Examining the Effects of Computerised Cognitive Training on Levels of Executive Function in Adults with Down syndrome: A Feasibility Study

A thesis submitted to the University of Dublin, Trinity College, for the Degree of Doctor of Philosophy

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Declaration

I hereby declare that the work contained in this thesis has not been submitted as an exercise for a degree at this or at any other University. The work described in this thesis, except where duly acknowledged, is my own. I hereby agree that the Library of Trinity College Dublin may lend or copy this thesis upon request. All mistakes and/or omissions are borne by the author.

Signed__________________________ Date: _____________________

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Abstract

Background

Down syndrome (DS) is diagnosed in approximately 1/650 – 1/1000 live births, thus making it the most common genetic cause of intellectual disability. People with DS have a life expectancy that has increased greatly in the past number of decades from 29 years in 1929 to 60 years of age and over in the present day. Adults with DS are at increased risk of developing Alzheimer's disease. By the age of 35 virtually all adults with DS have the neuropathological features of Alzheimer's disease. Unlike the progression of Alzheimer's disease in the general population, those with DS appear to present early with personality and behavioural changes associated with executive dysfunction rather than short term memory loss.

Introduction

It is clear that those with DS are at much greater risk of developing AD, and that one of the early clinical symptoms of AD is executive dysfunction. Thus training executive functions may help in extending the quality of life of people with DS. In the general population, cognitive training has shown some promising results in relation to maintaining or improving cognitive processes.

Aims and Objectives

The aim of the study is to assess the use of using cognitive training to influence levels of executive function in adults with Down syndrome. Within this, the specific objectives are (i) to examine the feasibility of conducting a cognitive training program using an iPad; (ii) To investigate whether cognitive training has a positive influence on executive function in adults with Down syndrome; (iii) To examine changes in behaviours related to executive functioning after cognitive training as perceived by family members/carers using the Behaviour Rating Inventory of Executive Functions; (iv) To investigate whether variables such as age, IQ, cognitive function, and time spent are predictive of change in scores post intervention

and (v) To investigate the relationship between cognitive reserve and executive function.

Methods

A quasi-experimental mixed factorial design with partial crossover was used involving an eight week intervention period with structured involvement in technology mediated brain training. Forty adults with Down syndrome, aged between 30 and 49 and with a mild or moderate level of intellectual disability participated in the study.

Participants were matched on age and then randomly assigned to either the intervention group or the delayed intervention group. All participants completed baseline assessments to measure IQ, cognitive function and cognitive reserve. All participants also completed baseline measures of executive function, using both neuropsychological assessments ("Cats and Dogs Stroop", "Tower of London", "Scrambled Boxes", "Spatial Reversal" and "Weigl Card Sorting Task") and a proxy rated measure of behavioural executive function (BRIEF-A).

The intervention group then began the cognitive training intervention, which was delivered on an iPad and which lasted for eight weeks. Participants were asked to complete the training for twenty minutes a day, five days a week for the duration of the eight weeks. When the intervention group completed the training, all participants again completed the executive function assessments. The delayed intervention group then completed the eight week cognitive training program. Following this, all participants completed the executive function assessments a third time.

An accessible structured questionnaire was completed each week to monitor level of enjoyment and adherence to the program, and to examine where the training was being completed and with whom.

Results

Feasibility was assessed based on parameters set out in relation to the participant, the support person and the environment. The average number

of minutes spent on the program was 930.73 (SD=848.4), a median of 711.29 and with an average of 34.7 days. Adherence to the program and levels of enjoyment were high, with 90% of participants completing the entire program and with 97% indicating a high level of acceptability. The environment in which participants completed the training did not appear to have an effect on the amount of time spent on the program.

The scores in the intervention group improved significantly, post training on the "Cats and Dogs Stroop" and "Tower of London", showing a large effect, with "Weigl Card Sorting" showing a trend towards significance. In the BRIEF-A, there was a significant improvement in scores of emotional control and in the global executive composite score with a large effect size, and with changes in initial and the metacognitive index coming close to significance. The delayed intervention group then improved significantly on all 5 neuropsychological measures of executive function post training also with large effect sizes. None of the behavioural executive function scores reached significance however emotional control and the behavioural regulation index approached significance, and again appeared to show a large effect in the delayed intervention group.

Conclusion

Based on a number of parameters to determine feasibility, from the point of view of both the person with DS and those caring for the person with DS, it was found that it was feasible to conduct such a program. The study also aimed to examine whether a cognitive training program could have an effect on levels of executive function. While, conclusions are limited due to small sample size, improvement was seen in neuropsychological assessments of executive function following cognitive training. Positive effects reflected in everyday behaviours were not as promising. These findings need further investigation with a larger sample size.

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Abbreviations

AAIDD	American Association on Intellectual and Development Disabilities
ACTIVE	Advanced Cognitive Training for Independent and Vital Elderly
AD	Alzheimer's disease
ADHD	Attention Deficit Hyperactivity Disorder
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
APOE	Apolipoprotein E
APP	Amyloid Precursor Protein
BEADS	Brain Exercises for Adults with Down syndrome
BPSD	Behavioural and Psychological Symptoms of Dementia
BRI	Behaviour Regulation Index
BRIEF-A	Behavioural Rating Inventory of Executive Function – Adult version
CEFA	Cambridge Executive Function Assessment
CR	Cognitive Reserve
CRIq	Cognitive Reserve Index Questionnaire
CRUNCH	Compensation Related Utilization of Neural Circuits Hypothesis
DLD	Dementia Questionnaire for People with Learning Disabilities
DS	Down syndrome
DSDS	Dementia Scale for Down syndrome
DSM-V	Diagnostic and Statistical Manual of Mental Disorders
DSMSE	Down syndrome Mental Status Examination
EF	Executive function
fMRI	Functional Magnetic Resonance Imaging
fNRS	functional Near Red Spectroscopy
GEC	Global Executive Composite
HAROLD	Hemispheric Asymmetry Reduction in Older Adults
HSE	Health Service Executive
IADL	Instrumental Activities of Daily Living
ICD-10	International Classification of Diseases-10
ID	Intellectual Disability
IDS-TILDA	Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing
IQ	Intellectual Quotient
MCI	Mild Cognitive Impairment
MeSH	Medical Subject Headings
MI	Meta Cognitive Index
ml	Myo-inositol
MMSE	Mini Mental State Examination
MRC	Medical Research Council
MRI	Magnetic Resonance Imaging
NETSCC	NIHR Evaluation, Trials and Studies Co-ordinating Centre
NIDD	National Intellectual Disability Database
NIID	National Institute of Intellectual Disability
NIHR	National Institute for Health Research
PET	Positron Emission Tomography
PFC	Pre Frontal Cortex
SD	Standard Deviation
SIB	Severe Impairment Battery
SPSS	Statistical Program for the Social Sciences
TCD	Trinity College Dublin
TSI	Test for Severe Impairment
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION AND CONTEXT

1 Introduction

1.1 Introduction

This chapter will introduce the thesis, both in terms of subject matter and also the structure and layout. As outlined in the aims and objectives below, the focus of the study is twofold; to examine the feasibility of conducting a cognitive training program with adults with Down syndrome (DS) and to examine the effects that cognitive training has on levels of executive function (EF) with this population. Specific characteristics of DS will then be discussed, with particular focus on dementia in people with DS. While this study cannot measure the impact of cognitive training on dementia, it is an issue that is key to the background of the study. Following on from this discussion, the rationale for the study will be presented. The definitions and terms used in the study will be delineated. Finally the structure and layout of the thesis will be outlined.

1.2 Research Aims and Objectives

The aim of the study is to assess the use of using cognitive training to influence levels of executive function in adults with Down syndrome.

The objectives of the study are set out as follows:

Objectives

1. To test the feasibility of using cognitive training with adults with Down syndrome by exploring ability to use the games, adherence, level of enjoyment and delivery parameters.

2. To investigate whether cognitive training has an influence on executive function in adults with Down syndrome.

3. To investigate whether cognitive training has an influence on behaviours related to executive functioning as perceived by family

members/carers using the Behaviour Rating Inventory of Executive Function.

4. To investigate the relationship between cognitive reserve and executive function.

5. To investigate whether variables such as age, IQ, cognitive function, and time spent are predictive of change in level of executive function post intervention.

1.3 Definition of Terms

This section defines some of the principle terms used in the study. These concepts are explored further in the literature review.

1.3.1 Down syndrome and Intellectual Disability

Intellectual disability is defined by the American Association of Intellectual and Developmental Disabilities (AAIDD, 2013) as a disability that is characterised by significant limitation in both intellectual functioning and adaptive behaviour, which covers many everyday behaviour and practical skills and where this disability originates before the age of 18. The AAIDD included as an additional consideration that assessments must assume that limitations coexist with strengths, and that with appropriate supports, an individuals' level of life functioning can improve.

As classified by the World Health Organisation (WHO), an IQ in the range of 50-69 indicates a mild level of ID, IQ range of 35-49 indicates a moderate level of ID, with 20-34 severe and an IQ of less than 20 indicating a profound level of ID.

Down syndrome is a chromosomal anomaly caused by an error in cell division that results in the presence of an additional third chromosome 21 or "trisomy 21". This extra genetic material results in the physical and learning characteristics of Down syndrome. Down syndrome is one of the most common known causes of intellectual disability (www.downsyndrome.ie).

1.3.2 Executive function

"An umbrella term that encompasses many different abilities that are mediated by the prefrontal areas of the lobes. These abilities include, but are not limited to, planning, working memory, attention, inhibition, self-monitoring, self-regulation and initiation" (Goldstein and Naglieri, 2014, p.32).

Issues around the definition of EF will be further discussed in the literature review.

1.3.3 Cognitive training

"Cognitive training involves guided practice on a set of tasks that aim to address specific aspects of cognition, such as memory, language, attention or executive function" (Clare, 2003, p.76).

1.3.4 Cognitive reserve

"Cognitive reserve postulates that individual differences in the cognitive processes or neural networks underlying task performances allow some people to cope better than others with brain damage" (Stern, 2009, p.2015).

1.3.5 Feasibility study

The definition of feasibility study as outlined by the National Institute of Health Research (2012) is a

"piece(s) of research done before a main study in order to answer the question 'Can this study be done?' ." (NETSCC, 2012).

A feasibility study may be indicated for a number of reasons, one being if the target population requires unique consideration which has not been examined in previous research (Bowen et al., 2009), as is the case with the current study.

1.4 Background to the Study

This section gives background information on intellectual disability and intellectual disability services in Ireland to contextualise the study.

1.4.1 Intellectual disability in Ireland

The national intellectual disability database (NIDD) in Ireland provides information on the current health services that are used or needed by people with an intellectual disability (ID). There were 28,108 people registered on the NIDD in December 2015, which represents a prevalence rate of 6.13 per 1,000 population. (Doyle and Carew, 2016). It is estimated that there are approximately 7,000 people with Ireland with Down syndrome (Down syndrome Ireland, 2013).

The percentage of people with ID over the age of 35 with a moderate, severe or profound level of ID has risen from 28.5% in 1974 when the database began to 48.7% in 2015 (Doyle and Carew, 2016). These data reflect the increase in life expectancy that is seen in people with ID across all aetiologies. Sixty-nine percent of people with ID lived at home with family in 2015 (Doyle and Carew, 2016).

The Intellectual Disability Supplement to the Irish Longitudinal Study on Ageing (IDS-TILDA) is a large scale nationally representative study of people aged 40 years and over with an intellectual disability in Ireland and is carried out in tandem with a national study on ageing in the general population. In a report published: Advancing Years: Different Challenges: Wave 2 IDS-TILDA, differences were noted between ageing individuals with ID compared to the general population in relation to family connections, and highlighted difficulties in maintaining family contact for older adults with ID. The importance of relationships with paid staff was also highlighted (McCarron et al., 2014).

Overall, 98.9% of people registered on the NIDD availed of at least one day program (Doyle and Carew, 2016). The Health Service Executive (HSE) published a report 'New Directions' in 2012 which aimed to modernise day service programs in line with person centeredness, accessibility and quality and a focus on personal outcomes (Health Service Executive, 2012). It was reported that the majority (95%) of people indicated that they were either very satisfied or satisfied with the day service (McCarron et al., 2014a). It was reported that the most frequent activities in day services were arts and crafts and music, but that 18.1% of individuals rarely or never chose their activities (McCarron et al., 2014a). The majority (82.7%) were not involved in further education and of those who were not yet involved, but who wished to complete further education, the most preferred courses were reading/writing and computers (McCarron et al., 2014a). At the time of the report, it was found that 35.6% had access to a computer but just 28.3% had access to the internet (McCarron et al., 2014a).

A number of differences were also reported in relation to health for people with ID compared to the general population. It was found that multimorbidity was high at 71%, and that the younger individuals in the sample (40-49 years) were comparable to the older age group (+70 years) in the general population (McCarron et al., 2013).

Results related specifically to those with DS found that mental health problems were almost 50% lower for individuals with DS than was reported for the non-DS population with ID (McCarron et al., 2014). In the first Wave of IDS-TILDA dementia in people with DS was at 15.8% and this increased to 29.9% in Wave 2 (McCarron et al., 2014).

The issue of dementia in people with DS and how it relates to the study will be discussed in the following section.

1.5 Study Rationale

As noted, the aim of this study is to examine the feasibility of cognitive training with adults with DS and to examine the effects that the training has on levels of executive function. It was not viable for this study to examine effects of training on dementia, as longitudinal follow up was not possible. The issue of dementia is however interrelated; this population is at high risk of developing dementia, executive dysfunction presents as early symptoms of Alzheimer's disease (AD) (Ball et al., 2008) and cognitive training has previously shown some positive effects on executive function in the general population (Kelly et al., 2014). Thus, while not directly measureable, it is important to understand the issue of dementia in this population, its neuropathology, prevalence, presentation and diagnosis. These are discussed below.

1.5.1 Down syndrome and Dementia

A clear link between DS and Alzheimer's disease has long been established in the literature, in terms of neuropathology, histology and clinically, (Prasher, 1995) with difficulties in timely diagnosis recognised as a challenge in the field (Tyrrell et al., 2001). People with Down syndrome have a life expectancy that has increased greatly in the past number of decades from 29 years in 1929 to 45 years in 1989 (Baird and Sadovnick, 1988), and this increase has continued to 60 years of age and over (Bittles and Glasson, 2004).

Brain development in people with DS appears normal at birth, however continues to develop abnormally (Pennington et al., 2003). By the age of 35 virtually all adults with DS have the neuropathological features of Alzheimer's disease (AD) (Holland and Oliver, 1995). Typically the brain is microcephalic, with greater reductions in the hippocampus, prefrontal cortex and cerebellum (Pennington et al., 2003). Structure specific reduction in the volume of white matter in the brain has also been noted (Weis et al., 1991). There is also evidence of deficits in functional connectivity, both within and between regions of the brain (Nadel, 1999). This is particularly evident between the frontal and parietal lobes – specifically in the inferior frontal gyrus and the thalamus (Wisniewski et al., 1985a). The thalamus relays information selectively to different parts of the cerebral cortex and this this thalamic deficit suggests responsibility for the problem with directed attention seen in individuals with DS.

1.5.2 Prevalence, Age of Onset and Duration of Dementia

Down syndrome is diagnosed in approximately 1/650 – 1/1000 live births (Bittles et al., 2007), thus making it the most common genetic cause of intellectual disability. As mentioned previously, life expectancy for people with DS has continued to grow, with estimates that 44% of people with DS will reach the age of 60 and 14% will reach 68 (Baird and Sadovnick, 1988). A number of population-based studies have reported on the prevalence of dementia (Coppus et al., 2006, Holland et al., 1998, Strydom et al., 2007, Strydom et al., 2010, Tyrrell et al., 2001, Sekijima et al., 1998, Cooper, 1997), with the consensual findings that AD is far more prevalent in individuals with DS than those with ID from other aetiologies or those in the general population.

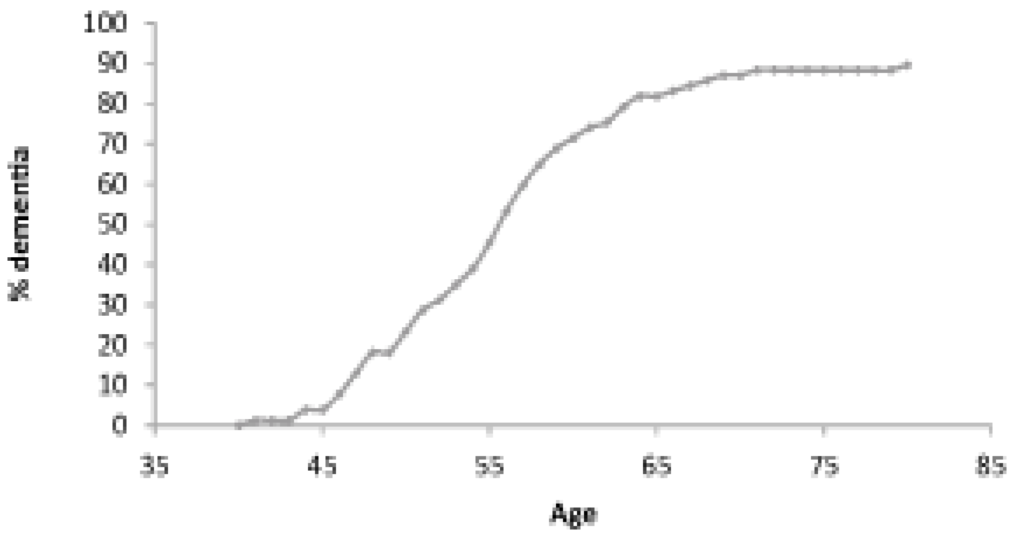
Strydom (2010) compiled a review of previous studies and found that prevalence of AD, in chronological order, was 21.6% (Cooper et al 1997), 15.1% (Sekijima et al (1998), 24% (Holland et al 1998), 13.3% (Tyrell et al, 2001), 16.8% (Coppus et al 2006), 13.1% (Strydom et al 2007). The unadjusted average prevalence rate of AD in people with DS is estimated at 15% (Nieuwenhuis-Mark, 2009).

A number of studies have looked at age specific prevalence and found that there is a sharp increase in AD from age 40-60. (See Table 1.1 below for results from two studies).

Table 1-1: Age specific prevalence of dementia

	Holland et al., 1998 %	Tyrell et al., 2001* %
30-39 *under 40	3.4	1.4
40-49	10.3	5.7
50-59	40	30.4

Coppus et al., (2006) reported that, from the age of 45, dementia prevalence doubled with each 5 year interval, up to the age of 60, after which prevalence declined, which would most likely be explained by higher mortality rates in this age group, as there was no decrease in incidence of dementia over the age of 60. Figure 1.1 below shows the cumulative risk of developing dementia by age from a 14 year longitudinal study (McCarron et al., 2014b), where a risk of 20% was found at age 50, 45% at age 55 and 80% risk of dementia at age 65.



(McCarron et al., 2014b)

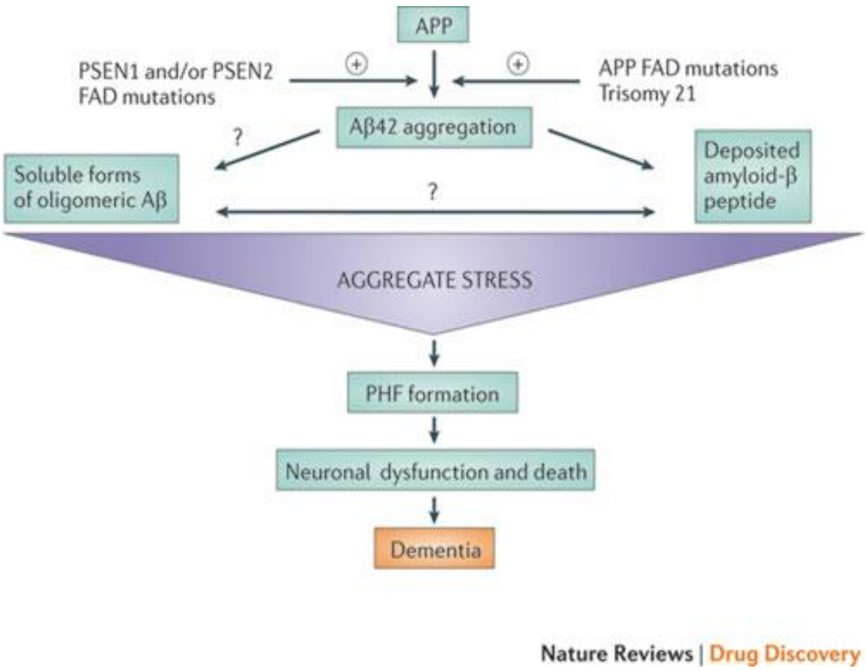
Figure 1-1: Cumulative risk of developing dementia by age

In this study, it was reported that the mean age of onset for people with DS was 55.4 years with a median survival of 7 years (McCarron et al., 2014b). This was slightly higher than had been reported in previous studies; 51.7 years (Prasher and Kirshnan, 1993).

1.5.3 Neuropathology of Down syndrome and Dementia

In individuals with DS, Alzheimer's disease has been reported to occur in 15-40% of people over the age of 35 (Prasher and Kirshnan, 1993), with neuronal loss, neurofibrillary tangles and neuritic plaques (Lassmann et al., 1995, Mann, 1991). Numerous studies have shown that by age 40, practically all individuals with DS will show neuropathological and neuro-imaging features of AD (Roizen and Patterson, 2003, Schupf et al., 2010a, Royston et al., 1996, Lamar et al., 2011) and that age related atrophy in DS is similar to the atrophy observed in early stages of AD in those without DS (Teipel and Hampel, 2006). The amyloid cascade hypothesis (Hardy and Higgins, 1992, Selkoe, 1991) (see figure 1.2 below) suggests that the deposition of Amyloid ß plays a critical role in the development of AD pathology, with Aß40 and Aß42 being the two major species generated by the amyloid precursor protein (APP) (Schupf et al., 2010b). Plasma levels of Aß42 and Aß40 are found to be higher at all ages in individuals with DS compared to age matched peers (Prasher et al., 2010) The increased levels of Aß, along with the neuropathological attributes found in people with DS have been attributed to the triplication and thus overexpression of the gene for APP, as this gene is located on chromosome 21 (Rumble et al., 1989). This results in a dementia syndrome in later life, which is phenotypically similar to AD (Krasuski et al., 2002). Despite this phenotypic similarity, some differences have been noticed in the pathological processes for dementia in DS as compared to AD, for instance, the long prodromal period for dementia in DS (Wisniewski et al., 1985b). Given that not all people with DS develop clinical symptoms of the disease, the increase in amyloid expression cannot account for the high risk of developing AD (Holland, 2000).

Some neuroanatomical differences have also been noted, including cortical thickness; cortical thickness is relatively stable with low biological variation, with AD the only condition so far reported that leads to significant thinning (Karlsen and Pakkenberg, 2011). In those with DS, however, cortical thickness remains relatively normal, despite the AD related neuropathology (Karlsen and Pakkenberg, 2011).



(Karran et al., 2011)

Figure 1-2: The Amyloid Cascade Hypothesis

While the APP gene is most studied, other genes found on chromosome 21 may also play a role in dementia (Lamar et al., 2011, Berry et al., 1995). Indeed, according to the European Bioinformatics Institute, there are believed to be 635 genes that are triplicated in DS, and some of these may also be expected to play a role in the AD phenotype (Hartley et al., 2015). Another compound located on this chromosome, and which has been known to affect neuronal osmolarity, signal transduction, cell survival and amyloid deposition is known as Myo-inositol (ml) (Mclaurin et al., 1998). As a result of these processes, an elevation in ml may directly affect neuronal dysfunction and death (Lamar et al., 2011). It has been noted in previous research that individuals with DS have increased levels of ml in the parietal and hippocampal regions compared to individuals without DS (Beacher et al., 2005). As a result, it could be that increased levels of mI may help to explain both some of the intellectual disability and the increased risk of dementia found in those with DS. It was suggested by Lamar et al (2011), that mI could be seen as likely to combine with the other known risk factors (APP gene and hippocampal atrophy) to act as a synergistic mechanism, rather than it increasing the risk for dementia independently.

While the full extent of the role of apolipoprotein E (ApoE) genotype is not fully understood, it is clear that it plays an important role, both as a risk factor (ApoE4) and as a modulator (ApoE2) of the age of onset of AD (Royston et al., 1996, Prasher and Haque, 2000, Deb et al., 2000).

Alternative explanations for the neuropathology of AD in people with DS have focused on the tau protein, which may help to explain neuronal death (Holland, 1994) and suggest that individuals with AD can be identified from control based on the amount of insoluble tau protein and phosphorylated tau species (Mukaetova-Ladinska et al., 1993). Changes in tau pathology have been shown to begin in the outer layer of the hippocampus, followed by neurofibrillary tangles in the hippocampal CA1 region, and neuronal loss in the entorhinal cortex (Head et al., 2003). It has been noted that the observed changes in neurofibrillary tangles appear to be similar for those with DS and AD, but with a higher density in those with DS (Head et al., 2016).

1.5.4 Diagnosis and Presentation of Dementia

1.5.4.1 Diagnosis

A number of challenges have been noted in diagnosing dementia within this population. While it is clear that the neuropathological symptoms of AD may be present in virtually all individuals with DS, a number of clinical studies have shown that not all individuals will present with clinical manifestations of dementia (Tyrell et al., 2001). Some theories have been presented to explain the difference between the time when neuropathological features appear and when clinical dementia is present. One theory suggests that people with DS may be protected from the clinical onset of dementia due to their brain anatomy. It was suggested by Tyrrell et al. (2001), that it could simply be due to the fact that clinical dementia can remain undetected in some cases due to difficulties in diagnosis within the DS population. This may be due to the pre-existing intellectual disability (Aylward et al., 1997) and to the fact that individuals do not reach the same cognitive ability as individuals without DS, thus decline specifically due to dementia may be more difficult to measure (Rowe et al., 2006) . Without a reliable longitudinal baseline level of functioning, scores on cognitive tests carry little significance.

In the general population it has been stated that

"The diagnosis of dementia remains clinically integrative based on history, physical examination and brief cognitive testing" (Feldman et al., 2008, pg. 285).

While this is true also for those with DS, difficulties in communication, lack of baseline measurements, difficulties in using standardised tests and high staff turnover present unique challenges in the diagnostic process (Mccallion and McCarron, 2004). In order to overcome these challenges, a model of best practice was developed for the diagnosis of people with ID (Burt and Alyward, 2000). This included: 1) a baseline assessment of people with ID >35 and an annual follow up assessment; 2) a comprehensive diagnostic workup if a decline is noted and 3) person centred approach to care including specialist staff training, standardised assessments, and further research (Burt and Aylward, 2000).

Although there are no guidelines in the International Classification of Diseases (ICD-10) (World Health Organization, 2004) or the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (American Psychiatric Association, 2013)for diagnosing dementia in people with DS or any other ID (O'caoimh et al., 2013), the same criteria can be used for people with DS as are used in the general population, as long as it is understood that any observed decline is relative to baseline functioning levels, rather than impairment to ‘normal’ functioning (Ball et al., 2004). There is no consensus as to which classification system is best suited, with some clinicians preferring the ICD-10 with others using the DSM-V, however a recent study has suggested that the DSM-V is more suited to this population (Strydom et al., 2007).

A number of assessments have been found to be useful and reliable in aiding the diagnostic process within this population, including Dementia Questionnaire for People with Learning Disabilities (DLD)(Evenhuis et al., 2007), the Dementia Scale for Down Syndrome (DSDS) (Gedye, 1995), Down syndrome Mental Status Examination (DSMSE) (Haxby, 1989), the Test for Severe Impairment (TSI) (Albert and Cohen, 1992), and the CAMDEX-DS (Ball et al., 2006a). The DSMSE was found to be the least sensitive instrument, and although designed for people with DS, may be more suited to those with less severe ID (McCarron et al., 2014b). In the same study, it was also noted that the DLD appeared to be the most sensitive instrument, with a progressive decline in functioning evident prior to a diagnosis of dementia.

1.5.4.2 Presentation of Dementia

While it has been established that neuropathological changes similar to AD occur for adults with DS, as mentioned in diagnostic issues, not everyone will develop clinical AD. With this in mind, it is imperative to understand the presentation and progression of dementia, so that a diagnosis of AD is not given, when in fact the true cause is manageable or reversible (O'caoimh et al., 2013). Similar to challenges faced with diagnosis, the discussion on the presentation of dementia in this population is made difficult, as the pre-existing level of intellectual disability means that presentation can vary largely between people (Strydom et al., 2010)

The presentation of dementia in people with DS is believed to be atypical (Smith, 2001) with many individuals presenting with neurological symptoms such as seizures and incontinence, which are more typically observed in advanced stages of dementia in the general population (Strydom et al., 2010). There are a number of similar symptoms such as memory loss (Cosgrave et al., 2000) confusion, deterioration in speech, change in behaviour or personality that are noticed, however unlike the progression of AD in the general population, those with DS appear to present early with personality and behavioural changes associated with executive dysfunction rather than short term memory loss (Ball et al., 2006b). The fact that behavioural changes predominate further complicate the diagnosis process, as these could be misdiagnosed as new onset behavioural disorder or depression (O'caoimh et al., 2013). Holland et al., (1998) reported that carers retrospectively reported that behavioural changes such as apathy, stubbornness, withdrawal were the earliest changes noticed prior to a clinical diagnosis. The behavioural changes seen have been described by Ball et al., (2006) as being more typical of dementia of the frontal type, and may be seen as preclinical AD, which occurs before the continued progression to clinical AD. The deterioration of activities of daily living (ADL) were noted as trigger symptoms also in 48%, with deterioration first noted in personal hygiene and continuing to spatial disorientation (Cosgrave et al., 2000). Behavioural and Psychological Symptoms of Dementia (BPSD) defined as 'heterogeneous range of psychological reactions, psychiatric symptoms and behaviours resulting from the presence of dementia' (Finkel, 2001) have been studied intensively over the past 2 decades in the general population, using scales such as the Behavioural Pathology in AD Rating Scale (BEHAVE-AD) (Reisberg et al.) or the Neuropsychiatric Inventory (Cummings et al., 1994). However, despite the increased prevalence of psychological and behavioural symptoms of dementia in this population, these scales have not been developed, adapted or validated for people with AD and DS (Dekker et al., 2015).

There are apparent health comorbidities associated with AD in those with DS compared to those without AD, including hearing and vision impairment, immobility and most significantly – epilepsy, which was reported in 55% of those with DS and AD compared to 11.4% of those with DS without AD (McCarron et al., 2014b).

1.6 Layout of the Thesis

Chapter 1: Introduction and Context: This chapter introduces the thesis and outlines the study aim and objectives. It also presents the rationale behind the study. The definitions used throughout the thesis are offered and finally it lays out the structure of the thesis.

Chapter 2: Literature review: This chapter reviews the relevant literature on the main study topics; it explores executive function including issues around definition and measurements, the theory of cognitive reserve is discussed and how it relates to the study. Finally the evidence for and against cognitive training is discussed.

Chapter 3: Methodology: This chapter details the methodological process of the study including the aims and objectives, with details of the feasibility parameters, the study design, ethical issues, the sample, the development of the protocol and the measures used and will also outline the intervention process and procedure.

Chapter 4: Feasibility of Cognitive Training: This chapter reports the findings of the study in relation to the first objective – the feasibility of conducting a cognitive training study. It begins with a description of the sample and the baseline scores of all assessments, including IQ, cognitive function and cognitive reserve. It continues to report on the feasibility of training as related to the parameters of feasibility already set out.

Chapter 5: The effects of cognitive training on levels of executive function: This chapter reports on the changes observed in levels of executive function as measured by the five neuropsychological assessments and by the proxy rated measure of behaviours of executive function; BRIEF-A. It reports on the changes within participants' scores post cognitive training compared to pre training. These results also indicate the differences between the intervention and delayed intervention group when the intervention group has completed the training but the delayed intervention group has not, and the interaction effect seen between groups (treatment/delayed intervention group) and time (pre/post intervention).

Chapter 6: Discussion: This chapter discusses the findings from chapters 4 and 5 and contextualises these findings.

Chapter 7: Conclusion and Recommendations: This chapter synthesises all findings from the study. It also presents limitations of the study and offers recommendations for future research, policy and practice.

1.7 Summary

This chapter has presented the aim and objectives of the study, has given a definition of the terms used and has outlined the background and rationale of the study. Finally the structure of the thesis was outlined with the main components of each chapter listed.

The Medical Research Council (2012) published guidelines in relation to the development and evaluation of complex interventions. These guidelines informed the development of the study. A complex intervention is described as an intervention that has a number of interacting components, number and variability of outcomes and has a degree of flexibility in the delivery of the intervention (Craig, 2008). The guidelines suggest that best practice is to develop the intervention using the best available evidence and theory. The following chapter will address this critical issues through a review of relevant literature of all components related to the study.

