

Hendrik J. Smit · Elizabeth A. Gaffan · Peter J. Rogers

Methylxanthines are the psycho-pharmacologically active constituents of chocolate

Received: 9 January 2004 / Accepted: 24 March 2004 / Published online: 5 May 2004
© Springer-Verlag 2004

Abstract *Rationale:* Liking, cravings and addiction for chocolate (“chocolism”) are often explained through the presence of pharmacologically active compounds. However, mere “presence” does not guarantee psycho-activity. *Objectives:* Two double-blind, placebo-controlled studies measured the effects on cognitive performance and mood of the amounts of cocoa powder and methylxanthines found in a 50 g bar of dark chocolate. *Methods:* In study 1, participants ($n=20$) completed a test battery once before and twice after treatment administration. Treatments included 11.6 g cocoa powder and a caffeine and theobromine combination (19 and 250 mg, respectively). Study 2 ($n=22$) comprised three post-treatment test batteries and investigated the effects of “milk” and “dark” chocolate levels of these methylxanthines. The test battery consisted of a long duration simple reaction time task, a rapid visual information processing task, and a mood questionnaire. *Results:* Identical improvements on the mood construct “energetic arousal” and cognitive function were found for cocoa powder and the caffeine +theobromine combination versus placebo. In chocolate, both “milk chocolate” and “dark chocolate” methylxanthine doses improved cognitive function compared with “white chocolate”. The effects of white chocolate did not differ significantly from those of water. *Conclusions:* A normal portion of chocolate exhibits psychopharmacological activity. The identical profile of effects exerted by cocoa powder and its methylxanthine constituents shows this activity to be confined to the combination of caffeine and theobromine. Methylxanthines may contribute to the popularity of chocolate; however, other attributes are

probably much more important in determining chocolate’s special appeal and in explaining related self-reports of chocolate cravings and “chocolism”.

Keywords Chocolate · Cocoa · Caffeine · Theobromine · Mood · Performance

Introduction

Liking, cravings and addiction for chocolate (“chocolism”) are often explained through the mere presence of its pharmacologically active compounds. Media favourites include the cannabinoid anandamide (Tomaso et al. 1996), and phenylethylamine (Liebowitz and Klein 1979; Hamilton 1992). These and other potentially psychoactive constituents in chocolate have been discussed in detail by Smit and Rogers (2001). “Mere presence”, however, does not guarantee psychoactivity (Di Marzo et al. 1998; Gibson and Desmond 1999; Smit and Rogers 2001). Additionally, and despite much speculation, the view that pharmacologically active constituents are responsible for certain mood and related effects of chocolate has not been tested very directly. A method for doing so takes advantage of the fact that these constituents are very largely confined to the cocoa fraction of chocolate (Michener and Rozin 1994). By administering cocoa powder in capsules, it is possible to assess the psychopharmacological activity of chocolate separately from its oro-sensory and expected effects. This approach has been used once before and it showed that consumption of cocoa powder, without tasting, fails to satisfy cravings for chocolate (Michener and Rozin 1994). However, no similar experiment has reported effects on mood or other measures of psychoactivity.

Of the various candidate compounds, theobromine (present in chocolate in uniquely high quantities) and caffeine (present in relatively small amounts) would appear to be the most likely to have some relevant effects. Many other compounds are ruled out because of dose and/or their metabolic fate when taken orally, including

H. J. Smit (✉) · P. J. Rogers
Department of Experimental Psychology, University of Bristol,
8 Woodland Road,
Bristol, BS8 1TN, UK
e-mail: henk.smit@bristol.ac.uk
Fax: +44-117-9288588

E. A. Gaffan
School of Psychology, University of Reading,
Harry Pitt Building, Earley Gate,
Reading, RG6 6AL, UK

phenylethylamine and anandamide (Rogers and Smit 2000; Smit and Rogers 2001). The present paper describes two double-blind experiments measuring psychoactive effects of cocoa powder, and its methylxanthine constituents theobromine and caffeine.

Theobromine (3,7-dimethylxanthine) is a metabolite of caffeine (Stavric 1988). Of all foods containing theobromine, cocoa products have by far the highest concentration, with dark chocolate containing 237–519 mg theobromine per 50-g portion (MAFF 1998). Despite its relationship with caffeine, the action of theobromine on the central nervous system is generally considered weak or even absent, although published work investigating effects of theobromine is restricted to relatively few articles. Mumford et al. (1994) provide some of the most relevant and up-to-date research in this respect. Their research showed a lowest reliable placebo-discriminable dose of theobromine to be 560 mg in four of seven participants, with one participant going as low as 100 mg. Basis for discrimination involved changes in mood and behaviour, including feeling more energetic, increased motivation to work, and increased alertness. The subjective effects phase of that study, however, showed some significant effects of theobromine (560 mg) in only a few individuals. Caffeine (178 mg), on the other hand, showed reliable group effects, apparently confirming theobromine's relatively weak psychoactive effects. The Merck Index places theobromine in the therapeutics categories “diuretic”, “bronchodilator”, and “cardiotonic” (Merck 1996). Although it was formerly used as a diuretic, and in the treatment of arteriosclerosis, some peripheral vascular diseases, angina pectoris and hypertension (Reynolds 1993; Landau 1986), there appears to be no current therapeutic use for theobromine.

