

Effect of Caffeine on Evoked Potentials

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Abstract : *Back ground: Caffeine a white crystalline xanthine alkaloid is the most widely used psychoactive stimulant in the world. In spite of being used as a substance of abuse, it is widely used as a CNS and metabolic stimulant for its short term and long term pharmacological action. A number of studies with dramatic results have proved that caffeine is a stimulant. Review of literature: Effects of caffeine have been studied on brain function and behavior using number of tests, but, however, studies on acute effects of caffeine on both visual and auditory evoked potentials are few. Aim of the study: To record the effect of caffeine in relation with the auditory and visual evoked potentials, as well as to highlight the individual differences in its effects in variation with age, sex and substance abuse. Materials and Method : 6 healthy volunteers were recruited for the study after a questionnaire analysis followed by routine ophthalmologic and auditory examinations. They were administered 2mg/kg body weight of caffeine (PO) after 12hr abstinence from caffeine in any form. Auditory and visual evoked potentials were recorded before and after 30 minutes of ingestion of caffeine by using RMS Polyrite. Latency and amplitude of P100 in VEP and absolute latency and amplitude, inter-peak latencies in BAEP were evaluated. Results and conclusion: The data obtained revealed the decrease in the latencies of P100 waveform in VEP and I-V inter-peak latency in BAEP as well, indicating that caffeine improves transmission in the peripheral and central brain auditory pathways.*

Keywords – caffeine, evoked potential, age variation, sex variation, substance abuse.

I. Introduction

Caffeine (1,3,7-trimethylxanthine) ,white crystalline xanthine alkaloid present in seeds, fruits and leaves of certain plants. Bioavailability of caffeine is almost 100% when administered orally. Within minutes of ingestion there is peak absorption, with volume of distribution similar to that of total body water. Plasma half-life is about 3-8 hrs. In brain the levels remain stable for at least a hour. It is metabolized in liver and excreted via kidneys¹.

Beverages like coffee, tea, soft drinks and energy drinks contain caffeine. It is the most widely used psychoactive stimulant in the world with per capita consumption 1-2cups a day².A cup of coffee on average contains 100 to 150 mg of caffeine/150 ml of coffee.Despite of being used as a substance of abuse, it is widely used as a CNS and metabolic stimulant for its short term and long term pharmacological actions.

Dixit et al., in their study on P3 evoked potential concluded that caffeine leads to facilitation of information processing and motor output response of the brain³. Whereas Soleimanian et al., studied the effect of caffeine on auditory brainstem response and concluded that adenosine receptor blocking brings about changes in conduction in the central auditory pathway⁴.Deslandes et al., concluded from their study on P300 evoked potential and neuromotor performance suggested that the positive tendency of caffeine to improve cognitive performance is probably associated with changes in the frontal cortex, a widely recognized attention area⁵.

A number of studies with dramatic results have proved that caffeine is a stimulant. Effects of caffeine have been studied on brain function and behaviour using mood questionnaires, reaction time tests, memory tests, EEG and off late by Event Related Potentials (ERPs).But, however, studies on individual differences on the acute effects of caffeine on both visual and auditory evoked potentials are few.

This study is designed to study the acute effects of caffeine on central processes through visual and auditory evoked potential and to bring out the individual differences that exist with the effect of caffeine, as well as to highlight its effects on age, sex and substance abuse.

II. Materials And Methods

Subjects: Six healthy volunteers (both the sex) with regular caffeine intake of about 2 cups a day were recruited for this study. They were grouped according to age like 20 years (n = 3), 25 years (n = 1) and 30 years (n= 2). Each 20 year male subject was paired with other three subjects to see the variation with age, sex and substance abuse. They were chosen after a questionnaire analysis according to the inclusion criteria. Institutional ethical committee clearance was obtained. A written informed consent was obtained from the subjects after briefing about the study.

Exclusion criteria: Recent Illnesses & Ongoing Medications, Alcoholics, H/o CNS and Mental Disorders, H/o Medical and Surgical Illness, Epilepsy, Pregnancy, Open Angle Glaucoma, Liver Disease.

