Effects of caffeine on visual attention
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The effects of caffeine on visual selective attention to colour: an ERP study

Abstract

Event-related potentials were recorded from 11 subjects under conditions of caffeine (250 mg) and placebo. Subjects were instructed to attend selectively to stimuli with a specified colour (red or blue) in order to react to the occurrence of a target within the attended category. Reaction times revealed faster responses for the caffeine condition, while no differences in strategy were observed. Colour attention effects were identified as frontal selection positivity, occipital selection negativity, and N2b, whereas target detection was reflected in P3b. Effects of treatment were found as a more positive going frontal P2 component in the caffeine condition. In addition, an interaction between attention and treatment could be observed on the N2b component. This pattern of results suggests that caffeine yields a higher overall arousal level, more profound processing of both attended and unattended information and an acceleration of motor processes.
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Introduction

A great deal of research has been done to examine the effects of caffeine on human performance and physiological responses. In general, it seems that the physiological responses to moderate and high doses of caffeine show a consistent reaction pattern: an increase in general arousal, as can be seen (for example) in an increase of blood pressure, although clinically insignificant, a higher Galvanic skin response and an increase in secretion of adrenaline (Davidson & Smith, 1989; Nehlig, Daval & Debry, 1992). The influence of caffeine on cognitive performance seems less consistent; among other aspects, results differ with the amount of caffeine administered and the state of the subject. In general reaction times shorten while absolute alertness and vigilance measures show an increase under the influence of moderate amounts of caffeine (Frewer & Lader, 1991; Lieberman, Wurtman, Emde, Roberts & Coviella, 1987; Loke, 1990). However, with higher doses of caffeine, 500 mg (Frewer & Lader) and 600 mg (Loke) deteriorating effects were found on performance.

These kind of inconsistent effects of caffeine on cognitive performance are also found for specific functions. Several authors investigated the influence of caffeine on different aspects of attention but the results from these studies do not yield a coherent conclusion. For example, no interactions were found between caffeine and performance on a stimulus-response compatibility task or a diagonal selection task, while performance on a task with intact and degraded stimuli and a time-uncertainty task did show an interaction with caffeine. In a study of selective attention by Kenemans and Lorist (1995) where participants had to make a selection of stimuli on the basis of spatial frequency, orientation or a conjunction of these dimensions, no interactions of treatment with the various task variables were found. Studying the effects of caffeine on a different type of selectivity, namely a nonspatial Stroop task (Hasenfratz & Bättig 1992; Kenemans & Verbaten 1998) evidence was found for improved selectivity (reduced Stroop interference) by caffeine, but only under very specific conditions. The conclusion from these studies could be that caffeine seems to have an attention specific effect at perceptual stages but less at response selection stages. However, most studies do not confirm a differentiation in the influence of caffeine on specific types of selectivity of attention, with an exception being the reduced Stroop interference.

Besides these results obtained by studies using subjective and behavioural measures, additional insight in the effects of caffeine can be obtained using neurological and pharmacological information. A number of studies (e.g. Bruce, Scott, Lader & Marks, 1986; Hasenfratz & Bättig, 1994; Rall, 1990) have investigated the influence of caffeine on the ongoing EEG by studying the distribution of the frequency power bands. They found that caffeine intake caused a shift towards faster spectral components and a reduction in alpha and delta power that has been interpreted as a reflection of elevated levels of energy. In addition, pharmacological studies have shown that caffeine inhibits the binding of adenosine to its receptor sites, thereby reducing the
inhibitory influence of adenosine on the ongoing neural activity, resulting in an increase in the function, turnover, and levels of different neurotransmitters, the most important being acetylcholine, noradrenaline, dopamine and serotonin (e.g. Fredholm, Herrera-Marschitz, Jonzon, Lindström & Ungerstedt, 1983; Fredholm et al. 1987; Nehlig et al. 1992). Since the affected neurotransmitters are widely distributed in the brain, these findings indicate additional support for the hypothesis of a general arousing effect of caffeine, which might be similarly and evenly distributed on all stages of information processing.

Although most pharmacological studies indicate that the drug effects are general, the behavioural studies argue for a more specific effect on the perceptual stage of information processing covering a limited number of functions. Within these perceptual processes, however, there is no strong evidence that caffeine would influence several types of selectivity in a different manner. To get more insight into the actual ongoing cognitive operations event-related brain potential (ERP) measurements can be used, that allow a more precise analysis of the timing and organisation of 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, thereby demonstrating the effect of attention. Moreover, ERPs can provide additional evidence on the question which stages (input, central, output) of information processing are influenced by caffeine. This way important insight about the influence of caffeine on selective attention could be uncovered, either showing a general improvement of information processing or a stage-specific improvement. In addition, using ERPs in a selective attention paradigm can possibly shed some light on the issue whether caffeine effects differ for specific types of selective attention.

In studies of focused non-spatial visual attention, when participants attend selectively to stimulus features such as colour (Aine & Harter, 1986; Hillyard & Münte, 1984; Wijers, Lamain, Slopsema, Mulder & Mulder, 1989; Wijers, Mulder, Okita & Mulder, 1989; Wijers, Mulder, Okita, Mulder & Scheffers, 1989), diagonal selection (Lorist, Snel, Kok & Mulder 1994; Lorist, Snel, Mulder & Kok 1995) or spatial frequency (Kenemans, Kok & Smulders, 1993; Kenemans, Smulders & Kok, 1995; Zani & Proverbio, 1995), different ERP components have been identified as sensitive to selective information processing and are made best visible in difference waves.

