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Influence of caffeine on information processing stages in well rested and fatigued subjects

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Abstract. The effects of caffeine on different information processing stages were examined by using choice reaction time tasks. Independent variables were stimulus degradation, stimulus-response compatibility, time-uncertainty, state of the subject, and caffeine treatment. The task variables were assumed to affect the following processing stages; encoding, response selection and motor preparation, respectively. A 200 mg dose at the beginning of the experiment and a maintenance dose of 50 mg caffeine or lactose half-way through the session were administered to well rested and fatigued subjects, double-blind and deceptively. Behavioural measurements, event-related potentials (ERPs) and mood questionnaires were used to assess caffeine effects. The data showed that caffeine shortened reaction time. This effect showed an interaction with stimulus degradation and time uncertainty. In addition, ERP results supported the view that caffeine increases cortical arousal and perceptual sensitivity. Stimulating effects of caffeine were mainly located at input and output stages of the information processing system. Central processes were unaffected by caffeine. Fatigued subjects showed larger improvements in performance after caffeine than well-rested subjects. The results also indicated that caffeine effects were not stimulating in all subjects: 6 out of 30 subjects did not show arousing effects of caffeine.

Key words: Caffeine – Stimulus degradation – Stimulus-response compatibility – Time uncertainty – State of the subject – Reaction times – Visual event-related potentials – N1 – P3 – Mood – Saliva caffeine concentrations

Although the effects of caffeine on human performance have been studied extensively over the last century, there still is no agreement concerning the actions of caffeine on mental performance (Hollingworth 1912; Weiss and Laties 1962; Bättig 1985). However, there are indications that caffeine alters the energetical state of subjects. After ingesting doses of 50–250 mg caffeine subjects usually experience a decrease in fatigue, which is also explained as less drowsiness, enhanced wakefulness or increased energy (Clubley et al. 1979; Koopmans and Van Boxtel 1988; Griffiths et al. 1990; Rall 1990; Zwyghuizen-Doorenbos et al. 1990). These subjective effects may persist up to 5 h after the caffeine ingestion. Furthermore, there is evidence that caffeine causes a shift in EEG power to faster spectral components (high frequency and low amplitude) (Goldstein et al. 1963; Künkel 1976; Bruce et al. 1986; Etevenon et al. 1989). These physiological findings can be interpreted as additional evidence for an effect of caffeine on energetical or arousal processes.

Recent information processing theories assume that there are multiple energetical resources, which are not directly involved in task performance, but modulate the on-going cognitive operations (Pribram and McGuinness 1975; Mulder 1983; Sanders 1983; Hockey 1986). Substances like caffeine are assumed to affect information processing stages, by changing these energetical mechanisms (Frowein 1981; Heemstra 1988). One of the questions to be answered in the present experiment is whether changes in energetic resources induced by caffeine will be relatively general and undifferentiated or whether the effects will be connected to specific information processing stages.

To verify this hypothesis, we used the additive factor method (AFM) (Sternberg 1969; Sanders 1980, 1983). The rationale underlying this method is that by systematically changing task variables, related to a certain information processing stage in reaction time (RT) tasks, differential effects of caffeine on input, central, or output mechanisms can be traced. The caffeine effects are evaluated as a function of changes in these task variables. If the effects of caffeine interact with the effects of a change in a certain task variable, both factors are thought to affect a common process. If the effects are additive, it suggests that the drug does not influence the mechanisms affected by the manipulated task variable (see also Frowein 1981

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and Gaillard 1988). For example, by degrading the quality of visual stimuli, input related perceptual processing is manipulated. Selective effects of caffeine on the input mechanism should then be evident from an interaction of caffeine with stimulus degradation. In a similar vein, manipulation of time uncertainty, by varying inter-stimulus interval, may be used to affect the output side of information processing, or the motor preparation stage. Finally, varying the compatibility between stimulus and response affects central processes between perception and output, or the response selection stage.

In measuring the effect of caffeine on information processing stages, ERPs may provide useful information in addition to RTs. In the past, ERP research has been very helpful in assessing the nature and time-course of information processing. Whereas RT reflects the end product of all stages, ERP components can provide important, more specific information about the duration and intensity of separate information processing stages (Renault et al. 1982; Ritter et al. 1982, 1983; McCarthy and Donchin 1983; Mulder et al. 1984; Kok 1990). More specifically, it has been argued that the latencies of different ERP components reflect the timing of information processing, while amplitude variations of the ERP signal are supposed to be mainly related to the intensity of information processing, and thus reflect energetical resources (Mulder 1986; Kok 1990). For example, the latency of the P3 component has been used as an index of stimulus evaluation time, whereas amplitude changes in the P3 area give an indication of the investment of energy associated with perceptual processing. Moreover, P3 latency seems to be independent of response related information processing (McCarthy and Donchin 1983; Mulder et al. 1984).

Very few studies so far have been concerned with the effects of caffeine in relation to ERPs. Spilker and Callaway (1969) and more recently Elkins et al. (1981) and Bruce et al. (1986) found no alterations in latencies or amplitude of evoked potentials after different amounts of caffeine. Ashton and colleagues (1974) and also Wolpaw and Perry (1978) found that 300 mg caffeine was associated with an increase in the N1 and P2 amplitude. Although these studies were not intended to make inferences about the effects of caffeine on underlying energetical mechanisms, which are related to certain stages of information processing, these amplitude effects point to a specific caffeine effect on input related energetical mechanisms.

In the present study the objective was to use ERPs as an index of the effects of caffeine on the timing of information processing and on the energetical resources necessary for mental performance. More specifically, the latencies of the N1 and P3 components were used as indices for the timing of early encoding and stimulus evaluation processes, respectively; while the amplitudes of these components were used as an index of phasic cortical arousal or orienting to environmental information. Based on the evidence found for influences of caffeine on energetical resources, effects should be expected on the amplitude rather than on the latency of ERP components. Caffeine effects tend to be most consistent in long-term performance or vigilance tasks (Keister and McLaughlin 1972; Regina et al. 1974; Elkins et al. 1981). These results might reflect that the compensation of fatigue effects is possibly the crucial factor in the actions of caffeine. Therefore, another objective of this study is to determine whether the effects of caffeine on performance depend on the state of the subject, such as fatigue caused by a lack of sleep.

