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The effects of age on the response to caffeine

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Abstract. Twelve healthy subjects, six young and six elderly, of either sex, took part in this two-period crossover study. In each session, a dose of trial drug – either 200 mg caffeine or a matching placebo – was given orally at 0900 hours. A battery of psychomotor tests and visual analogue scales was administered before treatment and at 1, 2 and 3 h post-treatment. The objective tests showed a significant increase in tapping rate in the young, while the elderly showed improved attention, faster choice-reaction time, and greater body sway on caffeine. The visual analogue scales showed that the young subjects felt more alert, calmer, more interested, and steadier on caffeine, while no significant changes were seen in the elderly. These results show that caffeine produces changes predominantly in the direction of improved performance and feeling of well-being, and suggest that the elderly are more sensitive to the objective effects of the drug, while reporting less subjective effect than the young.

Key words: Age-related changes – Caffeine – Drug effects – Human – Psychomotor performance

It has become increasingly recognised that the response to drugs acting on the central nervous system may be altered in the elderly. This is best documented for sedative/anxiolytic drugs, in particular the benzodiazepines, for which an increase in sensitivity has been shown in a number of controlled studies (Castleden et al. 1977; Swift 1983; Cook et al. 1984; Swift et al. 1985a, b). The precise mechanisms involved, however, are not known.

Caffeine (1,3,7-trimethylxanthine) is a central stimulant widely consumed as a component of coffee, tea and cocoa, and is also contained in a variety of over-the-counter medicines. Subjectively, caffeine produces a felling of alertness, increased interest, and reduction of fatigue, as well as increased sleep latency. Objective measures show a mixed picture, with improvements in performance of tasks involving attention and vigilance, reaction times and tapping, but a suggestion of impairment of some motor functions, e.g. body sway, eye-hand co-ordination and the motor component of a reaction-time task (Weiss and Laties 1962; Goldstein et al. 1965; Baker and Theologus 1972; Clubley et al. 1979; Putz-Anderson et al. 1981; Sawyer et al. 1982).

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The related xanthine derivatives theophylline and aminophylline are widely used in the treatment of respiratory disorders in patients of all ages. They are comparable to caffeine in their CNS stimulant effects (Rall 1985).

Since no investigations have so far been undertaken of possible changes with age in the effects of central stimulant compounds, it was decided to carry out a comparative study of the effects of caffeine on psychomotor performance in young and elderly healthy volunteers.

Subjects and methods

Twelve subjects, six young and six elderly, took part in the study. The young group consisted of two males and four females, and were aged from 18 to 37. The elderly group comprised three males and three females, aged from 65 to 75, all living independently at home. All subjects were healthy non-smokers, with a normal caffeine intake, who were not currently taking any medication.

The study used a two-period crossover design. Each subject first took part in a familiarisation session in which the tests of psychomotor performance were administered, in order to minimise practice effects. They then took part in two 1-day sessions spaced at least 1 week apart. In one session subjects received 200 mg caffeine, in the other session, a matching placebo. The order of the treatments was randomised, and treatment was double-blind. Each session began with the administration of the test battery, after which the subject received the capsule containing caffeine or placebo at 0900 hours. The test battery was repeated at 1, 2, and 3 h post-treatment. The following measures were used:

Tapping. The subject tapped with the index finger of the preferred hand on a morse key as fast as he could for 1 min.

Body sway. The subject stood with feet slightly apart, hands by the sides, eyes open. Sway in the anterior-posterior plane was measured using the Wright-Codoc ataxiameter. The mean of two 1-min recordings was taken (Swift 1984).

Continuous attention. A series of geometric patterns was flashed on a screen, each pattern being shown for 0.1 s, the interval between patterns being 2–4 s. The subject's task was to respond whenever two consecutive patterns were the same. A total of 240 presentations, with 40 repetitions, was used in each test. The total number of errors (both

Table 1. Performance of young and elderly subjects on placebo. Figures are mean ± standard deviation. CAT: Continuous Attention Task; CFF: Critical Flicker Fusion Threshold; CRT: Choice Reaction Time; DMT: Decision Making Test

Measure	Young	Elderly	Significance
CAT (total error score)	2.67 ± 1.41	17.4 ± 27.1	$P<0.1$
CFF (Hz)	38.7 ± 2.8	37.1 ± 3.6	n.s.
CRT (ms)	525 ± 66	634 ± 75	$P<0.05$
DMT	574 ± 76	673 ± 98	n.s.
Sway (1/3° arc)	6.9 ± 1.6	9.8 ± 3.0	$P<0.1$
Tapping	330 ± 51	286 ± 65	n.s.

false-positive and false-negative) was recorded (Tiplady 1985).

