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Saccharide effects on cognition and well-being in middle-aged adults:

A randomised controlled trial.

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Abstract

The current study used a randomised, double-blind, placebo-controlled design to investigate the effects of saccharide supplementation on cognition and well-being in middle-aged adults. Participants (N=109; 45 - 60 years) took a teaspoon of a combination of saccharides or a placebo twice daily for 12 weeks (3.6 g per day). Before and after this supplementation period, participants completed alternate forms of standardised tests of cognition and self-report measures of well-being. Significant beneficial effects of saccharide supplementation were found for memory performance and indicators of well-being. The potential for these nutrients to optimise cognitive function and well-being in older adults warrants on-going investigation.
Introduction

The role of nutrition in physiological and psychological health is an emerging area of scientific research (Dye, Lluch, & Blundell, 2000). Recent definitions of health suggest that it is more than the absence of disease, but rather the ability to achieve an optimal level of function (Fillit, et al., 2002) and maintain this as long as possible throughout the life-span.

Recent research has focused on the effects of various nutrients on the performance of cognitive tasks and has found evidence to suggest that nutrition can assist in achieving and maintaining cognitive function with age. In particular, beneficial effects of folate, vitamins B6 and B12, thiamine, niacin, zinc and iron as well as antioxidants, fatty acids and amino acids have been documented (Bryan & Calvaresi, 2004; Bryan, Calvaresi, & Hughes, 2002; Morris, et al., 2004). Emerging evidence also suggests a beneficial role for saccharides for cognition (for a review see Best, Kemps, & Bryan, 2005).

Saccharides are complex biological sugars found in certain vegetables, fruits and nuts, and are on the surface of all cells, cell membranes and in the extracellular space of tissues. Saccharides serve as recognition markers and as receptors that are critical for transmitting biochemical signals into and between cells (Sasisekharan & Myette, 2003). Thus, the body uses saccharides and saccharide-containing molecules (called glycoforms) to facilitate, guide and allow the cell-to-cell communication that is essential for normal physiological function.

Whilst there are over 200 known saccharides, at present, eight have been identified as important for the functioning of the human body. These are glucose, mannose, galactose, fucose, xylose, n-acetyl-glucosamine, n-acetyl-neuraminic and n-acetyl-galactosamine (Murray, Granner, Mayes, & Rodwell, 1996). These saccharides, both individually and as glycoforms are involved in the functioning of synapses and neurotransmitters needed for mood regulation (Backstrom, Westphal, Canton, & Sanders-Bush, 1995), the electrical activity of neurons (Kleene & Schachner, 2004; Martin, 2002) as well as the integrity of the
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central nervous system in general (Bandtlow & Zimmermann, 2000). Hence, because of the role of saccharides in brain function, saccharides are likely to affect cognition and mood. Of these, only the effect of glucose on cognitive performance in humans has been well researched, with several studies demonstrating positive effects of this monosaccharide on cognitive performance, especially memory (D. Benton, Owens, & Parker, 1994; Craft, Murphy, & Wemstrom, 1994; Donahoe & Benton, 2000; Hall, Gonder-Frederick, Chewning, Silveria, & Gold, 1989; Riba, 2004; Sunram-Lea, Foster, Durlach, & Perez, 2001).

In addition, there is emerging evidence from clinical and placebo-controlled studies that report positive effects of other saccharides, namely polysaccharides, on cognitive performance (E. W. Benton, 1997; Dykman & Briggs, 1997; Dykman & Dykman, 1998). For example, saccharide supplementation with fucose over 9 months administered by gastrointestinal tube improved the speech and language abilities of a young child with leukocyte adhesion deficiency type II (Marquardt, et al., 1999). Furthermore, supplementation with a combination of saccharides over 4 weeks improved the cognitive abilities, including auditory processing and retrieval from short-term memory, of an 8-year-old boy with dyslexia (E. W. Benton, 1997).

In addition, there have been two preliminary, peer-reviewed double-blind, placebo controlled studies that have investigated the short term effect of polysaccharide supplementation on cognition in non-clinical samples (Best, Bryan, & Burns, 2008; Wang, Szabo, & Dykman, 2004). Specifically, Wang and colleagues (Wang, et al., 2004) investigated the effect of a combination of saccharides on the task-associated brain activity of college students as measured by electroencephalograph (EEG). The EEG activity recording of those in the saccharide treatment group was characterised by significantly greater power in the theta, alpha and beta bands reflecting an increase in attention and arousal, compared to the placebo group. However, it is not clear to what extent these changes in the EEG reflected
improvements in cognitive performance, as cognition was not directly assessed in this study.