The study was conducted in the Research Laboratory, Department of physiology, SBMCH. The subjects were instructed to abstain from caffeine, nicotine and any substance of abuse for the last 12 hrs before the study. Auditory and visual evoked potentials were recorded using RMS Polyrite instrument. After which they were administered 2mg/kg of caffeine (PO) added with sugar and milk. After 30 minutes auditory and visual evoked potentials were again recorded⁶.

Recording of visual evoked potential: After a routine ophthalmologic examination. The subjects were prepared for the recording of visual evoked potential. Standard silver – silver electrode disc electrodes were placed according to the International 10/20 system⁷. Impedance kept low below 5 kilo ohms. The stimulus was of pattern reversal type using checker board. Contrast was maintained at about 80%. Pattern reversals were at a frequency o about 0.5-1.0Hz. The evoked potentials were amplified, averaged and recorded for 300 stimuli. Parameters measured were - Latency of N75, P100 and N145 in milliseconds and Amplitude of P100 wave (N75-P100) in microvolts.

Recording of auditory evoked potential: After a routine auditory examination. The subjects were prepared for the recording of auditory evoked potential. Standard silver –silver electrode disc electrodes were placed according to the International 10/20 system⁷. Impedance kept low below 5 kilo ohms. Stimuli were of clicks with intermediate rates at about 11-30 per second. In ipsilateral ear the clicks were about 90 dB, whereas in the contralateral ear white noise was given. The evoked potentials were amplified, averaged and recorded for 2000 stimuli. Parameters measured were Latency of waves I,II,III,IV and V in milliseconds and inter peak latencies – I-III,I-V and III-V in milliseconds.

The results obtained were tabulated and expressed as mean ± standard deviation, and the significance of the parameters was obtained by using non-parametric tests.

III. Results

In order to study the individual variation in the effect of caffeine, each 20 year male subject was paired with other three subjects to see the variation. Subject 1 (20 year male) was paired with subject 2, who is a 30 year male, to see if there is any variation in the effect of caffeine with age. Subject 3 (20 year male) was paired with subject 4 ,who is a female to see if there is any variation with sex. And subject 5 (20 year male) was paired with subject 6 who is a smoker for 5 years, to study if there is any variation in the effect of caffeine with substance abuse.

Table 1: Latencies and Amplitude of the waveform in VEP to see the effect of caffeine.

	N75(ms)		P100(ms) (120.3±1.17)		N145(ms)		P100-N75(µV) (10.1±4.2)	
	LT	RT	LT	RT	LT	RT	LT	RT
Before Caff.	82.6±4.8	83.1±4.	115.7±4.1	114.9±4.	165.3±8.7	166.7±7.3	5.7±1.8	5.4±2.2
After Caff.	80.5±3.5	80.9±3.	110.7±2.7	110.6±3.	159.6±10.	163.4±6.2	6.2±1.6	5.8±2.2

Graph 1 & 2: latencies and amplitude of the waveform in VEP to study the effect of caffeine.

