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Original Article

Acute Caffeine Effect on Repeatedly Measured P300

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Abstract

The acute effect of a single-dose of caffeine on the P300 event-related brain potential (ERP) was assessed in a study using a repeatedly presented auditory oddball button-press task. A dose (5mg/kg body-weight) of either caffeine or placebo lactose, dissolved in a cup of decaffeinated coffee, was administered double-blindly to coffee drinkers who had abstained from coffee for 24hrs, with the presentation order of the sessions counterbalanced and separated by 2-4 weeks. The caffeine-treatment condition demonstrated a smaller P300 amplitude and a shorter latency overall than the placebo treatment condition. The mean P300 amplitude value difference (caffeine minus placebo) increased with the successive trial blocks. Caffeine ingestion appears to yield a lower resource-consumption and a net increase in allocating attention resources for task performance across repeated measurements.

Key words: caffeine, event-related brain potential (ERP), repeated measurement, P300, oddball

Introduction

Caffeine is the most widely consumed psycho-stimulating constituent worldwide through coffee, tea, soft drinks, confectioneries, and medications such as tonic drugs and over-the-counter remedies for colds and flu. A cup of coffee usually contains some 100-150 mg of caffeine, and tea contains slightly less [1,2]. People in many countries habitually drink tea and/or coffee every day to get refreshed and to maintain a sense of well-being. The daily caffeine intake of adults in Western societies is averaged to be 200-300 mg [3]. An estimation shows that more than 85% of Americans consume caffeine, yielding a daily per capita consumption of 1-2 cups, and the annual total caffeine consumption in the U.S. alone is 15 billion grams [1,4]. To these people, caffeine provides an indispensable, positive, and reinforcing stimulus in their daily lives, as it is long and widely-alleged to be able to elevate mood, reduce fatigue, and improve physical and mental efficiency, possibly by increasing alertness, attention, energy, and motivation for work [1,5-7]. For some individuals, however, caffeine may introduce clinically significant detrimental effects such as discomfort or anxiety, etc.; and dependent or withdrawal symptoms such as headaches, sleepiness, fatigue, and depression, etc. [8-11]. It is obvious that caffeine plays an important role in the daily life-events of human society, and exerts a far-reaching impact on the public health and well-being of the majority of the world's population. Empirical observation has also demonstrated a possibility for caffeine to play a more active rule in the so-called 24-hour society in the future, because it offers a "natural" and widely available manipulation of human arousal, vigilance and the sleep-alarm cycle. Therefore, better knowledge of the psychophysiological actions of caffeine will enable us to find solid strategies to utilize caffeine to promote public health and elevate work efficiency, as well as to tackle its detrimental effects more effectively.

Since the last century, the overwhelming popularity of daily caffeine consumption has attracted investigations into its effects on human performance and mood [9,12]. Despite extensive studies, however, the psychophysiological actions of caffeine have not yet been well-established [9,13,14]. Recent evidence suggests that caffeine improves vigilance and performance of cognitive tasks [15,16], and enhances sustained auditory attention and selective visual attention [12,13,17]. It improves the selection of relevant and irrelevant information by facilitating more rapid mental processing and more efficient allocation of attention to relevant stimuli [13,18]. Evidence also suggests that caffeine exerts its cognitive and behavioral actions by interacting with a multitude of variables, such as intake levels, type of environment (novel vs. boring), and dosages, etc. [19]. This predisposes a major difficulty in caffeine research, since so many variables, both known and unknown, will potentially affect the results. Nevertheless, the prevalence of daily caffeine consumption throughout the world and its beneficial actions, as well as the clinical importance of its unwelcome mental effects on the general public, make it essential to further characterize its psychophysiological effects.

The amplitude of P300 event-related brain potential (ERP) demonstrates a systematic decline across repeated measurement [20,21]. This important characteristic suggests that the P300 reflect

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Table 1 Reaction time, mean percentage of (artifact-) rejection and error rate (no miss in all cases) for task performance from each drug treatment condition and trial block.