In contrast, a double-blind, placebo controlled study, using a battery of sensitive cognitive outcome measures, found a trend for a positive effect of a single dose of a combination of saccharides on the memory performance in middle-aged adults (Best, et al., 2008). The absence of a statistically significant short-term effect of saccharide intake on cognitive performance may be because of the nature of the role of saccharides in the brain. Given that saccharides are likely to play a longer-term structural and functional role in the brain, any effects on cognition might only be seen after longer-term intake.

Assessment of usual saccharide intake in the diet presents one method for examining potential longer-term effects of saccharide intake. To date, there are only two studies that have investigated the relationship between intake of saccharides through the diet and cognition. The first provides cross-sectional evidence to suggest a positive association between the intake of specific saccharides and self-reported cognition in middle-aged adults (Best, Kemps, & Bryan, 2009). The second study used a food diary to capture the exposure of middle-aged adults to food believed to be rich in saccharides through the diet (Best, Kemps, & Bryan, 2007). The results of both studies indicated a small but significant positive relationship between higher intakes of saccharides through the diet and better memory performance using both self-report and objective outcome measures. This relationship persisted even after controlling for health variables such as exercise, alcohol consumption, smoking and self-rated health.

The observed relationship between saccharide intake and memory functioning is consistent with the hypothesised mechanism that saccharides enhance the activity of hippocampal cells associated with memory performance, as suggested by animal research (H. Matthies, Staak, & Krug, 1996). However, because saccharides participate in the general cellular structure and function of the brain, saccharides are likely to affect a variety of
cognitive functions in addition to memory, as well as an overall sense of psychological well-being.

Effects of saccharides on psychological well-being may occur through the stable transport and receptor efficiency of neurotransmitters such as serotonin, which are known to affect mood (Backstrom, et al., 1995; Tate & Blakely, 1994). Because the serotonergic system of the brain plays a regulatory role in the development and plasticity of neural circuits that are involved in mood states, such as anxiety and depression (Martinowich & Lu, 2008), it is plausible that saccharides may have an effect on psychological well-being. In support, a 5-week case study of saccharide supplementation in participants with clinically diagnosed alcoholism revealed a significant effect on mood (Dykman & Briggs, 1997). Specifically, there was a significant decrease in the subscale assessing anger and significant increases in the subscales assessing energy and positive outlook on life as assessed by the Profile of Mood States questionnaire (POMS). A trend for improvement on the subscales assessing depression was also noted. Thus, the results suggest that saccharide supplementation may have an effect on psychological well-being (Dykman & Briggs, 1997).

In the dietary saccharide intake studies reviewed here, effect sizes were small and may, in part, be a result of saccharide intakes that were too low to bring about large effects on tasks of cognition and well-being. In the modern western diet, the consumption of fruits and vegetables, the major source of saccharides, is particularly low. Specifically, many adults consume less than 2 servings of fruit and 5 servings of vegetables per day, as recommended by the World Health Organisation and the Australian National Health and Medical Research Council guidelines (Best, et al., 2007; National Health and Medical Research Council 2005; National Health and Medical Research Council 2003; Fletcher & Fairfield, 2002). Although there are no intake guidelines for saccharides, it is likely that adults are not obtaining adequate amounts of saccharides from the diet because of their low fruit and vegetable intakes. Another
method for examining longer-term effects of saccharide intake is through supplementation. Increased intake of saccharides through longer-term supplementation, therefore, may increase the likelihood of detecting saccharide effects on cognition. Thus, the aim of the current study was to focus on the effects of longer-term intake of saccharides on the cognitive performance and psychological well-being in middle-aged adults through supplementation.

A 12-week supplementation period was used based on previous longer-term supplementation studies of nutrient effects on cognition. These have typically used supplementation periods of 8-12 weeks (Bryan, et al., 2002; Carrero, Fonollá, Marti, & Jiménez, 2007; Chambers & Camire, 2003; Fearon & al, 2003). Middle-aged adults were chosen for the current study because middle-age is when the first signs of age-associated cognitive decline appear and before cognitive difficulties become apparent (McDaniel, Maier, & Einstein, 2002; Nicolas, Nourhashemi, Lanzmann-Petithory, & Vellas, 2001).

