect of caffeine on the exogenous frontal P2 component is concerned, the CSD maps revealed no observable difference between the placebo and the caffeine condition, and the component seems to originate from a fronto-central source. However, trying to fit a dipole model on these data is speculative since little is known about dipole modelling in this time-range and the possible underlying brain mechanisms or structures being responsible for the observed results. At this time the authors were not able to develop a model based on the observed results that seemed trustworthy enough to present in this paper. More research is needed to develop firm dipole models of enlarged P2 components by caffeine.

Discussion
The present study addressed the issue whether caffeine influences spatial information processing, as was suggested by previous studies of Lorist (1995). This issue was examined by presenting participants with an often-used spatial-selective attention task in both a placebo and a caffeine condition, thereby investigating possible interactions between visual attention and treatment.

Attention effects
The amplitudes of ERP components elicited by relevant stimuli showed a more negative going occipital N196, parietal N164, and frontal and central N148 peak compared to the irrelevant stimuli, as well as a more positive going occipital P136 peak. In addition, attention related enhanced components were found for the occipital N284, parietal P236, central and frontal P204 and frontal N296. These results closely correspond to these of earlier research regarding the selective spatial attention paradigm
Effects of caffeine on visual attention

(e.g., Mangun et al., 1993; Gomez Gonzales et al., 1994; Johannes et al., 1995; Clark & Hillyard, 1996). Also in accordance with these studies, the occipital and parietal NP96 components were not influenced by attention. Although a trend towards a significant effect of attention was found for the P120 component in the parietal region, this component was found to have a more pronounced occipital, lateral maximum, as can be seen in Figure 1 on O1, O2 and P03, P04 leads (see also Mangun et al., 1993).

Taken together, it is concluded that the observed pattern of results represents the effects of spatial-selective attention. Since the attention related effects that were found are comparable to those from previous spatial attention studies it can be concluded that the spatial attention task was performed and perceived by the participants in the expected way.

Interactions of Treatment and Attention
The main hypothesis that caffeine clearly affects spatial-selective attention, as would be suggested by an interaction between Treatment and the attention modulated N1 and P1 components of the ERP could not be confirmed. The research, on which this hypothesis was based, used different tasks to investigate the effects of caffeine on general information processing. For example, in the Lorist, Snel, Kok and Mulder study (1994) a diagonal spatial selection task was used. Results showed an enlargement of the posterior N1 component due to caffeine, which was interpreted as an influence of caffeine on spatial selection. However, this result was based on analyses of data concerning all stimulus categories (including attention drawn to relevant and irrelevant targets) as opposed to analysing the spatial attention effect separately (by subtracting irrelevant from relevant nontargets). In other words, it was not the attentional N1 component per se that was influenced by treatment. Therefore it can not be ruled out that the effects reported by Lorist et al. reflect a more general improvement in stimulus processing and evaluation.

Evidence for a general effect of caffeine on early information processing comes from a study by Lorist, Snel and Kok (1994). In this study a nonspatial stimulus-degradation task was used, in which a response had to be given to all types of stimuli. Caffeine increased the amplitude of the posterior N1 peak, while it decreased the amplitude of the P2 peak. In the same study, these authors also found an enlargement of the N1 component by caffeine using a spatial stimulus-response compatibility task and a time uncertainty task. In addition, an increased N1 amplitude by caffeine was also found in a diagonal selection task (Lorist, Snel, Kok & Mulder, 1994). Thus, caffeine does seem to influence early ERP components, which are said to reflect basic perceptual processing (Csisbra et al., 1994) in tasks requiring both spatial and nonspatial stimulus processing. However, in two other studies in which a gratings task (Kenemans & Lorist, 1995) and a colour selection task (Ruijter, de Ruiter & Snel, in press) were used, the effects of caffeine on early ERP components could not be found. An explanation for these contradictory results can possibly be found in the different task parameters. However, more research is needed to draw firm conclusions about this.
Chapter 4: Influence of caffeine on spatial selective attention

The results of the present study suggest that caffeine does not have a specific influence on spatial attention per se, but rather has a more general influence on early information processing by either widening the visual field of attention (in spatial selection tasks), thereby enlarging the amount of information that can be processed or, alternatively, intensifying the information processing in case a reaction has to be given to all stimuli. In support of this interpretation is the observed increase of the number of correct reactions and the increase of sensitivity (A') by caffeine, as derived from the signal detection parameters. A' is considered to reflect an input-stage related sensitivity, which could point to a caffeine induced improvement of early perceptual information processing in the present study.

