Original research paper

# Acute effects of a dietary non-starch polysaccharide supplement on cognitive performance in healthy middle-aged adults

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Objective: Certain plant polysaccharides may provide psychological health benefits. The aim of this study was to evaluate whether they can acutely improve mood and cognitive function.
Method: In a randomized, double-blind, placebo-controlled, between subjects design trial, 73 middle-aged adults consumed 4 g of a proprietary mixture of non-starch polysaccharides (NSPs) (Ambrotose® complex), a rice flour placebo, or a sucrose control. Participants completed testing at baseline and 30 minutes post-consumption. Acute effects of consumption on mood, cognition, and blood glucose were evaluated during mental tests designed to induce mental fatigue.
Results: Significant improvement in recognition and working memory performance was observed in the group that consumed NSP compared with placebo or sucrose. Improvements in memory performance following NSP intake were independent of changes in blood glucose.
Discussion: This is the first report of acute behavioural improvement following plant polysaccharide intake in healthy middle-aged adults under conditions of mental fatigue. The findings suggest that certain NSP may enhance memory performance through mechanisms other than elevated blood glucose.

**Keywords:** Memory, Cognition, Middle-aged adults, Saccharides, Arabinogalactan, Plant polysaccharides, Dietary polysaccharides

## Introduction

Certain non-starch polysaccharides (NSPs) have been shown to elicit biological effects through direct or indirect mechanisms, including immunomodulatory antioxidant and antidiabetic activities, as well as gastrointestinal and prebiotic activities.[1,2] Distinctive NSP, especially mannans (such as galactomannan, glucomannan, and acemannan) and arabinogalactans are derived from algae, fungi, bacteria, and plants. These polysaccharides are relatively non-toxic and do not cause side effects when consumed orally following acute and chronic intake in humans.[3] However, the basic categorization of these polysaccharides lacks precision in terms of chemical and biological functions and metabolic characteristics. For example, the terms 'polysaccharides' and 'non-starch polysaccharides' can refer to the same polysaccharide but do not necessarily represent a single chemical component and/or health benefit. Each polysaccharide contains a range of compounds with different glycosidic linkages, substituents (e.g. acetyl and sulphate groups), and glycan structures. It is the complex glycan (sugar) structures of NSP that are unique and are yielding significant scientific advances in medicine, materials, food, and healthcare.[4]

At present, the metabolic fate of orally ingested NSPs such as mannans, glucans, and fucoidans is yet to be clearly identified. To our knowledge, no study has determined the specific pathways of orally ingested NSP in human tissue. So, there is little information in humans regarding the pharmacokinetics and metabolism of these carbohydrate polymers in neurological health.

Growing evidence shows neurological effects of oral and intravenously administered NSP in animals and humans.[5] These include, central nervous system development and function, cell migration and

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proliferation,[6] and increased synaptic plasticity and electrical activity of neurons within the hippocampus[5] that could underpin aspects of cognitive function such as memory, speed of processing, and attention. The potential impact of NSPs as bioactive carbohydrate polymers on cognitive function and the potential mechanisms of action remain largely unknown. A number of preliminary studies indicate positive effects of distinctive NSP on cognitive function in humans.

### *Dietary polysaccharides and cognitive function*

Placebo-controlled experimental studies show that the consumption of a standardized, commercially available blend of arabinogalactans, gluco- and galactomannans, acemannan, and glucosamine (Ambrotose® complex, Mannatech Incorporated, Coppell, TX, USA) improves cognitive performance following both acute and chronic intake.[7–9]

Using the same blend (Ambrotose® complex), two studies in young adults show acute cognitive benefits 30 and 45 minutes after consuming an estimated 4–7 g dose (one tablespoon) of these NSP. The first study assessed acute effects on electroencephalograph-associated changes in brain activity compared with placebo. The results showed increased brain activity that was associated with the cognitive ability of attention and concentration, compared with placebo 30 minutes after consumption.[10] The second study used a placebo-controlled, cross-over design with a similar estimated 4–7 g dose (one tablespoon). The results showed enhanced perceptual memory and working memory performance, measured by the same–different visual discrimination task and the reading span task, respectively, following acute NSP intake compared with placebo, 45 minutes post-ingestion.[7]

One other study has investigated the acute effects of NSP intake on cognitive performance in middle-aged adults.[11] Compared with glucose (25 g) and placebo, inspection of the means showed that a single, standardized dose of 7 g of Ambrotose® complex may have increased performance on memory tasks, but the differences between treatment conditions was not statistically significant (placebo $M = 48.13$, $SD$ 8.27; glucose $M = 48.40$, $SD = 9.43$; polysaccharides $M = 52.27$, $SD = 7.54$, $F(2, 42) = 0.65$, $P = 0.52$). A recent study[9] with middle-aged adults showed beneficial effects of the same NSP blend using a standardized 4 g dose for cognition and mood following chronic (12 weeks) supplementation. Specifically, when compared with placebo, those individuals who consumed the NSP performed significantly better on tasks of recall and recognition memory and reported significantly reduced scores for tension and low mood.[9]

Taken together, these preliminary studies provide evidence of the positive cognitive effects of these NSP following acute and chronic intake. However, there is limited understanding of the potential mechanism through which they may be impacting cognitive performance. One possible, well-documented mechanism of action of carbohydrates on cognition is through blood glucose. As complex carbohydrate polymers, due to the amount of constituent sugars and glycan structures, it is possible that NSP are converted into glucose following ingestion. While preliminary studies show that the arabinogalactans, galacto-, and glucomannans are metabolized by the human gut[1] and incorporated into glycoconjugates in humans,[3] little is known about a potential glucose mediated effect on cognitive function. Thus, it is important to determine whether these distinctive NSPs or their metabolic substrates elicit a blood glucose response that may mediate cognitive effects.