By contrast, caffeine (1,3,7-trimethylxanthine) is the most exhaustively researched methylxanthine consumed. It occurs naturally in the coffee bean, cola nut, guarana (the latter two both being used in cola beverages), tea and the cocoa bean, maté and in cassia (Tarka 1982; Barone and Roberts 1984; Landau 1986). It is an ingredient in various soft drinks, either in the form of a natural extract (e.g. cola nut or guarana) or as an added chemical “as such” (MAFF 1998), and in medicines (Barone and Roberts 1984). The amount of caffeine found in a typical serving of coffee and tea varies between about 40 and 130 mg, whereas a 50 g bar of dark chocolate contains 17–36 mg caffeine (James 1991; MAFF 1998). Moreover, effects of caffeine are well established compared with those of theobromine. In a recent review article (Smit and Rogers 2002b), we concluded that caffeine increases mainly energetic arousal (feelings of alertness and mental energy), with a smaller improvement in hedonic tone (feelings of well-being) at lower doses. Additionally, caffeine reliably affects cognitive and psychomotor performance (e.g. Smit and Rogers 2000), although the extent to which these and the subjective effects represent a net benefit gained from caffeine consumption is unclear. This is because studies have generally failed to rule out the possibility that the observed psychostimulant effects of

caffeine are in fact due to “withdrawal reversal” (see, e.g. Rogers and Dernoncourt 1998; Rogers et al. 2003).

Stimulatory effects of caffeine are believed to be mainly caused by means of adenosine receptor antagonism (Fredholm et al. 1999). Although the two methylxanthines here do not exhibit a clear difference in relative affinity for adenosine A₁ versus A_{2a} receptors, theobromine exhibits a noticeably lower overall level of such affinity than does caffeine (Fredholm and Lindström 1999), which would explain the differences in subjective effects between caffeine and theobromine as found in Mumford et al. (1994).

The purpose of the present studies was to test for psychopharmacological activity of chocolate, and for the role of the methylxanthines caffeine and theobromine in these effects. Because the main psychopharmacologically active constituents of chocolate are likely to be confined to, and present in much higher concentrations in, cocoa solids (Michener and Rozin 1994), we used encapsulated cocoa powder representative of a 50 g bar of dark chocolate and compared this to placebo in study 1. Next, we compared the effects of the amount of methylxanthines found in the same amount of chocolate, to placebo in study 2. The main dependent variables were self-reported mood and alertness, and performance on a long-duration simple reaction time (SRT) task and a rapid visual information processing (RVIP) task. A double-blind, within-subjects repeated measures design was used as described in Smit and Rogers (2002a).

Materials and methods

Participants

Ethical approval for the following experimental procedures was obtained from the Institute of Food Research Human Research Ethics Committee, and participants gave their informed consent prior to taking part in either study. They were told that the treatments “contain ingredients in the amounts found in commercially available chocolate”. All participants were recruited from a participant database by telephone, were chocolate consumers, had no adverse symptoms associated with chocolate or caffeine intake, were not pregnant, and were native English speakers.

Treatments

Study 1

The psychopharmacological effects of the active constituents in chocolate were investigated by testing two active treatments containing identical amounts of methylxanthines representing a 50 g bar of dark chocolate [11.6 g of Cadbury's Bournville cocoa powder (CP), and 250 mg theobromine+19 mg caffeine (CA+TB); (Smit and Rogers 2001)], against placebo. In order to increase the reliability of the control data, two identical placebo conditions were

included in this study. Each of the treatments was presented in 21 opaque red capsules size 0, and was consumed with lukewarm water to speed up the release of the capsule content through improved gelatine solubility. Microcrystalline cellulose (an inert food grade product) was used as filler in the methylxanthine and placebo treatments. Sources of these materials were: caffeine BP, Merck Industrial Ltd, Poole, Dorset, UK; theobromine USP, City Chemical, New York, USA; micro-crystalline cellulose: FMC Corporation Ltd, Leicester, UK; capsules: Davcaps, Hitchin, Hertfordshire, UK.

Study 2

Study 2 complemented study 1 by using more ecologically valid treatments. Visually identical 60 g portions (12 squares) of chocolate were prepared containing: no methylxanthines (zero MX), 8 mg caffeine+100 mg theobromine (low MX), and 20 mg caffeine+250 mg theobromine (high MX), matching the amounts of methylxanthines present in standard portions of white, milk and dark chocolate, respectively. Zero MX chocolate contained no methylxanthines, and therefore served as a placebo against which low and high MX chocolate were tested. The basic recipe for the chocolate was 44% icing sugar, 29% full cream milk powder, 4% skimmed milk powder, 22% cocoa butter, 1% emulsifier, 500 ppm brown food colour, and 30 ppm vanillin flavouring. The ingredients were ground to a paste in a ball mill, followed by tempering and moulding using standard chocolate manufacturing procedures. A fourth treatment consisting of 60 ml water served as a placebo for oro-sensory effects, tested against zero MX chocolate. Chocolate treatments were manufactured and supplied by Reading Scientific Services Ltd.

