Special Article

NUTRITION REVIEWS

Effects of chocolate on cognitive function and mood: a systematic review

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A systematic review was conducted to evaluate whether chocolate or its constituents were capable of influencing cognitive function and/or mood. Studies investigating potentially psychoactive fractions of chocolate were also included. Eight studies (in six articles) met the inclusion criteria for assessment of chocolate or its components on mood, of which five showed either an improvement in mood state or an attenuation of negative mood. Regarding cognitive function, eight studies (in six articles) met the criteria for inclusion, of which three revealed clear evidence of cognitive enhancement (following cocoa flavanols and methylxanthine). Two studies failed to demonstrate behavioral benefits but did identify significant alterations in brain activation patterns. It is unclear whether the effects of chocolate on mood are due to the orosensory characteristics of chocolate or to the pharmacological actions of chocolate constituents. Two studies have reported acute cognitive effects of supplementation with cocoa polyphenols. Further exploration of the effect of chocolate on cognitive facilitation is recommended, along with substantiation of functional brain changes associated with the components of cocoa.

INTRODUCTION

Chocolate originates from Mexico, where an ancient tribe called the Olmecs (1200 BC to 300 BC) were the first to domesticate the plant and use the beans. The Olmecs had a name for these bitter seeds to which secrets of health and power were ascribed: "kakawa," or "cacao." Cocoa became an integral part of the mythology and culture of the Mesoamerican civilizations and was regarded as a gift of the gods. The Mayans worshiped a goddess of chocolate/cocoa named "Ixcacao" and were the first civilization to cultivate cocoa plantations in the lowlands of the southern Yucatan Peninsula around AD 600. The Toltecs emerged to challenge the empire of the Mayans and also saw cacao as a divine gift, believing the god Quetzalcoatl had given the bean to humans and taught them how to cultivate it. This legend continued centuries later into the age of the Aztecs. Chocolate, considered an aphrodisiac, was available only for special occasions and for those with wealth and power. Cocoa trees were being grown by the Aztecs of Mexico and the Incas of Peru when the Europeans discovered Central America in the 1520s. At that time, chocolate, mixed with vanilla and sugar, was introduced by the early Spanish explorers to Europe, where it was consumed as a drink. There, too, chocolate was reserved for the nobility. Eventually, because of its high cost, chocolate as a beverage was displaced by coffee and tea. The introduction of the "dutching" process, which removed some of the more bitter flavors of cocoa, and, in the late 1820s, the application of the industrial press to the manufacture of cocoa products led to solid chocolate becoming a favorite confection in Europe and, subsequently, in North America. Although today cocoa is harvested primarily in West Africa, Indonesia, and Sri Lanka, the consumption of chocolate as a confection is widespread in most developed countries, with consumption being highest in Europe and the United States.[1]

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Cocoa and chocolate differ in that, while cocoa is the nonfat component of cocoa liquor (finely ground cocoa beans), chocolate contains a combination of ingredients that include cocoa, cocoa butter, sugar, and other constituents formed into a solid food product.[2] Commonly available, traditional chocolate is derived from the cocoa bean; this is a rich source of flavanols, which is a subgroup of the naturally occurring flavonoids that are natural bioactive plant compounds found in foods such as tea, red wine, and fruits.[3]

POTENTIAL FUNCTIONAL INGREDIENTS OF CHOCOLATE

Chocolate contains a number of ingredients that have the potential to influence neurocognitive function. Among these are carbohydrates, which have known behavioral effects.[4] However, given the large body of literature on the effects of carbohydrates and glucose on cognition, for purposes of this review the potential neurocognitive effects of carbohydrates in chocolate are restricted to the effects of carbohydrates on chocolate craving. Additionally, given the lack of specificity to chocolate and the absence of any studies using a carbohydrate arm when examining behavioral effects of components of chocolate, it was not possible to include carbohydrate effects in this systematic review.

The other major psychoactive components of chocolate are flavanols and the methylxanthines (MXs) caffeine and theobromine. A review of the effects of caffeine on behavior is beyond the scope of this review, but the most consistent behavioral effect of caffeine is to improve alertness and psychomotor function, particularly under conditions of fatigue.[5,6] There is also some debate regarding the extent to which, in habitual caffeine consumers, caffeine imparts absolute cognitive benefits as opposed to simply relieving the effects of caffeine withdrawal.[7,8] In addition to caffeine, chocolate also contains other MXs, notably theobromine, which may also be psychopharmacologically active. Theobromine, a caffeine derivative and metabolite found primarily in chocolate, is highly fat soluble, with levels peaking in the plasma 1–2 h after ingestion.[9] Like caffeine, theobromine binds adenosine receptors, indicating a potential for psychoactive properties similar to those of caffeine, although the functional binding properties of these two MXs are distinct. The other major, widely researched, potentially psychoactive components of chocolate are the flavonoids, a diverse type of natural compound that is ubiquitous in the plant kingdom. In the human diet, high levels of flavonoids are found in both green and black teas, grapes, red wine, apples, and, of particular relevance here, cocoa and cocoa-containing products.[10] Cocoa is particularly rich in flavonoids and contains a distinct complement of flavanols (a subclass of flavonoids). Cocoa contains simple monomeric (single unit) flavanols [primarily (–)-epicatechin] as well as two-unit dimeric and longer-chain oligomeric forms, the procyanidins.[11] There is a growing body of literature indicating that caffeine, theobromine, and cocoa flavanols (CF), in isolation and in combination, may have measurable neurocognitive effects.

The widespread consumption of chocolate and the evidence of health benefits from the constituents of chocolate were the basis for this systematic review of studies that evaluated the effects of whole chocolate and its potentially psychoactive components on mood and cognition. This review focuses on the direct effects of chocolate, ingested in experimental settings, on mood and cognition.

METHODS

Literature search

The following databases were searched: Medline, PsycINFO – Psychology, Web of Science, Google Scholar, Scirus, and Scopus – Food Science and Technology Abstracts.

Search strategy and search terms. Electronic databases were searched in early 2012. The following search terms were combined using the Boolean operators "AND" and "OR." Terms were nested by being enclosed in parentheses. Words beginning with "cognit" were truncated by the asterisk (*). In PubMed, the following limits were set: humans; clinical trial; randomized controlled trial. In PsycINFO, the limits were as follows: population group; human, methodology; empirical study. In Web of Science, search terms were refined by categories (neurosciences OR integrative complementary medicine OR behavioral sciences OR psychology multidisciplinary OR psychiatry OR psychology social OR psychology biological OR physiology OR psychology OR psychology clinical OR psychology applied OR psychology experimental) AND document type (= article).

The search terms in all databases were as follows: (chocolate OR cocoa OR theobromine) AND (mood OR cravings OR brain OR performance OR psychological test OR cognit* OR arousal OR thinking OR attention OR memory OR psychomotor OR concentration OR executive function OR affect OR emotion OR social).

All potentially relevant articles were categorized as belonging to one of four categories: 1) studies of the direct effects of chocolate/cocoa/theobromine on mood and cognition; 2) reviews and/or meta-analyses; 3) mechanistic studies, such as those in which the outcome measures of chocolate/cocoa/theobromine administration were physiological, e.g., cardiovascular effects, blood

lipid levels, etc.; or 4) studies of eating behavior in which chocolate/cocoa/theobromine was used as a stimulus rather than an intervention to examine differences in eating behaviors, e.g., cravers versus noncravers.

Of these four categories, only articles assigned to category 1 were subject to inclusion/exclusion criteria. These articles were tabulated and form the main focus of this review. Reviews and meta-analyses (category 2) were also searched for independently and are discussed when they provide context for empirical articles. Similarly, articles generated by the search that investigated physiological mechanisms or eating behaviors (categories 3 and 4) are discussed if they provide information that might provide a physiologically plausible mechanism for mood or neurocognitive effects.

Inclusion criteria. Several inclusion criteria were used to evaluate articles obtained by the search. Studies examining both male and female participants of any age were included. Only studies in which chocolate, cocoa, or theobromine was administered to human participants as an independent variable and as the central manipulation were included. Only research in which an appropriate placebo or control group was compared to one or more active treatment group(s) was included.

Outcomes. Studies using standardized outcome measures of both mood and cognitive performance were included. Studies examining quantitative measures of cognitive function alone were considered. For studies of mood, experiments employing both quantitative and qualitative measures were examined.

LO performed the initial data extraction, and the data were independently checked and audited by AS.