In summary, the aim of the present study is, first, to determine whether the effect of caffeine is a general effect or whether it is affecting specific energetical mechanisms underlying information processing, and second, to investigate the effects of caffeine at different levels of fatigue.

Materials and methods

Subjects

Thirty healthy, non-smoking students from the University of Amsterdam between 18 and 25 years old (mean = 21.2, SD = 1.7) participated in this study. The subjects were randomly assigned to the well rested ($n = 15$) or fatigued ($n = 15$) group. Random assignment was done with the one restriction that both groups got the same number of male ($n = 8$) and female ($n = 7$) subjects. The subjects either received study credits or money for participation. Because of evidence that caffeine users and non-users differ in some behavioural and physiological effects of the substance, and for the relevance of the study for daily life, only regular coffee consumers were selected (Robertson et al. 1981; Zahn and Rapoport 1987; Loke 1988). All subjects were self-reported coffee drinkers accustomed to a daily caffeine ingestion ranging from two to seven cups. They also met several additional criteria, namely they did not work night shifts, did not use prescription medication, had normal sleep patterns and normal or corrected-to-normal vision.

Treatment manipulation

The treatment conditions consisted of 200 mg + 50 mg (maintenance dose) caffeine or lactose with normally brewed decaffeinated coffee as vehicle. The substances in the beverages could not be detected by taste or smell. Treatments were double-blind and deceptive; subjects were led to believe that they were consuming normal caffeine containing coffee on both experimental sessions. This design permits the evaluation of the degree to which the combined psychological and pharmacological effects of caffeine administration exceeds effects owing to response expectancy (Kirsch and Weixel 1988). Concerning the treatment manipulation, a cross-over design was applied in order to use each subject as its own control and thereby to minimize the impact of inter-individual differences in performance.

State manipulation

To induce a suboptimal level of energetical resources, half of the young subjects were kept awake during the night and were tested between 04.00 and 06.30 a.m., when people are least alert and most likely to fall asleep (Marks and Folkard 1984; Czeisler and Jewett 1990). The other subjects were tested after a normal night of sleep, and were supposed to be in a more optimal state.

Experimental tasks and apparatus

General aspects. During the experimental sessions the subjects sat in a dimly lit experimental room facing a micro computer (MacIntosh, screen diagonal 22 cm) at a distance of 80 cm. Stimuli were

digits presented black on a white screen. Each of the three tasks was preceded by two instruction frames, both lasting for 10 s. The first frame told the subject to sit at ease and to be attentive. The second frame informed the subjects about the relation between stimulus and response for the subsequent task. A fixation mark was on the screen when no stimulus was present. Stimulus presentation time was 400 ms. Subjects were requested to respond to the stimulus with a button press as quickly and as accurately as possible.

The following tasks were administered to the subjects:

The *stimulus degradation* task, manipulating the perceptual or encoding stage, was a discrete four choice reaction task, with stimulus degradation as task variable. The digits 2, 3, 4 and 5 consisted of a dot pattern surrounded by a rectangular frame of dots. In the degraded condition the stimuli were covered with a pattern of random dots, replaced from the frame. Seven different degradation versions of each digit were used. There was no objective difference in recognition difficulty between these versions. Intact and degraded stimuli were presented in a random sequence with equal probabilities, at a visual angle of $0.9° \times 1.1°$. The digits 2 and 3 had to be responded to by pressing a button with the left hand (middle- and index finger, respectively); the digits 4 and 5 required a right hand response (index- and middle finger, respectively). A total of 224 stimuli was presented to the subject. The first 24 trials were used as practice trials and were discarded for further analysis. Inter-stimulus intervals varied randomly between 2210 and 2810 ms.

In the *stimulus-response compatibility* task, manipulating response selection processes, the digits 2 and 3 ($0.7° \times 0.5°$) were presented either at the left or the right of a fixation mark. In this task the fixation cross was visible during the entire task. A mask ($0.7° \times 0.5°$) appeared opposite to the presented digit, and the distance between both figures was 6 cm. In the compatible task subjects were instructed to give a reaction with the hand ipsilaterally to the location of the stimulus. In the incompatible condition, subjects had to respond with the contralateral hand. Subjects had to respond to the digit 2 either with the left middle or right index finger. The digit 3 corresponded to the left index or right middle finger. In the incompatible condition 112 trials were presented to the subjects. In the compatible condition the subject received a block of 560 trials to assess time on task effects, but for the aim of the present study the compatible and incompatible condition were made comparable by analyzing only the first 112 trials of the compatible condition. The first 12 trials in both condition were regarded as practice trials. The inter-stimulus intervals varied between 2350 and 2850 ms.

The *time uncertainty* task was a choice reaction task used to evaluate caffeine effects on the motor preparation stage. One of two digits (3 or 4) randomly appeared at the centre of the screen. Subjects were instructed to press a button with the left hand if the digit on the screen was a 3 and to give a right hand response in case the digit was a 4. During the first 112 trials the inter-stimulus interval was held constant (3250 ms). Thereafter stimuli were presented with variable inter-stimulus intervals, varying between 1000 and 4000 ms. The first 12 trials of each sequence of 112 trials were regarded as practice trials and were discarded from analysis.

Self-ratings of mood

In order to measure changes in mood, the short version of the *Profile of Mood States* (POMS) (Wald and Mellenbergh 1990) was used. Subjects indicated how they felt at that moment for each of 32 adjectives on a 5-point scale ranging from "not at all" (0) to "very much" (4). The five clusters of adjectives representing specific mood states, depression, anger, fatigue, vigour and tension, were measured three times during the experiment.

Procedure

Subjects passed through an extensive training session, followed by two experimental sessions, which were separated by at least 1 week. Except for the treatment both experimental sessions were identical. The subjects were asked to abstain from all caffeine containing substances for at least 12 h preceding each experimental session. Their compliance was checked by taking a saliva sample for caffeine analysis at the beginning of each experimental session. The method of using saliva samples for determining the plasma caffeine concentrations has been proven reliable (Newton et al. 1981; Zylber-Katz et al. 1984). Subjects who participated in daytime, arrived at the laboratory at 08.30 a.m. after a normal night of sleep. The subjects in the night group reported to the laboratory at 22.30 p.m.. Until the start of the experiment at 03.00 a.m. they were kept awake by the experimenter and were restricted to passive activities (e.g. talking, reading).