Critical flicker fusion threshold. The subject observed a group of four lights which flickered at an increasing frequency. The subject responded when the lights appeared to be steady. The test was then repeated in the opposite direction, the subject responding when the lights appeared to begin flickering. The mean of three observatons in each direction was taken as the threshold (Hindmarch 1975).

Choice reaction time. This used an apparatus with five buttons arranged in a semi-circle, by each of which was a light. The subject initially placed his finger on a sixth button in the centre of the semi-circle. At random intervals one of the lights was illuminated, whereupon the subject responded by pressing the appropriate button as quickly as possible. The mean latency and total response time over 30 responses was taken (Hindmarch 1975).

Decision making. A series of line drawings was displayed on a screen. The subject responded to each drawing by pressing a YES button if the picture was of an animal, a NO button otherwise, as quickly as possible. The mean reponse time to 32 presentations was taken (Thompson et al. 1981; Tiplady 1985).

In addition to these measurements, subjective changes were recorded using visual analogue scales. These were 10 cm lines, the ends of which were marked Steady/Dizzy, Alert/Drowsy, Calm/Tense, and Interested/Bored. The subject made a mark across the line to indicate how he felt at that time.

All test scores were calculated as changes from the Oh (pre-treatment) score. The differences between treatments were analysed using the the Wilcoxon signed-ranks test. The differences between the two age-groups were assessed using the Wilcoxon rank-sum test. The critical level of significance used was $P<0.05$ (two-tailed).

Results

Under placebo conditions there was, as expected, a consistent trend to lower levels of performance in the elderly, which was statistically significant only for CRT (Table 1).

The effects of caffeine versus placebo on the objective measures are shown in Fig. 1. In the young, the only measure to show a significant difference was tapping, which was faster with caffeine than with placebo ($P<0.05$ at 2 h). The elderly subjects made fewer errors on the attention

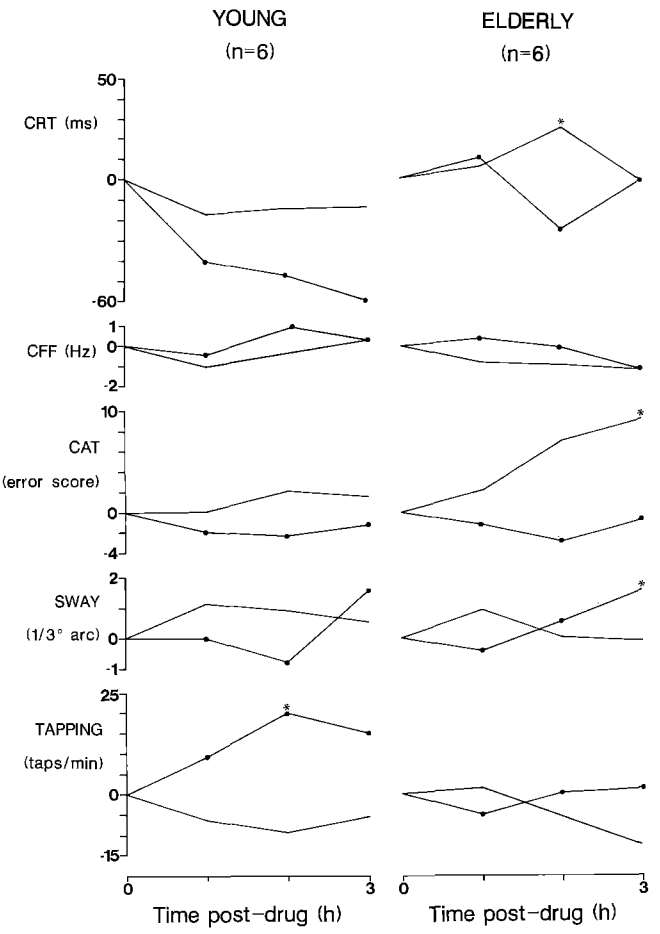

Fig. 1. Effects of caffeine on objective measures. Data are shown as mean changes from baseline (0 h) values. Significant results ($P<0.05$) are marked with an *asterisk*. ●—— caffeine; —— placebo

