Immediate and residual effects of functional chewing gum on sustained attention and mood

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Abstract

Objectives: Chewing gum has been shown to improve aspects of cognition and mood with sustained attention being particularly receptive to the effects of chewing. Chewing gum may also be a useful vehicle for administering functional ingredients. The herbal extract Rhodiola rosea and certain B-vitamins have previously been shown to improve aspects of cognition and subjective state, but their combined effects have not been studied to date. Methods: The current randomised, placebo-controlled, double-blind, balanced crossover study compared the effects of a functional gum containing Rhodiola rosea and B-vitamins to flavour-matched regular chewing gum and a flavour-matched placebo. Thirty-six healthy young participants completed measures of attention and mood at baseline, during chewing, and 1-hour after chewing. Results: Chewing both functional and regular gum was shown to reduce errors on a digit vigilance task compared to placebo irrespective of whether measured during or after chewing. There were no benefits to adding functional ingredients to the gum. Discussion: Future chewing research should consider different formats of placebo. Sex differences in response to chewing and the impact of rate and intensity of chewing should also be explored.

Keywords: Chewing, Functional gum, B-vitamins, Rhodiola rosea, Cognition, Cognitive, Attention, Mood

Introduction

Chewing gum influences several cognitive and mood outcomes (Smith 2010) through the stimulation provided by the masticatory exercise. Whilst a preferential effect on memory has been observed (Wilkinson et al. 2002), the majority of studies demonstrate improvements to attention, particularly sustained attention (see Hirano and Onozuka 2015 for review). Increases to self-rated alertness have also been observed in a number of studies (see Johnson et al. 2013). A study showing that chewing gum-related improvements in performance on the sustained attention response task (SART) were no longer significant when controlling for changes in self-rated alertness, indicates that effects on sustained attention may be underpinned by increases to alertness (Johnson et al. 2013). Improvements to mood have also been observed in the form of increased hedonic tone (Allen and Smith 2012), more positive mood (Smith 2010), and increased calmness and contentedness (Johnson et al. 2013).

Support for behavioural data showing chewing gum-related improvements to attention and processing speed (Allen and Smith 2012; Hirano et al. 2013) is provided by studies showing increased activation in the fronto-parietal network during gum chewing versus sham chewing (Takada and Miyamoto 2004). Increased cerebral blood flow has been proposed as a mechanism for performance enhancement during chewing (Scholey et al. 2009) due to the increased supply of oxygen and glucose, which may in turn improve cognition (Johnson et al. 2013). Flavour has also been proposed to be important to effects of chewing gum, with a previous EEG study showing differences in alpha, beta and theta bands that were indicative of increased arousal following flavoured gum compared to base gum (Morinushi et al. 2000). Chewing gum with a sweet taste and lemon odour was also shown to produce significantly higher haemodynamic signals when compared to a control gum (Hasegawa et al. 2013), suggesting a synergistic effect of chewing and flavour on cerebral blood flow.

Food supplements and herbal extracts have also been shown to influence cognitive functions in similar ways to those achieved from chewing gum. B-vitamins have been positively reviewed by the European Food Safety Agency (EFSA) for the maintenance of a healthy nervous system and psychological function. B-vitamins have been proposed to maintain brain health (Kennedy 2016) and reductions in mental tiredness have been observed following a single dose (Dodd et al. 2020). The extract Rhodiola rosea has been studied extensively for its adaptogenic properties (Ishaque et al. 2012) and has been shown to reduce mental fatigue and improve psychomotor function and wellbeing following 20 days' consumption when compared to placebo (Spasov et al. 2000). Increased capacity for mental work has also been observed following a single dose when measured at 1 hour (Shevtsov et al. 2003).

Chewing a gum with added vitamins comprising riboflavin (vitamin B2) and pyridoxine hydrochloride (vitamin B6) has previously been shown to increase B2 and B6 plasmatic levels after one chewing episode (Khoo et al. 2018), but it still remains to be investigated if this translates into acute effects on psychological function. Research investigating the effects of Rhodiola rosea has been limited to the use of capsules (Ishaque et al. 2012). Therefore, to verify if functional ingredients in chewing gum may exert an additional influence on cognitive functions, a chewing gum containing Rhodiola rosea extract and three B-vitamins (B2, B6, and B7) was developed. The current randomised, controlled trial examined the acute effects of chewing functional gum on measures of concentration and mental acuity in healthy participants. To assess any synergistic effects of combining functional ingredients with chewing, the effects were compared to chewing regular gum as well as a placebo tablet. As flavour has been suggested as a potential mechanism for effects of chewing gum, the current study addressed this by comparing the effects of chewing mint-flavoured gum to those of a mint-flavoured control tablet.

Materials and methods

Design

A randomised, placebo-controlled, double-blind, counterbalanced crossover design was utilised. Participants were assessed immediately prior to, during, and 1-hour after treatment consumption. The study was approved by the University Ethical Approval System at Northumbria University (approval date: 24th May 2022; approval number: 46799) and was conducted according to the Declaration of Helsinki (2013). The study was pre-registered on clinicaltrials.gov (identifier: NCT05544500).

Participants

Volunteers were recruited through opportunity sampling within Newcastle upon-Tyne, UK and the surrounding areas. A power calculation based on a medium effect size indicated that 36 participants with a complete dataset would allow detection of significant effects with a power of 0.8 at α=0.05.

All participants were healthy, non-smokers and had a body mass index (BMI) within the range of 18.5-30 kg/m2. Participants confirmed that they did not have any pre-existing medical conditions, were not habitually taking any medication (excluding the contraceptive pill), had not habitually used supplements within the last month (excluding existing and consistent use of vitamin D). No participants had undergone any dental treatment in the week before testing or were planning any dental treatments during the study. Participants were paid £70 following completion.

