Review Paper

International Physiology
Vol. 4 No. 1, January - June 2016
DOI: https://dx.doi.org/10.21088/ip.2347.1506.4116.7

Caffeine and Cognition: What do Event Related Potentials Say?

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Abstract

Caffeine is a stimulant that is present in various drinks like tea, coffee and colas. It acts on the body via different mechanisms like altering intracellualar calcium, acting on benzodiazepine receptors and inhibition of phosphodiesterases. The main mechanism of action is blocking of adenosine receptors and alteration of the neurotransmitters in the brain.

The event related potentials are electrical signals in response to stimuli and represent the processing of information by the brain. Various studies have been done to evaluate the effect of caffeine on cognitive processes using event related potentials. This review summarizes the evidence of the effect of caffeine on cognition.

Keyword: Caffeine; Cognition; Evoked Potentials.

Introduction

Caffeine (1, 3, 7-trimethylxanthine) is one of the most widely used psychoactive drug in the world. It is consumed in various forms like tea, coffee, colas and many over the counter medicines. The amount of caffeine in food items ranges from 40-180 mg/150 ml of coffee, to 24-50 mg/150 ml of tea and 15-29 mg/180 ml for colas [1]. Caffeine is known to affect various body systems. In low doses of 50-250 mg per sitting, caffeine produces relaxation, increased alertness, feeling of well being and increased concentration. In doses ranging from 400-800 mg in one sitting, it causes tachycardia, nervousness, aggressiveness, insomnia, trebling and anxiety.

Caffeine is readily absorbed from oral, rectal and parenteral routes. The half life of caffeine is 3-7 hours [2]. Significant levels of caffeine are observed in brain within 5 minutes of oral intake with peak levels being observed within 30 minutes [3]. Metabolism of caffeine occurs mainly by demethylation to paraxanthine. A little amount of caffeine is also demethylated to form theobromine and theophylline [4].

Caffeine increases the amount of epinephrine and norepinephrine secreted by adrenal medulla leading to stimulation of respiratory centre with an increase in respiratory rate, oxygen consumption and carbon dioxide elimination. The cardiac muscle is directly stimulated by caffeine leading to increase in heart rate, cardiac output and force of contractions. Caffeine also causes stimulation of medullary vagal nuclei that in turn decreases the heart rate. Action of caffeine on smooth muscles of coronary, pulmonary and general systemic blood vessels causes them to dilate: at the same time stimulation of vasomotor centre causes vasoconstriction of these vessels [5].

Mechanism of Action of Caffeine

Various hypotheses have been formulated regarding the possible mechanisms of actions of caffeine at cellular level.

(i). One of the mechanisms of action of caffeine is mobilization of intracellular calcium. At a concentration of 1-2 mM caffeine decreases the excitability threshold and promotes translocation of calcium through plasma membrane and cytoplasmic reticulum [6]. However it has been found that mechanism occurs at doses higher than those attained by human consumption [1].

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(ii) Another mechanism which is proposed is Inhibition of phosphodiesterases by caffeine in the CNS [7].

(iii). Binding of caffeine to benzodiazepine receptors has also been observed [8]. It has been seen that caffeine antagonizes or modifies the effects of benzodiazepines on human behavior [9,10].

(iv). Via blocking of adenosine receptors: There is evidence that adenosine acts to decrease the rate of firing of neurons [11]. It has been observed that caffeine increased the amplitude of EPSP and population spike of hippocampal CA1 pyramidal cells. A reversible and concentration dependent antagonism of adenosine-evoked inhibition of EPSP was seen. The excitation reflected four changes in the neuronal membrane properties i.e. a depolarization from resting membrane potential, a decrease in membrane conductance, in long duration hyperpolarisation and that of accommodation [12].

The Adenosine receptors are present in almost all areas of brain with the maximum concentration being in hippocampus, cerebral and cerebellar cortex and certain thalamic nuclei [13]. Morgan et al reported that caffeine caused a dose dependent (30-75mg / Kg) increase in dopamine in the striatum [14]. Caffeine by blocking adenosine receptors thus brings about changes in the turnover of various neurotransmitters like adrenaline, dopamine, serotonin, acetylcholine, glutamate and GABA [15].

Evoked Potentials

Evoked potentials are electrical responses of the brain that are "evoked" in response to a stimulus. They are further classified as Stimulus Related Potentials and Event related Potentials.

Stimulus Related Potentials (SRPs) are records of the changes in electrical potentials in the nervous system in response to an external stimulus e.g. Auditory Brainstem Response, Visual Evoked Response etc. They are obligatory responses that are independent of attention or interest of the subject in the stimulus.

The term Event Related Potentials or ERPs refers to the responses evoked due to various mental workloads when a stimulus and the problem related with that stimulus are applied. They occur only when the subject is selectively attentive to the stimulus and are elicited in conditions where the subject has to distinguish a target stimulus from non target stimuli [16].