In order to distinguish the cognitive effects of such dietary interventions, outcome measures need to be sensitive to change and eliminate the potential effects of prior learning and experience on performance. In addition, the concept and experience of mental fatigue in middle-aged adults is relevant to the everyday cognitive experience of many adults. This study will evaluate the extent to which polysaccharides may impact the performance of demanding cognitive and memory performance tasks. The cognitive demand battery (CDB) consists of repeated cycles of Serial Threes, Serial Sevens, the Bakan rapid visual information processing (RVIP) task, and self-rated mental fatigue. Previous studies have shown that, over six or more repetitions of this battery, mental fatigue ratings are reliably increased and performance reliably declines.[12] Thus, this study will explore the acute effects of NSP intake in middle-aged adults under conditions of mental fatigue, while monitoring changes in blood glucose.

## Method

### *Overview*

This was an acute, between subjects, double-blind, randomized controlled trial conducted at two centres involving single administration of polysaccharides, placebo (rice flour), or sucrose control. Participants attended one, 3.5 hours testing session involving baseline and post-treatment assessments of cognitive performance and mental fatigue, plus a 30-minute absorption time. The study was granted ethical approval by the University of South Australia and Swinburne University of Technology Human Research Ethics Committees, and was registered with the Australia and New Zealand Clinical Trials Registry (ACTRN12610000624088).

### *Participants*

Seventy-three healthy middle-aged volunteers (age 45–60 years, 26 male, 47 female) took part in the study. Prior to participation, volunteers provided written informed consent and completed a background health questionnaire to determine the following: age, height, and weight (in order to calculate body mass index (BMI)), years of education, the number of hours of work per week, self-rated health, (rated on a scale from 1 = poor to 5 = excellent), the number of dietary supplements used, the number of medications used, the number of hours of exercise per week, and alcohol consumption (the number of standard drinks consumed in a typical week). Descriptive statistics for the three treatment groups, including gender by the treatment group, are presented in Table 1. Participants were eligible to take part if they self-reported they were in good health and reported, at most, low dose, stable, preventive health medication use (e.g.: hormone replacement therapy or other consistent and stable medication use for blood pressure, cholesterol, or thyroid), no history of head injury, stroke or neurological condition, heart disease, diabetes, or gastrointestinal condition that may impact food metabolism.

### *Procedure*

Participants attended the research facility on a single day for a period of 3.5 hours during which they completed two testing sessions: one baseline test and one post-treatment test. All testing took place between 08:00–12:00 and 13:00–18:00. On testing days, 2 hours before their visit, participants were to fast and abstain from consuming any stimulants (e.g. tea, coffee, other caffeine-containing products). Compliance was assessed through self-report before commencement of session. Each study day comprised of a practice module, a pre-treatment baseline testing session on the mood and cognitive measures, followed immediately by a pre-treatment blood glucose measurement, and administration of treatment. A 30-minute absorption time was used based on blood glucose peak response time used in similar research designs. Following the 30-minute absorption period, a finger-capillary blood glucose measurement was taken and post-treatment assessment, using alternate forms of tests was completed, followed by a final blood glucose measurement. Fig. 1 shows the running order for the study day.

**Table 1 Descriptive statistics for baseline health and demographic characteristics for treatment conditions**

| | Treatment condition | | |
|---|---|---|---|
| Background variable | Polysaccharides *N* = 23 | Sucrose *N* = 24 | Placebo *N* = 26 |
| Gender | M = 8, F = 15 | M = 9, F = 17 | M = 9, F = 15 |
| Age in years | 53 (4.41) | 52 (4.35) | 53 (4.49) |
| BMI (kg/m$^2$) | 27 (4.48) | 29 (8.00) | 26 (3.82) |
| Years of education | 16 (4.70) | 15 (3.32) | 15 (3.99) |
| Self-rated health | 4.0 (0.90) | 4.9 (0.62) | 4.1 (0.56) |
| Hours of work/ week | 23.5 (15.81) | 21.4 (19.04) | 19.5 (18.24) |
| Hours of exercise/ week | 4.5 (4.01) | 4.3 (3.77) | 4.4 (3.49) |
| Number of supplements | 1.91 (1.37) | 2.66 (2.28) | 2.86 (1.88) |
| Number of medications | 1.61 (1.19) | 1.38 (0.76) | 1.62 (0.51) |
| Number of alcoholic drinks/ week | 5.7 (6.18) | 5.5 (6.11) | 5.2 (4.56) |

M, male; F, female.

### *Treatments*

The treatment received by participants, depending on randomization was one of the three, powdered treatments: a mixture of polysaccharides (Ambrotose complex), sucrose (icing sugar), or placebo (rice flour). To ensure blinding, a research assistant who was otherwise uninvolved in the study delivered a 4 g dose of the supplement to each participant on a tablespoon with 100 ml of water. This dose was used based on the standardized dose of 4 g used in the previous research that detected positive effects on cognitive function.[9]

The plant polysaccharide and placebo products were manufactured and supplied by Mannatech Incorporated in separate individual 100 g containers that were stored in a cool, dry environment. The pure sucrose powder was Australian-made icing sugar. The mixed plant-polysaccharide supplement contained a standardized mixture of saccharide biopolymers having 64% of their molecular weight higher than 1 700 000 Da: 48% arabinogalactan, 10% aloe vera gel extract, 10% gum ghatti, 10% gum tragacanth that contain gluco- and galactomannans, acetylated mannans, and acemannan, 10% glucosamine HCL, together with 12% rice starch. The placebo supplement was rice flour. Table 2 shows the energy and carbohydrate content of a 4 g dose of each treatment.

