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Feasibility and Acceptability of a Cognitive Training Study in Individuals with Type 2 Diabetes Mellitus

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Abstract: Individuals with type 2 diabetes mellitus (T2DM) are at an increased risk of cognitive dysfunction. Growing evidence supports the use of cognitive training to target cognitive dysfunction in T2DM, but only limited evidence exists surrounding its feasibility and acceptability. The primary aim of this research is to determine the feasibility and acceptability of a cognitive training study in T2DM. Adults diagnosed with T2DM were randomly allocated to either a 6-week cognitive training group or a usual care control group. Feasibility outcomes (recruitment, adherence, retention, motivation, data collection, and intervention design) were evaluated using a traffic light progression criterion. Qualitative interviews were conducted to explore study acceptability. Cognition was measured at baseline and post-intervention. Forty-one participants completed the study (age 66 ± 9.8 years; HbA1c 54.0 ± 13.3 mmol.mol). Feasibility was shown in the adherence, retention, and motivation of participants, whilst minor amendments were proposed to the study design, recruitment, and data collection. Participants described cognitive training as highly enjoyable, with study components broadly reported as acceptable. Data signalled improvements in cognition, with large improvements observed in executive function. This study provides evidence for the potential feasibility, acceptability, and efficacy for cognitive training in T2DM. Recommendations for future studies are provided.

Keywords: type 2 diabetes mellitus; cognitive training; cognition; feasibility; acceptability

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1. Introduction

An estimated 3.9 million individuals are currently diagnosed with diabetes across the UK, with a further 1 million individuals undiagnosed [1]. Almost 90% of these cases are attributed to type 2 diabetes mellitus (T2DM) [1]. In addition to the well-recognised microvascular and macrovascular complications [2–4], there is substantial evidence to suggest that T2DM is linked with an increased risk of cognitive dysfunction [5–8]. Cognitive dysfunction refers to the gradual loss or impairment of cognitive abilities [9], and there is evidence to suggest that the development and prognosis of cognitive dysfunction is markedly worse in individuals with T2DM [5,6,10–13]. Even in the earliest stages of T2DM (e.g., newly diagnosed and adolescents with T2DM), worse cognitive performance has been observed compared with non-diabetic controls [14–16]. Regardless of age, subtle cognitive deficits exist that are observed to be 0.3–0.5 standard deviations lower compared with individuals without diabetes [5,6]. Furthermore, although the pathophysiology for mild cognitive impairment (MCI) and dementia are similar in both individuals with and without T2DM, the impairment of cognitive function in individuals with T2DM and MCI is suggested to be 1–1.5 standard deviations lower compared with individuals with MCI but without diabetes [5,6]. It is important to highlight at this point that the development and progression of cognitive impairment is complex and may be influenced by several factors. For example, obesity, poor glucose control (i.e., hyperglycaemia), and disease duration have

been identified as important confounders of cognitive impairment in T2DM in addition to comorbid conditions such as macrovascular complications (e.g., cardiovascular and cerebrovascular diseases) [17–19]. Whilst cognitive dysfunction may affect a wide range of cognitive domains in T2DM, the most notable deficits have been shown in the domains of executive function, memory, attention, and psychomotor functions [20–22].

The development and progression of cognitive dysfunction in T2DM may be problematic, with studies suggesting that changes in cognition can have a negative impact on disease self-management behaviours and self-care outcomes [23–25], potentially contributing to the development or worsening of diabetes-associated complications. Lifestyle interventions, including physical activity [26–29] and dietary interventions [30–33] have showed promising outcomes in improving cognition in T2DM populations, but studies have consistently reported poor adherence and long-term compliance to these types of interventions [34–37], significantly limiting their impact. It is therefore important to identify strategies that are not only effective in improving cognition in T2DM, but most importantly, strategies that are feasible and acceptable, allowing for long-term behavioural compliance. Cognitive training interventions (i.e., mental exercises used to target one or more cognitive domains) have previously been identified as a potential strategy for targeting cognitive dysfunction [38–40], in which there is now growing evidence for their effective use in T2DM [41–47], particularly in relation to improving diabetes self-management [45,46]. There is a clear and important need for the development of these types of interventions, especially in the context of frameworks that advocate for strategies that assist in implementing and sustaining the skills, abilities, and knowledge required for optimal diabetes self-care [48,49]. However, to date there is limited exploration and understanding surrounding the feasibility and acceptability of cognitive training interventions in T2DM.

The primary aim of this research is to determine the feasibility (recruitment, adherence, retention, motivation, data collection, and intervention design) and acceptability of a 6-week cognitive training study in individuals with T2DM. This study will also explore the impact of cognitive training on outcomes of cognition in T2DM. Exploring the feasibility and acceptability of an intervention represents a fundamental step within the intervention development process, as outlined by the Medical Research Council's framework for the development and evaluation of complex interventions [50]. Furthermore, this research will help contribute to a deeper understanding of the impact of this type of intervention in T2DM, in addition to helping clarify which cognitive domains are most responsive to cognitive training in this population.