Waveforms of unattended standard stimuli are subtracted from waveforms of attended standard stimuli, thereby forming an "on-line" index of the selective brain activity. Three different attention-related components seem very robust and in general can be quite easily distinguished:
- A frontal selection positivity (FSP), maximal at frontal leads with an onset latency between 140 and 160 ms post stimulus (Kenemans et al. 1993; Wijers, Lamain et al., 1989; Wijers, Mulder, Okita & Mulder, 1989) and is said to reflect initial selection on the basis of the primary dimension;
- A centro-frontally maximal N2 component called the N2b (Wijers, Lamain et al., 1989; Näätänen & Gaillard, 1983; Wijers, Mulder, Okita & Mulder, 1989; Wijers,
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Mulder, Okita, Mulder & Scheffers, 1989). The N2b is also described as a "covert orienting response", with an onset between 200 and 250 ms. This component appears to be a feature-non-specific response. Recently Wijers, Lange, Mulder, and Mulder (1997) stated that the N2b component is likely to originate from the anterior cingulate cortex and is related to "selection for action";

- An early occipital maximal negativity known as "selection negativity" (SN; Harter, Aine & Schroeder, 1982; Harter & Aine, 1984; Wijers, Mulder, Okita, Mulder & Scheffers, 1989), with a latency onset between 150 and 200 ms. This component also appears to reflect early selection of stimulus features but differs from the FSP in that they probably stem from different brain sources. Support for this hypothesis can for example be found in the fact that the OSN could not be observed in the diagonal selection task, while the FSP was present.

Using a focused nonspatial visual selective attention paradigm, Lorist, Snel, Kok, and Mulder (1994) and Lorist, et al. (1995) found an enlarged N2b component in the caffeine condition (300-450 ms post stimulus range) using a diagonal selection task. In the Lorist, Snel, Kok & Mulder (1996) study, in which a visual focused selective search task was used the amplitude of the N2b was also increased by caffeine. This effect of caffeine was carefully interpreted as more selectivity, in that caffeine would reduce distractibility by task-irrelevant information by an inhibition of the processing of irrelevant stimuli. However, Kenemans and Lorist (1995) did not found a difference in amplitude of the N2b component between the placebo and caffeine conditions. Caffeine had no influence on FSP and OSN components in any of the studies mentioned above. Possible reasons for the inconsistency on the influence of caffeine on the N2b component could be related to the different tasks that were used. For example, primary selection may be more difficult for participants in a diagonal selection task than in a spatial frequency task. Based on the findings that for the spatial frequency task shorter mean reaction times were found and an increase in the number of hits by caffeine (which is in general only found on simple tasks), it may be concluded that this task was overall simpler. Another aspect that could have influenced the modulation of the N2b component by caffeine is the interstimulus interval that was used in these tasks. In the spatial frequency task used by Kenemans and Lorist interstimulus intervals (ISIs) between 750 and 950 ms were used as opposed to 2050 and 2450 ms for the diagonal selection task.

These varying results from ERP and reaction time studies suggest a specific effect of caffeine, meaning that the effect would only be present with specific cognitive processes and that the drug effect seems to vary as a function of specific task variables. In contrast, Daly (1993) and Phillis (1991) argue for a general arousing effect by caffeine. An important point remains how does caffeine exactly influence information processing and does caffeine increase the selectivity of attentional processes as indexed by FSP, N2b and OSN. The present study examines the effects of caffeine treatment on visual non-spatial selective attention. By using a colour selection task, which is known to yield the three selection components that were discussed above (Van der Stelt, Kok,
Smulders, Snel & Gunning, 1998; Van der Stelt, Gunning, Snel & Kok, 1998) it can be examined whether caffeine has the same effect on processing of this non-spatial feature (colour) as compared to studies that used other non-spatial features. This study will try to verify and add to the finding of the Lorist group that caffeine especially suppresses the processing of irrelevant information. In addition, the same task will be used in two versions with different ISIs, to be able to examine the influence of this factor on the modulating effects of caffeine on the selection processes. Possible variations of the amplitude of ERP components and the topography might reveal which cortical areas are activated during different task conditions and different treatment conditions. It will be examined whether these topographic scalp distributions to different stimulus categories differ as a function of caffeine intake.

Based on previously reported modulation of the ERP by caffeine, a fourth component will be investigated: a parietally maximal positive P3 peak, which is maximum on the detection of the target stimulus (relevant target). The P3 peak latency (between 300 and 700 ms) is often said to be related to stimulus evaluation time, while the P3 amplitude could be interpreted as an indicator for the amount of energy that is needed to process information (e.g. Donchin, Kramer & Wickens, 1986; Magliero, Bashore, Coles & Donchin, 1984; Ragot, 1984; Polich & Kok, 1995). In the Lorist, et al. (1995) study as well as in the Lorist, Snel, and Kok (1994) study it was found that the P3 amplitude was more positive under caffeine while no effects on P3 latency were found. In addition, in the Kenemans and Lorist study (1995) it was found that caffeine had an amplitude modulating effect, eliciting more late positivity (290 to 400 ms post stimulus) especially at the Cz electrode and independently of task conditions. In contrast, in a study by Hasenfratz and Bättig (1994) where the effect of caffeine on the late positive deflection (P3) in the ERP was investigated with a choice reaction time task, no evidence was found of differences in amplitude or latency of the P3 component as a result of caffeine treatment.

In summary, this study examines the effects of caffeine on different stages of information processing by examining performance data and specific components of the ERP that have been defined on the basis of a selective attention paradigm as used in several other studies.

Method

Participants

Eleven healthy volunteers, 4 men and 7 women, aged 20-25 ($M = 22.4, SD = 2.0$) participated in this study as a requirement of their introductory psychology course. Data of a twelfth participant were rejected for analysis due to equipment failure. All subjects were right-handed non-smokers, had normal or corrected-to-normal vision and were
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Habitual coffee drinkers accustomed to a self-reported daily caffeine ingestion ranging from 3 to 6 cups of coffee a day ($M = 4.9$, $SD = 1.3$). Participants also met several additional criteria: they did not work night shifts, did not use prescription medication except for birth control and did not report to have any history of brain damage.

