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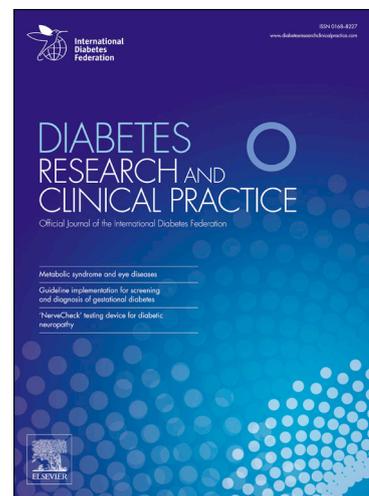
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Does working memory training improve dietary self-care in type 2 diabetes mellitus?**Results of a double blind randomised controlled trial.**

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Abstract

Aims: Controlling food intake despite adequate knowledge remains a struggle for many people with type 2 diabetes. The present study investigated whether working memory training can reduce food intake and improve glycaemic control. It also examined training effects on cognition, food cravings, and dietary self-efficacy and self-care.

Methods: In a double-blind multicentre parallel-group randomised controlled trial, adults with type 2 diabetes mellitus were randomly allocated to receive 25 sessions of either active ($n = 45$) or control ($n = 36$) working memory training. Assessments at baseline, post-training and 3-month follow-up measured cognition, food intake (primary outcomes), glycaemic control (HbA1c) and cholesterol (secondary outcomes). Semi-structured interviews assessed participants' experiences of the training.

Results: Intention-to-treat ANOVAs ($N = 81$) showed improved non-trained updating ability in active compared to control training from pre-test (active $M = 34.37$, control $M = 32.79$) to post-test (active $M = 31.35$, control $M = 33.53$) and follow-up (active $M = 31.81$, control $M = 32.65$; $\eta^2 = 0.05$). There were no overall effects of training on other measures of cognition, food intake, HbA1c, cholesterol, food cravings and dietary self-efficacy and self-care. In post-hoc analyses, those high in dietary restraint in the active training group showed a greater reduction in fat intake pre to post-test compared to controls. Interviews revealed issues around acceptability and performance of the training.

Conclusions: Transfer of working memory training effects to non-trained behaviour were limited, but do suggest that training may reduce fat intake in those who are already motivated to do so.

Trial registration: Current Controlled Trials ISRCTN22806944

Keywords: working memory training, type 2 diabetes mellitus, food intake, self-control, dietary restraint, dietary self-care

1.0 Introduction

Overweight/obesity is linked to the development of many health complications, including type 2 diabetes mellitus [1]. An estimated 422 million adults had diabetes in 2014 [2]. Just as trends in obesity are predicted to rise, so is the incidence and prevalence of type 2 diabetes mellitus [3]. Poorly controlled diabetes leads to health complications, which have direct and indirect costs to society and the economy [3]. The majority of these complications are preventable through well controlled glycaemic levels.

Lifestyle changes are the first line of treatment for reducing hyperglycaemia in type 2 diabetes mellitus [4, 5]. People with diabetes are advised to adopt a high-fibre, low fat, low-glycaemic-index carbohydrate diet and to reduce consumption of foods high in saturated and trans fat [5]. Lifestyle interventions may improve glycaemic control [6] but dietary changes can be difficult to maintain [7] especially in the context of the current obesogenic environment in which low-cost energy dense foods are readily available [8]. Education can provide the knowledge needed to make dietary changes [9] but resisting tempting foods presents a different challenge. Dual-process theories of cognition argue that two competing systems determine overt behaviour: one promotes automatic, impulsive behaviour (the impulsive system) and the other promotes controlled, deliberative behaviour (the reflective system) [10]. It has been argued that difficulties controlling the quality and quantity of food intake may be due to poorer ability to engage the reflective system and exert control over pleasure-seeking impulses [11]. Indeed, people with lower impulsivity are less likely to overeat [12] and be overweight/obese [13].

Working memory (WM) may underpin the ability to exert control over behaviour [14, 15]. Important WM functions include the ability to hold in mind information retrieved from long-term memory, maintain focused attention and shield goals from distraction [14]. WM may be key to retrieving and holding long-term healthy eating goals in mind [16], resisting

distraction from environmental cues (e.g. tempting foods) and reducing food cravings [17]. Indeed, research has found that better WM is associated with greater fruit and vegetable intake [18] and impulsive processes are weaker predictors of energy dense food intake for people with higher WM capacity [14]. Moreover, both obesity and diabetes are associated with WM deficits [19, 20].

WM can be improved via training and there may be transfer of learning gains to related but non-trained aspects of cognition and behaviour, such as fluid intelligence [21] and alcohol consumption [22]. There is also preliminary evidence that WM training can improve food choices [23, 24]. The current study examined whether WM training can reduce food intake and improve glycaemic control in type 2 diabetes mellitus. Near and far transfer effects to non-trained measures of cognition were also examined. Based on the results of studies published since the protocol for this study was published [25], we additionally investigated the effect of individual differences on training efficacy and the effects of the training on food cravings and dietary self-care.

2.0 Subjects, Materials and Methods

2.1 Study design

The study methodology and power calculation has been described elsewhere [25]. Briefly, this was a parallel group double-blind randomised controlled trial. Participants with type 2 diabetes mellitus were randomly allocated to either active or control working memory training. Assessments were conducted at baseline, immediately post-training and 3-month follow-up. Middlesex University Ethics Committee and West Midlands National Research Ethics Service Committee provided ethical approval.