2. Materials and Methods

2.1. Study Design

A randomised study design [51] was used to investigate the feasibility and acceptability of a cognitive training study in T2DM. Participants diagnosed with T2DM were randomised to either a computerised cognitive training group or a usual care control group on a 1:1 ratio using computer-generated random numbers, through which the sequence allocation was concealed from the principal investigator. Recruitment ran from August 2018 to July 2019, with data collection running from August 2018 to August 2019. All baseline and post-intervention assessments were conducted at the University of Lincoln. Cognitive training sessions were conducted either at the University of Lincoln or in the participant's own home. The study was conducted in accordance with the Declaration of Helsinki, and was approved by the Health Research Authority, England (IRAS no. 227672 on 1 May 2018). Written and informed consent were obtained from all participants prior to participation. This study was reported in accordance with the CONSORT 2010 extension to randomised pilot and feasibility trials checklist [51,52], see Supplementary Material (S1).

2.2. Study Population

Individuals were recruited to participate in this study if they met the following inclusion criteria: (1) diagnosed with T2DM (identified through GP (general practice) registers

or self-declared), (2) aged 45 and above, and (3) willing to take part in a 6-week structured cognitive training programme. Individuals were excluded from participating in this study if they met the following exclusion criteria: (1) diagnosed with pre-diabetes or type 1 diabetes mellitus, (2) below the age of 45 years, (3) identified as cognitively impaired as indicated using the mini-mental state examination (MMSE), (4) required support for specific literacy or communication skills, (5) reported any co-morbidities that affected computer use, (6) recently (within the previous 6 months) changed diabetes treatment, e.g., new medication, medication to insulin, or the type of insulin treatment, (7) recently undertaken (within the previous 3 months) a structured cognitive or physical training regime, and (8) did not speak English.

2.3. Recruitment

To assist participant recruitment, a public patient involvement (PPI) group was established involving members of local diabetes support groups, public representatives, and healthcare professionals. Specifically, the PPI group played an important role in identifying and establishing key participant recruitment pathways, in addition to reviewing study documentation. The primary recruitment pathway involved screening GP databases and posting study information packs to eligible patients. Potential participants registered their interest either by returning an expression of interest form or by directly contacting the principal investigator. Secondary recruitment methods included radio advertisements and the dissemination of posters and flyers in local GPs, community centres, community boards, diabetic clinics, and social media platforms. Advertisement emails were sent to both staff and student mailing lists at the University of Lincoln, along with poster invitations advertised on the staff and student news feeds. Invitation emails containing study information were also sent to local diabetes support groups.

2.4. Study Procedure

2.4.1. Baseline Assessment

Participants were firstly screened for any cognitive impairments using the MMSE. If any indication for cognitive impairment was identified, participants were excluded from the study. It was clearly communicated to the participants that the MMSE does not provide a clinical diagnosis and that it only provides a potential indication for cognitive impairment. Participants were recommended to contact their GP for further information. Height and weight were recorded, and participants were then seated for the measurement of glycated haemoglobin (HbA1c). Capillary blood was drawn from the index finger using an automated lancet and analysed instantly using a HemoCue 501 HbA1c analyser (HemoCue, Ängelholm, Sweden).

Participants then completed a computerised cognitive test battery comprising a selection of neuropsychological tests derived from CANTAB (Cambridge cognition Ltd., Cambridge, UK). The following tests were administered: (1) Reaction time (RTI) (reaction time and motor response), (2) Paired Associated Learning (PAL) (visual memory and new learning), (3) Spatial Working Memory (SWM) (executive function/working memory), (4) Pattern Recognition Memory (PRM) (visual pattern recognition memory), (5) Delayed Match to Sample (DMS) (visual matching ability), and (6) Rapid Visual Information Processing (RVP) (sustained attention). See supplementary material (S2) for further details. These tests were chosen as they measured performance in cognitive domains that have previously been shown to be sensitive to cognitive decline in T2DM populations [20–22]. The test battery took approximately 45–60 min to complete. Post-assessment visits were conducted following the 6-week intervention period and replicated the same procedure outlined in the baseline visit except for the recording of height, weight, and HbA1c measurements. All participants were asked to refrain from consuming caffeine on the day of testing and from consuming alcohol on both the day of testing and previous evening.

2.4.2. Intervention

Individuals allocated to the intervention group participated in 12 h of structured computerised cognitive training completed over a 6-week period, with sessions being performed 2 times per week. The intervention components were selected based on a sub-group analysis of the moderators of cognitive training in healthy adult populations proposed by Lampit et al. [38]. Each session required the participant to complete a cognitive training battery comprising a series of computerised cognitive tasks derived from CANTAB (Cambridge Cognition Ltd., Cambridge, UK). Tasks included: (1) Choice Reaction Time (CRT) (reaction time and motor speed), (2) Verbal Recognition Memory (VRM) (verbal memory and new learning), (3) Attention Switching Task (AST) (attentional set shifting), (4) Spatial Span (SSP) (visuospatial working memory), (5) Stop Signal Task (SST) (response inhibition), and (6) One Touch Stockings of Cambridge (OTS) (spatial planning and working memory). See supplementary material (S2) for further details. These tasks provided an overlap in the domain trained, but not an overlap in tests with respect to the neuropsychological test battery described in the baseline visit. Each training battery lasted approximately 60 min in duration. Participants were given a choice to complete the cognitive training sessions either at the University of Lincoln or in their own home.