All sessions started with taking the first saliva sample. This was followed by the administration of 200 mg caffeine or placebo dissolved in decaffeinated coffee. Milk powder and sugar were added to suit the taste of the subject. Subsequently, the electrodes were applied and mood was measured. A second saliva sample was taken and subjects were seated in the experimental room. On average 45 min after the coffee administration subjects started to perform the experimental tasks. During the two experimental sessions a total of four tasks was performed. In this paper the first three task will be discussed, dealing with stimulus degradation, stimulus-response (S-R) compatibility and time uncertainty.

The tasks were presented in the same order for all subjects. The average half-life of caffeine is approximately 3–7 h (Rall 1990), and although a relative homogeneous group of caffeine users participated, a large interindividual variance in caffeine clearance rate remained. In order to avoid an increase in intra-individual variance of the caffeine level, caused by a different level at the time of performing a specific task, a fixed task order was used. In addition to this, we tried to maintain a relatively constant level of caffeine in the subjects, by giving a maintenance dose of caffeine during the experimental session.

Another issue is the presentation of the task conditions in a fixed order (except for the intact and degraded stimuli, which were presented in random order). In the case of random presentation of the task conditions differential carryover effects could be expected, due to the different nature and different length of the task conditions. As argued by Maxwell and Delany (1990), counterbalancing is useless in case of differential carryover effects. Instead a between subject design would be favoured, but the power to detect true treatment effects then decreases. The design of the present experiment permitted us to vary relatively many variables and still to maintain a sufficiently high level of power. The problem of carryover effects due to practice was handled by the extensive training session.

In order to assess remaining effects of a fixed task condition order, the present results were compared to those of Smulders et al. (1991), who presented these task conditions in a counterbalanced sequence. No differences in results were found, therefore we conclude that the caffeine effects observed in the present study are not confounded with the order of tasks or task conditions.

After each task the subjects were allowed to take a 3 min rest period. The three tasks were followed by a longer rest period (about 15 min) in which a second cup of coffee was served. In the caffeine condition this cup of decaffeinated coffee contained a maintenance dose of 50 mg caffeine. The POMS was filled out for the second time. Thereafter, the remainder of the experimental procedure was conducted. At the end of the session the third saliva sample was taken and the POMS was filled out for the last time. Subjects were fully debriefed at the end of the second session.

Recordings

The EEG was recorded using an Electro-cap containing pure tin electrodes. Recordings were made from Fz, Cz, Pz, and Oz locations referred to linked earlobes. Impedance was always kept below 5 kΩ. To record vertical and horizontal eye movements bipolar electrooculogram (EOG) tin electrodes were used, placed at the outer

canthi of both eyes and above and below the left eye. The recorded signals were amplified with a bandpass set at 35 Hz and digitized at a rate of 100 Hz, using an IBM PC-AT, the hard- and software functions of which were extended with a Keithley data acquisition set.

Data reduction and statistical analysis

For each subject in the three groups, average ERPs were computed for each electrode position separately, for each task variable (intact-degraded, compatible-incompatible and time certain-time uncertain) within each treatment condition. The averaging epoch started 200 ms prior to stimulus onset and lasted until 1080 ms post-stimulus. Trials containing amplifier-saturation artifacts, errors (commission and omission errors) and premature (<150 ms or <mean RT −2.5 SD) or too late reactions (>2000 ms or >mean RT + 2.5 SD) were excluded from further analysis. Commission errors were wrong button presses occurring between 150 and 2000 ms, omission errors occurred when no button press was made to a stimulus. Horizontal and vertical eye movement artifacts and blinks were controlled according to Woestenburg et al. (1983). The average ERPs were evaluated using a 200 ms prestimulus baseline. For further analysis each ERP was divided into 14 periods of 50 ms, from 100 to 800 ms post-stimulus. The mean amplitudes of the ERPs in these intervals were submitted as dependent variables to SPSS MANOVA for repeated measurements (SPSS Inc. 1986). The factors were group (well rested, fatigued), treatment (placebo, caffeine), task variable (intact-degraded, compatible-incompatible, time certain-time uncertain) and electrode-site (Fz, Cz, Oz, Pz). When the main design indicated a significant interaction ($\alpha = 0.05$) of effects with electrode-sites, analyses were performed for each electrode-site separately. If significant effects are found in a particular range the smallest and largest F-value will be reported.

Latency of the N1 was denoted as the most negative going deflection in the 130–250 ms range of the averaged ERP at the Oz electrode where the peak was most pronounced. P3 latency was determined as the most positive going point between 300 and 800 ms computed at the Pz electrode. The latencies, RTs and subjective measurements were subjected to SPSS MANOVA for repeated measurements as well.

Saliva caffeine analysis

Three 5-ml samples of saliva, taken during each experimental session (see procedure), were centrifuged for 5 min at 3000 rpm and thereafter stored at −20°C for later analysis using the high-performance liquid chromatography method (by courtesy of Dr. van der Stegen, Douwe Egberts, Utrecht).

Results

Saliva caffeine levels

The average pre-treatment saliva concentrations of caffeine (mean = 0.3 mg/l, SD = 0.4) demonstrated that the subjects adhered to the abstinence instructions. As expected, after the administration of coffee a significant difference in saliva caffeine levels emerged between the caffeine (mean = 5.2, SD = 3.4) and placebo (mean = 0.6, SD = 0.9) condition [$F(1,28) = 41.7$, $P < 0.000$]. This difference remained significant at least till the end of the experiment [$F(1,28) = 15.5$, $P < 0.000$], and did not differ between the well rested and fatigued subjects [$F(1,27) = 0.1$, n.s.].