Components of ERPs

The long latency response to a rare auditory stimulus consists of different waves i.e. N1, P2, N2 and P3 (also called P300). The P300 component of ERPs was first described by Sutton in 1965 [17]. The N1 and P2 components are believed to reflect the activity in neural areas that are activated by sensory modality and are independent of the subject's attention [18]. The N2 component is related to the unexpectedness of the stimulus [19]. Thus any event related potential includes an early sensory evoked potential and a late (cognitive) response P300 component. Various other component waveforms have also been identified such as P165, N2 and P3a [19-21]. P300 (the positive wave occurring after 300msec of stimulus) is found more consistently than other waveforms. This occurs as the other components are of relatively small amplitude and thus more difficult to separate from background noise. Also these components occur at short latencies and overlap with the simultaneously occurring stimulus related potentials.

Various theories have such as Context Updating Theory, Wicken's Multiple resource model, Context Closure and Template matching have been put forward to interpret the meaning of P300 [22-25]. ERPs are a way of observing the functioning of the human brain as they allow the cognitive processes to be observed "from within" [26]. The most widely accepted views for interpretation of P300 are that it is evoked by unexpected stimuli, that it reflects the updating of working memory and that its amplitude indicates the amount of processing needed by a given stimulus.

Caffeine, CNS and Event Related Potentials

Various researchers have done studies to evaluate the effects of caffeine on central nervous system using EEG, psychological tests, reaction time, and of late evoked potentials. Hollingsworth in 1912 noted that 65-130 mg of caffeine improved typing speed. A dose of 390 mg resulted in poor motor performance and tremor [27].

Wolpaw and Penry examined the acute effects of 300 mg caffeine on N1P2 peak to peak amplitude in 31 subjects [28]. They found a decrease in N1P2 amplitude with placebo. This decrease was not seen with caffeine. Caffeine has been found to increase auditory vigilance in doses of 75-300 mg compared to a lactose dummy. In the same study it was seen that auditory reaction times were shortened, tapping rates increased and subjects felt more alert following caffeine consumption [29].

Tharion et al studied long latency evoked potentials during performance of visual vigilance task following

administration of 200 mg caffeine [30]. They found a significant decrease in P2-N2 amplitude after caffeine intake. Jarvis surveyed 9003 adults in UK and found that increased levels of coffee and tea were associated with improved performance on a range of cognitive tasks [31].

Study by Lorist et al demonstrated a decrease in RT and decrease in error rate following caffeine ingestion [32]. There was a more negative going N1 with a shorter latency. P3 amplitude revealed an increase with no significant change in its latency. Caffeine has been demonstrated to lead to a decrease in RT and increase in amplitude of visual evoked potentials. Azcona et al were of the view that this effect was not due to reversal of caffeine withdrawal as the subjects were not heavy caffeine consumers [33].

Lorist et al examined the effects of caffeine on specific information processing activities and on search processes [34]. They found that reactions were faster in focused attention condition than in divided attention condition. Caffeine led to a decrease in P3b (Stimulus evaluation processes) latency in focused attention and low display load conditions and thus accelerated stimulus evaluation. There was an increase in amplitude of N2b also. Kawamura et al investigated the effects of 500 mg caffeine on ERPs in 10 subjects [35]. The oddball paradigm showed that P300 amplitude and area were significantly increased after 30 minutes of caffeine intake. These effects disappeared after 210 minutes. P300 latency and Reaction time showed no significant change with oddball paradigm.

Another study by Lorist and Snel evaluated the effects of 3mg / Kg body weight of caffeine by using a visual selective attention task [36]. In the after caffeine condition the time taken to localize the target letter decreased and the information about the location of the target was passed earlier to the response system. The process of feature analysis was not affected by caffeine.

In their study Seidl et al found that Reaction time improved in response to target stimuli after administration of drink having caffeine [37]. The subjects showed shorter latencies of P300 though it was not statistically significant. A larger frontocenterally distributed P2 was found by Ruijter et al after caffeine intake [38]. The N2b component showed an increase in negativity. In the after caffeine intake condition the irrelevant target yielded a P3, thereby indicating that the subjects processesed the irrelevant target as well. There was a decrease in RT although the number of hits and false alarms showed no change.

Warburton et al evaluated the effects of caffeine on information processing using participants who had minimal deprivation from caffeine [39]. Their study also evaluated the effects of sugar using a sugar containing and a sugar free control drinks. A comparison of the two control drinks showed no significant difference, thereby indicating that glucose was not the substance responsible for improved performance in their study. The caffeine containing drink led to an increase in attention and verbal reasoning without affecting memory.

In a study on 30 subjects Yeomans et al observed a decrease in RT and increased response accuracy on a performance task [40]. These effects were however seen in subjects who were given caffeine after being in a caffeine deprived state. Preloading the subjects with caffeine had no significant effects on performance or mood. They suggested that the effects of caffeine were due to reversal of caffeine withdrawal condition.

Dixit et al evaluated the effect of caffeine on Event Related Potentials and reported non-significant decrease in latency of N1, P2, N2 and P3 after caffeine consumption [41]. The amplitude of P3 showed a significant increase after intake of caffeine. They concluded that caffeine led to facilitation of information processing and motor output response of the brain [41].

The consumption of caffeine has been shown to improve cognitive performance. There is increase in alertness and shorter reaction times. Thus caffeine leads to an overall improvement in cognitive functions. However more work is needed in the field to characterize if the improvement in cognition is global or in specific domains.

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