Effect of chronic caffeine intake on choice reaction time, mood, and visual vigilance

Daniel A. Judelson a,*, Lawrence E. Armstrong a,b,c, Bülent Sökmen a, Melissa W. Roti a, Douglas J. Casa a, Mark D. Kellogg d

a Human Performance Laboratory, Department of Kinesiology, University of Connecticut, 2095 Hillside Rd., U-1110, Storrs, CT 06269, USA
b Department of Nutritional Sciences, University of Connecticut, Storrs, CT 06269, USA
c Department of Physiology and Neurobiology, University of Connecticut, Storrs, CT 06269, USA
d Department of Laboratory Medicine, Children’s Hospital and Harvard Medical School, Boston, MA 02115, USA

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Abstract

The stimulatory effects of acute caffeine intake on choice reaction time, mood state, and visual vigilance are well established. Little research exists, however, on the effects of chronic caffeine ingestion on psychomotor tasks. Therefore, the purpose of this study was to evaluate the effects of 5 days of controlled caffeine intake on cognitive and psychomotor performance. Three groups of 20 healthy males (age=22±3 years, mass=75.4±7.9 kg, body fat percentage=11.2±5.1%) twice completed a battery of cognitive and psychomotor tasks: after 6 days of 3 mg·kg⁻¹·day⁻¹ caffeine equilibration (Day 6), and after 5 days of experimental (0 [G0], 3 [G3], or 6 [G6] mg·kg⁻¹·day⁻¹) caffeine intake (Day 11). Groups were randomized and stratified for age, mass, and body composition; all procedures were double-blind. Cognitive analyses involved a visual four-choice reaction time test, a mood state questionnaire, and a visual vigilance task. Experimental chronic caffeine intake did not significantly alter the number of correct responses or the mean latency of response for either the four-choice reaction time or the visual vigilance tasks. The Vigor–Activity subset of the mood state questionnaire was significantly greater in G3 than G0 or G6 on Day 11. All other mood constructs were unaffected by caffeine intake. In conclusion, few cognitive and psychomotor differences existed after 5 days of controlled caffeine ingestion between subjects consuming 0, 3, or 6 mg·kg⁻¹·day⁻¹ of caffeine, suggesting that chronic caffeine intake (1) has few perceptible effects on cognitive and psychomotor well-being and (2) may lead to a tolerance to some aspects of caffeine’s acute effects.

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1. Introduction

By many accounts, caffeine is the most widely used psychologically active drug. Predominantly through adenosine receptor antagonism [1], acute caffeine doses (32–400 mg) benefit numerous psychomotor variables, including choice reaction time [2–4], mood state [5–7], and sensory vigilance [3,5–10]. Conversely, ingestion of larger caffeine doses (>500 mg) may be less beneficial (and potentially detrimental) to performance of these cognitive tasks [10–12], suggesting an inverted-U dose–response relationship between acute caffeine intake and cognitive and psychomotor well-being.

Although the acute effects of caffeine intake have been well studied, previous research sheds little light on the psychological and cognitive effects of typical, chronic caffeine ingestion. Obviously, the relevancy of this topic is great as millions of people consume caffeine on a daily basis, many for its purported cognitive and psychomotor benefits (unpublished observations). Responses to recurrent caffeine consumption (i.e., 1–5 days) may significantly differ from acute dosages, however, because routine caffeine
exposure results in tolerance to the drug’s physiological effects [13,14]. It is unclear, however, to what degree these physical adaptations alter performance of cognitive and psychomotor tasks, and if a similar tolerance develops to caffeine’s cognitive effects. The few studies that examined this topic have presented inconclusive results: research documents complete [15,16], partial [17], or no [18] psychological tolerance to caffeine. This lack of clarity may be due to different caffeine doses, psychomotor tasks, and subject populations used; additionally, some research has failed to acknowledge significant confounding variables (e.g., tobacco or oral contraceptive usage) or measured caffeine’s effects during suboptimal conditions (i.e., during fatigue or caffeine withdrawal). Therefore, the purpose of this study was to examine the effects of 5 days of chronic, controlled caffeine intake on caffeine-sensitive cognitive and psychomotor tasks (choice reaction time, mood state, and visual vigilance) in moderate doses typically consumed by healthy males.