## Measures

### *Learning and memory*

The Rey Auditory Verbal Learning Test (RAVLT)[13] was used to assess immediate recall, delayed recall, learning, and recognition memory. The examiner read aloud 15 nouns (list A) over five trials and, after each trial, participants were asked to recall, in any order, as many of the 15 words as possible. Correct responses for the five trials were summed to produce a measure of immediate recall. After a sixth trial consisting of 15 different words (list B), participants were again required to recall the words that

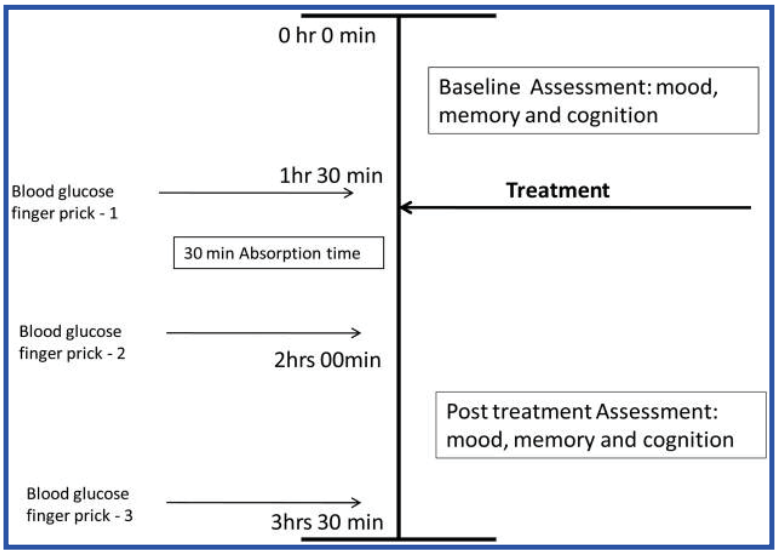


**Figure 1 Running order for testing day.**

were presented in list A (trial 7), and then again after an interval of 60 minutes (trial 8). The scores from trials 7 and 8 were summed to produce a measure of delayed recall. After trial 8, participants were presented with a sheet of 50 words containing the words from lists A and B among 20 distracter words. Participants were asked to recognize the words from lists A and B and indicate the list they came from. Each word correctly identified was awarded one point, producing a measure of recognition.

### *Cognitive measures*

The computerized CDB was comprised of six repetitions of a 10-minute assessment that measured the speed, accuracy, and mental fatigue of performance during continuous, cognitively demanding tasks. Each 10 minutes cycle of this battery comprised two serial subtraction tasks (Serial Threes – 2 minutes, and Serial Sevens – 2 minutes), a RVIP task (5 minutes), and a visual analogue scale (VAS) for mental fatigue (1 minute). The individual tasks are described below.

**Table 2 Energy and carbohydrate composition of treatment conditions**

| | Treatment condition | | |
|---|---|---|---|
| Composition | Ambrotose® complex (polysaccharides) (4 g) | Sucrose powder (4 g) | Placebo (rice flour) (4 g) |
| Energy (kcal) | 0.01 | 16 | 16 |
| Total carbohydrates (g) | 3.3 | 4 | 3.4 |
| Glucose (g) | 0.4 | 2 | 3.4 |
| Other sugars (g) | 2.7* | 2** | 0 |
| Dietary fibre (g) | 2.2 | 0 | 0 |
| Protein (g) | 0.04 | 0 | 0.32 |

*Arabinose, fucose, galactose, galactosamine, galacturonic acid, glucosamine, glucuronic acid, mannose, rhamnose, and xylose.
**Fructose.

#### Serial Threes subtraction task (2 minutes)

Participants were required to count backwards in threes from a random starting number between 800 and 999 presented on the computer screen, and enter their answer as quickly and as accurately as possible by using the linear number keys at the top of the computer keyboard. The starting number was cleared from the screen once participants entered their first response. Each subsequent three digit response by participants was presented on the screen as asterisks. Participants pressed the enter key to signal the end of each response and clear the three asterisks from the screen. The task was scored for the number of correct and incorrect responses, the average reaction time, and the proportion of correct responses made, given the average reaction time (i.e. accuracy vs. speed).

#### Serial Sevens subtraction task (2 minutes)

This task was identical to the Serial Threes task, above, except that participants were asked to subtract sevens.

#### RVIP task (5 minutes)

Participants were required to monitor a continuous series of digits for target strings of three consecutive odd or three consecutive even digits. The digits were presented on the screen at a rate of 100 per minute and there were 8 targets per minute. The participant responded by pressing the space bar as quickly as possible when they detected a target string of digits. The task was scored for the number of target strings correctly detected, the percentage of correct answers, the

number of false alarms, the average reaction time for correct detections, and the proportion of correct responses made, given the average reaction time (accuracy vs. speed).

#### 'Mental-fatigue' VAS (1 minute)

Participants rated their subjective feelings of mental fatigue on one 100 mm VAS with anchors of 'not at all' and 'very much so'.

### *Mood and well-being measures*

Background general mood and well-being were assessed with the profile of mood states (POMS) and SF-36 health survey to determine any background differences between the groups. On the testing day, subjective mood states, as outcome measures, were assessed with the paper-and-pencil State-trait anxiety questionnaire, and the Bond–Lader VAS that measured three mood states, alertness, calmness, and contentedness.

1. The POMS[14] is a self-report 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.
2. The SF-36 health survey[15] provides a measure of functional, physical, and psychological health across seven general health and well-being concepts: (1) limitations in physical activities because of health problems; (2) limitations in social activities because of physical or emotional problems; (3) limitations in usual role activities because of physical health problems; (4) general mental health (psychological distress and well-being); (5) limitations in usual role activities because of emotional problems; (6) vitality (energy and fatigue); and (7) general health perceptions.
3. The State-trait anxiety questionnaire[16] contains 20 items that record the presence (e.g. 'I am tense') or the absence (e.g. 'I feel at ease') of anxiety symptoms. Participants are asked to rate each item according to how they are generally feeling on a 4-point scale ranging from 'not at all' or 'almost never' to 'very much so' or 'almost always'. These are combined to provide a sum score between 20 and 80 (a lower score representing lower anxiety).
4. The Bond–Lader VAS[17] consists of $16 \times 100\ mm^2$ VASs. Participants indicate their current subjective state of mood for the 16 pairs of linked antonyms (e.g. attentive–dreamy, trouble–tranquil, happy–sad, alert–drowsy) by using the computer mouse to click on the line at a position that reflects their levels of mood. The results are combined to provide measures of self-rated alertness, calmness and contentedness.

