

## The Cognition and Flow Study (CogFlowS)

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## Title

The Cognition and Flow Study (CogFlowS): A mixed method evaluation of a randomised feasibility trial of cognitive training in dementia

## Running title

The Cognition and Flow Study (CogFlowS)

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## Declarations

### Ethical approval and consent to participate

Ethical approval for the study was granted by the Bradford Leeds Research Ethics Committee (YH/18/0396), and all participants provided written, informed consent or personal consultee declaration. All methods were performed in accordance with the relevant guidelines and regulations, including the Declaration of Helsinki 1971.

### Consent for Publication

All participants provided consent for quotes obtained during interviews to be used in publications.

### Availability of data and materials

Data are available on request from the corresponding author.

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## Key words

Brain training

Mild cognitive impairment

Alzheimer's disease

Cognitive intervention

Qualitative

## **Abstract (250 words)**

### **Background**

Cognitive training (CT) may be beneficial in delaying the onset or slowing dementia progression. CT has been evaluated quantitatively and qualitatively, but none have used mixed methods approaches.

### **Objective**

The aim of this study was to use a mixed methods approach to identify those who may selectively benefit from CT.

### **Methods**

This was an explanatory sequential mixed methods study involving a quantitative randomised trial of 12 weeks multi-domain CT in healthy older adults (HC, n=20), and people living with mild cognitive impairment (MCI; n=12) and dementia (n=24). Quantitative outcomes included: cognition, mood, quality of life and activities of daily living. 28 (10 HC, 6 MCI, 12 dementia) training participants completed semi-structured interviews with their carer. Quantitative and qualitative data were integrated using joint displays.

### **Results**

Three participants dropped-out from the training early-on, leaving 25 participants with follow-up data for full integration (10 HC, 6 MCI, 9 dementia). Drop-outs and lower adherence to training were more common in dementia participants with greater non-modifiable barriers. High adherers were more resilient to negative emotions, and poorer or fluctuating performance. Integrated analysis found the majority of participants (n=24) benefited across outcomes, with no clear profile of individuals who benefited more than others. Participants made a number of key recommendations to improve adherence and minimise drop-out to CT.

### **Conclusion**

Reasons for drop-out and low adherence were identified, with recommendations provided for the design of CT for dementia. An individual approach to training should be adopted and low adherence should not preclude engagement with CT.

## 1. Background

There are currently few effective treatments for dementia, and the number of people living with dementia worldwide is expected to almost double to 74.7 million by 2030 [1]. Thus, non-pharmacological strategies that are shown to be effective are of increasing interest to patients, clinicians and society.

Cognitive interventions are an emerging preventative strategy to both delay the development of dementia in healthy older adults, and slow cognitive and functional decline in mild cognitive impairment (MCI) and dementia [2, 3]. Cognitive interventions can be broadly considered under three main categories: cognitive training (CT), cognitive rehabilitation and cognitive stimulation [4, 5]. CT consists of a structured programme of standardised tasks designed to provide repeated practice on specific cognitive domains [4, 5]. In contrast, cognitive rehabilitation focusses on goal setting, and directs exercises that focus on deficits in activities of daily living [4, 5]. Cognitive stimulation is typically undertaken as a group but can be delivered individually, and uses more general activities (e.g. discussion, reminiscence, social activity) to improve cognitive function indirectly [4, 5].

Home-based computerised CT is attractive given it has fewer side effects, lower costs, and greater flexibility and accessibility over group-based programmes for people with mobility and transport difficulties [6]. However, the effectiveness of CT in dementia remains unclear [7]. Recent systematic reviews and meta-analyses suggest CT may be effective in healthy older adults [3] and individuals with MCI [2, 6], but less-so in dementia [2, 4]. This is further hampered by the poor quality of clinical trials and lack of adequate control conditions [7, 8]. Furthermore, whilst CT does not have any pharmacological side-effects, there may be negative psychological consequences, such as: reduced

self-esteem and confidence, carer strain, and increased anxiety and depression [9-11]. Thus, understanding for whom CT has greatest benefit and applicability is important when considering widespread use and adoption of CT programmes. There are a number of unique challenges to introducing behavioural interventions in dementia, with apathy and depression commonly co-existing, and progressive adaptation of the programme in line with advancing cognitive decline [12].

To date, no study has utilised a mixed methods approach to identify participants who may selectively benefit from CT by integrating data from both quantitative and qualitative streams. This could prevent the inappropriate use of CT programmes for certain people living with dementia, avoiding the adverse psychological and emotional consequences for susceptible participants. This study was a feasibility randomised controlled trial of CT in healthy older adults, and people living with MCI and AD. **The primary outcome of this trial was feasibility, and secondary outcomes included: changes in cerebral haemodynamics, cognition, mood, quality of life, and activities of daily living. Quantitative results on feasibility, effect sizes and sample size calculations, and qualitative results on participant experiences and engagement have been published and can be accessed here [13, 14].**

In this analysis, we present the results of a mixed methods approach, with the intention of using the qualitative data to explain results from the quantitative trial in respect of drop-outs and low adherence. The rationale was that the qualitative phase would provide insights to the quantitative results that would otherwise have remained unknown. Quantitative baseline demographic data were linked to qualitative themes from participants with low adherence or drop-out to identify those who may not benefit from CT. A further aim of this analysis was to integrate the quantitative and qualitative outcomes for each participant to identify whether integrated participant profiles can help identify those who may selectively benefit from training. Through this mixed methods design, the overall objective of this analysis was to facilitate a targeted approach to CT programmes for healthy older adults and those living with dementia and develop a set of key recommendations for the development of CT programmes specifically for people living with dementia.

## 2. Methods

### 2.1 Sample selection

The Cognition and Flow Study was an explanatory sequential mixed methods feasibility trial of CT in healthy older adults, MCI and Alzheimer's disease (AD). Participants were recruited from the Leicestershire Partnership Trust and University Hospitals of Leicester NHS Trust between January 2019 and April 2020. Recruitment was closed early due to the Covid-19 pandemic, but all enrolled participants completed the training unless they dropped-out from the trial. All participants provided written, informed consent, or personal consultee declaration where the participant lacked sufficient capacity. The study had research ethics committee approval (Bradford Leeds ref: YH/18/0396), and all study procedures were conducted in accordance with the declaration of Helsinki. The protocol for the study has been published previously [15]. In total, 20 healthy older adults, 24 people living with dementia, and 12 with MCI were recruited to the study. Eligibility criteria and any changes to these are reported elsewhere [13].

### 2.2 Study design

The first phase of the study was a quantitative randomised trial of a 12 week multi-domain CT programme provided by Lumosity®. Participants were either randomised to the intervention (30 minutes, five times per week for 12 weeks) or waiting-list control (1:1). Allocation was performed by Sealed Envelope®, an online programme to which the researcher was unaware of the treatment allocation until the point of randomisation. A block size of four was used to ensure equal distribution of participants in control and training arms given this was a small study and the primary aim was feasibility. In the second qualitative phase of the study, at the end of the 12 week period, participants in the intervention arm were invited to semi-structured interview on the experiences of the CT programme. One investigator (LB) enrolled, randomised and assigned participants to interventions. Where possible, participants with dementia or MCI were interviewed with their carers. Given the



primary aim of this trial was feasibility, blinding was not performed. A flow chart describing the study design is provided in Figure 1. The trial was prospectively registered on ClinicalTrials.Gov (NCT03656107, 04/09/2018).

### 2.3 Sample size

The sample size for the mixed methods analysis was limited to those that completed the training (12 AD, 6 MCI, 10 healthy older adults), with data for both quantitative and qualitative outcomes. Three participants dropped-out from the training early on, leaving 25 participants (10 healthy older adults, 9 AD, 6 MCI), with follow-up data for analysis of integrated profiles. The three participants who dropped-out were interviewed and have been included in the other analyses in this paper.