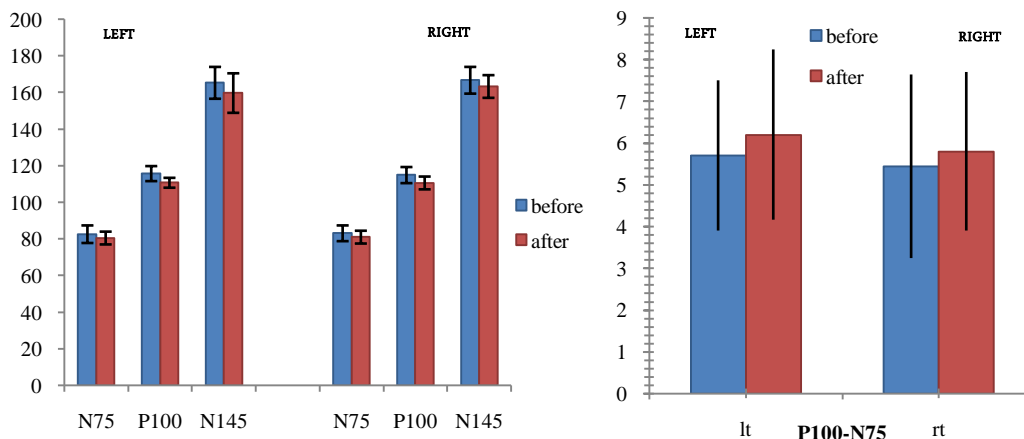
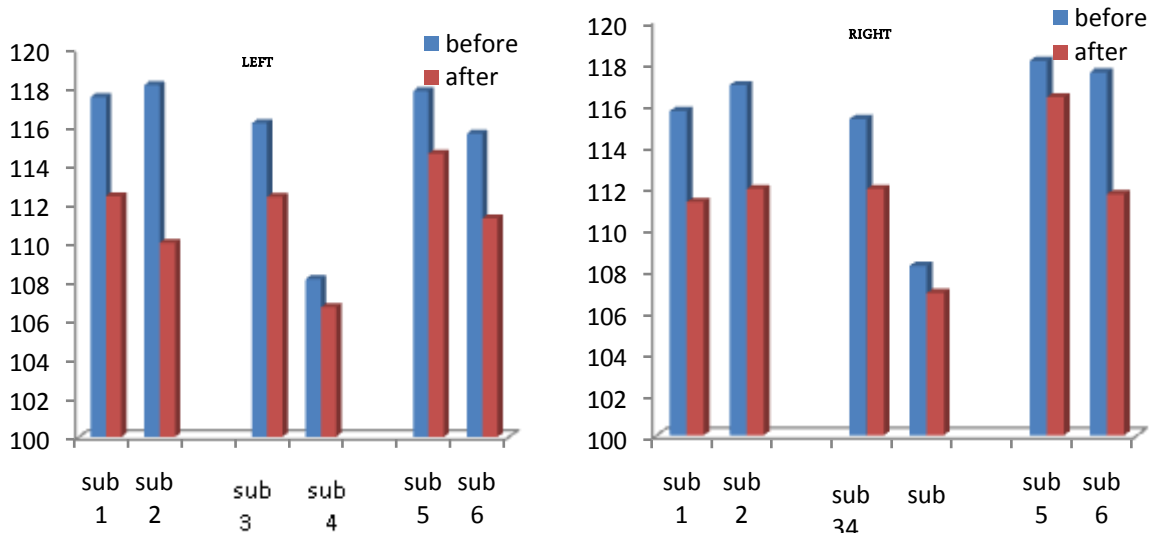


Table 1 , graphs 1 & 2 : represents the mean ± standard deviation of the latencies N75,P100 and N 145 and amplitude of P100 waveform. We can note that there is a decrease in the latencies and an increase in the amplitude of P100 wave after the ingestion of the caffeine.

Graph 3 & 4 : individual differences in the waveform P100 in VEP



Graphs 3 & 4 : represents the latency of P100 waveform in all the six subjects. We can note that there is a variation in the decrease in the latencies in all the subjects, after caffeine ingestion.

Table 2 : latencies of the waveforms in BAEP to study the effect of caffeine

	I		II		III		IV		V	
Normal Range	1.7±0.17		2.78±0.21		3.65±0.22		5±0.30		5.72±0.3	
	LT	RT	LT	RT	LT	RT	LT	RT	LT	RT
Before Caff	1.7±0.21	1.7±0.19	2.9±0.17	2.9±0.21	3.8±0.09	3.9±0.18	4.9±0.0.16	4.9±0.23	5.6±0.21	5.6±0.21
After Caff	1.6±0.12	1.6±0.21	2.8±0.19	2.9±0.13	3.6±0.13	3.6±0.24	4.9±0.15	4.8±0.28	5.3±0.15	5.3±0.14