### *Blood glucose measurement*

Blood glucose samples were measured using an automated analyser (ACCU-CHEK®, optimal blood glucose monitor and testing strips, Roche Diagnostics). Blood samples were collected using self-administered single-use capillary blood sampling lancet tips. Alcohol soaked cleansing swabs were used for pre-sampling sterilization. The blood glucose readings were recorded at three testing points: pre-treatment, post-treatment and post-cognitive testing.

### *Statistical analysis*

The primary outcomes were memory performance on the RAVLT, performance on the CDB, and mood and subjective ratings of mental fatigue. To test for chance baseline differences, which may have influenced change-from-baseline scores, prior to the primary statistical analysis, all pre-dose baseline measures were subjected to a one-way analysis of variance with Bonferroni correction, including demographics, general mood and well-being measures, and all cognitive and memory measures.

All data were analysed using SPSS for windows, Version 17, Chicago: SPSS Inc. as 'change from pre-treatment baseline scores'. Change from baseline scores were used to take into account chance baseline differences between treatment conditions and reduce the impact of regression to the mean[18] Analysis of covariance with baseline scores included as a covariate were used on those measures that significantly differed at baseline.

## Results

### *Baseline health and well-being group characteristics*

There were no significant differences between groups in demographic measures, including age, BMI, education, or overall self-rated health, so they were not used as covariates (Table 1). There was a significant difference between groups on the baseline POMS scale of anxiety ($F(3,68) = 3.25$, $P = 0.044$) (data not shown), but *post hoc* comparisons revealed that no group was significantly different from another. The direction of means, however, suggested that the placebo group was less anxious than the polysaccharide and the sucrose groups ($P = 0.06$ and 0.08, respectively). The anxiety sub-scale from the POMS was used as a covariate in analysis for differences between post-treatment changes from baseline for measures of memory, cognitive demand tasks, and subjective mood ratings.

There were no significant differences between groups on measures of memory (RAVLT) or subjective mood ratings (State-trait anxiety and Bond–Lader alertness, calmness, and contentedness) at baseline

(data not shown). There was a marginal difference between groups on the percentage correct and the number correct on the RVIP task from the CDB, but these differences did not reach statistical significance ($P = 0.052$ and $P = 0.053$, respectively). While not significant, those in the polysaccharide group tended to exhibit a higher mean performance than those in the placebo group ($P = 0.08$) but not the sucrose group ($P = 0.14$) (see Table 4 for baseline scores).

## *Effects of acute treatment*

### Memory (RAVLT)

The post-treatment 'change-from-baseline' RAVLT data are presented in Table 3. There was a significant difference between groups in change-from-baseline performance on tasks of recognition memory, sum ($F(2,68) = 3.28$, $P = 0.004$), list A ($F(2,68) = 3.28$, $P = 0.044$), and list B ($F(2,68) = 4.99$, $P = 0.009$), respectively. *Post hoc* analysis showed that those in the polysaccharide group recognized significantly more words overall than those in the sucrose group ($P = 0.004$) post-treatment, due to recognition of more words from list B ($P = 0.007$), but not list A ($P = 0.083$). There was a trend for those in the polysaccharide group to recognize more words than those in the placebo group ($P = 0.07$), but this was not significant. Fig. 2 shows the change in recognition memory scores (sum) between the three treatment conditions.

### Cognitive demand battery

Table 4 provides means and standard error for each task of the CDB, as pre- and post-treatment scores for each cycle.

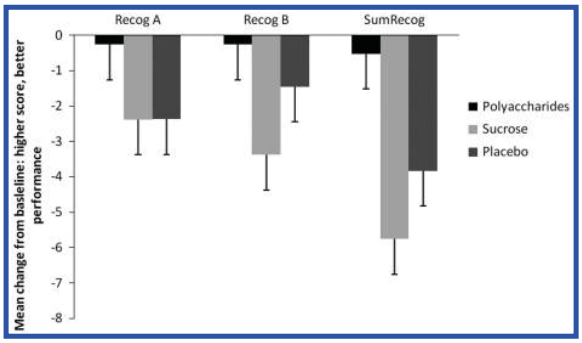


**Figure 2 Means and standard errors of RAVLT recognition memory scores: post-treatment change from baseline for treatment conditions.**

### *Serial Threes*

There was a significant main effect of time across the six repetitions of the CDB post-treatment on the number of correct answers ($F(5,340) = 2.16$, $P = 0.05$), and a trend towards a main effect of treatment ($F(2,68) = 2.70$, $P = 0.07$), with the direction of means indicating a higher number correct responses in the polysaccharide group compared with those in the sucrose group ($P = 0.07$), but not the placebo ($P = 0.83$). There was no significant time by treatment interaction ($F(10,340) = 0.94$, $P = 0.48$). There was a significant main effect of time on the proportion of correct answers given the average reaction time ($F(5,340) = 3.94$, $P = 0.002$) and a trend towards a main effect of treatment ($F(2,70) = 2.96$, $P = 0.058$), with the direction of means indicating a higher proportion of correct responses given the average reaction time in the polysaccharide group compared with those in the sucrose group ($P = 0.058$) but not the placebo

