Review Article

Is Caffeine a Cognitive Enhancer?

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Abstract. The effects of caffeine on cognition were reviewed based on the large body of literature available on the topic. Caffeine does not usually affect performance in learning and memory tasks, although caffeine may occasionally have facilitatory or inhibitory effects on memory and learning. Caffeine facilitates learning in tasks in which information is presented passively; in tasks in which material is learned intentionally, caffeine has no effect. Caffeine facilitates performance in tasks involving working memory to a limited extent, but hinders performance in tasks that heavily depend on working memory, and caffeine appears to rather improve memory performance under suboptimal alertness conditions. Most studies, however, found improvements in reaction time. The ingestion of caffeine does not seem to affect long-term memory. At low doses, caffeine improves hedonic tone and reduces anxiety, while at high doses, there is an increase in tense arousal, including anxiety, nervousness, jitteriness. The larger improvement of performance in fatigued subjects confirms that caffeine is a mild stimulant. Caffeine has also been reported to prevent cognitive decline in healthy subjects but the results of the studies are heterogeneous, some finding no age-related effect while others reported effects only in one sex and mainly in the oldest population. In conclusion, it appears that caffeine cannot be considered a 'pure' cognitive enhancer. The indirect action of caffeine on arousal, mood and concentration contributes in large part to its cognitive enhancing properties.

Keywords: Alertness, attention, caffeine, cognition, learning, memory, mood, performance

INTRODUCTION

Cognitive processes can be natural or artificial, conscious or unconscious. The concept of cognition (from the Latin word *cognoscere*, "to know" or "to recognize") refers to a capacity for information processing, applying knowledge, and changing preferences. Cognition is a complex notion that involves at least memory, attention, executive functions, perception, language, and psychomotor functions. Each of these individual aspects are themselves complex entities. Indeed, memory includes encoding, storage, and retrieval of information and can be divided into short-term, long-term and working memory. Attention can be selective, divided, or sustained, and perception includes several stages of processing to achieve object recognition in different modalities (visual, auditory, and tactile). Executive functions involve reasoning, planning, evaluation, strategic thinking, etc. Language concerns–verbal expression, vocabulary, fluency and language comprehension, and finally, psychomotor functions–are related to programming and motor execution. Moreover, all the functions detailed above are influenced by various factors, such as mood (being happy or sad), the level of arousal reflecting alertness and energy, physical well-being, and motivation.

The objectives of the present document are to review the components of cognition that can be influenced by caffeine, under either acute or chronic dosage. These aspects have been the subject of numerous studies over the past four decades. In all these studies, some biases can be found. It must first be reminded that everyone consumes caffeine in the form of drinks (coffee, tea, mate, hot chocolate, soft drinks, energy drinks), food (mainly chocolate), or medication. Therefore, it is very difficult to control for the intrinsic effects of caffeine, since groups of non-exposed true control subjects with

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zero exposure almost do not exist. Second, most studies considering the acute effect of caffeine have imposed a period of abstinence of caffeine before testing, typically overnight. This led to a debate of whether or not the effects of caffeine are true effects or partly due to the reversal of more or less prolonged abstinence [1].

Caffeine absorption from the gastrointestinal tract is rapid and reaches 99% in humans in about 45 min after ingestion. Pharmacokinetics are comparable after oral or i.v. administration of caffeine in humans and animals. The hydrophobic properties of caffeine allow its passage through all biological membranes, including the blood-brain barrier. Peak plasma caffeine concentrations are reached between 15 and 120 min after oral ingestion in humans, and most studies reported here were performed between 45 and 120 min after caffeine ingestion. Caffeine half-life ranges from 2.5 to 4.5 h in humans (for review see [2]).