2.2 Participant recruitment and randomisation

Recruitment was primarily through diabetes clinics (Royal Free London, Southern Health, Central London Community Healthcare and University Hospitals Birmingham NHS Trusts), but also via information distributed by relevant charities and local newspapers. Inclusion criteria for the study were: difficulty following a healthy diet, HbA1c >8.0% (64 mmol/mol), body mass index (BMI) ≥ 25 kg/m², type 2 diabetes mellitus diagnosis of ≥ 2 years and in general good health. Exclusion criteria were: neurological or psychiatric disorders, major changes in diabetes treatment in the last 6 months (e.g. transfer to insulin), treatment by GLP-1 agonists or DPP4 inhibitors and alcohol and/or substance abuse. Participants were screened by a researcher according to self-report of the criteria.

The randomisation sequence was created using the website Sealed Envelope (<https://www.sealedenvelope.com/>) with a 1:1 allocation (block sizes of 10). Greater dropout rates occurred in the active training condition, therefore, an unequal allocation ratio was subsequently used to maintain balanced groups. Prior to trial commencement one author who would not have contact with participants (KH) designated the two conditions either the number 1 or 2, VW then created allocation sequences using these codes. Blinded researchers would select the appropriate coded condition when signing participants up to the training program. Participants were blind to which training was active and control.

2.3 Intervention

The working memory training program is described in detail elsewhere [25]. Briefly, there were three tasks: backwards digit, letter and visuospatial span tasks. In each task participants had to remember a sequence of items and re-enter these in the correct (visuospatial span task) or reverse (backwards digit span task) order. In the letter span task the nth item in the sequence was cued and participants had to recall this item (which was cued was random).

There were 25 training sessions (both groups), each session comprised 30 trials of each task. In the active training condition the difficulty level increased by 1 after 2 consecutive correct responses, thereby closely following the working memory capacity of the participant. In the same tasks, each sequence always contained only 3 items for the control condition, hence WM capacity was not trained. One training session could be completed per day, and each session had to be completed within 48 hours. Participants could miss up to 5 training sessions. However, to reduce the amount of missing data at follow-up sessions, this limit was removed and participants were encouraged to complete as many sessions as possible.

2.4 Primary outcome measures

2.4.1 Working memory capacity (trained tasks). Performance on the training tasks was assessed by increasing the difficulty level until two consecutive incorrect responses were given. The longest sequence of items recalled on each task was then summed and averaged.

2.4.2 Cognition (non-trained tasks). Cambridge Neuropsychological Test Automated Battery tasks (CANTAB, Cambridge Cognition, Cambridge, UK) were used to assess transfer effects to different tests of WM and non-trained aspects of cognition. More detailed descriptions of the tasks are provided in the methods section of the electronic supplementary material.

2.4.2.1 Near transfer effects. The Spatial Span task is a computerised version of the Corsi blocks task, a validated measure of visuospatial WM capacity [26]. The outcome measure was span length (the longest sequence correctly recalled). The Spatial Working Memory test assessed updating ability. The outcome measure was the extent to which a strategy was used to perform the task: a higher score indicates poorer strategy use [27].

2.4.2.2 Far transfer effects. The Attention Switching Task assesses ability to ignore task-irrelevant and distracting information [28]. Outcome measures were switching cost and

congruency cost. Positive scores reflect a preference (i.e. faster responding) to non-switching and congruent trials. Scores closer to zero indicate little preference between switching/non-switching and congruent/non-congruent trials. The Paired Associates Learning task assesses visual memory and new learning (specifically episodic memory), and is reliable and able to discriminate mild cognitive impairment [29, 30]. First trial memory score was the outcome measure for this task and reflects how well participants remembered the location of patterns on the first attempt, with a higher score indicating better new learning.

2.4.3 Lab-based food intake (lunch buffet). Both high (crisps, cookies and cheese and onion rolls) and low (carrot sticks, rice cakes, tomatoes) energy dense food items were provided, along with a staple lunch item (sandwiches) (total energy ~1197 kcal). The cover story was that the researchers were interested in changes in taste-perceptions over time and participants were asked to make taste ratings to corroborate the cover story. The exact quantities of foods provided are described elsewhere [25]. Outcome measures were the amount of sandwiches, high and low energy dense foods consumed (grams).

2.4.4 Non-lab-based food intake (24-hour guided recall). Participants were asked to recall everything they ate and drank the day before in a guided recall procedure [31]. Participants also indicated the portion size they ate using the book “Carbs & Cals” [32]. The original outcome measure for this task was the number of high and low energy dense food items reported [25]. However, it was decided to score the dietary recalls using the McCance and Widdowson’s composition of foods database [33]. This allowed calculation of total kilocalories, as well as relevant macronutrients, since people with type 2 diabetes mellitus are advised to control their consumption of carbohydrates and fats [5].

2.5 Secondary outcome measures

2.5.1 HbA1c and lipids. Blood samples were collected to assess HbA1c and cholesterol levels. Samples were analysed at one of three hospital laboratories: Royal Free London Hospital, University Hospital Birmingham and University Hospital Southampton. To assess HbA1c, London and Birmingham laboratories used High Performance Liquid Chromatography (Tosoh, model G8), whereas Southampton used capillary electrophoresis (Sebia, Capillarys 2 flex-piercing). These methods provide comparable results [34]. All sites used the enzymatic colorimetric method to measure cholesterol (London and Birmingham used the Cobas 8000, c702 module; Southampton used a Beckman Coulter AU analyser).

