The effect of prior caffeine consumption on neuropsychological test performance: a placebo-controlled study

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Abstract

Background: The aim of this study was to investigate whether the prior consumption of 200mg of pure caffeine affected neuropsychological test scores in a group of elderly participants aged over 60 years. *Method*: Using a double blind placebo vs. caffeine design, participants were randomly assigned to receive 200mg of caffeine or placebo. A neuropsychological assessment testing the domains of general cognitive function, processing speed, semantic memory, episodic memory, executive function, working memory and short-term memory was carried out. *Results*: Significant interaction effects between age, caffeine and scores of executive function and processing speed were found; participants who had received caffeine showed a decline in performance with increasing age. This effect was not seen for participants who received placebo. *Conclusion*: The results highlight the need to consider and control prior caffeine consumption when scoring neuropsychological assessments in the elderly which is important for accuracy of diagnosis and corresponding normative data.

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Introduction

Previous longitudinal studies have investigated the relationship between habitual coffee consumption and cognitive performance [1,2,3]. Prior caffeine consumption in the period just before the time of testing is less well studied. If caffeine does affect test scores this will have implications for the accuracy of scoring these tests and consequently any interpretations made. Previously Lesk and Womble [4] found strong interactions between prior consumption of 200mg of caffeine (approximately the same amount of caffeine in one strong cup of coffee) or placebo and, phonological priming, on the tip-of-the-tongue state in both young participants [4] and in a patient with anomic aphasia [5]. Lesk et al. [6] then investigated the effect of prior caffeine intake on neuropsychological test scores in the elderly. This study used a questionnaire that simply asked participants about their intake of Caffeine Containing Foodstuffs (CCFS) (tea, coffee, chocolate and cola) four hours before testing. An interaction effect of age and intake of CCFS prior to neuropsychological assessment was found on six of the nine assessments used whereby the older elderly (over approximately the age of 80) performed significantly worse if they had consumed CCFS and the younger elderly performed significantly better if they had consumed CCFS. It remained unclear whether it is the caffeine contained within these foodstuffs causing the interaction effect or whether it is because of other substances in CCFS. For example, coffee also contains chlorogenic acid, cafestol and kahweol [1] and tea is concentrated in polyphenols which have been shown to enhance memory [2]. Furthermore, Walters and Lesk [7] found an interaction effect between 200mg of caffeine, the time of day assessments were administered and scores on the Mini Mental State Examination (MMSE)[8] and Graded Naming Test (GNT) [9]. The present study analyses this data set further.

Materials and Methods

The data set used in this paper is that used to investigate time of day effects and caffeine in Walters and Lesk [7]. The methods of data collection, tests used, inclusion criteria and procedure are described in detail there [7]. In the present study the aim is specifically to investigate whether prior caffeine and age influence performance on the same battery of cognitive tests. Forty participants from the University of Bradford, Division of Psychology cognitively-healthy elderly participant pool, were recruited to take part in the study. Ethical approval was obtained from the Humanities, Social & Health Science Research Ethics Panel at the University of Bradford**.** The study was performed double blind and there were an equal number of participants in both the placebo (n=20) and caffeine condition (n=20).

A cognitive battery was administered to each participant in the same order which consisted of the MMSE [8], word recall [10], Stroop [11], Pattern Comparison Speed (PCS) [12], Letter Comparison Speed (LCS) [12], digit span [13]; Dual Tasks [14], SDMT [15] Cambridge Neuropsychological Test Automated Battery Paired Associates Learning (CANTAB PAL) [16] and GNT [9]. See Walters and Lesk [7].

Results

The aim of the current study was to investigate whether 200 mg of prior caffeine can affect scores on neuropsychological tests in a group of participants over the age of 60. There were no main effects of gender or education on any of the tests administered and no main effect of drug group on any of the assessments used.

Following on from Lesk et al. [6], to assess formally whether prior caffeine consumption has an effect on performance with increasing age, all cognitive tests were submitted to a multivariate analysis of covariance (MANCOVA) with drug group (caffeine or

placebo) entered into the model as a fixed factor and age as a covariate. An interaction term was included in the model. The results of this analysis can be seen in table 1. Significant interactions between caffeine/placebo, age and scores on the SDMT, Dual Task Ratio, Dual Tasks T1-T2 interval, Stroop Interference, the PCS and LCS were found. No significant interaction effect is seen for the MMSE, digit span and digit score, the PAL, the GNT, word recall or the Stroop colour. Figure 1 contains scatter plots of those test scores that showed a significant interaction between drug group and age. There were no significant linear trends for the placebo group on any of the tests. Although there is no interaction between drug group and age for the GNT, a regression analysis did reveal a linear decrease in performance with age for those participants who received caffeine.