Method

Participants

109 participants (aged 45-60 years) were recruited from the Adelaide metropolitan community through word of mouth, local newspaper and television media advertisements. Participants were required to be proficient in English as many of the tasks were English language rich. Participants who had experienced recent major surgery, were taking medications for, or had a history of head/brain, neurological or psychiatric conditions were unable to take part in the study because of the adverse effect of such conditions on cognitive performance (Chamelian & Feinstein, 2006; Hokkanen, Kauranen, Roine, Salonen, & Kotila, 2006; Kumari & Marmot, 2005).

There were 138 middle-aged Caucasian adults who were screened for eligibility for the study: 7 were ineligible due to ongoing serious medical conditions, 19 decided not to participate, 109 participants completed the time 1 assessment, and 92 completed the time 2
assessment at 12 weeks. There were 17 people who withdrew at varying time points: 11 participants from the saccharide condition and 6 from the placebo condition. Of these, 11 participants withdrew due to time commitments, 2 felt bloated, 2 had the flu, 1 had a pre-existing reflux condition, and 1 had pre-existing irritable bowel syndrome. The 17 participants who did not complete the study had completed an average of 5 weeks and 1 day of supplementation. These participants were included in the final analysis in order to maximise sample size and to yield more informative results regarding the possible effectiveness of the intervention, consistent with the intent-to-treat principle. This analysis likely provides a truer estimate of the findings at population level, and is appropriate for a pre-test/post-test measurement design (Salim, Mackinnon, Christensen, & Griffiths, 2008; Ten Have, et al., 2008). Thus, the 17 participants were assigned a post supplementation score using the expectation-maximisation algorithm missing values analysis in SPSS for inserting missing data via the maximum-likelihood method. This method is considered to be the best for estimating missing data, because unlike other methods such as mean substitution, it consistently yields good parameter estimates, close to the population average (Graham, 2009; Salim, et al., 2008). Within the sample, there were 71 females and 38 males. In the saccharide condition (N= 59) there were 40 females and 19 males, and in the placebo condition (N= 50) there were 31 females and 19 males.

**Design**

A randomised, double-blind, placebo controlled experiment was used to assess the effect of saccharide supplementation on cognitive performance and well-being. Participants were randomly allocated to one of two supplement conditions, saccharides or placebo, as they entered the study. The condition allocation occurred by providing each participant with the next randomly allocated set of supplement containers.
Each set of containers, provided in a brown paper carry bag, came with a teaspoon, adherence intake card, and contact details of the experimenter. Each container had a lot number, arranged by the provider Mannatech, Inc. (Coppell Texas), to indicate which container corresponded with the saccharide and placebo conditions. The lot numbers were kept in a sealed envelope until completion of the study. Thus, both experimenter and participants were unaware of the allocation to saccharide or placebo conditions.

Materials

Supplements

The saccharide supplement was a combination of plant polysaccharides, Ambrotose®Complex, a proprietary and patented blend that per .44 g serving (approximately ¼ teaspoon) contained 342.2mg of polysaccharides (from aloe vera (44mg), Larix decidua (211.2mg), Astragalus gummifer (44mg) and Anogeissus latifolia (44mg)), 52.8mg rice starch and 44mg glucosamine hydrochloride. The combination of saccharides included mannose, galactose, fucose, xylose, glucose, n-acetyl-glucosamine, n-acetyl-neuraminic acid and n-acetyl-galactosamine. The placebo supplement was a rice flour starch powder.