CAFFEINE AND INCIDENTAL VERSUS INTENTIONAL LEARNING

In learning and memory tasks, there are several components which include the variable tested but also many other parameters such as the level of vigilance and attention, the speed of reaction time, and mood. It has been repeatedly demonstrated that caffeine decreases reaction time, increases vigilance and attention, and has positive effects on mood (at the doses used in most studies that will be considered here). The effects of caffeine on learning were tested in different types of situations. In some experiments, the subjects were aware that they would be tested for learning, while in others they were not. The paradigms used also differed with the studies: in some tests some cue for recall was provided, while in other ones it was free recall from lists of words.

In paired-associate learning, subjects are usually given word pairs of a high or low degree of semantic association (e.g., tree-apple; car-sea). Subjects have some time to learn the word pairs and then are given the first word of each pair and have to recall the second one. This situation is a learning task that is different from free recall since the experimenter is giving the cue for recall. Caffeine does not affect paired-associate learning performance when recall is assessed immediately [3–5], nor when tested after a delay of 20–30 min [4].

In serial or intentional learning, the effect of caffeine has been assessed on the recall performance of words from lists (immediate or after up to 20 min). Caffeine (100–400 mg, or 3–6 mg/kg) does not significantly influence word learning across 2-6 presentations [6–12]. Nevertheless, high to moderate users recall more words than low users, particularly at the beginning of the lists, reflecting a potential beneficial effect of habitual caffeine consumption on learning [7,10,13,14].

In incidental learning, subjects are not told that they will be tested for memory. In this paradigm, it is considered that the experimenter is able to gain more knowledge over information processing activities at the time of learning, since subjects cannot use additional processing activities (rehearsal, memory aids) to improve performance. In one study, performed on 7414 subjects over 18 with daily coffee intakes ranging from zero to over 7 cups per day, subjects performed dosedependently better and older people appeared more susceptible to the performance-improving effects of caffeine [15]. In another incidental learning paradigm, 300 students, aged 19-24 years, were tested 30 min after 1-4 m/kg caffeine on different encoding processes. Subjects were non-drinkers or occasional low coffee drinkers and were told to abstain from caffeinated beverages for 10 h before testing. They were categorized by impulsivity level, knowing that a key characteristic of impulsive behavior is inappropriate attention to irrelevant information and susceptibility to distraction in working memory [16]. In this test, caffeine facilitated acquisition and recall in high-impulsive subjects after rhyming acquisition, but hindered it after semantic acquisition. Caffeine did not reliably influence recall in low-impulsives [17].

In summary, caffeine facilitates learning in tasks in which information is presented passively; in tasks in which material is learned intentionally, caffeine has no effect.

CAFFEINE AND MEMORY

Human memory can be divided into short-term (sometimes called working) memory, and long-term memory. Working memory stores information over brief intervals of time during which further processing can be performed (e.g., recognition). Only limited amounts of information can be stored in this working memory of which we are aware. Working memory provides the ability to maintain and manipulate information in the process of guiding and executing complex cognitive tasks. It can be described as a multicomponent system guided by an executive component consisting of a number of processes that provide attentional control over other components of working memory and other cognitive abilities. Two of the subcomponents are domain specific, providing the ability to hold phonological and visuospatial information in separate stores. A third subcomponent enables the integration of information into complex multi-modal representations linking working memory to long-term memory [18].

Long-term memory contains large amounts of information stored for longer periods that can extend to lifetime. All information stored within the human brain for a period exceeding two minutes is usually considered to involve long-term memory [19]. We are not aware of this information until it is activated and becomes part of working memory. Long-term and working memories can be deliberately accessed during task performance, they become then explicit memories. Implicit memories are memory representations which cannot be directly accessed.

Most experimental studies concerning the potential effect of caffeine on memory have focused only on limited simple measurements of newly established episodic memory, i.e. acquisition, short-term storage, and retrieval of related or unrelated word lists. Some exceptions concern a few studies measuring (i) paired associated learning where the rate of acquisition of two unrelated items is assessed, (ii) spatial memory related to the location of items, or (iii) semantic memory where access to stored representations of factual or lexical information is the variable of interest. A few studies considered working memory, assessing the ability to retain and manipulate the information store in a transient space, for example solving arithmetic problems. In most of these studies, the effects of caffeine were not really robust and were frequently entangled by interaction with other variables [20]. Therefore, in the following part of this review we will focus mainly on short and long term memory.