Graph 5 & 6: latencies of the waveforms in BAEP to study the effect of caffeine

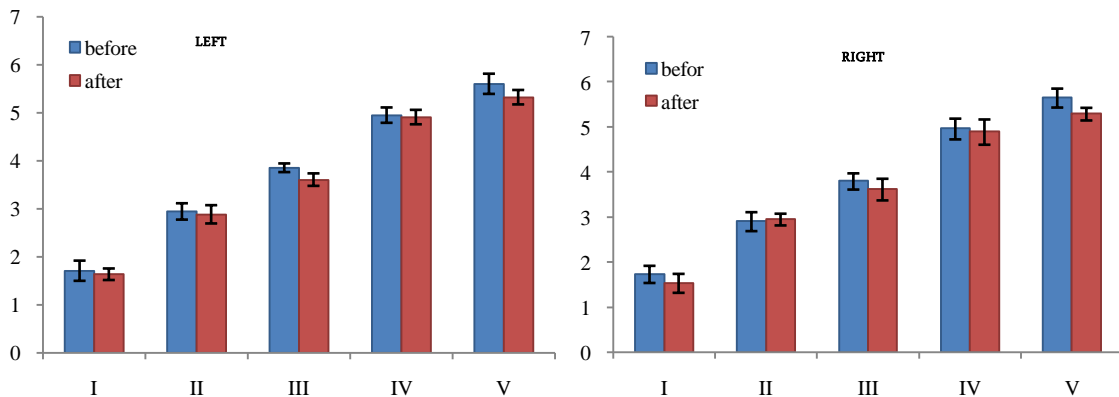


Table 2 , graphs 5 & 6 : represents the mean ± standard deviation of the latencies of the I,II,III,IV and V waveforms. We can note that there is a decrease in the latencies of almost all the waveforms after the ingestion of the caffeine.

Table 3 : interpeak latencies of the waveforms in BAEP to study the effect of caffeine

	I-III		I-V		III-V	
Normal Range	2.1±0.15		4.0±0.23		1.9±0.18	
	LT	RT	LT	RT	LT	RT
BeforeCaff	2.1±0.17	2.1±0.23	3.9±0.36	3.9±0.4	1.7±0.21	1.85±0.21
After Caff	1.9±0.18	2.0±0.31	3.7±0.37	3.7±0.31	1.71±0.18	1.7±0.2