2. Methods

2.1. Subjects

Subjects for this study were 60 healthy, nonsmoking males (age = 22 ± 3 years, mass = 75.4 ± 7.9 kg, body fat percentage = 11.2 ± 5.1%). Subjects were recruited via campus postings and personal contact. Preliminary analysis revealed most subjects habitually consumed low to moderate quantities of caffeine; individuals regularly ingesting greater than 600 mg of caffeine per day were excluded. Prior to data collection, the University of Connecticut Institutional Review Board approved all procedures and subjects provided written informed consent. Throughout testing, procedures adhered to standard national and international regulations regarding the use of human subjects in research. Subjects refrained from drug use, excessive alcohol consumption (more than 1–2 drinks per week), and changes in eating and exercise pattern during the course of the study.

2.2. Research design

This project was a subset of a larger study designed to evaluate the effect of chronic caffeine ingestion on hydration status, fluid-electrolyte balance, and responses to exercise in the heat. These alternate study purposes had no effect on the current investigation, as all exercise sessions and heat exposures occurred ~24 h after the final cognitive and psychomotor testing. To assess the effects of moderate caffeine intakes, subjects were divided into three randomized, balanced, blinded groups of 20 subjects (see Fig. 1). Groups were matched such that age, body mass, and percent body fat did not statistically differ between groups. On days 1–6, the equilibration phase, all subjects consumed 3 mg·kg⁻¹·day⁻¹ of caffeine in capsular form. On days 7–12, the experimental phase, group doses were altered: one group decreased caffeine intake to 0 mg·kg⁻¹·day⁻¹ and ingested only placebo (G0), one group maintained caffeine intake at 3 mg·kg⁻¹·day⁻¹ (G3), and one group increased caffeine intake to 6 mg·kg⁻¹·day⁻¹ (G6). Previous research on the time course of withdrawal symptoms (typically declining after 48 h of abstinence) [19] and physiological tolerance (typically within 5 days) [13,14] supports the present study design. These doses represent the typical caffeine intake of a caffeine-abstainer, an average US citizen, and a heavy caffeine user, respectively [20]. Regardless of concentration, half the caffeine dose was ingested from 7:00 a.m. to 9:00 a.m. under investigator observation; the other half was consumed from 11:00 a.m. to 2:00 p.m. and verified by telephone contact.

To maintain subject and investigator blinding, pills were pre-packaged by a registered dietician not involved in the research, subjects received no more than four capsules (regardless of dose), and subjects in the same group consumed differing numbers of capsules. Each subject, however, consumed the same number of capsules on all days of the equilibration and experimental phases. Caffeine and placebo (lactose) capsules were visually identical. Throughout the study, subjects refrained from ingesting foods that contained caffeine or altered caffeine metabolism (e.g., cruciferous vegetables and charbroiled meats [21]); compliance with caffeine restriction was verified on days 1, 6, and 11 by withdrawing 3 mL blood from an antecubital vein into a glass test tube (Vacutainer, Becton Dickinson, Franklin Lakes, NJ). Resulting serum aliquots were frozen at −80 °C and overnight shipped for commercial determination of serum caffeine via high performance liquid chromatography (Pennington Biomedical Research Laboratory, Baton Rouge, LA). Results indicated that all subjects fully complied with the experimental protocol.
2.3. Cognitive and psychomotor evaluations

On days 6 and 11, subjects completed a battery of four cognitive and psychomotor tests 1 h after receiving the afternoon caffeine dose. Tests were presented in the same order and under identical environmental conditions each day. Prior to data collection, subjects were familiarized with the tasks and completed two full-duration testing sessions (once 2 to 3 days prior to beginning the equilibration phase and once on Day 1 of equilibration) to become acquainted with the necessary demands and requirements.