### 2.4 Quantitative outcomes

Participants underwent assessment of cognition (Addenbrooke's Cognitive Examination III [ACE-III]) [16], mood (Geriatric Depression Scale 15 item [GDS-15]) [17], quality of life (Dementia Quality of Life [DEMQOL]) [18], and instrumental activities of daily living (Lawton IADL) [19] at baseline and follow-up. In addition, participants underwent an assessment of their neurovascular function using transcranial Doppler ultrasonography measured task-activation. Detailed methods and results from the quantitative phase of the study have been published [14, 15]. In brief, participants underwent a five minute resting baseline recording with continuous monitoring of cerebral blood flow velocity (CBFv, transcranial Doppler ultrasound), blood pressure (BP, Finometer), end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>, nasal capnography).

Following this, task-activated CBFv responses were measured using five cognitive tasks from the ACE-III (attention – subtracting serial sevens, fluency – naming words beginning with “p”, language – repeating words and phrases, visuospatial – drawing a cube and infinity diagram, and memory – recalling three words learnt previously). The remaining ACE-III tasks were completed separately. Data were extracted on the peak percentage in CBFv relative to a twenty second baseline prior to task

activation. A novel method was applied to calculate the presence or absence of a response to each cognitive task, based on a two-parameter method described previously [20]. The number of responses from each task, and in each hemisphere, were combined to give a cumulative response rate (CRR) (total out of ten). Three participants did not have data on blood flow changes due to remote follow-up during the Covid-19 pandemic.

Data were tested for normality prior to analysis using the Shapiro-Wilk test. Non-normally distributed continuous data are presented as median (inter-quartile range [IQR]), and normally distributed as mean (standard deviation). For the purpose of this analysis, tests of effectiveness and sample size calculations were not used, as these results have been published previously [13]. The quantitative analysis had input from a statistician and the clinical trials unit based at the University of Leicester.

## 2.5 Qualitative outcomes

All participants (n=28) who completed the training were invited with their carer to a semi-structured interview at the end of the intervention period. All participants agreed to take part in the qualitative study. The theoretical framework against which the interviews were constructed was the Health Belief Model (HBM). The HBM has six core constructs to conceptualise behaviour change: risk susceptibility, risk severity, benefits to action, barriers to action, self-efficacy, and cues to action. Semi-structured interviews were conducted iteratively, and new themes that emerged were explored in later interviews. Issues that arose during the quantitative phase were explored in the qualitative interviews (e.g. technology issues, drop-outs, anxiety).

Interviews were audio-recorded, transcribed verbatim, and open coded by LB using NVIVO version 11 for Windows. Coding of the initial transcripts was checked by RE to ensure consistency in the coding. Respondent validation was used to check the accuracy of transcripts with LB, and all participants had few or minor changes to the transcripts. Four major themes were developed from the initial coding: barriers, benefits and efficacy, threat, and behaviour. Framework analysis was undertaken by LB and supervised by RE. Analytical frameworks were generated using NVIVO and used to analyse data under

these major themes. The methods and results from the QUAL strand have also been published separately [14].

## 2.5 Mixed methods

High adherers were classified as those completing at least 20 hours of training (minimum required to induce changes and ~67% of allocated sessions). Consensus is lacking on the optimal training dose required to induce plasticity [21]. However, studies suggest that between 20 and 40 hours are required to induce clinical or radiological changes [21, 22]. A previous study evaluating Lumosity® classified high adherence as >70% of allocated sessions completed [23].

The key participant demographics and baseline scores were displayed using a typology, and statistics merged data analysis display (joint display) to identify those who may be more likely to drop-out, have low adherence, or few benefits, and the reasons why. The suggestions by participants on improving adherence and completion were also arrayed to identify which group of participants may need additional support or resources, and who may benefit from an adapted CT programme and how. Finally, the characteristics of participants who had, increased, neutral, or reduced CBFv responses to CT, were arrayed with their positive and negative experiences identified from the qualitative strand. This identified participants who were more likely to benefit from engaging with a CT programme using an integrated outcome profile for each participant..

The joint displays were examined for congruencies and discrepancies between the data streams. Data transformation (conversion of qualitative to quantitative data) of qualitative was not undertaken as this was unlikely to provide any additional or meaningful data above the joint displays.

The mixed methods analyses were conducted to answer three key research questions that were not explored by the separate quantitative and qualitative phases of the research study:

- 1) How do barriers, facilitators and constructs from the HBM explain the reasons for drop-outs or non-adherence with the CT programme, and can the associated baseline characteristics predict these individuals?
- 2) Can the integrated quantitative and qualitative profiles, based on the outcome measures and experiences of participants identify individuals who will selectively benefit from CT?
- 3) What recommendations can be drawn for future CT programmes from the experiences of participants with few benefits, low adherence or drop-out from the study?

### 3. Results

#### 3.1 Adherence and drop-outs

Twenty-eight participants were included (10 healthy older adults, 6 MCI, 12 AD). A full description of trial participants has been reported previously [13]. Participants were dichotomised into two groups: those that trained more than 20 hours over the study (high adherence, n=20), and those that trained less than 20 hours over the study (low adherence, n=5) or dropped-out (n=3). The median hours trained for high adherence group was 37.8 [IQR: 30.5-52.2], compared to 17.1 [IQR: 16.8-18.8] in the low adherence group. The majority of high adherers were healthy (n=10, 100% of healthy), or MCI (n=5, 83% of MCI), with fewer from the AD group (n=5, 42% of AD). In contrast, the low adherence group consisted mainly of AD (n=7, 88% of low adherers), with only one MCI participant. Barriers and facilitators from the qualitative analysis are arrayed against the high and low adherence groups in Table 1.

There were a greater number of barriers amongst the low adherence and drop-out group. In particular, barriers that were not present amongst the high adherence group were: apathy, severity of cognitive impairment, fluctuating symptoms, ability to remember instructions, difficulty with new situations and skills, fear of failure, patient-carer friction, carer reliance, lack of insight, lack of computer literacy, and higher levels of anxiety, stress and frustration. In contrast to participants with low adherence, barriers were more easily overcome by high adherers, which were viewed as a challenge.

Barriers in the high adherence group were more likely to be modifiable; for example, minimising distractions, having a suitable environment, training when less tired and busy, in comparison with less modifiable factors present in the low adherence group, such as dementia severity, apathy, lack of insight, and carer reliance. Although high adherers also experienced frustration and negative feelings related to poor performance, they were more likely to overcome this by “taking time out” or accepting

their performance was likely to fluctuate. High adherers were particularly facilitated and motivated by achievement, challenge, and visible progress. Similar facilitators were present in the low adherence group (ability to complete exercises, visible progress and satisfaction), but they were more likely to need facilitator or carer support to complete the training, including carers being able to step-back when needed in some instances.

### 3.2 Integrated participant profiles

Twenty-five participants (10 healthy older adults, 6 MCI, 9 AD), completed the training and interview study with follow-up assessments. Three participants underwent remote follow-up due to the covid-19 pandemic and did not have data on CRR changes. Participants were divided into three quantitative groups: increase in CRR (n=6), no change in CRR (n=9), and reduction in CRR (n=7) post-training. In Table 2, the quantitative outcomes are arrayed against the qualitative experiences for each participant in their respective CRR groups, to identify whether benefits in the quantitative arm translated into qualitative benefits, or where the two are discordant.