Short term memory

In immediate free recall tasks, subjects are presented a list of unrelated words, exceeding their memory span, and then asked to recall as many words as possible in any order. Words placed at the beginning and end of the list are recalled better than words in the middle of the list, producing so-called primacy and recency effects, respectively. This recall pattern is referred to as the serial position effect. It is usually hypothesized that the more recent words are retained in the primary, working memory, while the earlier ones are retained in the secondary, long-term memory. Caffeine was found to either (1) exert no effects on free recall performance in sixteen studies [7–9,11,21–32]; (2) improve recall in six studies [33–38]; or (3) impair recall in three studies [8,12,39].

In one study, females performed better than males in a recall task after 300 mg caffeine. This effect may be specific to the task used (digit memory task) and to different lateralization in both genders [38]. Gender also influenced the effects of caffeine (2 and 4 mg/kg) on the recall performance of lists of words presented at a fast or slow rate. Caffeine inhibited females' recall at the slow rate but not at the fast rate and had no effect in males. The data were not influenced by the daily caffeine consumption. Thus, caffeine may impair the efficiency with which females rehearse information in working memory [39], reflecting possible variation with the level of circulating estrogens.

In focused and divided selective attention tasks, subjects are instructed to detect the appearance of a memory item in relevant positions among items displayed on a screen [40–42]. Increased reaction times with increasing task load suggest that subjects apply serial, limited capacity searches, in which each memory item is compared sequentially with all other items. An increase of the number of targets to be memorised or of the items presented on the display results in search processes of longer duration and more pronounced negativity of recorded brain activity [43].

A 3 mg/kg caffeine dose decreased reaction times in a low display load but not in a high display load condition [42]. This differential effect indicates that caffeine facilitates performance only in simple or moderately complex tasks. In more complex tasks, caffeine may either have no effect or even impair performance [44, 45]. Thus, performance tested with caffeine improves as long as energetic supplies increase up to a certain level, beyond which it may deteriorate.

In summary, caffeine does not seem to consistently improve immediate free recall of words, letters and digits. Caffeine facilitates performance in tasks involving working memory to a limited extent, but hinders performance in tasks that heavily depend on working memory.

The discrepancies among the studies may originate in the fact that the studies vary from one another in the memory assessment method (recall or recognition), time frame (immediate versus delayed), sex and age of subjects. One possible explanation lies in the inverted U-shaped arousal-performance function [46]. Supporting this conceptualization, Kaplan and colleagues [47] found that low doses of caffeine enhance working memory performance, while higher doses decrease it. Other studies reported that caffeine facilitates low-difficulty performance on low-load memory tasks and impairs it on high-load tasks [48,49]. This could be due to increased arousal induced by high load tasks, which, in the presence of caffeine, could produce over-arousal leading to a decrement in memory performance. However, most studies did not control for memory load. In addition, arousal increments produced by novel stimuli and white noise improved performance on a recall task, while the further addition of caffeine-induced arousal decreased performance. The additional arousal generated by novelty pushed the subjects over the top of the inverted-U curve and so decreased their memory performance [50]. Thus, caffeine appears to rather improve memory performance under conditions that otherwise produce low arousal.