2.5.2 Qualitative interviews. Semi-structured interviews were conducted with 32 participants in the active training group. Interviews were recorded, transcribed verbatim and imported into NVivo for analysis. Thematic analysis was conducted to identify themes important to participants' experiences of the training [35].

2.6 Other measures

To characterise the sample we assessed a number of measures, including BMI calculated as kg/m^2 , eating styles (General Food Cravings Questionnaire, GFCQ [36]; Three Factor Eating Questionnaire-18, TFEQ [37]; Dutch Eating Behavior Questionnaire, DEBQ [38]) diabetes-related behaviours (Diabetes Specific Quality of Life Questionnaire, DSQOL [39]; Summary of Diabetes Self-Care Activities Scale, SDSCA [40]; Dietary Self-Efficacy Scale, DSES [41]), depressive symptoms (Patient Health Questionnaire-9, PHQ-9 [42]; physical activity (International Physical Activity Questionnaire, IPAQ [43]; physiological data (blood pressure, blood glucose levels) and demographic information (gender, age, ethnicity, education level, currently employed or not, length of diabetes diagnosis, how the diabetes is controlled, existence of co-morbid conditions). Mood and hunger were measured throughout the assessment sessions, as these can influence task performance [44]. Food-specific

inhibition was assessed using a food go/no-go task (see methods section of the electronic supplementary materials for further information).

2.7 Procedures

After providing informed consent, participants completed the hunger and mood questions, blood pressure was measured and blood samples taken. Height and weight were then measured with shoes and heavy clothing removed. Participants then completed the hunger and mood questions again, followed by the computer tasks (go/no-go, CANTAB, WM assessment and sign-up to training) and another set of hunger and mood questions.

Participants were then given 15 minutes to eat what they wanted from the buffet lunch and completed the taste ratings. Participants then completed the hunger and mood questions again, followed by the guided 24-hour recall and questionnaires measuring eating styles, diabetes-related behaviours, depressive symptoms, physical activity and demographic information. All assessment sessions were the same, with the addition of the semi-structured interviews at post-test and questions about awareness of the purpose of the buffet lunch at follow-up.

2.8 Statistical analyses

Data were analysed according to an intention-to-treat protocol, with the last observation carried forward for missing data [25]. Per protocol analyses were also conducted, including participants who completed all assessment sessions, the pre-specified minimum number of training sessions (20) and excluding major protocol violations [25]. As stated in the published protocol baseline group differences were analysed using ANOVA (Analysis of Variance) and Pearson's chi square test for categorical variables, although such tests are no longer recommended for randomised controlled trials [45]. Primary and secondary outcomes were

assessed using 2 (condition: active, control) x 3 (time-point: pre, post, follow-up) ANOVAs, with contrasts comparing post-test and follow-up to pre-test to examine significant effects (Bonferroni corrected, $p / 2$). The p value for main and interaction effects was set at $p < 0.05$.

Since the protocol for this study was published, it was reported that WM training in overweight/obese adults reduced food intake only in participants high in dietary restraint [23]. This was assessed in the current study in post hoc analyses using model 1 in the PROCESS macro for SPSS on the intention-to-treat sample [46]. Change in food consumption from pre-test to post- test and follow-up were entered as the dependent variables, condition as the independent variable and baseline dietary restraint (DEBQ) as the moderator. Houben and colleagues [23] also reported changes to psychological eating styles, and so we assessed the effect of WM training on state food cravings (GFCQ), general and specific dietary adherence (SDSCA), and dietary self-efficacy (DSES) using mixed ANOVA. No corrections for multiple tests were applied.

3.0 Results

3.1 Study sample

Eighty-one participants (intention-to-treat sample) were recruited and randomised to condition (between January 2015 and October 2016) across London ($n = 46$), Southampton ($n = 33$) and Birmingham ($n = 2$). Recruitment continued until the planned sample size after dropouts had completed all assessment sessions ($N = 40$) [25]. Forty-seven were maintained in the per protocol analyses (active training $n = 24$; control training $n = 23$). See study flowchart (Figure 1) for exclusions.