**Table 3 Means and standard errors for RAVLT post-treatment change-from-baseline scores for treatment conditions**

| | Treatment condition | | | |
|---|---|---|---|---|
| Measure | Polysaccharides $N = 23$ | Sucrose $N = 24$ | Placebo $N = 26$ | $F(2,68)$ |
| *RAVLT* | | | | |
| Immediate recall | | | | |
| Trial 1 | −0.78 (0.41) | −0.26 (0.39) | −0.54(0.42) | 0.429 |
| Trial 2 | −0.60 (0.45) | −0.57 (20.42) | −0.95 (0.46) | 0.017 |
| Trial 3 | 0.21 (0.37) | −0.42 (0.35) | −0.58 (0.38) | 1.35 |
| Trial 4 | −0.04 (0.41) | −0.42 (0.39) | −0.08 (0.42) | 0.263 |
| Trial 5 | 0.08 (0.35) | −0.19 (0.33) | 0.58 (0.36) | 0.918 |
| Sum immediate recall | −1.13(1.22) | −1.88 (1.15) | −1.58 (1.25) | 0.103 |
| Trial 6 (list B) | −0.08 (0.44) | −0.84 (0.42) | −0.25 (0.45) | 0.821 |
| Trial 7 | −0.82 (0.60) | −1.53 (0.57) | −1.08 (0.62) | 0.369 |
| Delayed recall | | | | |
| Trial 8 | −1.91 (0.63) | −3.23 (0.60) | −2.29 (0.65) | 1.18 |
| Recognition memory | | | | |
| Recog A | −0.26 (0.70) | −2.38 (0.66) | −2.37 (0.72) | 3.28 |
| Recog B | −0.26 (0.72) | −3.38 (0.68) | −1.45 (0.74) | 4.99* |
| Sum recognition memory | −0.52 (0.70) | −5.76 (0.66) | −3.83 (0.72) | 3.28* |
| Interference (trial 7 – trial 5) | −0.91 (0.55) | −1.34 (0.51) | −1.66 (0.56) | 0.417 |
| Learning (trial 5 – trial 1) | 0.86 (0.51) | 0.07 (0.48) | 1.12 (0.53) | 1.20 |
| Forgetting (trial 8 – trial 7) | −1.08 (0.65) | −1.69 (0.61) | −1.20 (0.67) | 0.254 |

*$P < 0.05$.