Caffeine and long-term memory

The effects of caffeine on long-term memory have not been studied in great detail. In one study, 12 subjects (6 males and 6 females) received 5 mg/kg before both the learning and retrieval sessions. Sixteen words were incidentally studied during the learning session and memory was evaluated by the number of words correctly recalled at the retrieval session two days later. Caffeine reliably increased arousal but did not produce any effects on memory [51]. Likewise, long-term memory retrieval functions measured at 30 min after a 15word learning test were not affected by 100 mg caffeine in middle aged (45-60 years) and older (60-75 years) healthy men and women studied in a cross-over design. Subjects were asked to abstain from caffeine in the evening preceding the tests. It is proposed that positive effects of cognition may occur at higher dosages (200–250 mg) in this age range [24], particularly for relatively complex cognitive functions. In elderly people, higher caffeine dosages may attenuate age-related arousal decrements, whereas young subjects may be more susceptible to caffeine-induced overactivation as they are already operating closely to an optimal arousal level under normal conditions [52].

The retrieval from the phonological system was studied using phonological priming and tip-of-the-tongue states in 64 participants of a mean age of 24 years. They received 200 mg of caffeine or placebo and were tested 40 min after intake. Caffeine produced a clear priming effect with phonologically related words. When primed with unrelated words, the caffeine subgroup produced an increase in tip-of-the-tongue states. This contrasting effect provides evidence that the positive priming effect of caffeine was not the result of increased alertness [53].

CAFFEINE, ALERTNESS AND MOOD

It is well-known that caffeine ingestion leads to dosedependent increased energetic arousal. At low doses, caffeine improves hedonic tone and reduces anxiety, while at high doses there is an increase in tense arousal, including anxiety, nervousness, and jitteriness. Caffeine improves concentration and help to focus mainly by eliminating distractors (for review see [2,54–60]).

In mood ratings, arousal state, i.e., changes in alertness, reaction time and attention have often been included. When mood per se is considered, a dose-related improvement in subjective measures of calmness and interest were found after caffeine. This relationship suggests that mood improvement may depend on baseline arousal. Older adults are more sensitive than younger subjects to mood-enhancing effects of caffeine. Mood effects are also influenced by the time of the day, with largest effects in the late morning. The repeated administration of 75 mg of caffeine (the equivalent of one cup of coffee) every 4 h confirmed a pattern of sustained improvement of mood over the day [61]. Highly fatigued subjects are more likely to experience larger subjective mood changes than non- or moderately fatigued ones. There are also indications of negative mood impact associated with over-arousal (for review see [20,60]).

Caffeine was also reported to slightly improve vigilance performance and reaction time in children who are habitual caffeine consumers but caffeine does not consistently improve performance in children with attention-deficit-hyperactivity-disorder (ADHD) [62]. In an animal model of ADHD, the spontaneously hypertensive rat (SHR), pre-training administration of caffeine attenuated the spatial learning deficit [63] and improved performance in an object-recognition task [64]. At the moment, there are no studies available on the effects of caffeine on cognitive abilities in children with ADHD, most studies were rather interested in whether caffeine could attenuate symptoms as well as the drug of choice in this pathology, methylphenidate.

CAFFEINE AND ATTENTION

The effects of caffeine on attention and psychomotor performance have been extensively reviewed (for review see [20,54,56–59,65]). Not all studies found effects of caffeine on the two variables, although most studies found improvements in reaction time. Likewise, when multiple tests were used, not all were affected by caffeine but there is clear evidence that caffeine can help sustain attention in demanding tasks. There is however, a debate, since most often testing was performed after a period of abstinence (typically overnight). The extent to which the effects of caffeine represent an absolute improvement in performance or a restoration of performance degraded by withdrawal is not clear. A recent study compared overnightwithdrawn consumers and non-consumers of caffeine. Caffeine generally improved mood and cognitive performance in both groups. These effects did not differ significantly between groups apart from three variables (fewer lapses of attention, ratings of alertness, and anxiety) where the effects of caffeine were larger in nonconsumers. These data led to the conclusion that the withdrawal hypothesis is not an adequate explanation for the effects of caffeine [66].

