BEST in Mental Health
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Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"In healthy adults, how effective is the consumption of cocoa flavanols/cocoa polyphenols, particularly drinking cocoa, for improving memory and cognitive function?"

Clarification of question using PICO structure

Patients:	Adults
Intervention:	Cocoa flavanols/cocoa polyphenols
Comparator:	Any
Outcome:	Memory; Cognition

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Clinical and research implications

Evidence from two small randomised controlled trials suggests that the consumption of high flavanol chocolate (520 to 994 mg), either as a bar or drink can improve cognitive outcomes. However these results only apply to healthy young adults aged between 18 and 35 years, and the cognitive outcomes were measured fairly soon after the chocolate consumption (between 90 and 120 minutes afterwards). Further research is needed into other populations, and whether these benefits are long-lasting.

Three other trials did not find any benefits for cognitive outcomes but also suggested areas for further research: in other populations and cognitive domains, over longer time scales, at different doses, and also monitoring relevant biomarkers and in other cognitive domains, and whether cocoa polyphenols can reduce symptoms of clinical anxiety or depression.

What does the evidence say?

Number of included studies/reviews (number of participants)
Five randomised trials were included (total number of participants = 311, ranging from 30 to 101). All compared different amounts of chocolate, given as a bar or as a drink.

Main Findings
One trial in 30 healthy young adults (aged 18 to 25 years), found that after consuming a bar of high flavanol chocolate (773 mg) the participants had significantly better performance on a contrast sensitivity test, a visual spatial test and also a faster reaction time, compared with low flavanol chocolate (trace amount). Another trial, in 30 healthy volunteers (aged 18 to 35 years) also found significant increases in a cognitive test (serial threes subtraction) for both high (994 mg) and low (520 mg) flavanol cocoa drinks compared with a control drink (46 mg). These were the only two trials to report positive findings for cognitive outcomes.

The three other trials did not find any benefits of cocoa on cognitive or memory outcomes. One reported a significantly higher pulse rate with a daily chocolate bar and cocoa drink and another reported a significant increase in self-rated calmness and contentedness with a high polyphenol chocolate drink compared to low polyphenol and control drinks.

Authors Conclusions
The authors of the two trials that found benefits of chocolate on cognition or memory concluded that: tests of visual system function in healthy young adults can be improved by the acute consumption of cocoa flavanols with effects likely to last several hours. Improvements in cognitive performance were also demonstrated (Field). The second trial concluded that their findings suggest that the consumption of 520 mg CF may be beneficial to performance and mood during highly effortful cognitive processing (Scholey).

The other trials concluded that: behavioral measures of accuracy and reaction time were not found to be significantly different between treatment groups, however, significant brain activation differences can be interpreted as evidence of increased neural efficiency in spatial working memory

function associated with chronic cocoa flavanol consumption (Camfield); this trial failed to support the predicted beneficial effects of short-term dark chocolate and cocoa consumption on any of the neuropsychological or cardiovascular health-related variables included in this research. Consumption of dark chocolate and cocoa was, however, associated with significantly higher pulse rates at 3- and 6-wk treatment assessments (Crews); and that a high dose of cocoa polyphenols, relative to placebo, was found to improve self-rated calmness and contentedness following 30 days of treatment but neither altered cognitive performance acutely or after 30 days of treatment (Pace).

Reliability of conclusions/Strength of evidence

The two trials providing evidence for the question were both fairly small (30 and 87 participants). The smaller trial used a cross-over design which is advantageous as it means all participants acted as their own control, however it was of moderate risk of bias as some aspects such as details of the randomisation were not reported. It was also the only single-blind trial as the participants knew which type of chocolate they were eating, but not the experimenters, and this could have influenced the results. The other trial was double-blind and used chocolate drinks matched for taste, overall this was a better quality trial and judged to be at a low risk of bias.

Overall, the trial conclusions appear to be reliable but as there was only evidence available from two small trials, the strength of evidence in this area is low.

What do guidelines say?

Neither National Institute for Health and Care Excellence (NICE) nor Scottish Intercollegiate Guidelines Network (SIGN) guidelines comment upon the use of coca flavanols or cocoa polyphenols for improving memory or cognitive performance.

Date question received: 13/11/2014
Date searches conducted: 04/12/2014
Date answer completed: 18/12/2014

References

1) Camfield, D. A., Scholey, A., Pipingas, A., Silberstein, R., Kras, M., Nolidin, K., ... & Stough, C. (2012). Steady state visually evoked potential (SSVEP) topography changes associated with cocoa flavanol consumption. *Physiology & Behavior*, *105*(4), 948-957.