Although significant shorter reaction times were observed for both groups, in the caffeine condition compared to the placebo condition [$F(1,28) = 8.7$–19.2, all $P < 0.01$], inspection of the single subject data indicated that two subjects in the well rested condition, and four subjects in the fatigued condition showed a slowing of performance after the caffeine treatment. These paradoxical effects of caffeine could not be explained by differences in factors measured during the experimental sessions or by selection criteria. In order to gain a more clear insight how caffeine influenced information processing in case of performance improvements, data of subjects showing performance deteriorations were discarded from further analysis, because these data might obscure the investigated effects (see also Discussion). Separate analyses on data of those subjects showing a slowing of performance after the caffeine treatment were not done because of lack of power.

No significant effects of order of caffeine treatment were observed in the data [$F(1,20) = 0.2$–0.6, all n.s.], therefore treatment order was omitted as a factor in further analysis.

Self ratings of mood

The fatigued subjects reported the lowest levels of vigour in comparison to the well rested subjects [$F(1,21) = 9.0$, $P = 0.007$]. All subjects felt more energetically in the caffeine condition than in the placebo condition [$F(1,21) = 12.1$, $P = 0.002$]. In accordance with this result are the scores on the POMS fatigue subscale. Feelings of fatigue were reduced by caffeine [$F(1,21) = 30.5$, $P < 0.000$] in particular for the fatigued subjects [$F(1,21) = 7.2$, $P = 0.014$]. In the caffeine condition the subjects reported to be less angry [$F(1,21) = 6.7$, $P = 0.017$], feelings of depression and tension did not change.

Stimulus degradation task

Behavioural results. The average reaction times (see Table 1) showed significant effects for caffeine treatment [$F(1,22) = 39.0$, $P < 0.000$], and task variable [$F(1,22) = 147.4$, $P < 0.000$]. The interaction between both factors [$F(1,22) = 6.8$, $P = 0.016$], indicates that, although caffeine induced shorter RTs to both intact and degraded stimuli, this effect was greater for the degraded stimuli. The lower part of Table 1 shows that not only the subjects reacted faster in the caffeine condition but also made fewer commission errors [$F(1,22) = 5.6$, $P = 0.027$] and omission errors [$F(1,22) = 5.6$, $P = 0.027$]. The positive effect on the number of false alarms of the caffeine treatment was most clear in the intact condition as deduced from the treatment × task variable interaction [$F(1,22) = 6.0$, $P = 0.022$]. Concerning the omission errors, the fatigued subjects showed the largest improvement after caffeine [treatment × group interaction: $F(1,22) = 7.1$, $P = 0.014$].

ERP results. The ERPs of the well rested and fatigued subjects (see Fig. 1) showed a consistent pattern of P2, N2

Table 1. Performance data (±SEM) for the two groups separately and averaged over all subjects as a function of task variables and treatment. The stimulus degradation task

Groups	Intact stimuli		Degraded stimuli	
	Placebo	Caffeine	Placebo	Caffeine
Reaction times (ms)				
Well rested	658 (28.4)	620 (31.7)	749 (35.5)	688 (31.9)
Fatigued	719 (38.6)	640 (28.5)	800 (35.4)	703 (31.2)
Grand mean	686 (23.8)	630 (20.8)	773 (25.2)	695 (22.0)
Commission errors (%)*				
Well rested	5.0 (1.0)	3.6 (0.8)	4.4 (1.1)	4.7 (1.1)
Fatigued	6.4 (1.2)	3.9 (1.2)	5.4 (0.9)	4.5 (0.9)
Grand mean	5.6 (0.8)	3.8 (0.6)	4.8 (0.8)	4.9 (0.7)
Omission errors (%)*				
Well rested	0.2 (0.1)	0.2 (0.1)	0.7 (0.4)	1.2 (0.9)
Fatigued	4.1 (1.9)	0.6 (0.4)	6.8 (3.0)	1.2 (0.6)
Grand mean	2.0 (0.9)	0.4 (0.2)	3.5 (1.5)	1.2 (0.6)

* Percentages are expressed to the number of trials within the specific stimulus category

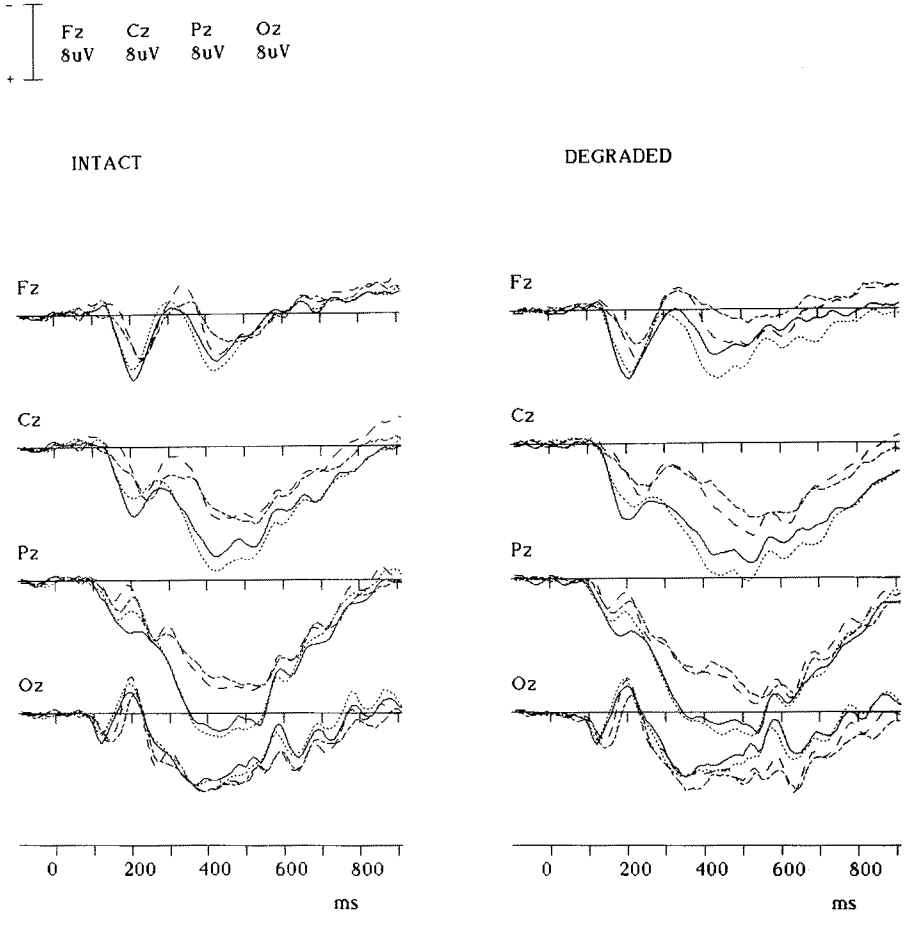

Fig. 1. ERP wave forms for well rested and fatigued subjects, superimposed for both treatment conditions. In the *left column* the ERPs evoked by intact stimuli are depicted, in the *right column* ERPs to degraded stimuli. ERPs are shown for four different electrode sites: Fz, Cz, Pz, and Oz. (——) Well rested placebo; (·····) well rested caffeine; (–·–·–) fatigued placebo; (– – –) fatigued caffeine