The first task, the four-choice reaction time test, is a visual modification of the Wilkinson four-choice reaction time test [22]. Subjects were presented with a visual stimulus in one of four predetermined locations on a computer screen. Each stimulus location was associated with one of four adjacent keys on the keyboard. When a stimulus was presented, subjects responded by pressing the appropriate key as quickly as possible. As soon as a stimulus was presented, subjects responded by pressing the appropriate key as quickly as possible. As soon as a

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The second task, the Profile of Mood States [24], is an inventory of emotions and feelings. Sixty-five adjectives were divided into six factors (Tension–Anxiety, Depression–Dejection, Anger–Hostility, Vigor–Activity, Fatigue–Inertia, Confusion–Bewilderment) and a Total Mood Disturbance score. These constructs are standardized factors with known psychometric properties, several of which have been demonstrated sensitive to the effects of caffeine [3,23].

The third task, the Scanning Visual Vigilance Test [27], is a test of visual alertness and attention. Subjects scanned a blank computer monitor for the random appearance of a small white rectangle (4 pixels × 2 pixels); stimuli brightness was individualized for each subject based on pretesting such that only 50% of objects were identifiable (thus avoiding the confounding potential of a ceiling effect [10]). In response to the rectangle, subjects pressed the keyboard space bar as quickly as possible. On average, one stimulus was presented for 2 s each minute, however, the inter-stimulus interval was randomized [7,27]. Thirty stimuli were presented. Dependent measures were number and mean latency of correct responses. This test has been shown to be sensitive to the effects of caffeine [7,23].

The final task was a 7-point Likert questionnaire regarding characteristic caffeine withdrawal and tolerance symptoms. Subjects were asked to rate 16 cognitive and psychomotor symptoms typically experienced during altered caffeine intake according to the following question: “Since I

last completed this questionnaire, I have noticed a change in ________.” Thus, Day 6 scores reflected changes in symptoms during the equilibration phase (subjects were familiarized with the cognitive and psychomotor tests on Day 1) and Day 11 scores reflected changes in symptoms during the Experimental phase (Day 6 to Day 11). Possible scores ranged from −3 (large decrease) to +3 (large increase), with 0 indicating no change. Specific symptoms evaluated were headache severity, alertness, fatigue, quality of sleep, energy level, anxiety/nervousness, jitteriness/shakiness, diarrhea, constipation, feelings of self-confidence, feelings of illness, mental concentration, quality of vision, crankiness/irritability, physical well-being, and emotional well-being. These symptoms were chosen based on the body of the caffeine literature (for review, see Ref. [25]).

2.4. Statistical analysis

Descriptive statistics (means, standard deviations, and standard errors) were calculated for all data. The main effect of caffeine ingestion on cognitive and psychomotor responses was evaluated with an analysis of covariance on data collected during the Day 11 testing; Day 6 scores were covaried to eliminate remaining subject differences after the equilibration period. When appropriate, pairwise differences were further evaluated post hoc by Tukey’s test of least significant differences. Additionally, effect sizes ($\eta^2$) were calculated for all test variables. Significance was set at $p \leq 0.05$.

3. Results

Table 1 presents the effects of chronic caffeine ingestion on four-choice reaction time measured on Day 11. Of the 60 subjects, 58 completed both experimental trials of this task (G0 = 20, G3 = 18, G6 = 20). No significant differences were found between groups for either number ($\eta^2 = 0.041$) or mean latency ($\eta^2 = 0.056$) of correct responses.

Table 2 shows the effects of chronic caffeine ingestion on mood state measured on Day 11. Of the 60 subjects, 59 completed both experimental trials of this task (G0 = 20, G3 = 19, G6 = 20). Vigor–Activity scores were significantly increased in G3 compared to G0 and G6 ($F_{(2,55)} = 3.427, p < 0.05; \eta^2 = 0.111$). No other mood construct was signifi-

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Four-choice reaction time</th>
<th>Scanning visual vigilance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hits (of 500)</td>
<td>Mean latency (ms)</td>
</tr>
<tr>
<td>G0</td>
<td>473 ± 3</td>
<td>415.22 ± 3.78</td>
</tr>
<tr>
<td>G3</td>
<td>479 ± 3</td>
<td>424.07 ± 4.05</td>
</tr>
<tr>
<td>G6</td>
<td>476 ± 3</td>
<td>423.11 ± 3.82</td>
</tr>
</tbody>
</table>

Values are covariate adjusted mean ± S.E. No values significantly differed from each other.
significantly altered by caffeine ingestion ($\eta^2$ range = 0.005–0.056), although large differences were apparent in some variables (e.g., Total Mood Disturbance).