INFLUENCE OF DAYTIME AND FATIGUE

Caffeine impaired [67] or did not affect [68] the immediate reproduction of numbers when testing was performed during the night. A study including 40 subjects over the age of 65 tested immediate and delayed memory in tasks consisting of the recall and recognition of 16 words from four semantic categories. They abstained from caffeine for 4 h prior to the session and received a cup of coffee containing 220–270 mg caffeine 30 min before testing. Caffeine counteracted the decline in performance from morning to afternoon, which suggests that time-of-day effects may be mediated by non specific changes in arousal [37].

Likewise, 200 mg caffeine given to 15 well-rested and 15 fatigued students aged 18-25 years led to larger improvements in performance in fatigued than in well-rested subjects [69]. In subjects fatigued after a long testing session, 1.5 mg/kg caffeine improved aspects of cognitive performance such as encoding of new information and detection of number of repeats [70]. Likewise, immediately after strenuous physical exercise (1 h time trial on a bicycle ergometer) in 15 trained athletes of a mean age of 23 years, 150 and 225 mg caffeine improved attention, psychomotricity and memory [71]. Subjects that consume higher levels of caffeine are more alert over the working day and have a significantly smaller slowing of reaction time. Caffeine consumption reduces the risk of frequent/very frequent cognitive failures and of accidents at work by about two-fold [72]. Also, beneficial caffeine effects on mood and performance are more prominent in low arousal

situations. Caffeine removes the drop in sustained attention after lunch, and is more effective during night work and prolonged work, and in subjects with upper respiratory tract illnesses [25].

After sleep restriction and exposure for 3 weeks to tea/coffee containing or not containing caffeine, the administration of 1.2 mg/kg caffeine after overnight deprivation did not improve cognitive performance in long-term caffeine-deprived participants but prevented further deterioration in overnight-deprived participants [73]. In another study, 21 healthy young men were sleep-deprived for 40 hours twice, one week apart. Subjects had to perform a random generation of 225 numbers at a low and high pace after placebo or 200 mg caffeine. Caffeine preserved simple aspects of cognitive performance but did not prevent the detrimental effects of sleep deprivation on more complex cognitive functions [74]. In US Navy trainees subjected to 72 h sleep deprivation, 200 or 300 mg caffeine improved cognitive function in terms of vigilance, learning, and memory [75]. Finally, 200 mg caffeine given to 36 male and female psychology students impaired the immediate reproduction of spatial relationships of verbal information after normal sleep, but improved it after sleep deprivation, indicating a compensation for fatigue [76]. Slow release caffeine tablets were effective for 13 h in alleviating fatigue-related decrements of vigilance and performance after limited sleep deprivation. The 300 mg dose was the most effective [77].

In summary, the larger improvement of performance in fatigued subjects confirms that caffeine is a mild stimulant.

INFLUENCE OF THE HISTORY OF CAFFEINE CONSUMPTION

The influence of daily caffeine consumption on cognitive performance and memory was tested in two types of situations, either with no addition of caffeine for testing or with consumption of a given amount of caffeine on top of the regular daily consumption.

In caffeine non-deprived young (20–25 years) and older subjects (50–65 years), 250 mg caffeine slightly offset the decline in performance found in the placebo group on a digit span memory test. However, caffeine did not improve performance in the immediate word recall task in either age group [11]. Caffeine (12.5–100 mg) given after overnight abstinence improved cognitive performance in a relatively difficult and stressful task involving rapid visual information processing and using a high load of working memory in 11 males and 12 females, aged 18–56 years. The effect was more marked in individuals with a high habitual caffeine intake [78]. In 68 volunteers consuming a regular daily amount of caffeine, 2 mg/kg caffeine improved the speed of encoding new information in a categorical search task [79]. Likewise, in a study comparing 24 non consumers (20 mg/day) to 24 consumers of caffeine (217 mg/day), there was no baseline difference between group performances. Caffeine improved numeric working memory reaction time and sentence verification accuracy; alertness was also increased, but in general caffeine tended to improve more the performance in non consumers [80].