Treatment

At each of the testing visits, one of three treatments was administered:

- Functional mint-flavoured sugar-free chewing gum containing 1.5% of a concentrated extract of Rhodiola rosea, delivering 3mg of total rosavins and 1mg of salidroside, and B-vitamins [0.7mg Riboflavin (vitamin B2), 0.7mg pyridoxine hydrochloride (B6), and 25µg Biotin (vitamin B7)] at doses compatible with fortified food (50% of daily nutrient reference value)
- Regular mint-flavoured sugar-free chewing gum without functional ingredients
- Mint-flavoured sugar-free placebo tablet

The order in which participants received each treatment was determined using computer-generated random allocation conducted by an independent 3rd party. During the second assessment at each visit, participants were instructed to chew two pieces of gum simultaneously (~2g each) or to suck two tablets consecutively for the duration of the tasks (~10 minutes). To aid in blinding participants to the treatment received, they were informed that the tablets would either include the same active ingredients as the functional gum or would be an inert placebo. Participants were visually isolated whilst consuming treatment. All treatments were flavoured with mint and were sugar-free.

Cognitive and mood measures

All cognitive and mood measures were delivered using the Computerised Mental Performance Assessment System (COMPASS, Northumbria University, Newcastle upon Tyne, UK), a purpose-designed software application for the flexible delivery of randomly generated parallel versions of standard and novel cognitive assessment tasks.

Tasks were presented in the same order on each occasion (Simple Reaction Time, Choice Reaction Time, Digit Vigilance, COMPASS VAMS and VAS) and responses were made using a response pad. The entire selection of tasks took approximately 10 min to complete.

Simple reaction time

An upwards pointing arrow is displayed on the screen at irregular intervals. Participants must respond by pressing the response button as quickly as they can as soon as they see the arrow appear. The task included 50 stimuli and the inter-stimulus interval varied randomly between 1 and 3.5 seconds. The outcome is speed of response (msec).

Choice reaction time

An arrow appears on the screen pointing to the left or to the right. Participants respond with a left or right response pad button corresponding to the direction of the arrow. The task included 50 stimuli and the inter-stimulus interval varied randomly between 1 and 3.5 seconds. The outcomes are reaction time for correct responses (msec) and accuracy (% correct).

Digit vigilance

A single randomly selected target digit is displayed to the right of the screen. A series of single digits are then presented in the left of the screen at the rate of 150 per minute. The participant is required to press the response button as quickly as possible every time the digit in the series matches the target digit. The task lasted for 3 minutes. Task outcomes are accuracy (%), reaction time for correct responses (msec) and false alarms (number).

COMPASS Visual Analogue Mood Scales (VAMS)

Participants rate their current subjective state by positioning an 'X' with a mouse cursor on lines on-screen. Individual scores are calculated as % distance along the line from the left. Composite scales assessing 'alertness', 'stress' and 'tranquillity' are produced, with higher values indicating higher ratings for each composite scale.

Visual Analogue Scales (VAS)

Participants rate their current subjective state by positioning an 'X' with a mouse cursor on lines on-screen. Scores are calculated as % distance along the line from the left, with higher values indicating higher ratings for each scale. Scales headed 'concentration' (anchored at either end by 'very high' and 'very low'), 'focussed' and 'mentally tired' (anchored at either end by 'not at all' and 'extremely') were included.

Procedure

Participants first completed a remote screening session via telephone call to assess their eligibility. Once informed consent was gained from participants via completion of an online consent form, participants were briefed on requirements of the study, then completed the health screening, collection of demographic data, and Caffeine Consumption Questionnaire (CCQ). Eligible participants visited the laboratory for a training visit, which began with physiological eligibility measures that could not be completed remotely (e.g. height and weight, waist-to-hip ratio) followed by training on the cognitive and mood measures.

Participants then attended the laboratory, at the Brain Performance and Nutrition Research Centre, at either 10am or 2pm on three separate occasions with testing time consistent within participants and counterbalanced across treatment orders. All testing days were identical, with the exception that participants consumed a different treatment at each visit. Participants were required to eat a standard meal at least 1 hour before testing and to abstain from alcohol and over the counter medications (including hay fever medications) for 24 hours and caffeinated products for 5 hours before testing (meal items were to be kept consistent across visits). Participants arrived at the laboratory at their allotted time and, following completion of the Case Report Form (to confirm continued eligibility), completed a baseline assessment for that day. They were then randomised to treatment order (Testing visit 1 only). Participants then had a 10-minute rest before completing the tasks again whilst 'chewing' their allotted treatment

for that day. They then disposed of their treatment and completed a final assessment 1 hour later (see **Figure 1**). During the 1-hour break they remained within the research centre where they could read or watch TV, but were not allowed to work, sleep, eat, or drink (other than water). At the end of the final visit, participants were fully debriefed.