**Treatment manipulation**

A cross-over design was applied in order to use each participant as his/her own control and to minimise the impact of inter individual differences in performance. All participants were asked to maintain a 12-hour abstinence of all caffeine containing foods and beverages prior to the experiment. They were told that saliva samples would be taken before and after each session. In fact, this was done to reinforce compliance. The order of treatment conditions was balanced across participants (five participants had placebo the first session and six participants had caffeine the first session).

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 were led to believe that they were consuming normal caffeine-containing coffee during both experimental sessions.

**Physiological and subjective measures**

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

A general health checklist which contained a segment that assessed to what extent participants were morning or evening types (Kerkhof, 1984) was used. Four questionnaires were used to measure subjective feelings: (a) The short version of the Profile of Mood States (POMS, Wald & Mellenbergh, 1990) was used in order to measure changes in mood. Participants indicated how they felt at that moment for each of 32 adjectives on a 5-point scale ranging from 0 (*not at all*) to 4 (*very much*). 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) was used to measure the current level of anxiety. Participants reported on 20 items on a 4-point scale ranging from 1 (*not at all*) to 4 (*almost always*). (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 & Hoofdakker, 1980) was used to measure participants’ sleep duration and quality.

**Stimuli and task**

Stimuli were presented using a Zenith Z-Select 100 PC, by the CSSP program of the Psychonomics department against a black background on a Nec Multisync 3FG monitor positioned at 80 cm from the participants’ eyes. A small fixation cross was continuously present except during presentation of the stimulus. Participants were tested individually in a dimly lit, sound-attenuated room. The participant was comfortably seated in an easy chair, while a response button was positioned on a table to the right of the chair.

All participants had to perform 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). The order in which the participants had to perform these tasks varied according to a rolling Latin square paradigm. In these tasks the participants were instructed to look continuously at the fixation cross and to respond as quickly and accurately as possible. In this article the colour selection task will be discussed.

A visual colour selection task was used, of which it was shown (Van der Stelt, Kok et al. 1998) that the before mentioned attentional ERP components are clearly distinguishable. The stimuli were red and blue circles, subtending a visual angle of 1.27°, presented in the centre of the monitor. The circles consisted of a line which thickness was one-fourth of the outer diameter. Eighty per cent of the circles had a small gap, the gap being distributed randomly over four possible positions (0°, 90°, 180° and 270°). The width of the gap was one-tenth of the outer diameter of the circle. The other 20% of the circles had no gap. Stimulus duration was 100 ms. Participants were given the instruction to focus on stimuli with a specified, task-relevant colour, while ignoring the other, irrelevant colour. Circles without a gap served as targets, circles with a gap as non-targets. The participant had to press the response button with the right index finger each time a target stimulus appeared among the relevant stimuli. The colour selection task consisted of a slow and a fast version. All participants first had to perform the slow task and then the fast one. During the slow task, the interval between successive stimulus onsets varied randomly between 1300 and 1900 ms, while during the fast task stimulus onsets varied randomly between 500 and 1100 ms (rectangular distribution). Both the slow and the fast task consisted of 6 experimental blocks of trials, each containing 80 stimuli, and the colour selection cue (red or blue) was alternated at each experimental block. Consequently, during the slow as well as during the fast task, both the colours red and blue served as selection criterion 3 times. Targets were presented among both relevant (attended) and irrelevant (unattended) stimuli. Accordingly, subjects were presented four types of stimuli (relevant target,
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probability .1, relevant non-target, probability .4, irrelevant target, probability .1 and irrelevant non-target, probability .4). The stimuli were presented successively and in random order, with the exception of relevant target stimuli, which did not occur in succession.

Recordings

During task performance, the EEG was recorded from 30 tin electrodes attached in 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 EOG changes, electrodes were attached above and below the pupil of the right eye. To monitor horizontal EOG changes, electrodes were attached at the outer canthi of both eyes. The right mastoid was used as a reference site and the right side of the nose was used as ground. The exact locations of the recording sites and the mastoid were assessed using the Polhemus 3 Space Isotrack II system. 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 department of Psychonomics.

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 filling out of a consent form and the general health questionnaire in the first session. Participants arrived at the laboratory at 9.30 a.m. where the first saliva sample was taken. Next, blood pressure and heart rate were measured on the left arm and participants were asked to fill out the POMS, STAI and sleep quality questionnaires after which they consumed their coffee. Subsequently, the electrodes were applied and participants were seated in the experimental room. On average 40 minutes after the coffee administration participants started to perform the experimental tasks. The tasks lasted for about 1 hour, after which participants filled out the POMS, STAI and subjective task load inventory. Blood pressure and heart rate were measured and a second saliva sample was taken. Thereafter, the electrodes were removed and the participants were thanked for their participation.

Data reduction

Button presses were classified as hits if they occurred in a 200-1000 ms time interval after the relevant target stimulus was presented. A second criterion for reaction times
was that they had to fall within a range of 2.5 SD from the participant’s average. Button presses to the other three types of stimuli were classified as false alarms while failures to respond to relevant targets were classified as misses. Overall comparison between conditions was done with a MANOVA, repeated measurements design.

For ERP analysis, the first two trials within each block, and trials with incorrect behavioural responses (defined above) were excluded. Trials containing amplifier blocking or in which the EEG showed flat lines (no voltage fluctuation for 10 or more consecutive samples) were detected automatically and omitted from further analysis. Ocular artefact in the EEG was controlled using regression analysis in the frequency domain (Woestenburg, Verbaten & Slangen, 1983). All intervals containing movement artefacts (change in amplitude of more than 40 \( \mu V \) between two adjacent samples) or electrical drifts (difference between lowest and highest amplitude more than 100 \( \mu V \) within one trial, 256 samples) were excluded from further analyses. For each participant, average stimulus-locked ERPs were computed separately at each scalp location for each of the four stimulus types and for both treatment conditions. The averaging epochs lasted for 880 ms post stimulus, using the last 100 ms of the 144 ms pre-stimulus 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.