These supplements were provided by Mannatech Inc, (Coppell, Texas). The saccharides and rice flour were in powdered form, and came in 75 g containers. They were matched for colour, texture and other characteristics (e.g., sweetness), so that taste and appearance was equivalent. Each participant received four containers for the 12-week supplementation period. Daily dosages were set at two teaspoons per day for a total intake of 3.6 grams per day. These dosages were based on those used in previous polysaccharide supplementation research (E. W. Benton, 1997; Dykman & Briggs, 1997; Dykman & Dykman, 1998; Dykman, Tone, Ford, & Dykman, 1998) and on the recommendation of the manufacturer. Teaspoons were provided so that dosages were equal across participants and condition.
Participants took one teaspoon of supplement with food in the morning and one in the evening. They were told that they would be consuming either a vegetable plant extract or rice flour extract. The supplement was consumed by either mixing the amount in a small glass of water or juice, or swallowing the amount straight from the teaspoon. Participants indicated on a small card that outlined the number of days to take the supplement, whether they had taken both teaspoon doses each day. This card was used to measure adherence and consistency across the 12 weeks, and was returned to the researcher for compliance analysis. As an additional assessment of adherence, participants were asked to return any unused amounts in the containers at the post-supplementation session. The amount consumed was determined by the number of teaspoon amounts left in the container out of the possible 168 serves (2 serves per day for 84 days).

Measures

Cognitive performance measures

Verbal Memory. The Rey Auditory-Verbal Learning Test (RAVLT) (Rey, 1964) was used to assess verbal memory performance. The examiner reads aloud 15 nouns (list A) over five trials and after each trial, participants are asked to recall, in any order, as many of the 15 words as possible. Scores for the 5 trials are summed to produce a measure of immediate recall. After a sixth trial consisting of 15 different words (list B) participants are again required to recall the words that were presented in list A (trial 7), and then again after an interval of 20 minutes (trial 8). The scores from trials 7 and 8 are used to produce a measure of delayed recall. After trial 8, participants are presented with a sheet of 50 words containing the words from lists A and B among 20 distracter words. Participants are asked to recognise the words from lists A and B and indicate the list they came from. Each word correctly identified is awarded one point producing a measure of recognition.
Visuo-Spatial Memory. Visuo-spatial memory performance was assessed by the Visual Pattern Span Recall (Della Sala, Gray, FBaddeley, Allamano, & Wilson, 1999) and the Visual Pattern Recognition (Wilson, Scott, & Power, 1987) tasks. In the Visual Pattern Span Recall participants are presented with black and white patterned grids that increase in difficulty two grid blocks at a time (2x2 to 5x6 grids). The participant views each pattern presented for 3 seconds only and then is asked to reproduce it by marking the cells in an empty grid of the same size. Three patterns of the same grid size make up a set. The score is the number of black cells in the largest pattern recalled, ranging from 2-15. The task is discontinued when all three patterns in a set are recalled incorrectly.

The Visual Pattern Recognition task is similar to the recall task, however, participants are asked to remember the grid pattern and then detect which one of the black cells is missing upon being presented with an identical pattern that has one black cell missing (Wilson, et al., 1987). Participants are presented with the black and white patterned grids (of increasing size) for 3 seconds, with a retention interval of 2 seconds. Scoring is the same as above.

Working Memory. Working memory was assessed by the Reading span (Daneman & Carpenter, 1980) and Computation Span (Salthouse & Babnock, 1991) tasks. For the reading span task participants are presented with series of unrelated sentences that they read aloud. Whilst reading the sentences, participants must memorise the final word of each sentence to recall after reading the last sentence in a series. The number of sentences in a series increases from two to six. Five trials are presented for each series. The task is discontinued when three out of five trials of a series are recalled incorrectly. The score is the total number of trials on which the participant has recalled the words correctly.

In the computation span task participants are presented with a series of simple arithmetic problems that they are asked to solve whilst simultaneously remembering the last digit from each problem to recall at the end of the series. The number of arithmetic problems
in a series increases from one to seven items. Three trials are presented for each series. The
task is discontinued when all three trials of a series are recalled incorrectly. The score is the
number of problems the participant has accurately recalled the digits for provided the
problems have been answered correctly.

Attention. Attention was assessed by the Stroop task (Trenerry, Crosson, DeBoe, &
Leber, 1989) and the Letter Cancellation task (Lezak, 1995). For the Stroop task, participants
are presented with a page of 112 colour names and asked to name aloud, as quickly as
possible, the colour of the ink in which the words are printed. In the first trial, the colour of
the ink is congruent with the colour word (e.g., the word “blue” is printed in blue ink). In the
second trial, the colour of the ink is incongruent with the colour word, (e.g., the word “blue”
is printed in red ink). The score for each trial is the number of correct minus incorrect
responses. The final score is the ratio of the incongruent task score to the congruent task
score.