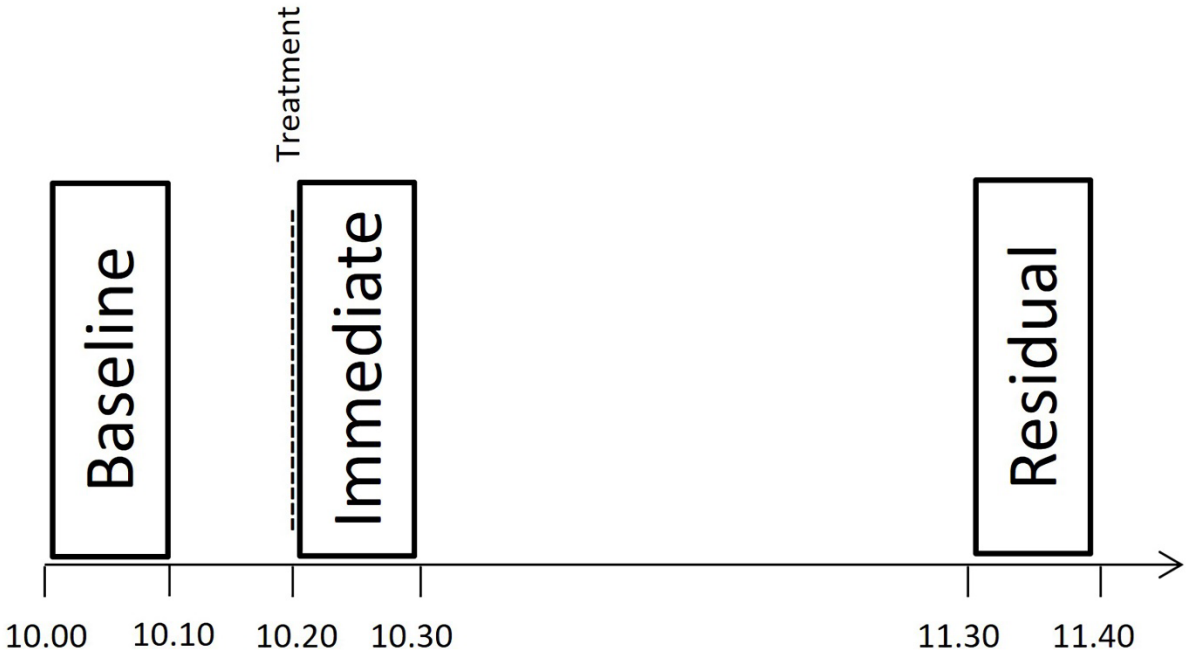

Figure 1 - Schematic of study procedures

Statistics

For the primary analysis, post-dose cognitive and mood outcome measures were modelled using the MIXED procedure in SPSS (version 26.0, IBM Corp., Armonk, NY, USA). This included the respective baseline values and the terms Treatment and Assessment as fixed factors, and Participant as a random factor. Sex and AM/PM were also included in the model as fixed factors but removed if no significant interactions between these factors and treatment were observed. Significant main effects of treatment and treatment interaction effects were

184 followed up with pairwise comparisons on baseline-adjusted means using placebo as the
185 reference category. Secondary analysis examined effects at assessment 2 only (during
186 chewing)**.** The respective baseline values and the term Treatment were included as fixed
187 factors, and Participant as a random factor. Sex and AM/PM were also included in the model
188 as fixed factors but removed if no significant interactions between these factors and treatment
189 were observed. Significant main effects of treatment and treatment interaction effects were
190 followed up with pairwise comparisons on baseline-adjusted means using placebo as the
191 reference category.

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Results

Demographics

Thirty-six participants (20 female) completed the study (see **Table 1** and **Figure 2**).