	Block 1	Block 2	Block 3	Block 4	Block 5	Block 6
Reaction time						
Placebo	309 ± 75.4	299 ± 59.9	317 ± 65.4	307 ± 55.8	316 ± 57.7	310 ± 60.9
Caffeine	306 ± 48.2	301 ± 43.8	306 ± 49.4	298 ± 42.2	290 ± 34.1	290 ± 33.1
Percent rejection						
Placebo	0.89 ± 1.36	1.00 ± 1.32	1.11 ± 1.27	0.67 ± 1.00	1.78 ± 2.33	1.00 ± 1.66
Caffeine	2.33 ± 4.82	2.78 ± 6.91	0.78 ± 1.99	0.67 ± 1.00	0.78 ± 1.39	1.44 ± 3.00
Percent false alarms						
Placebo	0.11 ± 0.33	0.22 ± 0.44	0.00 ± 0.00	0.00 ± 0.00	0.11 ± 0.33	0.00 ± 0.00
Caffeine	0.00 ± 0.00	0.11 ± 0.33	0.00 ± 0.00	0.11 ± 0.33	0.11 ± 0.33	0.22 ± 0.44

Mean ± SD

fundamental neurophysiological activities related to changes in the mnestic representation of the stimulus environment resembling the orienting response[20-24]. It also has been linked to changes in the amount of attention resources allocated as required time-on-task increases[24,25]. Moreover, repeated measurement will provide more "close-to-nature" testing conditions for the caffeine's psychophysiological effects, because in the real world, the majorities of human life-events (writing, speaking, reading, and walking, etc.) occur in repeated fashion.

The present study assessed how caffeine affects P300 measurements with repeatedly presented stimuli in order to look for new insights on the psychophysiological mechanism that may underlie the beneficial as well as detrimental effects of caffeine.

Materials and methods

Nine healthy male (M=30.7, SD= ± 3.8 years) regular coffee consumers (1-2 cup/day), with normal sleep patterns, free from prescribed medication and naïve to electrophysiological studies, signed a consent form and volunteered their time or were paid for their participation. The subjects were administered either caffeine or a placebo once in two sessions separated by 2-4 weeks under double-blind and counterbalanced presentation conditions[13,14,18]. They abstained from caffeine-containing substances, alcohol and smoking for 24hrs before each test, had lunch before 12:00 noon and were assessed between 5:00 to 6:30 p.m. Each subject received 5mg/kg (275-375 mg) caffeine or lactose dissolved in a cup of normally brewed decaffeinated coffee. About 30 min after consumption, when caffeine reached its peak plasma level[26], the ERP recording began.

A simple and widely used auditory oddball button-press task has been employed to elicit the P300. The stimuli were sinusoidal tones (70 dB SPL, 10 ms rise/fall, 50 ms plateau), presented binaurally through earphones, at 3 sec inter-stimulus-intervals (ISI). The target stimulus was always a 2000 Hz tone randomly occurring with a probability of 0.2; the standard stimulus was always a 1000 Hz tone with a probability of 0.8. They were delivered continuously until approximately 20 artifact-free target trials were averaged, which defined one trial block. A total of 6 blocks was obtained from each subject, since this procedure would produce robust P300 habituation[23]. The inter-block interval was about 40 sec, during which the subjects rested and the recorded data was stored.

The subjects were seated in a comfortable chair, and instructed to fixate on a point 0.8 m directly ahead and avoid eye-blinks or eye-movement to prevent artifact-rejection. They were also instructed to respond only to the target stimulus by pressing a button as quickly as possible, with the response time, artifact-rejection and error rate being recorded. Electroencephalographic (EEG) activity was recorded using Ag/AgCl plated electrodes at Fz, Cz and Pz of the 10-20 systems, referred to linked earlobes with a forehead ground. Two additional electrodes were placed at the outer canthus and supraorbitally to the left eye with a bipolar recording made of electro-ocular (EOG) activity. Electric impedance of all electrode sites was kept below 5 KΩ. EEG was recorded using a 0.02-30 Hz bandpass and digitized at 0.8 ms per point for 800 ms with a 100 ms pre-stimulus baseline. Waveforms were averaged online, with EEG or EOG trials exceeding ± 100μV rejected automatically.

Results

Table 1 is a summary of the behavioral performance from each drug-treatment and trial block. A two-factor analysis of variance (ANOVA) (2 drug-treatment × 6 trial blocks) of the response time, rejection and error rate showed neither a significant drug treatment effect nor an interaction of this variable with the trial block (*P>0.05* in all cases). Thus the drug treatment did not affect performance across the trial blocks, most likely because of the very simple nature of the target detection response task.