**Table 4 Means and standard errors of CDB task performance for treatment conditions**

| | | Pre-treatment baseline score | | Change from baseline scores for each 10 minutes cycle | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 10 minutes | | 20 minutes | | 30 minutes | | 40 minutes | | 50 minutes | | 60 minutes | |
| Measure | | M | se | M | se | M | se | M | se | M | se | M | se | M | se |
| Serial Threes, correct | Polysaccharides | 31.04 | 2.80 | 1.39 | 1.27 | 3.86 | 1.30 | 1.82 | 1.54 | 4.13 | 1.35 | 3.56 | 1.44 | 3.00 | 1.36 |
| | Sucrose | 33.57 | 2.05 | −1.57 | 1.19 | 0.69 | 1.22 | −1.88 | 1.45 | −0.15 | 1.27 | 1.46 | 1.35 | −0.30 | 1.27 |
| | Placebo | 29.83 | 2.74 | 0.37 | 1.24 | 0.83 | 1.27 | 2.75 | 1.51 | 0.87 | 1.32 | 2.45 | 1.41 | 2.41 | 1.33 |
| Serial Threes incorrect | Polysaccharides | 2.30 | 1.86 | −0.47 | 0.55 | −0.78 | 0.60 | −0.30 | 0.58 | −0.56 | 0.71 | −1.04 | 0.63 | 0.26 | 0.64 |
| | Sucrose | 2.19 | 2.96 | 0.15 | 0.51 | 0.11 | 0.56 | 0.23 | 0.54 | 0.42 | 0.67 | 0.76 | 0.59 | 0.76 | 0.61 |
| | Placebo | 2.41 | 2.22 | 0.41 | 0.51 | −0.29 | 0.58 | −0.33 | 0.57 | 0.95 | 0.69 | −0.20 | 0.62 | −0.20 | 0.63 |
| Serial Threes reaction time (milliseconds) | Polysaccharides | 4251.0 | 458.22 | −247.69 | 269.61 | −351.00 | 235.98 | −54.60 | 324.44 | −425.69 | 246.32 | −352.91 | 255.86 | −181.00 | 245.5 |
| | Sucrose | 3569.7 | 189.55 | 109.69 | 253.58 | −93.73 | 221.95 | 312.65 | 305.15 | −50.84 | 231.68 | −232.23 | 240.65 | −147.73 | 230.9 |
| | Placebo | 4382.1 | 504.65 | −393.37 | 263.93 | −256.66 | 231.01 | −451.41 | 317.61 | −452.54 | 241.14 | −394.20 | 250.47 | −547.08 | 240.3 |
| Serial Threes proportion correct/ reaction time | Polysaccharides | 10.09 | 1.59 | 0.53 | 0.68 | 2.332 | 0.75 | 1.11 | 0.77 | 2.43 | 0.64 | 2.15 | 0.80 | 2.18 | 0.77 |
| | Sucrose | 10.92 | 1.23 | −1.03 | 0.64 | −0.43 | 0.71 | −0.64 | 0.72 | −0.00 | 0.60 | 1.39 | 0.75 | −0.01 | 0.72 |
| | Placebo | 9.39 | 1.35 | 0.29 | 0.66 | 0.38 | 0.74 | 1.45 | 0.75 | 1.04 | 0.62 | 1.86 | 0.78 | 1.38 | 0.75 |
| Serial Sevens correct | Polysaccharides | 20.47 | 1.99 | −0.60 | 1.24 | 1.65 | 0.79 | 1.39 | 1.01 | 2.39 | 1.03 | 1.17 | 1.23 | 0.08 | 0.98 |
| | Sucrose | 21.76 | 1.79 | −1.53 | 1.17 | 1.26 | 0.74 | −0.15 | 0.95 | −0.19 | 0.97 | −0.73 | 1.15 | 0.93 | 0.92 |
| | Placebo | 19.04 | 2.02 | −0.16 | 1.21 | −1.37 | 0.77 | 2.45 | 0.99 | 0.12 | 1.01 | 1.62 | 1.20 | 1.70 | 0.96 |
| Serial Sevens incorrect | Polysaccharides | 3.08 | 0.35 | −0.34 | 0.57 | −0.91 | 0.45 | −0.47 | 0.60 | −0.13 | 0.70 | 0.17 | 0.50 | 1.30 | 0.88 |
| | Sucrose | 2.53 | 0.51 | −0.07 | 0.54 | −0.30 | 0.43 | −0.34 | 0.57 | 1.00 | 0.66 | 0.38 | 0.47 | 0.65 | 0.83 |
| | Placebo | 3.00 | 0.49 | 0.66 | 0.56 | 0.45 | 0.44 | −0.33 | 0.59 | 0.66 | 0.69 | −0.16 | 0.49 | −0.41 | 0.87 |
| Serial Seven reaction time (milliseconds) | Polysaccharides | 5933.8 | 640.47 | 1335.9 | 491.22 | 347.08 | 342.91 | 20460 | 356.25 | −283.39 | 355.09 | 70.17 | 356.46 | −56.56 | 331.6 |
| | Sucrose | 5455.3 | 417.92 | 278.53 | 462.01 | −439.65 | 322.52 | −225.38 | 335.07 | −150.00 | 333.98 | −156.88 | 335.26 | −547.11 | 311.9 |
| | Placebo | 6296.7 | 566.22 | 290.79 | 480.88 | 658.29 | 335.69 | −753.29 | 348.75 | −131.62 | 347.61 | −108.16 | 348.95 | −180.58 | 324.6 |
| Serial Sevens proportion correct/ reaction time | Polysaccharides | 4.81 | 0.82 | 0.01 | 0.44 | 0.69 | 0.28 | 0.50 | 0.35 | 1.25 | 0.46 | 0.77 | 0.51 | 0.32 | 0.38 |
| | Sucrose | 5.11 | 0.74 | −0.50 | 0.41 | 0.47 | 0.27 | 0.13 | 0.33 | 0.19 | 0.43 | −0.36 | 0.48 | 0.44 | 0.35 |
| | Placebo | 4.32 | 0.74 | 0.21 | 0.43 | −0.37 | 0.28 | 0.84 | 0.35 | 0.20 | 0.45 | 0.75 | 0.50 | 0.64 | 0.37 |
| RVIP correct | Polysaccharides | 19.47 | 1.45 | 1.52 | 1.08 | 1.17 | 1.20 | −1.45 | 1.14 | 0.24 | 1.30 | 1.50 | 1.29 | 0.61 | 1.28 |
| | Sucrose | 14.57 | 1.68 | −0.10 | 1.00 | −0.43 | 1.12 | −0.28 | 1.06 | 0.51 | 1.21 | −1.45 | 1.20 | −0.79 | 1.19 |
| | Placebo | 15.75 | 2.20 | 1.23 | 1.04 | 0.47 | 1.16 | −0.29 | 1.10 | −0.95 | 1.25 | −2.15 | 1.25 | −0.14 | 1.23 |
| RVIP false alarms | Polysaccharides | 5.69 | 0.84 | −1.82 | 4.22 | −0.69 | 2.56 | 0.13 | 2.47 | −0.26 | 3.63 | −0.52 | 2.64 | −1.69 | 3.28 |
| | Sucrose | 9.26 | 3.79 | 4.88 | 3.97 | 1.11 | 2.41 | −1.88 | 2.33 | 1.84 | 3.41 | 1.38 | 2.49 | −3.50 | 3.09 |
| | Placebo | 8.04 | 3.74 | −5.33 | 4.13 | −4.91 | 2.51 | −5.20 | 2.42 | −5.12 | 3.55 | −3.91 | 2.59 | −4.58 | 3.21 |
| RVIP% accuracy | Polysaccharides | 48.77 | 3.66 | 3.74 | 2.70 | 2.92 | 3.01 | −3.62 | 2.85 | −0.56 | 3.25 | 3.70 | 3.24 | 1.46 | 3.20 |
| | Sucrose | 36.47 | 4.20 | −0.29 | 2.52 | −1.12 | 2.80 | −0.75 | 2.66 | 1.25 | 3.03 | −3.65 | 3.02 | −1.99 | 2.98 |
| | Placebo | 39.38 | 5.51 | 3.05 | 2.60 | 1.15 | 2.89 | 0.72 | 2.75 | −2.35 | 3.13 | −5.36 | 3.12 | −0.38 | 3.08 |
| RVIP reaction time (milliseconds) | Polysaccharides | 516.66 | 11.77 | 4.86 | 25.12 | 12.02 | 17.95 | 8.63 | 17.97 | 4.24 | 14.26 | 14.74 | 13.10 | 18.73 | 12.93 |
| | Sucrose | 497.93 | 23.67 | 20.92 | 23.63 | 3.57 | 16.88 | 39.26 | 16.90 | 26.81 | 13.42 | 10.63 | 12.32 | 2.46 | 12.16 |
| | Placebo | 482.56 | 31.76 | 14.69 | 25.12 | 14.74 | 17.95 | −0.86 | 17.97 | 10.67 | 14.26 | 25.83 | 13.10 | 22.39 | 12.93 |