and P3 at all electrode sites, with the exception of Oz, where the P2 was overlaid by the N1 component, and preceded by a P1. Visual inspection of Fig. 1 shows that the stimuli in the caffeine condition elicited a larger N1 component and a smaller P2 component compared to the placebo condition, which was confirmed by statistical analysis. In the 100 to 200-ms area, there was a significant main effect of treatment on ERP amplitude [$F(1,22)=4.4$–10.9, both $P<0.048$]. The N1 peak latency (at Oz) was 191 ms in the placebo condition and 185 ms in the caffeine condition [$F(1,19)=6.2$, $P=0.022$]. The ERPs in the 400 to 500-ms range, showed a more positive going waveform under the caffeine treatment [$F(1,22)=6.3$–9.6, both $P<0.048$] than in the placebo

Table 2. Performance data (±SEM) for the two groups separately and averaged over all subjects as a function of task variables and treatment. The stimulus-response compatibility task

Groups	Compatible stimuli		Incompatible stimuli	
	Placebo	Caffeine	Placebo	Caffeine
Reaction times (ms)				
Well rested	619 (34.7)	570 (33.6)	725 (54.3)	668 (47.3)
Fatigued	720 (34.0)	622 (37.6)	830 (56.6)	740 (42.5)
Grand mean	665 (26.1)	594 (25.1)	773 (40.0)	701 (32.4)
Commission errors (%)*				
Well rested	2.0 (0.7)	2.1 (0.6)	4.9 (2.0)	2.9 (0.8)
Fatigued	4.6 (1.5)	2.4 (0.5)	6.8 (1.8)	4.6 (1.5)
Grand mean	3.2 (0.8)	2.2 (0.4)	5.8 (1.3)	3.7 (0.8)
Omission errors (%)*				
Well rested	0.9 (0.7)	0.6 (0.5)	1.3 (1.2)	0.9 (0.9)
Fatigued	6.2 (2.7)	0.3 (0.2)	6.5 (2.8)	1.6 (1.0)
Grand mean	3.4 (1.4)	0.5 (0.3)	3.7 (1.5)	1.3 (0.6)

* Percentages are expressed relative to the number of trials within the specific stimulus category

condition. This positive shift was most pronounced for the degraded stimuli with a frontal maximum [treatment × task variable × electrode site interaction in the 450 to 600-ms epoch: $F(3,20)=3.8$–4.6, all $P<0.027$]. No significant treatment effects were observed on the P3 peak latency.

Task variable effects started around 200 ms, with a smaller P2 followed by a larger N2 for the intact stimuli compared to degraded stimuli [200 to 400-ms area: $F(3,20)=4.4$–12.9, all $P<0.016$]. A somewhat earlier onset of these effects was found in the placebo condition than in the caffeine condition [$F(3,20)=3.3$, $P=0.040$], and for well rested subjects compared to fatigued subjects [$F(1,22)=4.9$, $P=0.038$]. Significant task variable effects were also found on the descending flank of the P3 component [$F(1,22)=14.1$–58.4, all $P<0.001$].

As can be seen in Fig. 1, the ERP amplitude in the P3 area (300–650 ms) elicited by the well rested subjects was more positive going than the amplitude of the fatigued subjects, and this effect was most pronounced on the centro-parietal electrode sites [$F(3,20)=3.8$–7.5,all $P<0.026$]. Effects of state on P3 peak latency did not reach the level of significance.

Stimulus-response compatibility task

Behavioural results. The RTs after caffeine were significantly shorter than after placebo [$F(1,22)=59.1$, $P<0.000$] (see Table 2), especially for the fatigued subjects [$F(1,22)=4.7$, $P=0.042$]. Shorter RTs were also observed for compatible compared to incompatible stimuli [$F(1,22)=53.6$, $P<0.000$]. No interaction between the caffeine treatment and task variables was observed [$F(1,22)=0.0$, n.s.]. As in the degradation task, fewer commission errors [$F(1,22)=6.9$, $P=0.015$] and fewer omission errors [$F(1,22)=7.6$, $P=0.011$] were made after caffeine than in the placebo condition. The beneficial caffeine effect on the percentage of omissions was most obvious for the fatigued subjects [$F(1,22)=5.8$, $P=0.025$]. In the compatible task condition fewer commission errors [$F(1,22)=9.1$, $P=0.006$] were made than in the incompatible task condition.

ERP results. Similar to previous results, caffeine produced a more negative going N1 component [150 to 200-ms area: $F(1,22)=5.2$, $P=0.032$] with an earlier onset [194 ms and 185 ms in the placebo and caffeine condition respectively: $[F(1,16)=17.9$, $P=0.001]$ compared to the placebo condition (see Fig. 2). The latency of the N1 was also influenced by state. A later N1 peak latency was observed for the fatigued subjects (196 ms) in comparison to the well rested subjects (183 ms) [$F(1,16)=4.5$, $P=0.05$]. In addition, caffeine produced a larger ERP amplitude in the 350 to 400-ms area, and this treatment effect was most clearly on Fz [$F(3,20)=4.5$, $P=0.015$]. Larger amplitudes in the P3 area, with a central-parietal maximum, were also seen for well rested subjects compared to the fatigued group (300 to 400-ms area: [$F(3,20)=3.3$–4.6, both $P<0.042$], although this group effect was diminished by caffeine in the 400 to 500-ms range [$F(3,20)=4.7$–4.9, both $P<0.012$]. The effects of caffeine in this area were independent of task variable, that is, the effects were similar for compatible and incompatible stimuli.