Study design and procedure

The two studies described here were carried out by the authors at the Institute of Food Research, Reading, UK, using a critically assessed methodology as described in Smit and Rogers (2002a), which allowed for the expression of both immediate and short-term effects of pharmacologically active constituents of chocolate.

Study 1

Participants were required to attend a practice visit to gain familiarity with the test procedures. During this visit, they also filled out a background questionnaire, and gave their written consent. They then returned to the laboratory for four test sessions (9:00 a.m. to 12:30 midday) according to the double-blind within-subjects design. Order effects and carry-over effects were addressed by using balanced (Williams) designs (Wakeling and MacFie 1995), or they were computed using Genstat, to counterbalance orders of

conditions over weeks and to assign participants to testing booths. Participants were required to abstain from consuming any caffeine or cocoa/chocolate-containing drink or food from 9:00 p.m. the previous evening. In order to encourage compliance with this instruction, a saliva sample (not analysed) was taken from each participant at the beginning of each test session.

Each test session involved the completion of one pre-test (baseline) and two post-test sets of tasks, at 1 and 2 h after receiving the treatment. Post-treatment testing times were chosen to coincide with absorption times of potentially psychoactive compounds in cocoa, including caffeine and theobromine (Drouillard et al. 1978; Mumford et al. 1994, 1996). Each set of tasks consisted of a mood questionnaire and three computerised cognitive performance tasks (see below).

Study 2

The task schedule of study 1 was repeated in study 2, although in addition, mood and task performance were also measured during an “extended treatment administration period” to assess immediate, sensory-related effects. During this extended treatment administration period, treatments were given over 30 min in four equal portions (three squares), where each portion was administered and consumed before commencing the next task in this second (interim) test battery.

Test battery

Mood questionnaire

A 25-item mood questionnaire, similar to Smit and Rogers (2000), was developed partly from the Profile of Mood States bipolar form (POMS-BI; Lorr and McNair 1988) and the short form of the activation-deactivation adjective checklist (AD ACL; Thayer 1989). It consisted of several descriptors of alerting and energising effects, aspects of positive and negative affect, and tension related moods, a measure of “overall mood”, and “hungry” and “thirsty”. Then, participants were asked to rate the intensity of several subjective “bodily sensations”, for example, “headache”, “heart pounding”, “nausea”, “chills”. All scales were 100 mm anchored visual-analogue (line) scales, with “not at all” and “extremely” as extremes, apart from “overall mood”, which was anchored “very bad” and “very good”, and “appetite for chocolate”, which was labelled “not at all” and “very much”. The questionnaire contained the following instructions: “Please answer all of the following questions by placing a vertical mark through the line for each question. Mark the lines according to how you feel at this moment. Regard the end of the lines as indicating the most extreme sensation you have ever felt”. The latter instruction was used to help avoid floor or ceiling effects in the mood data. No definitions of the mood adjectives were imposed upon the participants.

Responses were measured in mm from the left hand end of the scale (=0).

Because improved mood can lead to improved performance on tasks sensitive to psychoactive effects, three cognitive tasks used in previous dietary and pharmacological experiments (e.g. Lloyd et al. 1994; Smit and Rogers 2000) were also included. These computerised performance tasks were programmed using Micro Experimental Laboratory (MEL version 2.00; Psychology Software Tools Inc., Pittsburgh, Pa., USA).

Simple reaction time (SRT) task

This task measures response times to simple stimuli, thereby suggesting measuring alertness. Within each task, for 160 consecutive trials, a stimulus (single star) was presented on the screen for a maximum duration of 1000 ms. Participants were instructed to press the space bar as quickly as possible upon stimulus appearance, and to press the space bar again to go on to the next trial, making this a self-paced task. Time delays for stimulus projection were 1, 3, 7, and 16 s. Each time delay was repeated 4 times for each of ten blocks of 16 trials per block, presented in randomised order. Task duration was approximately 20 min.

Rapid visual information processing (RVIP) task

This relatively difficult task places a high load on working memory. Stimuli (single digits of 1–9) appeared in the middle of the computer screen in a semi-random order. Participants were required to press the space bar as soon as they detected a sequence of three odd or three even numbers appearing on the screen. The stimulus duration was 600 ms with no inter-stimulus interval. There were eight target sequences (i.e. potential correct hits) per minute, and the whole task lasted 10 min. The scores recorded were the number of correct hits for each minute and reaction times for correct hits.

Thurstone tapping task

This task assesses manual dexterity. On four stars appearing on the screen, subjects had to tap the “1” and “2” key on the keypad alternately and as fast as possible, until 300 taps were made. The dependent variable was tapping speed (taps/second). This task lasted around 1 min.