2.4.3. Control Group

Participants allocated to the usual care control group attended the baseline and post-intervention assessments only. Participants were asked to continue their usual diabetes care and routines for the 6-week duration.

2.5. Participant Characteristics

Measurements including age, sex, body mass index, MMSE, diabetes duration, education status, and HbA1C were recorded.

2.6. Feasibility

2.6.1. Design

Changes to any element of the study design, including enrolment procedures, assessment visits, cognitive training visits, and control group design, were recorded.

2.6.2. Participant Recruitment

The total number of individuals who met the study eligibility criteria at each GP, the number of mail-out study information packs posted, the number of those who expressed an interest in the study at each GP, and the number of individuals who enrolled onto the study through each GP were recorded. The number of individuals recruited from secondary recruitment strategies was also recorded.

2.6.3. Adherence and Retention

The number of individuals who provided consent to take part in the study and the number of individuals who dropped out of the study were recorded. The number of training sessions attended by those allocated to the cognitive training group was also recorded.

2.6.4. Data Collection

Outcome data from each participant were collected at predetermined time points, as outlined in the study protocol. The completeness of outcome data, along with the time point in which outcome data were collected, was recorded.

2.6.5. Motivation

Motivation was recorded digitally at the start of each session using visual analogue scales (VAS), a set of psychometric scales that measure subjective states. A sliding scale was presented on screen, with two 'extremes' or opposing answers reading at either end;

the participant responded to the questions as they appeared on the screen by selecting the on-screen slider and moving it to the appropriate position on the scale. Scales were graded 0–100, in which a lower score reflected attitudes/moods associated with the left extreme of the scale and a higher score reflected attitudes/moods associated with the right extreme of the scale. Participants completed 4 sliding scales, including (1) interested–bored, (2) attentive–dreamy, (3) alert–drowsy, and (4) energetic–lethargic.

2.7. Acceptability

Semi-structured interviews were conducted to better understand the acceptability of this type of intervention in T2DM. An interview guide was developed, informed by the wider qualitative literature concerning the acceptability of cognitive training in T2DM [42], in addition to theory-linked interview approaches [53,54]. See supplementary material (S3) for the study interview guide. Interviews were conducted post-intervention.

2.8. Cognition

Cognition was measured using the CANTAB neuropsychological test battery (Cambridge Cognition Ltd., Cambridge, UK) as outlined in the study procedure. Cognition was measured at baseline and post-intervention.

2.9. Progression Criteria

Feasibility outcomes were assessed using the following criteria: proceed/green (e.g., where there are no issues of concern that threaten the success of the trial), amend/amber (e.g., where there were remediable issues in which modifications may be needed before progressing), and stop/red (e.g., when there are intractable issues that could not be remedied) [55]. See Table 1, which outlines study traffic light progression criteria.

Table 1. Traffic light progression criteria used to assess the proposed cognitive training intervention.

Feasibility Outcome	Proceed (Green)	Amendments (Amber)	Stop (Red)
Design	No changes required	Minor changes required	Substantial changes required
Participant recruitment	n ≥ 70	n ≥ 35–<70	n ≤ 35
GP recruitment	n ≥ 4 GPs recruited	*n* = 1–4 GPs recruited	*n* = 0 GPs recruited
Retention rate	>80%	50–80%	<50%
Adherence rate	>80%	50–80%	<50%
Data collection	All data collected in timeframe	>50% of data collected in timeframe	<50% of data collected in timeframe
Motivation	<30 average on each outcome	>30–<70 average on each outcome	>70 average on each outcome

Notes: GP = general practice, VAS = Visual Analogue Scale.

2.10. Data Analysis

All cognitive data are presented as mean and 95% confidence intervals and were quantified using SPSS (IBM SPSS statistics for Windows, version 22.0, Armonk, New York, NY, USA). Effect sizes for each cognitive outcome were quantified using Review Manager 5.3. Audio data were transcribed verbatim and entered into NVivo 12 quantitative data analysis software system (QSR International Pty Ltd.) to organise data and facilitate analysis. Qualitative data were collected to the point at which it was agreed that replication of data had occurred, and no novel themes or concepts could be generated. Analysis of qualitative data was conducted in accordance with the six phases of thematic analysis outlined by Braun and Clarke (2006) [56], see below.

- **Phase 1 (familiarisation)**—interview transcripts and audio-recordings were repeatedly read and listened to in order to facilitate an in-depth knowledge of, and engagement with, the data set.