Significant task variable × electrode site interactions were found in the 200 to 250-ms area [$F(3,20)=3.8$, $P=0.028$] and 600 to 800-ms latency area [$F(3,20)=3.3$–4.1, all $P<0.043$]. The task variable effects in the 200 to 250-ms area were influenced by group and caffeine [$F(1,22)=6.0$, $P=0.023$]. Especially in the incompatible condition caffeine produced an enlarged P2 component in the ERPs of fatigued subjects. This effect was absent or reversed for the well rested subjects.

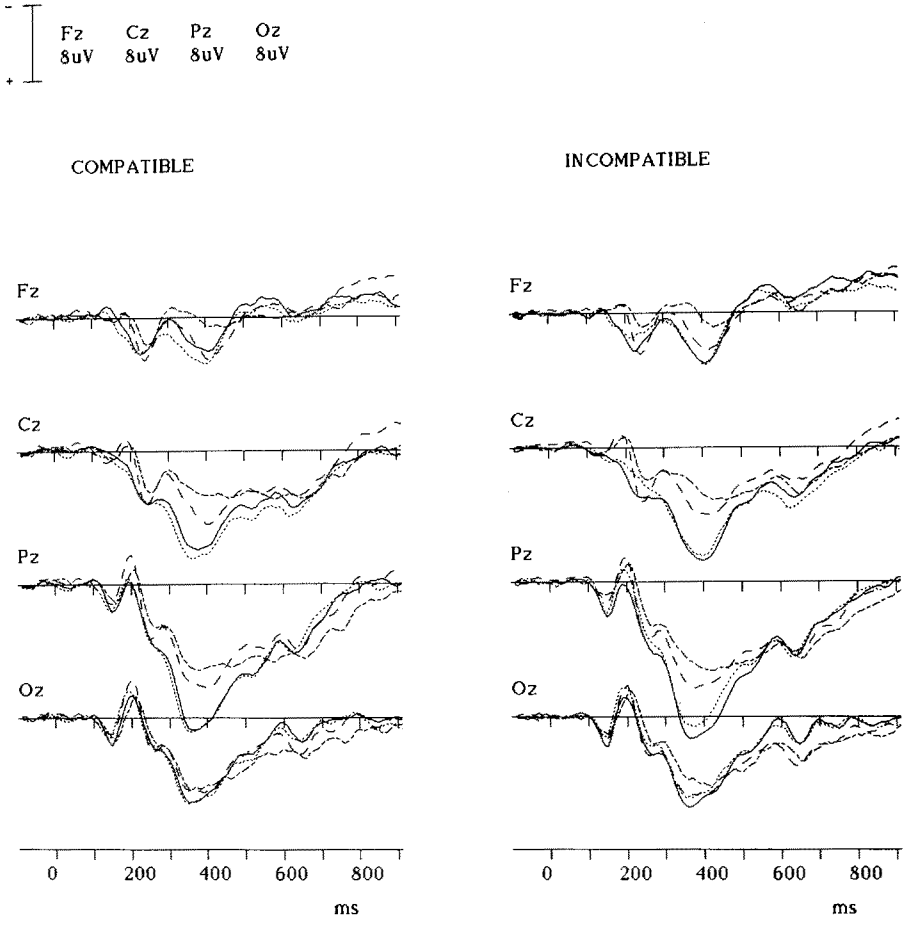

Fig. 2. ERP wave forms for well rested and fatigued subjects, superimposed for both treatment conditions. In the *left column* the ERPs evoked by compatible stimuli are depicted, in the *right column* ERPs to incompatible stimuli. ERPs are shown for four different electrode sites: Fz, Cz, Pz, and Oz. (——) Well rested placebo; (·····) well rested caffeine; (–·–·–) fatigued placebo; (– – –) fatigued caffeine

Table 3. Performance data (±SEM) for the two groups separately and averaged over all subjects as a function of task variables and treatment. The time uncertainty task

Groups	Time certain stimuli		Time uncertain stimuli	
	Placebo	Caffeine	Placebo	Caffeine
Reaction times (ms)				
Well rested	404 (15.0)	393 (12.2)	448 (17.4)	427 (16.8)
Fatigued	439 (24.2)	419 (14.4)	485 (28.0)	447 (16.6)
Grand mean	420 (13.9)	405 (9.5)	465 (16.0)	436 (11.8)
Commission errors (%)*				
Well rested	0.8 (0.3)	1.2 (0.4)	2.2 (0.5)	1.2 (0.5)
Fatigued	1.3 (0.3)	1.1 (0.4)	1.6 (0.3)	1.5 (0.5)
Grand mean	1.0 (0.2)	1.1 (0.3)	1.9 (0.3)	1.3 (0.4)
Omission errors (%)*				
Well rested	0.0 (0.0)	0.0 (0.0)	0.3 (0.3)	0.6 (0.6)
Fatigued	1.6 (1.1)	0.0 (0.0)	3.0 (1.4)	0.4 (0.2)
Grand mean	0.7 (0.5)	0.0 (0.0)	1.5 (0.7)	0.5 (0.3)

* Percentages are expressed relative to the number of trials within the specific stimulus category

The time uncertainty task

Behavioural results. In this task, as expected, the RTs in the caffeine condition were again shorter than after placebo [$F(1,22)=10.4$, $P=0.004$] (Table 3). The data revealed also a main effect of task variable [$F(1,22)=43.7$, $P<0.000$] and an interaction between caffeine and task variables [$F(1,22)=5.9$, $P=0.023$]. The time to react to stimuli presented with variable inter-stimulus intervals was longer but benefited more from caffeine than stimuli presented with fixed intervals. As in the previous described tasks, the beneficial effect of caffeine on the num-