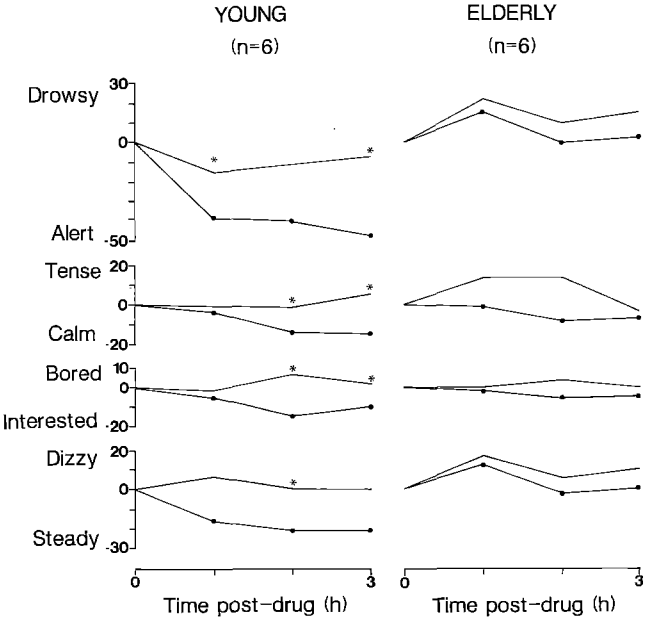

Fig. 2. Effects of caffeine on subjective measures (visual analogue scales). Data are shown as mean changes from baseline (0 h) values in mm. Significant results ($P<0.05$) are marked with an *asterisk*. ●—— caffeine; —— placebo

task ($P<0.05$ at 3 h), showed greater body sway ($P<0.05$ at 3 h), and responded more quickly to the choice-reaction test ($P<0.05$ at 2 h) on caffeine than on placebo. When the times from the choice-reaction test were broken down into latency and movement time, significant differences were found only for movement time, this again being faster with caffeine than with placebo ($P<0.05$ at 1 h and 2 h).

The results from the visual analogue scales are shown in Fig. 2. The young subjects felt more alert ($P<0.05$ at 1 h and 3 h), calmer ($P<0.05$ at 2 h and 3 h), more interested ($P<0.05$ at 2 h and 3 h), and steadier ($P<0.05$ at 2 h) on caffeine than on placebo. No significant differences were seen on these scales in the elderly, although trends in the same direction were seen for calm-tense and interested-bored.

No significant differences in the effects of caffeine were found between the two age groups.

Discussion

These results show changes in subjective and objective measures which are generally in the directions of improved performance, alertness, and subjective well-being with caffeine. The increase in body sway with caffeine is the exception to this, and may relate to the slight impairment in hand-eye co-ordination reported by Putz-Anderson et al. (1981); however the change in this measure with time is not straightforward and appears rather difficult to interpret (Fig. 1).

Although the differences between groups are not statistically significant, the data suggest that the elderly show a greater response to caffeine on the performance tests than do the young. A study of the pharmacokinetics of caffeine did not show any marked differences between young and elderly (Blanchard and Sawers 1983). Hence any change in response to caffeine in the elderly would be expected to have a pharmacodynamic basis. The stimulant effects of caffeine are generally considered to be mediated by inhibition of central adenosine receptors. Although there is some evidence from in vitro studies for increased tissue sensitivity to adenosine in aged animals (Hoffman et al. 1984), data from intravenous administration of adenosine to elderly human subjects showed no age-related difference in respiratory and cardiovascular responsiveness (Watt et al. 1986). A receptor-independent mechanism may therefore be involved.

These results may have significance for elderly patients undergoing treatment with methylxanthines for obstructive airways disease, in whom unwanted central stimulant effects, such as hyperexcitability, sleep disturbance and mental confusion are not uncommon.

The results from tapping are different from the other objective measures, this being the only such measure which was affected by caffeine in the young, while no such effect was observed in the elderly. This task has previously been shown to be sensitive to the effects of caffeine in young subjects (Fagan et al. in preparation). These results are therefore in agreement with previous studies, which suggest that tasks involving predominantly motor speed are less sensitive to the effects of centrally acting drugs in the elderly (Castleden et al. 1977; Swift 1983; Swift et al. 1985b).

By contrast to the objective measures, the visual analogue scales were significantly affected by caffeine in the young, but not in the elderly. This finding may be compared to previous work with sedative drugs, in which the young, but not the elderly, showed significant changes on the visual analogue scales. In this case, the changes were in the direction of increased drowsiness and dizziness (Swift 1983; Fagan et al. 1986). These results suggest that the elderly may be less able than the young to report the acute subjective effects of psychotropic drugs, and emphasise the importance of using both objective and subjective measures in drug studies of this sort.

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