RESULTS

Research studies

The search of PubMed for human clinical trial studies retrieved 233 articles. PsycINFO generated 251 articles. Web of Science generated 287 articles. There were a total of 771 articles; of these, 161 were duplicates. The use of the search term "Theobromine" generated many hits related to the drug pentoxifylline. A number of articles were also related to caffeine, and a few articles also used chocolate-flavored foods or drinks as a vehicle for other drugs. In total, 465 articles were clearly not relevant to the subject area and were rejected on the basis of the title and abstract. Of the remaining articles, 75 were related to eating behaviors, 49 were related to mechanisms of action, and 21 were related to mood and cognitive function (4 of which were included under both mood and cognition categories). Of the 21 articles identified, 12 articles included measures of cognition and 13 included measures of mood. Four of the articles measured both mood and cognition, so these were included in both categories. Of these, eight that measured mood and five that measured cognition (one covering both categories) did not meet the inclusion criteria. Table 1 summarizes the characteristics of the excluded studies related to mood[12–18] and cognitive function.[12,19–22] The remaining 10 articles (6 mood, 7 cognition, with 3 covering both categories) form the basis of this review (Tables 2 and 3). Figure 1 shows the flowchart for the systematic review.

Reviews

The search of PubMed for reviews and meta-analyses used the same search terms as the original search, but the limit was set to reviews and meta-analyses. This search generated 115 articles, of which 26 were potentially relevant. In PsycINFO, the following limits were set: methodology; literature review. This search revealed 11 articles, of which 2 were potentially relevant. In Web of Science, when the search was restricted to literature reviews, 6 articles were identified, 2 of which were potentially relevant. A total of 30 reviews were identified.

Quality rating

Each of the selected articles was analyzed for methodological quality using a modified augmented Jadad scale,[23] as first developed by Sarris and Byrne.[24] Methodological quality is assessed on the Jadad scale using three factors: randomization, blinding, and reported withdrawals. The modified version used for this review is a 10-point scale that assesses the following additional methodological factors: 1) Was the study described as randomized? 2) Was the randomization protocol detailed and appropriate? 3) Was the study described as double blind? 4) Was the blinding process detailed and appropriate? 5) Did the study have a control group? 6) Was the control detailed and appropriate? 7) Were there adequate exclusion criteria? 8) Was the amount administered documented? 9) Was there a description of withdrawals and dropouts? 10) Were the data reported clearly and adequately?

Affirmative answers were given one point, and negative answers received no points; thus, the maximum possible rating was 10 points. Note that criterion 8 has been modified from "Was the intervention at a therapeutic dose?" to "Was the amount administered documented?" Two authors independently rated the studies and cross-compared answers. The modified Jadad scale is extremely prescriptive, so there was very little disparity between the two raters. In fact, ratings differed for only two articles (by 1 point in each case), and these differences

Table 1 **Reasons for exclusion of studies that examined associations between chocolate and mood and between chocolate and cognition.**

Excluded study	Reason(s) for exclusion
Studies examining chocolate and mood	
Beck et al. (2010)[12]	Treatment was a combination therapy and therefore it is impossible to discern the contribution of chocolate. The exact treatment was also not specified. Design was not specified (presumed between-subjects). The number of subjects per group was not specified. The mood or "social engagement" measure is a proxy measurement, as it was rated not by the participants but rather by nursing staff
Macht et al. (2002)[13]	No control condition was used for comparison
Martin et al. (2009)[14]	Outcome measures were biological rather than behavioral. "Mood" was discussed in relation to stress hormone response. All subjects ingested chocolate, and thus there was no control group for comparison
Mumford et al. (1994)[15]	Study was very underpowered, not balanced, and nonblinded. The statistical analysis was also inappropriate to demonstrate statistically significant differences in mood outcome
Nakamura et al. (2009)[16]	Chocolate was enriched and used as a vehicle for gamma-aminobutyric acid (GABA); therefore, effects of chocolate and GABA could not be dissociated
Radin et al. (2007)[17]	No control condition was used. There was some lack of reporting in some methodological areas
Smit & Blackburn (2005)[18]	No direct assessments of mood were included in this experiment. The study evaluated the participants' liking of methylxanthine
Studies examining chocolate and cognition	
Beck et al. (2010)[12]	Treatment was a combination therapy, and therefore it is impossible to discern the contribution of chocolate. The exact treatment was also not specified. Design was not specified (though was presumed between-subjects). The number of subjects per group was not specified. The cognitive outcome measures were not quantitative
Ingram & Rapee (2006)[19]	Task data were qualitative. Randomization was not specified. Inappropriate statistics and absence of post-hoc comparisons
Jones & Rogers (2003)[20]	No control condition for comparison to treatment. Cohort consisted of "dieters" and "non-dieters," with outcomes comparisons made between these two groups rather than with respect to the chocolate intervention
Rolls & McCabe (2007)[21]	Amount and type of chocolate treatment were not specified. Outcome measures relate to brain activation in response to taste and imagery in cravers verses non-cravers
Small et al. (2001)[22]	Amount of chocolate ingestion was not specified, as participants ate past satiety. No control condition was included. Outcome variables relate to brain activation in response to reward and punishment rather than cognition

were resolved upon reinspection of the articles. Overall the cognitive studies had a higher quality rating (ranging from 7 to 10; median 8) than the mood studies (range 5 to 9; median 6).

CHOCOLATE AND ASPECTS OF MOOD

Chocolate and eating behavior

There is a large body of research examining the effects of chocolate as a mood-enhancing agent as well as several plausible hypotheses for the possible effects of how food may produce a comforting or mood-ameliorating effect. Several inclusive reviews explored eating behavior in relation to chocolate.[25–29] Parker et al.[27] list several explanations of cravings for chocolate and carbohydrate, including self-medication, homeostatic correction, hedonic experience, addiction to psychoactive substances, and emotional eating. A complete review of the literature on eating behaviors is beyond the scope of this systematic review, but the uniqueness of chocolate as an often highly craved food merits some attention. Chocolate is the most commonly craved food, and, for most chocolate cravers, nonchocolate substitutes are inadequate.[30]

The capacity of carbohydrates (including chocolate) to have a comforting effect and to also promote "feel-good" sensations has been noted previously.[27] The possibility that chocolate consumption is a form of self-medication, inducing neurotransmitter activity that may have antidepressant benefits in seasonal affective disorder[31] and atypical depression,[29] has been also been suggested. Furthermore, using functional brain imaging, Chambers et al.[32] demonstrated that oral exposure to a glucose drink (swilling in the mouth, but not ingested) activated reward-related brain regions, including the anterior cingulate cortex and striatum, which were unresponsive to saccharin. The authors suggested the possibility of a class of yet

Table 2 **Summary of studies examining the effects of chocolate, cocoa, or theobromine on mood.**