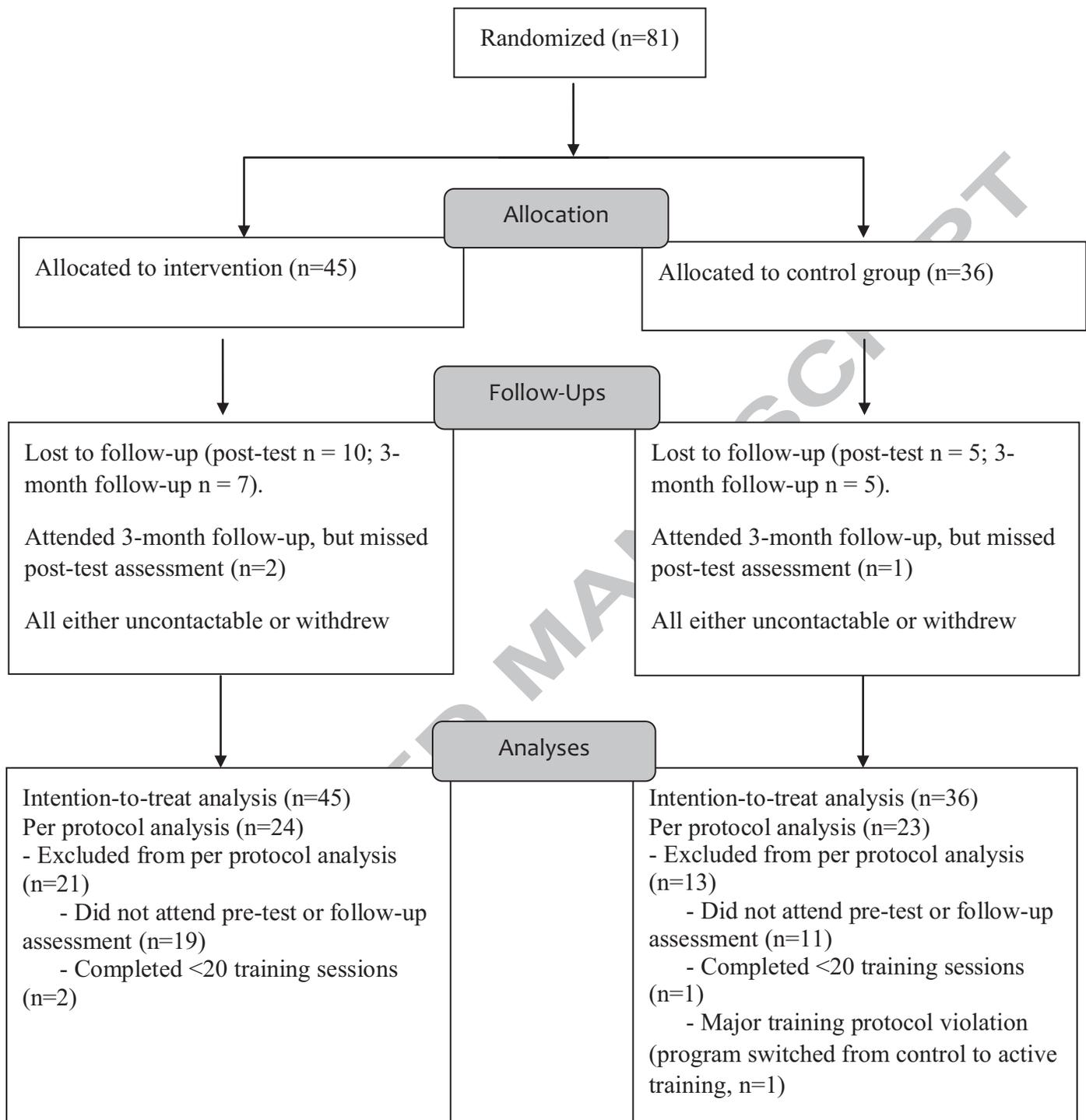


Figure 1. Flowchart of participants' progress through the trial.

All participants self-reported difficulty controlling food intake. Table 1 describes the characteristics of the intention-to-treat study sample, and shows that the mean characteristics of both conditions were within the study inclusion criteria, with the exception of HbA1c. Recruitment was based on self-reported information and due to the nature of the blood tests, the results were not available until after patients had been randomised to condition, meaning that actual HbA1c varied from that self-reported. It also became apparent after randomisation to condition that some patients were taking GLP-1 and DPP-4 treatment. Participants completed on average 20.09 training sessions (out of 25; $SD = 7.44$). The control group had higher diastolic blood pressure than the active training group (see Table 1). Due to an error in running the go/no-go task, non-food object data was unusable, and so groups were compared on food-specific commission errors only. The per protocol analyses did not affect the pattern of the results for the interaction between time and condition, and so only the intention-to-treat analyses are reported.

Table 1. Characteristics of intention-to-treat sample.

Characteristic	Active training Mean (<i>SD</i>) <i>n</i> = 45	Control training Mean (<i>SD</i>) <i>n</i> = 36	Range	<i>F</i> / χ^2	<i>p</i>
Age (years)	59.69 (8.77)	62.14 (10.29) ^a	33.00–80.00	1.32	0.25
BMI (kg/m ²)	33.22 (6.18)	32.31 (6.30)	18.71–48.98	0.43	0.51
Blood glucose (mmol/l)	8.46 (3.36) ^d	8.98 (3.54) ^a	2.90–18.20	0.43	0.51
HbA1c (mmol/mol)	55.33 (14.90) ^b	58.22 (12.44) ^c	30.00–90.20	0.79	0.38
HbA1c (%)	7.21 (1.36) ^b	7.48 (1.14) ^c	4.89–10.40		
Systolic blood pressure (mmHg)	135.82 (14.35)	140.39 (19.95)	109–191	1.43	0.24
Diastolic blood pressure (mmHg)	84.56 (10.16)	90.42 (11.56)	63–118	5.89	0.02
Duration of diabetes (years)	7.42 (6.24) ^a	7.79 (7.42)	0.8–30.0	0.06	0.81
Physical activity (total MET minutes per week)	3918.69 (3923.07) ^a	3770.38 (5589.33) ^b	0.00–26037.00	0.02	0.89
Gender (male, <i>n</i>)	29	19		1.13	0.29
Ethnicity (<i>n</i>)				1.50	0.68
White	36	27			

Asian/Asian British	6	6		
Black/African/Caribbean/Black British	1	0		
Other	2	3		
Employment (working, <i>n</i>)	24 ^c	19 ^c	0.01	0.94
Highest level of education			6.00	0.11
Secondary school	6	11		
College	6	8		
Higher education	28	14		
Other	5	3		
Diabetes treatment (<i>n</i>)				
Diet	23	19 ^a		
Exercise	20	19 ^a		
Tablets	36	29		
Insulin	9	4		
GLP-1 agonist	2	3		
DPP4 inhibitors	2	5		