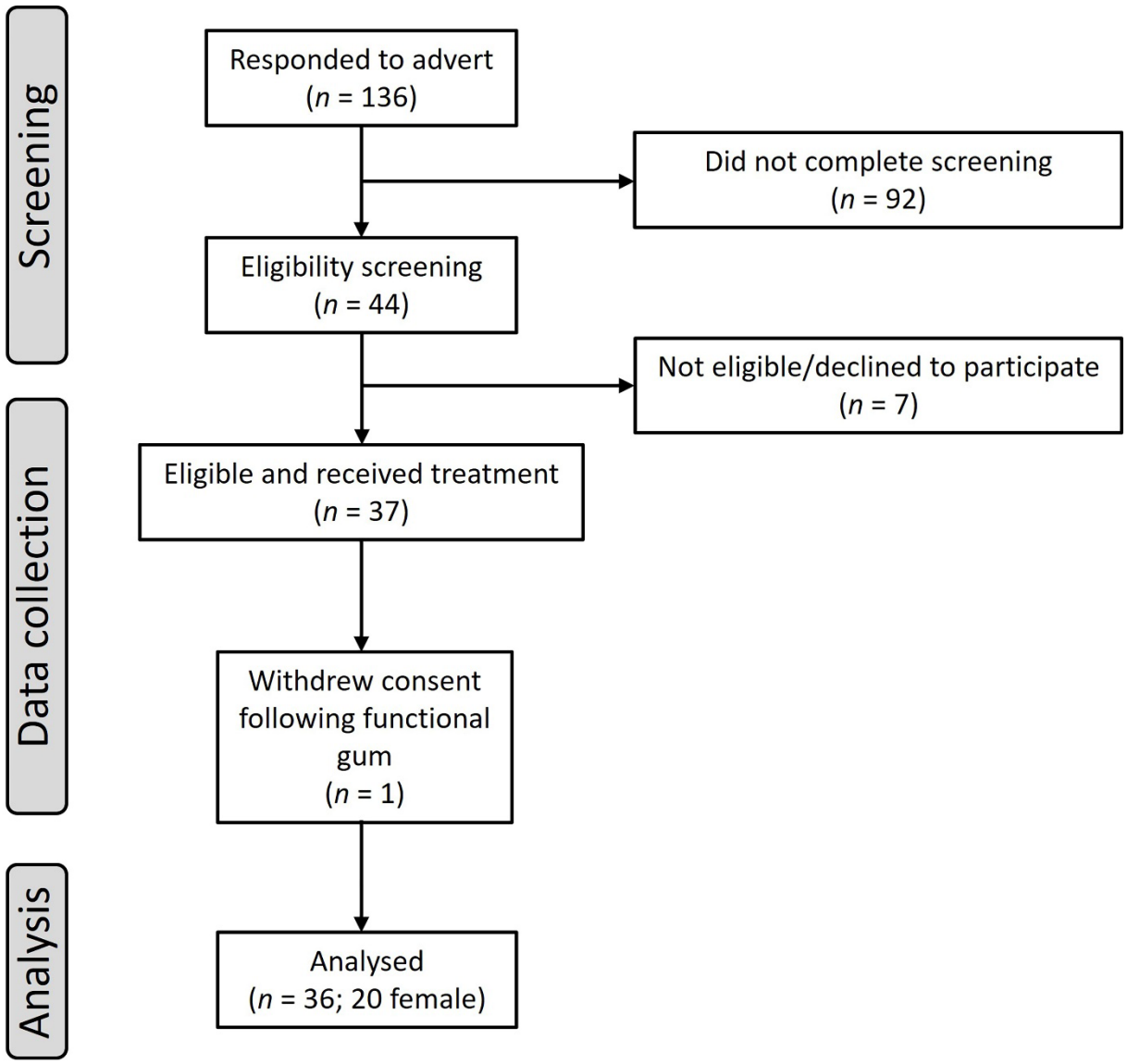

Figure 2 – Participant disposition flowchart

Table 1 – Participant demographics

	Female		Male	
	Mean	**SD**	**Mean**	**SD**
Age	23.1	3.88	24.19	4.58
Years in education	16.15	2.30	16.5	2.31
Body Mass Index (BMI)	24.75	4.25	24.52	3.69
Caffeine consumption (mg/day)	104.19	75.38	69.64	95.30
Fruit and vegetables (portions/day)	3.35	1.57	2.03	1.58

Significant main effects and interactions are reported below. See **Table 2** for means, standard deviations, F, and p values.

Primary analysis

Digit vigilance

A significant main effect of treatment was found for digit vigilance false alarms ($F(2, 169.895) = 3.466$, $p = 0.033$). Pairwise comparisons showed significantly lower false alarms in the regular gum condition ($p = 0.019$) and functional chewing gum condition ($p = 0.030$) compared to placebo (Figure 3a). There were no significant differences for reaction time or accuracy.

VAMS Tranquillity

There was a significant interaction between treatment, sex, and AM/PM for 'tranquillity' ratings ($F(3, 61.681) = 3.464$, $p = 0.021$). Pairwise comparisons showed that ratings of tranquillity were significantly lower in the functional chewing gum condition compared to

placebo (p = 0.023) in females tested in the afternoon (Figure 3b). There were no effects in males, nor in females tested in the morning.

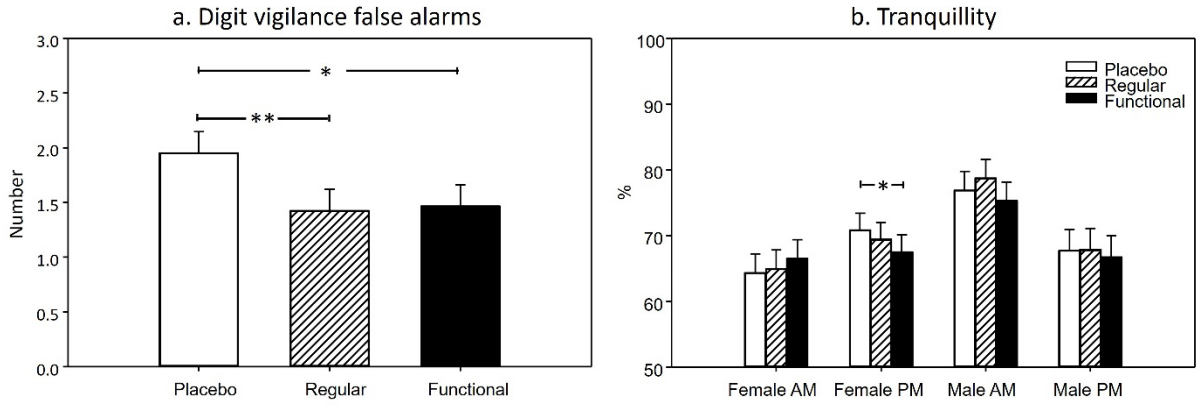

Figure 3 – Adjusted means and standard error for Digit vigilance false alarms (a) and Tranquillity (b). Significant effects of treatment are shown (* <0.05, **<0.01)

Secondary analysis

Digit vigilance

A significant main effect of treatment was found for digit vigilance false alarms (F(2, 66.761) = 5.906, p = 0.033). Pairwise comparisons showed significantly lower false alarms in the regular gum condition (p = 0.002) and functional chewing gum condition (p = 0.011) compared to placebo. There were no significant differences for reaction time or accuracy.

VAMS Alertness

There was a significant main effect of treatment on alertness (F(2, 63.794) = 3.814, p = 0.027). Pairwise comparisons showed that ratings of alertness were significantly higher in the regular chewing gum condition compared to placebo (p = 0.008). An interaction between treatment and AM/PM was also observed (F(2, 63.55) = 3.416, p = 0.039). Pairwise comparisons showed

234 that ratings of alertness were significantly higher in the regular chewing gum condition
235 compared to placebo ($p < 0.001$), and in the functional gum condition compared to placebo (p
236 $= 0.017$), when tested in the morning.