Reference	Study design	Participants & treatment	Mood outcomes	Findings	Comments	Quality rating
Macht & Dettmer (2006)[48]	RM, OC, CO, R	$n = 37$ (age 19–30) healthy women. Two treatment conditions: 1) chocolate bar (50 g) 2) apple (approx. 170 g)	Mood was assessed at 5, 30, 60, and 90 min. Measures of hunger, desire to eat, nervous/tension, active/energetic, mood, guilt, anger/annoyed, fear, sad/depressed, joy/happy, and loneliness were measured on a bipolar scale from 1 (extremely bad) to 10 (extremely good)	Participants reported elevated mood during both the chocolate and the apple conditions, with this effect being greater at all time points in the chocolate condition. Participants in the chocolate condition also experienced greater feelings of guilt	A number of mood measures were evaluated in this experiment. An improvement was observed in ratings of "Stimmung," which translates as "mood" or "tendency." No effects, however, were observed on more specific mood indices, i.e., sadness, happiness, tension, etc	5/10
Macht & Mueller (2007)[49] (study 2)	IG, OC, R	$n = 48$ (age 19–49) men and women. Two treatment conditions: 1) 5 g of chocolate "Ritter Sport" ($n = 24$) 2) spring water ($n = 24$)	Neutral, positive, and negative mood states were induced using film clips. Mood was then measured using a 25-point scale divided into five categories (very good, good, medium, bad, and very bad). Participants selected a mood state "mood," "joy," or "sadness" and then gave a numerical value	Eating chocolate reduced negative mood, whereas only marginal differences were observed following the neutral and positive states	Mood measures were somewhat crude and ill defined. The study would have benefited from using a reliable and valid questionnaire to measure mood states	5/10
Macht et al. (2007)[49] (study 2)	IG, OC, R	$n = 113$ (age 18–43) men and women. Three treatment conditions: 1) highly palatable chocolate (5 g) ($n = 38$) 2) unpalatable chocolate (5 g) ($n = 37$) 3) nothing ($n = 38$) One type of milk chocolate and four types of plain chocolate with varying levels of cocoa were previously rated for palatability	Neutral, positive, and negative mood states were induced using film clips. Mood was then measured using a 25-point scale divided into five categories (very good, good, medium, bad, and very bad). Participants selected a mood state "mood," "joy," or "sadness" and then gave a numerical value	Negative mood was improved after eating highly palatable chocolate compared with unpalatable chocolate. This effect was short-lived, disappearing after 5 min	The highly palatable and unpalatable chocolate was rated by participants in the previous experiment, so not all the interventions were the same, i.e., differences in preference of light or dark chocolate. Therefore, no effects of the "active" constituents of the chocolate can be inferred	5/10
Mitchell et al. (2011)[55]	RM, PC, DB, CO, R	$n = 24$ (mean age 51.1 ± 12.7 years) healthy women. Four treatment conditions: 1) theobromine (700 mg) 2) caffeine (120 mg) 3) theobromine (700 mg) and caffeine (120 mg) 4) placebo (microcrystalline cellulose)	The Bond–Lader Visual Analogue Scale, a 16-item measurement scale divided into three factors (alert, calm, and content), was used	Theobromine alone decreased self-reported calmness 3 h after ingestion. Caffeine alone increased self-reported alertness at 1 h, 2 h, and 3 h after ingestion and increased contentedness at 1 h and 2 h after ingestion. The results found with the combination of caffeine and theobromine were similar to those found with caffeine alone but did not reach significance	Authors concluded that caffeine may have more CNS-mediated effects on alertness, while theobromine acts via peripheral changes. However, the in the combination condition, the dose of caffeine was the same as that in the caffeine alone, condition suggesting that theobromine may have a depressive effect on CNS and mood measures	9/10
Scholey et al. (2010)[56]	RM, PC, DB, CO, R	$n = 30$ (age18–35) men and women. Three treatment conditions: 1) 520 mg CF 2) 994 mg CF 3) 46 mg CF (control drink) 3-day washout between drinks	"Mental fatigue" scale (part of the Cognitive Demand Battery), a single visual analog scale measuring present feelings of fatigue, was used	Increases in self-reported mental fatigue were significantly attenuated by consumption of 520 mg of CF beverage only	This was a well-designed and well-conducted study but would have benefited from additional mood measures and a long-term administration protocol	7/10
Smit et al. (2004)[50] (study 1)	RM, DB, PC, R	$n = 20$ (age 18–56) men and women. Two active treatments: 1) 16 g of Cadbury's Bournville cocoa powder 2) 250 mg theobromine + 19 mg caffeine) 3) placebo (microcrystalline cellulose)	Tasks were performed at baseline and at 1 h and 2 h following treatment. Mood outcomes were measured using a 25-item visual analog scale derived from other validated mood measures. This scale was split into four factors: "energetic arousal", "hedonic tone", "appetite" and "nervous/dysphoric tension"	Following intake of the cocoa powder with the combination of caffeine and theobromine, energetic arousal was significantly increased compared with placebo. Hedonic tone was also increased. Energetic arousal was improved by both active treatments, but this effect only reached significance following the caffeine + theobromine combination	An excellent study, but the methodology is slightly lacking and would be difficult to replicate from the reported material	9/10
Smit et al. (2004)[50] (study 2)	RM, DB, PC, R	$n = 22$ (age 18–70) men and women. Three treatment conditions: 1) 8 mg caffeine + 100 mg theobromine (low MX dose) 2) 20 mg caffeine + 250 mg theobromine (high MX dose) 3) placebo (zero MX dose) 4) 60 ml water (to control for orosensory effects)	Tasks were performed at baseline and at 1 h and 2 h following treatment. Mood was measured as in study 1 (see above)	Energetic arousal and hedonic tone were greater following low and high MX doses compared with the water and zero MX treatments, but this effect failed to reach significance	As above	8/10
Weisenberg et al. (1993)[47]	IG, OC, R	$n = 100$ (age 18–21) men and women. Five treatment conditions. An impossible task was used t induce learned helplessness: 1) no impossible task, no treatment ($n = 20$) 2) impossible task, no treatment ($n = 20$) 3) impossible task and aerobic exercise ($n = 20$) 4) impossible task and chocolate ingestion ($n = 20$) 5) impossible task and guided imagery ($n = 20$)	Rating of anxiety (no further details are given)	Learned helplessness task increased anxiety in all conditions compared with the control condition (condition 1). All interventions (exercise, chocolate, and guided imagery) appeared to ameliorate this effect to a level comparable with that observed in the control condition	The rating of anxiety requires more explanation. Since all treatment conditions improved anxiety, it is possible that merely the presence of an intervention created interference, which reduced anxiety	5/10

Abbreviations: CF: cocoa flavanols; CNS, central nervous system; CO, crossover; DB, double-blind; IG, independent groups; MX: methylxanthine; OC, other control; PC, placebo-controlled; R, randomized; RM, repeated measures.

Table 3 **Summary of studies examining the effects of chocolate, cocoa, or theobromine on cognitive and neurocognitive function.**

Reference	Study design	Participants & treatment	Cognitive and neurological outcomes	Findings	Comments	Quality rating
Camfield et al. (2012)[61]	IG, DB, PC, R	$n = 63$ (age 40–65) men and women. Three treatments, 30-day daily administration: 1) 250 mg flavanol ($n = 21$) 2) 500 mg flavanol ($n = 21$) 3) placebo ($n = 21$)	Spatial working memory used as an activation task. Primary outcomes were amplitude and phase of SSVEP during 13 Hz flicker	No behavioral effects. Difference in phase and amplitude of SSVEP at parietal and frontal sites consistent with increased neural efficiency	The lack of treatment-associated behavioral effects is not unexpected, as the tasks were designed for activation only	9/10
Crews et al. (2008)[62]	IG, DB, PC, R	$n = 101$ (age ≥ 60) men and women. Two treatments, given daily for 6 weeks: 1) 37 g of a dark chocolate bar and 237 mL of an artificially sweetened cocoa beverage ($n = 51$) 2) similar placebo (not specified) ($n = 50$)	Validated neuropsychological tests: Selective Reminding Test, Wechsler Memory Scale III – Faces I and Faces II subtests, Wechsler Adult Intelligence Scale III – Digit Symbol-Coding subtest. Data obtained before and after 6 weeks of treatment	Failed to support the predicted beneficial effects of short-term consumption of dark chocolate and cocoa on any of the neuropsychological measures	No neuropsychological assessment at 3 weeks. Sensitivity of tests to interventions is potentially questionable	10/10
Field et al. (2011)[63]	RM, SB, OC, CO, R	$n = 30$ (aged 18–35) men and women. Two treatments: 1) dark chocolate containing 720 mg CF in 35 g 2) 35 g white chocolate (control condition). 1-week interval between testing sessions	Visual contrast sensitivity, motion sensitivity. Cognitive performance was assessed using a visual spatial working memory for location task and a choice reaction time task designed to engage processes of sustained attention and inhibition	Relative to the control condition, CF improved visual contrast sensitivity and reduced the time required to detect motion direction, and CF improved spatial memory and performance on some aspects of the choice reaction time task	Control was white chocolate, which differed in levels of CF but also in levels of caffeine and theobromine	7/10
Francis et al. (2006)[64]	RM, DB, OC, CO, R	$n = 16$ (age 18–30) healthy women. Two treatments, both of 5 days' duration (semichronic): 1) high-flavanol cocoa drink (172 mg flavanols per drink) 2) low-flavanol cocoa drink (13 mg flavanols per drink)	Alphabetic choice reaction time task with two switching sets of rules measuring reaction time and "switching cost." Participants were pretrained on cognitive tasks prior to test and then performed during an fMRI scan. BOLD contrasts were measured	Compared with low CF, high CF increased the BOLD signal intensity in response to a cognitive task. No significant differences were evident in behavioral reaction times, switch cost, or heart rate after consumption of CF	Training on tasks prior to study may have led to ceiling performance	8/10
Mitchell et al. (2011)[55]	RM, DB, PC, CO, R	$n = 24$ (age 18–70) healthy women. Four treatments. duration (acute administration): 1) theobromine (700 mg) 2) caffeine (120 mg) 3) combination of theobromine (700 mg) and caffeine (120 mg) 4) Placebo (microcrystalline cellulose)	Psychomotor/working memory performance (DSST) and blood pressure before and at 1 h, 2 h, and 3 h after administration	Treatment interaction effect on DSST performance reported but not interpretable from information given	Discrepancies describing DSST effects within text and inconsistencies between text and data presented make interpretation difficult	8/10
Scholey et al. (2010)[56]	RM, PC, DB, CO, R	$n = 30$ (age18–35) men and women. Three treatment conditions: 1) 520 mg CF 2) 994 mg CF 3) 46 mg CF (control drink) 3-day washout between drinks	Cognitive Demand Battery comprising two serial subtraction tasks (Serial Threes and Serial Sevens), an RVIP task, and a "mental fatigue" scale	Consumption of both 520 mg CF and 994 mg CF significantly improved Serial Threes performance. The 994-mg CF beverage significantly speeded RVIP responses but also resulted in more errors during Serial Sevens. Increases in self-reported "mental fatigue" were significantly attenuated by the consumption of the 520-mg CF beverage only	Findings suggest that cognitive demand may be an important determinant of acute cognitive enhancement	7/10
Smit et al. (2004)[50] (study 1)	RM, DB, PC, R	$n = 20$ (age 18–56) men and women. Two treatments (acute administration): 1) 16 g of Cadbury's Bournville cocoa powder (250 mg theobromine + 19 mg caffeine) 2) placebo (microcrystalline cellulose)	Tasks were performed at baseline and at 1 h and 2 h following treatment. Three tasks were used: SRT task, RVIP task, and Thurstone tapping task	SRT was significantly faster after cocoa powder and after the caffeine + theobromine combination than after placebo. For number of correct hits in the RVIP task, performance was marginally improved by cocoa powder compared with placebo, and was marginally and significantly improved by caffeine + theobromine compared with placebo. No significant effects were found for the tapping task	Slight differences between the magnitude of responses to cocoa powder and the magnitude of responses to the caffeine + theobromine combination	9/10
Smit et al. (2004)[50] (study 2)	RM, DB, PC, R	$n = 22$ (age 18–70) men and women. Three treatments: 1) 8 mg caffeine + 100 mg theobromine (low MX) 2) 20 mg caffeine + 250 mg theobromine (high MX) 3) placebo (zero MX)	Tasks were performed at baseline and at 1 h and 2 h following treatment. Three tasks were used: SRT task, RVIP task, and Thurstone tapping task	Higher levels of MXs improved reaction times over those obtained with placebo, but lower levels did not. Higher and lower levels of MXs also improved RVIP, with a more significant effect observed with higher levels	Measurement of other forms of cognitive function not dependent on reaction time and attention would have added useful data to this study	8/10