- **Phase 2 (coding)**—a systematic process of searching, identifying, and coding data into subcategories within NVivo was completed to identify emerging patterns throughout the data set.
- **Phase 3 (searching for themes)**—major categories were then formed by clustering together similar codes/subcategories to create a plausible mapping of key patterns in the data.
- **Phase 4 (reviewing themes)**—potential themes were reviewed to ensure they exhibited a good fit with coded data along with the entire data set, and each had a distinct or organising concept.
- **Phase 5 (defining and naming themes)**—a thematic map was then created in which theme names were defined, ensuring the conceptual clarity of each theme.
- **Phase 6 (writing the report)**—themes were then used to provide a framework for the analysis, in which the researcher combined the analytic narrative and data extracts to form the final report. See Supplementary Material (S4).

3. Results

3.1. Participants

Seventy-five individuals expressed initial interest in the study, of which $n = 11$ did not respond to follow-up contact, $n = 8$ declined to participate, $n = 5$ did not meet the eligibility criteria, and $n = 5$ lived too far away. Forty-six consented to take part in the study, of which $n = 4$ lost interest and were removed from the study prior to randomisation. Forty-two participants were randomised into the study, with only $n = 1$ drop out occurring during the study. Forty-one participants (age 66.5 years $\pm$ 9.8, HbA1c 54.0 $\pm$ 13.3 mmol.mol, MMSE 28.1 $\pm$ 1.7) were included in the follow-up analysis. See Table 2 for participant characteristics.

Table 2. Participant characteristics.

Demographic	Total ($n = 41$)	Intervention ($n = 20$)	Control ($n = 21$)
Age (Years)	66.5 $\pm$ 9.8	66.3 $\pm$ 8.4	66.6 $\pm$ 11.1
Sex (M/F)	23/18	11/9	12/9
Height (cm)	172.0 $\pm$ 11.0	173.1 $\pm$ 11.8	170.9 $\pm$ 10.3
Weight (kg)	90.6 $\pm$ 20.0	92.7 $\pm$ 19.0	88.6 $\pm$ 21.1
Body Mass Index	30.4 $\pm$ 5.3	30.8 $\pm$ 5.3	30.0 $\pm$ 5.3
HbA1c (mmol.mol)	54.0 $\pm$ 13.3	52.3 $\pm$12.4	55.6 $\pm$ 14.2
Duration (years)	9.2 $\pm$ 5.4	8.2 $\pm$ 4.7	10.2 $\pm$ 5.9
MMSE	28.1 $\pm$ 1.7	28.0 $\pm$ 1.7	28.1 $\pm$ 1.8
GCSE	$n = 15$	$n = 8$	$n = 7$
BTEC/HND	$n = 5$	$n = 2$	$n = 3$
A-Levels	$n = 4$	$n = 1$	$n = 4$
Degree	$n = 10$	$n = 5$	$n = 4$
Postgraduate	$n = 7$	$n = 4$	$n = 3$

Notes: M = male, F = female, cm = centimetres, kg = kilograms, mmol.mol = millimoles per mol, BTEC= Business and Technology Council, HND = Higher National Diploma.

3.2. Feasibility

3.2.1. Design

Only one minor change was made to the training visits, in that additional time was incorporated into the initial training sessions to allow for participant orientation of training tasks. No modifications were made to enrolment procedures, assessment visits, or control group design. Offering the choice of training location resulted in $n = 10$ opting for home visits and $n = 10$ opting for university visits. Whilst this may have increased recruitment numbers, it did add a significant travel burden on the researcher. See Table 3 regarding all feasibility progression recommendations.

Table 3. Progression decision and proposed feasibility modifications.

Feasibility Outcomes	Decision	Proposed Modifications
Design Training duration Travel burden	Amend (Amber)	Extra time required in training visits for task orientation. Restrict home training visits to targeted postcodes or mileage cap.
Recruitment Participant recruitment GP recruitment Study uptake	Amend (Amber)	Approach and recruit more GPs as early as possible. Minimise burden and responsibility placed on GPs. Ensure optimal communication between researcher and GPs. Liaise with GPs to avoid busy periods, e.g., vaccinations. Include follow-up recruitment phone calls and/or texts.
Retention/Adherence No issues identified	Proceed (Green)	No modifications required.
Data collection Data collected outside timeframe	Amend (Amber)	Consider an alternative control group design, e.g., active cognitive training, educational workshops, or wait-list. Include data collection telephone, text, or email reminders.
Motivation No issues identified	Proceed (Green)	No modifications required.

Notes: GP = general practice.