In adult subjects, a higher habitual caffeine intake with no additional caffeine administration on the day of testing was positively related to better performance on incidental verbal learning and visuospatial learning tasks [15]. There was also an association between estimated caffeine intake and performance in a choice reaction time task, and in delayed recall of a verbal word learning task [81]. In the former study, older subjects appeared to benefit more from higher caffeine intake [15], while this was not the case in the latter study [81]. Also, in real life activities, regular caffeine consumption might benefit cognitive functioning in a non-working population [82].

CAFFEINE AND AGE-RELATED COGNITIVE DECLINE IN HEALTHY SUBJECTS

Between 20 and 60 years, cognitive functions in terms of reaction time and rate of perception and treatment remain relatively stable. Between 60 and 80 years, there is a general slowing down of cognitive function. It was hypothesized that caffeine could in part compensate for this decline because of its effects on vigilance, mainly in situations of reduced alertness, as mentioned earlier [25,37,72]. In many studies, young and elderly subjects appear to be differently affected by caffeine. In two studies, elderly subjects showed improved attention, psychomotor performance, and cognitive functioning on caffeine. Caffeine predominantly improved performance and feeling of well-being, and the elderly appeared more sensitive to the objective effects of caffeine than the young subjects, particularly in offsetting declining performance over time [83,84]. Likewise, in a study comparing young (18-37 years) and elderly (60-75 years) receiving an acute dose of 225 mg caffeine, caffeine was reported to improve performance

during distraction only in simple tasks in young subjects, and in more complex tasks requiring sustained attention in elderly subjects in which the treatment of complex tasks is usually less effective [85]. Finally, the administration of 250 mg caffeine to young and old subjects that are moderate caffeine consumers (250– 600 mg daily) shows that caffeine improves the performance in elderly, i.e., the treatment of information and the speed-accuracy trade-off. Caffeine is able to reverse the effects of cognitive aging, making more energy resources available in elderly subjects [86].

When considering the relationship between cognition and regular coffee/caffeine intake, two Dutch studies considering 1875 and 1376 subjects, respectively, aged 24-81 years found positive effects on cognition, mainly in terms of reaction time and verbal memory, but no age-related difference [81,87]. Conversely, a British study concerning 9003 adult subjects reported a dose-related trend to improved performance with higher levels of coffee consumption. Higher overall caffeine consumption (from coffee and tea) improved simple and choice reaction time, incidental verbal memory and visuo-spatial reasoning. Older people appeared more susceptible to the performanceimproving effects of caffeine than younger [88]. In the Rancho Bernardo study comprising 1538 participants, 890 healthy women and 638 healthy men from Southern California (mean age 73 years), higher lifetime caffeine consumption appeared beneficial for cognitive performance. Indeed it was associated with better performance in 6/12 tests with a trend on two other cognitive tests. Among women aged 80 or more years, lifetime coffee intake was not significantly associated with better performance in 11/12 tests. Current caffeinated coffee intake was associated with improved performance in two tests, with a trend in a third one. No relation was found between coffee intake and cognitive function in men, or between decaffeinated coffee intake and cognitive function in either sex [89]. These studies gave some support to the notion that habitual caffeine consumption may boost to some extent the cognitive reserve of the subject. However, these studies were cross-sectional, which makes the causal interpretation of a relationship between caffeine intake and performance somewhat speculative. In the longitudinal Three City cohort study including 4197 healthy women and 2820 healthy men over 65 years, women consuming over 3 cups of caffeine daily for over 4 years showed less decline in verbal retrieval and visuospatial memory than women consuming one cup or less. The protective effect of caffeine increased with age with a