The majority of participants whose CRR increased were in the AD group (n=5, 83%), with one MCI participant. No healthy participants had an increase in CRR post-training. Changes in the other quantitative outcomes for this group were variable (cognition, QoL, mood, function), but most had stable or improving cognition (n=4), stable QoL (n=5), or mood (n=4). The majority did not improve in function, and this was consistent across quantitative and qualitative measures. On average, cognition improved by 1.7 (5.8) points on the ACE-III, consistent with few participants identifying improvements in memory, and those that did, felt they were either stable or marginally improved. On average, mood improved by 0.5 (2.2) points on the GDS; however, the qualitative data were more variable and complex. Participants could be frustrated by the programme, and negative feelings were linked to poorer performance, but participants also reported positive experiences linked to greater awareness, progress and achievement. Majority of participants in this group benefited from the programme both in quantitative and qualitative measures, despite three participants (AD 11, 15, and 19) being in the low adherence group.

In the neutral CRR group, the majority were healthy or MCI (n=8), with only one participant from the AD group. Mean quantitative benefits were small on average in this group [cognition 1.3 (2.7), GDS 0.2 (1.1), QoL 2.4 (5.1), IADL 0.1 (0.8)] which was reflected in few participants identifying qualitative benefits. Three participants benefited from improved cognition, which was also identified in the

qualitative data. Only one participant improved in function on IADL, but this was not identified in the qualitative data. All participants, except one, identified more positive benefits to training (interest, enjoyment, learning, brain activity, challenge and achievement), than negative (mild frustration and anxiety), suggesting an overall benefit to training.

In the CRR reduction group, all participants were either healthy (n=5), or MCI (n=2), with none from the AD group. The majority reported benefits (active mind, enjoyment, progress, improved awareness), which were greater than the negative aspects (frustration, disappointment with scores). No participant identified improvement to ADL, consistent with quantitative data. Four participants identified effects to mood (3 positive, 1 negative), consistent with quantitative data in two participants. Two participants identified improved memory which was consistent with quantitative data in one case.

Three participants were not classified by CRR due to inability to complete the haemodynamic assessment at follow-up. These participants all had a diagnosis of AD, and reported benefits to the programme, including memory improvement in two cases. Quantitatively, mood deteriorated in all three, despite largely positive qualitative experiences.

Overall, participants demonstrated benefits from training, either both from quantitative and qualitative analysis, or in one of the domains. Only one participant had limited benefits from both (Healthy #4), and there was no clear integrated profile that did not demonstrate benefits to training.



### 3.3 Demographics, experiences, and recommendations of those that dropped-out, had low adherence or fewer benefits

Nine participants (1 healthy older adult, 1 MCI, and 7 AD) were classified as low adherers, dropped out from the study, or had few quantitative or qualitative benefits. Table 3 summarises the qualitative experiences and recommendations from participants with low adherence, fewer training benefits, or drop-out from the study. The mean age of this group was  $71.2 \pm 7.9$  years and the majority (78%) were male. Seven (78%) participants had a diagnosis of AD (low adherence or drop-out), and only one with MCI (low adherence) and one healthy participant (few benefits on quantitative and qualitative analysis). Mean years of education were  $16.1 \pm 3.8$  years, and median alcohol intake was 6 [IQR: 0-14] units per week. The majority (67%) were established on anti-dementia drugs, and deficits were mild at baseline (mean ACE-III score:  $80.5 \pm 16.8$ ). There was some evidence of reduced mood, QoL of life, and function at baseline (Table 3).

One healthy participant had few benefits to training, from both quantitative and qualitative analysis. Their perception and experiences of training were strongly influenced by their preconceptions on the effectiveness of CT, and in particular, the commercial nature of CT programmes. Participants with low adherence or drop-out reported friction with carers, high levels of anxiety, stress, and frustration, and more difficulty with following the instructions or understanding the purpose of the exercise. However, many of the participants identified benefits to training: enjoyment, progress, achievement and stability of cognition over the study.

Participants with dementia and their carers recommended commencing the programme earlier in the diagnosis, with better screening and tailoring to cognitive abilities and education. Participants with both AD and MCI needed clearer instructions with more reminders throughout the exercises, and some participants with dementia would benefit from a more graded programme from pencil and paper to computer, and more facilitator support. All participants valued greater personalisation of feedback with more explanation on the purpose or objectives of the exercises.

## 4. Discussion

### 4.1 Summary of results

In summary, there was no particular integrated profile which identified participants who were more likely to benefit from CT. In particular, although AD participants were more likely to have lower adherence, and greater drop-outs, they also had significant quantitative (increased CRR) and qualitative (positive experiences) gains. Despite negative experiences associated with training, these were often out-weighted by the benefits (e.g., AD participants #11, #15, #19). Some of these benefits were not always captured quantitatively (e.g. increased awareness, stimulation, challenge and achievement). Thus, if CT proves to be an effective intervention, it should be offered on a case-by-case basis, using a more tailored approach. Participants should be screened for potential barriers, and more support provided to participants with greater symptomatology, or with friction between patients and carers. Low adherence should not preclude enrolment into a CT programme, as these participants still demonstrated benefits on quantitative and qualitative outcomes. It is important to screen for, and address any negative preconceptions, as this may hamper engagement, and limit benefits to training. However, for some participants, barriers (especially internal) will be insurmountable, and careful screening of pre-morbid education, and anxiety and depression symptomatology may help identify those for whom training may be less beneficial.

### 4.2 Results in context

To our knowledge, this is the first study to use a mixed methods approach to investigate how integrated profiles may identify individuals with higher training-related gains, and those who may be less likely to benefit from CT. Previous studies have used mixed methods approaches to investigate the utility of a mindfulness programme [24], and a community-based falls prevention programme [25]. However, unlike our study, they did not fully integrate the quantitative and qualitative strands to

profile individual participants in response to interventions. Previous quantitative studies of CT in dementia have shown conflicting results, and recent Cochrane reviews question the quality of the evidence base [7, 8].

Meta-analyses suggest there may be a benefit to cognitive function in healthy older adults [3] and MCI [2], but the benefits are less clear for people living with dementia [2]. Given that CT is potentially time consuming, and not without adverse effects (anxiety, stress, reduced self-esteem), it is important to identify and understand the benefits and losses to the individual. In the results reported here, benefits were identified in both quantitative and qualitative measures, and integration of data did not identify a particular profile that benefited from training. The majority of participants with an increase in CRR post-training had a diagnosis of AD, and only one individual with a diagnosis of MCI. No participant with AD had a reduction in CRR, and only one participant with AD had a stable CRR. An increase or stable CRR in participants with dementia could suggest training-induced neuroplasticity, as CBFv responses have been shown to decline with poorer cognitive function [26, 27]. Whereas a decrease in CRR in healthy older adults or those with early MCI could represent restitution of evoked CBFv responses more in-line with that of younger people, indicating improved processing efficiency [28, 29].

Importantly, a number of participants who experienced training-related haemodynamic gains were also in the low adherence group, and had a number of critical barriers that may have hampered engagement with training. Thus, while participants with dementia may have the most potential to gain from training, they also have greater barriers to successful engagement. These results suggest an individualised approach should be taken, particularly assessing for and addressing potential barriers. This requirement for a personalised approach is echoed by qualitative studies previously investigating cognitive interventions in people living with stroke [30], MCI [31] and dementia [12].

Lack of insight has previously been identified as a barrier to successful cognitive rehabilitation in patients with HIV and schizophrenia associated cognitive impairment [9]. Lack of awareness of

cognitive deficits inhibits the perceived need for treatment, and is thus difficult to address [9]. However, in this study, participants with reduced insight, maintained adherence and engagement with sufficient carer support and prompting, and may not completely preclude cognitive intervention in this group.