The peak latencies and mean amplitudes of the ERP components of interest were determined on the basis of previous research (Aine & Harter, 1986; Hillyard & Münte, 1984; Kenemans, et al., 1993, 1995; Van der Stelt, Kok, et al. 1998; Van der Stelt, Gunning, et al. 1998; Wijers, Lamain, et al. 1989; Wijers, Mulder, Okita & Mulder, 1989; Wijers, Mulder, Okita, Mulder & Scheffers, 1989) in terms of experimental task (i.e. attention and target) effects in a given latency range, at specific scalp locations. Colour selection effects manifested by FSP, SN, and N2b were determined from the difference wave obtained by subtracting the ERPs elicited by irrelevant nontargets from those elicited by relevant nontargets. FSP was defined as the frontally distributed positivity occurring 100-300 ms in the post stimulus latency range, SN as the occipitally distributed negativity in the 100-300 ms range, and N2b as the centro-frontally distributed negativity in the 175-450 ms range of the obtained difference wave. The attention effect on P3b, referred to as P3b_{attention}, was defined as the parietally distributed positivity in the 300-700 ms latency range of this difference wave. To evaluate possible target effects within relevant and irrelevant stimulus categories on P3b amplitude (300-700 ms), difference waves were computed by subtracting the ERPs to relevant nontargets from those to relevant targets, referred to as P3b_{relevant target} and by subtracting the ERPs to irrelevant nontargets from those to irrelevant targets, referred to as P3b_{irrelevant target}. For the latter two measures only mean amplitudes were calculated. Finally, the target P3b peak and mean amplitude were determined from the (unsubtracted) ERPs, and defined in terms of the parietal maximum positive peak occurring between 300 and 700 ms after the presentation of a relevant target stimulus, allowing the target P3b results to be compared with those of previous studies.
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Determination of peak latency

Using the difference waves from midline locations, a 50% proportional onset method (Smulders, Kenemans & Kok, 1996) was applied to estimate the onset latencies of FSP at Fz, N2b at Cz, SN at Oz and P3b\textsubscript{attention} at Pz. For each single difference wave, the point in time was determined at which 50% of the maximum amplitude of a given ERP component was reached. These onset latency measures were determined automatically by a computer program and were all checked visually to determine their accuracy. In cases where the computer yielded inaccurate onsets, which could result from the presence of multiple peaks in the latency range, the search epoch was restricted and the onset estimate again determined. Maximal peak latencies of absolute target P3b at Pz were also determined automatically. In a few cases where a component was not visible at the midline location, the onset latency measure was obtained from a selected lateral location. The individual onset latencies of FSP, N2b, SN and P3b\textsubscript{attention} could be extracted in 82%, 82%, 91% and 91% of the cases, respectively. The individual latencies of the maximal target P3b peak could be extracted in 91% of the cases. In addition, correlations between the obtained onset latencies of target P3b and reaction times were calculated.

Determination of mean amplitude and scalp topography

Amplitude values were determined by computing the mean voltage of consecutive 20 ms intervals from 140-300 ms and in 100 ms intervals from 300-700 ms. Based on the previously mentioned studies the following attentional components were defined from the present results on which all statistical analysis were performed: FSP and SN were defined in the 200-240 ms range on Fz and Oz respectively, the N2b in the 240-280 ms range on Cz, P3b\textsubscript{attention} was defined in the 300-500 ms range on Pz while target P3b, P3\textsubscript{relevant target} and P3b\textsubscript{irrelevant target} were defined in the 400-600 ms range on Pz.

Topographic mapping of the scalp potentials and corresponding current source density (CSD) distributions were performed with the Brain Electric Source Analysis (BESA) software (Scherg, 1990) for each treatment and each attention condition, as well as for the difference waves. 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).

Statistical analysis

Repeated-measures multivariate analyses of variance (MANOVAs), using multivariate test statistic, the exact F-transformations of Hotellings $T^2$ were performed on mean
amplitude and peak latency measures separately, for the following ERP components: FSP, SN, N2b, P3battention target P3b, P3brelevant target and P3birrelevant target (all defined as described above, at a predetermined time-interval and a predetermined lead). Hence the overall MANOVA design for this first series of analyses was: Attention (2: Attended/Unattended) x Task (2: Slow/Fast) x Treatment (2: Placebo/Caffeine). When interactions between factors emerged, subsequently follow-up simple tests (2 x 2 design) were used to determine which factor levels were responsible for the differences in amplitude or latency. In addition, to be able to investigate possible treatment, attention or task related differences in scalp topography of the ERP components, a second series of ‘regional’ repeated-measures (MANOVAs) were performed on mean amplitude data for different scalp regions. For the FSP and N2b components regional MANOVAs were performed on 20 ms consecutive time-intervals from 200–280 ms for the data from the midline (Fpz, AFz, Fz, Cz, Pz, Oz), fronto-polar (Fp1, Fpz, Fp2), frontal (F7, F3, Fz, F4, F8) and central (T7, C3, Cz, C4, T8) scalp regions. For the SN component the regional MANOVAs were restricted to midline, parietal (P7, P3, Pz, P4, P8) and occipital (O1, Oz, O2) scalp regions on 20 ms consecutive time-intervals from 200–240 ms. For all P3 related components, the regional effects were examined on midline, parietal, occipital and centro-parietal (CP5, CP1, CP2, CP6) scalp locations for 100 ms consecutive time-intervals from 300–600 ms. The overall MANOVA design for these analyses was the following: Attention (2: Attended/Unattended) x Task (2: Slow/Fast) x Treatment (2: Placebo/Caffeine) x Location (3, 4, 5 or 6 levels). Significant two or three way interactions of Treatment, Attention and Task with Location or Hemisphere if present in the multivariate analyses, were followed by a second MANOVA with normalised data (according to the vector length scaling method proposed by McCarthy and 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.