Table 1 shows the effects of chronic caffeine ingestion on visual vigilance measured on Day 11. Of the 60 subjects, 46 completed both experimental trials of this task (G0 = 17, G3 = 13, G6 = 16). A greater number of subjects were eliminated in this data set (as compared to other tests) because (1) three subjects correctly responded to all stimuli (indicating the presence of ceiling effect), (2) three subjects failed to respond to any stimuli (and therefore, were unable to correctly perform the test, regardless of caffeine ingestion), and (3) eight subjects were eliminated due to tester error. No significant differences were found between groups for either number of stimuli detected ($\eta^2 = 0.030$) or mean response time ($\eta^2 = 0.026$).

Of the 60 subjects, 59 completed both experimental trials of the Likert tolerance/withdrawal symptoms questionnaire (G0 = 20, G3 = 19, G6 = 20). Mean scores showed very little change in symptom severity between Day 6 and Day 11 (range –0.55 to +0.50 of a possible –3 to +3); no significant differences were found between groups for any symptom.

### 4. Discussion

The primary finding of this study was the similarity of choice reaction time, most aspects of mood state, and visual vigilance despite controlled, chronic ingestion of three different but representative caffeine doses. Given the specific testing parameters and research frame of reference, these results suggest that in healthy, rested individuals, (1) regular consumption of caffeinated foods and beverages may have few perceptible effects on cognitive and psychomotor well-being, and (2) within 5 days, a tolerance may develop to specific aspects of caffeine’s acute cognitive benefits [2–10].

Previously, several research-related obstacles precluded definitive conclusions regarding the effects of caffeine intake. The use of caffeine-insensitive cognitive tasks [5,10,28,29] coupled with inter-individual differences in subjects’ prior caffeine usage [5,7,8,16,30], tobacco habits [5,7], and pharmacological sensitivity [9,16,31,32] frequently obscured the subtle effects of caffeine [28,33,34]. While the present research design eliminated the majority of these concerns (i.e., by employing documented caffeine-sensitive tasks, equilibrating caffeine during the initial 6 days, and testing only non-tobacco users), we recognize that a potential limitation of the study design was the relatively short experimental duration (5 days). Our model is supported, however, by the typical decline in withdrawal symptoms after 48 h of caffeine abstinence [19], the physiological tolerance that develops to high doses (up to 12 mg·kg$^{-1}$·day$^{-1}$) of caffeine within 5 days [13,14], and the lack of adverse effects subjects reported on the symptoms questionnaire. Additionally, repeated measures analysis of variance on G0 data showed no significant change from Day 6 (end of equilibration) to Day 11 (end of the experimental phase) in any of the six POMS constructs previously shown sensitive to the effects of caffeine withdrawal [25], suggesting these subjects were not experiencing acute withdrawal symptoms during testing. Although these results could be construed that G0 (and hence any experimental group) were unaffected by the caffeine dose during equilibration, we believe this is unlikely, given the magnitude of the dose (3.0 mg·kg$^{-1}$·day$^{-1}$), duration of ingestion (6 days), and previous research [13,14]. Instead, we interpret G0’s lack of withdrawal symptoms as evidence that subjects developed a tolerance to caffeine during equilibration, experienced withdrawal during the initial days of the experimental phase, but readjusted to their new caffeine intake (0 mg·kg$^{-1}$·day$^{-1}$) by Day 11. We also acknowledge that the number of subjects in each group, especially for the visual vigilance task, may be too low to definitively assess cognitive performance. The extremely low effect sizes calculated (0.005–0.111), however, suggest that the lack of significance noted between groups was not a result of low sample size and that a Type II error did not occur.