Micro-vascular co-morbid conditions (<i>n</i>)	18	11			
Macro-vascular co-morbid conditions (<i>n</i>)	8	8			
DSQOL (burden scale) ^c	76.89 (16.97) ^e	70.21 (21.42) ^a	19.30 – 99.30	2.17	0.15
SDSCA					
General diet	3.86 (2.36)	4.28 (2.05)	0 – 7	0.72	0.40
Specific diet	3.89 (1.76)	4.01 (1.57)	0 - 7	0.11	0.74
DSES	58.10 (19.97)	51.81 (22.39)	5.33 – 97.33	1.78	0.19
PHQ-9	5.38 (4.31)	7.19 (5.80)	0 – 21	2.62	0.11
DEBQ					
Restrained eating	2.91 (0.78)	2.82 (0.76)	1.20 - 4.40	0.27	0.61
Emotional eating	2.16 (0.89)	2.30 (0.83)	0.46 – 4.23	0.55	0.46
External eating	2.82 (0.66)	2.97 (0.61)	1.20 – 4.10	1.07	0.30
TFEQ (uncontrolled eating)	34.98 (19.65)	38.17 (20.99)	0 – 96.30	0.50	0.48
GFCQ					
State	23.31 (9.95)	26.58 (12.39)	15 – 69	1.74	0.19
Trait	52.96 (22.03)	57.69 (21.69)	21 - 119	0.94	0.34

Commission errors	1.58 (2.92)	1.41 (1.71)	0-43	0.21	0.65
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Note. HbA1c = glycated haemoglobin; DSQOL = diabetes-specific quality of life; SDSCA = summary of diabetes self-care activities; DSES = dietary self-efficacy scale; PHQ-9 = patient health questionnaire; DEBQ = Dutch eating behaviour questionnaire; TFEQ = three factor eating questionnaire; GFCQ = general food cravings questionnaire; MET = metabolic equivalent; SD = standard deviation; F = F value for ANOVA; χ^2 = Chi square value for Pearson's chi square test'; p = p value; ^aMissing information for 1 participant; ^bMissing information for 2 participants; ^cMissing information for 4 participants; ^dMissing information for 5 participants; ^eMissing information for 8 participants.

3.2 Primary outcome measures

3.2.1 Working memory (trained tasks). There were significant main effects of time and condition, and a significant interaction between time and condition. Contrasts for the main effects showed that the active training group had greater WM span than the control group, and both post-test and follow-up WM span were significantly greater than pre-test. Contrasts for the interaction showed that WM span increased significantly more from pre-test to post-test and follow-up in the active training compared to the control group (see Table 2 for the statistical results and Figure 2).

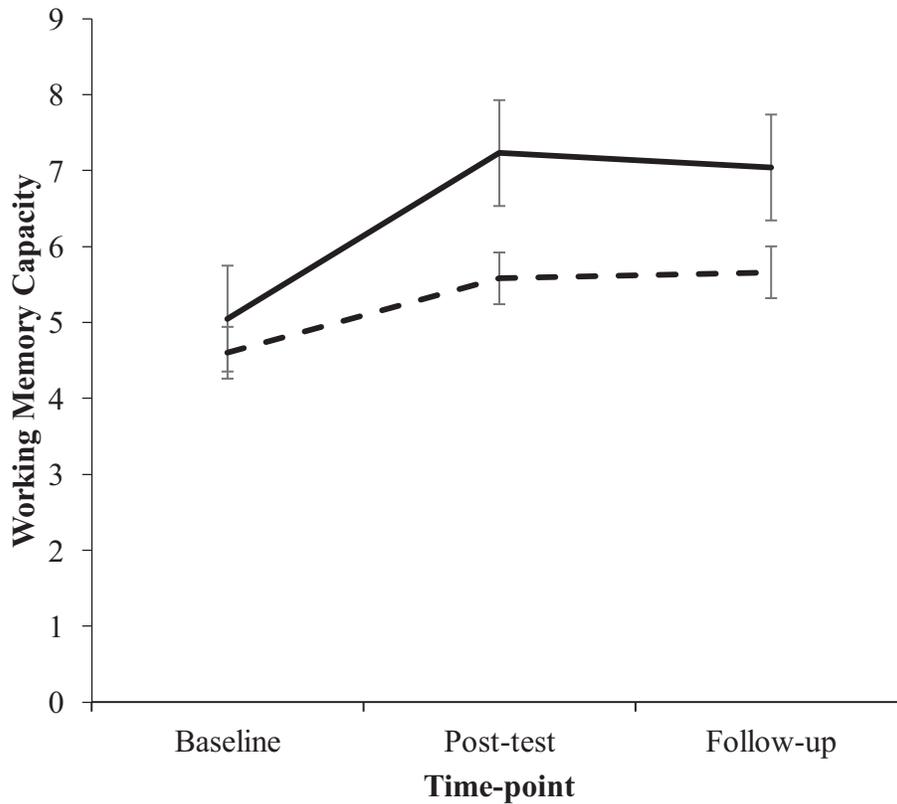


Figure 2. Means and standard errors for working memory capacity as a function for active training (solid line) and control training groups (dashed line) over time in the intention-to-treat sample. Statistical results are reported in Table 2.