Abbreviations: BOLD, blood oxygenation level-dependent; CF, cocoa flavanols; CO, crossover; DB, double-blind; DSST, Digit Symbol Substitution Test; fMRI, functional magnetic resonance imaging; IG, independent groups; MX, methylxanthine; OC, other control; PC, placebo-controlled; R, randomized; RM, repeated measures; RVIP, rapid visual information processing; SB, single-blind; SRT, simple reaction time; SSVEP, steady-state visual evoked potential.

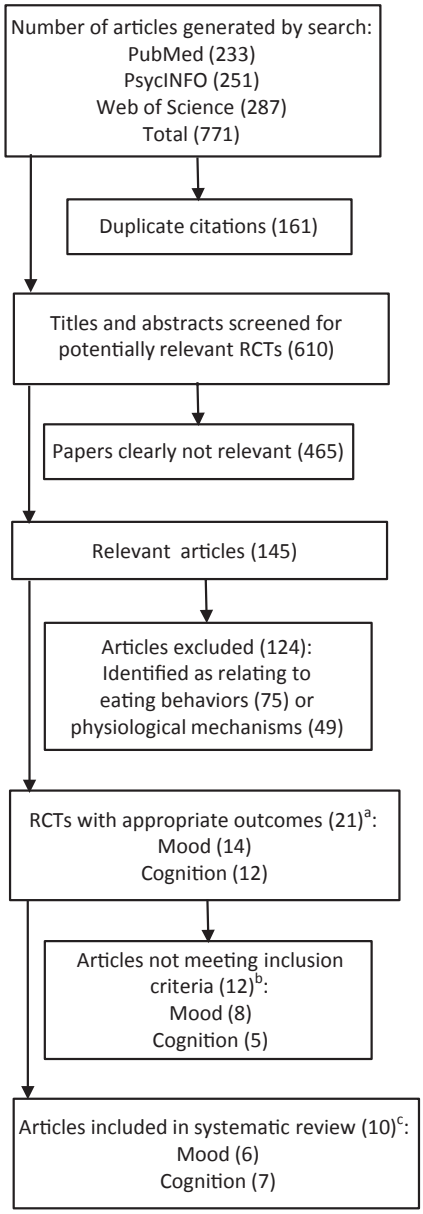

Figure 1 **Flowchart showing numbers of articles at each stage of the search.** Footnote a, b, and c include 5, 1, and 3 articles, respectively, describing studies that examined both mood and cognitive outcomes.

"unidentified oral receptors that respond to carbohydrate independently of those for sweetness." These findings suggest that carbohydrate orosensory detection prior to digestion may be associated with reinforcing effects, which may contribute to positive feelings and attributes related to chocolate consumption.

Potential psychoactive ingredients of chocolate have been evaluated in this context largely because chocolate craving appears to share some features with addiction. Several candidates have been identified (e.g., the biogenic stimulant MXs caffeine, theobromine, tyramine, and phenylethylamine). However, several authors have argued that these substances are present in concentrations are too low to have a significant psychoactive effect and, moreover, they are also present in higher concentrations in other noncraved foods.[26,27,30]

The prevailing view is that cravings can be explained fundamentally by the following specific orosensory qualities of chocolate: highly palatable, very sweet, and produces an optimal mouthfeel. It seems likely that the desire for chocolate arises from the unique flavor and synergistic relationship among its components. For example, milk chocolate appears to be the most preferred by subjects when milk chocolate, dark chocolate, white chocolate, and cocoa powder (powdered cocoa mass with some cocoa butter extracted) are compared. If cravings are elicited solely by psychoactive substances within chocolate, then cocoa powder should satisfy craving and dark chocolate should be the most preferred.[33]

Chocolate is frequently described as "sweet," but its high fat content is not always acknowledged. Drewnowski et al.[34] have therefore suggested that the term "carbohydrate craving" is a misnomer when applied to such foods.[34] Wurtman and Wurtman[31] initially presented a "serotonin hypothesis" of craving, which is described in many reviews and rejected as a potential mechanism underlying chocolate cravings. Other authors have also discussed the possibility of dopaminergic and opioid activity after chocolate consumption. However, while Parker et al.[27] noted the plausible relationship between the anticipatory pleasure of eating and the dopaminergic system, they also argue that any contribution of the dopaminergic system is unlikely to be chocolate specific. Drewnoski[35] has argued that carbohydrate craving is more strongly linked to the opioid system. Since then, Mercer and Holder[36] have proposed an opioidergic theory of food craving.[36] The opioid system appears to play a role in the palatability of preferred foods.[37] It has been suggested that endogenous opioid peptides enhance dopaminergic activity in the mesolimbic pathways to alter the reward value of food.[38]

Chocolate and cocoa contain the unsaturated *N*-acylethanolamines (*N*-oleoylethanolamine and *N*-linoleoyl ethanolamine), which are chemically and pharmacologically related to the endogenous cannabinoid anandamide. Anandamide, which translates as "internal bliss," is the endogenous brain lipoprotein that binds to and activates cannabinoid receptors within the brain, mimicking the psychoactive effects of cannabinoid drugs and resulting in heightened sensitivity and euphoria.[39] The researchers also found that the two *N*-acylethanolamines appear to interfere with the brain's ability to hydrolyze anandamide, hence they may extend the consequent sense of well-being. Again, it is possible that the concentration of anandamide analogs in chocolate is insufficient to induce these neurochemical effects.

The specific mechanism or, more likely, mechanisms of action responsible for the modulation of behavioral affect, craving, and mood produced by cocoa/chocolate are still not fully elucidated. Individual factors such as gender, age, dietary restraint, and susceptibility to various affective disorders have been proposed as major influences affecting chocolate cravings and/or "addictions." For example, being female and exercising a high level of dietary restraint makes it likely that guilt will be experienced after giving in to chocolate craving.[40,41] Self-reported "addicts" appear to display a relatively high level of affective or behavioral disturbance.[41,42] Associations between cravings and the premenstrual syndrome[43–45] or the seasonal affective disorder[46] suggest the contribution of hormonal fluctuations.

There appear to be several reasons why humans enjoy ingesting chocolate, and it is clear that, for many individuals, the particular combination of constituents may be specifically and uniquely craved. A number of potential psychomodulating mechanisms have been proposed, but the general consensus among the research community is that, while many psychoactive substances are present in chocolate, the amounts of these substances (at least in the forms of chocolate consumed today) are relatively small and are unlikely to cause behavioral modulation. A large body of research has demonstrated that individual factors may have specific influences on chocolate craving.