Table 2 – Means, SD, F and p values for each outcome

			Baseline		Assessment 1		Assessment 2				
	Treatment	N	Mean	SD	Mean	SD	Mean	SD	F	p	
Simple Reaction Time	Placebo	36	318.44	35.88	365.84	55.88	330.25	42.20	0.07	0.93	Treatment
	Regular gum		319.72	42.01	372.49	70.03	326.86	43.82	0.54	0.59	Treatment x Assess
	Functional gum		317.41	35.41	372.22	61.90	326.09	42.84			
Choice Reaction Time Accuracy	Placebo	36	95.33	3.45	96.50	3.49	95.33	3.51	1.49	0.23	Treatment
	Regular gum		95.28	3.03	96.72	2.44	96.33	2.81	1.00	0.37	Treatment x Assess
	Functional gum		96.17	2.92	97.06	2.64	95.56	3.86			
Choice Reaction Time	Placebo	36	425.29	56.26	450.49	58.63	433.82	60.76	0.63	0.54	Treatment
	Regular gum		434.91	66.38	445.41	55.38	440.96	57.12	1.05	0.36	Treatment x Assess
	Functional gum		426.29	51.26	446.55	66.16	433.69	56.65			
Digit Vigilance Accuracy	Placebo	36	91.11	8.55	88.46	12.85	91.16	8.52	0.70	0.50	Treatment
	Regular gum		91.49	7.71	90.78	11.72	91.33	9.11	0.66	0.52	Treatment x Assess
	Functional gum		90.80	9.16	90.33	9.74	91.10	9.44			
Digit Vigilance Reaction Time	Placebo	36	471.93	32.08	486.62	32.68	480.25	33.83	2.42	0.09	Treatment
	Regular gum		478.16	28.29	484.70	27.38	478.63	29.00	0.04	0.97	Treatment x Assess
	Functional gum		472.76	32.31	483.85	31.19	476.36	35.16			
Digit Vigilance False Alarms	Placebo	36	1.44	1.44	2.25	1.81	1.64	1.84	3.47	0.03	Treatment
	Regular gum		1.58	1.59	1.39	1.46	1.50	1.42	1.36	0.26	Treatment x Assess
	Functional gum		1.44	1.66	1.53	1.25	1.39	1.46			
Alertness	Placebo	36	61.59	16.30	64.54	12.72	64.59	12.97	0.24	0.79	Treatment
	Regular gum		60.26	14.17	66.72	11.80	61.96	14.59	2.30	0.10	Treatment x Assess
	Functional gum		62.39	14.42	66.46	11.81	63.00	13.87			

Stress	Placebo	36	32.74	11.91	32.67	13.85	32.23	13.09	0.48	0.62	Treatment
	Regular gum		35.79	12.29	32.72	13.58	34.22	13.47	0.75	0.47	Treatment x Assess
	Functional gum		34.99	15.68	33.41	15.32	33.90	15.21			
Tranquillity	Placebo	36	69.10	12.62	70.17	11.75	70.23	10.90	1.23	0.29	Treatment
	Regular gum		67.26	11.30	70.10	11.52	69.95	11.76	0.15	0.86	Treatment x Assess
	Functional gum		69.31	11.93	68.88	12.18	69.50	11.40			
Concentration	Placebo	36	58.14	19.64	61.78	16.87	64.36	15.28	0.65	0.52	Treatment
	Regular gum		57.50	15.51	62.97	17.13	60.61	16.57	2.53	0.08	Treatment x Assess
	Functional gum		60.83	14.88	64.25	13.44	60.81	14.94			
Focused	Placebo	36	56.56	18.20	61.72	16.55	60.92	15.62	0.07	0.93	Treatment
	Regular gum		57.39	15.12	64.47	15.64	57.78	15.00	1.63	0.20	Treatment x Assess
	Functional gum		59.28	17.14	62.69	14.86	60.50	14.82			
Mentally tired	Placebo	36	39.61	18.41	34.64	17.37	39.25	17.63	0.51	0.60	Treatment
	Regular gum		39.36	17.23	38.06	16.62	37.50	15.68	1.38	0.25	Treatment x Assess
	Functional gum		44.44	20.63	34.47	15.89	40.08	17.31			

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Discussion

Chewing gum led to improved sustained attention in the form of a reduction in the number of false alarms on a digit vigilance task when compared to placebo. This beneficial effect on sustained attention was observed following both regular chewing gum and functional gum enhanced with Rhodiola rosea and B-vitamins, suggesting that the added ingredients provided no additional benefit. Functional gum also had an unexpected effect in reducing tranquillity, but this effect was only observed in females tested in the afternoon. There were no effects on tranquillity in males, nor in females tested in the morning. Previous studies have shown beneficial effects of chewing gum and for added ingredients in the form of herbal extracts with caffeine (Davidson 2011), but no previous study has examined the impact of Rhodiola rosea and B-vitamins on cognition or mood when administered in a chewing gum.

The findings from the current study argue against combining these functional ingredients into a chewing gum using the paradigm employed here. However, further support for beneficial effects of chewing on sustained attention is provided. Mechanistically, chewing gum has been reported to increase heart rate at rest (Suzuki et al. 1992) and during mental demand (Walker et al. 2016), and to increase energy expenditure at rest (Kresge and Melanson 2015) and during physical demand (Hamada et al. 2018; Kanno et al. 2019). Alongside these circulatory and metabolic effects, chewing also leads to increased brain activation, which further enhances the supply of glucose and oxygen to the brain via increased blood flow (Momose et al. 1997; Wada et al. 2011). Chewing-related increases in blood oxygenation level-dependent (BOLD) signals have been observed in areas of the brain associated with movement: sensorimotor cortex, supplementary motor area, insula, thalamus, and cerebellum; but also, throughout the striatum, pre-frontal and parietal cortices (Onozuka et al. 2002), and the hippocampus (Feng et al. 2019). Chewing was also shown to increase

activation in brain regions related to motor function and attention during completion of the Attention Network Test (ANT) (Hirano et al. 2013), and a conjunction analysis of gum chewing minus sham chewing revealed activity in pre-frontal and parietal regions, leading to the suggestion of a fronto-parietal network that contributes to the effects of chewing on information processing (Takada and Miyamoto 2004). Activation of pre-frontal and hippocampal regions has been linked to reduced endocrine and autonomic stress responses during mastication (Ono et al. 2010), but there was no evidence of reduced stress based on the subjective responses in the current study. The role of chewing in higher order cognitive functions is also demonstrated by mastication studies showing that tooth loss is associated with risk of cognitive decline (Galindo-Moreno et al. 2022). Whilst it is possible that poor cognitive function precedes poor oral hygiene, or that other factors relating to periodontal disease are responsible for this association (Tada and Miura 2017), the role of mastication is highlighted by studies showing that replacing teeth is associated with better cognitive performance (Khalaila et al. 2022) and the wearing of a denture prothesis increases activation in the prefrontal cortex (Narita et al. 2009). Dietary hardness has also been linked to better cognition and brain activation (Al-Manei et al. 2023). However, the impact of reduced mastication is difficult to explore as food hardness has been linked to nutrient intake, which may explain any benefits to cognition (Fujiwara et al. 2023), therefore studies of gum chewing may represent a useful tool in studying this relationship further without the confound of nutrient intake.