For the Letter Cancellation task participants are required to search for and put a line
through two target letters (P and D) from an A4 page matrix of letters (32 letters wide, 45
letters in length) as quickly as possible within a 2-minute time period. The score is the
number of correct identifications.

Speed of Processing. Speed of processing was assessed by the Digit Symbol Coding
task, a subtest of the Wechsler Adult Intelligence Scale (WAIS III: Wechsler, 1997) and the
Boxes test (Earles & Salthouse, 1995). In the Digit Symbol Coding task, participants are
required to complete 133 digit symbol substitutes on a printed page as quickly as possible.
The score is the number of squares filled in correctly in 120 seconds. For the Boxes Test,
participants are presented with a printed sheet of 100 boxes, each with one side missing.
Participants are required to complete as many boxes as possible by drawing in the missing
side. The score is the number of boxes completed in 30 seconds.
General Cognitive Ability. General Cognitive Ability was assessed by Matrix Reasoning, a subtest of the WAIS III (Wechsler, 1997), and Spot the Word, a measure of general verbal ability (Baddeley, Emslie, & Nimmo Smith, 1992). In Matrix Reasoning, participants are presented with a series of 26 problems that are solved by selecting the correct item from five alternative choices. The task is discontinued when 4 consecutive wrong answers have been made. Scores are the total number of correct items. In Spot the Word, participants are presented with two sheets containing 60 real word/nonword pairs. Participants are asked to identify the real word in the pair and instructed not to guess. The score is the number of words identified correctly minus the number of errors; missed responses are not included.

Well-being measures

Three measures were used to assess overall mood and psychological well-being: the Profile of Mood States (POMS), the Depression Anxiety and Stress Scale (DASS), and the Perceived Stress Scale-10 Item (PSS-10). The POMS (McNair, Lorr, & Droppleman, 1992) is a questionnaire that contains 65 items pertaining to six mood states: tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment. Participants are asked to rate these on a 5-point scale (0= not at all to 4= extremely) indicating how they have felt during the past week including today.

The DASS (Lovibond & Lovibond, 1995) is designed to measure three negative emotional states; depression (e.g., self-depreciation and lack of interest), anxiety (e.g., autonomic arousal and anxious affect) and stress (e.g., difficulty relaxing and easily upset). Participants are asked to use 4-point severity/frequency scales to rate the extent to which they have experienced each state over the past week across 42 items. Scores for Depression, Anxiety and Stress are calculated by summing the scores for the relevant items (Lovibond & Lovibond, 1995).
The PSS-10 is a rating scale developed to measure the degree to which individuals appraise situations in their lives as stressful (Cohen, Kamarck, & Mermelstein, 1983). Participants are asked to rate how often they experienced specific feelings in the last month on a 4-point scale (0 = never to 4 = very often). PSS-10 scores are obtained by reversing the scores on the four positive items (items, 4, 5, 7, and 8) and then are summed across all 10 items.

Demographic and health questionnaire
This questionnaire asked for information about gender, age, height and weight in order to calculate body mass index (kg/m²), years of education, number of hours of work per week, self-rated health, (rated on a scale from 1 = poor to 5 = excellent), number of dietary supplements used, number of medications used, number of hours of exercise per week, number of cigarettes smoked per day and alcohol consumption (number of standard drinks consumed in a typical day).

Food Diary
A food diary was used to provide a measure of dietary saccharide intake in order to account for any diet difference between groups and ability to detect effects of supplementation. The diary provided a record of what a person ate on three non-consecutive days in one week. The diary requested participants to report all food eaten during the day, morning, afternoon and evening. Identifying the foods believed to contain saccharides amongst the foods that the participant recorded was the basis for analysis of the diary. The overall “exposure” to foods that contain saccharides, regardless of portion size, was recorded as the total number of servings of possible sources of saccharides. The number of different foods eaten that are thought to contain saccharides was also recorded to capture a secondary measure of exposure to saccharides in the diet.