Fig. 1 illustrates the representative averaged P300 for the

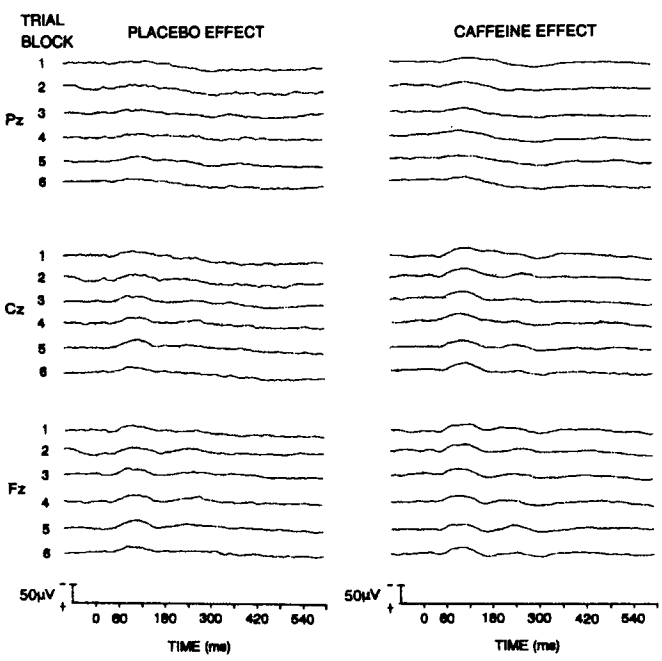

Fig. 1 Representative averaged P300 for target stimulus from each drug treatment condition and trial blocks at each electrode site.

target stimulus from each drug treatment and trial block at each electrode site. The P300 amplitude was defined as the maximum positive peak (relative to the 100 ms pre-stimulus baseline) after the N100-P200-N200 complex within a 250-400 ms time window, and the component latency was defined as the time point of maximum amplitude relative to the stimulus onset. Fig. 2 illustrates the mean (+0.5 SE) P300 amplitude (top) and latency (bottom) values from each drug-treatment and electrode site as a function of the trial block. A three-factor ANOVA (2 drug-treatment × 6 trial blocks × 3 electrodes) was applied to each dependent variable.

The caffeine treatment produced a smaller P300 amplitude and a shorter latency overall compared to the placebo treatment, $F(1,298)=14.91$, $P<0.001$, *and* $F(1,298)=5.65$, $P<0.05$, respectively. The P300 amplitude increased from the frontal to the parietal electrode sites, $F(2,30)=54.96$, $P<0.001$. No reliable interaction between either drug-treatment condition and trial block was found ($P>0.05$ in all cases). A separate two-factor ANOVA (6 blocks × 3 electrodes) on the P300 amplitude and latency from the placebo treatment and caffeine treatment conditions did not find a significant trial block effect for either condition ($P>0.05$), although the P300 amplitude after the caffeine treatment demonstrated a general increase over the trial blocks. Hence, the P300 amplitude did not demonstrate a habituation effect for either of the drug treatment conditions. Fig. 3 illustrates the mean (+0.5 SE) value difference (caffeine minus placebo) of the P300 amplitude that showed a successive increment from block 2 to block 6. Linear regression demonstrated that this difference correlated with the trial block, $F(1,160)=5.41$, $P<0.05$. The mean value difference of P300 latency did not show such a trend ($P>0.05$).

Discussion

The present results demonstrated that caffeine ingestion produced a smaller P300 amplitude and a shorter P300 latency overall compared to the placebo condition across the successive trial blocks, and the subjects performed the tasks equally well under both conditions. These findings suggest that caffeine yields quicker mental processing and less overall demand on attention resources required for task performance [18,27-30]. It may originate from an improved mental efficiency as suggested in previous studies that caffeine enables more efficient allocation of attention to relevant stimuli and accelerates mental processing [13,14], since an analogous discrimination between relevant and irrelevant information is also essential in performing oddball tasks [30]. The overall shorter P300 latency following caffeine-treatment provides further supportive evidence for this hypothesis [13,14]. Furthermore, the mean value difference of the P300 amplitude showed a successive net increment across repeated stimulus presentations. These results suggest that caffeine may have prevented a P300 amplitude decline with the trial blocks, possibly by preventing a decrease in allocating attention resources for successive task performance.