The outline of the thesis will continue to follow the MRC guidelines, where the methodology will detail the development of the intervention, from pilot testing to implementation. Assessing the feasibility of a study is recommended by the MRC followed by exploratory analysis. Feasibility is detailed in Chapter 4, with exploratory analysis reported in Chapter 5.

CHAPTER 2

LITERATURE REVIEW

2 Literature Review

2.1 Introduction

This study aims to examine the impact of cognitive training on levels of executive function (EF) in those with Down syndrome (DS). Thus a broad literature search was necessary to understand the role of EF, and how EF may differ in those with DS compared to the general population. The theory of cognitive reserve (CR) is also explored as this is integral to the understanding of protective factors for Alzheimer's disease (Stern, 2009), though to date, there has been little research on the idea of cognitive reserve specifically in relation to those with DS. Finally, there has been much debate over the past decade on the benefits of cognitive training (Kelly et al., 2014), both in the general population and to a lesser extent those with an intellectual disability, and thus it was necessary in the literature review to address this debate and to discuss its impact on the current study.

In order to successfully complete the study, a number of issues needed to be addressed. It was necessary to understand the difficulties in measuring both EF and CR, and to identify the most suitable measures for both constructs for this population It was necessary also to identify the most suitable cognitive training program to use in the intervention. The literature review will explore each if these concepts in depth where each concept will be introduced separately, with a final summary that will consider how they interrelate in the current study.

2.2 Search Strategy

It was necessary to cover a number of disparate topics in order to gain an understanding of the many facets that could lead to an improvement in executive functioning following a cognitive training intervention, and to understand why this improvement may be relevant. As a result, a systematic review was not feasible, as there was no one overall cohesive subject to be explored. Rather, a series of discrete systematic searches were carried out on the following subjects; Down syndrome, executive function, cognitive reserve and cognitive training, with combinations of these search terms also employed, where appropriate.

A detailed search strategy was developed, with PubMed, CINAHL, PsycInfo and EMBASE databases used to conduct the search. The search terms used were adapted accordingly for each database, no time period restrictions were placed on the searches, and searches were for English language text from established peer reviewed journals. Search updates were created to notify the researcher of newly published or indexed articles for the search terms. Further manual searches were carried out after scrutinising the reference lists of the articles identified and including reference lists from seminal work in order to identify any studies not found by the electronic search.

Search terms used were Down syndrome, Alzheimer's disease, Executive Functions, Cognitive Training and Cognitive Reserve. Alternative terms were used for each word, using the OR function, in order to capture as many articles as possible, as well as title and abstract searches. MeSH terms were used in PubMed and terms were exploded in CINAHL. See Table 2.1 below for alternative search terms and MeSH terms used. These concepts were also combined using the AND function. Elements of grey literature and personal communication with experts in the field were also included.

Table 2-1: Terms included in Search Strategy

Down syndrome OR Down's syndrome OR Downs syndrome OR Trisomy 21
Alzheimer's disease OR Alzheimer's OR Alzheimers OR Alzheimer OR Dementias
Brain training OR Brain Games OR Cognitive Remediation OR Brain remediation OR Cognitive Intervention OR Cognitive Rehabilitation OR Cognitive Games OR Mental exercise OR Brain Exercise OR Cognitive exercise OR Mental exercise OR Brain fitness OR Cognitive fitness OR Mental fitness
Executive functions OR Executive functioning OR Cognitive control OR Supervisory Attentional System OR Executive system OR Central executive system OR executive control OR executive processes OR cognitive control OR cognition
Cognitive Reserve OR Brain Reserve OR Neural Reserve

Based upon the review of articles, the following section will discuss executive function, including a brief overview of the history, neuropathology and definition, and will specifically examine executive function in adults with DS and how this differs from the general population.

2.3 Executive Function

2.3.1 Introduction to Executive Function

Executive Functions (EF) represent one of a number of central neurocognitive domains. In any given activity of daily living, a number of both higher level and lower lever processes can come into play, for example, in going to the shop, there are both overt behaviour components such as making a list, getting money together and covert behaviours such as engaging long and short term memory to visualise the route to the shop, planning the budget, initiating the activity, behaving appropriately in the shop. These represent a range of cognitive abilities that fall under executive functions (Alvarez and Emory, 2006).

Executive Functioning has been described as a multifaceted neuropsychological construct which consists of a set of higher order processes that allow us to engage in purposeful, goal directed and future orientated behaviour (Baddeley, 1996). Humans have the most evolved executive function of all species, allowing us to use not only pre practised, often used and over learned responses, but allows us to consider our options and select a specific response based on previous acquired knowledge and situational context (Suchy, 2009). It is believed that there has been significant growth in the prefrontal cortex in humans, as well as neural reorganisation and rewiring compared to other primates (Semendeferi et al., 2001).

EF has been used as an umbrella term for a number of cognitive processes, including planning, attention, set shifting, working memory, inhibition, initiation, self-regulation (Goldstein et al., 2014). The importance of a well-functioning executive system is not disputed and it is understood that these processes are essential in regulating human cognition. Despite this, a clear understanding of the process has yet to be established. In the mid-70s a model of working memory was proposed (Baddeley and Hitch, 1974) which discussed the importance of the central executive, however by the mid-80s Baddeley described how the lack of development "had become an embarrassment to the model" (Baddeley and Hitch, 1974, p.6) and an attempt was made to address this (Baddeley, 1996). While the theory was developed, with many advances in specific domains or processes, it was thought in 1996 that the field of knowledge explaining how cognitive processes are controlled and coordinated was "an embarrassing zone of almost total ignorance" p.96 (Monsell, 1996). A brief outline of the history and development of executive function is presented in Table 2.2.

Table 2-2: Brief History of Executive Function

(Adapted from Goldstein et al., (2013), (Suchy, 2009) and (Stuss and Alexander, 2000)	
1835	First description of executive dysfunction
1840	Phineas Gage – first well known case of executive dysfunction Changes in personality noticed associated with damage to prefrontal cortex
1953	Donald Broadbent described differences between automatic and controlled processes
1960s	Alexander Luria examined the relationship between frontal lobe injuries and emotional and behavioural dyscontrol – using the term frontal lobe syndrome
1974	Baddeley proposed theory of Working Memory stating there must be a component to manipulate short term memory, which he termed the 'Central Executive'
1975	Michael Possner coined the term 'Executive Control' in a book chapter 'Attention and Cognitive Control'
1988	Shallice hypothesises that attention must be regulated by a supervisory system that can override automatic response in favour of plans and intention
1990s	Consensus that the processes occur in the Pre Frontal Cortex
1996	Baddeley, Sala Robbins – Central Executive Unified System – A homunculus
1997	Fuster – Cross Temporal Model Interference control, planning and working memory Organising Behaviour most important
2001	Miller and Cohen – Top down processing system in which sensory and motor processes interact for goal directed behaviour
2002	Shallice – Supervisory Attentional System
2009	Banich – Dorsolateral Prefrontal Cortex (DLPFC) activates first with top down processing to activate brain regions necessary for the appropriate action.
2011	Barkley (2011) Extended Phenotype
2013	Operational definition proposed by McCloskey and Goldstein

2.3.1.1 Frontal Lobes and Executive Functioning

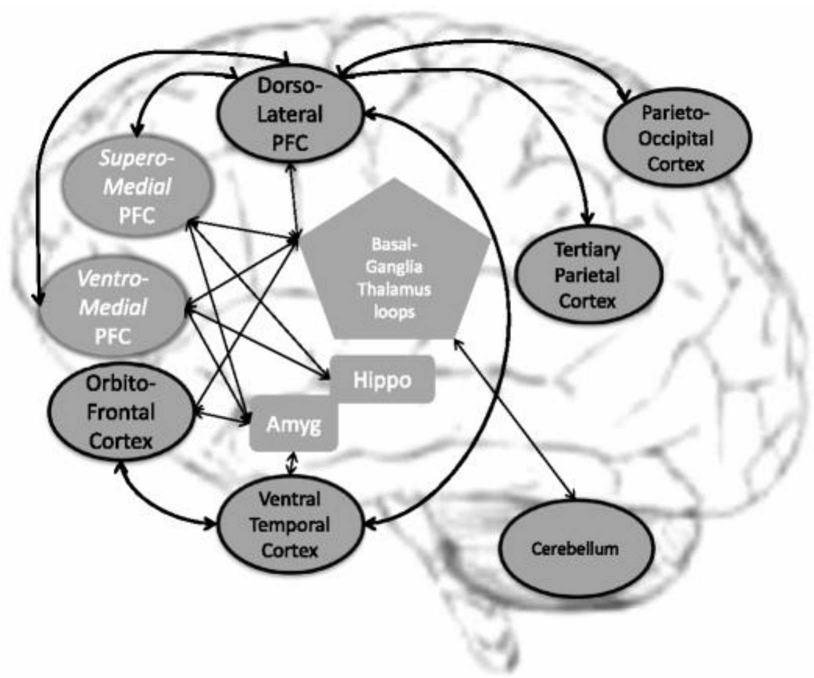
From the early observation in 1940 of Phineas Gage, who suffered frontal lobe damage, most research has focused on the prefrontal cortex (PFC) in order to better understand executive functioning.

The frontal lobes are the largest part of the brain; they comprise one-third of the cerebral cortex (Blumenfeld, 2010), and include the primary motor cortex, the premotor cortex, supplementary motor cortex, Brocas area, frontal eye fields and the prefrontal cortex (Otero and Barker, 2014).

The PFC can be divided into three main convexities 1) the dorsolateral PFC, often the associated substrate of working memory planning, set shifting (Cummings and Miller, 2007). The dorsolateral frontal cortex connects primarily to the head of the dorsolateral caudate nucleus (Alvarez and Emory, 2006), 2) the superomedial PFC, often the associated substrate of sustained attention and motivation and 3) the ventral PFC (orbitofrontal and ventromedial) often as the substrate for inhibition and social appropriateness (Suchy, 2009). Lesions in the orbitofrontal cortex can lead to disinhibition while lesions in the ventromedial circuit can lead to apathy and decreased social interaction (Cummings, 1995).

The cerebral hemispheres of the PFC are also subdivided according to function, with the left PFC associated with initiation of response, and the right PFC associated with inhibition of response (Stuss et al., 2002).

Perhaps due to the volume of research focusing on the prefrontal cortex, a popular belief emerged that the physiological underpinning of executive functions was allocated to this area (Chung et al., 2014) whereas executive functioning relies on different networks throughout the brain as part of a complex integration of neural circuits that span many regions, as no part of the brain works in isolation (Otero and Barker, 2014). EF processes are complex and rely not only on the frontal lobe region but also on a series of complex networks throughout the brain. (See Figure 2.1 below)



(Suchy, 2009)

Figure 2-1: Reciprocal connections between convexities of the prefrontal cortex and limbic and subcortical structures

A metaphor for the frontal system in relation to executive functioning, put forward by Otero et al., (2014) was that of driving a car, whereby the driver of the car has all of the control and uses the various parts – the mirrors, the pedals, the brakes of the car to engage in driving, with all these parts being necessary for the act of driving. In addition to these processes there are numerous automatic sub cortical processes operating while driving also.
Throughout the literature, there is discussion on whether the frontal lobes are indeed inextricably linked to executive function (Stuss and Alexander, 2000, Miyake et al., 2000, Alvarez and Emory, 2006), and this is further seen, in the ambiguity of the definition of EF, discussed in the section below.

Throughout the literature there is a circularity of reasoning between frontal lobe deficits and executive dysfunction. Executive function assessments were occasionally used interchangeably with frontal lobe measurements, and where low scores were attained in executive function tasks, it was concluded that it was due to frontal lobe deficit (Stuss and Alexander, 2000). While there is clearly a relationship between the two, it is important to differentiate between the anatomy (frontal lobes) and the neuropsychological construct (executive functions).

To further highlight the difference between frontal deficit and executive function, some studies have shown that people with frontal lobe deficits did not present with executive dysfunction and others found that some who presented with executive dysfunction did not have frontal lesions or deficits (Damasio et al., 1994, Andrés, 2003, Baddeley and Wilson, 1988).

2.3.1.2 Defining Executive Function

Throughout the decades there have been at least 33 definitions of executive function (Goldstein et al., 2014), without any clear universal definition to date. Goldstein et al., (2014) summarised EF as a single concept, conceptualised as the efficiency with which we acquire knowledge and how well problems can be solved across nine areas (attention, emotional regulation, initiation, organisation, planning, self-monitoring and working memory), however this is not universally accepted as definitive. A number of definitions have many similarities, with many focusing on goal-oriented behaviour (Pennington et al., 2003), problem solving (Burgess, 1997), behaviour regulating (Dawson and Guare, 2010), and many including the various neuropsychological constructs such as planning, inhibition, problem solving, set shifting (Lezak, 1982, Fuster, 2000, Mccloskey et al., 2008, Stuss and Alexander, 2000, Delis et al., 2001). While these cognitive processes have been labelled as 'executive', there is a large amount of overlap and many are highly interdependent, which add to the challenge of creating a satisfactory model of the complex multidimensional construct (Otero and Barker, 2014).

A number of researchers in recent years have tried to summarise the various theoretical models that have been put forward in an attempt to define EF. Although a firm definition has not been agreed upon, there is general consensus that executive functions are not unitary, but rather are multifaceted (Eslinger and Damasio, 1985, Otero and Barker, 2014, Goldstein and Naglieri, 2013, Suchy, 2009).

Suchy (2009) discussed how not only is there no universally accepted definition of EF, the approaches used in attempting to define it vary considerably. Approaches taken have addressed (Suchy, 2009):

- Its overarching evolutionary purpose
- The clinical syndromes associated with it
- The list of associated complex skills (e.g. planning, problem solving, attention)
- The list of associated elemental neurocognitive processes (e.g. working memory, inhibition, initiation)
- Atheoretical approaches driven by available populations
- The neuroanatomic substrates underlying the complex skill and elemental neurocognitive processes
- Constructivist theories that offer a framework

McCloskey et al (2008), proposed an operational definition of EF (see Table 2.3 below), which included six interrelated concepts.

Table 2-3: Operational Definition of Executive Functions from McCloskey (2008)

1	EF are multiple in nature; they do not represent a single unitary trait
2	EF are directive in nature; they are mental constructs that are responsible for cueing other mental constructs
3	EF cue mental constructs in four broad domains; perception, emotion, cognition and action
4	EF use can vary greatly across four areas of involvement; intrapersonal, interpersonal environment and symbol system use
5	EF begin development in early childhood and continue to develop at least into the third decade, and most likely throughout the lifespan
6	The use of EF is reflected in the neural network in the frontal lobes

Goldstein summarised the above operational definition, as was stated above, to provide the definition of EF as 'an umbrella term that encompasses many different abilities that are mediated by the prefrontal areas of the lobes. These abilities include, but are not limited to planning, working memory, attention, inhibition, self-monitoring, self-regulation and initiation' (Goldstein and Naglieri, 2013). An agreed model which could be universally adopted would assist in the development and interpretation of the most appropriate EF assessments to employ, in understanding everyday cognition and EF development (Anderson, 2002). For these reasons the Goldstein operational definition of EF was used for the current study, while also recognising that there is no fully adopted universal definition.

2.3.1.3 Measuring Executive Functioning

There are a number of challenges in the measurement of EF. Some of these challenges arise from the previously discussed fact that there is no universally adopted operational definition of EF. Due to these challenges in definition and the circularity of relating the anatomical to the neuropsychological, the literature on construct validity of executive function tasks is limited (Barceló, 2001, Alvarez and Emory, 2006). Indeed, the question has been posed; how does one measure the construct validity of a group of tests, when the construct itself is not clearly defined? (Jurado and

Rosselli, 2007). This problem becomes apparent, as discussed previously, when individuals with frontal deficit show no impairment in EF tasks, while others with no deficits in the frontal system do show executive dysfunction. The complex multifaceted nature of EF also means that an impairment on an EF task, may be due to a deficit in any component process (Chan et al., 2008). This means that practically it is not possible to measure EF in isolation without also measuring other nonexecutive processes (Suchy, 2009). Conversely, while there is undoubtedly an overlap and interconnection between different EF processes, there is also fractionation of different executive functions, whereby success or failure in one EF task, may not be predictive of success or failure in another EF task (Burgess, 1997, Shallice, 1988, Miyake et al., 2000) and may not sufficiently reflect complex real world situations (Fan et al., 2002). This multifactorial aspect also contributes to the low correlations among EF tests (Stuss and Alexander, 2000).

In order to focus on EF tasks, an attempt has been made in the literature to differentiate between 'complex' and routine' tasks i.e. that the level of complexity of the EF task requires more than that of routine processing. As with all things neural, a simplistic view does not suffice, and cannot be applied to all cases. What may be a routine overlearned task to one individual, may involve a complex process for another, and similarly, the interpretation of the task may influence the perceived level of complexity. Stuss et al., (2000) gave the example of the Card Sorting task, where an 'intelligent control subject' completely failed on the task because they had hypothesised far more complicated sorting strategies than was required.

The challenges discussed above mean that there is still controversy over the measurement of EF, with the prevailing approach being the measurement of the functions of the frontal lobe, as the best current proxy for EF measurement. Common measures of executive function are presented in Table 2.4 below. It has been suggested that perhaps a perfect test of frontal lobe functioning may be impossible to establish due to the many subcortical connections involved, whereby posterior and subcortical lesions will cause frontal impairment, due to their many connections (Jurado and Rosselli, 2007).

Table 2-4: Common tests of executive function

Assessment	**Executive Function**
The Tower of London	Planning
Brixton Spatial Awareness Test	Rule Detection
Wisconsin Card Sorting Task	Set Shifting
Stroop	Inhibition
Trail Making Test	Set Shifting; Inhibition
Verbal Fluency	Fluency

Another criticism noted in the measurement of executive function is related to the ecological validity, whereby the tests don't reflect real world problems. As a response to this criticism, the addition of function and adaptive scale to the traditional assessments were suggested (Chaytor et al., 2006). A further development was made to improve the ecological validity with the development of the Behaviour Rating Inventory of Executive Function (BRIEF), which uses real-life scenarios to measure executive functions in pre-school children, including those with an intellectual disability (Isquith et al., 2004). The BRIEF was adapted also to be used with adults (BRIEF-A) (Roth and Gioia, 2005).

2.3.2 Executive Functioning and DS

As was discussed previously, individuals with DS present with certain neuropathological abnormalities, including hypoplasia of the frontal cortex, where the cortex is smaller and underdeveloped (Holland et al., 2000). Structural neuroimaging studies have shown decreased total intracranial volume, with evidence that the frontal lobes show some of the greatest volumetric differences (Aylward et al., 1999). The volume of the prefrontal lobe has shown a positive correlation with performance on executive function tasks (Gunning-Dixon and Raz, 2003).

DS does not determine IQ, but it does have an effect on the IQ distribution (Pennington et al., 2003). A study conducted by Rowe et al., (2006) examined the difference in scores on EF tests between 26 individuals with DS and 26 individuals with ID from other aetiologies. The EF assessments used were Tower of London, Weigl Card Sorting Task, Raven's Coloured Matrices, Digit Span, Spatial Span, Finger Tapping Task and Verbal Fluency. It was found that individuals with DS scored lower on all tasks of EF than those with ID from other aetiologies, in particular on the Weigl Card Sorting Task, the Sustained Attention task, Ravens Coloured Matrices and the Tower of London task. It was also found that people with DS had similar scores on the visual short term memory task, but scored lower on verbal short term memory, supporting previous research on language impairment (Lanfranchi et al., 2004, Silverman, 2007). Overall it was concluded that those with DS presented with impairment in EF, relative to level of ID, and that this impairment may be as a consequence of impaired development of the PFC (Rowe et al., 2006). The challenges in measuring EF were outlined above, however, there are further challenges in measuring EF in individuals with DS, where low scores on EF tasks may be a result of failure to understand the rules and requirements of the task, as opposed to an impairment in EF (Ball et al., 2008). Attempts can be made to address this issue by ensuring that all instructions are given in a clear and accessible manner, that tasks are chosen that require minimal verbal instruction, demonstrations can be given and practice trials allowed (Ball et al., 2008).

Other studies have suggested that differences in EF tasks may be age related and connected to the presence of AD. Nelson et al. (2005) found that impairment on the object reversal learning tasks in twenty adults with DS was related to the presence of dementia, as assessed by the Dementia Questionnaire for People with Learning Disabilities (DLD) (Evenhuis et al., 2007). Ball et al (2010) reported similar findings - that EF functions are compromised early in AD and DS, as observed by the relationship between changes in behaviour and performance on tests of EF (Ball et al., 2010). Another study similarly found that scores on EF tasks such as planning and attention were poorer in older (50-62years) adults with DS compared to younger (40-49years) adults with DS, but that the same was not found for older vs younger adults with ID from other aetiologies, when matched for age and level of ID (Das et al., 1995). Typically impairment in EF is associated with individuals with pathology that extends primarily to the dorsolateral prefrontal cortex, more than is seen with those who have pathology mainly in the orbitofrontal cortex. However for individuals with AD, performance on EF tests was associated with orbitofrontal dysfunction. This suggests that EF in people with AD may show dysfunction in both orbitofrontal prefrontal cortex and dorsolateral prefrontal cortex (Ball et al., 2010) .

Kittler et al. (2008) reported on the differences between individuals with DS and Williams's syndrome and found greater weaknesses in dual task processing, as a measure of EF, for people with DS compared to Williams's syndrome. These studies point to a specific deficit in individuals with DS in relation to EF when compared to either people with ID from other aetiologies or to people in the general population. In contrast to this however a study conducted by Pennington found no difference on prefrontal functioning tasks in adults with DS compared to a control group matched on mental age, but rather found an impairment in hippocampal tasks (Pennington et al., 2003). Further research is required to better understand the relationship between EF dysfunction and the clinical and preclinical features of AD, especially in understanding the sequence of cognitive impairment and decline (Ball et al., 2008).

As previously discussed, in the progression of AD in DS, personality and behaviour changes have been retrospectively reported by carers as some of the earliest signs of AD (Holland et al., 1998). Ball et al., (2008) conducted a study with one hundred and three people with DS and found that informant-reported behaviour changes were a significant predictor of performance on two executive function tasks (Scrambled Boxes and Tower of London tasks). While this suggests that personality and behaviour changes and EF dysfunction results from AD neuropathology in the frontal lobes, this needs to be investigated further. It is currently unclear whether the observed frontal lobe changes prior to the clinical features of AD are a result of differences in the distribution of AD neuropathology or due to the underdevelopment of the frontal lobes in people with DS (Ball et al., 2010).

From this literature, it is clear that EF plays a crucial role in everyday behaviours and that individuals with DS are at increased risk of executive dysfunction. However there is evidence also regarding individual differences showing that neuropathology on its own does not necessarily determine the clinical outcome. The following section discusses the theory of cognitive reserve, which may address this issue.

2.4 Cognitive Reserve

2.4.1 Introduction to Cognitive Reserve

The concept of reserve refers to a theory that has been put forward to explain the disparity between the degree of brain damage or brain pathology and the clinical outcome (Stern, 2009). As was noted earlier, people with DS can show neuropathological signs of dementia without associated clinical features of dementia. Similarly, in the general population, Esiri et al. (2001) reported that a quarter of older adults met full pathologic criteria for Alzheimer’s disease, but showed no clinical impairment as measured by neuropsychological tests. Likewise, Katzman et al. (1988) found that the brains of ten women, who had shown no cognitive deficit, had the pathology of dementia. The brains of these women were heavier and contained more neurons, which were thought to help prevent clinical symptoms.

2.4.1.1 Cognitive Reserve, Brain Reserve and Neural Reserve

There are two models of reserve, one of which is passive (brain reserve), and the other is active model (cognitive reserve) (Stern, 2009). The brain reserve model proposes that reserve relies on physical features of the brain itself, including brain size, neuronal count or number of synapses (Katzman, 1993). Following from this model, (Satz, 1993) proposed a sub model of brain reserve; the threshold model, which recognises differences in brain reserve capacity, and postulates that once reserve falls below a critical threshold then clinical deficits appear. Thus high reserve capacity would be protective, with low reserve capacity being vulnerable (Stern, 2002). These models are described as passive due to the fact that there are set cut-off points, below which clinical symptoms will appear for everyone following a brain insult. As noted earlier in the discussion of EF, there are individual differences in how the brain processes cognitive tasks, and these passive models do not take these individual differences into account.

In contrast to this, the cognitive reserve model is active. It suggests that pre-existing cognitive processes are used in an attempt to manage brain damage, and thus the way in which tasks are processed determine how well the individual will cope with brain pathology (Stern, 2011). That is, those with higher cognitive reserve use more efficient processing mechanisms, and thus can suffer more brain insult without displaying decline in outward functioning. This means that there is no single cut-off point, and that an individual with higher cognitive reserve would be able to sustain more brain insult than a peer with the same brain reserve, but with lower cognitive reserve. In addition to this, it takes into account the mechanism with which the brain may cope with an insult. A cognitive system may still be able to operate effectively after sustaining an insult, or it could also be that it adopts an alternative paradigm to handle a task, if the standard approach is no longer functioning due to the brain insult (Stern, 2002).

The neural aspect of cognitive reserve may come from either neural reserve or neural compensation (Barulli and Stern, 2013).

Neural reserve refers to inter-individual differences in cognitive processing that occur in the healthy brain (Stern, 2009). These differences could be due to either the efficiency of networks or the flexibility of the networks. Efficiency of a network is associated with the change in neural activity that occurs with increased task difficulty, and can be measured using functional MRI (fMRI). An individual with low efficiency will require a bigger increase in neural activity to complete a demanding task than will a person with higher neural efficiency.

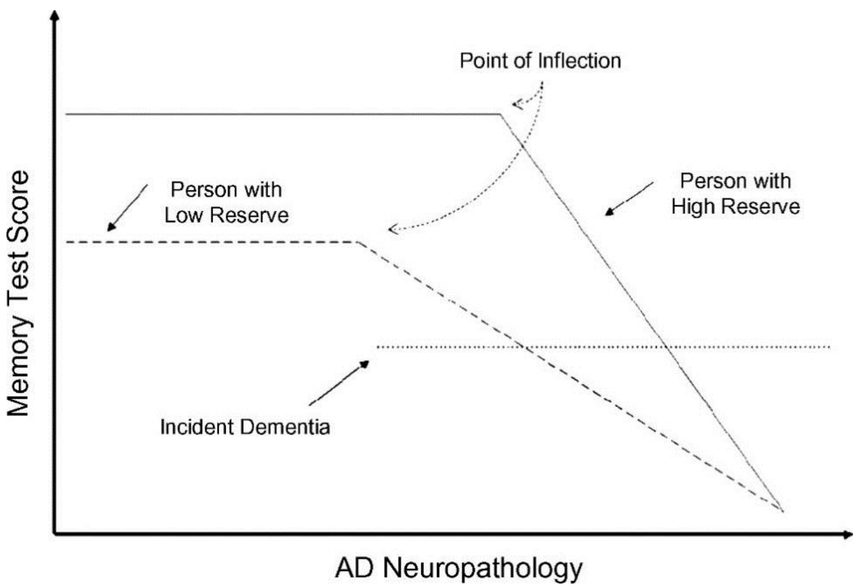
Neural compensation refers to the use of an alternative brain network due to damage or insult to the network usually associated with the task; the alternate network will compensate for the damaged network, thereby using alternate cognitive strategies (Steffener and Stern, 2012). A number of neuroimaging studies comparing impaired and unimpaired have shown increased activity in alternative brain regions for the impaired group as compared to the unimpaired group, perhaps compensating for deficit in the principle brain region involved in the task (Stern et al., 2004).

In recent years it has become more accepted that separating brain reserve and cognitive reserve may not be straightforward, and that both reserve hypotheses are inherently interlinked (Stern, 2009). Moreover, these reserve hypotheses are linked to the larger concept of brain plasticity (Fratiglioni and Wang, 2007). Brain plasticity allows the brain to continuously change and adjust, and it is the foundation of memory and learning processes. Both mental and physical exercise can have a positive effect on plasticity, with mental stimulation increasing synaptogenesis and physical exercise increasing non-neuronal aspects, such as vasculature (Fratiglioni and Wang 2007) and greater induction of neurotrophic growth factors (Kramer et al., 1999).

2.4.2 Cognitive Reserve and Dementia

These reserve hypotheses were applied to the study of dementia at the beginning of the 90s and have developed from anatomical concepts to exploring their functional implications (Fratiglioni, 2007). A systematic review on brain reserve and dementia, (Valenzuela and Sachdev, 2006) based on data on over 29,000 individuals, found that high brain reserve was associated with an approximate 50% reduction in the incidence of dementia. Similarly the National Institute on Ageing, (2012) at the U.S Department of Health and Human Services released a report in which they commented on the impact of ordinary activities such as listening to the radio, reading newspapers, playing puzzle games and visiting museums. After 4 years of following a cohort of 700 individuals in the general population, it was found that those engaged in these activities on a regular basis were, on average, 47% less at risk of developing Alzheimer's disease than those who engaged in these activities less frequently.

In a four year longitudinal study conducted by Stern et al. (1994) with 593 adults, who did not have dementia at the beginning of the study, it was found that those with fewer than eight years of education were over twice as likely to develop dementia than those with more education, and similarly those with low occupation achievements were over twice as likely to develop dementia as those with higher lifetimes occupation achievements. This finding was supported by more recent research also (Smart et al., 2014). It was, however, noted in a later study (Stern et al., 1995b) that those with a higher degree of reserve showed a sharper and steeper decline once clinical signs of dementia appeared. (See figure 2.2 below)



Stern (2009)

Figure 2-2: Potential Mediation of Cognitive Reserve in AD Neuropathology

There has been a further wealth of cross sectional and retrospective studies that have indicated that engagement in rich social networks and leisure activities may slow down or stop the onset of dementia, however it was suggested that perhaps a decrease in these activities in later life may in fact be a subtle symptom that precedes dementia (Coyle, 2003). Verghese et al. (2003) conducted a prospective study, which found that, even excluding persons with possible early symptoms of dementia, the protective factors of leisure activities continued. Furthermore, it was found that this protective factor was limited to activities that required mental effort, and no effect was found involving physical activity alone (Verghese, 2003). This type of mental effort may not only strengthen existing synaptic connections, but also create new connections, particularly in the hippocampus (Coyle, 2003).

Cognitive reserve has been most associated with childhood intelligence and educational achievement (Richards and Sacker, 2003). Similarly, low childhood intelligence has been observed as a risk factor for late onset dementia (Whalley et al., 2000). It was pointed out by Farfel et al. (2013), that the relationship between cognitive reserve and education may not be that straightforward, in that it may be that those with higher reserve continue to higher education, or that higher education leads to higher reserve.

Positron Emission Tomography (PET) studies have provided some evidence in support of the cognitive reserve theory, where it was reported that participants with AD had negative correlations between resting cerebral blood flow and education, IQ, occupation and leisure, where resting cerebral blood flow is taken as a proxy for AD pathology (Stern et al., 2004). In a study by Landau et al. (2012) a significant association was found between cognitive activity and [^{11}C]PiB uptake measured by PET. This suggests that high levels of cognitive activity may slow the deposition of β-amyloid, which in turn could affect the progression of AD (Landau et al. (2012). The effect of noradrenergic activity in cognitive reserve has also been examined where the key elements of cognitive reserve – IQ, education, mental and social activity are all associated with increase in the noradrenergic system (Robertson, 2013).

2.4.3 Cognitive Reserve and Down syndrome

To date, there has been a dearth of research specifically examining levels of cognitive reserve in people with DS, with direct tests still needed to better understand the impact of reserve with the population (Zigman and Lott, 2007). Although little direct research has been conducted, it could be hypothesised that there may be a relationship between level of ID, level of cognitive reserve and its impact on the onset of AD (Bush and Beail, 2004). We know from findings in the general population, as mentioned above that lower levels of education, lower levels of occupation attainment, lower IQ level, lower neuronal count, all for which many people with DS would be at greater risk, are risk factors for lower cognitive reserve. Cognitive Reserve has been linked to crystallised verbal ability (Richards and Sacker, 2003), with childhood intelligence the strongest contributor to estimate cognitive reserve (Whalley et al., 2004), which again would lead to the hypothesis that those with DS would be at greater risk of having low cognitive reserve.

There is evidence, as proposed by Holland et al., (2000) in the progression of AD in people with DS, that compromise of a particular brain region is more likely if there is less reserve in this region. As discussed above, we know that there are early executive function changes in people with DS when AD presents, that the frontal lobes are integral in executive functioning and that this region is compromised early in the neuropathological progression in DS.

From the literature above, it is hypothesised that those with DS are at greater risk of low cognitive reserve, and this, coupled with the neuropathology of AD results in early behaviour changes that are associated with executive dysfunction. The following section discusses the issue of cognitive training and its potential to modulate executive dysfunction.