2) Crews, W. D., Harrison, D. W., & Wright, J. W. (2008). A double-blind, placebo-controlled, randomized trial of the effects of dark chocolate and cocoa on variables associated with neuropsychological functioning and cardiovascular health: clinical findings from a sample of healthy, cognitively intact older adults. *The American Journal of Clinical Nutrition*, *87*(4), 872-880.

3) Field, D. T., Williams, C. M., & Butler, L. T. (2011). Consumption of cocoa flavanols results in an acute improvement in visual and cognitive functions. *Physiology & Behavior*, *103*(3), 255-260.

4) Pase, M. P., Scholey, A. B., Pipingas, A., Kras, M., Nolidin, K., Gibbs, A., ... & Stough, C. (2013). Cocoa polyphenols enhance positive mood states but not cognitive performance: a randomized, placebo-controlled trial. *Journal of Psychopharmacology*, 0269881112473791.

5) Scholey, A. B., French, S. J., Morris, P. J., Kennedy, D. O., Milne, A. L., & Haskell, C. F. (2009). Consumption of cocoa flavanols results in acute improvements in mood and cognitive performance during sustained mental effort. *Journal of Psychopharmacology*.

Results

RCTs

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Camfield et al. (2011)	*Participants*: Aged between 40-65 years; non-smokers; no history of anxiety, depression, psychiatric disorders or epilepsy; no history of heart disease or high blood pressure; not taking any medications; no health conditions that would affect food metabolism. *Intervention*: (1) High flavanol. 10g Acticoa dark chocolate per day for 30 days, containing 500mg flavanol polyphenols; (2) Medium flavanols. 10g standard dark chocolate per day for 30 days, containing 250mg flavanol polyphenols. *Comparator*: Placebo – low flavanol. 10g dark chocolate per day for 30 days, containing 0mg flavanol polyphenols. All treatments were given as a chocolate drink in 200 ml of water. *Outcome*: Spatial working memory (SWM), assessed using an experimental computer task. Two or three dots appeared in random locations on a screen, then disappeared for 3000ms. A circle appeared	N = 63	The mean participant age was 52.3 years. Two were excluded from the analysis, leaving a total of 61. The mean accuracy of the SWM test was measured at baseline and after 30 days. The mean accuracy (percentage correct) on the SWM task was significantly improved at 30 days compared to baseline, but there was no statistically significant difference between the low, medium and high flavanol groups. For the mean response time there was no statistically significant change over time, or between the three groups.	Low Treatment order was made using random allocation to a Latin square. The randomisation method was appropriate but it was unclear if allocation concealment was maintained as it was not reported when this happened (e.g. before or at the first assessment). This study was double-blind and used placebo drinks, all were given in the same quantity. As outcomes were measured on a computer, the outcome assessment was also blinded. Two participants were

	on the screen and participants were required to answer 'yes' or no', depending on if they thought the circle appears where a dot initially was. Two blocks of 40 trials.			excluded from the analysis but this was not enough to affect the reliability of the results. All outcomes appear to have been reported.
Crews et al. (2008)	*Participants*: Healthy adults with no history of dementia or neurocognitive impairment, hypertension, head injuries, learning disabilities, psychiatric or substance abuse disorders. Not using additional chocolate or cocoa-related products during the study. They had to have a total MMSE score ≥24 out of 30. *Intervention*: Dark chocolate and cocoa: one flavonoid-rich chocolate bars (11g natural cocoa) and one cocoa drink (11g natural cocoa), taken daily for 6 weeks. *Comparator*: Placebo: products which were matched to the active intervention in terms of appearance, taste, smell, and caloric content. Daily for 6 weeks. *Outcome*: Verbal learning and memory (Selective Reminding Test, SRT) memory (Wechsler Memory Scale-III Faces I and Faces II subtests), executive functioning including visual attention and task switching (Trail Making Test, TMT)	N = 101	The mean participant age was 68.7 years and 42% were male. Treatment adherence was98% in both groups. The analysis was per-protocol and based on 90 (89%) out of the 101 participants randomised. There were no statistically significant differences between the chocolate and placebo groups for any of the neuropsychological outcome measures (measured as mean change from baseline). The largest difference was seen for the change in the Wechsler Adult Intelligence Scale-III digit symbol test (3.36 for chocolate and 3.51 for placebo) but this was still not significant (p=0.094). The only outcome to be statistically significantly different between the groups was the pulse rate. At the midpoint 3 week assessment the mean pulse rate for the chocolate group was significantly higher (p <	Low Computerised randomisation was performed by an independent researcher. Products were labelled with randomisation numbers and issued in sequential order, so allocation concealment was maintained. This study was double-blind and chocolate bars and drinks were matched for appearance, smell, taste and calorie content. Due to the types of outcome measures, this meant that outcome assessment was also blinded.