The tasks were administered in order of least to most stressful, to minimize carry-over effects within each set of tasks: mood questionnaire; SRT; TT; RVIP. Between sets of tasks (approximately 30 min), participants were allowed to relax by reading a magazine whilst remaining confined to their testing booth. The complete time schedule for testing is summarised in Table 1.

Table 1 Schedule of experimental session. Names in plain text refer to computerised performance tasks

	<i>Time</i>	Duration (min)
Saliva sample	–33	3
Mood Qu 1	–30	3
SRT task 1	–27	20
Tapping task 1	–7	1
RVIP task 1	–6	6
STUDY 1		
<i>TREATMENT</i>	0	3
<i>BREAK</i>	3	57
STUDY 2		
<i>TREATMENT part 1</i>	0	2
Mood Qu 1a	2	3
<i>TREATMENT part 2</i>	5	2
SRT task 2	7	20
<i>TREATMENT part 3</i>	27	2
Tapping task 2	29	1
<i>TREATMENT part 4</i>	30	2
RVIP task 2	32	6
<i>BREAK</i>	38	22
Mood Qu 2	1h	3
SRT task 2	1h3	20
Tapping task 2	1h23	1
RVIP task 2	1h24	6
<i>BREAK</i>	1h30	30
Mood Qu 3	2h	3
SRT task 3	2h3	20
Tapping task 3	2h23	1
RVIP task 3	2h24	6
TOTAL	2h30	3h3

Data analysis

All analyses were performed using the statistical software SPSS. First, mood data were subjected to z-score transformation (mean of 0; SD of 1) on a participant by dependent variable basis to eliminate between-participant variations in scale use. These “z-scores” were then subjected to principal component analysis (PCA) in order to reduce the number of variables in the analysis. The “Eigenvalue-greater-than-one” rule and the Scree plot method were used, in combination with interpretability, to determine the number of factors to extract. Factors were extracted using oblique rotation, as relevant mood dimensions are not necessarily independent. Only mood constructs with a high reliability (Cronbach’s alpha ≥ 0.7) were used in the subsequent analysis. Factor scores were calculated by summarising individual mood adjective scores (e.g. energetic arousal = Alert+Clearheaded+Energetic+Lively–Drowsy–Sluggish–Tired). For the remaining dimensions, individual mood states were analysed.

Next, performance and compound mood data were analysed by using pre-treatment data (baseline measures)

as a covariate in a repeated measures ANOVA followed by a priori planned comparisons between active treatments and placebo. Least significant differences (LSDs) were calculated using a Bonferroni correction. In study 1, two planned comparisons reduced the probability level from testing against 0.05 down to 0.025; in study 2, three planned comparisons reduced it to 0.0167. Half these LSD values were used in the graphical representations as error bars. Hence, a significant difference can be identified by non-overlapping placebo and active treatment error bars (additionally indicated by one or more asterisks in Figs 1, 2). Reported fractional degrees of freedoms indicate the use of a Greenhouse–Geisser correction where the sphericity assumption in repeated measures ANOVA was violated.

Results

Study 1

Participant characteristics

Of the 27 participants recruited, 20 (three men and 17 women) finished the study. They were 32.6 (± 11.2 ; ranging from 18 to 56) years of age, were of normal weight for height, and had a mean caffeine intake of 330 mg/day (± 194 ; ranging from 9 to 670) and a mean theobromine intake of 100 mg/day (± 204 ; ranging from 14 to 952).

General

ANOVA revealed no significant “treatment” effects for any of the baseline (pre-treatment) measures taken; all $P > 0.05$.

Performance tasks

SRT was significantly faster after cocoa powder (CP) and caffeine+theobromine (CA+TB) than after placebo [$P=0.007$ and 0.0004 , respectively; overall treatment effect: $F(2,42)=6.50$; $P=0.003$; see Fig. 1a]. Although there was not a significant overall treatment effect for the number of correct hits in the RVIP task [$F(2,42)=1.71$; $P=0.194$], the results showed a similar profile to the SRT results, with CP marginally, and CA+TB significantly improving performance compared with placebo ($P=0.070$ and 0.035 , respectively; see Fig. 1b). No significant effects were found for the tapping task ($P > 0.05$).

Mood

A PCA on the dataset which excluded the “physical symptoms” data showed a clear interpretable, optimally clustered structure when extracting four factors. On these