2.5 Cognitive Training

2.5.1 Introduction to Cognitive Training

There are few subjects as controversial in neuropsychology as cognitive training. However, before undertaking a discussion on cognitive training, it is important to note that some of the controversy is not relevant to this particular study. Commercial brain-training games are a lucrative industry, with expected revenues by 2020 of more than $6 billion (Boot and Kramer, 2014). As with any industry, there is a substantial incentive for commercial companies to show the benefits of using their product and in promoting the theory of brain training as a whole. This has led to a plethora of funded, potentially partisan studies being conducted, and bold claims being made as to what brain training can achieve. In response to this, there was a severe backlash, where it was claimed that there was no benefit to brain training and no scientific evidence to support any claims. This backlash appeared to group 'brain training games' all together as a homogenous entity, as though saying that all pills either do or don't work (Merzenich, 2016). The disagreement among scientists is far from being resolved, with one of the problems in the discussion being the confusion over what is being debated; some are debating whether it is effective for specific areas of focus, whereas others are debating whether it can improve overall cognitive ability, and others on its effects or lack thereof in relation to dementia. Similarly, there is a lot of focus in the literature on specific programs or studies. When discussing cognitive training as a whole, certain reviews have focused and placed weight on a particular study or program, which is ineffective in discussing the concept in its entirety, such as Ratner and Atkinson (2015a).

2.5.2 Cognitive Training in the General Population

In this section, the controversy will be discussed, and in particular, the focus will be on the systematic reviews and meta-analyses that have been conducted to date. These data will be taken from studies involving healthy adults and adults with mild cognitive impairment and adults with dementia in the general population.

Cognitive training encompasses specifically designed training programs that provide guided practice on a standard set of cognitive tasks, aimed at improving performance in one or more cognitive domains (Martin et al., 2011). Cognitive training can also provide information on the extent and mechanisms of brain plasticity in older adults (Belleville et al., 2011). The HAROLD (Hemispheric Asymmetry Reduction in Older Adults) proposes that healthy ageing relies on recruitment of regions on the opposite hemisphere to the one specialised for the impaired process, thus reducing hemispheric asymmetry (Cabeza, 2002). Specifically, in relation to activity in the pre frontal cortex, it was found that older adults showed a more bilateral pattern compared to younger adults, reflecting functional compensation (Cabeza et al., 1997). The psychogenic view of the HAROLD suggests that this difference in bilateral pattern is due to the use of different cognitive strategies, whereas the neurogenic view is that the changes are due to change in neural architecture, and that the same cognitive processes are mediated by a more bilateral pattern of brain activity (Cabeza, 2002).

The CRUNCH (Compensation Related Utilization of Neural Circuits Hypothesis) proposes that a combination of both the recruitment of areas normally involved in the recruitment process and also the recruitment of new brain areas are needed for brain compensation (Reuter-Lorenz and Mikels, 2006). According to CRUNCH, the ageing brain has to recruit and activate more neural resources in order to perform at a similar rate to the younger brain. It is hypothesised that this compensation is successful for more simple tasks, but that age related deficiencies may be noticeable as task demand increases, and an intervention or training may increase the resources available and increase the potential for compensation (Reuter-Lorenz and Cappell, 2008). These concepts are directly related to cognitive reserve and the compensatory neural reserve that was discussed in section 2.5.1.

Thus the HAROLD model suggests that cognitive training should increase bilateral recruitment, whereas the CRUNCH model suggests that memory training might increase activation in both areas that are normally recruited for memory and also in other brain networks (Belleville, 2011). Overall, however, both models suggest that increased activation should lead to an improvement. The relationship between cognitive reserve and cognitive training was investigated in a study by Mondini et al., (2016). The authors found that cognitive reserve was a significant predictor of change in scores on the Mini Mental State Examination (MMSE), for individuals with mild to moderate dementia, following a period of cognitive training. Specifically, it was found that those with low levels of cognitive reserve appeared to benefit more from cognitive training than those with high levels of cognitive reserve (Mondini et al., 2016).

Transfer of effects to everyday functioning has been noted as a concern in the literature, with few studies including this as an outcome measure. In a review on brain plasticity and training induced learning, Green and Bavelier (2008) discuss the mechanisms of learning and how this differs in real life learning situations compared to a targeted cognitive training intervention. In 'natural' training regimens, for example athletics or musical training, there are multiple and complex systems acting in parallel, whereas in cognitive training, these domains are most often purposefully separated, that is, memory is trained separately to inhibitory control. It was suggested separating domains increases learning in the acquisition phase, but is detrimental to the retention phase, which in turn would impact the transfer to other generalizable domains (Green and Bavelier, 2008b). Some recommendations were given in the review by Green and Bavelier (2008) to encourage learning transfer;

- Task Difficulty: Using small, incremental increases in task difficulty, beginning at an easy level and advancing to a higher level of difficulty only when sufficient mastery of the current level has been demonstrated.
- Motivation and Arousal were deemed as key components for effective learning. Motivation was discussed as internal, rather than external, and linked to the individual's belief of his/her level of ability, and that motivation would be at its highest if the task at hand is just slightly above the current ability. A task much too difficult or much too easy

has been shown to decrease motivation, and thus learning substantially. The Yerkes-Dodson law, is an inverted U shaped relationship between arousal and function (Cohen, 2011), with excessively high or low levels of arousal detrimental to learning; thus a game should attempt to elicit an arousal effect between the two extremes. It was hypothesised that challenging tasks have a lower level of optimal arousal than routine tasks (Robertson, 2014).

- The role of feedback is not well understood, with contradictory evidence as to whether it is beneficial or detrimental to learning, and is an area that requires more research.
- The final factor as recommended in Green et al., (2008) was that variability is important for flexible learning.

From their systematic review Kelly et al (2014) recommended that in order to see a benefit in everyday functioning, cognitive training should focus on improvements in executive function.

A significant study in modern cognitive training suggested that training on working memory tasks may improve attention and reasoning in children with ADHD (Klingberg et al., 2002). A subsequent study in 2008 appeared to show that working memory training increased fluid intelligence (Jaeggi et al., 2008). These studies, particularly the latter, caused much debate in the scientific community. There continues to be much controversy surrounding the benefits of cognitive training, with meta-analyses producing divergent conclusions (Makin, 2016). Some of these meta-analyses are presented in Table 2.5 below.

In a systematic review on the impact of cognitive training and mental stimulation on cognitive and everyday functioning of healthy older adults, involving thirty one randomised controlled trials, it was found that those who completed cognitive training showed improved performance on measures of executive function. Specifically working memory and processing speed were improved compared to those in an active control group, and improvements in memory and subjective cognitive function were found when compared to those in the passive control group (Kelly et al., 2014). This review was noteworthy, as it showed a positive effect when compared to an active control group, where other studies have shown that while there was an improvement in scores post training, this did not exceed those seen in active control conditions (Martin et al., 2011). Kelly et al (2014) found that compared with 'no intervention control', improvements were found in seven of the sixteen measures of executive functioning, but that these differences in EF were not found compared to the active control.

Of the eleven systematic reviews and meta-analyses below, nine showed that cognitive training had a positive effect, but without strong evidence of generalisability and little evidence of far transfer effects. It was noted by a number of reviewers that studies did not use an outcome measure to examine changes in everyday function. Two of the systematic reviews found that cognitive training has no beneficial effect. The first examined working memory training and the second examined the effects of training on adults with mild or moderate dementia. There has been little discussion and no consensus on the dosage of training needed to see an effect.

Of significant note also is the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) which was the first large scale randomised trial to find that cognitive training improved cognitive function. The ACTIVE trial recruited 2832 individuals aged between 65 and 94 (Ball et al., 2002b). Participants were randomly assigned to three intervention groups and received ten training sessions on either memory, reasoning or speed of processing. Four booster sessions were given after 11 months and again at 35 months. In a ten year follow up, participants in all training groups showed less decline when compared to the control group in self-reported instrumental activities of daily living (IADL). Improvement was seen in targeted cognitive abilities for those in the reasoning and speed of processing groups at the ten year follow-up (Rebok et al., 2014). This study was significant due to the large number of participants, the longitudinal nature and also because it examined effects of training on everyday function, which was noted previously as lacking in the majority of studies.

Table 2-5: Summary of meta-analyses conducted on cognitive training studies

Author (year)	Paper	Number of Studies included in Review	Main Findings
Au., J., Sheehan, E., Tsai, N., Duncan, G., (2015)	Improving Fluid Intelligence with Training on Working Memory: A Meta-Analysis	20 Studies (n-back training studies with Gf outcome measures only	• Small but significant positive effect of n-back training on improving Gf • Improvements seen irrespective of using active or passive control group
Bahar-Fuchs, A., Clare, L., Woods, B., (2013)	Cognitive Training and Cognitive Rehabilitation for Mild to Moderate Alzheimer's Disease and Vascular Dementia	11	No evidence of improving cognitive functioning, mood or activities of daily living in people with mild or moderate Alzheimer's or vascular dementia Quality of the studies was low
Karbach, J., Verhaeghen, P., (2014)	Making Working Memory Work: A Meta-Analysis of Executive Control and Working Memory Training in Younger and Older Adults	49	• WMT and EF training lead to significant and large improvements in trained tasks • WMT and EF show clear and large near transfer effects • WMT and EF show clear but small transfer effects • Dosage did not appear significant • No data on generalisability to everyday life
Kelly, M. E., Loughrey, D., Lawlor, B. A., Robertson, I. H.,	The Impact Of Cognitive Training And Mental Stimulation On Cognitive And Everyday Functioning Of Healthy Older	31	• Improved memory and subjective measures of cognitive function compared to no intervention • Improved composite cognitive function and executive function compared to active controls

Walsh, C. & Brennan, S. (2014)	Adults: A Systematic Review And Meta-Analysis. Ageing Res Rev, 15, 28-43.		• Recommended adaptive program with at least 10 sessions and long term follow up for maintenance and transfer • Recommended targeting executive functions for changes in everyday settings.
Kueider, A., Parisi, J., Gross, A., Rebok, G. (2012)	Computerized Cognitive Training with Older Adults: A Systematic Review	38	• Classic cognitive training tasks, neuropsychological software and video games showed promise for improving cognitive ability • Effect sizes comparable or better than those reported in non-computerised cognitive training interventions
Lampit, A., Hallock, H., Valenzuela, M., (2014)	Computerized Cognitive Training in Cognitively Healthy Older Adults: A Systematic Review and Meta-Analysis of Effect Modifiers	52	• Modest effect at improving cognitive performance in healthy older adults • Effects found for memory, speed, visuospatial, but not for executive functions • Group based intervention more effective • 3 or more training sessions a week ineffective compared to less than 3
Melby-Lervåg, M., Hulme, C., (2013)	Is Working Memory Training Effective? A Meta-Analytic Review	23	• Working memory training (WMT) produced some short term improvements, but were not maintained • No convincing evidence of generalizable to other skills

			• Cast doubt on WMT as enhancing cognitive function
Papp, K., Walsh, S., Snyder, P., (2009)	Immediate and Delayed Effects of Cognitive Interventions in Healthy Elderly: A Review of Current Literature and Future Directions	10	• Training improves immediate memory performance on related tasks, but no evidence of generalizability
Reijnders, J., van Hrugten, C., van Boxtel, M., (2013)	Cognitive Interventions in Healthy Older Adults and People with Mild Cognitive Impairment: A Systematic Review	35	• Evidence of improvement in memory performance, executive functioning, processing speed, attention, fluid intelligence and subjective cognitive performance • Little evidence of generalisability • Recommend follow up assessments
Simon, S., Yokomiza, J., Bottino, C. (2012)	Cognitive Interventino in Amnestic Mild Cognitive Impairment: A Systematic review	20	Some evidence that individuals with Amnestic Cognitive Impairment benefit from cognitive interventions, and show that they can; learn new information using different strategies, use visual iagery, errorless learning and spaced retrieval Some positive effects on daily life activities, self-perception of memory and mood, emotional features and quality of life Impact of education background needs to be investigated

Valenzuela, M., Sachdev, M., (2009)	Can Cognitive Exercise Prevent the Onset of Dementia? A systematic Review of Randomized Clinical Trials with Longitudinal Follow-up	7	Strong effect size observed for cognitive exercise interventions Persistent protective effects on longitudinal neuropsychological performance Some transfer to general cognition and daily functioning reported Cognitive exercise yet to show to prevent incident dementia

As mentioned previously, there is some confusion in the ongoing debate on cognitive training, as to what exactly is being refuted. In response to the article Computerized Cognitive Training is Beneficial for Older Adults (Lampit et al., 2015), it was argued that there was no evidence of the protective nature of cognitive training against the pathophysiology of dementia (i.e. the development of plaques and tangles) (Ratner and Atkinson, 2015a). This claim, however, was never made in the original article. Indeed, there is no evidence that cognitive training could influence Alzheimer's pathology, but rather that there is some evidence that cognitive training may influence the relationship between Alzheimer's pathology and clinical symptoms of Alzheimer's.

Similarly, in the article *Why Cognitive Training and Brain Games Will Not Prevent or Forestall Dementia* (Ratner and Atkinson, 2015b), the quote below was used to strengthen the argument. The quote comes from a consensus statement, published in 2014 by seventy-six neuroscientists; A Consensus on the Brain Training Industry from the Scientific Community (Allaire et al., 2014)

"In the judgement of the signatories below, exaggerated and misleading claims exploit the anxiety of adults facing old age for commercial purposes. Perhaps the most pernicious claim, devoid of any scientifically credible evidence, is that brain games prevent or reverse Alzheimer's disease".

The above statement, is not arguing against claims made by scientific studies that have suggested some benefits in relation to particular cognitive domains, but rather against misleading claims that commercial companies may have made. As noted previously, this type of argument is pervasive in the cognitive training debate, where it is viewed as a binary – works or does not work, but this type of argument is neither useful, nor does it reflect the numerous studies that have examined the effects on targeted domains.

2.5.3 Cognitive Training and Intellectual Disability

There is much evidence to support the idea that individuals with DS are at higher risk of developing dementia at an earlier age (Coppus et al., 2006), and in experiencing problems with levels of executive functioning. While the evidence of benefits gained from cognitive training is not conclusive at present, some studies have shown promising results in the general population (Rebok et al, 2014). Yet although those with DS are at higher risk, little research has been done to date on the subject of cognitive training in this population. Rates of computer usage among adults with ID are very low compared to the general population (Hoppestad, 2013, McCarron et al., 2014a), which could explain the lack of research in this area.

A review of all studies using cognitive training with individuals with Down syndrome was conducted, with results of this review summarised in Table 2.6 below. The review was conducted using CINAHL, PUBMED, PsychInfo and EMABSE. MeSH terms were used in PubMed and terms were exploded in using the terms below

Down syndrome OR Downs syndrome OR Down's syndrome OR Trisomy 21 OR intellectual disability OR learning disability OR developmental disability OR mental retardation AND Brain training OR Brain Games OR Cognitive Remediation OR Brain remediation OR Cognitive Intervention OR Cognitive Rehabilitation OR Cognitive Games OR Mental exercise OR Brain Exercise OR Cognitive exercise OR Mental exercise OR Brain fitness OR Cognitive fitness OR Mental fitness

Seven studies were identified that used a cognitive training program with individuals with ID, however one of these studies one was published after the development of the current study (Siberski et al., 2015) and thus was not used to inform the methodology or development of the current study.

At the time of development of this study, all studies reviewed focused on children or adolescents with intellectual disabilities. Of the seven studies reviewed, four were computer based training courses and three were non-computer based training programs. Four of the studies used random allocation to active or control group. Overall, five of the studies found a positive overall effect following training and two did not find an effect.

Working memory plays a central role in almost every cognitive activity, (Connors, 2001). It has been noted that working memory and memory span are impaired in individuals with DS, however two studies have shown an improvement in working memory, following a training program with people with DS (Connors et al., 2001, Bennett et al., 2013). In order to develop learning or memory strategies for this population, it is necessary to have an understanding of which learning and memory systems are disproportionately impaired in DS and also which of these can be ameliorated and which cannot (Nadel, 1999). Broadley and Macdonald (1993) conducted a study which involved two non-computerised memory training programmes and found that the programmes were successful in increasing memory performance, but that this was not generalisable to other areas of learning. Similarly, Comblain (1994) examined the effects of a rehearsal training strategy, using letter span, digit span and word span on verbal short term memory. While the sample was small (n=24), for those who completed the training there was a significant improvement in memory span compared to the control group. These improvements were maintained six months after the intervention was completed. The findings from Comblain (1994) were further advanced with a more recent study which found that improvements in memory of lists of digits were seen during the training sessions (Conners et al., 2008). These improvements could be seen in the primary outcome measure, digit span, but no improvements were noted in more distal outcome measures of working memory or sentence span (Conners et al., 2008). Furthermore, it was found that improvements were correlated with language comprehension and verbal working memory.

As stated above, four studies have used computerised working memory training with children with ID, with similar results

1. A computerised working memory training was found to be effective for ninety-five adolescents with mild to borderline ID, with higher scores post intervention on visual short term memory, arithmetic and story recall (Van Der Molen et al., 2010). Individuals in this study were randomly assigned to an adaptive WM group, a non-adaptive WM group or a control group. Both adaptive and non-adaptive training groups improved following the intervention compared to the control group.
2. In a double blind randomised, intervention study, non-verbal reasoning and working memory in children with ID aged six to twelve was found to improve during training, but without lasting effects at one year follow up using computerised training. Training was completed for 20 minutes a day, 5 days a week over a period of 5 weeks (Soderqvist et al., 2012). This study recommended a longer training period for future research.
3. When participants were randomly allocated to either the intervention or control group, both trained and non-trained tasks on visuospatial short term memory were found to have improved following a computerised memory training program with twenty-one children with DS, and these improvements were sustained four months after the intervention (Bennett et al., 2013b). The training was completed as part of a structured school setting.
4. Of particular interest was a recent study which examined the effects of computerised cognitive training for adults with ID across fifteen cognitive processes, including divided attention, eye-hand coordination, inhibition, monitoring, naming, planning, response time, recognition, shifting, spatial perception, visual scanning and working memory (Siberski et al., 2015). Thirty two adults with ID participated in the ten week study, which used the cognitive training program CogniFit. This program was used both for pre and post

evaluation and as the intervention program, although the pre/post evaluation tasks bore no resemblance to the training tasks. An active control group was used, with games designed by CogniFit also, which acted as a placebo. Siberski et al., (2015) found that the program was suitable for all participants, with some support needed. Within-group comparisons found that those in the training group improved on eleven of the fifteen cognitive measures.

The results from these studies were encouraging, as it helped to promote the idea that, with support, a cognitive training program can be used for a population with ID, and can help to improve aspects of cognitive functioning. Of note, however, with the exception of Siberski et al., (2015), which was published after the development of the current study, all studies focused solely on children or adolescents. While these studies are useful as they also deal with a population with ID, there was a gap in the literature in relation to adults with ID. This is particularly important for individuals with DS, due to the genetic pre disposition to AD. The current study specifically chose adults with DS between the ages of 30 and 49, as neuropathology of Alzheimer’s disease could be seen, however without clinical dementia yet present. This age range was identified by Belleville (2011) as a critical stage at which to target interventions aimed at promoting brain plasticity. This study was therefore necessary to examine firstly whether an iPad based training program was feasible for an older population with DS. Secondly, while studies above found promising effects in relation to training with children or adolescents, it was important to examine this with an older population, where neuropathology of dementia would be expected, to determine if training at this stage of life could have a positive impact on levels of executive function.

Title and Author of Article	Participants	Design Type	Dosage	Main Findings
Bennett, S. J., et al. **(2013)**. "Computerized Memory Training Leads to Sustained Improvement in Visuospatial Short-Term Memory Skills in Children with Down Syndrome." American journal on intellectual and developmental disabilities 118(3): 179-192.	21 Children Aged 7-12	Computerised Training Random allocation to either intervention or wait list control group Training was completed in a school setting and as part of the school timetable	25 minute per session 10-12 weeks Total of 25 sessions Total Dosage: 450-750 minutes)	• Working memory training (WMT) was found to be feasible to conduct as part of a school setting with children with DS • WMT found to lead to improvements on visuospatial STM • Was not found to have an effect on WM or verbal STN • Improvements maintained 4 months post intervention

Broadley and MacDonald **(1993).** Teaching short term memory skilly to children with Down syndrome. Down syndrme Research and Practice, (2)56-62	51 children aged 4-18 years	Non-Computerised Training Non randomised to experimental or control group	6 weeks No information on specific dosage	• Training program was effective in improving the trained memory skills
Comblain, A. **(1994)**. Working memory in Down syndrome: Training the rehearsal strategy. Down Syndrome Research and Practice, 2(3), 123-126.	24 children and adolescents	Non Computerised Training Non-random allocation to intervention or control group Testing 6 weeks and then 6 months post training	8 weeks No information on specific dosage	• Rehearsal Training increased memory span • Participants were using a rehearsal strategy post training
Conners, F., **(2008)**. Improving memory span in children with Down syndrome. Journal of Intellectual Disability Research, 52, 244-255.	11 Children aged 6-14	Non randomised to intervention or control group Non computerised training – Auditory WM training Intervention group do 3 months memory training, followed by 3 months visual activities and finally another 3 months memory training	9 months No information on specific dosage	Preliminary results Auditory memory training improved auditory working memory

		Control group compete schedule in the opposite order: Visual activities, memory training, visual activities		
***Siberski (2015)**. Computer based cognitive training for individuals with intellectual and developmental disabilities ***This article did not inform study preparation or design, as the study was underway when this was published.**	21+	Computerised cognitive training Randomised blind intervention study Cognitive training were compared to an active control group and a passive wait list control group.	20/30 minutes, 3 times a week for 10 weeks = 600-900 minutes	High adherence rates to program Neither between group or within subject differences reached significance with a stringent alpha but a trend toward improvement was found in cognitive function.
Söderqvist, S., et al. **(2012)**. "Computerized training of non-verbal reasoning and working memory in children with intellectual disability." Frontiers in human neuroscience 6.	Children with DS 7-12	Computerised training Double blind and randomised to intervention group or active control group	20 minutes a day 5 days a week Minimum 20 training sessions for inclusion in analysis	Did not have an effect after 1 year follow up - Recommended more intense training for longer period

			5 weeks 500 minutes	
Van der Molen, M., et al. **(2010)**. "Effectiveness of a computerised working memory training in adolescents with mild to borderline intellectual disabilities." Journal of Intellectual Disability Research 54(5): 433-447.	95 adolescents 13-16 years Mild/borderline ID	Randomly assigned to adaptive WM group, non-adaptive WM group or control group	6 minutes per session 15 sessions 5 weeks 450 minutes	Both adaptive and non-adaptive group showed improvement post training comparted to the control group

Table 2-6: Previous studies using cognitive training with a population of people with intellectual disability

2.6 Summary of Literature Review

While the increasing life span of people with DS is to be celebrated, nevertheless there is the question of whether an increase in longevity also means an increase in the number of years living with a secondary disability, or whether this disability can be confined to the last few years of life (Holland, 2000). What is important is not only adding years to life, but also life to years. It is clear that those with DS are at much greater risk of developing AD, and that one of the early clinical symptoms of AD is executive dysfunction. Thus training executive functions may help in extending the quality of life of people with DS, as was recommended by Kelly et al. (2014). The theory and process of cognitive training is linked to that of cognitive reserve, in that training may increase cognitive reserve, and also existing cognitive reserve may impact on success of training. This idea of modifying the clinical symptoms may be of particular import to individuals with DS, since we know that while everyone with DS will have the neuropathological traits of AD, the clinical symptoms may not present, and cognitive training may show potential in delaying the onset of these clinical symptoms. The associations between these study concepts are illustrated in Figure 2.3.

There is currently a gap in the literature in relation to cognitive training for adults with DS. At the time of development of the study, only six studies were identified on cognitive training which included people intellectual disability and of these, all were focused on children or adolescents. People with DS comprise the largest group of people with genetically determined AD, but to date, have not played a large part in non-pharmacological interventions that seek to modulate clinical symptoms of dementia.

In order to address this gap, this study aims to first examine the use of a cognitive training program with a population of people with DS, and then to examine whether the program has an impact on levels of executive function. The specific objectives of the study are (i) to examine the feasibility of conducting a cognitive training program using an iPad with this population; (ii) to investigate whether cognitive training has a positive influence on executive functions in adults with Down syndrome; (iii) To examine changes in behaviours related to executive functioning after cognitive training as perceived by family members/carers using the Behaviour Rating Inventory of Executive Functions; (iv) to investigate whether variables such as age, IQ, cognitive function, and time spent are predictive of change in scores post intervention and (v) to investigate the relationship between cognitive reserve and executive function.

The following chapter details how the study was carried out, including the research design, the measures used and the procedure adopted to conduct the training.

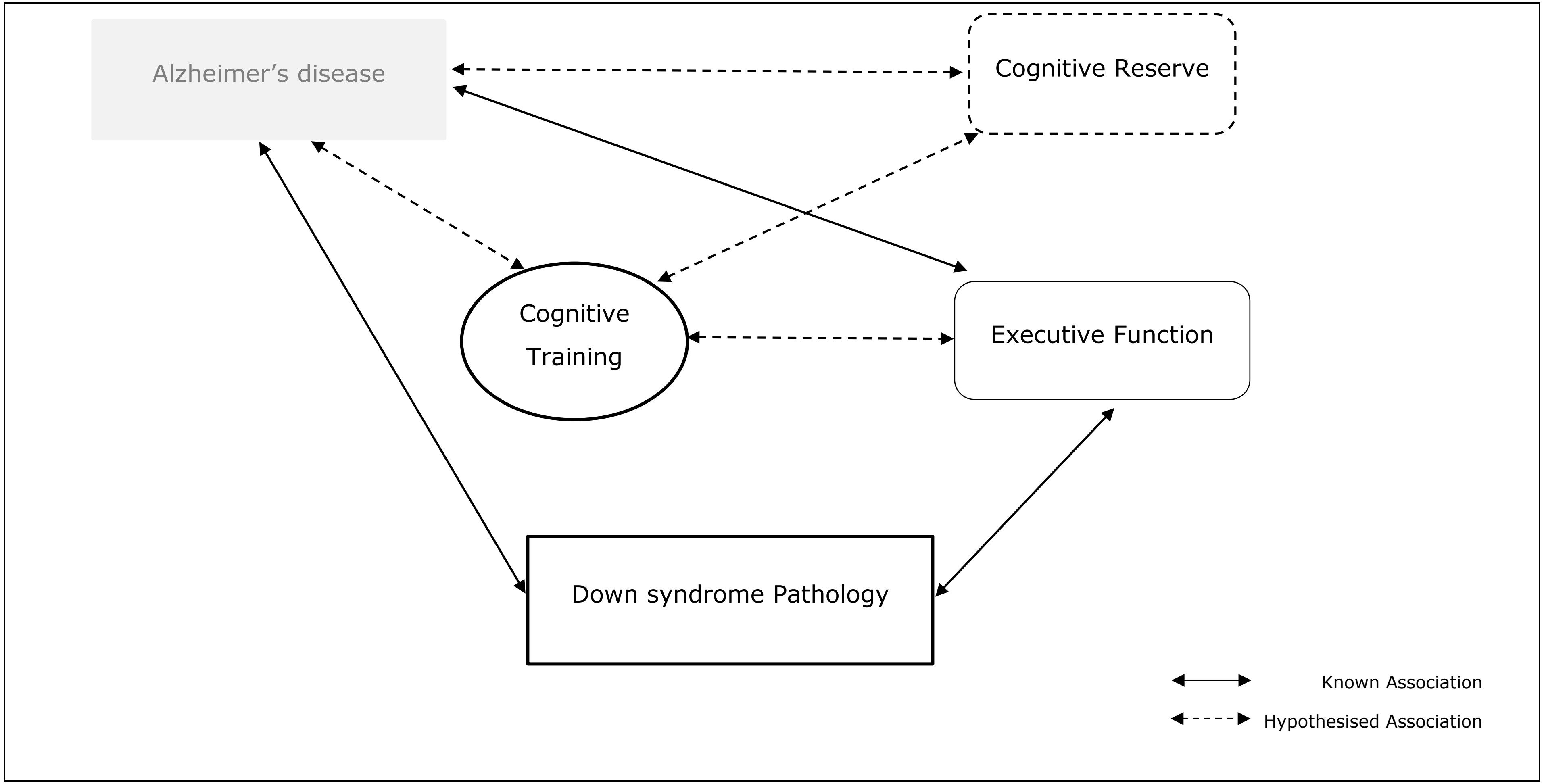


Figure 2-3: Relationship between study concepts

CHAPTER 3

METHODOLOGY

3 Methodology

3.1 Introduction

This chapter details the methodological process of the current study along with rationalisations for measures and tools used. This study examines the feasibility of conducting a cognitive training program with adults with DS, and also examines the effect of the training on levels of executive function. This chapter will outline all of the steps involved in the process to enable replication. A quasi-experimental mixed factorial design with partial crossover was used involving an 8 week intervention period with structured involvement in technology mediated brain training.

This chapter is divided into 8 sections (See Figure 3.1). In section 1, the research design chosen for the study will be discussed, together with the rationale and the measures taken to mediate internal validity concerns. In section 2, the ethical considerations involved in working with a sample of people with Down syndrome will be discussed and the measures taken to ensure that all ethical considerations were upheld throughout the study and the issue of data storage and confidentiality will be explained. Section 3 will deal with the sampling method used and the sample yielded. In section 4, the development of the protocol will be discussed including how executive function measures were chosen, the cognitive training program that was used for the intervention and the inclusion of a focus group with a group of adults with ID to help with the development of the research protocol. Section 5 will discuss the accessible material used in the study. The measures used in the study will be discussed in section 6, which include the dementia assessment used prior to participation, pre and post measures of executive function, baseline measures of IQ, cognitive function, cognitive reserve and the structured questionnaire developed to gauge usability and enjoyment. Section 7 will deal with the intervention process itself, the recruitment process and the structure of the intervention procedure. Section 8 will briefly outline the data analysis procedure for both the quantitative and qualitative data analysis.

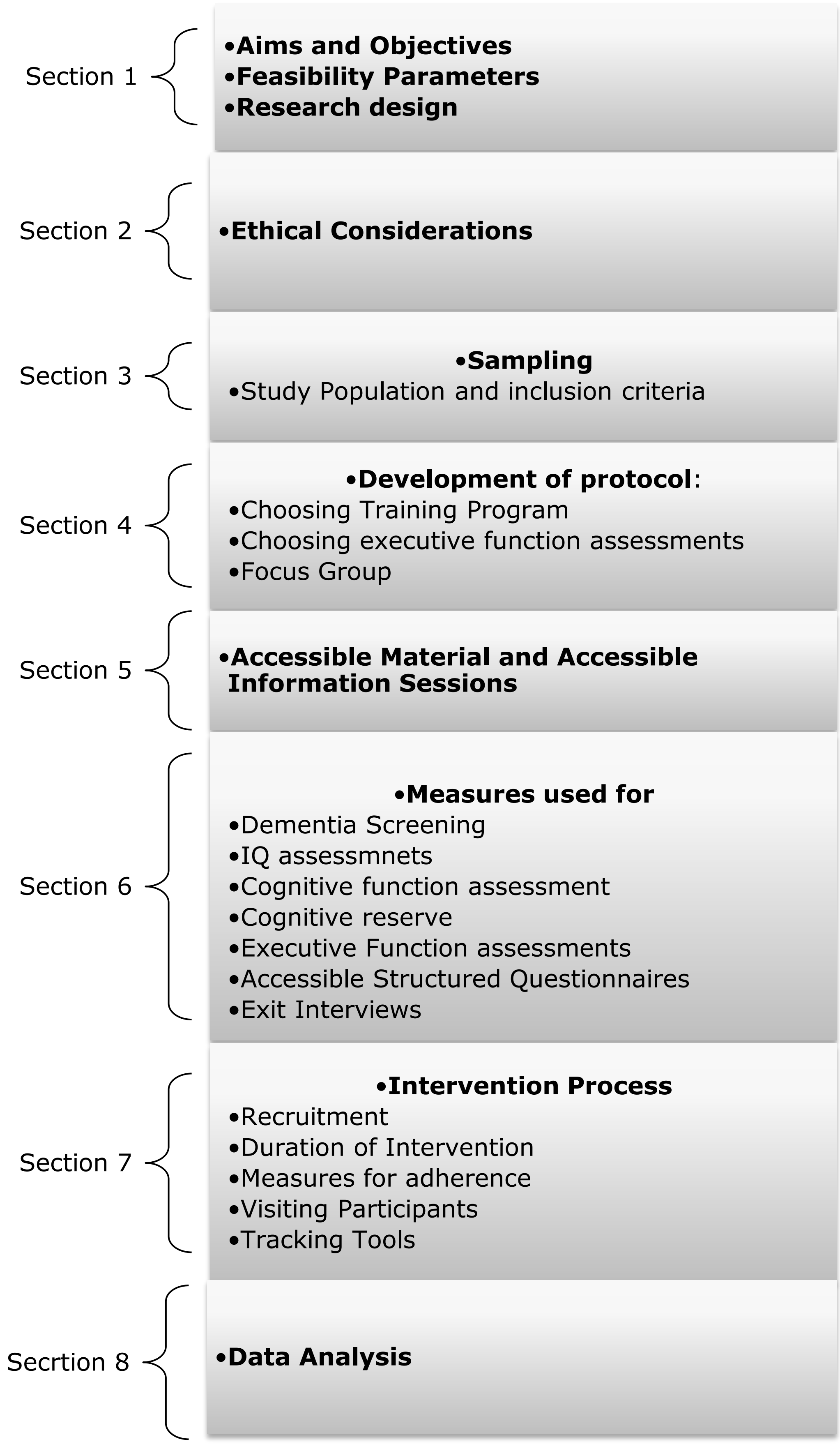


Figure 3-1: Layout of Chapter

3.2 Aims and Objectives

Aim

To assess the feasibility of using cognitive training to influence levels of executive function in adults with Down syndrome.