Little previous research has documented the effect of routine caffeine intake (i.e., greater than 1 day) on cognitive task performance. The current study, where 5 days of chronic ingestion of zero, average, and high caffeine doses [20] had no observable effect on four-choice reaction time, most aspects of mood, and visual vigilance agrees with some previous studies [15–17], but conflicts with other research [18]. Interviews of 7414 British adults concerning their typical caffeine intake and concomitant measurement of their cognitive and psychomotor performance yielded a positive relationship between habitual caffeine consumption and cognitive functioning [18]. It is difficult to interpret
those findings, however, because caffeine ingestion prior to data collection was apparently uncontrolled and recorded caffeine intake was based solely on subjects’ self-reports. Alternatively, that study and the present one may not be strictly comparable because of differences in subject samples (males age 18–35 vs. males and females over 18) or duration of caffeine ingestion (5 days of experimental dosages vs. the volume of coffee or tea subjects “usually” drank per day).

That cross-sectional survey [18] also reported that tolerance to the cognitive and psychomotor benefits of caffeine ingestion did not develop (i.e., high-routine caffeine users performed statistically better than low-routine caffeine users). Although the physiological tolerance to caffeine has been well-demonstrated [13,14], the extent to which users performed statistically better than low-routine caffeine ingestion did not develop (i.e., high-routine caffeine tolerance to the cognitive and psychomotor benefits of caffeine concentration during the tasks [29,36,37]), the results of the four-choice reaction time and the Visual Vigilance tests offer three interpretations: (1) caffeine ingestion has no cognitive effects, (2) the testing protocols were not sufficiently sensitive to identify effects, or (3) a tolerance develops to the effects.

Given the documented benefits of acute caffeine ingestion on the cognitive and psychomotor tasks used in the present study [2–10], the initial explanation seems unlikely. The sensitivity of the test battery, however, must be considered. Previous research has demonstrated a 120-min Scanning Visual Vigilance Test is sensitive to caffeine [7], but no studies validate this test with the 30-min duration used in the current investigation. Although one previous report demonstrated caffeine improved performance of a 21-min vigilance task [10], the majority of tests evaluating sensory vigilance meet or exceed 60 min [3,5–7,9]. In the present study, other subject requirements coincident with cognitive and psychomotor testing precluded the use of a full 120-min Scanning Visual Vigilance Test. Additionally, no prior studies have validated this task in a between-subjects research design; regrettably, a crossover study of this magnitude and detail would have created prohibitive subject demands. As such, the present results on caffeine and sensory vigilance should be evaluated in light of these methodological limitations.

The similarity among G0, G3, and G6 responses to the four-choice reaction time test, however, suggests that a tolerance may develop to the typically observed acute benefits of caffeine on choice reaction time. If it occurs, caffeine tolerance most likely results from adenosine receptor upregulation [38,39]; the ubiquitous role of the adenosine receptor in the nervous system [40] implies that this mechanism is likely to affect the complex of nerve tissue controlling the psychomotor traits measured in the current study.

The lone statistically significant difference between groups (see Table 2) occurred in mood state: the Vigor–Activity subset of the POMS, a trait sensitive to caffeine [5–7,9,41–43], was statistically greater in G3 (15±6) than G0 (9±5) and G6 (11±5). Although this result may be due to Type I error, increased Vigor–Activity was matched by a significantly longer exercise-heat tolerance time 1 day after cognitive and psychomotor testing (data reported elsewhere), suggesting that this difference is not statistical artifact. Interestingly, other aspects of mood (Tense, as measured with the UWIST Mood Adjective Checklist [44]) have also resisted tolerance to chronic caffeine use [17], suggesting that tolerance to caffeine’s effects on mood may develop slower, to a lesser degree, or not at all. The increased Vigor–Activity score in G3 further documents the sensitivity of this measure to caffeine intake; the similarity of Vigor–Activity in G0 and G6 results also supports the concept of an inverted-U dose–response curve. This relationship has been hypothesized for several other psychomotor traits including reaction time [11], vigilance [10], information processing [32], and overall mood state [23,35], and may result when caffeine saturates membrane receptors in the neuromuscular system and begins to interfere with other physiological processes [11].

In conclusion, within the frame of reference of the present research, ingestion of caffeine in 0, 3, and 6 mg·kg⁻¹·day⁻¹ doses for 5 days had no perceptible effects on choice reaction time, most aspects of mood, and visual vigilance. Additionally, a tolerance may develop to specific aspects of the acute cognitive and psychomotor benefits of caffeine intake.

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