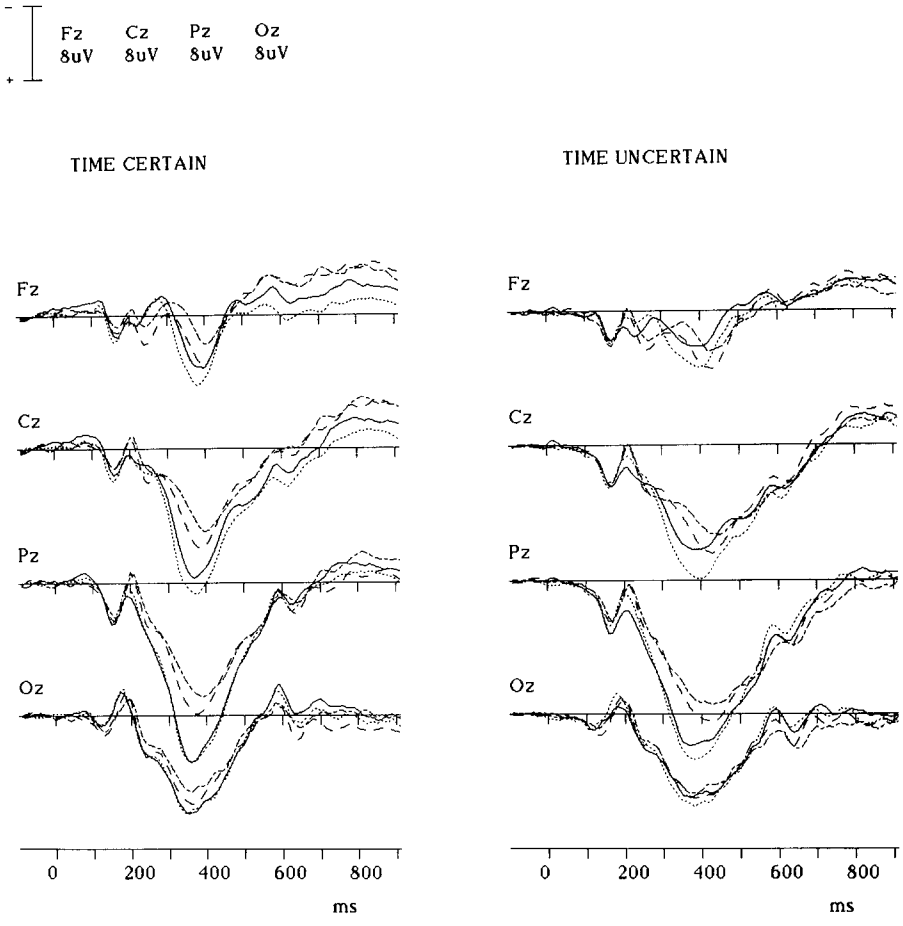

Fig. 3. ERP wave forms for well rested and fatigued subjects, superimposed for both treatment conditions. In the *left column* the ERPs evoked by time certain stimuli are depicted, in the *right column* ERPs to time uncertain stimuli. ERPs are shown for four different electrode sites: Fz, Cz, Pz, and Oz. (——) Well rested placebo; (·····) well rested caffeine: (–·–·–) fatigued placebo; (– – –) fatigued caffeine

ber of omission errors was most obvious for the subjects tested during the night [$F(1,22)=4.6$, $P=0.043$].

ERP results. In accordance with the tasks discussed before, a more negative N1 component was observed after the caffeine treatment [150 to 200-ms area: $F(3,20)=3.1$, $P=0.049$], and the N1 peak latency was on average 5 ms earlier after caffeine than in the placebo condition [$F(1,14)=5.1$, $P=0.041$] (see Fig. 3). The P3 amplitude was enhanced after subjects took caffeine [300 to 400-ms period: [$F(1,22)=5.7$–11.2, both $P<0.026$]. This effect was more broadly spread over scalp locations for the fatigued subjects, while for the well rested subjects this effect was more pronounced and could mainly be seen on the anterior electrodes [250 to 450-ms area: $F(3,20)=3.6$–9.8, all $P<0.033$]. As can be seen in Fig. 3, fatigued subjects elicited smaller P3 amplitudes in the 300 to 450-ms area [$F(3,20)=3.7$–4.3, all $P<0.029$].

Manipulation of time certainty revealed significant main effects in the 100 to 200, 250 to 300, 400 to 650-ms latency areas [$F(1,22)=7.0$–57.5, all $P<0.015$] and task variable × electrode site interactions between 100 to 800-ms [$F(3,20)=4.1$–19.0, all $P<0.020$]. The task variable effects in the 300 to 800-ms area are mainly caused by a latency shift of the P3 component, which was most pronounced for fatigued subjects as deduced from the group × task variable interaction [$F(1,21)=7.3$, $P=0.013$]. In the time uncertain condition the P3 peak latency occurred 21 ms and 65 ms later for well rested and fatigued subjects respectively, compared to time certain stimuli.

Discussion

The present study investigated the effects of caffeine on separate components of information processing under different levels of arousal. In order to do so, we used RT and ERP measures complemented with questionnaires on subjective feelings. Firstly, it has to be noted, that the caffeine manipulation was successful and subjects adhered to the abstinence instruction, as indicated by the caffeine concentration in the saliva samples. In addition to this, we succeeded in maintaining a relatively constant level of caffeine in the subjects during the experimental session, by giving a maintenance dose of caffeine.

Concerning the behavioural data, interactions between caffeine treatment and stimulus quality in the stimulus degradation task and with response related information processing in the time uncertainty task point to the involvement of caffeine in the actions of encoding and motor preparation mechanisms. The effects of S-R compatibility and caffeine on RT were found to be additive. These latter results indicate that the response selection stage is unaffected by caffeine. Thus the present behavioural results strongly argue that caffeine has specific,

rather than general effects on human information processing.

Several RT studies have suggested that increases in speed are usually associated with a decrease in accuracy (Pachella 1974; Wood and Jennings 1976; Wickelgren 1977). The data of the present experiment show, however, that shorter RTs were accompanied by a decrease in error rate. This pattern of results does not indicate that subjects applied different response strategies in the two drug conditions, but rather that the processing of information is facilitated by caffeine.