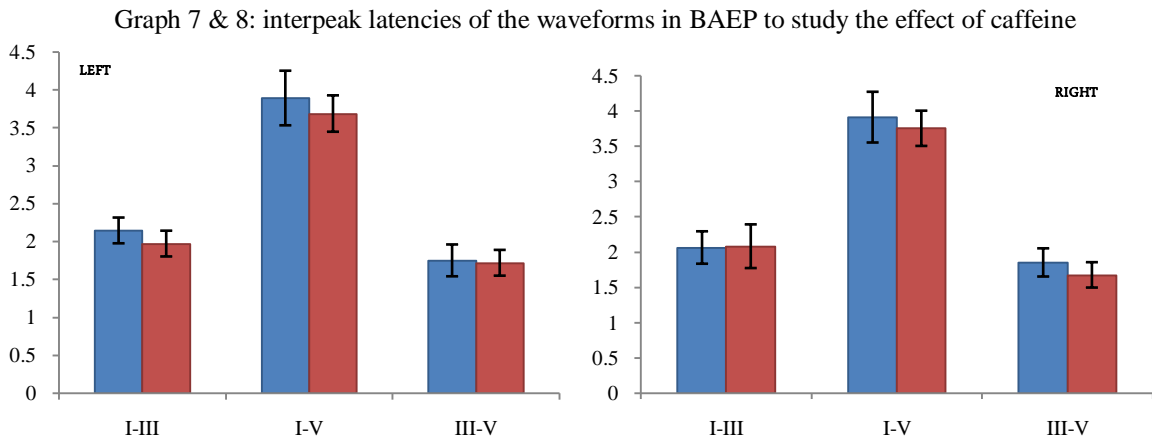
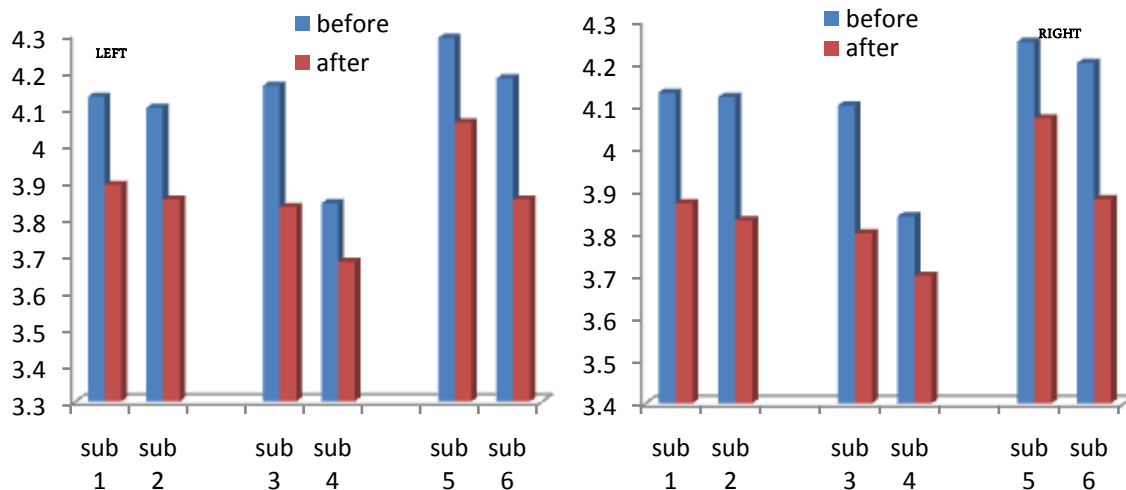


Table 3, graphs 7 & 8 : represents the mean \pm standard deviation of the interpeak latencies of the I-III,I-V and III- V waveforms. We can note that there is a decrease in the latencies of almost all the waveforms after the ingestion of the caffeine.

Graph 9 & 10: individual differences in the interpeak latency I-V in BAEP.



Graphs 9 & 10 : represents the latency of P100 waveform in all the six subjects. We can note that there is a variation in the decrease in the interpeak latency after the administration of caffeine in all the subjects.

Visual evoked potential: There is a decrease in the latencies of all the waveforms, and an increase in the amplitude of P100 waveform in the visual evoked potentials after the administration of caffeine.

Considering each pair of subjects, we can observe a variation in the decrease of the latencies in subjects 1 & 2 on the right side, however, not much of difference is observed on the left. On comparing the decrease in the latencies in subjects 3 & 4 we can observe that the decrease in the latency in the female subject is less when compared to that of the male subject, on both the sides. Similarly, in case of subjects 5 & 6, we can observe that the decrease in the latency of the subject who smokes is much more when compared to the 20 year male subject. Brainstem auditory evoked potential: We can clearly observe that there is a decrease in the latencies of all the waveforms, and the inter peak latencies of the brainstem auditory evoked potentials after the administration of caffeine.

Considering each pair of subjects, we can observe a variation in the decrease of the latencies in subjects 1 & 2 on both the sides. On comparing the decrease in the latencies in the subjects 3 & 4 we can observe that the decrease in the latency in the female subject is less when compared to that of the male subject, on both the sides. Similarly, in case of subjects 5 & 6, we can observe that the decrease in the latency of the subject who smokes is much more when compared to the 20 year male subject.

Even on comparing the decrease in the latencies among the three 20 year male subjects, we can observe that the decrease in the latencies in these subjects is not similar.

IV. Discussion

In our study, we included only 6 subjects which might be considered as a limitation of this study, however, we would prefer to suggest that this study design was undertaken to highlight the individual differences that exist with the effect of caffeine, which would have been masked when a large population, is considered in the study.