The objectives of the study are set out as follows:

Objectives

- To test the feasibility of using cognitive training with adults with Down syndrome by exploring ability to use the games, adherence, level of enjoyment and delivery parameters.

- To investigate whether cognitive training has an influence on executive functions in adults with Down syndrome.

- To investigate whether cognitive training has an influence on behaviours related to executive functioning as perceived by family members/carers using the Behaviour Rating Inventory of Executive Functions.

- To investigate whether variables such as age, IQ, cognitive function, and time spent are predictive of change in scores post intervention.

- To investigate the relationship between cognitive reserve and executive function.

Table 3.1 below gives specific details on how the feasibility of the study was measured (Objective 1). Table 3.2 gives an overview of the measures and processes used to achieve research objectives 2-5.

Table 3-1: Feasibility Parameters of the Cognitive Training Program

Feasibility parameter	How was this recorded?
	Participants
Can participants play and progress in the games?	Data from games played were available remotely through the cognitive training program. This allowed the researcher to view performance on individual games, in addition to time spent on individual games Participants' perception of level of difficulty of the games each week was recorded in the weekly structured questionnaire, completed with researcher
Do participants enjoy the cognitive training program	Gathered through weekly questionnaire and explored further in exit interview and through the use of field notes.
Do participants adhere to the training program?	Level of adherence recorded by program
	Staff
How much support is needed to complete the training program?	Question in weekly structured questionnaire asked how many days participant completed game 'on own/with researcher/ with staff/with family. Data from this questionnaire were used for descriptive analysis on whether participants could progress to independent game play during the 8 weeks.
How much training is involved for those supporting participants?	Training for supporters would typically involve the support worker sitting in on 1 training session, which lasted approx. 30-40 minutes. Any further training required by supporters was recorded
	Environment
Can the program be implemented in different environments? (e.g. at home and in day service)	Location of training was recorded in the weekly structured questionnaire

Table 3.2 Matching measures used and process to research objectives

Objective	Measure Used	Process
To investigate whether cognitive training has an influence on executive function in adults with Down syndrome	"Cats and Dogs Stroop" "Tower of London" "Scrambled Boxes" "Spatial Reversal" "Weigl Card Sorting Task" (Cambridge Executive Function Assessment–CEFA) (Ball et al., 2008)	Changes in levels of executive function as measured by EF assessments were analysed. EF assessments was completed at 3 time points. (see Figure 3.5 for explanation). This aided in discounting practice effects and allowed examination of retention of effects after a period of 8 weeks
To investigate whether cognitive training has an influence on behaviours related to executive functioning as perceived by family members/carers using the BRIEF-A.	Behaviour Rating Inventory of Executive Functioning, Adult version (BRIEF-A) (Roth et al., 2014)	The BRIEF-A was completed by a carer/ family member both pre and post intervention. Changes in score were analysed to estimate the effect of the cognitive intervention program in relation to behavioural executive functions.
To investigate whether age, IQ, cognitive function, cognitive reserve and time spent are predictive of change in scores post intervention.	Demographic variables Leiter 3 Test for Severe Impairment (TSI) CEFA	TSI and Leiter 3 scores, demographic information were used to investigate whether baseline IQ, cognitive function, age or gender are predictors of a positive change in EF as a result of the intervention
To investigate the relationship between cognitive reserve and executive function.	Cognitive Reserve Index questionnaire (CRIq) (Nucci et al. 2012) CEFA BRIEF-A	Scores from the CRIq were compared to scores from the EF assessments and BRIEF to investigate how closely cognitive reserve is related to executive function

The acronym BEADS (Brain Exercises for Adults with Down Syndrome) was devised as the name of the project in order to give an identity to the process and so that participants could relate and recognise the study and logo. It was felt that this would have greater impact rather than referring to the project as part of a PhD thesis and would promote a sense of identification with the project. An accompanying picture was added to the name to act as a logo for the study and was used on all material in relation to the study for easy identification. See Figure 3.2.

Figure 3-2: BEADS study logo

3.3 Research Design

This study uses a quasi-experimental mixed factorial design with partial crossover, using a delayed intervention group. This will be discussed including the rationale behind choosing this research design. Possible threats to the internal validity of the project and how these threats were overcome will also be discussed.

3.3.1 Quasi-Experimental Design

An experiment is defined as 'A scientific procedure undertaken to make a discovery, test a hypothesis, or demonstrate a known fact' (Oxford English

Dictionary, 2006). A common feature in all experiments is to deliberately manipulate one variable to see if another variable has changed later – or to ascertain the effect of presumed causes (Shadish et al., 2002). True experimental design necessitates randomisation of groups, which is not always possible in social research for both ethical and practical reasons (Reichardt, 2009, Handley et al., 2011), and will be discussed below in relation to the current study.

The purpose of a quasi-experimental design is to estimate the effects of a treatment (Campbell, 1963), and thus the definition of 'treatment effect' is paramount. To fully understand a treatment effect is impossible, as it requires what Reichardt (2009) describe as 'the ideal comparison'. This refers to the unachievable situation whereby a treatment can be given and not given to the same group of people at the same time. In experimental research, a treatment can be given to one group of people and not given to another at the same time, or a treatment can be given and not given to the same group of people at different times, which results in the estimation of treatment effects being inherently imperfect (Reichardt, 2009). This idea of the ideal comparison reflects the counterfactual model that was discussed by philosopher David Hume in the 18th century (Campbell, 1963) whereby the counterfactual is the knowledge of what would have happened if the experiment did not take place.

While the ideal comparison cannot be achieved, it provides the background to which research design aspires, and thus experiments aim to create a reasonable approximation to this phenomenon. To achieve this, a comparison group should be matched as closely as possible to the intervention group and information collected across groups should be as comparable as possible.

While randomised controlled trials are often seen as the gold standard, there is the risk of not knowing why they worked, if there is no previous research to guide the process.

"If the process is ignored, trivialized, or mismanaged, we'll be measuring the wrong outcome with high reliability, the right outcome with low reliability, or, in the worst case, we won't know what we are measuring. (Raudenbush 2005, p. 29).

As above, true experimental design necessitates randomisation of individuals to groups (Handley et al., 2011, Reichardt, 2009). As was discussed in the literature review, it would be expected that the older adults in the study (those 40-49) would be at greater risk of having the neuropathology of AD than those in the younger age group (30-39), and this could be expected to impact scores of executive function. As the number of participants is small in the current study, the risk of mismatched treatment and delayed intervention groups was too great, and thus participants were assigned to groups based on age. This was essential, as comparing a predominantly younger (e.g. 30-39) 'intervention group' to an older (e.g. 41-49) 'control group' would not give a true reflection of the impact of the cognitive training program.

With a sample size of 40, simple randomisation posed too great a risk of mismatched groups and posed a threat to the reliable estimation of the treatment effect, and thus true experimental design was not suitable. In this study, matching method was used with respect to dividing the treatment and delayed intervention group in relation to age. Matching can balance subjects on covariates to produce comparable groups in relation to a desired characteristic (in this case, age) thus controlling for the potential confounding factor (Sedgwick, 2015). Matching attempts to imitate, as closely as possible the randomisation process, which is the ideal (Stuart and Rubin, 2008). The process for allocation is illustrated in Figure 3.3. Participants were first matched on age within a 3 year age band and subsequently randomised to either the treatment or delayed intervention group, using a coin toss.

When participants first consented to participate in the study, a dementia assessment was completed for all. Following assessment, it was found that no one who had consented had a current diagnosis of dementia, and thus all forty individuals were included in the study. All participants were added to the participant list in the order in which they consented to participate. When a participant was added to the list they were matched with the next person in the list who was within a three year age band. The individual was not matched with anyone that did not fir this criterion, but rather stayed on the list until another participant was added who was within the three year age band. At this stage these two participants were matched. Once all participants were matched, they were randomly allocated to either the intervention group or the delayed intervention group. This allocation was completed using a coin toss

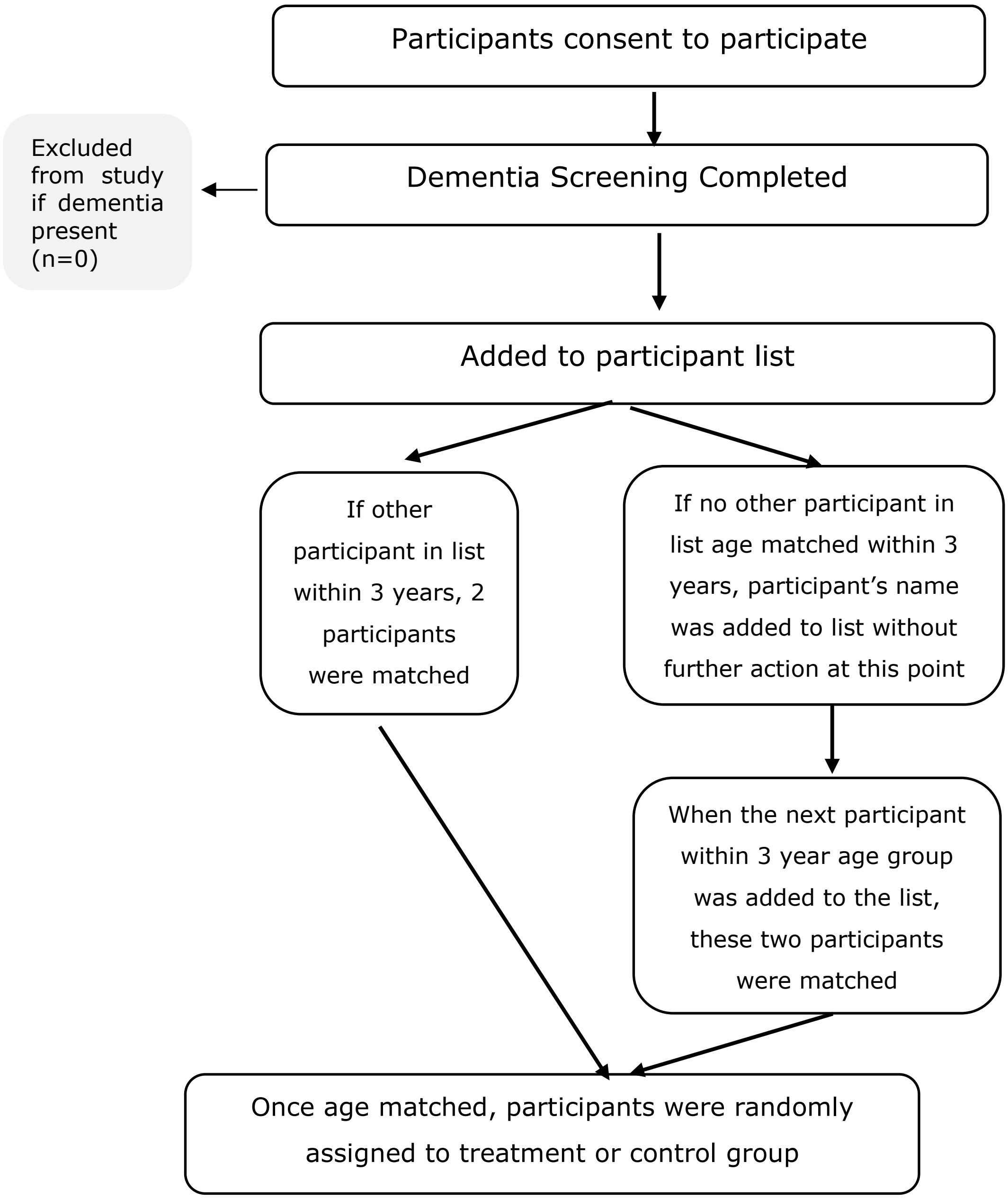


Figure 3-3: Process for Allocation to Groups

Adopting a quasi-experimental approach allowed the current research to assign participants to the intervention group and to the delayed intervention group based on age. This was of particular import with the current study, due to the likelihood of increased neuropathology of dementia of those in the older cohort (Holland and Oliver, 1995), which if groups were severely unmatched could threaten the internal validity of the study. Due to the reasons discussed above the design chosen best suited the study, considering sample size. It is acknowledged, however that the lack of full randomisation limits the conclusions that can be drawn from the study. Without full randomisation, the study can detect and association, but there is the possibility that any association found is the result of a third factor linked to both intervention and outcome.

3.3.2 Delayed intervention group

The delayed intervention group acted as a control group at the beginning of the study in order to control for practice effects of the executive function assessments, with a view to increasing internal validity. This group then received the intervention. See figure 3.4 below for representation of the process. Ensuring all participants received the intervention was essential for the recruitment process where the use of a control group can discourage participation (Slavin, 2007). This adds to the design a partial crossover offering an opportunity to confirm findings from the initial experiment (McCallion et al., 2013).

A mixed factorial delayed intervention group design was used in this study. This is a design that best suited the demands of the current research and provided the most useful and credible results. The mixed factorial design refers to the analysis of both the within subjects (pre/post intervention) and between groups (treatment and control group) EF scores.

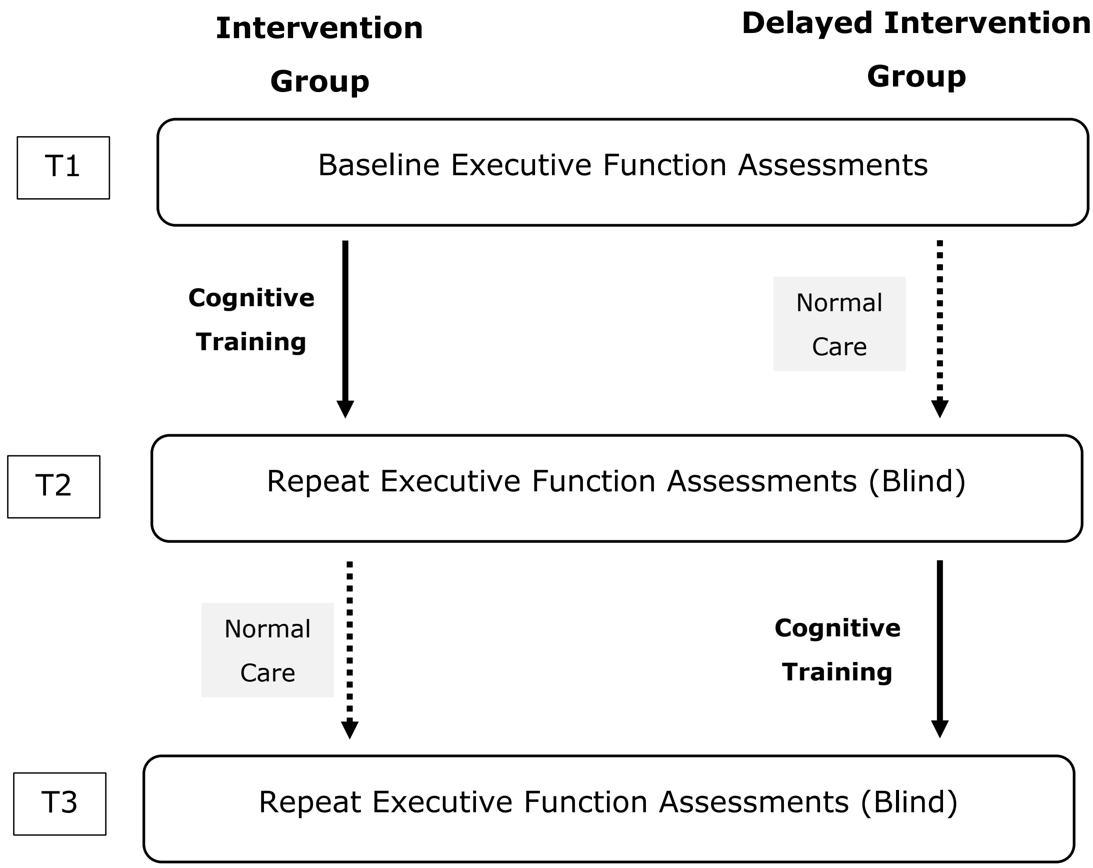


Figure 3-4: Training Process for Intervention group and Delayed intervention group

3.3.3 Internal Validity

Internal validity is the fundamental facet of any experimental design, without which, the results are uninterpretable (Campbell, 1963) and is related to the idea of the ideal comparison that defines the treatment effect (Bryman, 2015).

There are seven threats to the internal validity of a study (Cook et al., 1979):

- maturation
- history
- seasonality
- testing
- instrumentation
- attrition
- statistical regression

Each of these presents a threat that the comparison drawn in the practical setting will differ from a comparison drawn in the ideal setting.
Table 3.2 below deals with each of these threats and how the current study attempted to overcome these.

Table 3-2: Threats to internal validity and how they were addressed

Threat	**Meaning of threat**	**Mediated for in study**
Maturation	Changes are due to time effect	Use of delayed intervention group
History	Event other than intervention could cause effect	Field notes were used by researcher throughout the study, where any changes could be recorded.
Seasonality	Cyclical variation in the outcome variable	N/A
Testing	Pre-test might produce a change in the outcome variable	Controlled for by using repeat of pre-test measures prior to intervention in delayed intervention group
Instrumentation	Change in pre-test to post test in measuring instrument, or instrument applied differently	Pre-test and post-test instruments and method of administration were identical
Attrition	Participants observed at pre-test but not at post-test	Development of BEADS booklet and regular contact with researcher to encourage adherence to the program.
Statistical regression	Refers to the fact that scores on the dependant variable may not be due to natural performers but could be measurement error or chance	The delayed intervention group acted as a control group at the beginning of the study. This allowed for re-measurement of the dependent variable when no intervention was given.

3.4 Ethical Considerations

In this section, the ethical considerations of the project will be outlined along with a discussion of the main challenges of conducting research within this population and how these challenges were overcome. The crucial guiding principles were inclusion of people with DS in the research process, right to privacy and confidentiality, informed consent, benefit to participants. A concerted effort was made to ensure that all material and content related to the research project were accessible to each participant, with a focus on engaging the participant in the research at every step. The researcher adopted a person-centred approach throughout the process, with the interests of the participant central to the research. Emphasis was placed on the potential benefit to the participant from engaging in the cognitive training program. This helped to promote empowerment in the individual to take an active role in promoting brain health. Given the vulnerable nature of the population, it was imperative to ensure that participants were fully aware that they could withdraw from the study at any time without any consequence. This was done through processed consent, where consent was taken at each point of the study. These factors are now discussed in more depth.

3.4.1 Ethical Considerations with population of people with ID

Research involving individuals with an intellectual disability is essential to providing the best care possible. There is however some reluctance to include individuals with ID in research for fear of being harmful, exploitative or unethical (D'abrera et al., 2013). While this precaution no doubt is derived from compassion, it leads to situations where people with ID are denied the opportunity to decide whether to participate in research, thus leading to a paucity in research that could inform high quality care methods (Oliver et al., 2002).

Ethical guidelines arose due to the growing prevalence of unethical research that was being carried out, including a study where children with intellectual disability were infected with viral hepatitis without their knowledge and the issue of informed consent from their parents was debateable (Iacono, 2006). Beecher (1976) paper on experimentation, listed the numerous studies in which unethical practices had taken place and called for the development of ethical guidelines, leading to the development of federal rules governing experimentation on human subjects (Harkness et al., 2001). Since then a number of codes of practice and regulations have been developed in order to ensure participants are protected from unethical practices (Arscott et al., 1998).

There is the possibility, however that the idea of protection has gone too far and that it has led to overly restrictive, and occasionally prohibitive requirements from ethics committees that in turn restrict research that might benefit people, particularly in the field of intellectual disability (Iacono, 2006).

Interestingly, Beecher was not an advocate of research ethics committees, but rather argued that

"the presence of an intelligent, informed, conscientious, compassionate, and responsible investigator offered the best protection for human research subjects" (Beecher, 1976, pg. 366).

3.4.2 Ethical Approval Process

Ethical Approval was granted by the Faculty of Health Sciences in Trinity College Dublin (See Appendix 1). An initial application for the ethics committee included brain imaging as an additional component of the study however it was felt that the inclusion of this component would create an inappropriate burden on the participants as many people with DS find the experience of an MRI quite stressful. On reflection, this decision was appropriate, as there was, at the time, no evidence that the intervention program would be feasible, and thus the inclusion of the brain imaging component had the potential to cause stress without yielding any new information. Following from evidence gleaned from the current study, it would be expected that future research into this area would have sufficient research based evidence on the feasibility of cognitive training and its effect on executive function to include a brain imaging component to further investigate this. All measures to be included in the study were submitted to the ethics committee for review, along with information booklets for family/carer, consent form, accessible information booklet, accessible consent form, and detail of the training program to be used. An amendment was sent to the ethics committee following approval due to a change in two of the measures used. Ethical approval was then granted for these changes.

Following receipt of ethical approval from TCD, ethical approval was sought and granted from the two intellectual disability services involved in the study. Identical material was forwarded for review as was given to TCD and the approval letter from TCD was also attached.

3.4.3 Ethical Principles

The four prima facie principles, introduced by philosopher WD Ross, were adopted in the study: respect for autonomy, beneficence, non-maleficence and justice (Ross and Stratton-Lake, 2002). These principles are binding unless one conflicts with another (Gillon, 1994). The implementation of these four principles in relation to the current study will be discussed.

3.4.3.1 Respect for Autonomy

Autonomy can be described as deliberate self-rule and is an attribute of all moral agents (Gillon, 1994), which, in terms of research encompasses the idea that participants are free to make their own decisions. Autonomy, in terms of Kant's categorical imperative of morality, is also applicable in terms of the research participant:

“Act in such a way that you treat humanity, whether in your own person or in the person of another, always at the same time as an end and never simply as a means” (Kant and Mary Gregor, 1785)

The current study adopted this moral guideline through the inclusion of a number of measures. The information on the study was given to and focused directly on the participant. All material used was accessible (discussed in section 3.7 of this chapter) to facilitate maximum understanding. This notion was carried throughout the study where communication was imperative, which included listening to participants’ opinions of how the training program was going. Information was also sent to key workers/family to inform them of the study, should the research participant wish to discuss any aspects with someone close to them. At each point in the study, the researcher acknowledged the right of the participant to withdraw at any time, and was mindful of noting any signs of distress in the participant, whether verbal or behavioural. No participant showed any signs of distress during the study, however one participant withdrew after one week.

Respect for autonomy also requires that no deception is involved, and thus all features of the study were fully transparent. Keeping appointments and remaining punctual for appointments also falls under the remit of autonomy, as an appointment is an agreement, and to cancel is to break this agreement. As the researcher aimed to visit each participant every week, it was important to ensure that all agreed appointments were respected.

3.4.3.2 Beneficence and Non-Maleficence

Attempting to give benefits to others carries with it the risk of causing harm. Beneficence with non-maleficence deals with the obligation to deliver maximum benefits with minimum harm. There were no known risks to participating in the current study, however the researcher acknowledged the possibility that participants may become bored or frustrated with the training program. The researcher aimed to lessen the possibility of these situations through constantly reviewing the performance of the participant and changing the game, or changing the level of difficulty when necessary, and this approach worked well throughout the training program.

The cognitive training program also encouraged empowerment in participants, both by learning new skills through the medium of the iPad and also through taking an active role in promoting brain health.

3.4.3.3 Justice

Justice in research means treating all participants fairly and equally and this right was respected in the study. This was particularly noted in choosing the design where no group acted simply as a control group, but rather all participants received the same intervention delivered in the same manner. All material was accessible, using both pictures and accessible language in order to increase the inclusion of all participants.

Training was provided to all participants prior to beginning the program to ensure that each individual had equal opportunities to benefit from the training program. During the weekly visit, the researcher was cognisant that participants may have needed extra assistance, and this was provided where necessary. All iPads were equipped with 3G so that participants had equal chance to complete the training.

To date, there has been little research with people with DS in relation to cognitive training. The inclusion of individuals with Down syndrome in a study on cognitive training aimed to lessen the gap between the opportunities afforded to this cohort and those to the general population. As participants in the study were aged between 30 and 49, level of education, and opportunities to develop skills in literacy and IT would have been less available than for the general population. While there is much research and publicity for the general population regarding methods to enhance brain health, especially in the field of dementia prevention/delay, people with Down syndrome, who are at higher risk for dementia are too often overlooked. The current study aimed to address this issue thus promoting justice for people with DS.

3.4.4 Consent

Information sessions were organised for potential participants (described in section 3.7.2) to give information on the study. Following the information sessions, a week was given for participants and family members to consider the information, to ask any outstanding questions and to consider the benefits and drawbacks of participation. Throughout the information sessions and the written information, it was reiterated that participants could withdraw from the study at any time without any consequence. In order for conditions of the Mental Capacity Act 2005 to be fulfilled the participant must be able to show a level of understanding to the researcher. In order to satisfy this, a quiz on key aspects of the project was given prior to receipt of consent (see Appendix 2).

The issue of consent is straightforward, in that it is accepted that research should not be conducted on human participants without their prior consent (Turnbull, 1977). Informed consent is a legal doctrine for practice that is put in place to ensure the rights of patients; this has been extended to research to guarantee that the rights of participants are upheld during the research process. Informed consent necessitates the knowing consent of the individual of their own choice, without any element of fraud, deceit or manipulation (Berg, 1998).

Process consent expands the idea of informed consent, and is an ongoing consensual process involving both patient (participant) and nurse (researcher) to ensure the participant is informed at all stages of the process (Usher and Arthur, 1998).

Process consent was used throughout the study, where it was ensured that the participant understood and felt involved and engaged in the research at all times.

3.4.5 Confidentiality

Participants' right to privacy and confidentiality were upheld throughout the study in accordance with the Data Protection Acts (Government of Ireland 1988, 2003). All participants were given a pseudonymous code and all data were stored under this code. A key was developed by the principal researcher who was the only individual with access to it. The names of the participants were never used for any purpose. No one other than the researcher and supervisors had access to the data.

The computer data were stored on a secure research drive hosted by TCD, accessible only to the researcher and supervisors. The key for the pseudonymised data was kept in a separate folder with separate access codes on a secure research drive.

Consent forms with original signatures were placed in a sealed envelope and did not leave the researcher's person while in transit to the research office. All documents were placed in a locked cabinet on the premise of Trinity College Dublin inside a locked office.

All steps taken were consistent with TCD data protection procedures.

3.5 Study population

A non-probability sampling method was used to recruit participants. To better manage logistical issues, intellectual disability services in the Dublin region were selected. It was necessary for the researcher to engage and meet with participants on a regular basis, and to be available should any problems arise for the duration of the study, which limited the geographical region to be included. Two intellectual disability services in Dublin and Down syndrome Ireland were involved in the study. Information on the study was sent by the gatekeeper to those who met the inclusion criteria (see Table 3.3 below), with an invitation to attend the information session, and a consent form, should the individual wish to return consent without attending the information session.

Participants were between the ages of 30 and 49 with a mild/moderate level of intellectual disability. This age range was chosen as the age range in which neuropathology of AD may begin to occur. This prodromal period was identified as a critical period in which to provide interventions to promote brain plasticity and to reduce cognitive decline (Belleville, 2011).

Table 3-3: Inclusion and exclusion criteria for participants

Inclusion Criteria	**Exclusion Criteria**
Has Down syndrome	Has Dementia
Aged 30-49	Severe/profound ID
Mild/moderate level of ID	Blind
Has no diagnosis of dementia	No hand movement
Lives within the Dublin/Meath/Wicklow/Kildare areas	

One hundred and eleven invitations to participate were sent out in total. Forty four participants consented to participate, however four withdrew prior to the commencement of the study. Two individuals withdrew due to the ill health of a member of their family, one person withdrew due to their own ill health, and one person began a new course, and felt they would be too busy to complete the cognitive training course. Fourteen males and twenty six females participated ranging in age from 30 -49 with 10 having a mild level of ID and 30 having a moderate level of ID.

A dementia assessment was conducted using the CAMDEX-DS for forty participants, and all forty participants continued to complete baseline assessments and began the training program.

Section 4 – Development of Protocol

3.6 Development of Protocol

This section will detail the steps taken in the development of the research protocol, including the cognitive training program that was used, the executive function assessments used, focus groups and development of accessible material.

3.6.1 Scientific Brain Training Pro

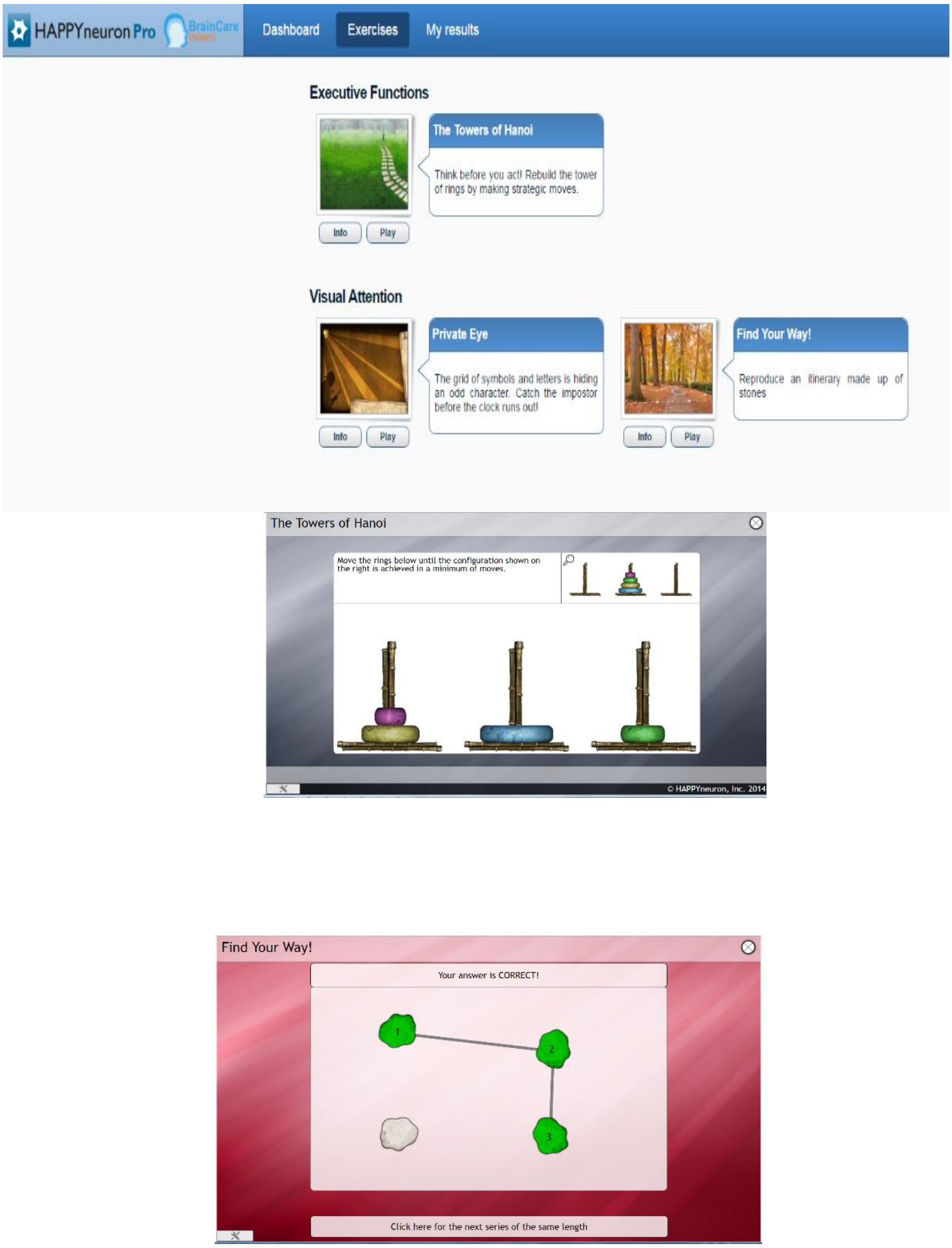
Scientific Brain Training Pro was the cognitive training program that was used to conduct the intervention.