Results

Subjective and physiological measurements

Subjects reported no differences in quality of sleep on the night before the experimental sessions. There were neither differences between males and females in reported amount of averaged daily caffeine ingestion in mg, nor were there differences between the sexes in reported sensitivity to the effects of caffeine. All items from the task load inventory were analysed separately. Participants reported no significant differences between the caffeine and placebo condition on subjective effort needed to perform the set of tasks. There were neither any differences in mood (as measured with the POMS
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and the STAI) between the conditions as measured upon the arrival of the participants, nor any mood differences due to the different caffeine doses 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 vigorously, $F(1,10) = 11.31, p = .007$, at the end of the experiment compared to the start of the experiment. 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 so that treatment order was omitted as a variable in further analysis, $F(1,20) = 0.06-0.38$, all $p$s n.s. In addition, no differences were observed regarding the physical aspect of the colour of the targets (red or blue) and no interactions between treatment condition and colour were revealed, $F(1,20) = 0.003-1.64$, all $p$s n.s. Based on these results, colour as a separate factor was also omitted in further analysis.

Overall there was a significant main effect of task version on reaction times, $F(1,10) = 12.02, p = .006$, with faster reactions for the slow version of the task ($M = 460.1, SD = 53.5$) as compared to the fast version of the task ($M = 489.5, SD = 52.2$). In addition a significant main effect of treatment was found on reaction times, $F(1,10) = 6.24, p = .032$, with faster reactions for the caffeine condition ($M = 464.2, SD = 54.5$) as compared to the placebo condition ($M = 485.4, SD = 51.1$), these effects are shown in Figure 1. A main effect of Task was found on the number of hits that were made, $F(1,10) = 9.45, p = .012$, with more hits in the slow version of the task ($M = 7.7, SD = 0.35$) as compared to the fast version of the task ($M = 7.0, SD = 0.76$), see also Table 1. No main effect of treatment on the number of hits and number of false alarms (either analysed all together or separately for all three categories) was found and no interaction effects were revealed between any of the variables mentioned above.

Table 1 Performance data ($SD$) for the two task versions, averaged over all subjects as a function of treatment.

<table>
<thead>
<tr>
<th>Performance measure:</th>
<th>Slow version</th>
<th>Fast version</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Caffeine</td>
</tr>
<tr>
<td>Reaction times (ms)</td>
<td>470 (49.8)</td>
<td>450 (57.1)</td>
</tr>
<tr>
<td>False alarms (%)</td>
<td>0.11 (0.12)</td>
<td>0.15 (0.35)</td>
</tr>
<tr>
<td>Misses (%)</td>
<td>2.5 (2.7)</td>
<td>1.7 (3.7)</td>
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</tbody>
</table>

Note: % is expressed relative to the number of trials within the specific stimulus category.
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**Figure 1** Mean reaction times in ms for targets on the slow and the fast task version of the colour selection tasks and for the placebo and caffeine condition. Vertical bars represent the SD in either positive or negative direction.

**ERP Measurements**

Figure 2 depicts the grand average ERPs from scalp midline locations during the slow and the fast version of the colour selection task. Superimposed are ERPs elicited by relevant nontarget and irrelevant nontarget stimuli under placebo and caffeine conditions. Only statistical significant effects with a $p < .05$ will be described below.
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![Graph showing effects of caffeine on visual attention](image)

**Figure 2** Grand average ERPs elicited by relevant and irrelevant nontarget stimuli, superimposed for the placebo and the caffeine conditions. ERPs for the slow and the fast task version are depicted in the left and the right column, respectively.
Figure 3 Grand average difference waves, obtained by subtracting the ERPs elicited by irrelevant nontarget stimuli from the ERPs elicited by relevant nontarget stimuli. The difference waves are superimposed for the placebo and the caffeine conditions. ERPs for the slow and the fast task version are depicted in the left and the right column, respectively.
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Effects of Colour Selection: FSP, SN, N2b and P3battention

The attention effects can be seen in figure 3, which show the superimposed difference waves for the placebo and caffeine condition, formed by subtracting the ERPs to irrelevant nontarget stimuli from the ERPs to relevant nontarget stimuli. Neither the effect of attention defined as the FSP, $F(1,10) = 15.96$, $p = .003$, nor the effect of attention defined as the N2b, $F(1,10) = 7.58$, $p = .020$, depended on task version. In contrast, $P3b_{attention}$ and the SN attention effects did show an interaction with task version, $F(1,10) = 10.05$, $p = .010$ and $F(1,10) = 6.84$, $p = .026$, respectively, with the $P3b_{attention}$ being larger and the SN being smaller in the slow task compared to the fast task version. In addition, analysis on the latency data revealed a significant effect of task on the FSP ($F(1,8) = 6.83$, $p = .031$) indicating that the onset latency of this component was 29 ms later in the slow task than in the fast task (188 ms versus 159 ms).

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Figure 4 ERPs of the exogenous effect, obtained by averaging the ERPs of relevant nontarget and irrelevant nontarget stimuli. Superimposed are ERPs for the placebo and caffeine conditions, averaged over task version.

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Chapter 3: Effects of caffeine on visual selective attention to colour

Effects of treatment

Exogenous effects  Figure 4 shows that the P2 amplitude was significantly larger in the caffeine than in the placebo condition at FPz from 200-280 ms, $F_{(1,10)} = 5.84-13.73, p = .036-.004$, and at Fz from 180-260 ms, $F_{(1,10)} = 5.14-8.13, p = .047-.017$. These results were found from an additional, unplanned analysis that was performed on the basis of visual inspection of the ERP waveform.