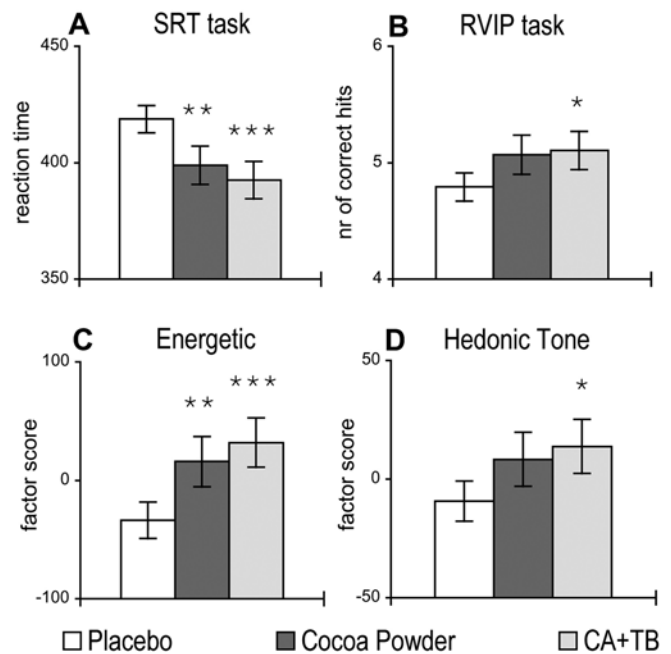


Fig. 1 Results for study 1. **a** Simple reaction time, **b** rapid visual information processing, and **c** mood constructs energetic arousal and **d** hedonic tone. Data shown are post-test treatment means $\pm 0.5 \times \text{LSD}$. Non-overlapping error bars between placebo and non-placebo treatments indicate significant difference after Bonferroni correction for multiple comparisons. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. Pre-treatment (baseline) overall means are: 389 (SRT); 4.8 (RVIP); -12.7 (energetic arousal); -14.1 (hedonic tone)

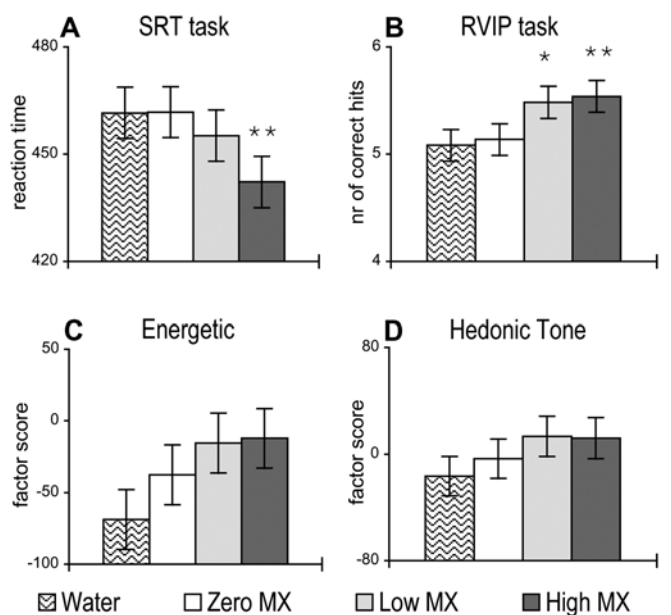


Fig. 2 Results for study 2. **a** Simple reaction time, **b** rapid visual information processing, and **c** mood constructs energetic arousal and **d** hedonic tone. Data shown are post-test treatment means $\pm 0.5 \times \text{LSD}$. Non-overlapping error bars between placebo and non-placebo treatments indicate significant difference after Bonferroni correction for multiple comparisons. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$. Pre-treatment (baseline) overall means are: 417 (SRT); 5.4 (RVIP); 44.5 (energetic arousal); -4.6 (hedonic tone)

factors, the following constructs, listing Eigenvalues (EV) and reliability (α), were identified: energetic arousal (“energetic”, “alert”, etc. versus “tired”, “sluggish”, etc.; EV=6.8; α =0.87); hedonic tone (“happy”, “content”, “calm”, etc. versus “angry”, “dissatisfied”, etc.; EV=2.8; α =0.79); appetite (“hungry”, “thirsty”, “appetite for chocolate”; EV=2.0; α =0.73); nervous/dysphoric tension (“nervous”, “uncertain”, “tense” and “sad”; EV=1.8; α =0.71). The four factors explained a total of 51.3% of the variance in the data.

Consistent with the effects on SRT performance, CP and CA+TB significantly increased energetic arousal scores compared with placebo [$P=0.010$ and 0.0007 , respectively; overall treatment effect: $F(2,41)=7.55$; $P=0.002$; see Fig. 1c]. For hedonic tone there was a marginally significant overall treatment effect [$F(2,41)=2.65$; $P=0.083$], where CP only marginally, and CA+TB significantly improved hedonic tone compared with placebo ($P=0.083$ and 0.025 , respectively; see Fig. 1d). A significant treatment \times time interaction, however, showed the peak of the effect to be delayed in the CP compared with the CA+TB scores, the latter peaking in the first post-test set of tasks [1 h after receiving the capsules; treatment \times time interaction: $F(2,42)=5.39$; $P=0.008$; data not shown]. No effects were found for tense arousal, thirst, or appetite for chocolate ($P>0.1$). Hunger, on the other hand, was decreased following CP, but not CA+TB, compared with placebo [$P=0.027$ and 0.167 , respectively; overall treatment effect: $F(2,42)=3.86$; $P=0.029$]. Finally, the only significant effect found for the “physical symptoms” measures was for “headache”, where CA+TB (but not CP) decreased headache scores compared with placebo [$P=0.0006$ and 0.345 , respectively; overall treatment effect: $F(2,42)=7.22$; $P=0.002$].