The interplay between self-esteem, negative emotions, and performance is complex and has been a significant barrier to successful rehabilitation in previous studies of cognitive disorders [9, 12]. In particular, people living with dementia are more likely to anticipate negative emotions and side effects prior to commencing the intervention which can hamper engagement [9, 12]. In keeping with this, participants with low adherence or drop-out had greater negative emotional consequences from training (qualitative- anxiety, stress, low mood and frustration), and quantitative evidence of low mood prior to commencing the intervention. In spite of common barriers between high and low adherence groups, barriers amongst high adherers tended to be more modifiable, and participants had greater resilience and acceptance of negative side effects. Internal barriers have been identified as more obstructive than external barriers in a previous study of diet and exercise in ~18,000 community dwelling adults [32]. Thus, barriers such as lack of motivation, low mood and anxiety are potentially more significant than lack of access to technology and may be more crucial when screening for suitability to cognitive intervention. Choi et al suggest a number of techniques to overcome these barriers including: embedding motivational training (cognitive vitality training) to increase motivation and self-efficacy, motivational interviewing, and compensatory cognitive training (focussing on skills rather than deficits) [12].

Figure 2 summarises a potential screening approach for enrolling participants into cognitive intervention and the additional support mechanisms that may facilitate adherence and engagement for those with more barriers to training.

In a multi-method study of 18 healthy older adults undergoing novel gaming experiences, those with lower cognitive test scores found digital games hard to learn, and were less likely to experience

enjoyment or interest [33]. However, performance was not related to cognitive function, although those with lower MoCA scores, experienced a non-significant increase in physiological stress (cortisol levels) [33]. Furthermore, older adults preferred games perceived to be “brain training” [33]. In keeping with these results, participants in this study who had greater deficits were more likely to have low adherence or drop-out, and reported anxiety, stress and frustration more frequently. However, for the majority, enjoyment and interest was maintained in spite of this, which may be due to the stronger focus on brain training in the intervention for this study.

In ten participants living with dementia, a virtual reality forest intervention resulted in increased alertness and reduced apathy, but also heightened fear and anxiety on quantitative measures [34]. Based on the qualitative results, the authors recommend enhanced facilitation of the intervention, and found that responses were highly individualised and dependent on the severity of the deficits [34]. Similar findings were reported in a mixed-methods feasibility randomised trial of cognitive stimulation therapy for Parkinson’s disease and Lewy body dementia [35]. Common barriers amongst this group included: challenges in managing symptoms, carer strain, lack of personalisation of activities, and additional strategies needed to improve adherence [35]. Despite these barriers, participants demonstrated significant quantitative benefits (high acceptability ratings for interest, motivation and sense of achievement) [35]. In keeping with the findings reported here, benefits were evident despite difficulty maintaining adherence, suggesting greater support and tailoring are required. In particular, greater facilitator support may reduce carer strain and improve adherence, as suggested by carers for participants with AD in this study [35].

#### 4.3 Limitations and future directions

This was a relatively small sample size and therefore may not be generalisable to the wider population. The drop-out rate for the study was relatively low (three in the AD group), and thus both drop-outs and low adherence were explored as one cohort. However, this may not fully capture the profiles of participants who drop-out from cognitive intervention, and there could be additional barriers not

identified here. Selection bias could have identified participants with higher computer literacy, and those with access to technology and the internet. Therefore, fewer benefits, lower adherence and higher drop-out may be seen if this intervention was applied more widely. Only participants who completed the training were included in this analysis given that the aim was specifically to investigate the engagement and response to CT on an individual basis. This may have introduced bias into the analysis as a result.

Defining what constitutes a haemodynamic benefit is problematic at present. It remains unclear whether an increase or decrease in CRR represents beneficial physiological adaptation to training and may be disease dependent. For example, increasing CRR may be positive and constitute neuroplasticity in people living with dementia, but could be maladaptive for healthy older adults, or those with earlier cognitive deficits, where decreasing CRR may indicate improved processing efficiency consistent with a more “youthful” pattern of brain activation. Therefore, participants were grouped according to their haemodynamic profile rather than a positive, negative, or absent response to training. Future studies should investigate the utility of mixed-methods approaches to identify participants who selectively benefit from cognitive or complex multi-modal interventions to facilitate a more targeted and personalised approach favoured by participants.

## 5. Conclusions

In conclusion, this mixed method study provided new insights into the place of CT in dementia. Through integrating quantitative and qualitative analysis strands, the results showed that healthy older adults and those living with dementia or MCI, demonstrated benefits from a 12 week CT programme. There was no specific integrated participant profile that can be used to identify those who may benefit more selectively from training. Low adherence to training should not preclude the use of CT as benefits are present, with higher potential gains amongst those living with dementia.

Instead, these participants may benefit from improved screening and support to facilitate higher adherence and engagement with training.

### **Competing interests**

The authors declare that they have no competing interests.

### **Author contributions**

LB collected and analysed the data and drafted the manuscript. VJH, HS, EML, RP, TGR contributed to the design of the study, interpretation of the findings, and drafting of the manuscript. CBJ contributed guidance on the mixed methods conduct, interpretation and analysis, and drafted the manuscript. RE supervised the qualitative and mixed methods data collection, analysis, interpretation, and drafting of the manuscript.



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Participant	Quantitative		Qualitative			Integration
	Drop-out Y/N	No. hours trained	Facilitators	Barriers	Example quotes	Interpretations
Completers and high adherence (>20 hours [23]) (n=20)						
Healthy 16	N	114.1	<ul style="list-style-type: none"> <li>• Benefit/relaxation</li> <li>• Timing</li> <li>• Enjoyment and interest</li> <li>• Determination</li> <li>• Look forward to</li> <li>• Competition</li> <li>• Acceptance</li> <li>• Achievement</li> <li>• Variety</li> <li>• Challenge</li> <li>• Repetition</li> <li>• Visible progress</li> <li>• Routine</li> <li>• Reminders</li> <li>• Learning</li> <li>• Carer support</li> <li>• Completer-finisher</li> <li>• Commitment</li> </ul>	<ul style="list-style-type: none"> <li>• Distractions</li> <li>• Confusing instructions</li> <li>• Environment</li> <li>• Busy/stressed</li> <li>• Tiredness</li> <li>• Low mood</li> <li>• Frustration</li> <li>• Negative feelings linked to performance</li> <li>• Holidays/illness</li> <li>• Technology problems</li> <li>• Lack of portability</li> <li>• Forgetting sessions</li> <li>• Difficulty level</li> <li>• Dexterity/arthritis</li> <li>• Visual impairment</li> </ul>	<p><i>“even though they were frustrating I enjoyed doing them because I wanted to do them better or get a better score because I knew I could do them”– healthy (15)</i></p> <p><i>“it showed you where you hadn’t done so well and where you had so there was an element of motivation from that” healthy (1)</i></p> <p><i>“just because I don’t like a game doesn’t mean to say you should stop doing it because I’ve got to keep getting used to it haven’t I? Respond to the challenge” MCI (10)</i></p> <p><i>“each time when you get a better score than last time..... I felt as though I was achieving something” AD (13)</i></p>	<p>More likely to see the challenge, accepting that performance would be fluctuant and less effects on mood with this. Participants more determined, if they experienced setbacks more likely to spur them on than deter them. Motivated by achievement, progress and challenge. Some required reminders.</p> <p>Fewer barriers and more were external than internal.</p>
AD 6	N	70.0				
Healthy 15	N	56.7				
MCI 12	N	53.2				
Healthy 10	N	52.3				
AD 17	N	52.2				
Healthy 19	N	46.1				
Healthy 11	N	45.8				
Healthy 1	N	40.7				
Healthy 20	N	38.8				
Healthy 4	N	36.8				
MCI 7	N	35.8				
MCI 5	N	33.3				
MCI 9	N	33.2				
MCI 10	N	30.8				
Healthy 6	N	29.6				
AD 13	N	29.2				
AD 26	N	26.3				
Healthy 7	N	25.7				
AD 21	N	23.7				
Median [IQR] hours trained		37.8 [30.5-52.2]				