Attention effects  An interaction of treatment with the N2b attention component was found, $F_{(1,10)} = 7.25, p = .023$, and is shown in Figure 5. Simple tests revealed that this interaction consisted of a main effect of attention for the caffeine condition, $F_{(1,10)} = 14.53, p = .003$, while there was no main effect of attention for the placebo stimuli. In addition, analysing the stimulus categories separately, it was revealed that there was neither an effect of treatment on the relevant stimuli nor on the irrelevant stimuli. In other words, this effect revealed a more positive going ERP for irrelevant standards in the caffeine condition as compared to the placebo condition as well as a more negative going ERP for relevant standards in the caffeine condition as compared to the placebo condition. None of the onsets of any of the attentional components was significantly altered by the intake of caffeine nor were there any interactions of Treatment x Task revealed for the onset latencies.

![Figure 5](image.png)  

Figure 5  Enlargement of the ERPs at Cz to show the modulatory effects of caffeine on the N2b component (240–280 ms), averaged over slow and fast task versions. ERPs elicited by relevant nontarget and irrelevant nontarget stimuli are superimposed for the placebo and the caffeine condition.
Effects of caffeine on visual attention

The correlations between the target P3b peak and reaction times were highly significant for both treatment conditions and for both task version: placebo $r = .70$, $p = .0006$; caffeine $r = .73$, $p = .0003$ (averaged over task version), revealing slower reactions as the onset of the target P3b peak was later. This would indicate that participants had evaluated the stimuli quite thorough before giving a response and that this strategy was not altered by the treatment condition.

For the P3bIrrelevant target component (irrelevant target compared to irrelevant standard, from 400-600 ms) a main effect of treatment was found, $F(1,10) = 5.40$, $p = .042$. This treatment effect was further manifested as a trend towards an interaction of Treatment x Target/non-target, $F(1,10) = 3.97$, $p = .074$, both effects are shown in Figure 6. Follow-up simple tests revealed that this interaction consisted of a significant target effect for the caffeine stimuli, $F(1,10) = 18.30$, $p = .002$, which was absent for the placebo stimuli. In addition, the effect of treatment on irrelevant targets was significant, $F(1,10) = 8.95$, $p = .035$, whereas this effect was not significant for irrelevant standards. In other words, the irrelevant target P3b was larger in the caffeine condition. Furthermore, this positive shift was attributable to a shift of the irrelevant target ERP in the caffeine condition as compared to the placebo condition but not to a shift of the irrelevant standard in the placebo condition as compared to the caffeine condition. No effects of treatment were found on the P3bRelevant target.

Figure 6 Enlargement of the grand average ERPs at Pz to show the modulatory effects of caffeine on the P3bIrrelevant target (400–600 ms), averaged over task version. ERPs elicited by irrelevant target and irrelevant nontarget stimuli, superimposed for the placebo and the caffeine condition are shown.
Regional MANOVAs of mean amplitudes and scalp topography

Main effects or trends towards a main effect of treatment, revealing a smaller amplitude for the placebo condition as compared to the caffeine condition, were found in a broad scalp region and a large time range: for midline locations from 200-260 ms, $F(5,6) = 3.41-5.16$, $p = .095-.046$, for frontal locations from 180-260 ms, $F(4,7) = 3.94-8.94$, $p = .075-.014$, for fronto-polar locations from 180-280 ms, $F(2,9) = 4.02-12.40$, $p = .073-.006$, and for central locations from 220-240 ms, $F(4,7) = 3.52$, $p = .090$, see also Figure 2. These effects are probably all due to the exogenous frontally distributed P2 peak that was larger under the caffeine than under the placebo condition.

A significant Attention x Location interaction from 200-220 ms, $F(5,6) = 23.02$, $p = .001$, across midline leads was revealed as can be seen in Figure 3, which remained significant after normalisation, $F(5,6) = 6.47$, $p = .021$, indicating that the attention effect differed among midline locations. In this time domain there is a frontal positivity (FSP) while at the same time there is an occipital negativity (SN). For the 240-260 ms time domain the following pattern could be seen on the midline locations: a significant Treatment x Location interaction, $F(5,6) = 5.16$, $p = .035$, and a significant Attention x Location interaction, $F(5,6) = 11.94$, $p = .004$; both interactions remained significant after normalisation, $F(5,6) = 6.79$, $p = .019$; $F(5,6) = 7.02$, $p = .017$, respectively, see Figures 3 and 4. The Treatment x Location interaction could be explained by the fact that there was an effect of treatment for fronto-central leads while at the same time this effect was absent on posterior leads. For the Attention x Location interaction a similar pattern could be observed: an attentional positivity at frontal leads combined with an attentional negativity at centro, parietal and occipital leads. These results indicated that there was not merely a difference in amplitudes that was measured on the midline leads in this time domain for the placebo and the caffeine condition but also a possible difference in topographic profiles. Therefore, an additional analysis was performed to investigate whether the topography of the N2b component was responsible for the observed interaction between treatment and location. Since the N2b attention component was more pronounced in the slow version of the task, this additional analyses was restricted to the slow task version only. This analysis in which 10 fronto-central location factors were included (F3, Fz, F4, FC5, FC6, C3, Cz, C4, CP1, CP2) revealed no significant interactions of Treatment x Location or Treatment x Attention x Location for the 240-280 ms time domain indicating that there were no differences in scalp topography as a result of the effect of treatment on the N2b component.

For the P3b component (300-500 ms) no main effects of treatment were found on parietal, centro-parietal, occipital or midline locations. An interaction between treatment and location was found for occipital locations in the 400-500 ms range ($F(2,9) = 5.06$, $p = .034$), indicating a somewhat greater difference between treatments for the O2 lead with the placebo condition having a more positive going amplitude. This interaction was no longer significant after normalisation.