Study 2

Participant characteristics

Of the 29 participants recruited, 22 (11 men and 11 women) finished the study. They were 35.4 (± 14.2 ; ranging from 18 to 70) years of age, had a BMI of 24.1 kg/m² (± 3.2 ; ranging from 20.3 to 30.1), had a mean caffeine intake of 386 mg/day (± 263 ; ranging from 10 to 1004), and a mean theobromine intake of 85 mg/day (± 71 ; ranging from 19 to 321).

General

ANOVA revealed no significant “treatment” effects for any of the baseline (pre-treatment) measures taken; $P>0.05$.

Sensory effects

An overall treatment effect [$F(3,63)=4.32$; $P=0.008$] indicated that high MX chocolate was perceived as bitterer than the other treatments. However, treatments did not differ significantly in terms of “liking” scores [$F(3,63)=1.58$; $P=0.202$], and relevant to this, analysis of the immediate post-treatment mood and task performance data revealed no significant treatment effects ($P>0.05$) except for scores on “thirsty” [overall treatment effect: $F(3,50)=3.72$; $P=0.017$], showing a highly significant difference in feelings of thirst between the “water” and the “zero MX” condition (data not shown).

Performance tasks

In contrast to the lack of oro-sensory effects on mood and performance, significant post-ingestional psychoactive effects related to methylxanthine content were apparent in the post-treatment data. High MX chocolate significantly decreased reaction time (increased reaction speed) compared with zero MX in the SRT task [$P=0.007$; overall treatment effect: $F(3,50)=3.12$; $P=0.034$; see Fig. 2a], and both the low and high MX chocolates improved RVIP performance compared with zero MX [$P=0.019$ and 0.007 , respectively; overall treatment effect $F(3,44)=6.12$; $P=0.001$; see Fig. 2b]. No significant effects were found for the tapping task ($P>0.05$).

Mood

A PCA on the mood-only dataset (thirst, hunger and appetite for chocolate were analysed separately) showed the clearest interpretable, optimally clustered structure when extracting three factors. On these factors, the following constructs, listing Eigenvalues (EV) and reliability (α), were identified: energetic arousal (“energetic”, “alert”, etc. versus “tired”, “sluggish”, etc.; EV=6.6; α =0.88); hedonic tone (“relaxed”, “overall mood”, “happy”, “content”, “calm”, etc. versus “angry”, “tense”, etc.; EV=3.5; α =0.84); Dysphoric moods (“dissatisfied”, “sad”, “uncertain”, and “muddled”; EV=1.5; α =0.544). Combined, the three factors explained 49.9% of the variance in the data. Admittedly, unlike the more typical and theorised hedonic tone dimension in study 1 (Thayer 1989), the similarly interpreted dimension in study 2 is, strictly speaking, a merge of HT and TA adjectives.

Energetic arousal [overall treatment effect: $F(3,50)=3.85$; $P=0.015$; see Fig. 2c] and hedonic tone [overall treatment effect: $F(3,49)=2.08$; $P=0.114$; see Fig. 2d] showed a treatment profile similar to the SRT and RVIP task. The higher mean scores for the methylxanthine-containing treatments were, however, not significantly different from white chocolate (all $P>0.2$). No effects were found for “dissatisfied”, “sad”, and “uncertain” ($P>0.1$). Muddled, on the other hand, showed an overall treatment effect [$F(3,50)=3.58$; $P=0.020$], with a main difference

between milk and dark chocolate only, expressed in the questionnaire data collected 1 h post-test only. As the comparison is not related to our hypotheses, and is lacking theoretical basis, this finding should be treated with caution. Finally, appetite related effects were found for feelings of hunger [overall treatment effect: $F(3,50)=3.32$; $P=0.027$; treatment \times time interaction: $F(3,51)=7.68$; $P<0.001$] and for “appetite for chocolate” [overall treatment effect: $F(3,50)=13.25$; $P<0.001$; treatment \times time interaction: $F(3,51)=4.20$; $P=0.010$], both suggesting a post-treatment increase in scores for these variables in the “water” condition versus the three chocolate conditions (data not shown). No significant effects were found for any of the “physical symptoms” measures ($P>0.10$).

Discussion

The present studies show that methylxanthines in chocolate provide psychostimulant effects, and that these effects are at the very least much greater in magnitude than those of any other potentially pharmacologically active constituents.

In study 1, strong treatment effects were found for the mood construct energetic arousal and the SRT task, but not for the RVIP task or hedonic tone, although even for these measures certain significant planned comparison effects were present. The cocoa powder and mixture of methylxanthines showed very similar effects, the former being if anything marginally less potent, perhaps indicating slower absorption rates of some of the active compounds due to the formation of complex structures with polyphenols in cocoa solids (Czok 1974; Mumford et al. 1996). The absence of an “appetite for chocolate” effect of cocoa powder versus placebo confirms the findings of Michener and Rozin (1994), in that the taste, and not the pharmacology of chocolate, has the ability to satisfy a craving for chocolate. Study 2 confirms the findings of study 1 in the presence of the main chocolate constituents (sugar and fat), thereby suggesting these macronutrients do not play a significant inhibitory role in the uptake of the methylxanthines in chocolate. Moreover, the results suggest no clear difference in effects between milk and dark chocolate methylxanthine levels, as is consistent with the reasonably flat dose-response curves found for caffeine (Smit and Rogers 2000). Of all physical symptoms tested, only one effect was found for “headache”, but this was not consistent between the two studies. Overall, the results show that (1) the cocoa content of a typical portion of dark chocolate has significant psychopharmacological activity; and (2) this activity can be accounted for by the presence of theobromine and/or caffeine, leaving no significant role for other putative psychoactive compounds. Whether caffeine, theobromine or the two compounds jointly were responsible for the observed pattern of psychoactivity is unclear; however, 19 mg is just within the lower end of the range of caffeine doses previously found to have detectable stimulant effects (Smit and Rogers 2000).