There is a paucity of research into cognitive training with adults with DS and as a result, suitable training programs for use with this population have not been standardised or validated. To date, there is no specifically developed cognitive training program for people with ID.

Scientific Brain Training Pro was developed by neuroscientists, clinicians and researchers as a rehabilitation and remediation program for a wide range of cognitive conditions, including those with intellectual disability. Prior to the current study, this program had not been used with a population of people with Down syndrome.

One of the advantages of Scientific Brain Training Pro was the clear format. The layout of the home screen, and screenshots of two of the games can be seen in Figure 3.5 below.

Figure 3-5: Screen shot of layout and two games used in the cognitive training program



Another important advantage of Scientific Brain Training Pro was that it consisted of a number of games targeting executive functions including attention, memory and planning, problem solving. A focus group was held with a group of students with ID to evaluate the cognitive training program (discussed in section 3.6.3). The researcher chose twelve games, based on the discussion and advice from the focus group, as games that appeared suitable and usable with this population. The games chosen and cognitive process involved are reviewed in Table 3.4 below.

Table 3-4: Games Used in the Program and Area of Focus

Name of Game	**Area of Focus**
Tower of Hanoi	Planning; Problem Solving
Find Your Way	Visual Attention
Private Eye	Attention
Ancient Writing	Visual Attention
Objects Where Are You?	Visual Working Memory
Chunking	Working Memory
Heraldry	Visual Memory
Point of View	Spatial Abilities
Shapes and Colours	Visual Abilities
Displaced Characters	Memory; Shifting
Writing in the Stars	Planning
Under Pressure	Inhibition; Processing Speed

The parameters of the exercises could be changed depending on the abilities of the individual participant. When a player twice achieved a score of 80% or higher in any game, they would continue at the next level the next time the player engaged. If a player achieved score of 50% or below they returned to the previous level of the game. This worked well, as it meant that participants were operating within a level that was challenging, but not so challenging that they were unable to engage in the game.

Another advantage of this particular program was that there was not an over reliance on literacy within the games; that is, literacy wasn't needed to achieve the aim of the game (with the exception of Writing in the Stars and

Heraldry). There was however a large amount of text involved in terms of instructions on the screen and the rules that were given. The researcher addressed this by explaining the rules of the games to participants at each session. After a few initial sessions, the majority of participants were able to navigate the program and the games without reviewing the written instructions for the program.

A number of other commercially available programs were researched and evaluated including Lumosity, Posit Science Brain HQ, MindGames and BrainAge, however none were thought to be useful for a population of people with DS due to overly complicated games, over reliance on literacy skills, or lack of ability to track progress of games. At the time this study began, the only published study of a computerised cognitive program (COGMED) with people with DS used a program which solely targeted working memory (Bennett et al., 2013a). COGMED is a working memory training program that has been used with adults with DS to improve working memory. This proved to be a feasible program for use with a population of children with DS (Bennett et al., 2013b) however as it targeted working memory only, it was not suitable for the current project, as transfer effects were not likely to be seen across all domains of executive function.

3.6.2 Executive Function Assessments

In order to choose the most appropriate measures of executive function for use with adults with DS, a review of literature of studies using executive function assessments with adults with ID was conducted. There was overlap in a number of studies that reported on EF measures with this population (Rowe et al., 2006, Lanfranchi et al., 2010, Ball et al., 2006b, Ball et al., 2008, Willner et al., 2010). In particular, The Tower of London and Weigl Card Sorting were used in both Ball et al., (2008) and Rowe et al., (2006).

On closer examination both measures were found to be suitable for use with this population and were included. Other measures of EF used in Rowe et al.

(2006) (Digit Span, Spatial Span, Motor Preservation) were found to be unsuitable due to high rates of floor effects.

The five measures of EF chosen (listed below) were selected from the battery of assessments used by Ball et al. (2008), which form the Cambridge Executive Function Assessments (CEFA). In an evaluation of executive functioning in adults with DS, Willner et al. (2010) found the CEFA to be suitable for use with a population of adults with DS.

The "Tower of London" and the "Weigl Card Sorting Task" have been validated as EF measures in the general population (Cazalis et al., 2003, Tamkin and Kunce, 1982) and used also by Rowe et al. (2006) with a population with DS. "Cats and Dogs Stroop" was adapted by Ball et al. (2008) from the Day and Night Stroop that has been validated for measurement of EF with children in the general population (Gerstadt et al., 1994). Scrambled Boxes and Spatial Reversal were modifications of tasks used in a number of EF studies in the general population (Espy et al., 1999, Ewing-Cobbs et al., 2004) and were found suitable for use with this population.

The five assessments of EF chosen as used by Ball et al. (2008) were:

- Cat and Dogs Stroop
- The Tower of London
- Scrambled Boxes
- Spatial Reversal
- Weigl Card Sorting Task.

3.6.3 Focus Group

Most commonly, focus groups are used to explore a topic that has not been heavily researched (Stewart and Shamdasani, 2014). It involves a small number of people in an informal discussion of that topic (Onwuegbuzie et al., 2009, Rabiee, 2004) .

3.6.3.1 Aim and Objectives of Focus Group

The aim of the focus group was to test the acceptability of the chosen cognitive training program with a group of adults with an intellectual disability.

The objectives were set as follows:

- To get the opinions of the focus group on the cognitive program selected – Scientific Brain Training Pro
- To assess which modules of the training program were most suitable for inclusion
- To ask advice on the most appropriate method of introducing the program to users
- To get opinions on accessible material developed for the research program (see section 3.7 for description of accessible material)

3.6.3.2 Sample Composite and Recruitment of Focus Group

Twelve students (5 male, 7 female) from the Certificate in Arts, Science and Inclusive Applied Practice in the National Institute of Intellectual Disability (NIID), TCD, participated in the focus group. Participants were aged between 20 and 28 and had either a mild or moderate level of intellectual disability and had ID from different aetiologies. A time was selected with a facilitator from the NIID where the researcher could meet with a group of students to explain both the overall research project and the nature of the focus group. As part of the course, all students completing the certificate in contemporary living engage in a module on research, and it was decided that the researcher would introduce the current study during a class for this research module. The researcher met with the group of students and explained the overall project and the purpose and structure of the focus group, should any student want to be involved. For this meeting an accessible information booklet on the project and on the focus group was developed (see Appendix 3) as well as an accessible consent form (see appendix 4). Any student wishing to take part was asked to fill out the consent form and to return same to the facilitator within a week, who would then pass this on to the researcher. The students decided on a convenient time for the focus group to be held, and a room in the NIID was then booked for this time. It was agreed that anyone who wished to participate in the focus group would meet in the assigned room at the assigned time.

3.6.3.3 Procedure for Focus Group

There were two distinct components to the focus group, which took place in a single meeting; the first was the individual exposure to the proposed training program, and the second was an open but focused group discussion on the accessible material and on the training program.

The focus group convened in a computer room in the NIID where all students had access to an individual computer. One individual used a personal iPad for the duration of the focus group. The researcher gave each member of the focus group access to the cognitive training program and asked each member to try out any of the games available. As the aim of the focus group was to gauge the usability and suitability of the cognitive training program for a population of adults with ID, no instruction was given at the outset. The researcher met with each group member to discuss progress and opinion on the selected game. Differences were found between members of the group in relation to initial engagement and understanding of the games. Some found the games quite simple and were eager to continue with new games, while others found the games challenging and required further instruction in order to successfully engage with the game. The researcher assisted those who found the program challenging, and gave instructions and explained the rules of the game in which the individuals were engaged. If the individual continued to find the game challenging, the researcher completed a game, while audibly explaining the reasoning behind each move and reaffirming the goal and the rule of the game. This was repeated with the focus group member if necessary. If after a given time, the game was found to be too challenging, a new game was picked and actions repeated as necessary.

Participants engaged with the training program for approximately 40 minutes, with the researcher spending time with each individual. At this time, the researcher asked participants to convene in a circle to discuss the program as a group. One previously noted advantage of a focus group is that is viewed as less threatening to participants than one to one interviews and that the environment is useful for discussing thoughts and opinions (Krueger and Casey, 2014). Participants gave their opinion on which games were most suitable and on the perceived level of difficulty of the games. The researcher also showed copies of the accessible information booklet and consent form to members of the focus group and a discussion ensued on whether the information accurately depicted the nature of the project and whether it was accessible.

Notes were taken by the researcher during the discussion. Following the focus group, notes were written up on observations and comments made during the focus group.

3.6.3.4 Analysis of Focus Group

The focus group discussed a number of issues with regard to the training program.

With respect to the first and second objectives;

1. To get the opinions of the focus group on the cognitive program selected
2. To assess which modules of the training program were most suitable for inclusion

The focus group discussion topics included.

<u>What did you think of the program overall?</u>

The response to the individual components were positive with members of the group speaking of their favourite component and what they most enjoyed. The most common remark was that the challenge of the games was enjoyable and gave a feeling of achievement on progressing to the next level. Some more negative comments about the program were directed at the simple graphic that is used. One individual noted that he thought it was going to be more like a video game and suggested that the graphical interface was not very exciting.

<u>What games were most enjoyable?</u>

While there was also a diverse response, with many individuals naming different games, there was a certain amount of agreement in relation to which games were most enjoyable to play: *Chunking, Find your Way, Objects Where are You?* and *The Towers of Hanoi* were named by a number of people in the group. The least tried components were those which relied on higher levels of literacy, including *Writing in the Stars* and *Restaurant*, with the exception of one group member who worked with these games almost exclusively.

" I like the memory game one – it's like the card game I sometimes play" (In relation to Objects Where are You?).

<u>What games were challenging?</u>

There was a very mixed response to this question, due to the difference in approach taken by members of the focus group. Some chose to spend the time trying as many components as possible, while others chose one or two and continued with that which resulted in that component increasing in difficulty.

"After 5 or 6 goes, the tower gets seriously hard" (In relation to *Tower of Hanoi*)

The researcher noted that special attention should be given to the *Sleight of Hand* component. This requires the player to select one of two options. One member of the group appeared to be progressing in this, however on speaking to the individual in relation to tactics used, it became clear that the progression was due to luck and that the individual was choosing at random. Other individuals, however were giving thought and adopting tactics for succeeding at Sleight of Hand, and so while it could be an appropriate game for certain individuals, monitoring progress would be essential.

The researcher then asked the opinion of the group in relation to the third objective that was set out for the focus group

<u>The most appropriate method of introducing the program to users</u>

There was a universal agreement within the focus group that the researcher should pick just a few games at first and to explain them thoroughly, rather than trying to go through the rules of many games

> "There's loads of them so it takes a while to get the rules"

Three members of the focus group had high levels of literacy and were able to progress through the different components of the program, reading the rules without the aid of the researcher. Other members, however were reliant on the researcher to explain the rules and format of the various components. One individual indicated that she wanted to go back to the first component that she tried as she understood the best what was required.

Due to time restrictions, some members of the focus group had to leave prior to discussing the accessible material. Four individuals remained and reviewed the information leaflet and consent form for the BEADS project. There was little discussion overall on the accessible material, with the remaining members simply stating that it was clear and that the information was useful.

It was noted that the lack of discussion around the material could have been due to the order in which it came in the focus group and that the majority of members of the group were not present, however the feedback given was still beneficial.

3.6.3.5 Conclusions from focus group

Overall, members of the group found the program suitable and usable, with some requiring more assistance than others in order to overcome initial challenges. The outcome of the focus group was encouraging in relation to the usability of the chosen program, with the main negative feedback in relation to the graphical user interface. The accessible information booklet and consent forms were reviewed and found to be useful, relevant and accessible. No changes were made to the cognitive training program following the focus groups, as overall the program was found to be usable and suitable. Formatting changes were made to the accessible material, most notable the layout of the BEADS booklet, where the initial design was found to be non-user friendly.

3.7 Accessible Material

Accessible material was developed for each aspect of the study, in accordance with Article 9 of the United Nations Convention on the Rights of People with Disabilities (United Nations, 2006). The Mental Capacity Act 2005 sets out limits in relation to research for those who lack the capacity to understand what the research entails. It specifies that an individual is not to be treated as unable to make a decision unless all avenues to aid in this understanding have been exhausted (D'abrera et al., 2013). All participants in the current study were deemed to have the capacity to understand the nature, purpose and requirements of the study with the aid of accessible material and clear explanations.

An accessible information booklet and consent form were developed for distribution (see Appendices 3 and 4) and reviewed by the focus group. An accessible PowerPoint presentation was also developed for the accessible information session.

3.7.1 Development of Accessible Material

The use of accessible material was an integral part of the research project, from an ethical standpoint and as part of the inclusive nature of the project. In addition to the printed accessible material, accessible information sessions were held and throughout the course of the project, all interactions with participants were conducted in an unhurried, respectful manner where every measure was employed to ensure the participant understood and was comfortable with the process.

All accessible material was developed using the guidelines from the Pathways project: Information for all, which outlines the European standards for developing material that is easy to read and understand. The Intellectual Disability Supplement to The Irish Longitudinal Study on Ageing (IDS-TILDA) published an accessible report of results from Wave 1 and

Wave 2 of the study; these accessible reports were also used as reference guides for developing the accessible material. Key elements for the development of accessible material included: using words that people will know and explaining any words that might be difficult, using headings, keeping sentences short, using the same words throughout the document, using active language rather than passive, using positive sentences rather than negative. All material was produced with a light coloured background with the text in black or dark font using Arial font, at size 14 minimum. Pictures were used alongside the text to assist in comprehension.

3.7.2 Accessible Information Session

Accessible information sessions were held for any potentially interested participants. The gatekeeper was involved in providing the participant with the necessary information so that they could attend these sessions.

3.7.2.1 Attendance at information session

Twenty two people attended the information session at the first intellectual disability session. The information session was held in the morning, as it was identified by the service as the time that was most convenient to the majority who were interested in attending. Fourteen potential participants and eight support persons attended the information sessions. No information session could be facilitated in the second intellectual disability service, as the participants were spread across a number of different centres, and it was felt by the gatekeeper that it would put excessive strain on staff and service users to try to arrange a session in one location. In order to redress this issue, a staff member at each of the centres made contact with each of the potential participants/carers to reiterate the point to make contact with the researcher should they have any questions. The researcher received two phone calls, following this, from family members with questions about the study.

3.7.2.2 Format of Accessible Information Session

The researcher first introduced and gave some background on herself and briefly explained the purpose of the information session. An accessible

PowerPoint presentation was given which highlighted the primary components of the study, including an introduction to the training program, the timelines involved and the measures used. The benefits of the study were also highlighted and the idea of healthy ageing was discussed. The presentation allowed the researcher to expand on the points made in the information booklets that the potential participants had received from the gatekeeper prior to attending the information session.

The presentation was given with the presenter sitting down in the circle to avoid any indication of power imbalance. Questions were welcomed and encouraged throughout the sessions.

In order to help with understanding of the time commitment, a sample timetable for completing the training sessions was drawn up. This illustrated how the training sessions might fit into the diary of a potential participant. Those in attendance at the information session were encouraged to contact the researcher with any further questions, concerns or thoughts on the study.

The information session was found to be particularly useful in opening up a discussion on any prerequisites that people perceived would be needed for the study. Three carers and one service user were concerned that the potential participant did not have any previous experience with using an iPad, and another carer was concerned that lack of literacy skills may preclude someone from taking part in the study. Although these issues were highlighted in the information booklets, it was useful to have a forum for discussing this, as it was an area of concern. The researcher offered reassurance that any previous experience with an iPad was not necessary and that training would be given on all aspects of the study.

3.8 Measures used

This section examines the measures used in the study. A summary of all measures used in the study and discussed in this section is listed below in Table 3.5

Table 3-5: List of measures used in study

Measures Used	To Measure (Screen for*)	When Measured
CAMDEX-DS	Dementia*	Pre-participation
Leiter-3	IQ	Baseline Only
TSI	Cognitive Function	Baseline Only
Cognitive Reserve Index questionnaire	Cognitive Reserve	Baseline Only
Cambridge Executive Function Assessment	Executive Function	3 Time-points
BRIEF-A	Behaviours of executive function	3 Time-points

3.8.1 Pre Participation Dementia Screening

It is a well-established fact that many of those with Down syndrome experience dementia at a younger age than those without DS. A dementia screening assessment was administered to all participants prior to beginning the training program, and if presence of dementia was detected, the individual would not be included in the study. No potential participants presented with signs of dementia, however, and thus all participants began the training program.

3.8.1.1 Measures for screening for dementia

A number of challenges have been identified in diagnosing dementia in this population; lack of baseline measures and lack of standardised measures are examples of such challenges (Tyrrell et al., 2001). A number of instruments are available for screening for dementia in adults with an intellectual disability, all with both advantages and disadvantages. Some instruments considered included the Dementia Questionnaire for People with Learning Disabilities (DLD) (Evenhuis et al., 2007), DSDS (Gedye, 1995), DSME (Haxby, 1989), DLSQ (National Institute of Ageing, 1989). In a 14 year study conducted by (McCarron et al., 2014b) the above mentioned instruments were used and all found to be sensitive to detection of dementia with the exception of the DSMSE. While these instruments were found to be useful and valid with this population, the most significant factor for inclusion in the present study was the need for repeated measures and reliance on change over time, and thus they were not deemed useful for the present study.

There was no longitudinal scope in this study for these measures, and thus, the CAMDEX-DS was chosen, as it is able to examine change in the individual with DS, as noted by a carer/family member.

CAMDEX-DS

The CAMDEX was developed in 1986 as an instrument to diagnose dementia in the general elderly population (Roth et al., 1986). The CAMDEX-DS is a modified version which places more emphasis on the informant interview (Gangadharan and Bhaumik, 2008). It distinguishes decline from pre-existing intellectual and functional impairments and emphasises change (Ball et al., 2004). Validity and reliability for use in the diagnosis of dementia in adults with DS is evidenced with inter-rater reliability of >0.6 for all items (Ball et al, 2004). The usual practice of determining validity of dementia diagnostic instruments has been established through comparison of findings of clinicians. One major flaw in this is that clinicians tend to use highly correlated assessment methods as the instrument to be validated, and thus high levels of agreement would be expected (Ball et al., 2006b). In order to test the concurrent validity of the CAMDEX–DS, a level of agreement was sought between the informant based interview and the objective measurement of decline from the previous 6 years. Predictive validity at a 6 year follow up was found to be high (Ball et al 2006). The CAMDEX-DS was also found to have high sensitivity (0.88) and specificity (0.94) (Gangadharan, 2008).

The researcher administered the CAMDEX-DS informant interview with a key worker or carer who knew the potential participant at least 6 months or more. The researcher then discussed the informant interview with a Clinical Nurse specialist in Dementia who was blind to the age, gender and cognitive function of the participant. A decision was made based on the CAMDEX-DS as to whether the individuals were likely to have dementia. It should be noted that the researcher was not making a clinical diagnosis, but rather included this measure for all participants as an indication that a diagnosis of dementia was not present at the beginning of the project.

3.8.1.2 Preparing for Dementia Screening and Dementia Screening Process

In order to prepare for the dementia screening process, the researcher attended a number of dementia screenings of individuals with ID with a clinical nurse specialist in dementia. The assessments helped to understand the process of dementia screening and how the history is taken. The CAMDEX-DS was also administered with a key worker/family member of an individual with DS and confirmed dementia in order to gain an insight into the types of answers given and to appreciate where further probing may be necessary.

Following the dementia assessments, these were discussed with the PhD supervisor, a leading expert in Down syndrome and dementia.

None of the participants were deemed to have dementia at the beginning of the study, and as such met the eligibility criteria to be included in the study.

3.8.2 Pre Intervention Assessments

Pre-intervention assessments were administered to acquire a baseline measure on a number of different aspects of the cognitive and environmental status of participants. This was done both to allow an understanding of whether the intervention had an impact on participants, and also, if there was a change as a result of the intervention, to allow an understanding of what pre-existing characteristics of the individual may have contributed to this change. All measures used in the study were administered at baseline, with some being repeated at different points during the study (See figure 3.1). Measures included, Leiter 3 as an IQ assessment, Test for Severe Impairment (TSI) as a measure of cognitive function, the cognitive reserve index questionnaire as a measure of level of cognitive reserve, BRIEF-A as a measure of behavioural executive function and five measures of EF ("Cats and Dogs Stroop", "Tower of London", "Scrambled Boxes", "Spatial Reversal" and "Weigl Card Sorting") as a baseline measure of executive function.

3.8.2.1 Baseline Measures not repeated

Three measures were administered at baseline and were not administered again. These measured IQ, cognitive function and level of cognitive reserve. The intervention program was not expected to have an effect on any of these constructs, and thus repeat administration was unnecessary. The purpose of all 3 measures was to investigate whether scores on the measure were a predictor of change/magnitude of change as a result of the intervention program.

3.8.2.1.1 Measure of IQ

High general intelligence factor or g(IQ) can be defined simply as the phenomenon whereby an individual is good at a wide range of tasks that demand high cognitive function (Flynn, 2007). There are many measures of IQ that are validated in the general population, but are not suitable for use with a population of adults with DS. Due to specific delay in language compared to other areas of ability, use of certain IQ scales in a population of adults with DS would risk underestimation of development level (Glenn and Cunningham, 2005).

One test of IQ that has been used in a number of studies with a population of children with DS is the British Pictorial Vocabulary Scale (Dunn and Dunn, 2009). This measure was considered, however it has not been normed for adults with DS.

Leiter 3

The Leiter 3 (Roid et al., 2013) is the most recent re-standardised version of the original Leiter International performance scale (Leiter, 1980). A re-standardisation of norms was necessary due to the Flynn effect, which sees an increase in IQ scores in newer generations of test takers, leading to an artificial assumption that the IQ of a population is rising (Deary et al., 2009). The Leiter 3 is re standardised and involves non-verbal measures which assess fluid reasoning and visual spatial ability, minimising the impact on verbal ability in assessing overall cognitive function (Glenn and Cunningham, 2005).

The Leiter-R (Roid and Miller, 1997) was standardised in over 2000 children and adolescents up to 20 years of age. The Leiter-R had high internal consistency (.94-.95), test re-test reliability (0.80) and construct validity and was suitable for use with a population with DS (Glenn and Cunningham, 2005). The Leiter 3 was re-designed to cover a wider age range (3-75+) and has been standardised in 1603 individuals, including those with intellectual disability.

The Leiter 3 has fewer subtests than its predecessor. The subtests retained from the Leiter R were kept because of high reliability co-efficient, with others that showed less reliability being discarded.

Four sections were used in the Leiter 3 to compute a total non-verbal IQ score; Figure Ground, Form Completion, Classification and Analogies and Sequential Order. Each of these sections yielded a raw score, which were converted to normative scaled scores according to chronological age. The scaled scores of the four subtests were summed and then converted to a composite non-verbal IQ score, where the mean is 100 (SD=15).

As classified by the World Health Organisation (WHO), an IQ in the range of 50-69 indicates a mild level of ID, IQ range of 35-49 indicates a moderate level of ID, with 20-34 severe and an IQ of less than 20 indicating a profound level of ID.

If a raw score of 0 is obtained, the total score is deemed to be indeterminate, and based on the Leiter 3, the true level of functioning for that individual is unknown (Roid et al., 2013). Data was missing for three individuals where an indeterminate score was found.

The test took approximately 30 minutes to complete.

3.8.2.1.2 Measure of Cognitive Function

Obtaining a measure of cognitive function was important in this study primarily for 2 reasons. Previous research has shown that those with DS often show signs of cognitive decline prior to an official diagnosis of dementia (McCarron et al., 2014b). A measure of cognitive function prior to intervention was necessary, as the intervention may have been successful, but only for those with relative intact cognitive function, but not for those who had already begun to decline. Recording a score of cognitive function pre intervention also allowed statistical analysis to be conducted on whether level of cognitive function was a predictor in a successful outcome of the cognitive intervention program.

Test for Severe Impairment (TSI)

The Severe Impairment Battery (SIB) (Saxton, McGonigle, Swihart and Boller, 1993), was considered, which had good test-re test reliability and validity, however a number of problems were identified in using this measure with a population with DS, including automatic failure for many participants due to the need to read an item aloud and repeated questions become tedious and patronising (Witts and Elders, 1998).

The Test for Severe Impairment (TSI) (Albert and Cohen, 1992) measures a range of cognitive functions including motor performance, language production, language comprehension, memory, conceptualisation, and general knowledge. The TSI has been shown to be a valuable measure for use in testing cognitive function in a population with DS and found to have high validity and reliability (Interrater reliability: 0.97, Test Retest Reliability: 0.98, Validity: 0.94 (Cosgrave, 1998), and good internal reliability (0.90)(Albert and Cohen, 1992). The TSI has 24 items, and has been found to be a useful assessment with this population, with participants in previous studies reporting high levels of acceptability (McCarron, 2011)

The TSI took approximately 10-15 minutes to complete.

3.8.2.1.3 Measure of Cognitive Reserve

Cognitive Reserve attempts to explain how there is not always a direct relationship between severity of brain damage and deficit in clinical symptoms (Stern, 2009) and suggests that those with high cognitive reserve would be able to withstand more age related brain changes and disease pathologies than those with low cognitive reserve, using pre-existing cognitive processes (Nucci et al., 2012).

The current study included a measure of cognitive reserve in order to investigate the relationship between level of cognitive reserve and level of executive function through comparing scores from the Cognitive Reserve Index questionnaire (CRIq) and the objective scores on the CEFA at baseline.

Cognitive Reserve Index questionnaire (CRIq)

The CRIq was developed by Nucci in 2011 as a means of collecting and quantifying the amount of cognitive reserve acquired during a person's lifetime (Nucci et al., 2011). The CRIq collects demographic information (date and place of birth, gender, place of residence, nationality, marital status) and a further 20 items grouped into three sections – education, working activity and leisure time, each of which returns a subscore. The questionnaire calculates each activity in terms of number of years and frequency of activity. A measure of IQ is not included in the index as although the two are related, they are nevertheless distinct. The CRIq has a reliability of .062; due to lack of other standardised measures for estimating cognitive reserve, concurrent validity could not be obtained (Nucci et al., 2011).

The CRIq took approximately 10 minutes to complete

3.8.3 Measures repeated at 3 time points

The neuropsychological EF assessments and the Behaviour Rating Inventory of Executive Function (BRIEF-A) as the primary outcome measures were repeated at three time points during the study. Both study groups completed the measures at baseline, with the intervention group then completing the intervention and the control group continuing with regular care, after which both groups repeated the measures again. The control group then went on to complete the intervention while the intervention group returned to normal care. The assessments were repeated again for a third time. This approach was designed to test if the findings of the initial pre/post assessment scores would be confirmed with the delayed intervention group. There was an additional opportunity to see whether the intervention group maintained scores following an 8 week period of no intervention (See Figure 3.6 for explanation).

3.8.3.1 Blind Assessment

Repeated measures of EF were administered by an independent assessor, who was blind to whether the participant had completed the cognitive training program, thus minimising bias and increasing validity (Kaptchuk, 1998, Hersen and Gross, 2008). There is also some evidence to suggest that desire to please the investigator may lead to temporary improvements in performance (Green and Bavelier, 2008a), and thus this may be diminished with the introduction of someone with whom the participant was not familiar. The independent assessor was trained in the administration of the EF assessments and had both observed the way in which the researcher administered the assessments and had completed mock assessments with a volunteer with an intellectual disability. In the mock assessment, the researcher was also present and also scored the assessments. The scores given by both were compared at the end of the mock assessments to ensure that researcher and independent assessor had the same interpretation and scoring methods. There was full consensus in the scores given on the EF assessments following the mock assessment.

Reasons for 3 time points for Intervention group

Time 1	**Time 2**	**Time 3**
Pre Intervention CEFA	CEFA repeated post intervention	CEFA repeated 8 weeks post intervention
Reason	**Reason**	**Reason**
Get Baseline Measure	To examine whether the intervention influences measures of executive function?	To examine whether there were changes (if any) in executive function retained after 8 weeks?

Reasons for 3 time points for Delayed Intervention group

Time 1	**Time 2**	**Time 3**
Pre Intervention CEFA	Repeat CEFA without completing intervention	CEFA post intervention
Reason	**Reason**	**Reason**
Get Baseline Measure	To examine whether repeating the CEFA increase scores even without intervention?	To examine whether the intervention influences measures of executive function?

Figure 3-6: Reasons for repeating EF measures at 3 time points

Executive function is an umbrella term for the cognitive processes involved in planning, working memory, attention, inhibition (Chan et al., 2008), and are thought to comprise a set of abilities in order to achieve a goal (Stuss, 2011). The Cambridge Executive Function Assessment was administered to all participants at three time points in the study. The specific measures were: Dogs and Cats Stroop, Spatial Reversal, Weigl Card Sorting Test, Tower of London and Scrambled Boxes. As may be seen in Table 3.6, these tests measure a range of executive function elements, including inhibition, set shifting, planning and working memory.

Table 3-6: Cognitive Process targeted by neuropsychological assessments

Assessment	**Cognitive Process**
Cats and Dogs Stroop	Inhibition, working memory
Tower of London	Planning, working memory
Scrambled Boxes	Working memory, inhibition, attention
Spatial Reversal	Set shifting, inhibition, attention
Weigl Card Sorting Task	Set Shifting

Procedure for Measures of Executive Function

3.8.3.1.1 Cats and Dogs Stroop:

The “Cats and Dogs Stroop” tested response inhibition and working memory. The “Cats and Dogs Stroop” was taken from Ball et al, (2008). A series of 16 drawings of cats and dogs were presented to participants in the following order ‘c,d,d,c,d,c,c,d,d,c,d,c,c,d,c,d’. In the first instance, the participant was asked to point to each picture as quickly as possible and to name either ‘cat’ or ‘dog’.

Following completion, and once the researcher was satisfied with the response, the experimental condition began. In this, the participant was asked to say ‘dog’ when pointing to a cat and ‘cat’ when pointing to a dog. The researcher demonstrated what was required before commencing.

There was a maximum score of 16 points, with 1 point for each correct response in the experimental condition.

3.8.3.1.2 Spatial Reversal

Two identical boxes were used for the assessment. At the beginning of the assessment, coins were hidden under both boxes, without the participant seeing. The participant was instructed to choose a box. The coin was then hidden under the box first picked by the participant until he/she made four consecutive correct responses, or until 10 trials had been completed. If after 10 trials the set had not been obtained, the assessment ended. After four correct responses, the coin was then switched to the opposite box (the reversal stage) and the procedure was repeated (Ball et al., 2008).

3.8.3.1.3 Weigl Card Sorting Task

The Weigl Card Sorting Task assessed extra dimensional set shifting and abstracting common principles (Ball et al, 2008). The participant was presented with 12 foam pieces which comprised of 4 colours (red, yellow, blue, green) and 3 shapes (square, circle, triangle). Participants were asked to sort these into piles that belonged together (i.e. either by colour or by shape). Upon completion, the participant was asked to sort the foam pieces in a different way. If the participant failed to sort them the researcher used prompts:

Prompt 1: "Here you have grouped them according to colour/shape. This time you must group them differently".

The next prompt given if the participant did not regroup was
Prompt 2: "Here you have put them in piles of red, green, blue, and yellow. This time try to make the piles differently".

The researcher then began sorting the shapes into piles according the new set and said
Prompt 3: "See if you can put the rest of the cards in piles like this".

After this, the researcher gave the rule explicitly.

Scoring for the Weigl Card Sorting was a maximum of 5 points for shifting set without any prompt. 1 mark was deducted for each prompt. The prompts were taken directly from Ball et al. (2008).

3.8.3.1.4 Tower of London

An adapted version of the Tower of London was used which was validated for use with people with intellectual disability (Masson et al., 2010). The Tower comprised a board with three poles of differing height, the tallest to accommodate 3 balls, the next 2 balls and the shortest 1 ball. There were 3 coloured balls which could be moved across the poles to achieve an end state goal, each requiring a minimum number of moves. The test was completed manually, with 2 identical sets, one for the researcher and one for the participant. The goal was for the participant to recreate the configuration of the researcher. At the end of each level, the participants' set were returned to a starting state and the researcher reconfigured the new level behind a screen.

At the start of the test the participant had to complete a one move challenge, which increased in difficulty upon success, up to a 6 move challenge. The configurations for all trials can be seen in Appendix 5. This was changed slightly from the study conducted by Ball et al, (2008) which began with a 2 move challenge up to a 5 move challenge. This was based on previous research by Rainville et al. (2002) and would allow a larger range of scores.