3.2.2. Recruitment

Primary recruitment through GP mail-out was the most successful recruitment approach. A total of four GPs were identified, with only three GPs agreeing to assist in study recruitment. A total of n = 1037 individuals diagnosed with T2DM were identified across the three GPs that met the study eligibility criteria (GP no.1 n = 332, GP no.2 n = 417, GP no.3 n = 288). One GP (GP no.3) dropped out of the study, leaving a total of n = 749 targeted mail-outs sent from two GPs. A total of n = 42 individuals expressed interest (GP no.1 n = 18, GP no.2 n = 24), with n = 25 enrolling onto the study (GP no.1 n = 13, GP no.2 n = 12). Secondary recruitment pathways generated a combined total of n = 33 individuals who expressed interest, of which n = 21 enrolled onto the study. This included n = 6 via posters/flyers, n = 5 via diabetes support groups, n = 5 via previous research, n = 3 via social media, and n = 2 via radio advertisement. Overall, the target recruitment rate for the current study, as well as the estimated recruitment rate per GP per month, was not met.

3.2.3. Retention and Adherence

Of the 46 participants who provided written and verbal informed consent, 89% remained in the study at the post-intervention follow-up (n = 4 were removed prior to randomisation and n = 1 dropped out during study). The adherence to training sessions of the twenty participants allocated to the cognitive training intervention was 99%, with only two participants missing one training session (n = 1 university training and n = 1 home training).

3.2.4. Data collection

There were no missing cognitive data in any of the 41 participants who were included in the follow-up analysis. Cognitive data were collected within the specified time frame in 36 of the 41 participants (intervention group n = 1 vs. usual care control group n = 4).

3.2.5. Motivation

Scores from the VAS scales indicated that participants were highly motivated to conduct cognitive training, with a group mean score of 15.3 $\pm$ 10.6 for interested/bored, 18.5 $\pm$ 11.9 for attentive/dreamy, 20.3 $\pm$ 14.0 for alert/drowsy, and 24.6 $\pm$ 13.9 for energetic/lethargic. There were no significant differences observed in any of the VAS outcomes between those who undertook training at the university or at home.

3.3. Acceptability

Face-to-face semi-structured interviews were conducted with 13 participants, including 10 participants from the cognitive training group and 3 participants from the usual care control group. Six overarching themes were identified relating to the acceptability of a cognitive training intervention in individuals with T2DM, including: (1) motivation to participate in research, (2) research communication, (3) feelings about the research, (4) facilitators and barriers to cognitive training, (5) delivery of training, and (6) desire to continue training. The six overarching themes and subthemes are provided in Table 4, along with supporting quotes. See supplementary material (S4) for further details of acceptability findings.

Table 4. Analytical themes, descriptive themes, subthemes, and supporting quotes.

Analytical Theme	Descriptive Theme	Sub-Theme	Supporting Quote
Motivation to participate in research	Family illness	Family suffering from dementia or Alzheimer's	"To be absolutely truthful I found it worrying because my mum has got dementia and since I've been going to visit her and seeing all these guys I am terrified, I am terrified of getting dementia, so because when this came up I thought well this would be interesting to see if you could do anything to help or alleviate it"
	Wanting to improve brain health	Concerned about brain health	"I was concerned, certainly. Undoubtedly as you get older you slow down your brain definitely and because of that you want to know how much you slowed down, and how much you're still in control over situations."
Research communication	Better communication required	Aims could have been made clearer	"I didn't fully understand the aims of the exercises maybe that could have been clearer."
	Understood the study aims and processes	Understood the aims	"I understood perfectly the aim of the study, we had various people in my group that were interested, we had 2 or 3 sessions, didn't we? I think where you explained the purpose of the study and yes, I understood."
Feelings about the research	Feelings towards cognitive training	Enjoyment	"Oh yes, yes it was enjoyable. Yes, I certainly would carry on doing it."
		Frustration	"I found it quite frustrating especially the ones that I wasn't progressing in so much."
	Feelings towards being in the control group	Greater study involvement needed	"Yeah there could have been something else. Yeah, I don't know what, but it would have been nice for there to be something else instead of sort of just being left alone."
Facilitators and barriers to cognitive training	Recruitment	Easy to manage when retired	"I mean ok I'm fortunate because obviously being retired meant that my time is easier to organise."
	Travel	Travel to and from university	"I mean the problem is always from anywhere in Lincolnshire is getting into Lincoln."
	Providing choice	Essential part of the study	"The fact that you give people the opportunity, either they come here or you go to them. I think that's an essential part of the study."
Delivery of training	University training visits	Academic environment	"I think if it's practical it would be better if they came here (university), the more academic environment."
		Opportunity to visit a new place and meet new people	"Yeah, I quite enjoy coming into different environments and meeting new people and seeing the big wide world rather than sitting at home moping around, especially in the wintertime there's not a lot I can do outside."
	Home training visits	Felt more relaxed training at home	"A bit more relaxed, you're not a little bit hyper because you had to rush through traffic or run out of breath because you had to run up the stairs or anything like that you're in your own zone, your own environment I think it's very useful."
		More convenient to train at home	"Yeah, I mean it's easier for me, It's as simple as that really particularly if you were going to do that number of home visits."
Desire to continue training	Continuing training	Using apps and puzzles at home	"I have been using the sudoku, (name of participant) has been busy using an app at the moment where you're given so many letters and how many words can you find out of it."
			"It's made me a lot more aware of it and I tend to do crosswords at home and try and keep my brain active probably more so now after those training sessions than I did before."