Stimulant effects of chocolate were apparently known to ancient Maya and Aztec cultures, as there are various accounts detailing how they used chocolate for endurance (in a more basic form without the addition of milk, sugar and extra cocoa butter; Coe and Coe 1996). Today, chocolate, coffee and tea are among “the most popular ingestants in the world” (Rozin et al. 1991). It is presumably no coincidence that these are the three principal dietary sources of methylxanthines. Why then is chocolate reputed to have much stronger and more varied mood effects than coffee or tea, and why does our society have so many “chocoholics” when there are relatively few self-proclaimed “coffeeholics”? We argue that this is because of a culturally based ambivalence towards chocolate (Rogers 1994; Rogers and Smit 2000). Chocolate fulfils two innate preferences: one for sweet taste, and one for creamy texture, making chocolate one of the most palatable foods available (Drewnowski and Greenwood 1983; Drewnowski et al. 1992). Indeed, cravings for chocolate are satisfied by the oro-sensory rather than the pharmacological effects of chocolate (Michener and Rozin 1994). However, chocolate is also perceived as an unhealthy food, lacking in nutritional value and stigmatised by associations with overeating, overindulgence, obesity, and even sin (Rozin 1987; James 1990). It seems very likely that craving, and the label of addiction, arises as a result of attempts to restrain intake of this irresistibly nice (but “naughty”) food, and guilt is felt when restraint fails (MacDiarmid and Hetherington 1995). Coffee and tea drinking, in contrast, generally cause little concern, to the extent that the use of these drinks as sources of pharmacological stimulation is openly acknowledged as acceptable.

While conflicting attitudes towards chocolate may better explain its capacity to arouse emotions such as euphoria and guilt, the present experiments provide for the first time unequivocal evidence of significant psychopharmacological activity of chocolate. The results are, moreover, directly relevant to the consumption of chocolate in everyday life because the observed stimulant effects occurred at doses of cocoa solids and methylxanthines found in standard portions of chocolate. Note that in the studies reported here, participants were deprived of caffeine and theobromine overnight. Previous research has found that acute caffeine deprivation is necessary for showing psychostimulant effects of caffeine (e.g. Rogers and Derroncourt 1998; Rogers et al. 2003). Moreover, in everyday life, coffee or tea (which contain caffeine but little or no theobromine), rather than chocolate, are typically consumed soon after waking as a first opportunity to reverse the adverse effects of overnight caffeine withdrawal. Therefore, if the psychostimulant effects of methylxanthines play a significant role in reinforcing consumption of chocolate, we propose that theobromine (or its unique combination with caffeine in chocolate), rather than caffeine alone, is the key candidate. Future research should address this, and investigate the possibility of synergism in the effects of these two methylxanthines.

Acknowledgement H.J.S. was supported by a grant from Reading Scientific Services Ltd, Reading, UK.