3.2.2 Cognition (non-trained tasks). There were significant main effects of time for spatial span length, switching cost and first trial memory score, such that performance was significantly better at follow-up than pre-test. Performance was also significantly better at post-test than pre-test on switching cost, but pre-post contrasts were non-significant for spatial span and first trial memory score (see Table 2). There were no significant main effects of condition for any measures. There was a significant interaction between time and condition for spatial working memory strategy use score. Contrasts showed that strategy score decreased significantly more from pre-test to post-test in the active training group than the control group. These effects were maintained at follow-up (see means in Table 2), however, the contrast shows no significant difference between groups on change in strategy score from pre-test to follow-up.

3.2.3 Buffet taste-test and 24 HR recall. There were no differences between groups prior to the lunch buffet in hunger or liking of the foods (see results section of the electronic supplementary material for details). There was a significant effect of time on sandwich intake, such that intake was significantly lower at follow-up and post-test compared to pre-test. There were no other main or interaction effects for food intake outcomes (see Table 2).

3.3 Secondary outcomes

3.3.1 HbA1c and lipids. There was a significant main effect of time for HbA1c, such that follow-up HbA1c was significantly higher than pre-test. There was no significant main effect of condition and no significant interaction between time and condition (see Table 2). For total cholesterol, there was no main effect of time or condition and no significant interaction between time and condition (Table 2).

3.3.2 Qualitative interviews. Two themes were identified in relation to participants' experiences of the training: acceptability and performance. See the results section of the electronic supplementary material for detailed descriptions and supporting quotes. In

summary, the acceptability theme demonstrated that key issues for participants included maintaining their enthusiasm for the training, managing to include it into their life, and the intrusive nature of the training. The performance theme showed that there were discrepancies between what participants expected to achieve and what they felt they actually achieved from doing it.

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Table 2. Means and standard deviations for primary and secondary outcome measures as a function of condition and time-point.

	Active training Mean (SD)			Control training Mean (SD)			Time	Condition	T x C	Time	Time	T x C	T x C
	Pre-test	Post-test	FU	Pre-test	Post-test	FU	$F(\eta^2)$	$F(\eta^2)$	$F(\eta^2)$	$F(\eta^2)$	$F(\eta^2)$	$F(\eta^2)$	$F(\eta^2)$
Trained working memory span	5.05 (1.02) ^a	7.23 (1.47)	7.04 (1.43)	4.60 (0.97)	5.58 (1.14)	5.66 (1.25)	116.40 (0.60) **	22.67 (0.23) **	14.40 (0.16) **	157.20 (0.67) **	155.96 (0.67) **	22.63 (0.23) **	14.74 (0.16) **
SSP span length	5.86 (1.05) ^a	5.84 (1.03)	6.11 (1.10)	5.51 (0.95) ^a	5.71 (0.67)	5.91 (0.82)	4.95 (0.06) *	1.57 (0.02)	0.57 (0.01)	0.92 (0.01)	7.00 (0.08) *		
SWM strategy use	33.37 (5.91) ^b	31.35 (7.05)	31.81 (6.90)	32.79 (7.51) ^b	33.53 (6.01)	32.65 (7.25)	1.53 (0.02)	0.32 (0.00)	3.68 (0.05) *			5.57 (0.07) *	2.26 (0.03)
AST congruency cost	62.33 (55.46) ^b	58.61 (57.44)	57.66 (56.70)	81.87 (44.64) ^a	76.93 (48.90)	77.37 (52.60)	0.70 (0.01)	3.04 (0.04)	0.02 (0.00)				
AST switching	327.78	314.47	293.88	397.12	359.50	354.49	7.08	2.77	0.71	4.78	11.83		

cost	(141.82) ^b	(172.42)	(162.27)	(155.09) ^a	(163.38)	(180.41)	(0.09)	(0.04)	(0.01)	(0.06)	(0.14)
							*			*	**
PAL first trial	10.12	10.91	11.21	10.89	10.54	11.74	4.33	0.22	1.48	0.48	6.75
memory score	(2.68) ^b	(3.54)	(3.87)	(2.73) ^a	(3.56)	(3.94)	(0.05)	(0.03)	(0.02)	(0.01)	(0.08)
							*				*
Sandwich intake	124.34	93.46	75.22	127.67	115.56	80.64	15.11	0.77	0.69	6.62	26.46
(g)	(63.75)	(56.02)	(38.58)	(68.21) ^c	(76.02)	(99.20)	(0.17)	(0.01)	(0.01)	(0.08)	(0.26)
							***			*	***
High energy dense	43.61	48.69	54.76	49.72	46.06	54.76	0.87	0.05	2.89		
food intake (g)	(31.15)	(38.33)	(39.36)	(33.18) ^c	(31.74)	(39.36)	(0.01)	(0.01)	(0.04)		
Low energy dense	107.58	108.06	109.57	95.22	97.91	94.81	0.05	0.99	0.10		
food intake (g)	(63.41)	(72.65)	(66.39)	(39.70) ^c	(45.91)	(53.49)	(0.00)	(0.01)	(0.00)		
Total (Kcal, 24-	1800.58	1816.28	1815.23	1743.08	1851.57	1617.31	1.24	0.26	1.24		
hour recall)	(653.76)	(634.75)	(686.93)	(881.40) ^a	(1005.25)	(599.37)	(0.02)	(0.00)	(0.02)		
Carbohydrates (g,	197.17	190.93	197.01	209.33	208.68	193.80	0.31	0.28	0.60		
24-hour recall)	(75.86)	(74.10)	(82.29)	(111.23) ^a	(123.91)	(76.00)	(0.00)	(0.00)	(0.01)		
Fat (g, 24-hour	78.87	78.55	78.52	77.27	78.36	64.47	1.42	0.44	1.35		
recall)	(39.96)	(37.81)	(39.87)	(49.44) ^a	(55.29)	(30.73)	(0.02)	(0.01)	(0.02)		
Saturated fat (g,	28.74	28.17	26.53	26.20	26.33	22.18	2.20	0.96	0.20		