Each challenge level (1 move, 2 move, 3 move, 4 move, 5 move, 6 move,) had 3 trials, with participant receiving 3 points if a correct solution was completed within the minimum moves on the first trial, 2 points if completed on second trial and 1 point if completed on the third trial. This was the same scoring method as used previously (Rainville et al., 2002, Ball et al., 2008, Krikorian et al., 1994). In order to avoid distress, the trial was

stopped if the participant did not get the correct response on three trials in two consecutive levels.
At the beginning of the trial, the researcher ensured that the participant could differentiate between the coloured balls, and also that the participant could count the 6 coloured balls (Masson et al., 2010). The researcher also checked that participants had the motor movement to place the balls on the poles. If these motor skills were not present, then researcher would ask the participant to explain where they wanted the balls to go and the researcher would place the balls for the participant.

The rules were explained to the participant and the researcher demonstrated a 2 move level that was not going to be used in the trial and followed next with a practice trial.

3.8.3.1.5 Scrambled Boxes

In the practice stage, there were three boxes marked with different shapes. The participant watched as a coin was placed underneath each of the boxes. After a short delay, the participant was asked to find a coin. If a coin was found, it was removed and the box was replaced, after which the participant was asked to find another coin, and this process was repeated until all three coins were found, or the participant made four errors. In the experiment stage, the same process applied, the boxes were scrambled in a random order during the delay. If the participant was successful with both the stationary and the scrambled components with three boxes, the process was repeated with six boxes. In this case, testing continued until all the coins had been retrieved or until seven errors had been made. (Ball et al., 2008).

3.8.3.2 Behaviour Rating Index of Executive Function – Adult

The Behaviour Rating Inventory of Executive Function – Adult Version (BRIEF-A) is a standardised measure that captures everyday behaviours of executive function, using either a self-report or informant report form (Roth et al., 2014). The informant report form was used in this study. The BRIEF-A has good test re-test reliability (0.88) and internal consistency (0.80-

0.98). This is a pen and paper measure and consists of seventy-five items, which are used to create nine clinical scales; Inhibit, Shift, Emotional Control, Self-Monitor, Plan/Organise, Initiate, Task Monitor, Working Memory, Organisation of Materials (See Appendix 6 for list of questions). These scales then combine to form two broad indices – Metacognition Index and Behaviour Regulation Index, a combination of which form an overall Global Executive Composite Score.

The measure also includes three validity scales;

- Negativity Scale measures the extent to which selected items are answered in an unusually negative manner, which may indicate the respondent may have an unusually negative response style
- The Infrequency Scale measures the extent to which the respondent may have answered questions in a haphazard manner, or perhaps may have attempted to portray the individual in a particularly positive or negative manner
- The Inconsistency Scale indicates whether the respondent answered similar items in an inconsistent manner.

Table 3.7 describes the behaviours of executive function measured by the scales in the BRIEF-A.

Table 3-7: Description of behaviours related to scales in BRIEF-A

Scale	**Behaviour**
Inhibit	Control impulses, appropriately stop on behaviour at proper time
Shift	Move freely from one situation to another; solve problems flexibly
Emotional Control	Modulate emotional responses appropriately
Self-Monitor	Keep track of effect of own behaviour on others; attend to own behaviour in social context
Initiate	Begin a task, fluidly create ideas
Working Memory	Hold information in mind for the purpose of completing a task
Plan/Organise	Anticipate future events; set goals; develop appropriate steps to achieve goals
Task monitor	Check work; assess performance during and after a task
Organisation of Materials	Keep workspace/living space in orderly manner

Taken directly from Roth et al., (2000)

3.8.4 Structured self-report questionnaire

3.8.4.1 Purpose of the questionnaire

A structured questionnaire was developed (See Appendix 7) to be administered with each participant during the weekly researcher's visits. The purpose of the questionnaire was:

- To examine the experience of the participant in participating in the training program and to track if and how this changed throughout the 8 week period, in terms of enjoyment and perceived difficulty.
- To examine amount and type of support that was received
- To gather information on where the training took place

The measure was very quick to administer, as the researcher was conscious not to overburden the participant each week. It was important to include this self-report measure to capture the subjective experiences of the participants while taking part in the intervention program.

3.8.4.2 Development of the questionnaire

The questionnaire was developed to the standard of accessible guidelines, including pictures to help to clarify the Likert scale used. In the past decade, research has been conducted on the validity and reliability of using Likert scales with a population of adults with ID. Hartley et al (2006) reviewed 51 studies conducted between the years 1979 and 2005, of which 20 reported response rates for Likert type scales. They found that response rates for Likert type scales were comparable and often higher than for yes/no or open ended questions (Hartley et al, 2006). In a study conducted by Mindham and Espie (2003), it was found that the three option response rate was useful and easy to use. The developed questionnaire used a 3 option response in order to better track any change that occurred over the 8 week period. Participants were asked 'how much did you like the games this week?', 'how hard did you think the games were this week?', 'how excited are you about continuing next week?'.

3.8.5 Exit Interview

Twenty exit interviews were conducted; 10 interviews were conducted with participants and 10 with carers. The questions posed to the participants and to the carers can be seen in Table 3.8. In qualitative research saturation is said to be reached when there is no new data, no new themes and no new coding (Fusch and Ness, 2015). There is no consensus on the number of interviews required to reach saturation, but a recommendation of six to twelve interviews was given by Guest et al. (2006). Following the 10 interviews conducted with participants and carers, it was felt that saturation had been reached.

The level of support given from carers varied widely, with some participants receiving no support, some receiving support but perhaps not from the same individual and some receiving support throughout the program. An exit interview was conducted with a carer who was consistently involved with the training, whether staff or family member. Interviews were recorded, with permissions from the individual and were transcribed.

Table 3-8: Exit Interview Questions

Participant
Did you like the games?
Did you find them hard?
Would you do it again?
What was your favourite thing about doing the training program?
Did you ever find it boring?
Would you have done it for longer?
Did you find 20 minutes long?
Would you make any changes if we were doing the program again?
Parent/Keyworker
What did you think of the training program?
Did you think it was worthwhile?
Do you think X enjoyed the program?
Do you think 8 weeks was long enough/too long…would you have done it for longer?
Would you make any changes if we were doing the program again?
Did you find that you had to do a lot of work to help X with the program?

3.8.6 Field Notes

Field notes were recorded throughout the intervention process to record information on the setting, behaviours and conversations that took place during the cognitive training sessions. These notes were recorded in as much detail as possible immediately following the training session. These notes provided insights into participants' and support persons' thoughts throughout the intervention process.

3.9 Intervention Process

In this section, the intervention process will be discussed, including recruitment, duration, the procedure, including the first training session and measures put in place to promote adherence to the training program. See Tables 3.9 and 3.10 below for a full summary of the intervention process. The lead researcher completed all dementia assessments, all baseline assessments including IQ, cognitive ability, cognitive reserve and baseline EF assessments. The lead researcher also completed all of the training sessions with participants throughout the study. In order to reduce bias, an independent researcher completed all follow up EF assessments, and was blind to whether the participant had completed the cognitive training.

In measuring IQ, cognitive ability, cognitive reserve, age and level of ID, an attempt was made to control for external variables that could have an effect on the outcome of cognitive training program. There were however a number of external components that could have had an active effect on the intervention. Figure 3.7 below displays these active components.

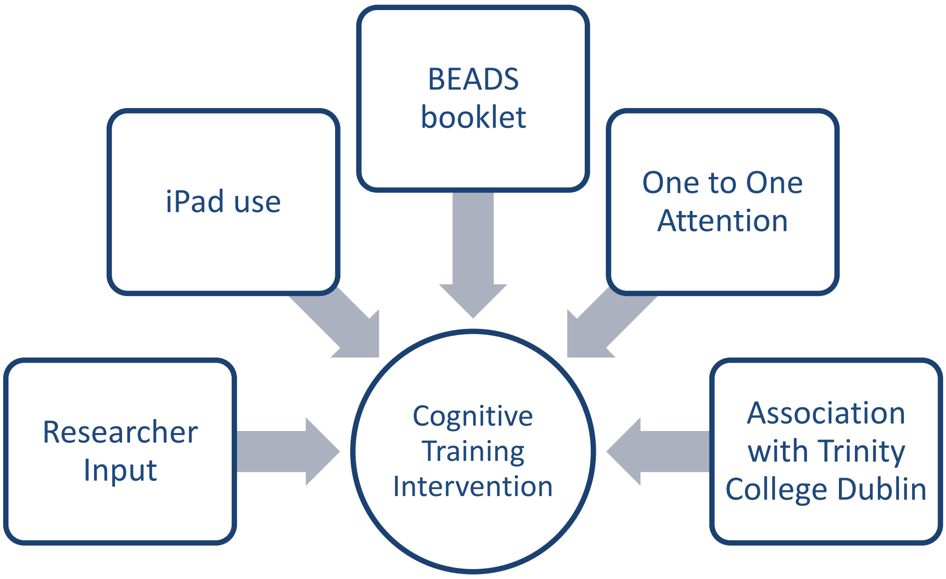


Figure 3-7: Active components of the intervention

The delivery of the training program was standardised to control for these components as much as possible. The fact that the training was delivered on an iPad, which was unfamiliar to half of the sample could have an effect on the individual. All participants who were previously unfamiliar with an iPad learnt to navigate this which enhanced their learning experience over and above the cognitive training program. Similarly, participants met with the researcher and had one to one time at least once a week which was novel. The input from the researcher while conducting the training sessions could have had an active effect on the intervention. Participants were very aware that the training was part of a study conducted in Trinity College Dublin, and regarded this with importance. This association could have influenced the decision to adhere to and complete the training program.

__Table 3-9: Delivery of baseline assessments__

Dementia Screening (no participant involvement) **Upon receiving consent a meeting was arranged with carer that knew the participant for at least 6 months to administer CAMDEX-DS** **Following CAMDEX-DS, consensus with specialist in dementia and down syndrome**	
Dementia Screening	<u>Presence of dementia noted</u> Advise to attend a clinical dementia screening. Did not participate in the study (n=0) <u>No dementia noted</u> Contact made with participant and carer to arrange a day for pre intervention assessments (n=40)
Leiter 3 and TSI **Average time spent approx. 60 minutes**	
TSI	Both Leiter 3 and TSI were delivered at the same time These were delivered in the same room which needed a table and two chairs The TSI was administered first

Leiter 3 assessment	After a very short break, the Leiter 3 was administered The format of the Leiter 3 was very different as it is non verbal At the beginning of this it was noted that "This is a different type of game, where we can't talk" Each component of the Leiter 3 has 3 different age groups 3-5, 6-9 and 9+ Each component began with the 9+ and if/after 1 fail went to 6-9; if/after 1 fail went to 3-5 (as per assessment guidelines) A clipboard was used to score discreetly Four components were completed in the Leiter 3. Each one was stopped once 7 cumulative fails was reached.
Carer involvement was not needed for either of these, but could sit in if desired. The carer was instructed not to assist and to sit behind the participant to avoid accidental/ non-verbal guidance/influence	
Executive function assessment and BRIEF and first training session (participant and carer) **Average time: Participant- 1 hr; Carer- 15 minutes**	
Executive Function Assessments	The CEFA was delivered in similar circumstances as previous assessment (rules and delivery of assessments described previously in section 3.8.3.1) (A room with table and two chairs was needed) Score sheets were discreetly as assessments completed

BRIEF-A and CRIq	Carer was asked to complete BRIEF-A and CRIq during the time participant was completing the executive function assessments. These were completed independently or with assistance from the researcher if necessary

Delivery of second and third executive function assessments

Executive Function Assessments	Executive function assessments at times 2 and 3 were blind assessments administered by independent assessor. Assessor received training in administration and had completed mock administration Administration of executive function assessments was identical to baseline procedure, except with blind assessor replacing the principal researcher

Table 3-10: Delivery of the intervention

First Training Session with participant and carer	Researcher met with participant and key worker/carer who would be primarily assisting with the training program. Completed the CEFA with participant and the BRIEF-A with carer (see above). Demonstrated how to turn on iPad and how to access training program to participant Demonstrated how to log in to program, with ID and Password Began with 3 games – Tower of London, Find Your Way, Private Eye Explained the rules of each game while demonstrating Asked participant to try the game. Re-explained rules/demonstrated again as necessary. Asked participant to go through steps again (turn off iPad first, ask participant to turn on, access game, play game). Assistance and support was given where necessary. Researcher sat with, and supported participant where necessary to complete first training session. Carer was asked to sit in on this session if they were going to be supporting the individual. Where support wasn't necessary, carer could sit in if desired by participant and carer. At this first session, the BEADS booklet was introduced, with stickers and the best time for completing the training was discussed with participant i.e. whether in the morning/evening and on what days, depending on other commitments and schedules.

	The amount of times the researcher would meet the participant was discussed at the first meeting. This was 2-3 times a week on average.
Contact with participant	For the first week, researcher made contact with participant to ensure that the participant was able to access/navigate the program and to discuss any issues that the participant may have had. A contact number was given if the participant/carer needed any assistance with the program at any point.
Weekly session	Researcher met with the participant at the agreed time(s) each week. Contact could be made if needed outside of these agreed times using the number given.
Where was the intervention delivered?	The most suitable place for the intervention was discussed at the first meeting and varied between individuals. The training took place either at home, at the day centre, or in a mixture of both If the training took place in both the home and day centre, the researcher met with carers (where necessary) in both settings.
How was delivery monitored?	Delivery of intervention could be monitored remotely as the researcher was able to log into each of the participants' account and see how long was spent, on what day, on what games. This allowed discussion for any problems that were being experienced with the delivery of the program

While Figure 3.7, below gives an overall timeline for the treatment and control group, it does not give a true reflection of the timeline in relation to the practicality of conducting the intervention. Each participant had a corresponding participant in the opposite group. This meant that both participants had to be available for the appropriate 8 weeks. For example the first participant had to be available for 8 weeks beginning on a certain date, while the corresponding participant had to be available to begin the training 8 weeks later, and to be then available to complete the training for a further 8 weeks. The researcher aimed to meet with participants two to three times a week, depending on the level of support needed, the level of support available, the participants' schedule and the participants' desire to meet.

	Intervention group	Delayed intervention group
	CAMDEX-DS	CAMDEX-DS
Week 1	CEFA BRIEF-A CRIq LEITER 3 Test for Severe Impairment	CEFA BRIEF-A
Weeks 1-8	Intervention	
	Intervention	
Week 9	CEFA BRIEF-A	CEFA BRIEF-A CRIq LEITER 3 Test for Severe Impairment
Week 9-16		Intervention
		Intervention
Week 16	CEFA BRIEF-A	CEFA BRIEF-A

Figure 3-8: Timeline for assessments and intervention

To keep track of the dates of Pre or Post Assessments, an Excel spreadsheet was used, with a code written to automatically generate a date 8 weeks from start date, and again after another 8 weeks. The researcher attempted as much as was possible to arrange a meeting for the exact date, or on as close a date as possible, and was within 5 days of the exact date in all cases. Data collection took place over a sixteen month period.

3.9.1 Recruitment Process

Recruitment was carried out within each of the services involved in the study and through the Down Syndrome Ireland website. Following receipt of ethical approval, the researcher contacted the gatekeeper in each service to explain the nature of the project and to provide him/her with detailed material on the nature, requirements and benefits of the project. The gatekeeper, who acted as a mediator between the researcher and potential participants, distributed the information to both staff members and to service users. Following a period of time for reflection and to allow any initial questions from staff or potential participants to be asked and directed to the researcher if necessary, consent was obtained.

Previous research has noted difficulties in recruiting individuals with ID in research, and one strategy to overcome such difficulties was the early recruitment of key workers and staff who work with individuals with ID on a daily basis, as opposed to senior members of staff (Lennox et al., 2005).

Thirty two individuals were sent invitations from one ID service, with thirteen people consenting to participate, a response rate of 40.6%, thirteen people consented from the other ID service from thirty five invitations sent out, a response rate of 37.1%. Forty five invitations were sent out from Down syndrome Ireland, with 17 responses, yielding a response rate of 37.7%.

As noted earlier, in one of the intellectual disability services, an information session was held for potential participants and support persons. Fourteen potential participants attended this session, and of these twelve consented to participate, yielding a response rate of 85.7%.

3.9.2 Duration of intervention

As mentioned above, previous research conducted using computerised cognitive training with a population of adults with DS is scarce, with only 5 other studies identified at the beginning of the current study. Although there are a number of published cognitive intervention studies in the general population, there was no consensus on dosage of training (Finn and Mcdonald, 2011) with dosage ranging from 600 minutes (Ball et al., 2002a) to 3000 minutes (Barnes et al., 2009). The dosage given in training may have a significant impact on outcome measures, where too low a dose may only increase lower level process involving neurotransmitters, without causing neurogenesis, synaptogenesis or the formation of new neural networks (Valenzuela et al., 2007). Dosage for the intervention needed to be lengthy enough to allow a chance for an effect but not so lengthy that it was not feasible or practical for participants with DS to complete successfully. A study by Bennett et al, (2013) with children with DS found that between 450 and 750 minutes, with an average of 517.2 minutes of training showed improvement on working memory tasks – the outcome measure of the study.

A dosage of 800 minutes was decided upon, based on the 6 previous studies discussed in the literature review that focused on cognitive training with a population with intellectual disability. It was theorised that this was above the dosage already shown to have significant effect, but not too much over that participants would not likely complete the training.

3.9.3 The first training session

Following pre-intervention measures, all participants began the intervention training within a one week period. On the first day of the intervention, the researcher met with participant and key worker/carer and all aspects of the study were explained again, and verbal process consent was affirmed. The iPad was given to the participant and the basic operations of the iPad were explained i.e. how to turn on the iPad, how to get on to the internet. Depending on the level of familiarity of the individual participant with any technology, the key worker was asked to provide assistance where needed to connect to the intervention program.

The intervention program was internet based, and so all iPads were supplied with a 3G connection, as it was understood that many participants may not have reliable, if any, access to the internet. The intervention program was set up so that the home screen appeared when the internet was launched.

Once the researcher was satisfied the participant was comfortable with the iPad, some of the exercises in the program were explored. The researcher picked up to 3 games during the first session, depending on the ability of the participant, that were deemed to have the most straightforward 'rules'. The games picked at this point varied between participants depending on level of ID and familiarity with certain game types, but the most common games used at this point were *Find Your Way*, *Objects Where Are You?* and *Private Eye*

The researcher sat with the participant for the duration of the first training session and returned at least once, and on average two to three times a week for the duration of the intervention.

3.9.4 Measures for adherence

At the beginning of the intervention program, the researcher met with the participants and carer to discuss the creation of a timetable. A training timetable was devised with the participant and key worker/carer, however it was agreed that this would be reviewed on a weekly basis as changes in the schedule of the participant occurred e.g. if the participant had an appointment or was attending a social event not normally in their schedule. This timetable took into account other work schedules and commitments in which the participant was involved. It also took into account the habits and mood of the participant, where some preferred the morning and some the evening. The participant was encouraged to stick to the timetable as it was thought that a prescribed schedule and time that suited both participants and key worker would be most likely to contribute to adherence rather than a simple instruction of 20 minutes on 5 days of the week. Deviation from the timetable, however, did not have any effect on the intervention itself.

In order to promote adherence to the program, a booklet was developed 'My BEADS Passport' (see Appendix 8) which showed one week per page, with the days of the week listed. There was a star shaped space beside each day of the week. When the researcher met with the participant each week the schedule for the following week was agreed upon. Participants were given star shaped stickers, which were to be stuck in the booklet for each day that training was completed. Encouraging pictures were included in the booklet.

3.9.5 Visiting Participants

The researcher met with participants on average two to three times a week to ensure that there were no specific difficulties in relation to the program and to discuss the exercises that had been carried out since the last meeting. If the participant was not enjoying a particular exercise or was finding it too challenging, an alternative exercise was chosen. In between meetings, the researcher was available to participants and key workers for any matters involving the study and was contactable via phone.

3.9.6 Tracking Tools

As this was partly a feasibility study, there was not an expectation or a reliance on particular exercises being completed, or on a certain number of different exercises being completed. As much as possible, the researcher suggested exercises that required the use of different cognitive processes, however this was not a primary goal. If the participant preferred a certain type of exercise or was happy to continue to progress in a particular exercise, this was acceptable.

The intervention program software monitored the time spent on any given day of each exercise. Thus it was possible to monitor how long was spent on which exercise, and to determine how much time overall was spent on the intervention program. This information was available to the researcher remotely through the internet based program and thus the researcher could be made aware of potential problems in between meetings with participants.

Having recorded data on the length of time spent on each task was useful in determining the most and least used exercise. It was also useful in conducting data analysis on the relationship between type of exercise completed most frequently in the intervention program and what measures of executive function were most influenced.

3.10 Data Analysis

SPSS 22 was used to analyse all quantitative data for the study. Descriptive and bivariate analyses were used to explore the data and the associations between variables. In order to explore the differences between the treatment and delayed intervention group, independent samples t tests were used for the continuous variables with chi squares used for the categorical variables. Paired samples t tests were used to compare within group differences at T1, T2 and T3. See Table 3.12 for the analysis used for each of the objectives in the study. A thematic analysis was conducted on field notes and exit interviews, with the steps involved described below.

Table 3-11: Analysis Plan

Objective	Analysis Type
To test the feasibility of using cognitive training with adults with Down syndrome by exploring time spent, frequency level of enjoyment and delivery parameters, support needed.	Descriptive statistics were used to explore aspects of feasibility including time spent, frequency level of enjoyment and delivery parameters, support needed.
To investigate whether cognitive training has a positive influence on executive functions in adults with Down syndrome.	Paired Samples t –test was used to examine pre/post scores Two Way mixed ANOVA was used to examine the Time x Group Effects
To examine changes in behaviours related to executive functioning after brain training as perceived by family members/carers using the Behaviour Rating Inventory of Executive Functions.	Paired Samples t –test was used to examine pre/post scores Two Way mixed ANOVA was used to examine the Time x Group Effects
To investigate the relationship between cognitive reserve and executive function.	Chi squared analysis and ANCOVA was used to examine the relationship between cognitive reserve and levels of EF
To investigate whether variables such as age, IQ, cognitive function, and time spent are predictive of change in scores post intervention.	ANCOVA was used to investigate whether age, IQ, cognitive function and time spent were predictive of change in scores post intervention

3.10.1 Comparisons

In order to examine the effects of the training, scores within the intervention group were compared at two time points; baseline (T1) and then post intervention (T2). The delayed intervention group were also measured at T1 and T2, having received no intervention at T2, in order to determine if changes were due to practice effects.

At T2, the relationship between the intervention group and the delayed intervention group was of interest, to examine the difference between the two groups when one has received the intervention and one has not. Through using a delayed intervention group, there was an opportunity to confirm the initial findings, where the delayed intervention group continued to receive the intervention. Following this, the effect cognitive training had on scores of executive function for the delayed intervention group from T2 to T3 was also examined. Maintenance effects of the training were also investigated, and thus the EF scores for the intervention group were also examined from T2 to T3.

These within participants and between groups comparisons were made also for the behavioural aspect of executive functions that are apparent in everyday life, as rated by an individual known to the participant. This allowed an extra dimension to the study, whereby it could be ascertained whether any changes in neuropsychological assessments of executive function transferred to everyday life.

Demographic factors including age, IQ, level of cognitive ability were examined along with the number of minutes spent on the training program also of interest, in order to determine if any factors emerged as predictive of whether a change would be seen in both the neuropsychological assessments and also in everyday life.

A two-way mixed ANOVA was conducted in order to understand if there was a two-way interaction between the within subjects (T1 to T2) and the between groups factors (Treatment and Control). This ascertained whether the effect of training was dependent on being in the treatment or control group.

3.10.2 Assumptions

Data were checked for normality using the Shapiro Wilks test of normality and Levene's test for equal variance. Both tests returned p-values of greater than .05, and thus satisfied assumptions of normality and equal variances for the t-tests.

For the two-way mixed ANOVA, Mauchly's test of sphericity was unnecessary as there were only 2 levels, thus only one set of difference scores, and thus only one correlation, meaning the assumption will always be met.

3.10.3 Bonferroni Correction

As multiple comparisons were made using t-tests, a Bonferroni correction was used to adjust the alpha level to reduce the risk of Type I error for each hypothesis. There is some dispute over the correct use of the Bonferroni correction, namely at what point the overzealousness of use to reduce the risk of a Type I error then increases the risk of a Type II error, with the line between the two often blurred (Cabin and Mitchell, 2000). Critics of the use of the Bonferroni correction have suggested that it trivialises the hypothesis testing outcomes by setting an alpha level which precludes the possibility of finding a positive effect (Rothman, 1990).

As the Bonferroni correction adjusts for multiple testing of each hypothesis, the neuropsychological assessments of EF were separated from the behavioural aspects of EF (using the BRIEF-A), as they relate to separate constructs and hypotheses. The neuropsychological assessments consist of 5 t-tests and relates to one hypothesis. The BRIEF-A consists of 12 t-tests and relates to a second hypothesis.

Figure 5.1 shows the different comparisons that were made in the study in order to understand the effects of the cognitive training. For the purposes of calculating the adjusted p-value, it was taken that those comparisons highlighted in blue in Figure 5.1 would be taken into account, as the comparisons in red are not directly related to the hypothesis. This leaves 5 comparisons.

When taking these into account, an adjusted stringent p-value was calculated:

$$.05/\ (12x5) = \alpha \quad 0.0008$$

All data were analysed using SPSS 22. The output yielded in SPSS gives a probability value, but rounds only to three decimal places. This means that a p value given in SPSS of .000 could be anything >.000 but < .001 (Hinton et al., 2014).

For this reason results will be discussed in relation to a significance level of .001.

While the p value indicates if an effect exists, it does not give information on the size of the effect. Thus reporting only the p value gives us statistical significance, but not substantive significance (Sullivan and Feinn, 2012). Effect sizes will be reported also in order to understand the size of the effect of cognitive training. Cohen's d will be used for reporting effect size for t tests and partial eta squared will be reported for the two-way mixed ANOVA. Interpretation of effect sizes is based on the following:

Table 3-12: Effect Sizes

	Cohen's d	Partial eta squared
Small effect	0.2	.01
Medium effect	0.5	.09
Large effect	0.8	.25

Cohen's d was calculated using Wiseheart online effect size calculator (http://www.cognitiveflexibility.org/effectsize/), where the correlation between the means was included for paired samples t-tests in order to correct the dependence between the means (Wiseheart, 2013).

3.10.4 Missing Data

Data were analysed using intent-to-treat analysis. Intent-to-treat analysis is described as "once randomised, always analysed", where all participants are included in analysis even following subsequent withdrawal (Gupta, 2011). This method is employed as there is no guarantee that those who do not comply have the same risk-factor profile as those who do comply, and exclusion may introduce bias to treatment comparisons (Heritier et al., 2003). In clinical trials, some missing data is often unavoidable, and thus two approaches have been suggested to reduce the effect of missing data; imputation and 'last observation carried forward' (Heritier et al., 2003).

One individual in the study withdrew after 1 week, and thus did not complete post assessments. 'Last observation carried forward' was conducted, and thus this individual's baseline scores were used also as post intervention scores. Scores for the BRIEF-A for 3 individuals were missing at T3, and in those cases scores from T2 were used.

3.10.5 Thematic Analysis

A thematic analysis was conducted, using the Braun and Clarke (2006) framework in order to identify the main themes to emerge from the interviews and field notes. Thematic analysis is a flexible method for identifying, analysing and reporting key themes in data (Braun and Clarke, 2006). The six steps outlined by Braun and Clarke (2006) were followed (Table 3.15), however as noted the process is not necessarily linear, but recursive where it is necessary to move back and forth through the phases as needed (Ely, 1997).

Table 3-13: Thematic Analysis process (Braun and Clarke, 2006)

Step	Description
1. Familiarise with Data	Reading, re-reading and immersing in the data.
2. Coding	Generating succinct labels for important features of the data. Collating all the codes for later analysis.
3. Search for themes	Identify potential themes from collated data.
4. Reviewing themes	Checking potential themes against data to make sure they fit. Refining themes.
5. Defining and naming themes	Deciding on informative name for each theme.
6. Writing up	Report findings.

To facilitate the thematic analysis, statements from the field notes and the transcribed interviews were exported to excel and were then colour coded and then grouped and classified into themes. The emerging themes were verified independently by researcher and PhD supervisor and then consensus was reached between the two on the emerging global themes.

CHAPTER 4

FEASIBILITY OF COGNITIVE TRAINING

4 Feasibility of Cognitive Training

4.1 Introduction

The aim of this chapter is to present the findings for Objective 1, that is, the feasibility of conducting a cognitive training program with a population of people with Down syndrome (DS). The study sample will first be described, including age, and levels of ID, IQ, cognitive reserve and cognitive function. The average scores for baseline assessments will also be outlined. Following this, the feasibility parameters of the study, discussed in Chapter 3 will be briefly outlined again and these parameters will then be examined with the supporting data presented. Relevant quotes taken from the field notes and exit interviews completed by the researcher will be included in the chapter. Key themes emerging from a thematic analysis of exit interviews will also be described.

4.2 Demographics of the Sample

Forty individuals with DS aged between 30 and 49 participated in the study, of whom 35% (14) were male and 65% (26) were female and with 25% having a mild level of ID, and 75% a moderate level of ID. The mean age of participants in the study was 36.9 (SD=5.7). Overall 62.5% were living at home or independently and 37.5% were living in the community.

All of the participants (n=40) completed baseline assessments, including a measure of IQ using the Leiter-3, cognitive function, measured using the Test of Severe Impairment (TSI), and baseline assessments of executive function using the Cambridge Executive Function Assessment (CEFA), which included the following elements as outlined in section 3.8.3; Dogs and Cats Stroop, the Tower of London, Scrambled Boxes, Spatial Reversal and the Weigl Card Sorting task. The cognitive reserve index questionnaire (CRIq) was answered by either the participant or by a carer. The Behaviour Rating Inventory of Executive Function – Adults version (BRIEF-A) was completed by a carer.

The executive function assessments named above were conducted to examine whether cognitive training had an effect on levels of executive function. The IQ, cognitive ability and cognitive reserve assessments were conducted to examine whether scores on these tests would be predictive of change in scores on executive function post intervention. These assessments were included to conduct exploratory analysis following cognitive training intervention. This exploratory analysis was an important factor in relation to the feasibility of conducting such a study in order to give an indication if such an intervention would likely have an effect on executive function. The results from these analyses will be discussed further in the Chapter 5.

The average scores on the baseline assessments for IQ, cognitive ability and cognitive reserve across the whole group are displayed in Table 4.1 below.

Table 4-1: Average scores on baseline assessment of IQ, Cognitive function and cognitive reserve

	Mean	SD	Median	Range
Non-verbal IQ	43.38[1]	7.08	43	2-20
TSI	21.88[2]	3.2	23	7-24
CRIq	84.63[3]	15.58	84	62-115

[1] corresponds to a moderate level of ID (World Health Organization, 1992)

[2] corresponds to high level of cognitive function

[3] corresponds to a medium level of cognitive reserve (Nucci et al., 2012)

4.2.1 Non-verbal IQ as measured by the Leiter 3

The average non-verbal IQ score, as measured by the Leiter-3 was 43.38 (SD=7.1), which corresponds to a moderate level of ID. The non-verbal IQ scores as measured by the Leiter-3 were compared to the classification of ID as was per participants' case records. Table 4.2 shows the relationship between the non-verbal IQ scores and the ID classification. The ID classification was taken from participants' records and verified by key worker or family member.

Table 4-2: Classification from IQ scores and from record

		Classification from IQ scores		
Classification from record		Mild	Moderate	Severe
	Mild	5	5	0
	Moderate	1	22	4
Missing Data = 3				

There was some discrepancy between IQ scores and previously recorded level of ID for 10 participants.

Of those who had a classification of mild ID, 5 individuals (50%) scored in the moderate range of ID based on scores on the Leiter 3. Of these, 3 individuals had a non-verbal IQ score of 47 and 2 had a non-verbal IQ score of 41.

Of those individuals who were classified from records as having a moderate level of ID, 1 individual had a non-verbal score of 55, which would fall within the mild range according to the WHO (1992). Four individuals scored below 35, which would be classified as a severe ID. Of these, 1 individual scored 32, another scored 33, and two individuals had a score of 34 according to the Leiter-3.

4.2.2 Cognitive ability as measured by the TSI

The Test for Severe Impairment yielded a score for 6 subtests and also an overall score, with a max score of 24. The results yielded for the subtests and total sample are below in Table 4.3

Table 4-3: Mean scores on Test for Severe Impairment

	Range	Mean Score	SD
Language Comprehension	2-4	3.88	0.46
Language Production	0-4	3.83	0.71
Immediate Memory	1-3	2.58	0.71
General Knowledge	1-4	3	0.64
Conceptualisation	0-4	3.7	0.94
Motor Performance	0-1	1	0
Total Score	7-24	21.88	3.20
n=40			

The average score on the TSI was 21.88 of a maximum score of 24, and ranged from 7 to 24. The majority of participants had a high level of cognitive function, where 90% (n=36) of participants scored 20 or above.