The present study has observed a smaller P300 amplitude following caffeine ingestion, while in the previous ERP studies using visual selective attention tasks, the P300 amplitude either was not affected by caffeine [13,14] or demonstrated an increment after caffeine ingestion [18]. Both the unaffected P300 amplitude from previous studies and the smaller P300 amplitude from the present study seem to imply that in these studies, caffeine exerted its psychophysiological effect mainly through a mechanism other than increasing alertness, since elevated arousal is generally related to a larger P300 amplitude [31]. The precise reason for the discrepancy among these studies is not yet clear, because the psychophysiological actions of caffeine are very complicated [9,13,14,19,26] and caffeine-related P300 research has just begun [31]. Moreover, how the P300 component may vary across different paradigms and response conditions has not yet been well-characterized [29,30,32]. Nevertheless, the specific procedural and parametric differences utilized by the present and previous studies have contributed a potential source of discrepancy in the P300 amplitude between these studies [26,30,32]. Further studies are needed to clarify these characteristics.

Caffeine may modulate the mental processing for repeated stimulus by reducing the overall demand on attention and producing a net increase in allocating attention resources for task performance. This effect, if it can be further clarified, may offer a

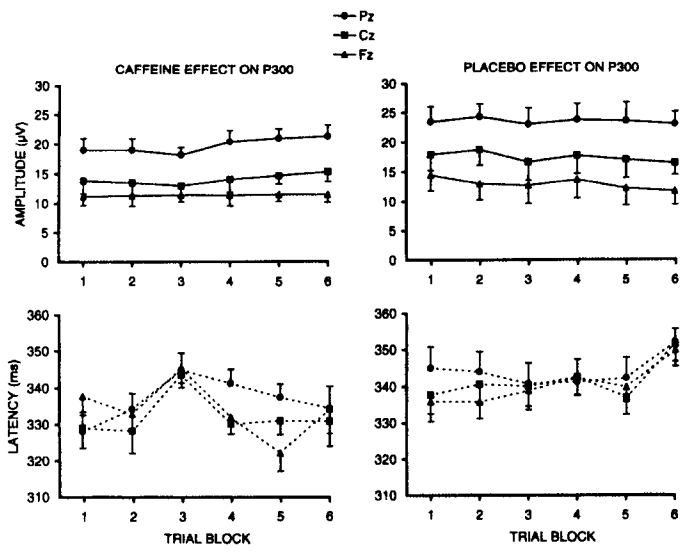

Fig. 2 Mean (+0.5 SE) P300 amplitude (top) and latency (bottom) values from each drug-treatment condition and electrode site as a function of successive trial blocks.

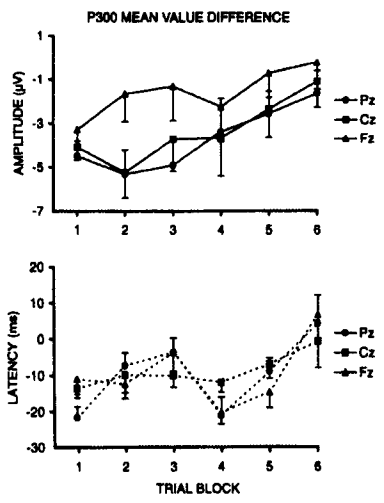

Fig. 3 Mean (+0.5 SE) value difference (Caffeine minus Placebo) of the P300 amplitude (top) and latency (bottom) from each drug treatment condition and electrode site as a function of successive trial blocks.

new hypothesis for the psychophysiological mechanism behind the prevailing caffeine consumption and/or its detrimental effects. For example, it is not unreasonable to assume that some regular caffeine drinkers may develop a level of psychophysiological dependence upon caffeine to sustain a higher level of mental efficiency for performing daily duties. Acute caffeine abstinence may cause a decline in their mental processing and "forces" them to consume extra attention resources to perform the same task. This might increase the brain energy consumption, etc., and play a role in their "easiness" to become tired and sick. It is also not impossible that constant mental "coercing" will result in anxiety and headaches.

In conclusion, the present results suggest that proper utilization of caffeine may help people feel more at ease with redundant information or repeated stimulation, and reduce performance failure (incident as well as accident) due to boring tasks and/or extended work conditions such as long-distance flying and driving. Nevertheless, caution must be taken to prevent the "over utilization" (in dosage or frequency) of caffeine to minimize its detrimental symptoms. It also calls for multidisciplinary studies to further elucidate the pertinent psychophysiological mechanisms and to circumscribe the optimum dosage, frequency and interval of caffeine usage to promote physical and/or mental health for the general caffeine consuming populations.

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