Shorter latencies of the P100 waveforms in the visual evoked potentials indicate an increase in information processing speed. As the generator site for P100 waveform in VEPs is believed to be the peristriate and striate occipital cortex, the latency and the amplitude of the wave P100 is usually considered, and analysis from previous studies on VEP indicated the topographic localization of the dipoles around the calcarine fissure. In VEP, latency of P100 wave is hardly affected by age, and these waves tend to vary after the age of 60⁸. The general male and female differences in the P 100 wave are suggested to be due to differences in the geometry of the head rather than to more general biological differences between males and females and no studies have highlighted the variation in the evoked potentials with the use of nicotine⁹.

Shorter latencies of the waveforms in auditory evoked potentials indicate an increase in information processing speed. Similar to VEP, in BAEP also the decrease in the interpeak latency is hardly affected by age, and these waves tend to vary after the age of 60⁸, and the male and female differences are suggested to be due to differences in the geometry of the head rather than to more general biological differences between males and females¹⁰ and no studies have highlighted the variation in the evoked potentials with the use of nicotine. This concludes that any variation in the evoked potentials before and after the administration is attributed by the effect of caffeine.

General discussion: Decrease in the latency of P100 waveform in VEP and the interpeak latency of I-V in BAEP, highlights the stimulating effect of caffeine. Shorter latencies of the waveforms in the visual and auditory evoked potentials indicate an increase in information processing speed¹¹. Caffeine stimulates the central nervous system first at the higher functions of the brain like cognition, memory, attention and concentration than altering the peripheral motor responses resulting in ergogenic action¹. However, we could see there is individual variation in its action on the visual and auditory central pathways.

Our study inferred that there is no difference with the stimulating effect of caffeine in variation with age. However, one of the previous study have concluded that there effect of caffeine varies with that of age, but , the study compared the effect of caffeine between 20 and 60 age groups, and the concluded difference would have been due to age related difference in either the metabolism or excretion, with each individuals¹². In consistent with the previous studies our study observed that the male subject experienced a greater effect compared to the female subject, which would probably due to the biological differences between males and females^{13,14}. The effects of caffeine are more pronounced in subject whose is under the influence of nicotine¹⁵. This variation with each individual in the effect of caffeine would have been contributed by the underlying cellular mechanisms that are triggered with the ingestion of caffeine.

Caffeine mainly acts by blocking adenosine receptors¹⁶, which are responsible for the “fine-tuning” of the neuronal communication. Thereby bringing about changes in the levels of various neurotransmitters like dopamine, adrenaline and glutamate¹⁷. Glutamate mediated action The check on the excitatory action of glutamate is lifted off with the blockade of adenosine receptors, which results in the profound action of glutamate¹⁸. Whereas there is a pituitary mediated release of catecholamines resulting in actions mediated Adrenaline¹⁸. Dopamine mediated action of caffeine requires a special mention. Here both D1 and D2 like receptors are involved in the reinforcing properties of different drugs of abuse, with D2 receptors mediating the stimulant drug reinforcement and D1 receptors playing a permissive role¹⁹. However, multiple components are needed to account for the totality of the effects of caffeine. Factors like, Difference in the number of adenosine receptors that are being blocked, difference in the neurotransmitter that comes into play, and the difference in the number of D1 and D2 like receptors that causes the reinforcement in the usage of caffeine. These varied underlying cellular mechanisms contribute to the individual variation in the effect of caffeine.

The stimulatory effect of caffeine as represented by the shorter latencies can also represent the speed at which the sensory information is being transmitted to their respective cortices – sensory memory, a part of brain’s cognition. Even though this study, has assessed the visual and auditory processing of information and their modification with the effect of caffeine, this ergogenic action of caffeine can be positively hypothesized to the whole of cortical activity as the sensory impulses are largely perceived and interpreted by the visual and auditory pathways.

V. Conclusion

This study concludes that, Caffeine acts as a stimulant, and that has the tendency to modify, the rate at which the sensory information is transmitted to the respective cortices, and this stimulating effect of caffeine varies with each individual as the underlying physiological mechanisms are varied. And caffeine might cause easy susceptibility for substance abuse.

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