24-hour recall)	(16.33)	(16.52)	(15.06)	(17.15) ^a	(21.10)	(12.76)	(0.03)	(0.01)	(0.00)		
HbA1c	55.33	56.29	56.44	58.22	59.50	60.62	4.30	1.13	0.61	3.42	5.9
(mmol/mol)	(14.90) ^b	(14.75)	(14.00)	(12.44) ^c	(13.49)	(14.42)	(0.06)	(0.02)	(0.01)	(0.05)	(0.08)
							*				*
HbA1c (%)	7.21	7.30	7.31	7.48	7.59	7.70					
	(1.36)	(1.35)	(1.28)	(1.14)	(1.23)	(1.32)					
Cholesterol	4.52	4.46	4.53	4.37	4.36	4.33	0.10	0.38	0.29		
(mmol/L)	(1.12) ^d	(1.04)	(1.01)	(0.89) ^d	(1.03)	(1.19)	(0.00)	(0.01)	(0.00)		

Note. SSP = spatial span task; SWM = spatial working memory task; AST: attention switching task; PAL = paired associates learning task; HbA1c = glycated haemoglobin; SD = standard deviation; F = F value for ANOVA; p = p value T x C = Time x Condition interaction, FU = Follow-up; * $p < .05$; ** $p < 0.01$; *** $p < 0.001$; ^aMissing information for 1 participant; ^bMissing information for 2 participants; ^cMissing information for 4 participants; ^dMissing information for 6 participants.

3.4 Post hoc analyses

The interaction between condition and time-point was non-significant for state cravings, dietary self-efficacy score and general and specific dietary self-care (all p 's > 0.05). Full statistical information is reported in the results section of the supplementary materials (Table S1).

3.4.1 Pre-test to post-test. Only significant interaction effects are reported here, significant main effects of restraint and condition are reported in the results section of the electronic supplementary material. There was a significant interaction between restraint and condition for change in fat intake from pre-test to post-test, $b = -26.78$, $t(76) = -2.69$, $p = 0.01$, such that in those high in dietary restraint (+ 1 SD) there was a marginally significant greater reduction in fat intake in the training group than the control group, $b = -21.80$, $t(76) = -1.99$, $p = 0.05$. This effect did not exist at low levels of restraint, $b = 19.55$, $t(76) = 1.67$, $p = 0.10$ (see Figure 3). The interaction between restraint and condition was also significant for change in saturated fat from pre-test to post-test, $b = -8.03$, $t(76) = -2.12$, $p = 0.04$. However, simple slopes for both low restraint, $b = 6.15$, $t(76) = 1.30$, $p = 0.20$, and high restraint, $b = -6.25$, $t(76) = -1.52$, $p = 0.13$, were non-significant. These results suggest that there was a greater short-term (pre-test to post-test only) reduction in fat intake in those high in dietary restraint in the active training group.

3.4.2 Pre-test to follow-up. There was a significant interaction between restraint and condition for change in total kJ, $b = -390.56$, $t(76) = -2.04$, $p = 0.04$. In those low in restraint (-1 SD) there was a non-significant trend for a greater increase in total kJ, $b = 446.70$, $t(76) = 1.78$, $p = 0.08$, in the active training than control group. There were no significant effects in those high in dietary restraint (+1 SD), $b = -156.38$, $t(76) = -0.88$, $p = 0.38$. These results suggest that in those low in dietary restraint, there was a slightly greater increase in energy intake over time in the active training group.

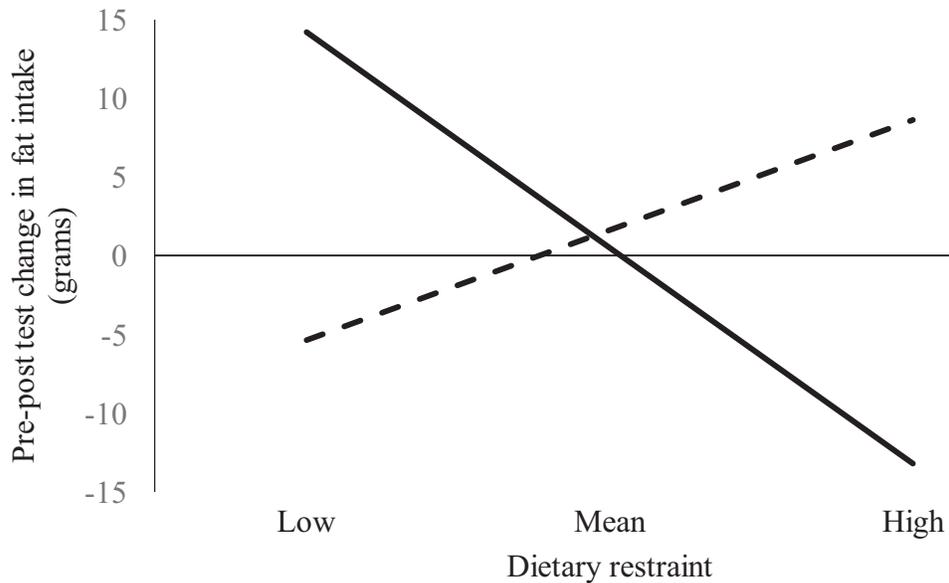


Figure 3. Change in fat intake from pre-test to post-test at different levels of dietary restraint in the active (solid line) and control (dashed line) training groups

4.0 Discussion

The current study assessed whether WM training can reduce food intake and improve diabetes control in adults with type 2 diabetes mellitus. It also assessed transfer effects to non-trained aspects of cognition, food cravings and dietary self-efficacy and self-care. The active training group improved significantly more than the control group on WM training tasks. There was some evidence of near transfer effects, whereby updating ability improved immediately after training in the active training group, and was maintained at follow-up.