Table 1: MANCOVA results for the interactions between age and drug group and the outcomes of the linear regression analysis for each group separately.

Testing domain	Assessment	Caffeine	Placebo	p and η^2 value of interaction caffeine/placebo × age	Caffeine regression	Placebo regression
General cognition	MMSE	28.75±1.21	28.40±0.94	n.s.	n.s.	n.s.
Episodic memory	CANTAB PAL 6 errors	7.35±6.40	7.90±6.67	n.s.	n.s.	n.s.
Semantic memory	GNT	26.30±2.98	25.65±2.64	n.s.	r = 0.44, p = 0.05	n.s.
Working memory	Digit Span	6.50±1.00	6.25±0.79	n.s.	n.s.	n.s.
	Digit Score	8.95±1.82	8.60±1.64	n.s.	n.s.	n.s.
Executive function	Dual Tasks T1–T2	7.30±11.66	3.65±6.17	f(2, 37) = 6.51, p < 0.01, η^2 =0.26	r = 0.49, p <0.05	n.s.
	Dual Task ratio	0.92±0.22	0.10±0.12	f(2, 37) = 7.55, p < 0.01, η^2 = 0.29	r = 0.64, p <0.05	n.s.
	SDMT total correct	40.10±9.03	38.70±7.45	f(2, 37) = 6.67, p < 0.01, η^2 = 0.27	r = 0.68, p < 0.01	n.s.
	Stroop interference	30.05±10.92	25.80±9.02	f(2, 37) = 5.64, p < 0.01 , η^2 = 0.23	r = 0.62, p < 0.01	n.s.
Processing speed	PCS	25.25±3.96	22.45±4.94	f(2, 37) = 3.65, p <0.05, η^2 = 0.17	r = 0.56, p < 0.05	n.s.
	LCS	15.35±3.72	12.80±2.95	f(2, 37) = 6.91, p < 0.01, η^2 = 0.27	r = 0.58, p < 0.01	n.s.
	Stroop colour	24.75±5.48	23.85±7.16	n.s.	n.s.	n.s.
Short-term memory	Word Recall	5.35±1.76	4.80±1.44	n.s.	n.s.	n.s.

n.s. = Not significant.