Drop-outs and low adherence (<20 hours) (n=8)						
MCI 3	N	19.8	<ul style="list-style-type: none"><li>• Interest and enjoyment</li><li>• Investment</li><li>• Completer-finisher</li><li>• Commitment</li><li>• Feedback</li><li>• Time (completed the exercises quickly)</li><li>• Routine</li><li>• High levels of pre-morbid education</li><li>• Carer support</li><li>• Carer step-back</li><li>• Facilitator support</li><li>• Ability to do the exercises</li><li>• Computer-literate</li><li>• Visible progress</li><li>• Repetition</li><li>• Satisfying</li><li>• Quiet environment</li></ul>	<ul style="list-style-type: none"><li>• Apathy</li><li>• Confusing or lack of instructions</li><li>• Remembering instructions</li><li>• Fluctuating performance</li><li>• Negative feelings linked with poorer performance</li><li>• Dementia symptoms</li><li>• Difficulty level</li><li>• Missed sessions, difficult to get started again</li><li>• New situations daunting</li><li>• Frustration</li><li>• Fear of failure</li><li>• Patient-carer friction</li><li>• More challenging than anticipated</li><li>• Lack of insight</li><li>• Forgetting sessions</li><li>• Illness</li><li>• Time</li><li>• Computer literacy</li><li>• Lack of portability</li><li>• Game purpose</li></ul>	<p><i>“he got irritated with me trying to get him to do them.....” Carer for AD (12)</i></p> <p><i>“I mean you used to love doing cross words and Sudoku, and you know all things like that, but now you have no interest in that have you?” Carer for AD (2)</i></p> <p><i>“when I get up in the morning some days I can get up and feel fine and I can get things done and other times I feel a bit woozy and not with it then everything’s difficult for me to do then” – AD (11)</i></p> <p><i>it made me feel stupid, it really did” AD (5)</i></p> <p><i>“I found that the- some of the puzzles it was difficult to work out how you were to proceed, whereas most of them had a little beginning session where you could learn how to do what you were going to do, some of them I couldn’t find any such learning aspects” MCI (3)</i></p>	Majority (7) of participants had a diagnosis of AD (1 MCI). The three drop-outs had high numbers of barriers, with relatively fewer facilitators. Carer support was the most common facilitator. Participants who didn’t drop-out but had low adherence experienced more enjoyment, interest, and better ability to complete the exercises with visible progress. Common barriers to both drop-out and low adherence were: difficulty interpreting the instructions, severity of the dementia and the difficulty level of the exercises. Frustration and lack of familiarity with technology were also common. Drop-outs were more likely to have apathy and lack of insight than those with low adherence. Drop-
AD 19	N	18.8				
AD 11	N	17.1				
AD 25	N	16.8				
AD 15	N	11.5				
AD 2	Y	-				
AD 5	Y	-				
AD 12	Y	-				
Median [IQR] hours trained		17.1 [16.8-18.8]				

			<ul style="list-style-type: none"> <li>• Patronising or “childish”</li> <li>• Tired/fatigue</li> <li>• Anxiety and stress</li> <li>• Speed of the exercises</li> <li>• Reliance on carer to set up and help with the training</li> <li>• Dexterity/arthritis</li> <li>• Visual impairment</li> </ul>	<i>“I think if somebody had been used to playing games on the computer they would find it much easier to do because they’d be that quicker, but he hadn’t really used the computer much for the last six months so you get out of the habit of using it...and that makes it more difficult” carer for AD (12)</i>	outs were more reliant on carer support and experienced friction with carers. Those with low adherence rates benefited from carer support, but also carers taking a step back.
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Table 1. Joint display of participants with high vs low adherence rates and drop-outs with barriers and facilitators to training arrayed against adherence.

	Quantitative			Qualitative		
Participant	CRR change	Other quantitative changes	Adherence (hours trained)	Positive experiences/outcomes	Negative experiences/outcomes	Interpretation
<b>CRR increased</b>						All participants with an increase in CRR (n=6) were from the AD or MCI group. Majority had positive experiences (enjoyment, increased awareness or brain activity, challenge), but few noticed significant effects to memory, mood or ADLs. Few negative effects, frustration was common. Change in other quantitative outcomes was variable, but the majority (n=4) had stable or improving cognition or improved or stable quality of life (n=5), or mood (n=4). These were consistent across QUAN and QUAL measures.
AD 19	+5	ACE-III 0 GDS 0 DEMQOL +4 IADL -1	Low (18.8)	<ul style="list-style-type: none"> <li>• “Makes you think about different things”</li> <li>• Focus and enjoyment</li> <li>• Visible progress in speed and ability</li> <li>• No memory decline = positive</li> </ul>	<ul style="list-style-type: none"> <li>• Frustration</li> <li>• Patient-carer strain</li> <li>• Increased awareness of deficits (negative)</li> <li>• No effects on ADLs</li> <li>• No mood effects</li> </ul>	
AD 15	+3	ACE-III -6 GDS +1 DEMQOL -1 IADL 0	Low (11.5)	<ul style="list-style-type: none"> <li>• Felt good when achieving something</li> <li>• Enjoyment</li> <li>• Visible progress</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No memory effects</li> <li>• No mood effects</li> </ul>	
AD 13	+2	ACE-III +10 GDS 0 DEMQOL +6 IADL +2	High (29.2)	<ul style="list-style-type: none"> <li>• “Made you think”, use logical thought</li> <li>• Felt challenged</li> <li>• Improved awareness</li> <li>• Possible memory effects</li> <li>• Satisfied, pleased with scores</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• Mild frustration</li> </ul>	
AD 6	+1	ACE-III +7 GDS +2 DEMQOL +1 IADL 0	High (70)	<ul style="list-style-type: none"> <li>• Active mind benefit</li> <li>• “Cheerful” when performing well, but could feel “down” when not</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• Occasional frustration (performance related)</li> <li>• No memory effects</li> </ul>	
AD 11	+1	ACE-III 0 GDS -4 DEMQOL +1 IADL -1	Low (17.1)	<ul style="list-style-type: none"> <li>• Pleased and happy with better ability</li> <li>• Good days more than bad days</li> </ul>	<ul style="list-style-type: none"> <li>• Frustrated and depressed with difficult exercises</li> <li>• No effects on ADLs</li> <li>• No memory effects</li> </ul>	