There were no effects of training on another measure of WM (spatial span task), inhibitory control or new learning/episodic memory. These results are in line with reviews of WM training, which suggest short-term near or intermediate transfer effects (such as other aspects of WM), but find little evidence of far transfer effects [47].

There were no effects of training on laboratory-based or non-laboratory based food

intake. However, there was a short-term reduction in fat intake pre-post test in those high in dietary restraint in the active training group. In contrast, those low in dietary restraint showed a trend to increase their energy intake. One interpretation of this is that WM training combined with being high in restraint may offset a gradual increase in food intake over time, but perhaps only in the short-term. Alternatively, these may be spurious findings. However, this is not the first study to find that WM training effects depend upon levels of dietary restraint and motivation to lose weight [23, 24]. Dietary restraint is an indicator of conscious effort to control food intake, therefore, these findings suggest that WM training brings actual food intake in line with dietary goals. Other studies support that in individuals with higher WM capacity, self-regulatory goals are a better predictor of food intake than in those with lower WM capacity [14]. WM improvements may be unlikely to benefit those who lack motivation to control food intake and so additional motivational training may be required to achieve dietary change.

There was no effect of training on cholesterol or glycaemic control. Considering the lack of overall training effects on food intake, this is not unexpected. Post-hoc analyses did not reveal any effects of training on self-reported dietary self-care, self-efficacy and food cravings. The qualitative interviews suggest that changes to the training programme would improve its acceptability, such as fewer and shorter training sessions and a clearer relevance to eating behaviour and diabetes control. The greater rate of study dropouts in the active than control training group also supports that the training was difficult and quickly became tedious. Introducing novel tasks during the training may help maintain enthusiasm and motivation.

4.1 Study strengths and limitations

We used a range of self-reported and objective outcome measures, and observed a consistent pattern of results. However, the study sample was highly educated and those who completed the training were likely more motivated than those who did not. The food intake results based on 24-hour recalls should be interpreted with caution, as this was not a validated measure of consumption. Further, average self-reported intake was ~2000 kcal for men and ~1400 kcal for women, suggesting an underreporting bias for this measure. Despite these limitations, it is promising that changes in non-laboratory based food intake were found in a sub-group of the sample, as changes in behaviour in daily life are more likely to continue after training than changes found in the laboratory. The fact that some patients were taking GLP-1 agonist and DPP-4 inhibitor medications during the trial may have reduced the chances of observing effects of the training, due to their effects on appetite. Average HbA1c post-randomisation was lower than intended, however, it was still above the clinical target of 6.5% (48 mmol/mol) [5]. Despite this, the chance of finding an effect of training on diabetes control was likely reduced as a result. A further limitation is the small per protocol sample size. The only similar study available at the time had found large effects [22], and therefore the power calculation for this study suggested that only a small sample size was needed to detect similar effects. The per protocol analysis sample size was therefore likely underpowered to detect smaller effects. Considering the age range of participants in the current study, it is possible that some participants were at risk of experiencing age-related cognitive decline. This may have reduced the chances of finding training effects, in particular on the non-trained cognition tasks.

4.2 Suggestions for future research

WM strategy training, which aims to improve a person's ability to remember information through teaching strategies such as rehearsal [48] may be an important addition to future working memory capacity training. Being able to efficiently use and maintain information held in WM is likely to influence food intake decisions [14, 15], for example, keeping long-term health goals active in mind may help a person to resist tempting food. Individual differences in dietary restraint and BMI have been shown to moderate the effectiveness of several cognitive training interventions [49]. Future research should continue to assess the moderating role of individual differences in sufficiently powered studies to identify for whom these types of training are likely to be successful. An interim solution is to combine different types of cognitive training which may have additive effects and/or be more effective for a wider range of people. Pilot testing of combined food response training supports the efficacy of this approach [50].

4.3 Conclusions

Working memory training in adults with type 2 diabetes mellitus improved performance on trained WM tasks and showed some near transfer effects to WM updating ability. There was also evidence that active training reduced fat intake in those with high levels of dietary restraint. There was no improvement on other aspects of cognition (spatial span, inhibitory control, new learning and memory), behavioural and biological measures of food intake or glycaemic control. There were no effects of training on food cravings and dietary self-efficacy and self-care. These findings suggest that WM training may change food consumption in people who are motivated to make such changes. Future research should continue to assess the effects of individual differences on training efficacy.

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Declarations of interest

None.

Contribution statement

AN, SH and KH conceptualised the study, and all authors contributed to the design of the study. VW conducted data collection and analysed the results. VW also drafted the manuscript with input from all authors. All authors have read and approved the final manuscript.

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Highlights

- Working memory training improved non-trained updating ability compared to controls.
- Dietary fat intake reduced in those motivated to control their food intake.
- Glycated haemoglobin and cholesterol levels did not improve.
- Food cravings, dietary self-efficacy and self-care did not improve.

ACCEPTED MANUSCRIPT