maximal effect in women over 80 years. No relation was found between caffeine intake and cognitive decline in men [90]. Another longitudinal study followed a population of 1376 subjects that were tested 6 years after the first time they enrolled in the Maastricht Aging Study. The subjects were stratified by age from 25 to 80 years. In this follow-up, there was no association between lifetime habitual caffeine intake and verbal memory performance [91]. On the other hand, a recent prospective study concerned the 10-year cognitive decline in 676 healthy men born between 1900 and 1920 from three European countries (Finland, Italy and The Netherlands). Men who consumed coffee had a 10-year cognitive decline of 4%. Non-consumers had an additional decline of 4.7%. The authors reported an inverse J-shaped curve between the number of cups of coffee consumed and the extent of cognitive decline, with the least cognitive decline for 3 cups coffee daily (2%). This decline was 4.3 times significantly smaller than in non-consumers [92]. Finally, the most recent cohort study included 923 healthy adults from Scotland belonging to the Lothian Birth Control 1936 Study, in which the IQ of the children was assessed at 11 years. Cognitive function was assessed at 70 years using tests measuring general cognitive ability, speed of information processing, and memory. In age- and sex-adjusted models, the authors found associations between total caffeine intake (coffee, tea, and total dietary caffeine) and general cognitive ability and memory. After adjustment for age 11 IQ and social class, a robust positive association remained between drinking ground coffee (filter or espresso) and performance at the National Adult Reading Test and the Wechsler Test of Adult Reading. No gender effects were observed, conversely to several previous studies. The latter study provides only limited evidence that caffeine consumption protects against cognitive decline. It seems that childhood IQ and factors such as social class, rather than caffeine intake, would drive the association with cognition in later life [93].

In conclusion, it appears that the effects of caffeine on cognitive decline still deserve further attention and research in order to clarify why some studies found effects only in one sex, and to better define the nature of the association between caffeine consumption and the potential prevention of cognitive decline during aging. Other data are available on the potential preventive effects of caffeine in Parkinson's and Alzheimer's disease. The reader can refer to chapters by Cunha, Arendash, Lunet and Costa in the same issue of the journal.

GENERAL CONCLUSIONS

Despite the wide variability (1) in the amount of caffeine given before testing, (2) in the period of caffeine abstinence observed before testing, (3) in the baseline caffeine consumption of the subjects tested, and (4) in the type of tests used, there was not much heterogeneity in the effects of caffeine on learning and memory.

Caffeine does not usually affect performance in learning and memory tasks. Occasionally, caffeine effects on memory and learning, facilitatory or inhibitory, were found. These effects were rather the result of complex interactions with dose, subject, and task variables. They may result from effects on encoding, or attention devoted to the information, rather than being direct and specific effects on the storage or retrieval of information in short-term and working memory. Caffeine can apparently improve performance directly over a wide variety of mental tasks, and indirectly by reducing decrements in performance under suboptimal alertness conditions. The efficacy of caffeine under states of reduced alertness is quite consistent. Many studies on the elderly population reported a preventive effect of caffeine on cognitive decline. However, the results of the different studies are still heterogeneous and deserve further attention. It may be that in the elderly population, higher caffeine dosages are necessary to attenuate age-related arousal decrements, whereas young subjects may more easily respond to lower doses while reaching overactivation at high caffeine dosages. This still needs to be clarified. The ingestion of caffeine does not seem to affect long-term memory.

Two general mechanisms may account for most of the observed effects of caffeine on performance: (1) an indirect, non specific 'arousal' or 'processing resources' factor, presumably explaining why the effects of caffeine are generally most pronounced when task performance is sustained or degraded under suboptimal conditions; and (2) a more direct and specific 'perceptual-motor' speed or efficiency factor that may explain why, under optimal conditions, some aspects of human performance and information processing, in particular those related to sensation, perception, motor preparation, and execution, are more sensitive to caffeine effects than those related to cognition, memory, and learning.

Thus, caffeine apparently cannot be considered a 'pure' cognitive enhancer. Its indirect action on arousal, mood and concentration contributes in large part to its cognitive enhancing properties.

DISCLOSURE STATEMENT

The author's disclosure is available online (http://www.j-alz.com/disclosures/view.php?id=261).

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