The lack of effects following functional ingredients in the current study may be explained by methodological considerations. It is possible that release and/or absorption of functional ingredients during the 10-minute chew may not have been sufficient to elicit positive effects during the chewing assessment. However, previous data shows salivary riboflavin level increases within 2 minutes of chewing vitamin-supplemented gum and peak pyridoxine

289 salivary levels within 5 minutes (Khoo et al. 2018). In addition, it is assumed that the Rhodiola
290 rosea extract is released due to the presence of OH groups in its marker molecules, salidroside
291 and rosavin. Moreover, the 1-hour post-chew time point was selected on the basis of previous
292 effects of Rhodiola rosea shown at this time point in terms of improved information processing
293 during fatigue (Shevtsov et al. 2003) and increased delta and theta power in frontal and occipital
294 brain regions during cognitive tasks (Dimpfel 2014). Similarly, whilst vitamins are typically
295 assumed to require repeated intake for effects to be observed on cognition and mood, previous
296 studies have indicated mood effects following a single administration of B-complex multi-
297 vitamins at 1 hour post-intake (Macpherson et al. 2015; Dodd et al. 2020). Therefore, effects
298 would be expected at the 1-hour assessment even if not observed during the 'chewing'
299 assessment. It is possible that different effects would be observed with different doses. Previous
300 studies of Rhodiola rosea have been highlighted as methodologically flawed (Ishaque et al.
301 2012), but studies that have used standardised extracts have tended to use higher doses than
302 employed in the current study (Shevtsov et al. 2003; Dimpfel 2014; Koop et al. 2020).
303 Moreover, whilst the B-vitamins administered in the current study were at 50% of daily nutrient
304 reference value, previous studies have employed doses above the recommended daily intake
305 (Macpherson et al. 2015; Dodd et al. 2020). As Rhodiola rosea has been highlighted as an
306 adaptogen able to offset fatigue (Hung et al. 2011), and as B-vitamins have also been shown to
307 be beneficial in counteracting physical and mental fatigue (Dodd et al. 2020), it is also possible
308 that any effects may be more prominent following an extended period of task completion rather
309 than the 10-minute task paradigm employed here.

310 Chewing gum was shown to reduce digit vigilance errors irrespective of which type of
311 gum was chewed. A lack of effects on simple reaction time and choice reaction time tasks
312 may point to a specific effect on sustained attention tasks, as is supported by the literature
313 (Hirano and Onozuka 2015). However, the lack of sensitivity of the reaction time tasks may

314 also be due to their completion earlier in the paradigm. Time on task has previously been
315 shown to be important when chewing gum during a sustained attention task (Tucha and
316 Simpson 2011; Morgan et al. 2014), with detrimental effects to speed shown during the first
317 10 minutes and positive effects shown after that. If decrements in performance, or reductions
318 in alertness, are necessary to observe effects of chewing gum then it would be expected that
319 longer tasks where the production of a response is relatively rare would be most susceptible
320 (Miquel et al. 2019), and tasks towards the end of the assessment period may also be more
321 susceptible. However, when the role of degraded task performance was explored previously,
322 no differential effects of chewing as a function of time were observed (Johnson et al. 2013),
323 and others have suggested that task order may impact findings (Allen and Smith 2012).
324 Therefore, the impact of time-on-task appears to be inconsistent and may depend on other
325 factors. The rate and intensity of chewing have been highlighted as potential factors to impact
326 on cognitive response. Faster chewing has been associated with slower simple reaction times,
327 whilst harder chewing was associated with faster encoding of new information on a categoric
328 search task. However, no effects of rate or intensity of chewing were observed on a digit
329 vigilance task (Allen and Smith 2015), and there are a limited number of studies exploring
330 this.

331 The limited number of studies exploring the impact of rate or intensity of chewing
332 make it difficult to draw firm conclusions, but future studies should consider inclusion of
333 monitoring of chewing to further assess any impact. Time of day may also be an important
334 factor. This has not been explored conclusively in previous studies but the findings from the
335 secondary analysis of the current study showing increased alertness during chewing only
336 when tested in the morning, alongside the primary analysis showing decreased tranquillity
337 following functional gum in females in the afternoon, but not when tested in the morning,
338 suggest that the effects of chewing gum may be more favourable in the morning. Time-of-day

effects may relate to cortisol, which has been shown to follow a diurnal pattern (Hucklebridge et al. 2005). Previous studies of chewing have shown mixed findings with regards cortisol, with one showing increased cortisol during chewing (Smith 2010), but others showing decreases to cortisol (Scholey et al. 2009; Tasaka et al. 2014), with greater reductions when chewing faster (Tasaka et al. 2008) and harder (Soeda et al. 2012). Despite inconsistencies, the impact of chewing on cortisol suggests that time-of-day may need to be taken into account. The effect of reduced tranquillity in the current study is unexpected and should be interpreted with caution given the 3-way interaction. As the study focused on functional nutritional ingredients, the controls implemented centred around dietary restriction. It remains a possibility that the effects observed are due to an uncontrolled confounding factor such as sleep, exercise, or baseline stress levels, which should be considered in future studies alongside endocrinological and autonomic stress responses. Nevertheless, sex differences in response to chewing warrant further investigation due to sex-specific features of masticatory jaw movements (Gerstner and Parekh 1997)

The use of a sugar-free mint as a control condition in the current study was intended to mimic the action of chewing as closely as possible, whilst also controlling for any impact of flavour and aroma. The use of this control may have masked some of the effects on cognition, as a previous study has shown sucking a mint to be beneficial to context-dependent memory (Baker et al. 2004). Previous studies of behavioural effects of chewing gum have either used sham chewing or simply a ‘no gum’ condition, both of which present problems; sham chewing because it may activate similar mechanisms to chewing gum, and no gum because it gives rise to the possibility of placebo effects in the chewing gum condition that aren’t present in the no gum condition. Future research in this area should consider implementing a flavour-matched placebo solution to address this issue.