Procedure
Each participant attended two sessions, one prior to supplementation and one post-supplementation. After initial contact and analysis of eligibility for participation, individuals selected mutually convenient times for their first testing session to visit the Flinders University Psychology Laboratory. Participants were then sent the demographic and health questionnaire, the food diary and well-being measures to be completed prior to the first session. Both pre and post supplementation testing sessions took approximately 1-1.5 hours. Alternative forms of cognitive performance tests were counterbalanced across participants at the pre and post testing sessions. Participants were tested individually in a quiet and well-lit interview room. Each participant completed the cognitive tests in the following order: Letter cancellation task, Rey Auditory Verbal Learning Test, Computation Span, Stroop task, Delayed Recall of Rey Auditory Verbal Learning Test, Visual Span Recall task, Digit Symbol coding, Reading Span, Boxes Test, Visual Span Recognition, Matrix Reasoning and Spot the Word. Matrix Reasoning and Spot the Word were administered in the pre-supplementation session only as these tasks were used to determine whether participants in the saccharide and placebo conditions differed on general cognitive ability.

Statistics

To detect covariates, baseline differences between the supplementation conditions on all variables were investigated using one-way Analyses of Variance (ANOVA) with an alpha of .05. The difference between pre and post supplementation cognition and well-being measures was explored using Analysis of Covariance (ANCOVA), with baseline performance used as a covariate. Between group effect sizes using Cohen’s $d$ were calculated using the formula $d = \frac{2\sqrt{F}}{\sqrt{\text{df}_{\text{error}}}}$, where .2 is considered a small effect, .5 a moderate effect and .8 a large effect.

Results

Pre-supplementation
**Demographics and health**

ANOVA’s were conducted to identify group differences in demographic and health indicators, saccharide intake through the diet, and tasks of general cognitive ability, for possible inclusion as covariates when assessing the effects of supplementation on cognition and well-being. Table 1 presents the descriptive statistics for these measures at baseline. As can be seen in the table, there were no significant differences between groups for most variables. There were, however, significant differences between conditions for self-rated health and number of supplements used such that individuals in the placebo condition rated their health as better than those in the saccharide condition, while those in the saccharide condition reported taking more supplements than those in the placebo condition. Thus, self-rated health and number of supplements were used as covariates in the comparisons of conditions on the post-supplementation cognitive and well-being measures.

**Post supplementation**

**Adherence to supplement protocol and supplement intake**

Adherence to the supplement protocol and supplement intake was assessed by the number of days on which participants took the supplement during the 12 weeks, and the percentage of the supplement consumed. There were no significant differences between conditions on either measure (adherence ($F(1,88) = .05, p = .98$): placebo condition $M = 80.22$, $SD = 6.11$, saccharide condition $M = 81.12$, $SD = 10.20$; percentage of supplement intake ($F(1,88) = .32, p = .57$): placebo condition $M = 97.66$, $SD = 5.15$, saccharide condition $M = 98.32$, $SD = 4.28$). Overall, the compliance was good with participants taking the supplement for 80 days out of 84, and consuming on average 294g of the possible 300g (4 containers at 75g each).

**Cognitive performance and well-being**
ANCOVA’s were conducted to examine differences between conditions in cognitive
performance and well-being. Baseline measures of self-rated health, number of supplements,
and pre-supplementation performance on the outcome measure were used as covariates.

Participants in the saccharide condition performed significantly better than those in the
placebo condition on tasks of immediate recall (RAVLT trial 2, $F(1, 101) = 3.94, p < .05, d = .40$; and RAVLT trial 5, $F(1, 101) = 7.48, p < .05, d = .54$), and recognition memory ($F(1,101) = 5.75, p < .05, d = .47$). The effect size on these measures was moderate. Across the non-significant trials, there were positive effect sizes in the same direction as the significant trials, with effect sizes ranging from .10 - .34. Descriptive statistics for all trials of the RAVLT are presented in figure 1. There were no other significant supplementation effects on any other measure of cognition. However, there was also a moderate sized difference between the saccharide ($M = 78.73, SD = 10.16$) and placebo ($M = 77.12, SD = 15.25$) conditions for digit coding that fell just short of significance ($F(1, 101) = 3.54, p = .06, d = .40$).

For well-being, participants in the saccharide condition scored significantly lower than those in the placebo condition on depression-dejection ($F(1, 101) = 6.12, p < .05, d = .50$) and anger-hostility ($F(1, 101) = 4.46, p < .05, d = .46$) subscales of the POMS. The effect size on these measures was moderate. Descriptive statistics are presented in figure 2.

Discussion

The current study, to our knowledge, is the first, randomised, double-blind supplementation study to investigate the longer-term effects of saccharides on cognition and well-being in middle-aged adults. Saccharide supplementation had a positive effect on several measures of cognition and well-being.