Spline and CSD maps for the exogenous effect of caffeine on the P2 component are shown in Figure 7. Although the maps are shown for a single time point, the
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topographic profiles were constant over a larger time window centred around this latency. Visual inspection of the observed scalp distributions of this time range revealed a very similar pattern for both treatment conditions suggesting no differences in source localisation. In addition, there is a slight increase in neural activity as can be seen by the number of iso-contour lines in the caffeine condition. This may indicate somewhat more activation or more general arousal.

**spline maps**

**c.s.d. maps**

**Figure 7** Spline and current source density (CSD) maps for the exogenous P2 effect for placebo and caffeine conditions at 212 ms post stimulus, averaged over task version. The isocontour lines for the spline map are separated by 0.7 μV; for the CSD map they are separated by 0.35 μV/cm². Non-shaded areas indicate positive voltages or outward current; shaded areas indicate negative voltages or inward current flow.
As can be seen in Figure 3, a remarkable interaction of Attention x Treatment was found on the fast task at the Cz lead from 160-180 ms, $F(1,10) = 11.00, p = .006$. This interaction consisted of a main effect of attention for the placebo condition, $F(1,10) = 26.49, p < .001$, and for the caffeine condition, $F(1,10) = 12.02, p = .006$, there was a trend for a treatment effect on relevant stimuli, $F(1,10) = 4.00, p = .073$, while there was no treatment effect on irrelevant stimuli.

**Discussion**

In this study a selective attention paradigm was used to assess differences between a placebo and a caffeine condition on four attention components of the ERP: FSP, SN, N2b and P3battention. In addition, the influence of caffeine on exogenous components of the ERP, scalp topographies, P3b related components and behavioural measures were studied. A slow and fast version of a colour selection task were used to investigate the influence of interstimulus interval on attention components and possible interactions of treatment with task version.

**Effects of attention**

Focused selective attention to colour of the stimulus was found to have profound effects on the ERP waveforms for both treatment conditions and for the slow as well for the fast version of the task. The earliest attention effects, associated with an increase in amplitude appeared as a centro-frontally distributed P2 peak (FSP) while at the same time an occipital negativity was apparent (SN). Following these early effects a centro-frontally distributed N2 peak (N2b) with a maximum at Cz became apparent, reflecting the covert orienting of attention toward relevant stimulus features (Naätänen & Gaillard 1983) indicating active, effortful orienting. A subsequent centro-posteriorly distributed P3b peak was apparent at Pz, probably indicating attentional effects on processes that follow stimulus identification.

**Effects of treatment**

One of the main questions we addressed in the introduction was whether caffeine has a general arousal increasing effect on information processing or a possible more specific effect, influencing only the information processing of certain types of information (e.g. relevant standards) or only certain stages of information processing. In the present study, a larger fronto-centrally distributed exogenous P2 peak was apparent in the caffeine condition as compared with the placebo condition. This effect was interpreted as an arousal increasing effect that was irrespective of the attentional category the stimulus belonged to (attended or unattended). These kind of early exogenous effects
are sometimes said to reflect basic perceptual processing (Csisbra, Czigler & Ambrò, 1994), since the results suggest that all stimulus categories are processed more thoroughly in this stage of information processing. Supporting this view, Lorist, Snel, and Kok (1994) interpreted the early exogenous effect of caffeine on ERPs they found as an increase of the receptivity of the nervous system to all external stimuli. It is suggested from the CSD maps (Figure 7) that the scalp distributions of the exogenous effect in the P2 time range are comparable for both treatment condition though the iso-contour lines in the caffeine condition indicate an overall somewhat stronger activation than in the placebo condition. Taken together, these results suggest that caffeine improves basic perceptual processes at the input stage of information processing.

A second major finding concerning caffeine treatment was the increase of the attentional N2b component, pointing to more selectivity by caffeine. This component is often interpreted as being sensitive to the state of the participant and to resource allocation (Gunter, van der Zande, Wiethoff, Mulder & Mulder, 1987) and to reflect a covert orienting response. An enlargement of this component under the influence of caffeine suggests therefor a more active, effortful orienting. It was suggested from the ERP figures (Figure 5) that this N2b effect can be accounted for by the ERP of the attended standards eliciting more “negativity” and the ERP on the unattended standards eliciting more “positivity” under caffeine conditions. On the basis of the simple tests, one could say that neither the differentiation in processing of relevant nor the processing of irrelevant information alone could account for this enlargement of the attention effect. In addition, in the Lorist, Snel, Kok, and Mulder (1994) study there was also an effect of treatment on the N2b, mainly caused by a positive displacement of ERPs to irrelevant stimuli under caffeine, whereas there was no difference between treatments in ERPs to relevant stimuli. This effect was interpreted by the authors as a reduced response to irrelevant stimuli under the influence of caffeine, which led to more selectivity. Speculating about the results from the present study this could mean that there was facilitation of the processing of relevant stimuli but also an inhibition of processing of irrelevant stimuli. In other words, this could point to more active processing of the relevant stimuli while the irrelevant stimuli were ignored more actively.