In conclusion, no beneficial effects of adding Rhodiola rosea and B-vitamins to chewing gum were observed in the current study. Chewing both regular and functional gum led to a reduction in errors on a sustained attention task, supporting previous findings in this domain. This study is novel in that effects were compared to a flavour-matched placebo rather than sham chewing or no gum. However, the act of sucking the mint placebo may have had effects on cognition, so future studies should consider a flavour-matched placebo solution. The rate and intensity of chewing may also impact on findings and should be monitored in future research.

Declarations

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Disclosure statement

No potential conflict of interest was reported by the author(s).

Notes on contributors

Emily Haworth is a Research Assistant in the Population Health Sciences Institute at Newcastle University. Emily's current research focusses on patient experience of cancer-related NHS procedures. Previously, Emily was a Research Assistant at the Brain, Performance and Nutrition Research Centre at Northumbria University where her interest lay in the role of nutrition on cognition.

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Data availability

The data that support the findings of this study are available from the corresponding author, [CH-R], upon reasonable request.

References

Al-Manei K, Jia L, Al-Manei KK, Ndanshau EL, Grigoriadis A, Kumar A. 2023. Food Hardness Modulates Behavior, Cognition, and Brain Activation: A Systematic Review of Animal and Human Studies. Nutrients. 15(5): 1168. eng.

Allen AP, Smith AP. 2012. Effects of chewing gum and time-on-task on alertness and attention. Nutr Neurosci. 15(4):176-185. eng.

Allen AP, Smith AP. 2015. Chewing gum: cognitive performance, mood, well-being, and associated physiology. Biomed Res Int. 2015:654806. eng.

Baker JR, Bezance JB, Zellaby E, Aggleton JP. 2004. Chewing gum can produce context-dependent effects upon memory. Appetite. 43(2):207-210. eng.

Davidson MG. 2011. Herbal-caffeinated chewing gum, but not bubble gum, improves aspects of memory. Appetite. 57(1):303-307. eng.

Dimpfel W. 2014. Neurophysiological effects of Rhodiola rosea extract containing capsules (a double-blind, randomised, placebo-controlled study). International Journal of Nutrition and Food Sciences. 3(3):157-165.

Dodd FL, Kennedy DO, Stevenson EJ, Veasey RC, Walker K, Reed S, Jackson PA, Haskell-Ramsay CF. 2020. Acute and chronic effects of multivitamin/mineral supplementation on objective and subjective energy measures. Nutr Metab (Lond). 17:16. eng.

Feng CZ, Li JF, Hu N, Jiang H, Wang YY, Liu HC. 2019. Brain activation patterns during unilateral premolar occlusion. Cranio. 37(1):53-59. eng.

Fujiwara A, Fukunaga A, Murakami K, Inoue Y, Nakagawa T, Yamamoto S, Konishi M, Mizoue T. 2023. Cross-Sectional Association between Estimated Hardness of the Habitual Diet and Depressive Symptoms in Older Japanese Men. Nutrients. 15(13). eng.

Galindo-Moreno P, Lopez-Chaichio L, Padial-Molina M, Avila-Ortiz G, O'Valle F, Ravida A, Catena A. 2022. The impact of tooth loss on cognitive function. Clin Oral Investig. 26(4):3493-3500. eng.

Gerstner GE, Parekh VV. 1997. Evidence of sex-specific differences in masticatory jaw movement patterns. J Dent Res. 76(3):796-806. eng.

Hamada Y, Yanaoka T, Kashiwabara K, Kurata K, Yamamoto R, Kanno S, Ando T, Miyashita M. 2018. The effects of gum chewing while walking on physical and physiological functions. J Phys Ther Sci. 30(4):625-629. eng.

Hasegawa Y, Tachibana Y, Sakagami J, Zhang M, Urade M, Ono T. 2013. Flavor-Enhanced Modulation of Cerebral Blood Flow during Gum Chewing. PLOS ONE. 8(6):e66313.

Hirano Y, Obata T, Takahashi H, Tachibana A, Kuroiwa D, Takahashi T, Ikehira H, Onozuka M. 2013. Effects of chewing on cognitive processing speed. Brain Cogn. 81(3):376-381. eng.

Hirano Y, Onozuka M. 2015. Chewing and attention: a positive effect on sustained attention. Biomed Res Int. 2015:367026. eng.

Hucklebridge F, Hussain T, Evans P, Clow A. 2005. The diurnal patterns of the adrenal steroids cortisol and dehydroepiandrosterone (DHEA) in relation to awakening. Psychoneuroendocrinology. 30(1):51-57. eng.

Hung SK, Perry R, Ernst E. 2011. The effectiveness and efficacy of Rhodiola rosea L.: a systematic review of randomized clinical trials. Phytomedicine. 18(4):235-244. eng.

Ishaque S, Shamseer L, Bukutu C, Vohra S. 2012. Rhodiola rosea for physical and mental fatigue: a systematic review. BMC Complement Altern Med. 12:70. eng.

Johnson AJ, Muneem M, Miles C. 2013. Chewing gum benefits sustained attention in the absence of task degradation. Nutr Neurosci. 16(4):153-159. eng.

Kanno S, Shimo K, Ando T, Hamada Y, Miyashita M, Osawa K. 2019. Gum chewing while walking increases fat oxidation and energy expenditure. J Phys Ther Sci. 31(5):435-439. eng.