	selective attention (Stroop Colour-Word Test, SCWT), visual-motor speed/motor co-ordination (Wechsler Adult Intelligence Scale-III Digit Symbol-Coding subtest, WAIS).		0.01) than for the control group.	Not all randomised participants were included in the analysis (11% excluded) so this might have introduced bias. All outcomes appear to have been reported.
Field et al. (2011)	*Participants*: Aged 18-25 years old, with normal visual acuity. Exclusions: having a medically restricted diet or any kind of ongoing illness. *Intervention*: High cocoa flavanols: 35g of commercially available dark chocolate (773mg cocoa flavanols) – one bar consumed, with cognitive testing occurring 2 hours later. *Comparator*: Low cocoa flavanols: 35g of commercially available white chocolate per day (trace amounts of cocoa flavanols) – one bar consumed, with cognitive testing occurring 2 hours later. The comparator tests occurred one week later. *Outcome*: Visual spatial working memory computer experiment (VSWM): Objects appeared on screen for 3 seconds, followed by a blank screen for 1 second. The objects re-appeared and participants	N = 30 (crossover design, with participants tested again a week later)	No information about the participants was provided. The percentage of digits read correctly was significantly higher with high cocoa flavanols than with control for 2 out of 6 stimulus contrasts, with mean improvements of 8.9% and 13.3%. The percentage correct on the visual spatial test was also significantly higher with high cocoa flavanols than with control (mean 87.1% compared with 83.5%). The predictable reaction time was significantly faster with high cocoa flavanols (median 517 ms compared with 557 ms).	Moderate No information was provided about the method of randomisation. This study was single-blind in that the participants knew which type of chocolate they were eating (dark vs. white), but the experimenters did not. As the experimenters were blind, and outcomes were measured by a computer, it is likely that the outcome assessment was also blinded. It was unclear if there were

	had to choose the two which had switched places. Six each of easy, medium and hard trials were included. Choice reaction time (CRT): Participants had to press one of three keyboard buttons as quickly as possible in response to letters or digits that appeared on screen.			any dropouts, or if all participants were in the analysis. All outcomes appear to have been reported.
Pase et al. (2012)	*Participants*: Healthy adults aged 40-65 years. Exclusions: history of heart disease or hypertension; psychiatric disorders or epilepsy; any physical illness affecting food metabolism; not currently taking vitamin supplements or illegal drugs. *Intervention*: (1) High dose: 20g dark chocolate drink containing 500mg cocoa polyphenols, daily for 30 days; (2) Low dose: 20g dark chocolate drink containing 250mg cocoa polyphenols, daily for 30 days. *Comparator*: Placebo: 20g dark chocolate drink containing 0mg cocoa polyphenols, daily for 30 days. *Outcome*: Cognitive performance	N = 87 randomised but 69 analysed	The mean participant age was 52 years and 34% were male. There was no statistically significant difference between the chocolate and placebo groups for any of the cognitive outcomes after 30 days. However, there was a significant increase in self-rated calmness and contentedness for the high polyphenol group compared with the low polyphenol and control groups.	Low Randomised was computer generated and performed by an independent third party. The trial was double-blind and all drink mixes were matched for taste, energy and calories. Outcomes were measured by the participants, so this was also blinded. Not all randomised

	(Cognitive Drug Research computerised assessment system, to measure: Quality of working memory, QWM; Quality of episodic secondary memory, QESM; Continuity of attention, CA; Speed of memory, SM; Power of attention, PA).			participants were included in the analysis (21% excluded) so this might have introduced bias. All outcomes appear to have been reported.
Scholey et al. (2010)	*Participants*: Health volunteers aged 18-35, and free from illicit drugs and prescription medication. Abstaining from caffeine, alcohol, and chocolate/cocoa for 12h prior to testing. *Intervention*: (1) High dose: one cocoa drink containing 994mg cocoa (2) Low dose: one cocoa drink containing 520mg cocoa flavanols *Comparator*: one cocoa drink containing 46mg cocoa flavanols. *Outcome*: Cognitive performance measured 90 mins after drink consumption. Outcomes were measured every 10 minutes for 60 minutes: Cognitive Demand Battery comprising two computerised tests (1. Serial Threes Subtraction Task – count backwards in 3s from a given number as fast and accurately as possible; 2. Serial Sevens Subtraction Task – count backwards in 7s from a given number as fast and accurately as possible); Bakan Rapid Visual	N = 30 (crossover design, with participants tested in all 3 conditions at least 3 days apart)	The mean participant age was 21.9 years and they were healthy, non-smoking undergraduate and postgraduate students. In the cognitive tests, the number of correct serial threes was significantly increased with both the high and low dose cocoa drinks compared with control (mean changes of 5.07 for low cocoa, 3.13 for high cocoa, and 1.93 for control; $p<0.001$). However the consumption of the high cocoa drink resulted in significantly more errors on the serial seven subtraction test compared with the other drinks. No significant differences were seen between the drinks for RVIP accuracy.	Low Random allocation used a Latin square design to allocate the order of treatments and this happened at the start of the first session. Drinks were identically packaged by a third party and labelled with a random number, so concealment was maintained. All drinks were identical in packaging and appearance so double-blinding was maintained. Outcomes were measured by the participants, so this was also blinded. It was unclear if there were