3.4. Cognition

The mean and 95% CI for all cognitive outcomes at baseline and post-intervention by group are presented in Table 5. Compared with the usual care control group, greater improvements were observed in the cognitive training group in the RTI simple reaction time task, RTI Five choice reaction time task, PAL total errors, and SWM strategy. An increase in RVP total hits and RVP A was also shown in both groups, indicating greater performance in these tasks. A greater increase in RVP total hits was made in the control group, whilst RVP A equally improved. Improvements in both DMS total correct and DMS latency were shown in the control group only, whilst the cognitive training group was shown to worsen both DMS total correct score and DMS correct latency score. An increase in PRM total correct score was shown in the cognitive training group, reflecting a greater performance in this task, whilst no change was observed in the control group. Small effects were identified across most cognitive outcomes except for SWM strategy, which showed a moderate to large effect (0.7). see Table 5 for further information.

Table 5. Cognitive performance across the cognitive and control groups.

Domains	**Cognitive (*n* = 20)**		**Control (*n* = 21)**		**SMD**
Outcomes	**Pre**	**Post**	**Pre**	**Post**	**(Hedge's g)**
Reaction Time and Motor Response					
RTI simple (ms)	**320.6** (280.0–361.2)	**306.7** (282.3–331.0)	**305.1** (283.1–327.0)	**298.2** (270.4–325.9)	**0.15**
RTI Five choice (ms)	**342.2** (309.4–374.9)	**331.7** (301.7–361.6)	**335.0** (311.9–358.0)	**333.2** (303.2–363.2)	**−0.02**
Visual Memory and New Learning					
PAL total errors	**31.3** (18.4–44.1)	**15.0** (8.4–21.6)	**23.1** (15.2–31.0)	**16.6** (10.5–22.6)	**−0.11**
Executive Function and Working Memory					
SWM strategy	**29.0** (24.8–33.2)	**25.9** (22.5–29.2)	**32.7** (29.3–36.0)	**31.1** (27.8–34.5)	**−0.70**
SWM total errors	**23.0** (10.1–35.3)	**21.2** (10.4–32.0)	**33.1** (23.4–42.8)	**29.2** (19.9–39.0)	**−0.36**
Visual Pattern Recognition Memory					
PRM total correct	**19.2** (17.9–20.5)	**20.6** (19.3–21.8)	**21.0** (19.8–22.2)	**21.0** (20.0–22.1)	**−0.16**
PRM correct latency (ms)	**1979.9** (1686.8–2273.0)	**1830.7** (1481.0–2180.4)	**2018.2** (1830.2–2206.3)	**1860.9** (1673.6–2048.0)	**−0.05**
Visual Matching					
DMS total correct	**12.6** (11.8–13.4)	**12.5** (11.7–13.3)	**12.0** (11.1–12.8)	**12.6** (11.9–13.2)	**0.25**
DMS correct latency (ms)	**3202.7** (2650.6–3754.7)	**3493.1** (2865.3–4121.0)	**3452.3** (3010.2–3894.5)	**3220.0** (2894.0–3546.2)	**−0.06**
Sustained Attention					
RVP total hits	**16.8** (14.6–18.9)	**17.1** (14.1–20.0)	**16.4** (13.6–19.3)	**17.1** (14.6–19.7)	**0.13**
RVP A	**0.90** (0.90–0.92)	**0.90** (0.87–0.92)	**0.89** (0.84–0.93)	**0.88** (0.84–0.93)	**0.00**

Notes: RTI = Reaction Time, SWM = Spatial Working Memory, PAL = Paired Associated Learning, PRM = Pattern Recognition Memory, DMS = Delayed Match to Sample, RVP = Rapid Visual Information Processing, SMD= Standardised Mean Difference.

4. Discussion

The use of cognitive training interventions to maintain and/or improve cognition is growing in T2DM. Whilst studies have predominately focused on the potential effectiveness of cognitive training, there remains limited understanding surrounding the feasibility or acceptability of this type of intervention. The aim of this research was to determine the feasibility and acceptability of a 6-week cognitive training study in individuals with T2DM. Our findings showed feasibility in the adherence, retention, and motivation of participants, whilst only minor remedial modifications were recommended to the intervention design, recruitment strategies, data collection procedures, and control group design. Findings

from the acceptability element suggested that the type and dose (frequency, duration, and length) of cognitive training was broadly acceptable, and providing flexibility of training location and timing was important in mitigating training barriers. The level of understanding regarding the purpose and design of the research study varied among participants, highlighting the need for more extensive PPI in both the design and participant communication of all future trials. Those allocated to the usual care control described feeling unmotivated, pointing to the need for greater control group involvement in future trials. Analysis of cognitive data signalled towards improvements in several cognitive domains including executive function (SWM task), visual memory (PAL task), recognition memory (PRM task), and reaction time (RTI tasks). Overall, our findings provide evidence to suggest that cognitive training may not only be a potentially effective strategy, but also a feasible and acceptable strategy for targeting cognitive dysfunction in T2DM.