References

- Barone JJ, Roberts H (1984) Human consumption of caffeine. In: Dews PB (ed) *Caffeine: perspectives from recent research*. Springer-Verlag, Berlin, pp 59–73
- Coe SD, Coe MD (1996) *The true history of chocolate*. Thames and Hudson Ltd, London
- Czok G (1974) Zur Frage der biologischen Wirksamkeit von Methylxanthenen in Kakaoprodukten. *Zeitschrift Ernährungswissenschaft* 13:165–171
- Di Marzo V, Sepe N, De Petrocellis L, Berger A, Crozier G, Frède E, Mechoulam R (1998) Trick or treat from food endocannabinoids? *Nature* 396:636
- Drewnowski A, Greenwood MR (1983) Cream and sugar: human preferences for high-fat foods. *Physiol Behav* 30:629–633
- Drewnowski A, Krahn DD, Demitrack MA, Nairn K, Gosnell BA (1992) Taste responses and preferences for sweet high-fat foods: evidence for opioid involvement. *Physiol Behav* 51:371–379
- Drouillard DD, Vesell ES, Dvorchik BH (1978) Studies on the theobromine disposition in normal subjects. *Clin Pharmacol Ther* 23:296–302
- Fredholm BB, Lindström K (1999) Autoradiographic comparison of the potency of several structurally unrelated adenosine receptor antagonists at adenosine A₁ and A_{2A} receptors. *Eur J Pharmacol* 380:197–202
- Fredholm BB, Bättig K, Holmén J, Nehlig A, Zvartau EE (1999) Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharmacol Rev* 51:83–133
- Gibson EL, Desmond E (1999) Chocolate craving and hunger state: implications for the acquisition and expression of appetite and food choice. *Appetite* 32:219–240
- Hamilton S (1992) Why the lady loves C₆H₅(CH₂)₂NH₂. *New Scientist* 132:26–28
- James A (1990) The good, the bad and the delicious: the role of confectionery in British society. *Sociol Rev* 38:666–688
- James JE (1991) *Caffeine and health*. Academic, London
- Landau SI (1986) *International dictionary of medicine and biology*. Wiley, New York
- Liebowitz MR, Klein DF (1979) Hysteroid dysphoria. *Psychiatr Clin N Am* 2:555–575
- Lloyd HM, Green MW, Rogers PJ (1994) Mood and cognitive performance effects of isocaloric lunches differing in fat and carbohydrate content. *Physiol Behav* 56:51–56
- Lorr M, McNair DM (1988) *Profile of mood states Bi-polar form*. Educational and Industrial Testing Service, San Diego
- MacDiarmid JJ, Hetherington MM (1995) Mood modulation by food: an exploration of affect and cravings in “chocolate addicts”. *Br J Clin Psychol* 34:129–138
- MAFF (1998) *Survey of caffeine and other methylxanthines in energy drinks and other caffeine-containing products (updated)*. Food Surveillance Information Sheet 144
- Merck (1996) *The Merck Index: an encyclopedia of chemicals, drugs, and biologicals*, 12th edn. Merck & Co., Inc., Whitehouse Station, N.J.
- Michener W, Rozin P (1994) Pharmacological versus sensory factors in the satiation of chocolate craving. *Physiol Behav* 56:419–422
- Mumford GK, Evans SM, Kaminski BJ, Preston KL, Sannerud CA, Silverman K, Griffiths RR (1994) Discriminative stimulus and subjective effects of theobromine and caffeine in humans. *Psychopharmacology* 115:1–8
- Mumford GK, Benowitz NL, Evans SM, Kaminski BJ, Preston KL, Sannerud CA, Silverman K, Griffiths RR (1996) Absorption rate of methylxanthines following capsules, cola and chocolate. *Eur J Clin Pharmacol* 51:319–325
- Reynolds JEF (ed) (1993) *Martindale: the extra pharmacopoeia*. Pharmaceutical Press, London
- Rogers PJ (1994) Mechanisms of moreishness and food craving. In: Warburton DM (ed) *Pleasure, the politics and the reality*. Wiley, Chichester, pp 38–49
- Rogers PJ, Dernoncourt C (1998) Regular caffeine consumption: a balance of adverse and beneficial effects for mood and psychomotor performance. *Pharmacol Biochem Behav* 59:1039–1045
- Rogers PJ, Smit HJ (2000) Food craving and food “addiction”: a critical review of the evidence from a biopsychosocial perspective. *Pharmacol Biochem Behav* 66:3–14
- Rogers PJ, Martin J, Smith C, Heatherley SV, Smit HJ (2003) Absence of reinforcing, mood and psychomotor performance effects of caffeine in habitual non-consumers of caffeine. *Psychopharmacology* 167:54–62
- Rozin P (1987) Sweetness, sensuality, sin, safety and socialization: some speculations. In: Dobbing J (ed) *Sweetness*. Springer-Verlag, London, pp 99–111
- Rozin P, Levine E, Stoess C (1991) Chocolate craving and liking. *Appetite* 17:199–212
- Smit HJ, Rogers PJ (2000) Effects of low doses of caffeine on cognitive performance, mood and thirst in low and higher caffeine consumers. *Psychopharmacology* 152:167–173
- Smit HJ, Rogers PJ (2001) Potentially psychoactive constituents of cocoa-containing products. In: Hetherington MM (ed) *Food cravings and addiction*. Leatherhead Food RA Publishing, Leatherhead, pp 325–349
- Smit HJ, Rogers PJ (2002a) Effects of “energy” drinks on mood and mental performance: critical methodology. *Food Qual Pref* 13:317–326
- Smit HJ, Rogers PJ (2002b) Effects of caffeine on mood. *Pharmacopsychologia* 15:231–258
- Stavric B (1988) Methylxanthines: toxicity to humans. 3. Theobromine, paraxanthine and the combined effects of methylxanthines. *Food Chem Toxicol* 26:725–733
- Tarka SMJ (1982) The toxicology of cocoa and methylxanthines: a review of the literature. *CRC Crit Rev Toxicol* 9:275–312
- Thayer RE (1989) *The biopsychology of mood and arousal*. Oxford University Press, New York
- Tomaso Ed, Beltramo M, Piomelli D (1996) Brain cannabinoids in chocolate. *Nature* 382:677–678
- Wakeling IN, MacFie HJH (1995) Designing consumer trials balanced for first and higher orders of carry-over effect when only a subset of *k* samples from *t* may be tested. *Food Qual Pref* 6:299–308