Using a Pearson bivariate correlation, it was found that IQ score was significantly correlated with the overall cognitive function score $r(37) = .506$, $p < .001$.

4.2.3 Cognitive reserve as measured by the Cognitive Reserve Index questionnaire

The cognitive reserve index questionnaire (CRIq) yielded 3 subscores; education, working activity and leisure time. These scores combine and an overall cognitive reserve was computed.

The cognitive reserve score was interpreted as follows (Nucci et al., 2012):

Low	Low-Medium	Medium	Medium-High	High
≤70	71-84	85-114	115-130	>130

The mean score of the total population was 84.63 (SD=15.58), indicating a medium level of cognitive reserve, with a range from 62 (low) to 115 (medium-high). See Table 4.4 below for cognitive reserve categories.

Table 4-4: Breakdown of cognitive reserve categories

	n	%
Low	10	25
Low-Medium	11	27.5
Medium	17	42.5
Medium High	2	5
High	0	0

The breakdown of the subsections for the CRIq are listed in Table 4.5 below

Table 4-5: Breakdown of CRIq subsection scores

	Mean	SD	Range
Education	85.6	26.6	50-13
Working Activity	89.1	5.2	80-99
Leisure Time	90.1	7.7	74-112
Total Score	84.6	15.6	62-115

Using a bivariate correlation, it was found that IQ score was significantly correlated with the overall cognitive reserve score $r(37) = .759$, $p < .001$.

4.2.4 Executive Function Assessments

The scores for executive function are discussed in detail in Chapter 5, with particular emphasis on the comparisons between the treatment and delayed intervention group throughout intervention process. In this section, only an overview of baseline scores for the whole group of 40 individuals is given.

Tables 4.6 and 4.7 give an overview of the baseline scores for EF. Table 4.6 shows the baseline neuropsychological EF assessments and table 4.7 shows the baseline scores on the behavioural component of EF as measured by the

Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A).

As can be seen in Table 4.6 below, floor effect were highest for 'spatial reversal' where 37.5% scored at 0 at baseline measurements. Floor effects for the 'Weigl card sorting task' were also relatively high at 22.5%. The floor effects found for 'spatial reversal' were similar to those found in the study by Ball et al., (2008). These high floor effects may suggest that this outcome variable may not be the most suitable for use with this population. For 'Dogs and Cats' 17.5% scored at 0 at baseline, however the scores were evenly distributed and where 12.5% scored at the top score of 16.

Table 4-6: Scores of Neuropsychological Assessments of Executive Function

	Range of Tool	Range of Scores	n at Min (%)	n at Max (%)	Mean	SD
Cats and Dogs	0-16	0-16	7 (17.5)	5 (12.5)	6.1	5.3
Tower of London	0-16	3-15	0 (0)	0 (0)	8.6	3.3
Scrambled Boxes	0-11	3-11	0 (0)	6 (15)	7.4	2.4
Spatial Reversal	0-7	0-7	15 (37.5)	7 (17.5)	2.9	2.7
Weigl Card Sorting	0-7	0-7	9 (22.5)	2 (5)	1.9	1.5

Table 4-7: T Scores on Behaviour Rating Index of Executive Function

	Mean	SD	Min	Max	Range of Tool
Inhibit	49.74	6.12	39	61	38-93
Shift	61.31	9.78	39	84	39-93
Emotional Control	52.36	8.43	39	67	39-89
Self-Monitor	56.69	8.35	39	71	37-91
Behaviour Regulation Index	55.18	9.15	41	88	36-100
Initiate	58.33	10.18	45	85	38-94
Working Memory	60.38	11.35	41	92	40-97
Plan/Organise	56.00	8.84	44	79	39-97
Task Monitor	59.36	10.04	41	84	38-95
Organise Materials	46.08	7.24	38	69	37-86
Metacognitive Index	56.23	8.14	43	76	36-101
Global Executive Composite	55.69	7.08	43	72	35-104

For the BRIEF-A, T-scores were calculated to provide information on individual scores relative to normative scores (Roth et al., 2005). A higher score on the BRIEF-A indicates a higher level of dysfunction. A score at or above 65 is considered clinically significant. Clinical significance refers to magnitude of the score and whether this would require clinical care (Skelly, 2011). All scores for the validity scales (negativity, infrequency and inconsistency scales) were in the acceptable range. Figure 4.1 shows the percentage of participants who scored above 65 for each of the subsections of the BRIEF-A. For the overall composite executive function score for behaviour, 10.3% scored at a clinically dysfunctional level. The subsections that showed the highest levels of dysfunction were working memory (33.3%), shift (30.8%) and task monitor (25.6%).

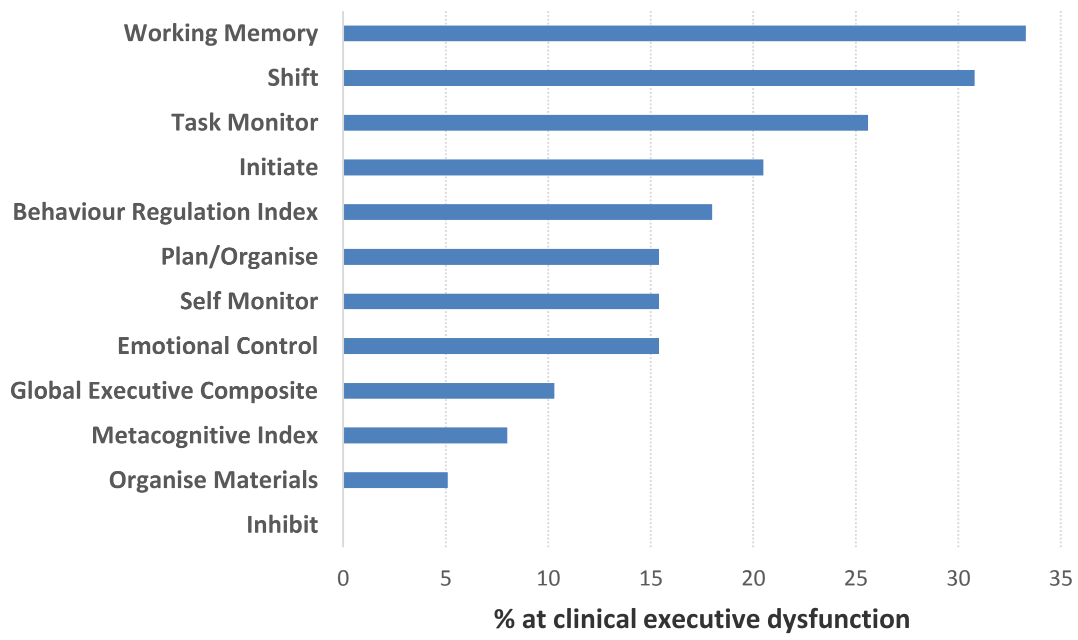


Figure 4-1: Percentage of participants at clinical level of behavioural executive dysfunction

4.2.4.1 Comparison between EF scores in the current study and EF scores in Ball et al., (2008)

Executive function scores in the current study were compared to scores on the same measures in a study by Ball et al., (2008). These results are presented in Table 4.8 below. It was found that Scores for Scrambled Boxes and Spatial Reversal were similar to scores found in Ball et al., (2008) study. Scores on the Weigl Card Sorting and Tower of London were higher in the BEADS sample than in Ball et al., (2008), whereas the BEADS sample on average had lower scores on the Tower of London task than in the study by Ball and colleagues.

Table 4-8: Comparison between EF scores in current study and Ball et al., 2008

	BEADS study 2016			Ball et al., (2008)		
	Mean	Min %	Max %	Mean	Min %	Max %
Dogs and Cats	6.1	17.5	12.5	8.8	17.9	28.6
Tower of London	8.6	0*	0	6.2	25	3.6
Scrambled Boxes	7.4	0	15	7.8	3.6	17.9
Spatial Reversal	2.9	37.5	17.5	3.2	35.7	0
Weigl Card Sorting	1.9	22.5	5	1.0	53.6	0

*An extra option of 1 move was added to this study (The BEADs study), whereas Ball et al., (2008) began at 2 moves. The comparable figure for the BEADs study is 7.5%

4.2.4.2 Correlation between neuropsychological assessments of executive function and behaviours of executive function

The correlation between scores of the 5 neuropsychological assessments of executive function and behaviours of executive function as measured by BRIEF-A were examined (See Table 4.9 below). A statistically significant correlation was seen between the two indices (Behavioural Regulation Index and Metacognitive Index) and 4 of the neuropsychological assessments. A significant correlation was observed between the Global Executive Function Composite score in the BRIEF-A and all 5 neuropsychological assessments of EF.

4.2.5 Summary of demographics and baseline scores

Participants in the study were aged between 30 and 49 with a mean age of 36.9 and where 75% had a moderate level of ID. Results from the IQ assessments, the Leiter-3, it was found that the average scores was 43.38, indicating a moderate level of ID also. Scores on the cognitive function assessment using the TSI showed that participants had a high level of cognitive function with an average scores of 21.88 found. The average score on the cognitive reserve assessment was 84.63, which corresponded to a moderate level of cognitive reserve.

Baseline scores of EF were also measured and compared to a study by Ball et al., (2008) in order to gain an understanding of how the EF baseline scores of this sample compared to the baseline scores of a similar cohort in a previously published study using the same measures.

Table 4-9: Correlation between neuropsychological executive function assessments and behaviours of executive function as measured by BRIEF-A

	Cats and Dogs		Tower of London		Scrambled Boxes		Spatial Reversal		Weigl Card Sorting	
	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
Inhibit	.533	**.000**	.430	**.006**	.321	**.046**	.449	**.004**	.407	**.010**
Shift	.452	**.004**	.488	**.002**	.430	**.006**	.369	**.04**	.423	**.007**
Emotional Control	.476	**.002**	.489	**.002**	.448	**.004**	.459	**.003**	.437	**.005**
Self-Monitor	.346	**.031**	.349	**.029**	.160	.331	.459	**.003**	.437	**.005**
BRI	.341	**.034**	.365	**.022**	.326	**.043**	.335	**.037**	.432	**.006**
Initiate	.555	**.000**	.462	**.003**	.468	**.003**	.218	.181	.339	**.035**
Working Memory	.317	**.049**	.274	.092	.242	.138	.172	.296	.192	.241
Plan/Organise	.345	**.032**	.386	**.015**	.304	.060	.265	.103	.212	.194
Task Monitor	.214	.192	.240	.141	.265	.104	.038	.818	.235	.149
Organise Materials	.245	.133	.158	.338	.157	.340	020	.904	.194	.237
Metacognitive Index	.510	**.001**	.508	**.001**	.478	**.002**	.235	.150	.430	**.006**
Global Executive Composite	.561	**.000**	.537	**.000**	.460	**.003**	.335	**.037**	.479	**.002**

4.3 Feasibility Parameters

The feasibility of the study was measured using the feasibility parameters that were outlined in the previous chapter, and which are summarised in Table 4.10 below. As noted earlier, participants had either a mild or moderate level of intellectual disability and some were living at home with family and some in community group homes. The level and type of support needed was thus also an important consideration, and one that must be considered when examining the overall feasibility of a cognitive training program, as was the environment in which the training program was delivered. The feasibility of the program was therefore examined in terms of the participant, the support person and the environment in which the training was completed.

Table 4-10: Feasibility parameters of the cognitive training program

Participant
Can participants play and progress the games?
Do participants adhere to the training program?
Do participants enjoy the cognitive training program
Support Person
How much support is needed to complete the training program?
How much training is involved for those supporting participants?
Environment
Can the program be implemented in different environments? (e.g. at home and in day service)

4.3.1 Participant

This section will examine the feasibility of the program as was related directly to the participant and the experience of the participant in terms of the usability of the program and perceived difficulty, level of enjoyment throughout the program and the extent to which participants adhered to the program.

4.3.1.1 Can participants play and progress in the games?

The first feasibility parameter examined whether participants were able to use and play the games in the cognitive training program, and whether progression could be seen throughout the games. In order for this to occur, the participant first had to be able to use and navigate the iPad.

4.3.1.1.1 Familiarisation with the mechanics of the iPad

The first training session explained the rules of the games, and how to manoeuvre the objects in the games. Overall 55% (n=22) of participants had previously used an iPad or similar tablet, and were thus familiar with the use of the touch screen. Of those who did not have previous experience, some needed extra training in the use of the touch screen. In *Tower of Hanoi*, some participants initially had difficulty in using the touch screen on the iPad to manoeuver the disks in the game.

> *"It's amazing how quick she has picked that up. She's never used anything like that before now. She can get into the games and all by herself"*
>
> - From support staff taken from Field Notes

Figure 4.2 shows screenshots of moving the yellow disk from the right hand pole to the left hand pole.

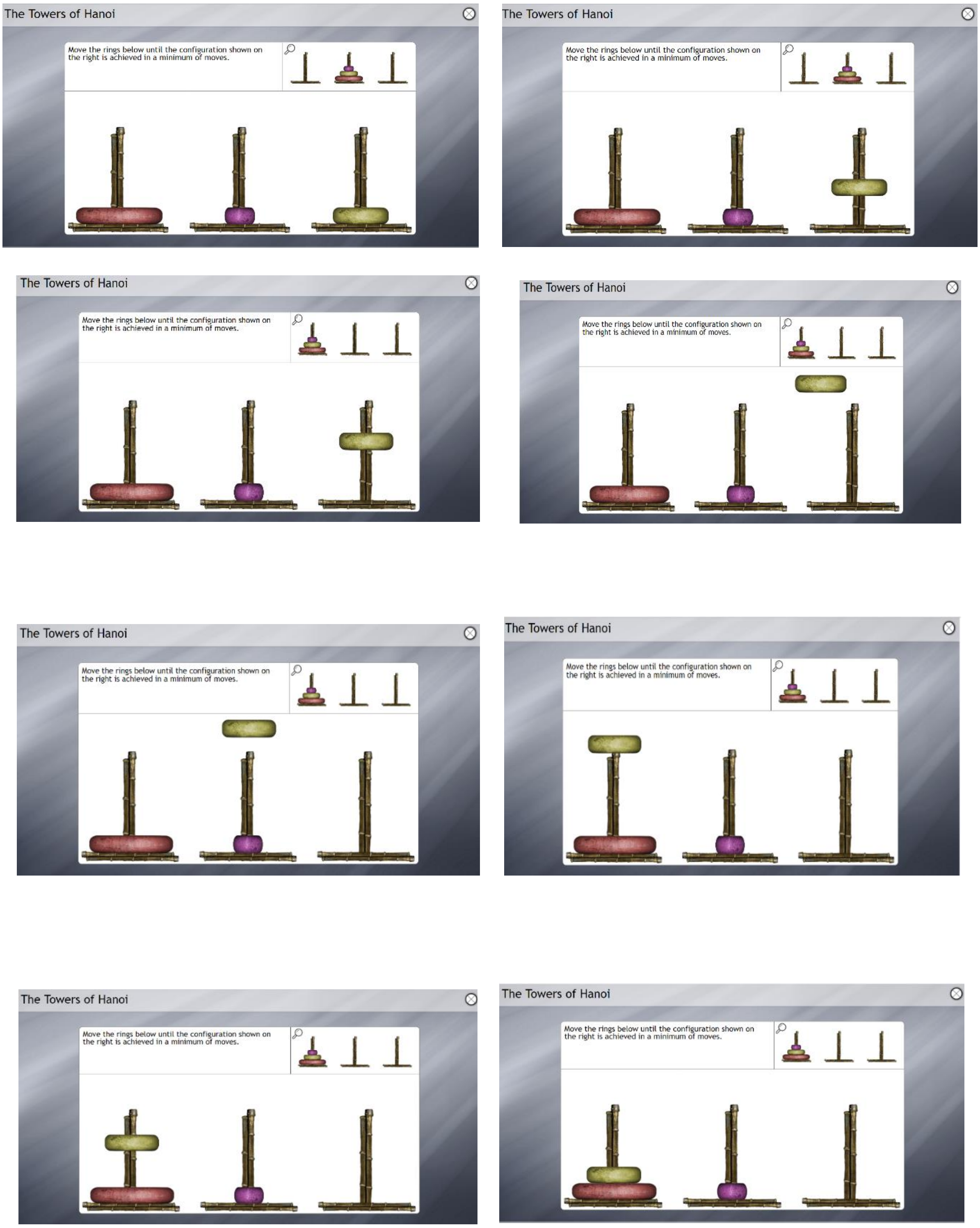


Figure 4-2: Using touch screen to manipulate game components

A common difficulty was the perceived need to press down very hard on the screen to move the objects. Another difficulty was not maintaining contact with the screen, which resulted in the disk 'falling' and returning to the start position. In the first training session, the use of the touch screen was practiced where needed. After some initial training all participants became proficient at the mechanisms of using the iPad, including the touch screen. Similarly, with initial training, 95% of participants proved capable of logging in to the cognitive training program using a username and password independently. The username and the password were both the same, and consisted of the participants' initials.

As was discussed in Chapter 3, twelve games were chosen, however not all participants played all twelve games. Figure 4.3 shows the number of games played by participants, with the highest percentage of participants played 4-5 games, followed closely by 6-8 games.

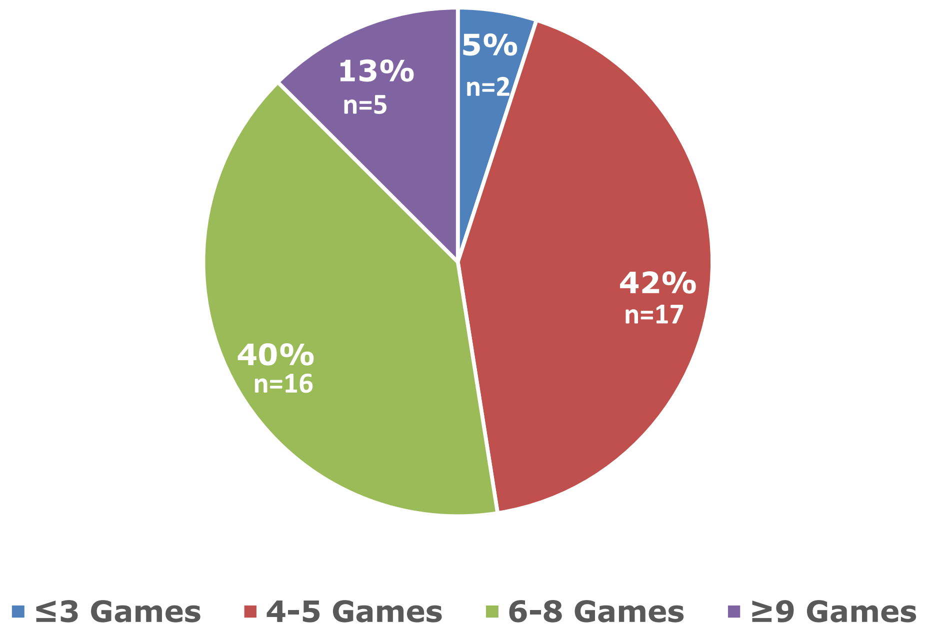


Figure 4-3: Number of games played by participants.

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(From support staff) – "I think it's better that she only had the 4 games. She really likes routine and that's very important to her. She liked going back to the same games all the time and she'd get to know them. I think if there had been too many or new ones (games) coming in all the time she would have been a bit overwhelmed

- Taken from exit interview

In order to examine the ability of participants to play the games, the progression of participants throughout the program was recorded. The games played by the most participants were:
Tower of Hanoi (100%), *Objects Where Are You?* (95%), *Find Your Way* (97.5%), and *Private Eye* (97.5%). Table 4.11 shows the percentage of participants that played the different games, and summarises again the cognitive area of focus of the game.

Table 4-11: Games played by participants

Name of Game	Area of Focus	% of participants that played
Tower of Hanoi	Planning; Problem Solving	100
Find Your Way	Visual Attention	97.5
Private Eye	Attention	97.5
Objects Where Are You?	Visual Working Memory	95
Chunking	Working Memory	52.2
Displaced Characters	Attention; Shifting	50
Point of View	Spatial Abilities	27.5
Ancient Writing	Visual Attention	25
Heraldry	Visual Memory	25
Shapes and Colours	Visual Memory	15
Writing in the Stars	Planning	10
Under Pressure	Inhibition; Processing Speed	7.5

As over 95% of participants played *Tower of Hanoi*, *Find Your Way*, *Private Eye* and *Objects Where Are You?*, the progression of participants in these games is presented. All games began at level 1 and progressed to level 9.

All participants reached level 2 in *Tower of Hanoi* and *Private Eye*, with 97.4% and 94.9% reaching level 2 in *Objects Where Are You?* And *Private Eye*, respectively. As Figure 4.4 shows, approximately one third or more of participants reached level 5 in all games (60% *Tower of Hanoi*; 30.8% *Find Your Way*, 33.3% *Private Eye*, 37.8% *Objects Where Are You?*). Approximately 20-30% of participants reached level 7 in *Tower of Hanoi* (22.5%), *Private Eye* (28.2%) and *Objects Where Are You?* (29.7%).

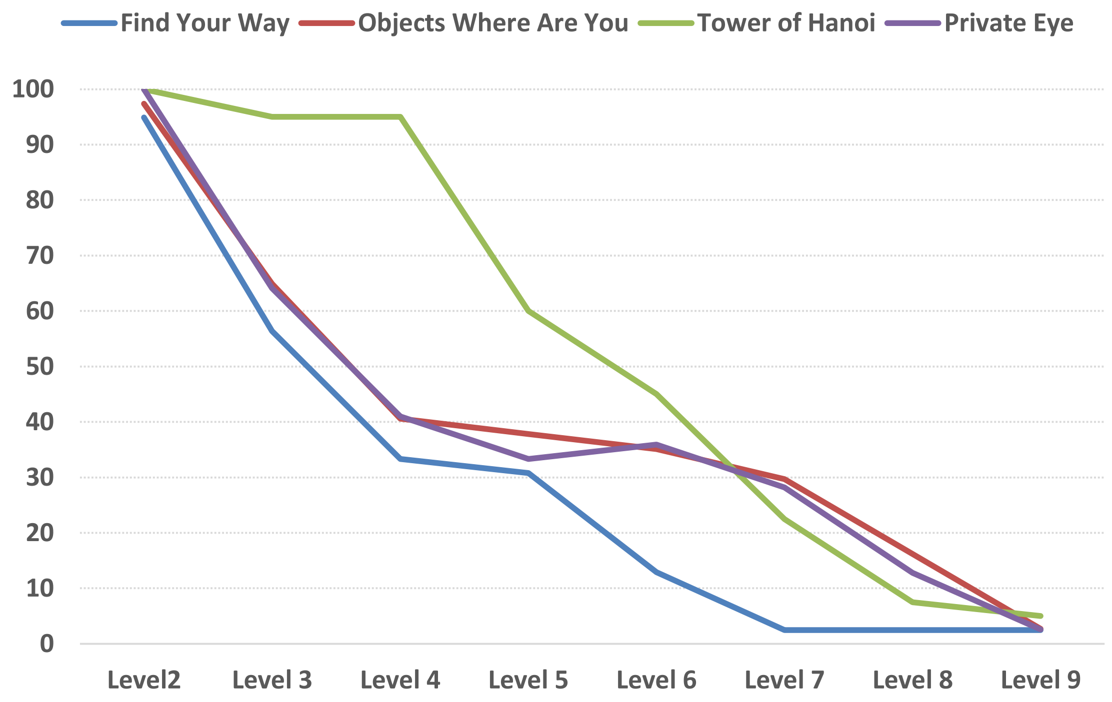


Figure 4-4: Progression through the levels across four games

Perception of difficulty of the cognitive training program was measured each week using the structured questionnaire.

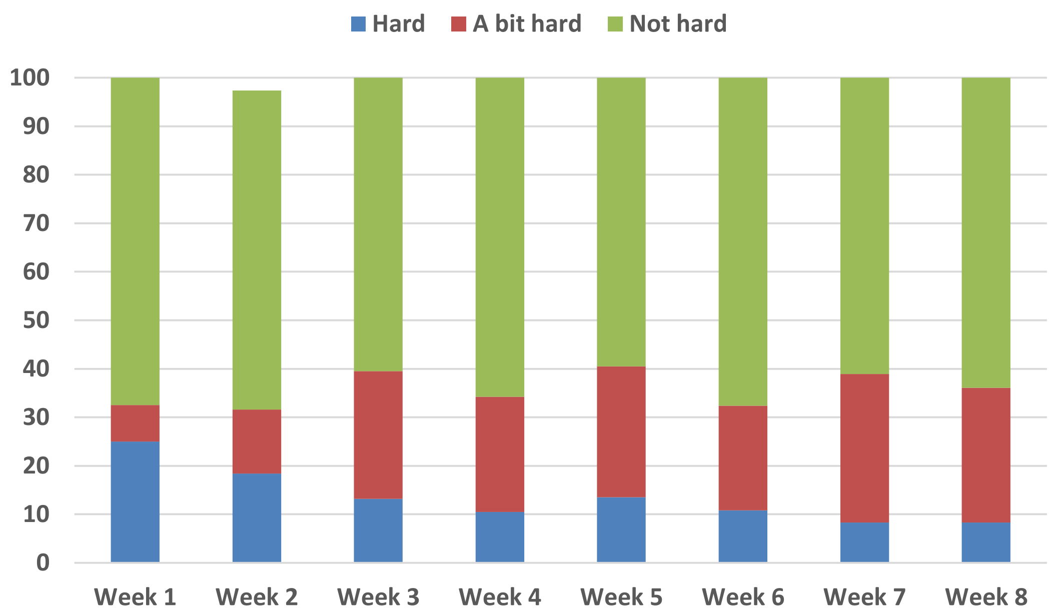


Figure 4-5: Perception of difficulty throughout the program

Perception of difficulty decreased throughout the program, with the majority of participants never perceiving the program to be difficult (Figure 4.5). At the end of the first week, 25% of participants thought the program was hard, and this fell to 10.3% by week four.

One participant had had difficulty with all of the games for the first 5 weeks. In one training session she grasped the concept of 'Tower of Hanoi' and went from Level 1 to Level 3 in that training session.

She was not literate, but when written instructions came onto the screen she 'read' aloud to herself….

"Well done [name]. I am so proud of you. You are wonderful"

Taken from Field Notes

4.3.1.2 Did participants adhere to the cognitive training program?

Adherence to the program was high with 90% (36) of participants completing the full 8 weeks of the program. Two individuals completed 7 weeks, with one discontinuing due to ill health and another due to other commitments. One individual completed 6 weeks and withdrew as was no longer interested. Follow up assessments were completed for these 3 individuals. One individual withdrew after 1 week, and no follow up assessments were completed.

The recommended dosage was 800 minutes, based on previous research in the ID literature. The recommended program was to spend 20 minutes a day, 5 days a week over 8 weeks (40 days). The average number of minutes spent on the program was 930.73 (SD=848.4) with an average of 34.7 days (Table 4.12).

Table 4-12: Adherence to the program

Mean minutes	930.73
SD minutes	848.4
Median minutes	711.29
Min; Max	339; 5353
Mean number of days	34.68
SD Days	11.43
Mean days per week	3.9

*Data on n=39; not included for 1 individual who completed 29 minutes

During the weekly completion of the questionnaire, if the training had not been completed on a particular day, the reason it was not completed was noted. Figure 4.6 displays the reasons given when training was not completed. The most frequently occurring reasons were that the participant was too busy to complete the training (24.8%, n=96), that no support was available when it was needed (18.9%, n=73) or that the participant didn't want to complete the training (15%, n=58).

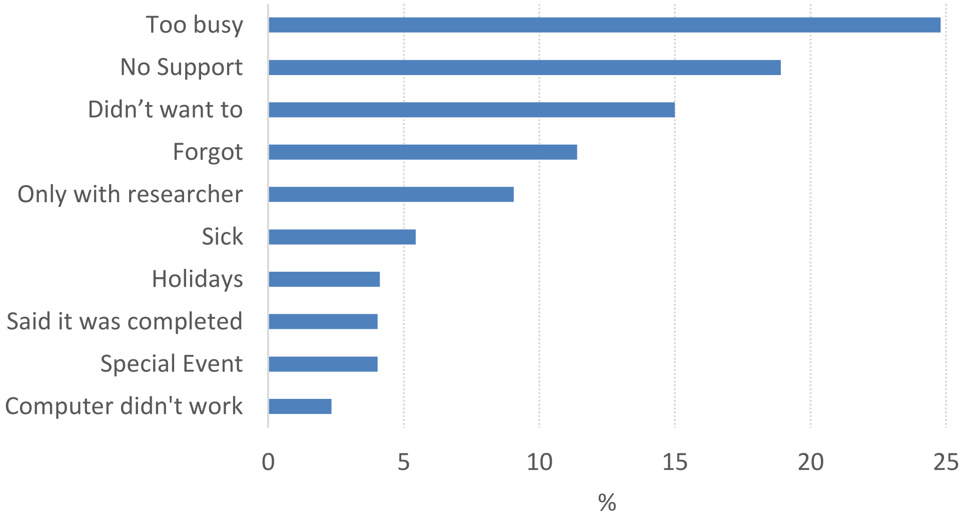


Figure 4-6: Reasons training was not completed

"I was at work all day, and I came home and it was dark and raining and I just wanted to watch TV"

"I didn't do it on Tuesday. Just didn't have time, I was in work all day"

(From support staff) - "I just don't have time to do it on a Wednesday. They go to Arch club and then come home, have dinner, have shower so when that's all finished it's too late. And it's just me on, so I can't sit with her alone for half an hour"

(From parent) – "We won't get it done now for the next few days. His sister's wedding is coming up and it'll all be manic here for the next while"

(From support staff) - "I tried to do it with her the other night but she didn't want to do it with me. She says she'll only do it with you [researcher]

- Taken from field notes

4.3.1.2.1 The BEADS booklet

The BEADS booklet was designed to encourage adherence to the program (See Appendix 8). Overall 70% (28) of participants used the BEADS booklet and of those that used it 100% reported finding it useful as an aid for recording the number of days of completed training. Of those that did not use it (n=12), 7 indicated that they did not want to use it and did not think it was necessary. The remaining 5 had intended to use it but forgot to use it, and then abandoned it.

"What picture is for next week?...I can't wait to get to the dog picture, that's my favourite"

"Nah, I don't need that (BEADS booklet), I'll just do it every day"

-Taken from Field Notes

4.3.1.3 Did participants enjoy the program?

Level of enjoyment was measured in the weekly structured questionnaire. The majority of participants found the cognitive training program enjoyable for the duration of the program. At the end of week 1 of the program, 92.5% (n=37) individuals indicated that they liked, or really liked the program (Figure 4.7).

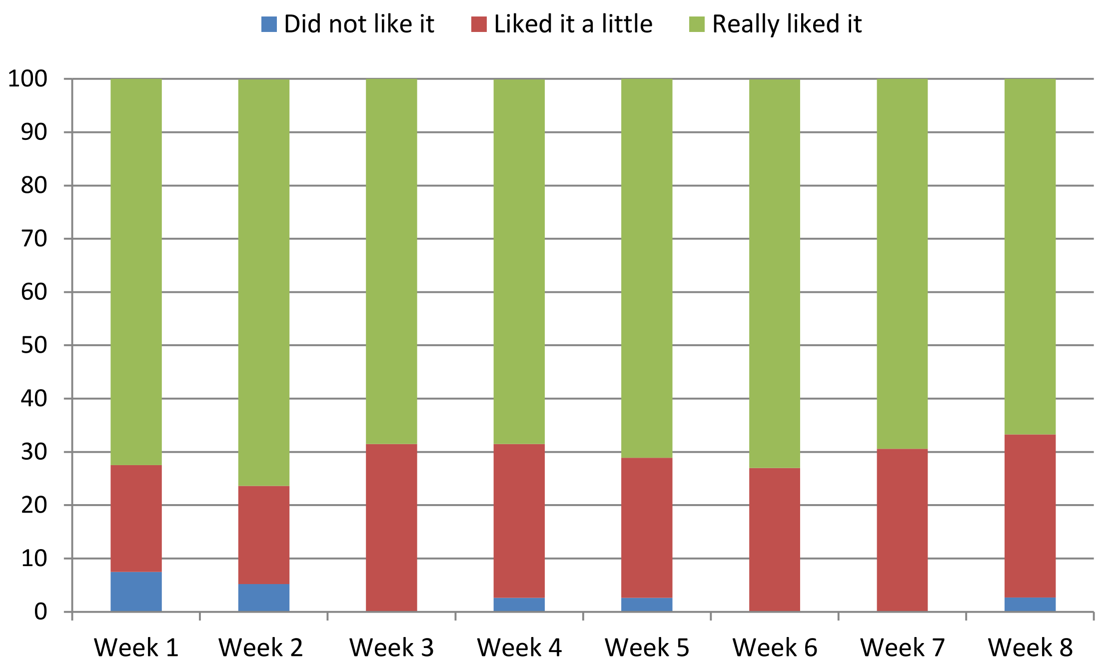


Figure 4-7: Level of enjoyment throughout the cognitive training program

"I just love it. It's just deadly [Irish colloquialism for very good]"

*"It's nothing short of a miracle. I thought there would be no way he'd do it and you'd be wasting your time, but he sits there and does it and he likes it. I think he's getting good at some of them. He does that now when he comes in instead of the TV" (*parent of participant*)*

"I don't know which one is my favourite. They're all my favourite, but if I had to pick one, I don't know, I'd just like to play all of them".