The high adherence (89%) and retention (99%) of participants demonstrates the potential feasibility of this type of intervention [57]. Similar to exercise training and medication regimens, cognitive training is unlikely to produce significant benefit unless individuals adhere to it [58,59]. Aside from reducing the generalisability of findings, poor compliance is often viewed as an adverse outcome that reflects the weakness of a trial independent of any treatment effect [60,61]. These findings fall in line with previous randomised controlled trials [62] and are comparable to, or greater than, participant retention and adherence rates previously reported in cognitive and exercise trials in T2DM [26,42,63,64]. The high adherence and retention observed in the current study may have been linked to the high levels of motivation maintained throughout the study. Participant motivation has previously been identified as a putative determinant of one's capacity to adhere to and benefit from health interventions [65–67], including cognitive enhancing therapies [68]. Coordinating post-intervention assessments with some control group participants was challenging, and it is acknowledged that missing or excluded data may significantly impact the generalisability of findings [69,70]. There is evidence to suggest that control group participants may become less motivated to remain in a trial if they view the experimental intervention as more efficacious compared with their usual care received [71], indicating the need for greater control group involvement in future trials. However, the importance of including a 'usual care' control group in trials is recognised when aiming to evaluate the effectiveness of a new approach compared with standard usual care [72,73].

Whilst GP mail-outs yielded the greatest number of participants, supporting previous evidence advocating the use of GP registers as a primary recruitment pathway [74–76], the recruitment of GPs was challenging, which meant that recruitment targets were not met. Challenges associated with the recruitment and retention of GPs to assist in trial recruitment have been widely documented [77–80] and include barriers such as a lack of time [81–84], lack of interest [85–87], overwhelming responsibilities [81], and inadequate study information [78,81]. Evidence points towards optimal communication with GPs [80,88] and reducing the responsibilities placed on GPs [88] as two key factors when recruiting and retaining GPs in trials. Furthermore, an earlier study [89] also reported that successful participant recruitment may be dependent on the early recruitment of GPs and not through reliance on the initial recruitment of a few key practices. Our findings also showed that a large proportion of individuals that returned the expression of interest form as part of the GP mail-out packs did not reply to follow-up recruitment emails, reflecting the need for greater follow-up strategies in future trials. For example, a prior systematic review [90] reported that telephone reminders to individuals who did not respond to postal invitation resulted in a 6% (95% CI 3–9%) improvement in participant uptake.

Only a limited number of trials exist that evaluate the impact of cognitive interventions in T2DM [42–47], of which only few explore the acceptability of these types of interventions. Our findings are consistent with recent evidence presented by Cuevas et al. [91] suggesting individuals with T2DM may be motivated to participate in cognitive activities due to their concerns of developing dementia. The programme format was found to be acceptable in the current study, and in line with previous research [92,93], cognitive training was found to be

challenging but enjoyable. Enjoyment is a key determinant of intervention acceptability and has been directly linked to increased adherence and long-term compliance to positive health behaviours [94–97]. Participants also reported an improvement in their confidence when attempting complex cognitive tasks upon study completion. The improved confidence may reflect improvements in cognitive self-efficacy [98], which would influence health behaviour change [99] and diabetes self-management [100,101]. This is supported by previous evidence that reported that the use of cognitive training and strategies provided participants with a greater sense of control and self-efficacy of diabetes self-management tasks [91]. A small number of participants expressed initial difficulty in understanding the study aims of the present study. The lack of participant understanding is a common problem in research, with several studies reporting participants having an incomplete or inaccurate understanding of trial aims and processes [102–105]. There is a clear need for the implementation of clear communication strategies in future trials, e.g., enhanced consent forms and extended decision time and discussions [106], as the participants' lack of understanding of the research process may potentially have adverse effects on trial outcomes.

In line with previous evidence [42], travel and work commitments were reported as prominent training barriers in the present study and are two prominent barriers acknowledged to influence participation and adherence [107–109]. Providing preference with respect to the location of training and timings was explored in the current study, and whilst this clearly introduces logistical challenges for research teams, providing choice is thought to have helped mitigate the potential logistical barriers [110]. Those allocated to the control group expressed disappointment in not being able to participate in cognitive training. This reportedly led to a decrease in motivation, with some suggesting the need to employ a different approach for control participants in future. Whilst the use of a usual care control group is advocated for testing interventions that are characteristically different to usual care practice [73], evidence presented in previous drug and health interventions do show greater retention of participants when employing an active control group or wait -list approach [111–113].