The effects of caffeine on the ERPs are consistent with these behavioural findings. A more negative going N1, in combination with a shorter latency of this component after the caffeine treatment, suggests that caffeine increases the receptivity of subjects to external stimuli and accelerates input related information processing (Hillyard and Kutas 1983). The second ERP component that is affected by the administration of caffeine is the P3 component. In the caffeine condition we found a more positive going P3. This enlargement of the P3 amplitude at the posterior electrode site represents an increase in phasic cortical arousal (Hillyard and Kutas 1983; McCarthy and Donchin 1983; Kok 1990). Both N1 and P3 have been found to be related to signal detection. The P3 component, however, reflects recognition or identification of stimuli (Parasuraman et al. 1982), while N1 reflects only an early phase of information processing activities. Therefore, the effects of caffeine on P3 amplitude seems to indicate that the intensity of encoding processes and thus the orienting toward stimuli in the environment is enhanced compared to the placebo condition. This interpretation is in accordance with Johnson (1986) who states that an increased positivity of the P3 component might reflect heightened information transmission during information processing activities, caused by less information loss during information transmission and by a more adequate orienting of attention.

A well known finding is also that the amplitude of endogenous components, such as the P3, is in general larger the easier the task (Kramer et al. 1983; Näätänen and Gaillard 1983). Therefore, it can be stated alternatively that the lower levels of fatigue and higher levels of vigour reported by the subjects in the caffeine condition, together with the increase of P3 amplitude, suggest that the task complexity is perceived as lower under the influence of caffeine.

The caffeine induced changes in mood could have confounded the effects of caffeine on the performance and electrophysiological measures. Indeed, caffeine lessened significantly feelings of fatigue and increased vigour as mentioned above. Also, the correlation between changes in mood with changes in RT of the placebo and caffeine condition moved around 0.50. This result, however, was only found for the scales depression and fatigue in the degraded, compatible and incompatible task conditions. It is our opinion that only the physiological effect of caffeine could have affected the performance and electrophysiological measures, since the subjects received caffeine and placebo deceptively. In other words in both the caffeine and placebo condition they expected to receive caffeine.

To our surprise, no significant effects of caffeine were found on the latency of the P3. Inspection of Fig. 1 suggests that either effects of caffeine and fatigue on the amplitude of P3 are much more conspicuous than on P3 latency, or the peak of P3 overlaps in time with a small positive/negative deflection that probably reflects a stimulus offset potential. The latter artefact could have interfered with a correct identification of small shifts in the latency of P3 which might have occurred in this time interval.

Summarizing the results so far, a specific effect of caffeine on the encoding stage of information processing has clearly been demonstrated in the RT and ERP data. Evidence for a caffeine effect on motor preparation has been found in the RT data of the time uncertainty task. A remaining question however is to what extent the processes taking place in the P3-RT interval are central motor related processes or more peripheral motor processes? Using measurements of peripheral motor activity (electromyography) in addition to cortical recordings might clarify the precise impact of caffeine on the different parts of response related processes.

The second objective of this experiment was to study the effect of caffeine under different levels of fatigue. The manipulation of the state of the subjects resulted in effects on mood. The fatigued group reported less vigour and higher levels of fatigue than the well rested group. The ERPs also showed an effect of state of the subject; for fatigued subjects the P3 amplitude was smaller than in those who had a normal night of sleep (see also Figs 1, 2, and 3). As has been mentioned before, amplitude effects can be used as an indication of energetical resources. Therefore the observed reduction in P3 amplitude suggests a reduction of the energetical levels in the fatigued subjects in comparison to the well rested subjects, this is, arousal or information transmission is reduced in fatigued subjects.

The state manipulation had no effect on RTs, but in all three tasks caffeine led to significantly less omission errors in the fatigued group than in the well rested group. This suggests that in the case of suboptimal arousal, caffeine helps to prevent "lapses of attention". According to this lapse hypothesis a suboptimal state is associated with periods of accurate performance intermitted with absences or pauses in performance, and this will lead to omission errors (Johnson 1982). In the signal detection theory the resolution of the information detection mechanism is called "sensitivity". In case more information is transmitted during information processing, the sensitivity is more optimal. It has been argued that fatigued subjects experience a loss in sensitivity (Wickens 1984). Tentatively, caffeine seems to be able to reduce these lapses, and enhances perceptual sensitivity. On the level of ERP measures, this is probably reflected in the increase of P3 amplitude.

A point of consideration in interpreting the effect of state is the confounding with time-of-day. Different levels of fatigue were induced by a combination of sleep deprivation and testing when the circadian arousal was at its trough. As a consequence, well rested and fatigued subjects were tested at two different points of their circadian

arousal rhythm. In order to gain more detailed information on the interaction of state, caffeine and the phase of the circadian rhythm, a study is in progress in which the effects of caffeine are assessed at a fixed time-of-day in extreme morning- and evening-types (Spreeuw 1992), who differ in the level of alertness due to a relative shift in circadian rhythm (Kerkhof 1981).

An important point left is that 6 out of 30 subjects did not show performance improvements after the administration of caffeine. One interpretation is in terms of the Yerkes-Dodson law (Yerkes and Dodson 1908). According to this theory performance and arousal are curvilinearly related. Caffeine is known to have arousal elevating properties. The absence of this effect can be explained by suggesting that caffeine increased arousal beyond an optimal level and therefore impaired performance in these subjects. If this indeed was the case disadvantageous effects of caffeine would be awaited in the well rested group instead of in fatigued subjects, due to their higher basic energy levels. What actually can be seen, is that the absence of performance improvements is observed in the fatigued group twice as often than in the well rested group. No systematic changes in the number of commission errors or in omission errors were observed, which might indicate that strategy effects are not involved in producing these differences. At the moment no satisfactory explanation can be offered for the performance deteriorations due to caffeine on RT.

In conclusion, this study provides evidence which suggests that caffeine specifically affects input and output related information processing mechanisms. The subject's level of task performance is enhanced after the caffeine treatment, because of an increase in the amount of transmitted information and a more efficient orientation to the environment. The preparation of response mechanisms seems to have improved, although further research is needed to determine whether the effects of caffeine on the motor preparation stage are located centrally or more peripherally. The findings further indicate that caffeine effects are most pronounced in fatigued subjects compared to well rested subjects.

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