	Information Processing task (RVIP – monitor a series of digits for 3 consecutive odd or even digits); Mental fatigue visual analogue scale (MF; participants rated their current subjective mental fatigue from 0-100).			any dropouts, or if all participants were in the analysis. All outcomes appear to have been reported.

Risk of Bias:

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Camfield et al. (2011)	☺	?	☺	☺	☺	☺
Crews et al. (2008)	☺	☺	☺	☺	☹	☺
Field et al. (2011)	?	?	☹	☺	?	☺
Pase et al. (2012)	☺	☺	☺	☺	☹	☺
Sholey et al. (2010)	☺	☺	☺	☺	?	☺

☺Low Risk ☹High Risk ? Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
SRs and Guidelines			
NICE	Cocoa memory (0) Cocoa cognition (0)	0	0
DARE	1 (cacao* or cocoa* or chocolat*) IN DARE 15 Delete 2 MeSH DESCRIPTOR Cacao EXPLODE ALL TREES 12 Delete 3 #1 OR #2 16 Delete	216	0
Primary studies			
CENTRAL	#1 MeSH descriptor: [Cacao] explode all trees 193 #2 cacao* or cocoa* or chocolat* 529 #3 #1 or #2 529 #4 MeSH descriptor: [Cognition] explode all trees 6916 #5 cognition* or cognitive* or memory or attention 47484 #6 #4 or #5 48780 #7 #3 and #6	35	5
PsycINFO	24. PsycINFO; (cacao* OR cocoa* OR chocolat*).ti,ab; 1016 results. 25. PsycINFO; CACAO/; 0 results. 26. PsycINFO; 24 OR 25; 1016 results. 27. PsycINFO; (cognition* OR cognitive* OR memory OR memories OR attention*).ti,ab; 580357 results. 28. PsycINFO; exp COGNITION/; 23523 results. 29. PsycINFO; 27 OR 28; 583785 results. 30. PsycINFO; 26 AND 29; 161 results.	161	0
Embase	10. EMBASE; (cacao* OR cocoa* OR chocolat*).ti,ab; 6579 results. 11. EMBASE; CACAO/; 4565 results.	745	

	12. EMBASE; 10 OR 11; 7372 results. 13. EMBASE; (cognition* OR cognitive* OR memory OR memories OR attention*).ti,ab; 705621 results. 14. EMBASE; exp COGNITION/; 1355781 results. 15. EMBASE; 13 OR 14; 1744160 results. 16. EMBASE; 12 AND 15; 745 results.		
Cinahl	3. CINAHL; (cacao* OR cocoa* OR chocolat*).ti,ab; 800 results. 4. CINAHL; CACAO/; 984 results. 5. CINAHL; 3 OR 4; 1281 results. 6. CINAHL; (cognition* OR cognitive* OR memory OR memories OR attention*).ti,ab; 88999 results. 7. CINAHL; exp COGNITION/; 24185 results. 8. CINAHL; 6 OR 7; 101409 results. 9. CINAHL; 5 AND 8; 56 results.	56	0
Medline	17. MEDLINE; (cacao* OR cocoa* OR chocolat*).ti,ab; 5477 results. 18. MEDLINE; CACAO/; 2392 results. 19. MEDLINE; 17 OR 18; 5811 results. 20. MEDLINE; (cognition* OR cognitive* OR memory OR memories OR attention*).ti,ab; 606393 results. 21. MEDLINE; exp COGNITION/; 118097 results. 22. MEDLINE; 20 OR 21; 664313 results. 23. MEDLINE; 19 AND 22; 258 results.	258	0
Summary	**NA**	**NA**	

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