The improvements in executive function/working memory (SWM task), visual memory (PAL task), recognition memory (PRM task), and reaction time (RTI task) complement the findings observed in previous randomised controlled trials [42,44] and further add to the accumulating evidence pointing towards cognitive training as a potential effective strategy for targeting cognitive dysfunction in T2DM [42–47]. Whilst the magnitude of effect was small across most cognitive outcomes, a moderate to large improvement (0.7) was identified in spatial working memory, a core construct of executive function [114]. Together, these findings may have important implications in the context of (1) evidence that identifies working memory, visual memory, and recognition memory as key cognitive domains that are sensitive to decline in T2DM [20–22] and (2) evidence that suggests deficits in executive function and memory may have a detrimental impact upon T2DM self-management behaviours [23–25]. A decline in cognition and the subsequent worsening of self-management abilities is of concern in this population, as it may potentially lead to a vicious downward spiral resulting in the development or exacerbation of vascular complications [24]. It may therefore be important to target cognition at the earliest stage of diabetes development, i.e., during prediabetes. As alluded to in the introduction, T2DM can be viewed as a disease continuum whereby even subtle changes in glucose metabolism may have significant implications on cognition and subsequent self-management abilities. For example, previous studies show that prediabetes is associated with worse cognition compared with non-diabetic cohorts [115], may alter brain metabolism [116], and decrease the probability of reverting back from MCI to normal cognition [117]. Our findings provide further evidence for cognitive training as an effective strategy for targeting cognitive dysfunction in T2DM, which may potentially help improve or maintain self-management abilities.

5. Study Limitations

This study has several potential limitations to consider. A longer-term follow-up assessment was not conducted, meaning that the long-term benefits of this 6-week cognitive training study remains unknown. There is a need for further research to explore different types and designs of cognitive training in addition to exploring the longer-term effects of these types of interventions in T2DM. Likewise, HbA1c was measured at baseline only in the present study to help define the study population. Recent evidence has shown that cognitive training may not significantly improve glucose control [45]; however, there remains a need to further explore changes in glucose control alongside other self-management indicators in response to differing types of cognitive training in T2DM. Whilst the current study did control for several confounding factors that may affect cognitive training performance (e.g., prohibiting the consumption of alcohol on both the day of testing and previous evening), no consideration was given towards wider confounding factors such as excessive or chronic alcohol intake. Regarding study acceptability, only $n = 3$ participants were interviewed from the control group, which is considered a limitation of the study. We recognise the need to include a greater number of control participants in the future to help provide a broader evaluation of this type of research. Finally, this study did not include any assessment or analysis of ethnic or cultural differences. The authors acknowledge the importance of considering ethnic and cultural factors when developing and implementing lifestyle interventions and this is therefore recognised as a limitation of the current study.

6. Recommendations for Future Research

The findings of this study provide informative evidence to help guide future researchers regarding the implementation and evaluation of future definitive cognitive training interventions in T2DM. Based on the feasibility, acceptability, and cognitive training components of the present study, the following recommendations are proposed:

- A detailed recruitment strategy should be developed and tailored specifically in line with the research questions and study population. This should include follow-up recruitment and data collection strategies, e.g., emails, phone calls, or text reminders to encourage study uptake and timely data collection. Researchers may also want to consider monetary incentives with respect to the recruitment of both GPs and participants.
- GPs should be considered as a primary recruitment pathway and must be recruited early into studies. Based on the findings of the current study, future research would need to recruit around 2–4 GPs to recruit approximately 25–50 participants.
- Trials should consider employing an alternative control group design, e.g., active cognitive training, educational workshops, or a wait-list to keep control participants engaged in future studies.
- Communication strategies should be co-produced involving PPI to better inform the participants' understanding of the study purpose and design.
- Future research should explore a wide range of cognitive training interventions that differ in format and design. These should include a long-term follow-up to assess the long-term impact of these and also include a comparison to non-diabetic cohorts to better validate these types of interventions in T2DM.
- Greater consideration should be given towards any potential confounding factors associated with cognition and T2DM (e.g., glucose control and disease duration) when designing, implementing, and evaluating these types of interventions. This should also include the consideration of key ethnic and cultural factors.
- Future trials should aim to measure a wide range of cognitive outcomes, including those that play a critical role in diabetes self-management, such as executive function. Trials should also aim to include measures of diabetes self-management (e.g., glucose control, diet, and medication adherence) to better assess the impact of cognitive training on disease management. The effect sizes presented in the current study could

be used to guide sample size calculations for relevant cognitive outcomes in future trials.

7. Conclusions

The findings from the current study suggest that cognitive training is both feasible and acceptable in T2DM. Recommendations are provided to help guide future researchers in designing, implementing, and evaluating future cognitive training studies in T2DM. There is still much work to be done in this promising area, including exploring the potential mechanisms underpinning changes in response to cognitive training in T2DM and further exploring how clinically meaningful any improvements in cognition are, particularly in the context of diabetes self-management.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/diabetology4020016/s1, File S1: CONSORT checklist, File S2: Training and test batteries, File S3: Study interview guide, File S4: Acceptability themes.

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