Additional interactions of Treatment with Attention were observed for the occipital scalp regions for the P236 and N284 components. For the P236 component the placebo condition showed a larger amplitude for stimuli at the attended locations, while the caffeine condition showed an opposite effect with a larger amplitude for stimuli at the unattended locations. These results could also be interpreted by the presumed enlargement of the amount of information that can be processed under caffeine conditions. A wider scope of attention is induced in the caffeine condition, resulting in increased attention to the irrelevant stimuli. The interaction of Treatment with the N284 component consisted of an effect of attention in the caffeine condition, while this effect was not significant for the placebo condition. This again could support the idea of extra information processing capacity in the caffeine condition. However, opposite to the Treatment x Attention effect on the P236, this effect seems to consist of more processing of the relevant nontargets and less processing of the irrelevant nontargets. While both interactions of Treatment with P236 and N284 could be explained by an enlargement of processing activity by caffeine, these results point to different ways on how this energy would be utilised.

Treatment effect
A main effect of Treatment on ERP amplitudes was found for the frontal exogenous P2 component with the caffeine condition showing a more positive going ERP compared to the placebo condition. This effect was independent of attention and was apparent in a time range from 180-240 ms poststimulus on a broad number of frontal leads. Similar frontal P2 effects of caffeine have been found by Ruijter, de Ruiter and Snel (in press) using a colour selection task. In this study the P2 amplitude was significantly larger in the caffeine than in the placebo condition at lead FPz from 200-280 ms and at lead Fz from 180-260 ms. In another study by Ruijter, Lorist and Snel (1999) in which a dual-task was used, an exogenous effect of caffeine was found on lead Fz in the 150-250 ms window; and in a study by Lorist, Snel, Kok and Mulder (1994) using a diagonal selection, an enhancement of the anterior P2 peak was found in the 200-300 ms epoch that was primarily restricted to irrelevant stimuli. Although CSD maps of this effect in the present study point to a fronto-central source, CSD maps in the Ruijter, de Ruiter
Effects of caffeine on visual attention

and Snel (in press) study point to a more frontal source. Taking these results together, one might conclude that in this time interval, roughly 180-250 ms, a frontally based source for this effect of caffeine seems a probable assumption. If true, it means that caffeine influences the prefrontal cortex, which is assumed to be related to working memory and a higher level control- and co-ordination mechanism (for an overview see for example Wickelgren, 1997).

Interaction of Treatment and Hemisphere, 3-way interactions with Treatment

An effect of caffeine on the left parietal region, but not on the right parietal region was observed in the early time interval of the NP96. However, using EEG power spectral analyses, Etevenon et al. (1989) concluded that the left temporal area appeared to be the most activated EEG location by caffeine. These authors recorded EEG from participants who were resting with their eyes either closed or open, for periods of 2.5 minutes, in both a placebo and a caffeine condition. Although the same pattern of results was found by these authors before, using the comparable substance yohimbine as a stimulant (Etevenon, Pidoux, Peron-Magnan, Lecrubier & Verdeaux, 1982), they do not offer a suggestion as to why especially the left temporal area is mostly activated by caffeine. In contrast, using the PET (Positron Emission Tomography) technique, Cameron, Modell and Hariharan (1990) did not observe any regional or hemispherical differences due to caffeine, in participants who were lying still. A major difference between these studies and the present study is the time scope in which these effects were found: a time period of 2.5 minutes, approximately 1 hour after caffeine intake (Etevenon et al., 1989), 15 and 45 minutes after intravenous caffeine administration (Cameron et al., 1990) and in the present study 96 ms after stimulus presentation, approximately 1 hour after caffeine intake. Whether or not the left parietal or temporal cortex areas are specifically influenced by caffeine intake and under what circumstances, remains an uncertainty for now. More research is needed before any conclusions can be drawn. The same conclusions can be reached for the results displayed by the three-way interactions of Treatment, Attention and Electrode Location and Treatment, Electrode Location and Hemisphere. These seem to point to an effect of caffeine that is differentially distributed over the scalp. However, these interactions are difficult to interpret and are not very informative without replication first.