It is interesting to relate the observed modulation of the N2b component by caffeine in the present study to earlier research. Kenemans and Lorist (1995) suggested that a critical variable responsible for the presence or absence of modulatory effects of caffeine on the N2b attention component could be the differences in ISI. However, for the ISI ranges used in the present study the results suggest that ISI is not the critical variable since no interactions of Treatment x Attention x Task were observed. In order to investigate the influence of different ISIs as a critical variable on this N2b effect, the task versions were also analysed separately to determine their contributions to this effect. Although no significant effects of attention (N2b) or Treatment x Attention interaction were observed for the fast task version, these effects were statistically significant when the data were averaged over task version. This indicates that both task
versions pointed to effects in the same direction but that smaller ISIs do have a modulatory effect on both attention and caffeine effects. Kenemans and Lorist also suggested task difficulty as a factor that may be responsible for the observed differences of the influence of caffeine on the N2b component. In contrast to former research (see review Koelega, 1993) the present study did not show any effects of treatment on the number of hits or false alarms and in addition, reaction times were slower (caffeine condition 464.2 ms, placebo condition 485.4 ms) as compared to the spatial frequency task of Kenemans and Lorist (caffeine condition 385.2 ms, placebo condition 408.7 ms). This could indicate that the present task was indeed quite difficult as compared to the spatial frequency task in which no modulation of the N2b was found and that task difficulty might be one of the factors that influences the effects of caffeine. A third factor that might be of influence is the time between caffeine administration and actual task performance. In the present study as well as in the diagonal selection task of Lorist, Snel, Kok, and Mulder (1994) this time was about one hour while in the Kenemans and Lorist study this time was about two hours. It is known from pharmacological studies (e.g. Daly, 1993) that caffeine reaches its peak plasma concentration in about 45 minutes to one hour. In addition, the metabolic half-life of caffeine lies between two and four hours, meaning that after two hours the level of caffeine in the brain is substantially lower than after one hour.

An additional ERP finding was the effect of caffeine on the P3b_irrelevant target, indicating more late cognitive processing of the irrelevant target in the caffeine condition as compared with the placebo condition. Moreover, this effect of treatment was not found for the irrelevant standard stimuli. This is in line with the results reported by Lorist, Snel, Kok and Mulder (1994) who also found that caffeine enhanced the P3 component of irrelevant stimuli (both target and standard) as compared to the relevant stimuli. Since the P3 component was not enhanced for relevant standards this pattern of results could suggest that early selection on the basis of a specific colour was relatively efficient. However, the irrelevant target did yield an ERP component that could be described as a P3 under the caffeine condition suggesting that the participant processed this target, although irrelevant, more thoroughly in the caffeine condition compared with the irrelevant target in the placebo condition and the standards of both conditions. Since this effect is rather late (400–600 ms post stimulus) it could point to a memory update-process after the correct response is given, indicating that participants recognised the irrelevant target as an important and deviant stimulus. Targets of both colours appeared infrequently in comparison with standard stimuli, and could therefore yield a deviance effect as observed in the P3. However, this effect on the P3b_irrelevant target was observed for the caffeine condition only and if it is a reflection of an update process of the occurrence of a deviant stimulus one expects this effect also to occur in the placebo condition. For that reason this effect was interpreted by the authors as more available processing capacity by caffeine. In contrast, an alternative interpretation could
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be that this extra processing capacity actually leads to more distractibility by caffeine since it seems not to serve a clear purpose to process irrelevant target more thoroughly.

Regarding the performance data significantly shorter reaction times for the caffeine condition than for the placebo condition were found. In addition, there were no differences in number of hits and false alarms (to any stimulus category) as a result of treatment. The latter result could be an indication that caffeine did not improve selectivity. However, since absolute numbers of misses and false alarms to both versions of the colour selection task were so low, this could also point to a ceiling effect. The same pattern of behavioural results (faster reactions in the caffeine conditions, while no differences were found in the number of misses and false alarms) was found earlier in a number of studies which addressed the influence of caffeine on performance measures (for example Kenemans & Verbaten, 1998; Lorist, Snel, Kok & Mulder, 1994; Lorist, et al. 1995). Although different tasks were used in these studies the authors concluded that it was the output motor-processes (either central or peripheral) that were accelerated. This interpretation was supported by the additional fact that there were no effects found of caffeine on LRP or input related stages of information. In contrast, Kenemans (1998) who looked at performance on a Stroop task under the influence of caffeine found a reduction of the errors and omissions and shorter reaction times by caffeine and concluded that caffeine reduces Stroop interference. Based on the same level of results, Kenemans' conclusion suggests that the influence of caffeine is probably not motor-response related but more probable could be related to input or central processing stages. Given the fact that in the present study several ERP components were also influenced by caffeine, the reaction time results could be related to the processes that are represented by these components and thus stem from the input or output stage of information processing, being either more perceptual or decision-making in nature. However, the observed effect of caffeine on the ERP components was only based on differences in amplitudes. Caffeine had no effect on the peak latencies of any of the ERP components and taking the pattern of performance data into account, the authors conclude that in the present study the reaction time effects point to a specific influence of caffeine on the motor response stage.

One wonders what the benefit of caffeine is when its effects can only be found in ERPs without manifest differences (except for RTs) in task performance. Caffeine did induce differences in the ERP however, pointing to a change in processing of information and it is possible that if a different task was used the effects of caffeine could have been observed also in the performance data. The benefit of caffeine could be a faster rejection of irrelevant stimuli or a faster recognition of relevant information. Both these selection processes could lead to an enlargement of the N2b component. However, the former does not necessarily lead to differences in task performance while the latter could very well result in faster reactions to target stimuli. This indicates that different experimental tasks are not equally sensitive to the influence of caffeine on task
performance or on the ERP measures and argues for both types of measurements on a broad scale of tasks to improve our insight on the effects of caffeine.

**Conclusion**

The results from the present study show that caffeine enhances the exogenous P2 and the attentional N2b components of the ERP and decreases reaction times, although no influence on the number of misses or false alarms could be observed. The P3b irrelevant target was more positive under caffeine, probably reflecting more processing capacity of the participants in this condition. The N2b effect seems quite specific, since the categories of stimuli were affected differently: the attended standard elicited a more negative amplitude while the unattended standards elicited a more positive ERP amplitude. Modulation of the N2b component by caffeine seems to be dependent on the difficulty of the task, although time between administration and task performance could also be a critical factor. From the present study it was concluded that inter-stimulus interval did not influence the modulation of the N2b by caffeine. The enhancement of the N2b component points to more selectivity by caffeine although it is not clear which information processing stages are exactly involved.