Studies included in the review

In this systematic review, evidence for effects on mood has been drawn only from research in which 1) a reported amount of chocolate (or components of chocolate) was ingested; 2) mood was measured as an outcome variable following chocolate ingestion; 3) an adequate control condition was employed; 4) statistical comparison between chocolate and control was conducted; and 5) quantitative measures of mood were used.

Following a literature search, a total of 14 relevant articles in which chocolate was consumed and mood was measured as an outcome variable were identified. Of these, eight did not meet the inclusion criteria, leaving six relevant articles describing eight studies (Figure 1 and Tables 1 and 2). These studies are discussed and appraised in detail below. Furthermore, some of the studies that were not considered to meet the inclusion criteria are also noted for their relevant contributions.

Effect of chocolate on mood

Several studies that were identified in the literature search examined the effect of chocolate on mood outcomes following experimentally induced mood states. The earliest of these, conducted in 1993, attempted to examine whether administration of exercise, guided imagery, or 50 g of chocolate could ameliorate negative emotions of learned helplessness. In this experiment, learned helplessness was induced by using an unsolvable task.[47] It was hypothesized that exposure to the unsolvable task would lead to higher levels of anxiety, engagement in more task-irrelevant cognitions, and poorer performance on a solvable task. It was also hypothesized that an intervention of 50 g of chocolate, 10 min of exercise, or guided imagery would improve these outcomes. A total of five groups were used in a parallel group design. In one group (control group), the participants were not primed with the impossible task for learned helplessness and were not given any intervention. Four other groups were exposed to the learned-helplessness task, after which chocolate, exercise, guided imagery, or nothing was administered. All participants in each of the five groups were then given the solvable task. As predicted, groups previously given the unsolvable task showed greater "anxiety arousal" compared with the group that was not given the unsolvable task. All interventions (exercise, chocolate, and guided imagery) appeared to ameliorate this effect to a level similar to that observed in the control group. For those who attempted the unsolvable task and were not given an intervention, anxiety levels remained unaltered. Weisenberg et al.[47] do not report the paired contrasts in this experiment, so it is difficult to ascertain the magnitude of difference between the three treatment conditions. Furthermore, while two control/comparison groups were employed in this study, it is difficult to discern whether the participants were affected by some form of placebo effect, since the control condition involved no intervention and all of the treatment interventions were similarly effective at reducing anxiety. Perhaps in the case of learned helplessness, simply having any form of intervention (compared with none) is perceived as having increased control, thereby contributing to the observed reduction in anxiety.

Three studies by Macht et al.,[13] Macht and Dettmer,[48] and Macht and Mueller[49] were identified in the literature search, the first of which[13] was excluded. Like the study of Weisenberg et al.,[47] this study also involved the induction of mood states prior to the administration of chocolate, followed by measurement of mood. The authors attempted to induce states of anger, fear, sadness, or joy by presenting emotive film clips to the participants. Unfortunately, this study did not employ a control condition for comparison, so it could not be included as part of the systematic review. Macht and Mueller[49] did, however, conduct a further study in 2007, in which mood states were again experimentally induced using film clips to emote feelings that were sad, happy, or neutral. This study used a parallel group design with a control condition: half

of the participants received chocolate (one piece, 5 g) and the other half received spring water. Mood was measured on a 25-point scale that was subdivided into five categories (very good, 21–25; good, 16–20; medium, 11–15; bad, 6–10; very bad, 1–5). The participants were instructed to first decide on their mood and then on the numerical gradation within that category (e.g., good mood, 18). In this study, two experiments were conducted. The first aimed to examine the immediate effects of chocolate consumption on mood. Specifically, it was hypothesized that eating chocolate would impact the mood of an individual when a negative mood had been induced, but not when a positive or a neutral mood had been induced. The authors confirmed this hypothesis, showing that negative mood was reduced in the chocolate eaters compared with the water drinkers. A second experiment compared the effects of eating palatable versus unpalatable chocolate on negative mood in order to ascertain whether a reduction in negative mood was due to a physiological effect of the chocolate or to the palatability of the chocolate. Negative mood was ameliorated only in the group that received palatable chocolate, and this effect disappeared after 3 min.[49] In this experiment, the authors suggested that eating a small amount of sweet food can improve experimentally induced negative mood.

In terms of chocolate's potential ability to ameliorate preexisting negative mood states, a study by Martin et al.[14] may shed some light on the mechanisms of this effect. Although this study did not meet the inclusion criteria for the present review, largely because the outcome variables were biological rather than behavioral, it is worth mentioning here. Participants were categorized as either "high" or "low" trait anxiety individuals (based on the State-Trait Anxiety Inventory). Biological fluids were collected during 3 test days at baseline, on day 7 (mid trial), and on day 14 (end of the trial). After the baseline measurement was taken, participants ingested 40 g of dark chocolate every day for the duration of the 2-week study. Subjects with higher "trait anxiety" showed a distinct metabolic profile indicative of a different energy homeostasis (lactate, citrate, succinate, *trans*-aconitate, urea, proline), hormonal metabolism (adrenaline, DOPA, 3-methoxy-tyrosine), and gut microbial activity (methylamines, *p*-cresol sulfate, hippurate). Dark chocolate reduced the urinary excretion of catecholamines and the stress hormone cortisol and partially normalized stress-related differences in energy metabolism (glycine, citrate, *trans*-aconitate, proline, β-alanine) and gut microbial activities (hippurate and *p*-cresol sulfate).[14] It is not possible to deduce whether these effects were the result of any one particular constituent of the chocolate, i.e., flavanols, MXs, or macronutrients with high caloric value. The authors themselves concluded that these markers of stress and metabolism may be modified through the actions of gut microbial activities and that administration of whole dark chocolate improves the activity of the symbiotic bacterial partners.[14] These findings require further evaluation and replication in conjunction with mood and stress measurements.

A further investigation by Macht and Dettmer[48] evaluated the effect of chocolate on mood, but this time in the absence of an induced negative mood. In this experiment, the notion that mood effects may be transient and due to simply ingesting a sweet snack was investigated. Mood was examined following ingestion of a chocolate bar, an apple, or nothing. This study used a repeated measures design for both treatment and time, with mood being rated at 5 min, 30 min, 60 min, and 90 min after ingestion. The following feelings were evaluated on a bipolar scale from 1 (extremely bad) to 10 (extremely good): "hunger," "desire to eat," "nervous/tension," "active/energetic," "mood," "guilt," "anger/annoyed," "fear," "sad/depressed," "joy/happy," and "loneliness."[48] The results showed that participants in both the chocolate and the apple groups reported elevated mood, with this effect being greater at all time points in the chocolate group. Participants in the chocolate group also experienced greater feelings of guilt.[48] It should be pointed out that no effects on any of the other mood measures were observed, and the term "mood" is perhaps the most ambiguous of the feelings measured.

In the studies listed thus far, the effects of whole chocolate administered in the form of chocolate bar/pieces were examined. No effects of individual constituents of chocolate can be inferred. In the studies by Macht and Dettmer[48] and Macht and Mueller[49] that are included in this systematic review, there is some disparity regarding the length of time these effects of chocolate on mood persist. In 2007, Macht and Mueller[49] observed that negative mood was ameliorated only after ingestion of palatable chocolate and that this effect disappeared after 3 min, whereas previous work by Macht and Dettmer[48] suggested that elevated mood following chocolate consumption was sustained for up to 90 min. In a review by Parker et al.,[27] it is suggested that eating chocolate may be a form of self-medication and that effects of chocolate on mood are as ephemeral as holding a chocolate in one's mouth.[27] The disparity in the work by Macht and Dettmer[48] and Macht and Mueller[49] may be the result of differences in experimental design, but clearly this large disparity merits further research. The observed effects of chocolate on mood in these studies seems likely to implicate the pleasurable consequences of consuming chocolate and the potential activation of reward pathways in the brain, as discussed above in the context of oral detection of the carbohydrate saccharin.[32] One avenue for future research might be to investigate the precise mechanisms by which these pathways become activated.