Kennedy DO. 2016. B Vitamins and the Brain: Mechanisms, Dose and Efficacy--A Review. Nutrients. 8(2):68. eng.
Khalaila R, Vitman-Schorr A, Cohn-Schwartz E. 2022. A prospective association between tooth status and cognitive performance among older adults in Europe. Aging Ment Health. 26(3):499-506. eng.
Khoo WY, Chrisfield BJ, Colantonio AJ, Lambert JD. 2018. Vitamin-supplemented chewing gum can increase salivary and plasma levels of a panel of vitamins in healthy human participants. Journal of Functional Foods. 50:37-44.
Koop T, Dienel A, Heldmann M, Münte TF. 2020. Effects of a Rhodiola rosea extract on mental resource allocation and attention: An event-related potential dual task study. Phytother Res. 34(12):3287-3297. eng.
Kresge DL, Melanson K. 2015. Chewing gum increases energy expenditure before and after controlled breakfasts. Appl Physiol Nutr Metab. 40(4):401-406. eng.
Macpherson H, Rowsell R, Cox KH, Scholey A, Pipingas A. 2015. Acute mood but not cognitive improvements following administration of a single multivitamin and mineral supplement in healthy women aged 50 and above: a randomised controlled trial. Age (Dordr). 37(3):9782. eng.
Miquel S, Haddou MB, Day JEL. 2019. A systematic review and meta-analysis of the effects of mastication on sustained attention in healthy adults. Physiol Behav. 202:101-115. eng.
Momose T, Nishikawa J, Watanabe T, Sasaki Y, Senda M, Kubota K, Sato Y, Funakoshi M, Minakuchi S. 1997. Effect of mastication on regional cerebral blood flow in humans examined by positron-emission tomography with ^{15}O-labelled water and magnetic resonance imaging. Arch Oral Biol. 42(1):57-61. eng.
Morgan K, Johnson AJ, Miles C. 2014. Chewing gum moderates the vigilance decrement. Br J Psychol. 105(2):214-225. eng.
Morinushi T, Masumoto Y, Kawasaki H, Takigawa M. 2000. Effect on electroencephalogram of chewing flavored gum. Psychiatry Clin Neurosci. 54(6):645-651. eng.
Narita N, Kamiya K, Yamamura K, Kawasaki S, Matsumoto T, Tanaka N. 2009. Chewing-related prefrontal cortex activation while wearing partial denture prosthesis: pilot study. J Prosthodont Res. 53(3):126-135. eng.
Ono Y, Yamamoto T, Kubo KY, Onozuka M. 2010. Occlusion and brain function: mastication as a prevention of cognitive dysfunction. J Oral Rehabil. 37(8):624-640. eng.
Onozuka M, Fujita M, Watanabe K, Hirano Y, Niwa M, Nishiyama K, Saito S. 2002. Mapping brain region activity during chewing: a functional magnetic resonance imaging study. J Dent Res. 81(11):743-746. eng.
Scholey A, Haskell C, Robertson B, Kennedy D, Milne A, Wetherell M. 2009. Chewing gum alleviates negative mood and reduces cortisol during acute laboratory psychological stress. Physiol Behav. 97(3-4):304-312. eng.
Shevtsov VA, Zholus BI, Shervarly VI, Vol'skij VB, Korovin YP, Khristich MP, Roslyakova NA, Wikman G. 2003. A randomized trial of two different doses of a SHR-5 Rhodiola rosea extract versus placebo and control of capacity for mental work. Phytomedicine. 10(2-3):95-105. eng.
Smith A. 2010. Effects of chewing gum on cognitive function, mood and physiology in stressed and non-stressed volunteers. Nutr Neurosci. 13(1):7-16. eng.
Soeda R, Tasaka A, Sakurai K. 2012. Influence of chewing force on salivary stress markers as indicator of mental stress. J Oral Rehabil. 39(4):261-269. eng.
Spasov AA, Wikman GK, Mandrikov VB, Mironova IA, Neumoin VV. 2000. A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of Rhodiola rosea SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen. Phytomedicine. 7(2):85-89. eng.

491 Suzuki M, Shibata M, Sato Y. 1992. Energy metabolism and endocrine responses to gum-
492 chewing. Journal of Japanese Society for Mastication Science and Health Promotion. 2(1):55-
493 62.
494 Tada A, Miura H. 2017. Association between mastication and cognitive status: A systematic
495 review. Arch Gerontol Geriatr. 70:44-53. eng.
496 Takada T, Miyamoto T. 2004. A fronto-parietal network for chewing of gum: a study on human
497 subjects with functional magnetic resonance imaging. Neurosci Lett. 360(3):137-140. eng.
498 Tasaka A, Tahara Y, Sugiyama T, Sakurai K. 2008. Influence of chewing rate on salivary stress
499 hormone levels. Nihon Hotetsu Shika Gakkai Zasshi. 52(4):482-487. eng.
500 Tasaka A, Takeuchi K, Sasaki H, Yoshii T, Soeda R, Ueda T, Sakurai K. 2014. Influence of
501 chewing time on salivary stress markers. J Prosthodont Res. 58(1):48-54. eng.
502 Tucha L, Simpson W. 2011. The role of time on task performance in modifying the effects of
503 gum chewing on attention. Appetite. 56(2):299-301. eng.
504 Wada M, Hoshi Y, Iguchi Y, Kida I. 2011. Near-infrared spectroscopic study on the effects of
505 chewing on short-term memory. Appetite. 57(3):749-752. eng.
506 Walker J, Hosiner A, Kergoat S, Walker JM, Somoza V. 2016. Chewing unflavored gum does
507 not reduce cortisol levels during a cognitive task but increases the response of the sympathetic
508 nervous system. Physiol Behav. 154:8-14. eng.
509 Wilkinson L, Scholey A, Wesnes K. 2002. Chewing gum selectively improves aspects of
510 memory in healthy volunteers. Appetite. 38(3):235-236. eng.
511