First, there was a significant effect of supplementation on memory performance, specifically on immediate recall and recognition memory. This is consistent with the findings of dietary saccharide intake studies that determined a relationship between saccharides and
Saccharide supplementation in mid-life memory performance (Best, et al., 2007, 2009; H. Matthies, et al., 1996). However, the current study yielded a stronger effect (i.e., moderate effect sizes) of saccharides on memory performance, with increases in scores of almost half a standard deviation. These results support the hypothesised mechanism of saccharide effects in the brain. Specifically, saccharide administration has been shown to enhance the cellular activity (long-term potentiation) required for memory formation in the hippocampus (H. Matthies, et al., 1996; H. J. Matthies, et al., 1999; Rose, 1989) and to improve performance on tasks of memory in animals (Dunbar, Lescaudron, & Stein, 1993; Dunn & Hogan, 1975; Zhuravin, Nalivaeva, Plesneva, & Dubrovskaya, 1999).

The moderate sized, albeit non-significant, supplementation effect on digit coding performance may suggest a potential benefit of saccharide intake to speed of processing. This tentative conclusion has support from animal research which has shown saccharide supplementation to enhance the speed with which older rats performed tasks (Dunn & Hogan, 1975; Mei & Zheng, 1993). However, future research is needed to clearly establish any effect of saccharide supplementation on processing speed in humans. Second, there was a significant effect of supplementation on well-being, with a significant reduction in anger-hostility and depression-dejection in the saccharide group. Specifically, participants in the saccharide condition felt less irritable, reported fewer instances of being “grouchy, and “annoyed”, were overall more positive and happy, and experienced fewer feelings of personal inadequacy than those in the placebo condition. Given the limited research in this area, there are few comparisons that can be made between the current findings and those of previous research. However, the case study by Dykman et al. (1997) found a significant effect of saccharide supplementation on measures of well-being as assessed by the POMS. Specifically, participants with clinically diagnosed alcoholism reported significant decreases on the Anger scale, and significant increases in the
Fatigue (energy) and Vigor (positive outlook on life) scales following 5 weeks of saccharide supplementation. The role of saccharides in the function of serotonin, a neurotransmitter involved in mood regulation, suggests a plausible direct mechanism on the brain for saccharide effects on well-being (Backstrom, et al., 1995).

Taken together, the findings suggest that there are beneficial effects of increased saccharide intake through supplementation for memory performance and well-being in middle-age. The strength of the current study is its randomised controlled design and the use of sensitive measures of cognitive performance across a variety of cognitive functions as well as measures that assess well-being across general mood, depression, anxiety and stress.

Despite these strengths, there are a number of limitations. First, the assessment of dietary intake, supplement use and medication use was somewhat crude. Future studies could benefit from a more detailed quantitative and qualitative assessment of these variables to more accurately control for the potential impact of such lifestyle choices in determining supplementation effects. Second, despite its strengths, a randomised, placebo-controlled design cannot fully control for sampling differences. Future studies might usefully adopt a cross-over design to control for such differences. However, consideration would need to be given to the potential longer-term effects of saccharides and determining an appropriate “wash out” period before utilising such a design. Third, given the large set of variables, it is possible that some of the significant results could have occurred by chance. However, it is unlikely that the observed supplementation effect on memory is a chance finding, as it is consistent with previous studies showing a relationship between saccharide intake and memory functioning (as opposed to other cognitive domains) (Best, et al., 2008; Best, et al., 2007, 2009), and with studies in animals showing effects of saccharide supplementation on specifically memory (H. Matthies, et al., 1996; H. J. Matthies, et al., 1999).
Importantly, the effect of saccharide supplementation for memory performance and psychological well-being were determined in a sample of middle-aged adults who were considered to be in good health. Moreover, the beneficial effects of saccharide supplementation were detected after controlling for self-rated health and dietary supplement use. Thus, it is possible that stronger saccharide supplementation effects could be found in less healthy and cognitively less intact individuals.