Effect of constituents of chocolate on mood

The effects of chocolate on mood and cognition have been theorized to be due to specific constituents of MXs (e.g., theobromine and caffeine) and CF. A few of the studies that were identified in the literature search have examined altered concentrations of these active ingredients in order to discern any selective benefit provided by individual components of chocolate. For example, Smit et al.[50] argued that MXs were the psychopharmacologically active component of chocolate. They describe two double-blind, placebo-controlled studies that measured the effects of cocoa powder versus MXs administered in opaque capsules (MX content equivalent to that of a 50-g bar of dark chocolate) on cognitive performance and mood. In the first study, participants received 11.6 g of cocoa powder, a caffeine and theobromine combination (19 mg and 250 mg, respectively), or placebo. Participants completed a test battery once before and twice after treatment administration. Mood was measured using a 25-item visual analog scale that was devised from other validated mood measures. This was the split into the following four factors: "energetic arousal," "hedonic tone," "appetite", and "nervous/dysphoric tension."[50] Following administration of both cocoa powder and the combination of caffeine and theobromine, energetic arousal was significantly increased compared with placebo. Hedonic tone was also improved by both of the active treatments, although this effect reached significance only with the caffeine-theobromine combination. In the second study, treatments were visually identical: 60-g portions of chocolate that contained no MXs (no MX), 8 mg of caffeine + 100 mg of theobromine (low MX), and 20 g of caffeine + 250 g of theobromine (high MX). These amounts are typically present in white, milk, and dark chocolate, respectively. Energetic arousal and hedonic tone again appeared to be greater following low and high doses of MX compared with water and zero-MX treatments, but this effect failed to reach significance. The authors argued that, while MXs may contribute to the popularity of chocolate, other attributes are likely to be more important in determining chocolate's particular appeal and in explaining related self-reports of chocolate cravings and "chocoholism."[50]

While the behavioral effects of caffeine have been well documented, those of the other major cocoa MX, theobromine, have been more tenuous. In fact, the lack of theobromine effects in preclinical behavioral research had previously led some authors to conclude that theobromine was behaviorally inert.[51–53] Theobromine is a caffeine derivative and metabolite found primarily in chocolate. It is highly fat soluble, peaking in the plasma 1–2 h after ingestion.[9] Theobromine is an adenosine receptor antagonist that appears to have equal affinity for A1 and A2A receptors, while caffeine shows a slightly lower affinity for A1 receptors.[54] Theobromine has one-fifth the stimulant effect of caffeine but has a longer elimination half-life.[9]

Only a few studies have examined the behavioral effects of theobromine in isolation. In two studies, Mumford et al.[15] aimed to determine whether participants could discriminate between the physiological sensations produced by 1) theobromine versus placebo (study 1), and 2) caffeine versus placebo (study 2). This study did not meet the inclusion criteria for the present systematic review because of the small sample size of seven subjects. Nevertheless, it showed that five of the seven subjects were able to discriminate a high dose of theobromine from a placebo or caffeine dose. In addition, it showed that the combination of caffeine (19 mg) and theobromine (250 mg) in capsules increased the self-reported mood construct "energetic arousal" and speeded simple reaction time compared with placebo capsules. More recently, Mitchell et al.[55] examined the potential synergistic and singular effects of theobromine and caffeine. They administered capsules of theobromine (700 mg), caffeine (120 mg), a combination of both, or placebo (microcrystalline cellulose) to 24 healthy female subjects. Aspects of participants' mood and psychomotor performance were measured using the Bond–Lader visual analog scale and the Digit Symbol Substitution Test (DSST), respectively. Blood pressure was also measured at baseline and at 1 h, 2 h, and 3 h after administration. Relative to placebo, theobromine alone decreased self-reported calmness at 3 h post ingestion and lowered blood pressure at 1 h. Caffeine increased self-reported alertness at all post-administration time points and increased contentedness at 1 h and 2 h. Caffeine was also associated with elevated blood pressure at 1 h. The combination of caffeine and theobromine had effects similar to those of caffeine alone on mood, except for the absence of blood pressure effects. The authors concluded that theobromine and caffeine could have differential effects on mood and blood pressure. It was tentatively concluded that caffeine may have more central-nervous-system-mediated effects on alertness, while theobromine may be acting primarily via peripheral physiological mechanisms.

Another potential active mood modulator in chocolate might be the CF. Scholey et al.[56] examined CF in a randomized, controlled, double-blinded, balanced, three-period crossover trial. In this trial, 30 healthy adults consumed drinks containing 520 mg of CF, 994 mg of CF, and a matched control, with a 3-day washout between drinks. Mood outcomes were assessed using the Spielberger State-Trait Anxiety Inventory and a "mental fatigue" scale, which was measured repeatedly over the course of 1 h. Increases in self-reported "mental fatigue" were signifi-

cantly attenuated by the 520-mg CF beverage only. The authors stated that the mechanisms of action in this trial may have been related to the potential vasoactivity of CF components on endothelial function and blood flow.

In summary, the data appear to demonstrate very reliable effects of chocolate and chocolate components in attenuating negative mood, i.e., learned helplessness,[47] negative mood associated with viewing a film,[13,49] or mental fatigue from repeated cognitive testing.[56] There have been some reports of improved mood in the absence of a prior negative mood state.[48] The most consistent mood-enhancing effects seem to occur following ingestion of whole chocolate rather than individual chocolate constituents (the latter being typically administered in capsules or drinks). This suggests such effects are derived from a combination of taste, texture, carbohydrate, and fat content rather than from individual psychoactive components or combinations thereof. However, some research has begun to examine the components of chocolate in order to discern any particular active constituents. Thus far, the evidence reviewed suggests that MXs (particularly caffeine) may have a role in the mood-altering effects of chocolate, particularly by increasing alertness, although it should be noted that the MX theobromine is also capable of conferring negative mood effects, including reductions in self-reported calmness.[15]

The total number of studies that could be considered for evaluation was only six. Considering the large body of research conducted to evaluate the effects of chocolate, there is clearly a scarcity of data available to answer the questions of whether, how, and for how long chocolate consumption affects mood. Additionally, neither publication bias nor the possibility that nonsignificant findings may be less likely to be published can be excluded.

FLAVANOLS AND NEUROCOGNITIVE FUNCTION

Neurocognitive effects

Epidemiological evidence supports the notion that long-term flavanol intake provides a number of health benefits, including neurocognitive enhancement and neuroprotective effects. A number of reviews in this area are recommended but are not scrutinized in detail here.[57–60]

Studies included in the review

Following a literature search, a total of 12 relevant articles in which chocolate was consumed and cognition was measured as an outcome variable were identified. Of these, five did not meet the inclusion criteria, leaving seven relevant articles describing eight studies (Figure 1 and Tables 1 and 3). These studies are discussed and appraised in detail below. Furthermore, some of the studies that did not meet the inclusion criteria are noted for their relevant contributions.

Of the articles met the inclusion criteria, all examined the cognitive effects of potentially psychoactive fractions of chocolate. Five studies focused on CF fractions of cocoa[56,61–64] and three (from two articles) on combinations of the MXs caffeine and theobromine.[50,55]

Effects of cocoa flavanols on cognitive function

Several studies have evaluated the cognitive effects of CF.

Francis et al.[64] studied the effects of CF on cognition and brain activation using functional magnetic resonance imaging (fMRI). Sixteen female subjects (aged 18–30 years) received 150 mg of CF and a control drink daily for 5 consecutive days in a study with a balanced, crossover design. On day 5 they underwent cognitive testing and fMRI. The cognitive assessment consisted of an attentional task in which letter-number pairs were presented in red or blue font. The task involved attending to the color of the font that signaled whether the letter (red) or digit (blue) was to be attended to. Depending on the color of the font, the correct response was then to press the left button (vowel/odd number) or right button (consonant/even number). Blocks of five letter-digit pairs were either "switch" (alternating colors) or "non-switch" (one color). Despite increased cerebral blood flow (CBF) and cortical activation following CF administration, there was no enhancement in task performance.[64] The trial used as an activation task a relatively demanding executive/attentional switching task. Such a task might be expected to be sensitive to CF. Prior to the treatment phase, however, participants were trained to a relatively high performance criterion (>95% accuracy). It is therefore possible that performance was already at asymptote, thus minimizing the possibility of detecting enhancement of task performance associated with CF administration.