				<ul style="list-style-type: none"> <li>Felt challenged, “pushed”, had to “think a lot”</li> </ul>		None improved in ADLs, consistent across QUAN and QUAL analyses.
MCI 9	+1	ACE-III -1 GDS -2 DEMQOL +3 IADL 0	High (33.2)	<ul style="list-style-type: none"> <li>Challenge</li> <li>Stable memory= positive</li> <li>Discipline</li> <li>“Exercise mind in a different direction”</li> <li>Increased awareness of brain activity</li> <li>Marginal memory improvement “a little sharper”</li> </ul>	<ul style="list-style-type: none"> <li>No ADL effects</li> <li>Frustration with visuospatial exercises</li> </ul>	
<b>CRR neutral</b>						Majority were healthy or MCI with no change in CRR (n=8), only 1 from the AD group. Three participants felt their memory had been improved by the training, which was consistent with the QUAN (ACE-III score) data. Only one person improved on the IADL which was not identified qualitatively. One participant qualitatively identified ADL improvement but this
Healthy 1	0	ACE-III -1 GDS +1 DEMQOL +4 IADL 0	High (40.7)	<ul style="list-style-type: none"> <li>Interest</li> <li>Competition</li> <li>Enjoyment</li> <li>Benefit</li> </ul>	<ul style="list-style-type: none"> <li>No effects on ADLs</li> <li>No memory effects</li> <li>No mood effects</li> <li>Mild frustration</li> </ul>	
Healthy 4	0	ACE-III +1 GDS +1 DEMQOL 0 IADL 0	High (36.8)	<ul style="list-style-type: none"> <li>Nil positive</li> </ul>	<ul style="list-style-type: none"> <li>No effects on ADLs</li> <li>No memory effects</li> <li>Frustration</li> <li>Anxiety – abated with time</li> </ul>	
Healthy 6	0	ACE-III +1 GDS 0 DEMQOL -2 IADL 0	High (29.6)	<ul style="list-style-type: none"> <li>Active mind</li> <li>“Taught a certain routine that could improve certain things”</li> <li>Learning &amp; enjoyment</li> </ul>	<ul style="list-style-type: none"> <li>No effects on ADLs</li> <li>Unsure if memory improved</li> <li>No mood effects</li> <li>Mild frustration</li> </ul>	
Healthy 16	0	ACE-III +4 GDS 0 DEMQOL +3 IADL 0	High (114.1)	<ul style="list-style-type: none"> <li>Felt memory improved in and out of the programme but unsure by how much</li> <li>Happy and pleased with scores and progress</li> </ul>	<ul style="list-style-type: none"> <li>No effects on ADLs</li> <li>Occasional frustration</li> </ul>	

				<ul style="list-style-type: none"> <li>• Achievement</li> </ul>		<p>was not consistent with QUAN measures. Majority (n=7) had improved or stable QoL which was supported by positive QUAL experiences. Majority (n=7) had stable or improved mood on QUAN analysis, but only four reported improved mood qualitatively.</p>
Healthy 20	0	ACE-III -1 GDS 0 DEMQOL +2 IADL 0	High (38.8)	<ul style="list-style-type: none"> <li>• Positive mood related to improved scores</li> <li>• Achievement</li> <li>• “Made you think”</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No memory effects</li> </ul>	
MCI 3	0	ACE-III +4 GDS 0 DEMQOL +2 IADL -1	Low (19.8)	<ul style="list-style-type: none"> <li>• Interest &amp; enjoyment</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No memory effects</li> <li>• No mood effects</li> </ul>	
MCI 5	0	ACE-III -3 GDS -2 DEMQOL +8 IADL 0	High (33.3)	<ul style="list-style-type: none"> <li>• Challenge</li> <li>• Mood improved</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No memory effects</li> <li>• Frustration</li> </ul>	
MCI 7	0	ACE-III +5 GDS -2 DEMQOL +11 IADL 0	High (35.8)	<ul style="list-style-type: none"> <li>• Challenge &amp; achievement</li> <li>• Enjoyment</li> <li>• Concentration</li> <li>• Improved mood</li> <li>• Active mind</li> <li>• Improved organisation</li> <li>• Improved memory</li> <li>• Improved multi-tasking</li> </ul>	<ul style="list-style-type: none"> <li>• Frustration with some exercises</li> </ul>	
AD 17	0	ACE-III +2 GDS 0 DEMQOL -6 IADL +2	High (52.2)	<ul style="list-style-type: none"> <li>• Had to “think very hard”</li> <li>• Improved abilities</li> <li>• Challenging</li> <li>• Improved awareness</li> <li>• Improved memory</li> </ul>	<ul style="list-style-type: none"> <li>• Frustration</li> <li>• No effects on ADLs</li> </ul>	
<b>CRR reduced</b>						<p>All participants that had reduced CRR were healthy or MCI. Majority reported benefits (active mind, enjoyment, progress,</p>
Healthy 11	-9	ACE-III -1 GDS 0 DEMQOL 0 IADL 0	High (45.8)	<ul style="list-style-type: none"> <li>• Active mind</li> <li>• “Use your brain differently”</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLS</li> <li>• No memory effects</li> <li>• No mood effects</li> <li>• Frustration</li> </ul>	
Healthy 10	-8	ACE-III -1	High (52.3)	<ul style="list-style-type: none"> <li>• Increased awareness</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLS</li> </ul>	



		GDS -1 DEMQOL 6 IADL 0		<ul style="list-style-type: none"><li>• Visible progress</li><li>• Enjoyment</li></ul>	<ul style="list-style-type: none"><li>• No memory effects</li><li>• No mood effects</li><li>• Frustration</li></ul>	improved awareness). No participant identified improvement to ADL, consistent with QUAN data. Four participant identified effects to mood (3 positive, 1 negative), consistent with QUAN data in 2 participants. 2 participants identified improved memory which was consistent with QUAN data in one case.
Healthy 19	-5	ACE-III +1 GDS -1 DEMQOL -2 IADL 0	High (46.1)	<ul style="list-style-type: none"><li>• Enjoyment</li><li>• “Making you push yourself”</li><li>• Challenging</li><li>• Visible progress</li><li>• Pleased with good scores</li></ul>	<ul style="list-style-type: none"><li>• No effects on ADLs</li><li>• No effects on memory</li><li>• No effects on mood</li><li>• Disappointed with scores</li><li>• Some tension</li></ul>	
Healthy 7	-1	ACE-III -1 GDS 0 DEMQOL 0 IADL 0	High (25.7)	<ul style="list-style-type: none"><li>• Competitive</li><li>• Enjoyment</li></ul>	<ul style="list-style-type: none"><li>• No effects on ADLs</li><li>• No effects on memory</li><li>• Frustration and anxiety</li></ul>	
Healthy 15	-1	ACE-III 0 GDS -1 DEMQOL 4 IADL 0	High (56.7)	<ul style="list-style-type: none"><li>• Active mind</li><li>• Challenge</li><li>• Visible progress</li><li>• Enjoyment</li><li>• Positive mood related to scores</li></ul>	<ul style="list-style-type: none"><li>• No effects on ADLs</li><li>• No memory effects</li></ul>	
MCI 10	-1	ACE-III +1 GDS +1 DEMQOL -1 IADL -1	High (30.8)	<ul style="list-style-type: none"><li>• Stimulating</li><li>• Enjoyment</li><li>• Improved memory</li><li>• Improved mood</li></ul>	<ul style="list-style-type: none"><li>• No effects on ADLs</li><li>• Frustration</li></ul>	
MCI 12	-1	ACE-III -5 GDS -1 DEMQOL -7 IADL 0	High (53.2)	<ul style="list-style-type: none"><li>• Pleased with abilities</li><li>• Challenge</li><li>• Enjoyment</li><li>• Improved awareness</li><li>• Improved memory</li><li>• Improved mood</li></ul>	<ul style="list-style-type: none"><li>• No effects on ADLs</li><li>• Frustration</li></ul>	
No CRR data						

AD 21	-	ACE-III +6 GDS +1 DEMQOL +10 IADL +2	High (23.7)	<ul style="list-style-type: none"> <li>• “Gets your brain working”</li> <li>• Challenging</li> <li>• Enjoyment</li> <li>• Satisfaction</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No effects on memory (possibly worse)</li> <li>• No effects on mood</li> <li>• Frustration</li> </ul>	No effects on ADLs identified qualitatively, although one participant did improve on IADL.
AD 25	-	ACE-III +1 GDS +2 DEMQOL -9 IADL -1	Low (16.8)	<ul style="list-style-type: none"> <li>• Felt “exercised”</li> <li>• Enjoyment related to performance</li> <li>• Memory improved</li> <li>• Visible progress</li> <li>• Satisfying</li> </ul>	<ul style="list-style-type: none"> <li>• No effects on ADLs</li> <li>• No mood effects</li> <li>• Significant frustration</li> </ul>	Two participants felt memory improved, one felt it had deteriorated, and only one corroborated with the QUAN data. No effects on mood qualitatively, but worsened in all participants quantitatively. All three reported benefits to the programme.
AD 26	-	ACE-III -1 GDS +1 DEMQOL +16 IADL 0	High (26.3)	<ul style="list-style-type: none"> <li>• Generally pleased</li> <li>• “Made me think more”</li> <li>• Memory improved</li> <li>• Challenging</li> <li>• Enjoyment</li> </ul>	<ul style="list-style-type: none"> <li>• Felt “could have done better”</li> <li>• No effects on ADLs</li> <li>• No mood effects</li> <li>• Frustration</li> </ul>	

Table 2. Joint display of participants grouped by quantitative response to training (CRR change), arrayed against their individual quantitative outcomes, and qualitative experiences from training.