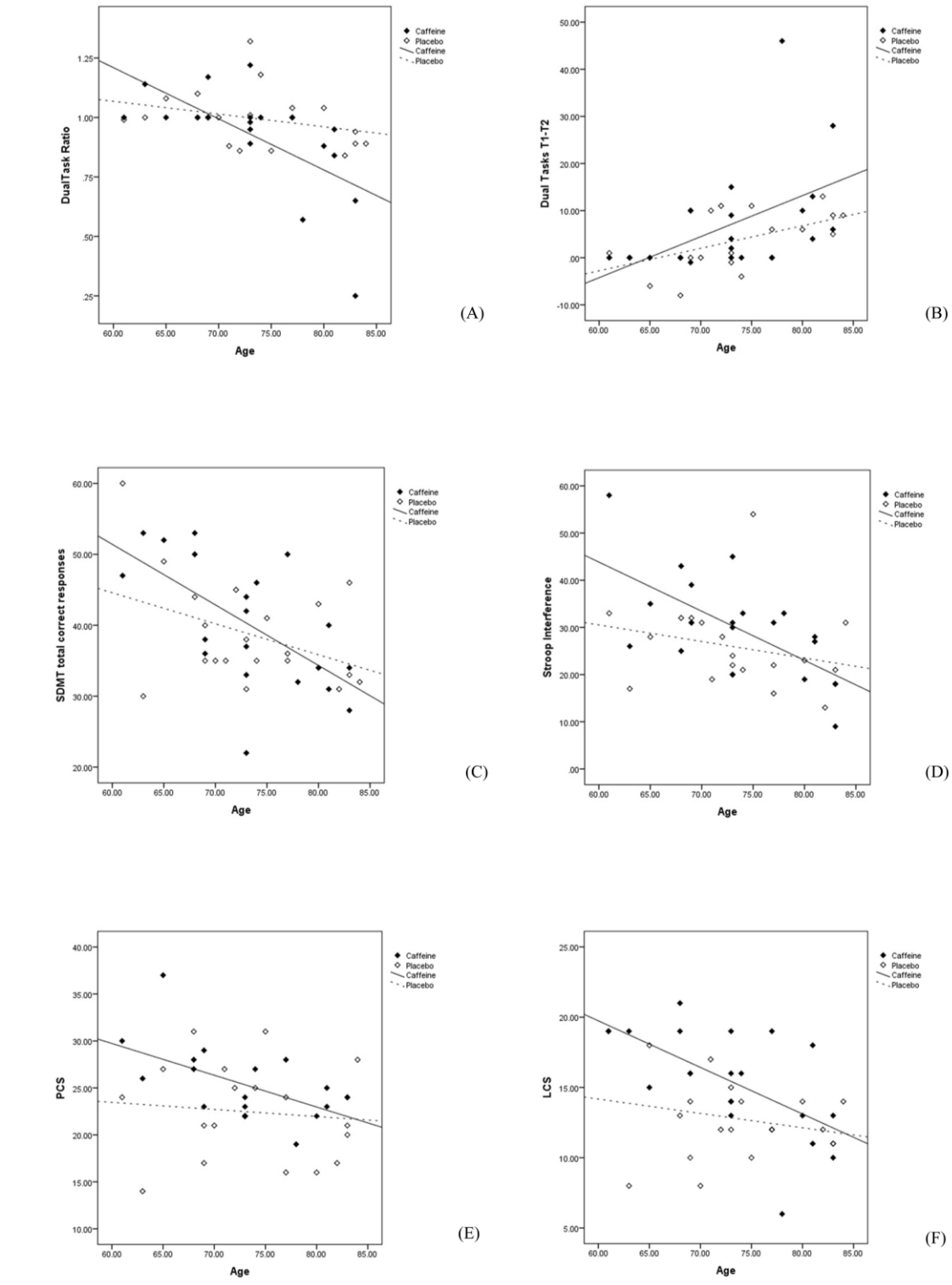

Figure 1: Scatter plots showing the interaction effects between caffeine x age and score for (A) Dual Task ratio, (B) Dual Tasks T1-T2 interval, (C) SDMT total correct responses, (D) Stroop Interference, (E) PCS and (F) LCS. There is a significant linear decrease in performance with increasing age for the caffeine group. A higher score for T1-T2 interval equates to poorer performance on this test.

Discussion

The aim of the present paper was to extend the results of Lesk et al. [6] by investigating whether 200mg of pure caffeine could influence score on cognitive tests in the over 60-year-old participants. No main effect of caffeine or placebo was found on any of the tests administered. Significant interaction effects between drug group, age and tests of ***executive function***, (specifically the Dual Task ratio score and number of boxes crossed at time point one v time point two, the SDMT total score and the score for Stroop Interference) and ***processing speed,*** (specifically the scores on the LCS and PCS tasks) were found. The third test for processing speed, the Stroop colour test, did not show the same interaction effects. In the tests that showed this interaction, for the caffeine subgroup, participants' scores declined with increasing age, an effect not seen in the placebo condition.

The present study and Lesk et al.[6], both show that if there is no caffeine in the system (no prior consumption of CCFS in Lesk et al. [6] and the placebo condition in this study) the results are the most controlled i.e. no significant interaction and no main effects in the regression analysis. One strong advantage of this study is that it focuses specifically on caffeine and no other CCFS showing that the effects are because of caffeine. The discrepancies between the two studies may therefore be because of the other components within CCFS [1,2,17]. This raises the question of whether participants should be asked to abstain from caffeine and CCFS for at least four hours before being given any neuropsychological assessment

Significant interactions in this cohort were only found on tests of ~~EF~~ executive function and processing speed which has implications for the diagnostic process of Alzheimer's disease. It is not possible to determine the specific reasons for the selectivity of

the effects of caffeine to these particular cognitive domains from the present data.

Executive function is specifically associated with the frontal lobes [18,19], which are highly susceptible to age-related changes compared to other areas associated with cognitive function [19,20,21]. Furthermore, caffeine is an adenosine receptor antagonist [22]. During aging, adenosine receptors are specifically upregulated in frontal cortex [23]. This may explain why the effects of caffeine alter with age in relation to executive function skills. This highlights the need to control for prior caffeine intake in neuropsychological assessment.

Conflicts of interest: There are no reported conflicts of interest.

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