A chronic (6-week) study by Crews et al.[62] assessed the neurocognitive effects of daily cocoa administration.[62] Older individuals (>60 years of age) ingested dark chocolate (37 g containing 397 mg of cocoa procyanidins) and a cocoa drink (273 mL containing 357 mg of cocoa procyanidins) or matching control products. Assessment included standardized tests of cognitive function, including tests of memory (Selective Reminding Test, the Wechsler Face Memory scale), psychomotor speed and working memory (Trail Making Test, DSST), and selective attention (Stroop Color and Word Test). There were no effects of treatment on cognitive function, nor were there changes in a range of physiological or other biomarkers measured at the 3-week midpoint or the 6-week endpoint

assessment. While these findings might suggest a lack of effect of CF (procyanidins) on cognition, there are a number of possible methodological reasons for the negative results. The authors themselves acknowledge the possibility that the cohort habitually consumed a flavonoid-rich diet. In addition, members of the cohort were cognitively high functioning, which decreased the likelihood of enhancement. It is notable that the cocoa condition was associated with a significantly increased heart rate at both the 6-week endpoint and the 3-week interim assessment, suggesting the treatment was bioactive and imparted physiological effects over and above the habitual diet. The authors suggest this may be attributable to the MXs (caffeine and theobromine) present in cocoa products, although this cannot be determined from the study. As in the study by Francis et al.,[64] the possibility that participants were already near ceiling performance, thereby minimizing the chances of capturing any positive effect of CF on cognitive function, cannot be excluded.[62]

Camfield et al.[61] conducted a randomized, double-blind, placebo-controlled trial whose primary aim was examination of changes in brain bioelectrical activity. Sixty-three middle-aged volunteers (aged 40–65 years) were administered a chocolate drink containing 250 mg or 500 mg of CF or a placebo drink daily over a 30-day period. Cognitive assessment consisted of a spatial working memory (SWM) task that involved remembering the location of onscreen stimuli, with a hold period of 3 s. Behavioral measures of accuracy and reaction time did not differ between treatment groups. The lack of effect on task performance is unsurprising, since the study was designed so that SWM was an activation task only.

Two studies that met the inclusion criteria for the present review investigated the acute effects of CF administration. Scholey et al.[56] investigated the acute cognitive effects of CF in a placebo-controlled, double-blind study of 30 young adult participants.[56] Following baseline measurements, subjects consumed drinks containing 520 mg or 994 mg of CF or a matched (low flavanol) control drink. Cognitive and mood assessments were administered over the course of 60 min and included the Spielberger State-Trait Anxiety Inventory ("State" portion), undertaken before and after a Cognitive Demand Battery comprising repeated cycles of two serial subtraction tasks (Serial Threes and Serial Sevens); a Rapid Visual Information Processing (RVIP) task measuring vigilance and working memory; and a "mental fatigue" scale. Compared with placebo, both 520 mg and 994 mg of CF significantly improved performance in the Serial Threes task. The 994-mg CF beverage significantly speeded RVIP responses but also resulted in more errors in the Serial Sevens task.

The authors point out that the greatest number of – and the most significant – effects on mood and cognition were observed during the fourth Cognitive Demand Battery cycle, which coincided with the 2-h peak CBF reported by Francis et al.[64] and the peak plasma epicatechin levels[65] measured in pharmacokinetic studies. The effects associated with 520 mg of CF on Serial Threes and "mental fatigue" ratings were evident during the first 10-min cycle of the Cognitive Demand Battery, raising the possibility that cognitive benefits may occur earlier than 90 min post administration (when the earliest cognitive data were gathered).

An acute study by Field et al.[63] examined the effects of CF on measures believed to be sensitive to blood flow changes. Thirty healthy young adults took part in a cross-over study. Outcome measures included contrast sensitivity (the point at which subjects could no longer distinguish between stimuli of increasingly similar luminance) and motion coherence threshold (the proportion of coherently moving dots required for subjects to detect them in an array of randomly moving dots). Participants also underwent two cognitive tests: an SWM task and a two-choice reaction time task. The latter had two phases – a block of predictable stimulus responses (alternating Y-N responses) and an unpredictable phase that also included a response inhibition element. Testing was administered 2 h after consumption of either a high-CF chocolate bar containing 773 mg of CF or a white chocolate control.

Both visual contrast sensitivity and motion sensitivity were improved in the high-CF group. There were also significant improvements in aspects of the cognitive tasks. The high-CF condition was associated with significantly better SWM accuracy and significantly faster choice reaction time during the predicable sequences only. The authors conclude that "increased cerebral blood flow may be producing an increase in motivation or attentiveness on the tasks." It should be noted that the study was not double-blinded, since the control treatment was a white chocolate bar. Moreover, the two treatments differed in their caffeine content (38 mg in the high-CF condition versus trace amounts in the control).

From the results of these two studies, it appears that CF administration can improve aspects of cognitive function following ingestion of single doses of 520 mg, 720 mg, or 994 mg.[56,63] In the one study that has compared different doses of CF, there was a better cognitive profile for 520 mg than for 994 mg.[56] The improved cognitive effects are detectable at 90 min post ingestion (and possibly earlier) and appear to peak at around 2 h post ingestion.

Studies on the cognitive effects of methylxanthines

Several studies have examined the cognitive effects of the major MXs, caffeine and theobromine, found in chocolate.

Mitchell et al.[55] examined the cognitive effects of caffeine (120 mg) and theobromine (700 mg) both alone and in combination in a cohort of women (age range, 18–70

years; mean age, 51.1 years). The study employed a placebo-controlled, four-period crossover design. Cognitive outcomes were scored using a computer-adapted version of the DSST and the Emotive Reaction Time Test (which also served as an implicit mood measure). The Motivation and Workload Questionnaire was also administered to gauge the level of effort required to perform the tasks. The effects on mood followed the predicted pattern. Caffeine alone and theobromine alone increased ratings of "interest in tasks," while caffeine alone had a similar effect on "eagerness to do tasks." The article is unclear about the effects of the treatments on DSST performance. Mean response times (fastest to slowest) are presented as follows: placebo, 2,110 milliseconds; caffeine-theobromine combination, 2,310 milliseconds; theobromine alone, 2,344 milliseconds; caffeine alone, 2,435 milliseconds. However, the text states that "the combination of theobromine and caffeine increased mean response time compared to the theobromine alone and decreased it compared to caffeine alone." Furthermore, the legend to Figure 1 in Mitchell et al.[55] and the key to groups also appear to be mismatched.

Smit et al.[50] reported two studies of the psychopharmacological actions of cocoa constituents. The first aimed to compare the effects of whole cocoa powder with the effects of MX content only. The effects of 11.6 g of cocoa powder (Cadbury's Bournville) and the effects of 250 mg of theobromine plus 19 mg of caffeine were compared with placebo (all treatments were encapsulated). Cognitive outcomes were measured using a variable-interval simple reaction time (SRT) task, the Thurstone tapping task of manual dexterity and psychomotor speed, and the RVIP task. The authors conclude that the cocoa powder and the MX treatments produced similar positive effects on SRT and RVIP results as well as on mood measures. It appears that the effects were more pronounced for the MX treatment than for the cocoa powder.

A second study reported in the same article examined the effects of two doses of MXs on the same tasks. The treatments were administered in a chocolate bar containing no MXs, a low dose of MXs (8 mg of caffeine, 100 mg of theobromine), or high dose of MXs (20 mg of caffeine, 250 mg of theobromine). A water control was also included. The results revealed a dose-response effect on SRT performance, with significant effects at the highest dose only, and with more significant effects on RVIP performance at the higher dose than at the lower dose. The authors conclude that the MXs are the psychoactive components of chocolate. This contention is partially supported by the findings of Mitchell et al.[55] and Smit et al.[50]; however, in light of the demonstrable acute psychoactive effects of other components of chocolate (notably, CF), this conclusion is premature. Future studies directly comparing the effects of caffeine, theobromine, and CF, both alone and in combination, might be useful.

Summary of neurocognitive effects

There is growing evidence of improved cognitive function with acute administration of CF and MXs. Attentional, working memory, and executive function were improved between 90 min and 150 min after administration of CF.[56] Working memory and reaction time were improved 2 h following administration.[63] A caffeine-theobromine combination produced cognitive effects similar to those of to cocoa powder and improved psychomotor function/attention and working memory in a dose-dependent manner.[50] There was also evidence of improved cognitive function with a caffeine-theobromine combination, although some inconsistencies in the reporting of the cognitive effects made interpretation difficult.[55] In addition, the levels of caffeine (120 mg) and theobromine (700 mg) administered were high compared with those that might be realistically found in chocolate products.

In summary, the literature on the neurocognitive effects of chocolate and its components shows that, despite seemingly strong evidence from epidemiological studies, no study has found cognitive effects in randomized controlled trials using subchronic or chronic administration. All these studies evaluated the subchronic/chronic effects of administration of a cocoa-flavanol-rich fraction. Dosing regimens have included 5 days,[64] 30 days,[61] 3 weeks, and 6 weeks.[62] In all cases, there are possible methodological reasons for the lack of positive findings. There is evidence that certain physiological processes underlying cognitive function are affected, including CBF[62,64] and region-specific brain activation.[64]

MECHANISMS OF ACTION OF CHOCOLATE

The exact mechanisms by which components of chocolate may benefit cognitive processing remain unknown. The following section briefly describes potential processes that might plausibly benefit neurocognition, most of which have focused on CF. Dietary intervention trials have shown that the consumption of flavanol-rich cocoa products can lead to changed patterns of neural activity, improved insulin sensitivity,[66] lowered blood pressure,[67] reduced platelet aggregation,[68] and improved endothelial function[69] and blood flow[66,70–74]; the role of antioxidant activity will also be briefly considered.