	Qualitative experiences	Qualitative Recommendations	Example quotes	Interpretation
<b>Participant</b>				
Healthy (4)	<ul style="list-style-type: none"> <li>• Perceptions of effectiveness influenced by pre-conceptions, commercial programme</li> <li>• Unlikely to have benefit above crosswords, jigsaws</li> <li>• No clear benefits identified qualitatively</li> <li>• Some anxiety and frustration</li> </ul>	<ul style="list-style-type: none"> <li>• Felt there are other activities more preferable i.e. walking, crosswords</li> <li>• Wouldn't choose to do CT specifically for dementia prevention</li> </ul>	<p><i>"I wouldn't have done the brain training program without the research that was behind it. I started off with the preconception that a brain training program was not terribly valid let's say. I finished it without any change of heart"</i></p> <p><i>"if you enjoy doing them, fine, are they any better than doing crosswords, are they any better than doing jigsaw, are they any better, I doubt it"</i></p>	<p>Participants with low adherence, few benefits, or drop-out tended to be older, male, with a diagnosis of AD. Mean education years was high, but the majority were on anti-dementia drugs, and had limitations to ADLs, and some evidence of low mood at baseline. Cognitive impairment was relatively mild.</p>
MCI (3)	<ul style="list-style-type: none"> <li>• Limited benefits identified qualitatively apart from interest and enjoyment</li> </ul>	<ul style="list-style-type: none"> <li>• Felt programme too short to identify benefits</li> <li>• Would prefer more/clearer instructions for the exercises</li> <li>• Would prefer more choice in the exercises and to skip those they didn't enjoy</li> </ul>	<p><i>"It's been too short I suppose, nine or ten weeks could I blame that programme on things that have happened in the last- I'm not sure that anything major has happened in those nine weeks so I can't blame the programme on anything"</i></p> <p><i>"well I found that the- some of the puzzles were, it was difficult to work out how you were to proceed, whereas most of them had a little beginning session where you could learn how to do what you were going to do, some</i></p>	<p>One healthy participant had good adherence (36.8 hours), but had few quantitative and qualitative benefits, largely due to significant preconceptions around CT effectiveness.</p> <p>Participants with low adherence or drop-out reported friction with carers, high levels of anxiety, stress, and frustrations, and more difficulty with following</p>

			<i>of them I couldn't find any such learning aspects"</i>	the instructions or understanding the purpose of the exercise. However, some still benefited from training with enjoyment, progress, achievement, and stability of cognition over the study.
AD (19)	<ul style="list-style-type: none"> <li>Participant and carer identified benefits in keeping mentally active, improving focus, stability of memory</li> <li>Did cause friction between patient and carer and lacked insight</li> <li>Increased awareness but this wasn't necessarily positive</li> <li>Enjoyed doing the training</li> </ul>	<ul style="list-style-type: none"> <li>No suggestions for improvement</li> </ul>	<p><i>"it makes you think about different things but I don't- I can't explain what it is its just I'm interested in doing what was in that" - patient</i></p> <p><i>"yeah despite that nagging it was good particularly if its, once it picked up again after we had that break but you [patient] were doing them more quickly and sometimes surprisingly quickly got through them and there's nothing wrong with having that little focus in the day as well" - carer</i></p> <p><i>"I think that for me it turned out to be more challenging than I'd expected, the difficulty day-to-day was the reminder to do it sometimes felt like nagging</i></p> <p><i>that was kind of a daily reminder of where you are when in fact sometimes you can forget where you are, it just sort of put it in your face and the other thing I found out quite quickly was it was better that I left [patient] to do all the puzzles on her own was much better than me at the start</i></p>	<p>Participants recommended commencing the programme earlier in the diagnosis, better tailoring to abilities and education, clearer instructions with more reminders, a more graduated programme from pencil and paper to computer, and more personalisation of feedback.</p>

			<i>hovering over, she got on better with them when I stepped back and she did it on her own"- carer</i>	
AD (11)	<ul style="list-style-type: none"> <li>• Struggled with some exercises and this negatively affected mood</li> <li>• Pleased with ability on other exercises</li> <li>• Enjoyed the challenge, saw benefit to mental activity</li> </ul>	<ul style="list-style-type: none"> <li>• Would like reminders of the instructions throughout the exercises</li> <li>• Instructions could be clearer</li> <li>• Speed could be slower with a more gradual increment in difficulty</li> <li>• Would have liked text-message reminders</li> </ul>	<p><i>"some days you did better and other days he'd do worse than the very first time he did it, then you got a bit down hearted"- carer</i></p> <p><i>"oh great, I thought I can do these look and then they come back and tell you I've done this better, I was a lot better with that one" - patient</i></p> <p><i>"I think it would help on some of them because some of them got a bit too quick and it's like when you're doing that memory one with the beach, the more you've answered, the faster, and the more things come down and the faster it seemed to be going"- patient</i></p>	
AD (25)	<ul style="list-style-type: none"> <li>• Saw benefit to keeping mentally active</li> <li>• Saw visible progress in the exercises and in memory</li> <li>• Enjoyed some exercises but very frustrated by others, particularly with poor/limited instructions</li> </ul>	<ul style="list-style-type: none"> <li>• Felt instructions could have been clearer</li> <li>• Would prefer more information on the purpose of the game and the transfer to daily life</li> <li>• More personalised feedback on performance</li> <li>• Missed sessions due to lack of portability</li> </ul>	<p><i>"well, the brain games exercised me and that was good, and I think that with some of the games I was doing pretty well and I improved a little bit as the time went on so that's been good"</i></p> <p><i>"I just got frustrated with those mind games that I thought the explanation that was given at the</i></p>	

			<p><i>beginning of the, of some of them, were just poorly written, very poorly written and so as a consequence it took me ages"</i></p> <p><i>"they've got to be explaining what you're supposed to be doing and a purpose other than the obvious thing of identifying sea urchins, sea animals, that's obvious what that's about but what is that actually helping? To get some feedback on my brain, I am coping, how I'm doing?"</i></p>	
AD (15)	<ul style="list-style-type: none"> <li>• Felt as though was achieving something, could see visible progress through the scores</li> <li>• Enjoyed the training</li> <li>• Main barrier was time and fitting the programme in</li> </ul>	<ul style="list-style-type: none"> <li>• More personalised feedback on performance or explanation of the scoring</li> </ul>	<p><i>"to see that I was actually achieving something, getting better at certain things than I started off I suppose that's really the ideal thing is to see an achievement isn't it? I felt it was achieving something"</i></p> <p><i>"because I've got a lot going on I've found it difficult to get the time to do it"</i></p> <p><i>"sometimes I got a five which I'm assuming was one of five got the top marks I don't know but probably to give an indication of what the marks were or where you stood with those marks"</i></p>	