*Continued*

**Table 4** *Continued*

| Measure | | Pre-treatment baseline score | | Change from baseline scores for each 10 minutes cycle | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 10 minutes | | 20 minutes | | 30 minutes | | 40 minutes | | 50 minutes | | 60 minutes | |
| | | M | se | M | se | M | se | M | se | M | se | M | se | M | se |
| RVIP proportion correct/reaction time | Polysaccharides | 39.05 | 3.50 | 0.91 | 2.27 | −0.19 | 2.54 | −5.29 | 2.30 | −2.07 | 2.62 | −0.68 | 2.80 | −2.51 | 2.74 |
| | Sucrose | 28.65 | 3.09 | 1.38 | 2.18 | 0.14 | 2.43 | 0.63 | 2.21 | 1.77 | 2.51 | −1.38 | 2.68 | 0.57 | 2.63 |
| | Placebo | 33.30 | 4.28 | 3.66 | 2.33 | 1.56 | 2.59 | 1.06 | 2.36 | -2.45 | 2.68 | −4.25 | 2.86 | −0.08 | 2.80 |
| VAS mental fatigue | Polysaccharides | 76.65 | 3.66 | −26.65 | 3.96 | −14.91 | 3.73 | −8.30 | 3.68 | −3.34 | 3.66 | −0.30 | 3.57 | 4.08 | 3.91 |
| | Sucrose | 68.46 | 4.16 | −11.11 | 3.73 | −5.92 | 3.51 | −0.53 | 3.46 | 2.65 | 3.44 | 6.69 | 3.36 | 9.42 | 3.68 |
| | Placebo | 70.54 | 4.73 | −21.41 | 3.88 | −12.50 | 3.65 | −9.79 | 3.60 | −2.70 | 3.58 | 2.91 | 3.49 | 1.20 | 3.83 |
| VAS mental fatigue reaction time | Polysaccharides | 5702.08 | 786.43 | 1819.8 | 967.18 | 138.87 | 2043.65 | 309.0 | 741.89 | −597.91 | 846.81 | −871.52 | 738.57 | −992.39 | 776.15 |
| | Sucrose | 5853.80 | 589.21 | 159.57 | 909.67 | 4457.96 | 1922.14 | −48.96 | 697.78 | −251.88 | 796.46 | −347.15 | 694.66 | −1491.5 | 730.00 |
| | Placebo | 5061.95 | 395.34 | 2010.0 | 946.82 | 1236.91 | 2000.62 | 49.12 | 726.27 | 270.54 | 828.99 | −606.29 | 723.02 | −747.79 | 759.81 |

M, mean; se, standard error.

($P = 1.00$). There was no significant time by treatment interaction ($F(10,340) = 0.898$, $P = 0.54$). There were no statistically significant effects associated with either time, treatment, or time by treatment interactions on the number of incorrect responses made or on the average reaction time.

### *Serial Sevens*

There was a significant main effect of time on the number of correct answers made ($F(5,340) = 2.52$, $P = 0.02$), but no significant main effect of treatment ($F(2,68) = 0.547$, $P = 0.58$). There was a significant time by treatment interaction ($F(10,340) = 2.53$, $P = 0.006$). *Post hoc* analysis showed a significant difference between groups during the second cycle (approximately 55 min post-treatment), with those in the polysaccharide group making significantly more correct responses than the placebo ($P = 0.02$), but not the sucrose ($P = 1.00$) groups and those in the sucrose group making significantly more correct responses than the placebo group ($P = 0.04$). There was neither a significant main effect of time on the proportion of correct answers given the average reaction time ($F(5,340) = 1.66$, $P = 0.14$), nor a main effect of treatment ($F(2,68) = 0.93$, $P = 0.39$). There was a significant time by treatment interaction ($F(10,340) = 1.91$, $P = 0.04$). *Post hoc* analysis showed a significant difference between groups during the second cycle with those in the polysaccharide group making significantly more correct responses than the placebo ($P = 0.03$), but not the sucrose ($P = 1.00$) groups. There were no statistically significant effects associated with either time, treatment, or time by treatment interactions on the number of incorrect responses made or on the average reaction time.

### *RVIP task*

There were no statistically significant effects associated with either time, treatment, or time by treatment interactions on the total number of responses, the number of correct or incorrect RIVP responses made.

### *Mental fatigue*

There was a main effect of time on subjective ratings of mental fatigue ($F(5,340) = 75.44$, $P < 0.001$), with increasing fatigue across time (Fig. 3). There was no significant main effect of treatment ($F(2,68) = 2.04$, $P = 0.13$) or time by treatment interaction ($F(10,340) = 1.39$, $P = 0.18$) on mental fatigue. *Post hoc* analysis showed a significant difference between groups at the first cycle, which is approximately 45 minutes post-treatment ($F(2,70) = 4.27$, $P = 0.018$), with those in the polysaccharide group reporting a significant reduction in feelings of fatigue approximately 45 minutes post-consumption, compared with those in the sucrose group ($P = 0.01$).

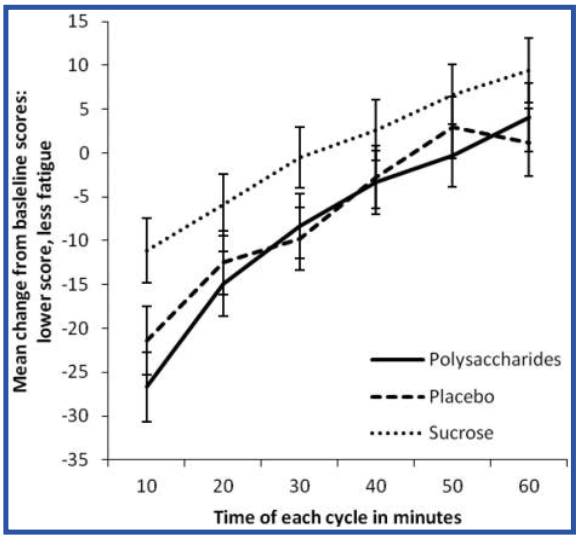


**Figure 3 Means and standard errors of mental fatigue VAS: post-treatment change from baseline for treatment conditions.**

### *Mood*

There were no statistically significant effects associated with either treatment on subjective levels of anxiety measured by the State-trait questionnaire, or on the Bond–Lader scales of alertness, contentedness, and calmness as change-from-baseline scores (data not shown).