Cocoa flavanols and neuroimaging

Francis et al.[64] evaluated the effects of CF administration on brain activation during an attentional switching task (described earlier). Compared with a control condition, CF administration resulted in higher levels of task-associated brain activation in the dorsolateral prefrontal cortex, the anterior cingulate cortex, and the parietal

cortex. The participants had ingested CF on the day of assessment (day 5 of the subchronic trial), thus the results did not preclude the possibility of acute effects on cerebral metabolism. Consequently, the authors conducted an additional small acute trial ($n = 4$ subjects) on the effects of CF on CBF. Ingestion of CF resulted in transiently increased CBF at 2 h, which returned to baseline levels by 6 h.

Camfield et al.[61] conducted a randomized, double-blind, placebo-controlled trial using a different brain-mapping methodology known as steady-state topography.[61] Steady-state topography is a variant of electroencephalography that has proven to be highly sensitive to nutritional interventions. Sixty-three middle-aged volunteers (aged 40–65 years) were administered chocolate drinks containing 250 mg or 500 mg of CF or a placebo every day over a 30-day period. The steady-state visual evoked potential (SSVEP) to a 13-Hz steady-state stimulus was recorded during the completion of an SWM task as described above. The primary outcomes were changes in the amplitude and the phase of the SSVEP response, both of which were compared between treatment groups at baseline and after 30 days. Both SSVEP amplitude and phase were significantly different between groups at posterior parietal and centrofrontal sites during memory encoding, the working memory hold period, and retrieval. These areas constitute a parietofrontal circuit that is reliably activated during working memory tasks. These differences can be interpreted as evidence of greater neural efficiency associated with CF consumption during working memory operations.

These neuroimaging studies demonstrate that CF or their metabolites are bioactive and centrally active and can influence cortical activity both acutely and after long-term (30-day) administration.

Antioxidant effects

It is commonly believed that many of the health benefits of CF are due to their antioxidant properties. It is now widely accepted, however, that these ex vivo effects may not translate to in vivo antioxidant properties (for reviews, see Frei[75] and Halliwell[76]). It is now known that flavanols undergo extensive biotransformation following ingestion, resulting in compounds with greatly diminished antioxidant capacity. An antioxidant role has yet to be substantiated in biological systems using physiologically realistic levels of orally administered CF. Furthermore, it should be noted that any effects of CF on antioxidant capacity, if present at all, are likely to be observed only after long-term administration of CF. In the light of the lack of any reported long-term cognitive effects of CF, antioxidant mechanisms are unlikely to play a role in cognitive changes in healthy individuals.

Effects on insulin sensitivity

Administration of flavanol-rich dark chocolate has been shown to increase insulin sensitivity in hypertensive[66] and healthy adults.[77] There is a great deal of evidence to suggest that increasing glucoregulatory control via improved insulin sensitivity can improve cognitive function. For example in healthy young adults, poorer glucoregulation is associated with worse performance on tests of memory[78,79] and vigilance,[79,80] and insulin resistance is directly related to impaired executive functioning.[81] Thus, insulin sensitivity is a modifiable factor that may impinge on cognitive function.[82] Again, such effects are more likely with long-term dosing.

Vascular effects

There is also increasing evidence that consumption of CF can improve a host of parameters that reflect increased peripheral and central blood flow.[66,70–74] While the mechanisms underlying these effects are still unknown, they may be related to changes in the pool of bioavailable nitric oxide (NO), known to be a key signaling molecule that mediates changes in vascular function.[69,83,84] Ingestion of 200–500 mg of CF resulted in an acute increase in blood vessel dilation.[70] It is known that the delivery of metabolic substrates can lead to improved performance of mentally effortful tasks.[85–88] It is not unreasonable to conclude that such effects may contribute to the acute cognitive benefits described for CF. Indeed, the peak effects described at 2 h post ingestion of CF in the two acute studies that met the inclusion criteria[56,63] coincide with the largest, dose-dependent increases in flow-mediated dilatation.[74] These results are consistent with literature showing that natural products that increase CBF or increase brain metabolism are particularly effective in enhancing cognitive performance during prolonged, effortful, cognitive processing.[86]

Effects on cerebral blood flow

CBF is particularly relevant to neurocognitive function. A number of studies have found direct effects of CF on CBF. Sorond et al.[89] reported no acute effect of 450 mg of CF on CBF in a healthy older cohort. After 1 and 2 weeks of CF supplementation, however, there was higher mean flow velocity (MFV) in the middle cerebral artery in treated versus untreated subjects, as measured by Doppler ultrasound. The effects reached significance at 1 and 2 weeks after daily CF supplementation. There were, however, no significant effects on MFV on day 1; indeed, there was a slight (though nonsignificant) decline in MFV 2–4 h after CF ingestion. These results suggest that subchronic (1 or 2 weeks) administration of CF can improve CBF.

Putative mechanisms in relation to cognitive function

How might these potential mechanisms relate to improved cognitive function? It is known that increasing the provision of metabolic substrates can be cognition enhancing. Thus, inhalation of pure oxygen[87,88,90,91] or imbibing glucose,[80,92] for example, can enhance cognitive performance. It also appears that such effects are more marked during cognitive processing that involves a relatively high level of mental effort.[85,86,92–94] Recruitment of local neural tissue during cognitive processing is tightly coupled to CBF, and NO, released from cortical neurons in an activity-dependent manner, is key to coupling neuronal activity to increased blood supply in active tissue.[95] There is good evidence that CF (and other polyphenols) can increase CBF. It might be tentatively speculated that the acute enhancement of cognitive performance associated with CF during high cognitive demand is related to the interaction between local tissue demands, which is mediated by NO-dependent central vasodilation.

Furthermore, the possibility that caffeine, theobromine, or other components of the drinks (such as magnesium[96]) interact differentially with CF to produce the neurocognitive effects of chocolate and its components cannot be ruled out.

CONCLUSION

The aim of this systematic review was to evaluate whether chocolate or its constituents are capable of ameliorating mood and cognitive function. Six studies met the inclusion criteria for mood assessment. Of these, five showed either an attenuation of negative mood or a facilitation of mood state when interventions were compared with their respective controls,[47–50,56] with the most robust mood effects being associated with whole chocolate rather than its constituents. Only one study failed to show a clear improvement.[55] In that study, the effects of theobromine and caffeine appeared to have differential mood effects, possibly due to different central nervous system effects. In terms of cognitive function, seven studies met the inclusion criteria, of which only three demonstrated clear cognitive facilitation.[50,56,63] Two studies that failed to demonstrate behavioral benefits, however, did identify changes in functional brain activity, reflected as differences in signal intensity and blood oxygen utilization (electroencephalography and fMRI) in treated versus control subjects.[61,64]

The articles evaluated in the present literature research utilized a wide range of cognitive and mood evaluations. Overall, the cognitive studies had a higher quality rating than the mood studies. The latter reported almost exclusively positive effects, though it is unclear whether this is due to the palatability or the mouthfeel of chocolate or to some aspect of psychopharmacological action. Cognitive effects appear to be less robust, although only two studies to date[56,63] have examined the acute cognitive effects of cocoa supplementation. In order to more fully understand the behavioral effects of chocolate and its components, further exploration of acute cognitive effects is required, along with examination of functional brain changes associated with CF.

Only one article[62] in this review scored 10 on the modified Jadad rating scale, and many of the articles might have been improved by including more details of key aspects of the methodology employed. In some cases, the precise nature of the intervention (including the constitution of chocolate used) was unclear or missing from the manuscript, while other studies were poorly controlled (Table 1). A wide range of mood and cognitive measures were included, sometimes making comparisons across studies difficult. Future studies should include as positive controls measures similar to those previously revealed as significant to the effects of chocolate and/or its components. Additionally, the inclusion of appropriate biomarkers, either as direct measures of absorption or as a means to evaluate putative mechanisms involved in behavioral effects, is recommended. Given the potential benefits to vascular function, particularly from CF, the latter might include measures of cardiovascular function and/or CBF. The use of more sophisticated neuroimaging methodologies such as fMRI and magnetoencephalography would help elucidate the underlying mechanisms of behavioral effects. Finally, since chocolate and cocoa contain multiple bioactive compounds, one approach might be to examine the neurocognitive effects of combinations of potential functional ingredients. Given the difficulties in disentangling pharmacological effects from those related to taste, palatability, and the mouthfeel of chocolate, studies directly comparing the same ingredients delivered in chocolate and in capsules may prove fruitful.

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