AD (2)	<ul style="list-style-type: none"> <li>Negatively increased awareness of dementia</li> <li>Training caused anxiety, stress, frustration, and friction with carer</li> <li>Engagement limited by apathy, severity of dementia, and lack of insight</li> </ul>	<ul style="list-style-type: none"> <li>Speed of the exercises was too fast</li> <li>Would prefer activities not using a computer</li> <li>Greater benefits from informal reminiscence with carer</li> </ul>	<p><i>"You just couldn't pass them. Couldn't pass the exercises could you. So it made you feel a failure that you couldn't cope with the exercises."- carer</i></p> <p><i>"We try and talk about things from the past, lovely holidays, travelling the world, and people that we've met, and you know I try and get you to remember things."- carer</i></p> <p><i>"Well it isn't fine really, I mean, I recognise that in me. But I feel that there is nothing there that I want to pursue."-patient</i></p> <p><i>"Well I had to use the computer to register your answers, but they were over so quickly, you became very stressed by how quickly it moved on to the next exercise" - carer</i></p>	
AD (5)	<ul style="list-style-type: none"> <li>Training caused significant anxiety, stress, fear of failure, frustration, and friction with carer</li> <li>Engagement hampered by low pre-morbid education, difficulty of</li> </ul>	<ul style="list-style-type: none"> <li>Better tailoring of training to education, occupation, and functional levels</li> <li>Slower increment in difficulty level</li> <li>Clearer instructions</li> </ul>	<p><i>"I was getting frustrated really wasn't I, that was the problem. I shouldn't get annoyed with you but it was happening which isn't good"- carer</i></p> <p><i>"I suppose it's very hard to tailor something that isn't yours to particular people, whether a bit</i></p>	

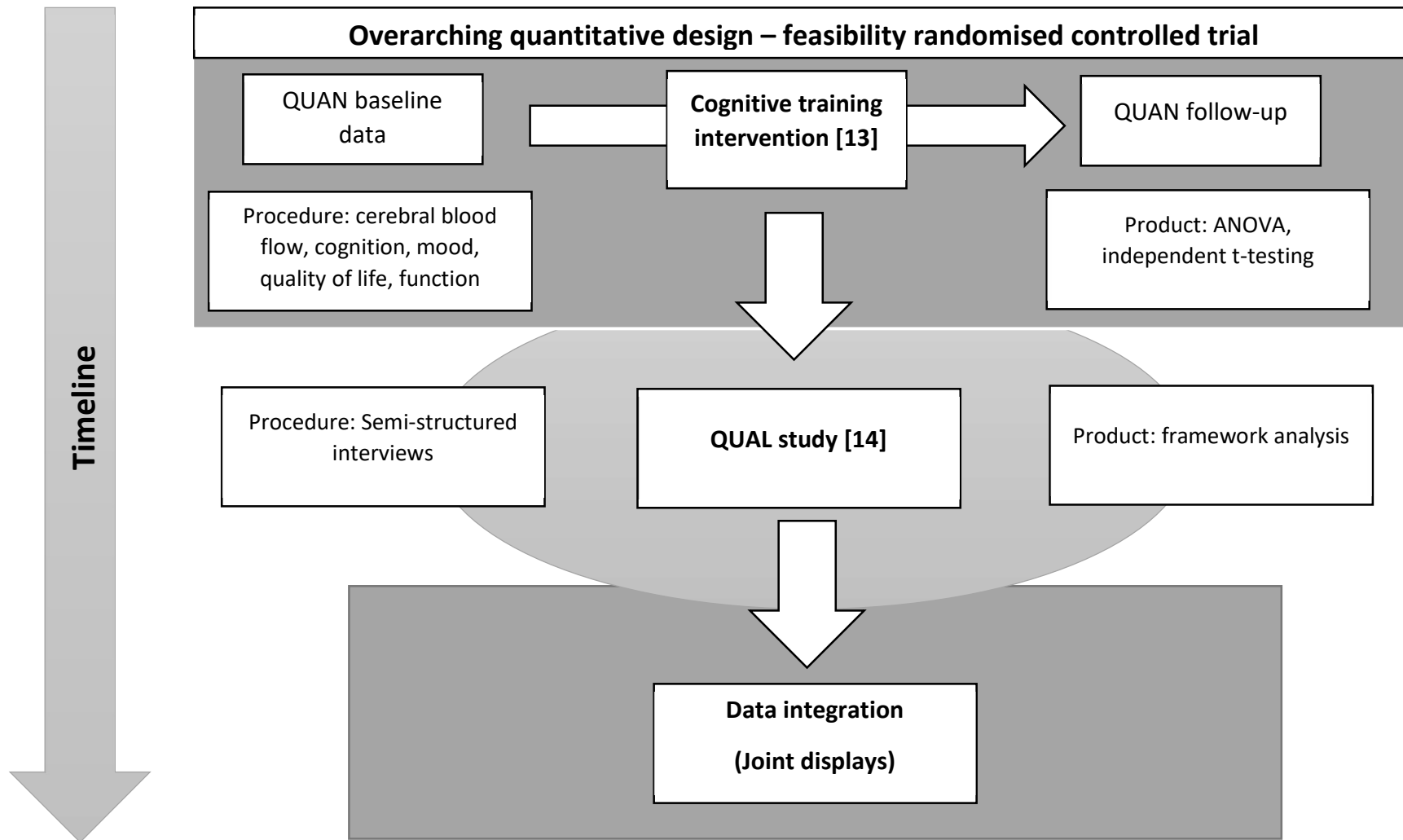
	exercises, and computer literacy		<p><i>more pre-interview or something to go a bit more depth into people's background"- carer</i></p> <p><i>"I'm not saying it should be words of one syllable but they weren't easily understandable for each game, what the premise was of that particular activity was going to do"- carer</i></p> <p><i>"because I never use one...I've never typed or text or emails I don't do anything because by the time I find the letter I've had enough"- patient</i></p>	
AD (12)	<ul style="list-style-type: none"> <li>• Training caused significant friction with carer</li> <li>• Engagement was limited by apathy, dementia severity, lack of insight</li> </ul>	<ul style="list-style-type: none"> <li>• Suggested CT earlier in the disease may have greater benefit</li> <li>• Slower increment in speed and difficulty</li> <li>• More personalisation of the exercises to current brain function</li> <li>• Facilitated sessions and paper and pen exercises may be more appropriate</li> </ul>	<p><i>"I just wonder whether if this was conducted in a room, where people got together apart from their families because I think though [patient] is really good with the kids, he gets, he tends to get, annoyed with me if I'm trying to get him to do something"- carer</i></p> <p><i>"getting somebody who its difficult at this stage to do more than one time a week say, it's difficult, the other thing was that perhaps if he had done this a year ago he might have been more ofay with doing it."- carer</i></p>	



			<p><i>"I would find it easier with paper and pen than I would be with a computer"- carer</i></p> <p><i>"you found it difficult I think you knew the answers to the questions but what you did find difficult to do was to operate the computer quickly"- carer</i></p>	
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Table 3. Joint display of participants with fewer benefits on quantitative analysis, lower adherence, or higher drop-out rates, arrayed against qualitative experiences and recommendations.

Figure 1. Schematic diagram of the Cognition and Flow study summarising the explanatory sequential mixed methods design, and stages of quantitative (QUAN) [13] and qualitative (QUAL) [14] data collection and integration.



**Figure 2. Suggested screening and adaptation to cognitive intervention for people living with dementia considering cognitive intervention.**