### *Blood glucose measurement*

There was a significant main effect of time ($F(2,140) = 37.28$, $P < 0.001$) and significant interaction of time and treatment condition ($F(4,140) = 8.39$, $P < 0.001$) on blood glucose concentrations. There was no significant main effect of treatment condition on blood glucose concentrations ($F(2,70) = 2.41$, $P = 0.09$). Importantly, gender was also considered in blood glucose analysis due to differences in blood glucose tolerance between genders (not shown in Fig. 4).[19]

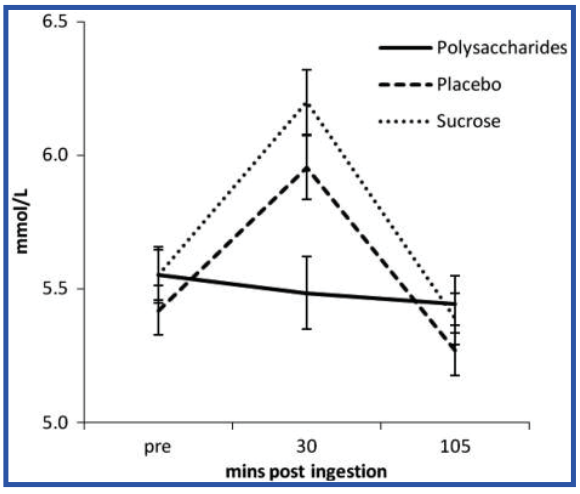


**Figure 4 Means and standard errors of capillary blood glucose levels for treatment conditions.**

There was a main effect of gender on blood glucose concentrations, not due to the presence of outliers ($F(1,59) = 26.40$, $P < 0.001$), that showed males have higher blood glucose concentrations than females (data not shown). There were no significant interactions of gender by treatment or gender by time. Pairwise comparisons show that at 30 minutes post-treatment, those who consumed the polysaccharide supplement had significantly lower blood glucose levels than those who had consumed placebo ($P = 0.038$) or sucrose ($P < 0.001$). Specifically, there was no rise in blood glucose response following polysaccharide intake compared with the blood glucose response for those individuals who consumed sucrose or placebo (Fig. 4).

## Discussion

This study explored the acute effects of a polysaccharide supplement, compared with sucrose and placebo (rice flour) treatments, on cognition and mood in middle-aged adults during effortful and mentally fatiguing conditions, and whether any effects may be explained through a glycaemic mechanism. The results of the first exploratory acute assessment showed consumption of NSP improved memory performance under conditions of mental fatigue in healthy middle-aged adults, not explained by raised blood glucose.

Specifically, the 4 g polysaccharides blend improved recognition memory performance compared with sucrose consumption, with a similar non-significant trend towards improved performance compared with placebo. This positive effect on recognition memory, as opposed to recall memory performance, suggests that those who ingested polysaccharides were differentially aided in cued retrieval of previously encoded stimuli, rather than aspects of learning or encoding information. With regard to performance on tasks in the CDB, there was a significant time × treatment interaction for performance on Serial Sevens task, with greater number of correct responses performed during the second, 10 minutes cycle (which is 45 minutes post-treatment) of the battery for those in the polysaccharide condition compared with those in the placebo condition.

There was a similar, non-significant trend towards a positive treatment effect of NSP on Serial Threes performance.

Performing Serial Sevens subtraction tasks is significantly more demanding than Serial Threes, and relies more heavily on working memory and executive resources. The current results suggest that consumption of these NSP helps to maintain working memory performance under conditions of subjective mental fatigue. Interestingly, the trends towards improved performance on Serial Threes following

intake of polysaccharides, may indicate potential working memory and attention effects, as performance on both Serial Threes and Serial Sevens tasks have attentional components.

In relation to mood, there were no significant treatment effects on acute subjective ratings of feelings of anxiety, alertness, contentedness, or calmness.

This is the first study to examine the blood glucose response to consumption of this combination of polysaccharides in humans. The absence of a rise in blood glucose following their intake, compared with starch and sucrose control, indicates that the improvements in recognition memory and working memory, were unlikely to have been mediated by glucose-related mechanisms. Perhaps, this finding is not surprising, given that the effective doses of the NSP mixture for improved cognition are in the range of 4–7 g (yielding <1 g of glucose), whereas glucose doses of 25–50 g are typically required for memory enhancement. Thus, we can now preclude with some confidence the possibility that glycaemic changes underlie the cognitive effects of a 4 g dose of polysaccharides. Importantly, the effects on recognition memory and Serial Sevens task performance are consistent with the effects of other carbohydrate-based interventions.[20] However, here, they were observed with a low-energy content of 4 g dose compared with the high-energy content of 37.5 g carbohydrate and 50 g glucose loads used in other studies. Thus, the current findings raise questions regarding the potential potency of active carbohydrate polymers in plant polysaccharide form.

Knowledge of the pharmacokinetics and tissue absorption of polysaccharides is limited. Consequently, the mechanisms by which NSP may benefit cognition remain largely unknown. However, it is well documented, that the hippocampus is involved in learning and memory, and is a crucial structure for the initial encoding and storage of memories involving synaptic plasticity. In addition, communication between the hippocampus and the pre-frontal cortex are needed for memory retention and working memory processes. Importantly, acute intake of polysaccharides in animal models increases hippocampal long-term potentiation, necessary for the formation of memory traces.[21] Taken together, the significant effects on overall word recognition, as well as working memory Serial Sevens task performance, implicates hippocampal and frontal lobe activation as a key element in a potential mechanism underpinning effects of plant polysaccharide consumption. Furthermore, applied research is needed to explore polysaccharide neuronal mechanisms in the hippocampus structure, given the potentially significant functional benefit for memory performance.

The results of this study provide the first preliminary evidence of acute beneficial effects following intake of specific dietary polysaccharides, primarily arabinogalactans, on demanding memory and cognitive performance tasks in healthy middle-aged adults. The results suggest that a single 4 g dose of polysaccharides may be beneficial to performance during highly demanding cognitive processes. This study extends previous research in both design and scope, by utilizing cognitive demanding tasks to elucidate a 'mental fatigue' in a middle-aged cohort, rather than young adults.

The beneficial effects of the blend of polysaccharides on memory were independent of any blood glucose mediated effect and deserve further investigation. Specifically, examining the effects of polysaccharides in other populations, such as older adults, and exploring different doses and other cognitive domains, would elucidate potential differential effects. Given that older adults may be more susceptible to a reduction in cognitive resources to perform cognitive demanding tasks, dietary NSP extracts might deliver a cognitive benefit to individuals with age-related cognitive impairment.

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