Hence, future research into the effects of saccharide supplementation in older adults with mild cognitive impairment would provide clearer evidence of longer-term saccharide effects for cognition. A recent investigation into the rates of cognitive change across 6 years and the dietary consumption of fruits and vegetables among older adults suggests that longer-term saccharide intake may indeed benefit cognitive aging. The results of the study revealed that high vegetable intake was associated with a 40% slower rate of cognitive decline with age (Morris, Evans, Tangney, Bienias, & Wilson, 2006). Specifically, intake of individual foods, such as zucchini, summer squash, eggplant, broccoli, lettuce, tossed salad, and greens/kale/collards, were significantly inversely associated with cognitive decline. Interestingly, these foods are believed to be rich in saccharides. Whilst the influence of other nutrients, such as antioxidants, may also have played a role in the positive effect of vegetable intake over time, it is possible that increased intakes of vegetables believed to be rich in saccharides over longer periods of time may have a beneficial effect on cognition with age. Further saccharide supplementation investigations in older adults could usefully determine whether saccharide intake guards against age-related cognitive decline.

Given the need for increased consumption of fruit and vegetables in the Western world, continued dietary counselling is important. However, despite the emerging prevalence of public health campaigns promoting fruit and vegetable consumption, a large proportion of the population still does not meet the recommended daily intakes (National Health and
Medical Research Council, 2003). Supplementation provides a ready alternative for meeting the required intake levels, particularly as many adults do not consume an optimal amount of vitamins and minerals from fruits and vegetables by diet alone (Fletcher & Fairfield, 2002).

In conclusion, because of the increased scientific interest in the effects of nutrition on cognition and well-being, there may be substantial advances in the use of saccharides in everyday functioning. Because of the relative low cost of altering dietary habits through healthy food choices or supplementation, further research in this area will benefit from collaboration between research groups from multiple disciplines and industry, in order to understand how best to utilise nutrition to produce optimal cognition and well-being.

Acknowledgements

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Saccharide supplementation in mid-life

References


Sasisekharan, R., & Myette, J. R. (2003). The sweet science of glycobiology: complex carbohydrates, molecules that are particularly important for communication among cells, are coming under systematic study. *American Scientist, 93*(5), 432-410.


Table 1

Descriptive statistics for background measures at baseline (i.e., pre-supplementation)

<table>
<thead>
<tr>
<th>Background Measures</th>
<th>Supplement Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>M</td>
</tr>
<tr>
<td>Age</td>
<td>52.44</td>
</tr>
<tr>
<td>BMI</td>
<td>25.76</td>
</tr>
<tr>
<td>Years of Education</td>
<td>13.53</td>
</tr>
<tr>
<td>Hours of work/week</td>
<td>27.84</td>
</tr>
<tr>
<td>Self rated quality of health*</td>
<td>4.22</td>
</tr>
<tr>
<td>Number of supplements**</td>
<td>1.36</td>
</tr>
<tr>
<td>Number of medications</td>
<td>.73</td>
</tr>
<tr>
<td>Hours of exercise/week</td>
<td>5.09</td>
</tr>
<tr>
<td>Number of cigarettes/day</td>
<td>.34</td>
</tr>
<tr>
<td>Number of alcoholic drinks/week</td>
<td>6.88</td>
</tr>
</tbody>
</table>

Dietary saccharide intake

|                                      | Placebo     | Saccharide |
|                                      | M          | SD | M    | SD |
| Number of serves                     | 18.33      | 6.67 | 18.08 | 6.97 |
| Number of different foods            | 9.27       | 2.80 | 9.37  | 2.93 |

General cognitive ability

|                                | Placebo     | Saccharide |
|                                | M          | SD | M    | SD |
| Matrix Reasoning               | 15.26      | 5.46 | 16.46 | 4.72 |
| Spot the word                  | 41.81      | 9.35 | 42.59 | 7.65 |

* F(1,104) = 5.10, p = .02
** F(1,104) = 5.79, p = .01
Figure Captions

Figure 1. Effects of supplementation on RAVLT measure of memory performance.

Figure 2. Effects of supplementation on POMS measure of well-being
Figure 1.

![Graph showing scores for different trials with the legend indicating Placebo and Saccharide. The graph includes trials labeled Ravlt 1 to Ravlt 8, with some trials having delayed recall. The x-axis represents trials, the y-axis represents scores, and the bars show the scores for each trial under Placebo and Saccharide conditions. Asterisks indicate a p-value of <0.05.]

* p < 0.05
Figure 2.

![Bar chart showing scores for Anger-hostility and Depression-Dejection under Placebo and Saccharide conditions.](image-url)