-Taken from Field Notes

At the final session, one individual reported not liking the program during the previous week.

"It was ok, but I was a bit tired of the games now."
-From Field Notes

Participants were also asked about excitement for completing the program in the coming week. Figure 4.8 shows that enthusiasm grew during the first 4 weeks and then waned slightly toward the end of the program.

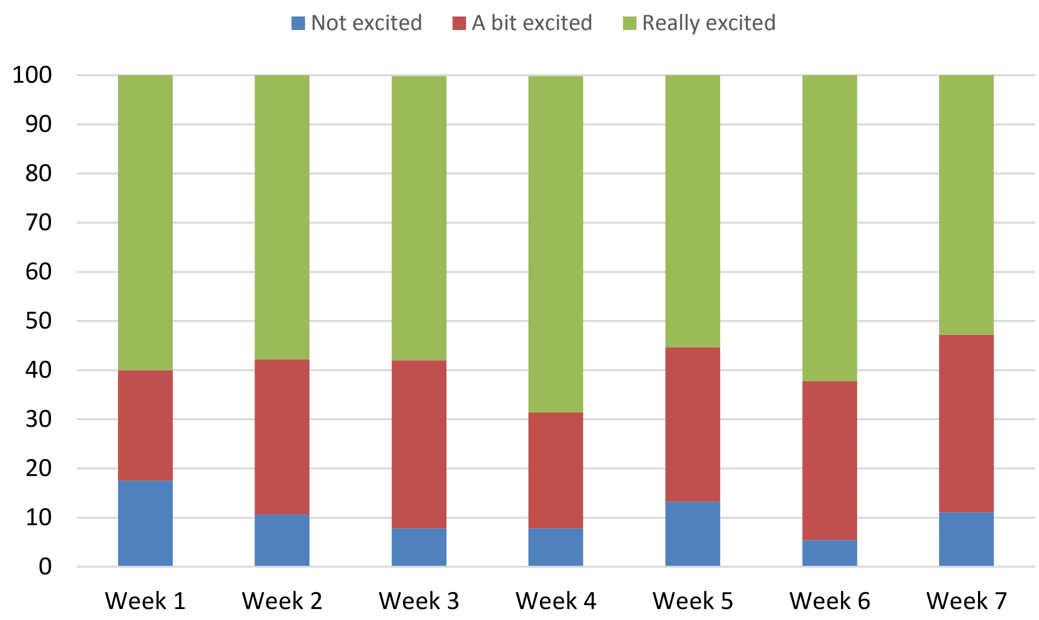


Figure 4-8: Excitement for completing program in the coming week

Overall, all parameters examined in relation to the individual indicated that from a person centred focus, conducting a computerised cognitive training program was feasible.

4.3.2 Support Person

This section will examine the feasibility of conducting a cognitive training program with adults with Down syndrome in terms of the amount of support that is needed from a support person, either family member or staff. While some participants did not need any support, over 80% (n=32) required some support at some stage of the program.

4.3.2.1 How much support is needed to complete the training program?

The role of the support person was to support the participant in completing the cognitive training, where necessary. The amount of support needed varied between participants; 17.9% (n=7) of participants were able to complete the training independently from the beginning and 40.5% (n=15) needed support until the end of the program (Figure 4.9). The figure shows the percentage of participants who required support throughout the program

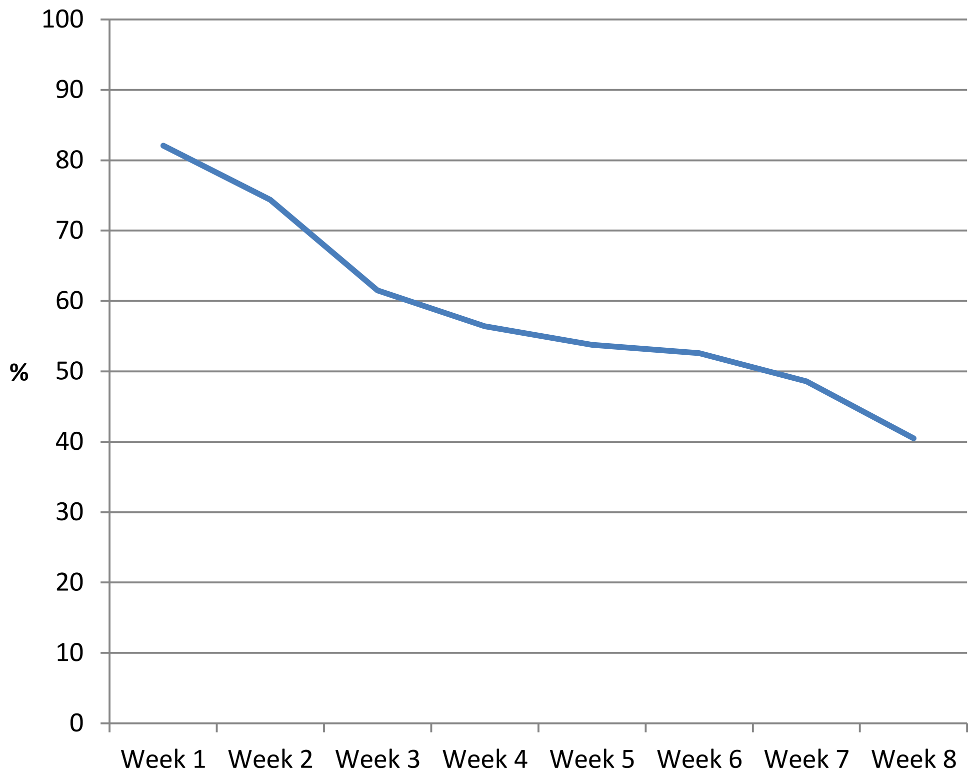


Figure 4-9: Level of support needed throughout the training program

(From support staff) - "At the start I'd sit with her all the time, but she's well able now so I just leave her to it."

Taken from Field Notes

The average amount of support given by the researcher, staff, family member, or training completed independently was calculated based on the average number of days support was given per week.

The majority of participants (62.5%) were living with family, and of these, some completed the cognitive training in day service on some days and at home on other days.

The average support given was calculated based on whether support was needed, and whether staff/family support was available to the individual.

Table 4.13 below outlines the percentage of time by whom support was given, when it was needed.

Table 4-13: Support given by whom

	% of time support was given
Researcher*	46.7
Staff	9.6
Family Carer	14.7
On own	29

*It should be noted that the researcher had made scheduled appointments with the individual, and thus, had the researcher not completed the training, the % for ‘staff’/’family’/’on own’ could have increased accordingly.

4.3.2.2 How much training is involved for those supporting the individual?

Training was given by the researcher to all supporters at the first training session. The individual who was to be the primary supporter sat in on the first training session. The majority of support persons were familiar and comfortable with the basics of an iPad or similar. If not, however, the training initially covered the basics of how to turn on the iPad, how to connect to the internet and how to log in to the cognitive training program, with username and password.

The support person then observed the researcher and participant going through the rules and gameplay. At the end of the training session, the researcher went through all steps again with support person. The researcher met with participants to complete the training 2-3 times per week, and thus any further questions from the support person or participant were addressed at the training session.

Support persons had a positive experience of the cognitive training program.

(From parent) – "I thought it was really good – really useful. I can see how it would be a good thing, because [name] would never have the chance to do anything like that"

(From parent) – "If you were doing something like that again we'd do it again. Maybe if we could have some different games next time, because I think she knows all of them now, so she'd prefer new ones"

(From parent) – "I think we'd need a break now alright, I think the 8 weeks was long enough, the last week we struggled a bit to get it done. Having said that though, after a break or if it was happening again, let us know"

(From parent) – "She seemed to enjoy it and she was getting better at the games alright. Once she's happy, I'm happy".

(From parent) – "Really interesting, and really great to see him do it and get so good at the games. We'll really miss it now that it's done"

From Exit Interviews

4.3.3 Environment

Overall, 62.5% (n=25) completed the training solely at home, 7.5% (n=3) completed the training solely in the day service and 30% (n=12) completed the training both at home and in the day service.

There was no significant relationship between the environment in which the training was completed and the amount of time participants spent doing the cognitive training program; Fisher's Exact Test (p=.50).

Three parents suggested in the exit interview that the program may be better delivered as part of the day service program.

(From parent) - "I think if you were doing it again it would be good to get the day service on board. I think it would be great for them to do it in there, because a lot of the time I feel they're a bit bored in there"

(From parent) – "It would be a lot easier to get it done if it was part of the program in the day centre. She has a routine when she comes home, and it's hard to change that, but she liked it, so she'd bemuch happier doing it in there"

(From support staff) – To be honest I think she'd do it better in there (day service). There's so many things going on when she gets home, it's harder to do it here"
Taken from exit interviews

Based on the parameters set out for the support required to effective conduct the cognitive training with this population, it was found that while support was indeed needed for some throughout the program, half of participants were able to complete the training independently by the end of the program. The environment in which the training was completed did not appear to have an impact on successful completion of the training.

4.4 Thematic Analysis of Interview and Field Notes

A thematic analysis was conducted on the field notes and the exit interviews using Braun and Clarke (2006) framework. Both participants and carers were satisfied with the program overall. All participants noted that they had really enjoyed the training program in the exit interviews and that they would complete a similar program again, given the opportunity. This was noted in the field notes also throughout the course of the program also. All the carers interviewed also reported being happy with the program overall. The most frequent challenge noted was scheduling the training, both in terms of researcher visits and scheduling training times. This challenge was noted from the participants, who had a number of other activities to also attend, and from staff who found it difficult to schedule individual time to complete training. While literacy was not a prerequisite for the games, there was a large amount of written instructions and this was noted as an inhibitor. Participants recommended that if the program were to be conducted again that the graphics on the program should be improved to increase stimulation and to include games with more action. Support persons recommended that the program should be integrated into the day service program. Two reasons for this recommendation emerged from the thematic analysis; 1) it was felt that it would enhance the time spent in the day program 2) it would make it easier to complete the training as scheduling the training was challenging, as mentioned. These themes that emerged from the thematic analysis are illustrated in Figure 4.10.

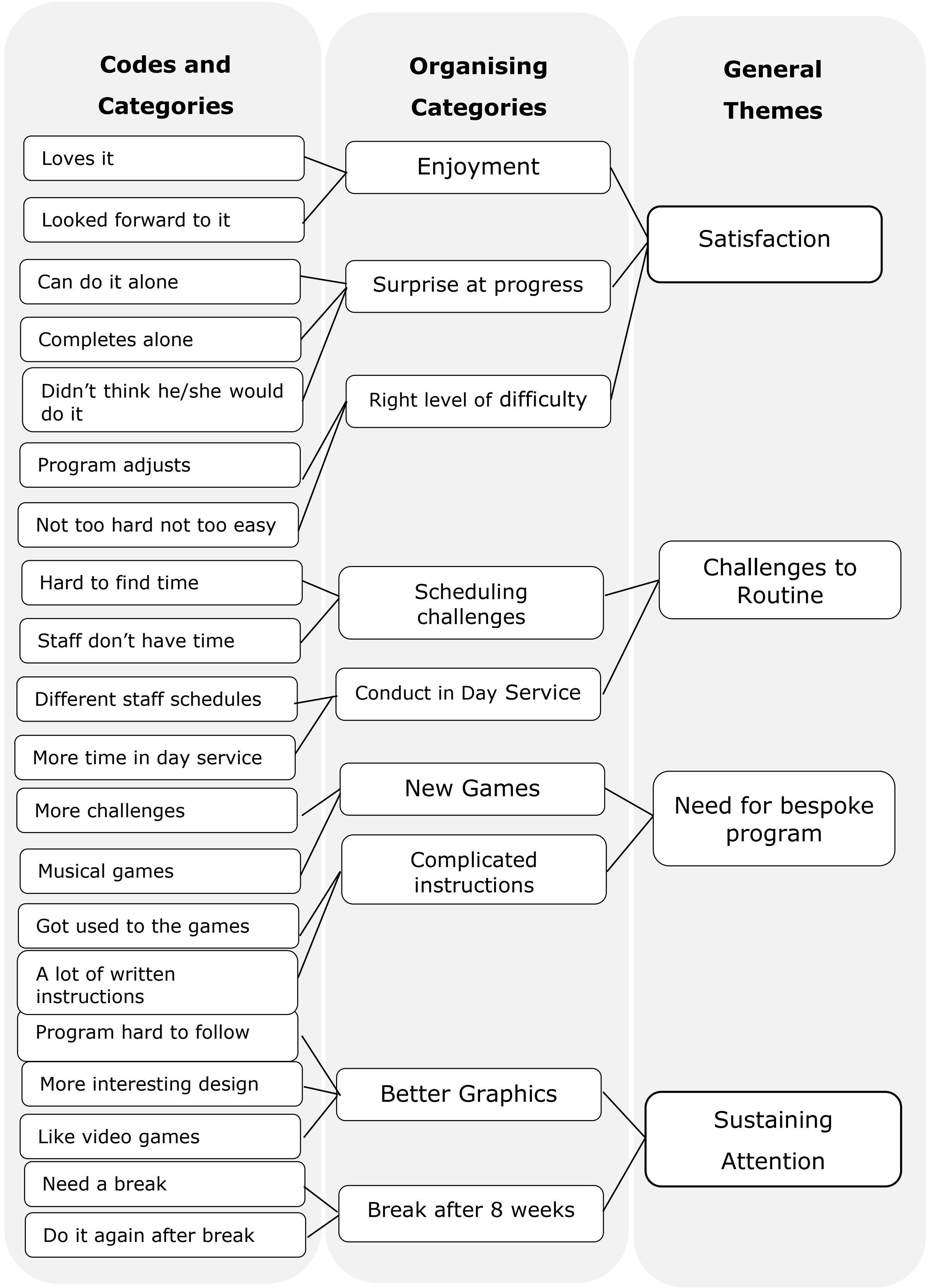


Figure 4-10: Themes emerging from exit interview and field notes

4.5 In Sum

Taken together, the findings support that conducting a cognitive training program with this population is feasible. Levels of enjoyment and adherence to the program were high, with 90% of participants completing the entire program, with 97% indicating a high level of acceptability. The environment in which participants completed the training did not appear to have an effect on the amount of time spent on the program.

Both participants and support staff and family were positive about the training program, with scheduling of training the biggest challenge. There were recommendations that it may be more beneficial for the training to be completed as part of the day service which may further increase use of this programming approach.

The following chapter will report on the effects of the training on levels of executive function, through comparison of executive function scores within participants, between groups and examining the interaction effects.

CHAPTER 5

IMPACT OF COGNITIVE TRAINING ON EXECUTIVE FUNCTION

5 Impact of cognitive training on executive function

5.1 Introduction

Chapter 5 presents the findings related to objectives 2 – 5, which are:

- To investigate whether cognitive training has an influence on executive function in adults with Down syndrome.
- To investigate whether cognitive training has an influence on behaviours related to executive functioning as perceived by family members/carers using the Behaviour Rating Inventory of Executive Function.
- To investigate whether variables such as age, IQ, cognitive ability, and time spent are predictive of change in scores post intervention.
- To investigate the relationship between cognitive reserve and executive function.

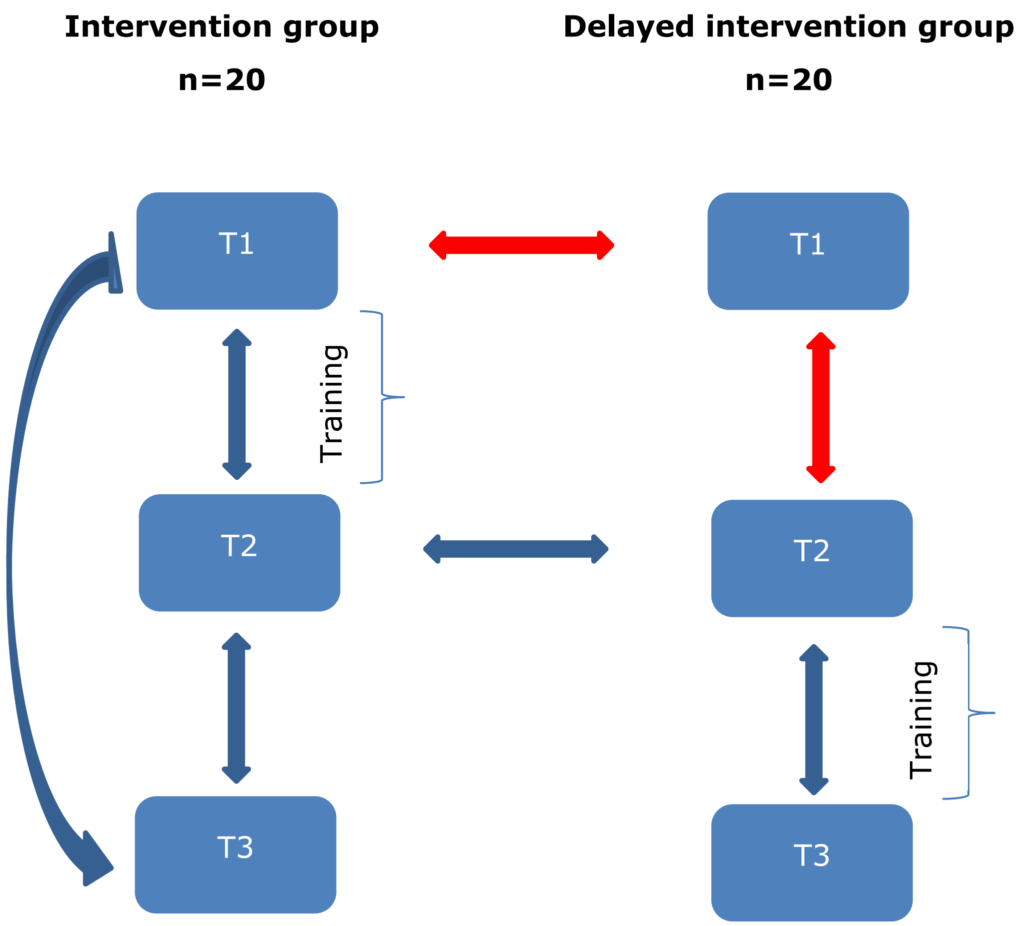
The related hypotheses are listed in Table 5.1

Study Objective	Null Hypothesis	Alternative Hypothesis
To investigate whether cognitive training has an influence on executive functions in adults with Down syndrome.	Cognitive training has no influence on executive functions in adults with Down syndrome	Cognitive training has an influence on executive functions in adults with Down syndrome
To investigate whether cognitive training has an influence on behaviours related to executive functioning as perceived by family members/carers using the Behaviour Rating Inventory of Executive Functions.	There are no changes in behaviours related to executive functioning after cognitive training as perceived by family members	Changes in behaviours related to executive functioning were seen after cognitive training as perceived by family members
To investigate whether variables such as age, IQ, cognitive ability, and time spent are predictive of change in executive function scores post following cognitive training.	Age, IQ cognitive ability and time spent on the program are not predictive of change in scores of executive function following cognitive training	Age, IQ cognitive ability and time spent on the program are predictive of change in scores of executive function following cognitive training
To investigate the relationship between cognitive reserve and executive function	There is no relationship between cognitive reserve and executive function	There is a relationship between cognitive reserve and executive function

Table 5-1: Study Objectives and Associated Hypotheses

The effect of cognitive training both within participants' (pre and post intervention) and between groups (intervention group and the delayed intervention group) is reported in this chapter. The comparability of the groups was assessed at baseline in terms of demographic data and baseline scores of executive function assessment.

Figure 5.1 below summarizes the associations of interest for both within subjects and between groups.



*Arrows in red represent comparisons between groups at baseline, and tests for practice effects

Figure 5-1: Associations tested for within subjects and between groups effects

The chapter is divided into five sections. The first section deals with baseline comparisons between the treatment and control groups on demographic and EF variables and therefore considers if there are alternative explanations to any effects seen following the training.

Section 2 of the chapter reports differences in scores from pre intervention to post intervention within groups, for both the treatment and delayed intervention groups and also the difference between the groups at T2. The interaction effect between the treatment and delayed intervention groups is also reported. Section 3 is focused on any maintenance effects seen in the intervention group. Section 4 examines the influence of external variables including age, IQ cognitive ability and minutes spent on the program. These 4 sections therefore address study objectives 2, 3 and 4. Finally section 5 addresses objective 5 by examining the relationship between cognitive reserve and executive function, including whether baseline level of cognitive reserve was predictive of change in score of EF following the cognitive training program.

Section 1

5.2 Comparability of Groups at Baseline

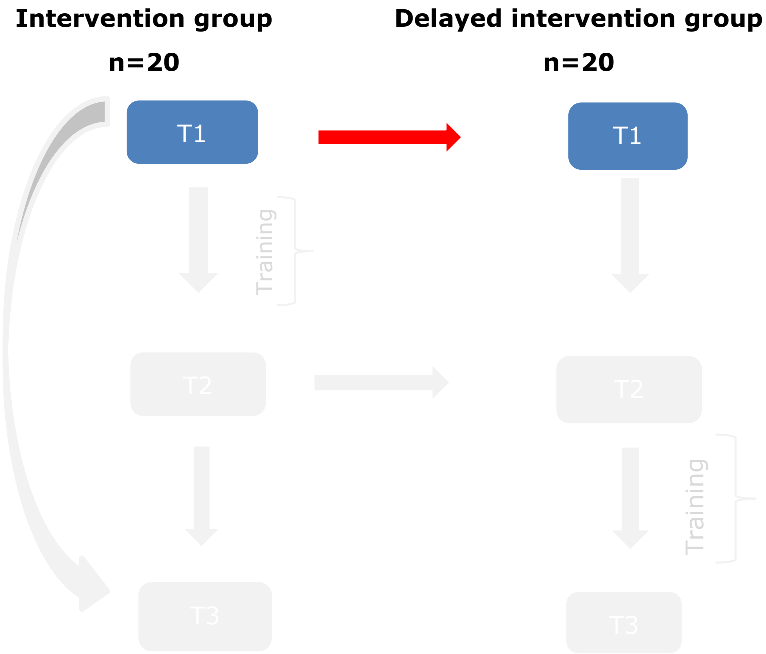
The treatment and delayed intervention groups were compared at baseline across the key demographic variables and on prior use of an iPad. A chi squared test of independence was conducted for the categorical variables; gender, level of ID and use of an iPad. An independent samples t-test was conducted for continuous variables; age, IQ and cognitive ability.

At baseline it was found that there were no significant differences between the treatment and delayed intervention group across the demographic variables (Age, IQ, cognitive function, gender, level of ID) as shown in Table 5.2 below. No significant difference was found either between the groups on previous use of an iPad. The minimal differences in age, IQ, cognitive function, gender and level of ID support the comparability of the groups

Table 5-2: Demographics at baseline

	Treatment		**Delayed Control**			
	Mean	**SD**	**Mean**	**SD**	**t- statistic**	**p-value**
Age	36.9	5.65	36.9	5.9	0	>.99
IQ	43.29	7.70	43.45	8.10	-.06	.96
Cognitive Ability	21.4	3.91	22.35	2.3	-.936	.36
	Treatment		Delayed Control			
	n	%	N	%	χ^2	p-value
Gender						
Male	9	45	5	25		
Female	11	55	15	75	1.78	.19
Level of ID						
Mild	3	15	7	35		
Moderate	17	85	13	65	2.13	.14
Use of iPad						
Yes	10	50	12	60	.404	.53

5.2.1 Executive Function comparisons at baseline



As with demographic variables, assessments of EF were measured at baseline to examine potential confounders that would impact the interpretation of the results post intervention. An independent samples t-test found no statistically significant difference in mean scores of EF between the groups at baseline, both on neuropsychological assessments and on behaviours of executive function.

See Tables 5.3 and 5.4 below.

Table 5-3: Neuropsychological executive function assessments at baseline

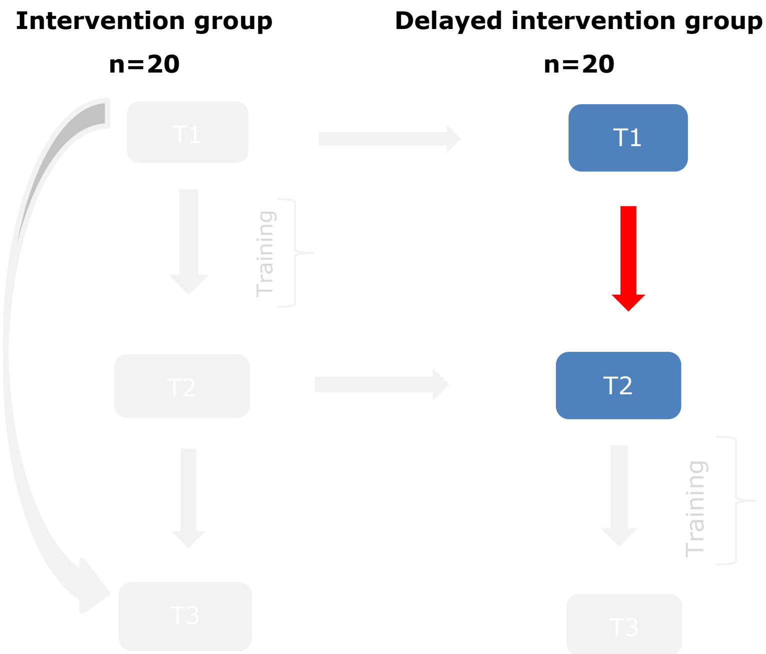
	Treatment		Delayed Control			
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**
Cats and Dogs	5.4	5.6	6.85	4.9	-.86	.393
Tower of London	8	3.7	9.1	2.9	-1.0	.304
Scrambled Boxes	7.4	2.6	7.45	2.2	-.07	.948
Spatial Reversal	2.95	2.9	3	2.5	-.06	.955
Weigl Card Sorting	1.9	1.4	1.95	1.6	-.11	.917

Table 5-4: Behaviours of executive function at baseline

	Treatment		Delayed Control			
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**
Inhibit	49.55	7.01	49.95	5.21	2.00	.843
Shift	62.75	11.15	59.79	8.11	.944	.351
Emotional Control	52.45	8.75	52.26	8.31	.068	.946
Self-Monitor	54.95	9.27	58.53	7.05	1.651	.185
BRI	54.2	5.56	56.21	9.85	.681	.500
Initiate	60.90	11.64	55.63	7.80	1.651	.107
Working Memory	62.30	12.44	58.37	10.00	1.084	.285
Plan/Organise	56.20	10.49	55.79	6.97	.143	.887
Task Monitor	59.05	11.82	59.68	8.06	.195	.847
Organise materials	46.2	7.95	45.95	6.63	.107	.915
MCI	57.65	9.48	54.74	6.36	1.121	.270
GEC	56.2	8.30	55.16	5.69	.455	.652

BRI=Behaviour Regulation Index; MCI-Metacognitive Index; GEC = Global Executive Composite

5.3 Delayed intervention group at T2



Scores for participants in the delayed intervention group on neuropsychological measures of EF, and on the proxy rated BRIEF-A at baseline (T1) were compared with their corresponding scores at T2 using a paired samples t-test.

It was found that there was no significant difference in EF scores between T1 and T2 in either the neuropsychological assessments or in behaviours of executive function for the delayed intervention group, suggesting that practice effects were not significant. See Tables 5.5 and 5.6 below.

Table 5-5: Executive function scores of neuropsychological assessments from T1 to T2 for delayed intervention group

	Neuropsychological assessments					
	T1		**T2**		**T statistic**	**p-value**
	Mean	**SD**	**Mean**	**SD**		
Cats and Dogs	6.85	4.97	5.9	5.6	1.8	.075
Tower of London	9.1	2.9	9.5	2.5	1.1	.288
Scrambled Boxes	7.45	2.5	7.25	1.7	.721	.479
Spatial Reversal	3	2.5	3.2	1.9	.58	.569
Weigl Card Sorting	1.95	1.57	1.95	1.66	.000	1.00

Table 5-6: Behaviours of executive function from T1 to T2 for delayed intervention group

	Behaviours of Executive Function					
	T1		T2		T statistic	p-value
	Mean	SD	Mean	SD		
Inhibit	50.22	5.22	49.56	7.23	.702	.492
Shift	60.11	8.22	61.00	8.23	.551	.589
Emotional Control	52.78	8.24	49.17	5.36	1.876	.078
Self-Monitor	58.44	7.25	60.78	8.95	1.637	.120
Behavioural Regulation Index	56.61	9.98	54.50	6.35	1.037	.314
Initiate	55.56	8.02	56.06	8.29	.337	.711
Working Memory	58.28	10.29	59.61	10.01	.539	.597
Plan/Organise	56.06	7.07	54.28	6.07	1.947	.068
Task Monitor	59.50	8.24	61.56	8.53	.882	.390
Organise materials	45.83	6.80	44.89	5.03	.991	.375
Meta Cognitive Index	54.72	6.54	54.33	5.67	.324	.750
Global Executive Composite	55.28	5.83	53.11	6.31	1.355	.193

*Lower score denotes lower level of dysfunction

Section 2

5.4 Examining the Impact of Cognitive Training on Level of Executive Function

This section will focus on the effect of cognitive training on both the intervention group and delayed intervention groups. This was examined in a number of ways. Firstly, a two way mixed ANOVA was conducted to examine the interaction effect between the group and intervention factors.

The pre-intervention baseline scores (T1) of the intervention group were compared to their post intervention scores (T2). As discussed, this procedure was then repeated by comparing the pre intervention scores for the delayed intervention group (T2) to their corresponding post intervention scores (T3). These comparisons were made using a paired samples t-test, in order to show the within subjects effect. In addition to the within subjects effect, the change in mean scores between the groups at T2 were examined, using an independent samples t-test.

5.4.1 Bonferroni Correction

Multiple comparisons were made and thus a Bonferroni correction was used, but results will be discussed with respect to both the adjusted alpha level and a less stringent alpha level. For clarity, the actual p-value will be reported in the tables below, except in cases where $p<.001$.

5.4.2 Examining the interaction effect between Group and Time

A two-way mixed ANOVA was conducted in order to understand if there was a two-way interaction between the within subjects (T1 to T2) and the between groups factors (Treatment and Control).

Figure 5.2 graphs the interaction effect for the neuropsychological assessments, where it can be seen that scores increased for the intervention group at T2, whereas this did not happen for the delayed intervention group in 4 of the assessments. This suggests that the completing the cognitive training had an effect on executive function. This effect was not as pronounced for behaviours of executive function, where Figure 5.3 shows that a statistically significant interaction was seen only in 3 of the 12 measures of behavioural EF. Results from the interaction are described in detail below. A higher score for the BREIF-A which measures behaviours of EF indicates a higher level of dysfunction. The decrease seen in Figure 5.3 thus indicates an improvement in behaviours of EF.

5.4.2.1 Neuropsychological Assessments

There was a statistically significant interaction effect between group and time for Cats and Dogs Stroop $F(1,38) = 26.512$, $p<.001$, $\eta^2 = .411$ and for Tower of London $F(1,38) = 33.409$, $p<.001$, $\eta^2 = .468$.

An interaction effect was seen for Scrambled Boxes $F(1,38) = 5.801$, $p = .021$, $\eta 2 = .110$, and for Weigl Card Sorting Task $F(1,38) = 7.12$, $p = .011$, $\eta^2 = .158$, however these were not statistically significant for alpha level .001.

No significant interaction effect was seen for Spatial Reversal $F(1,38) = 1.114$, $p = .298$ $\eta^2 = .028$.

5.4.2.2 Behavioural Executive Function Assessments

An interaction effect was seen for the initiate component of the BRIEF-A, showing a trend towards significance $F(1,38) = 8.61$, $p = .006$, $\eta^2 = .181$, for working memory; $F(1,38) = 5.29$, $p=.027$, $\eta^2 = 119$, and for the metacognitive index; $F(38) = 4.833$, $p = .034$, $\eta^2 = .116$. These however were not significant to the alpha level of .001

Figures 5.2 and 5.3 below graph the interaction effect for assessments that were trending to significance, with level of significance indicated. See Table 5.7 for interaction effects for all neuropsychological and behavioural assessments.

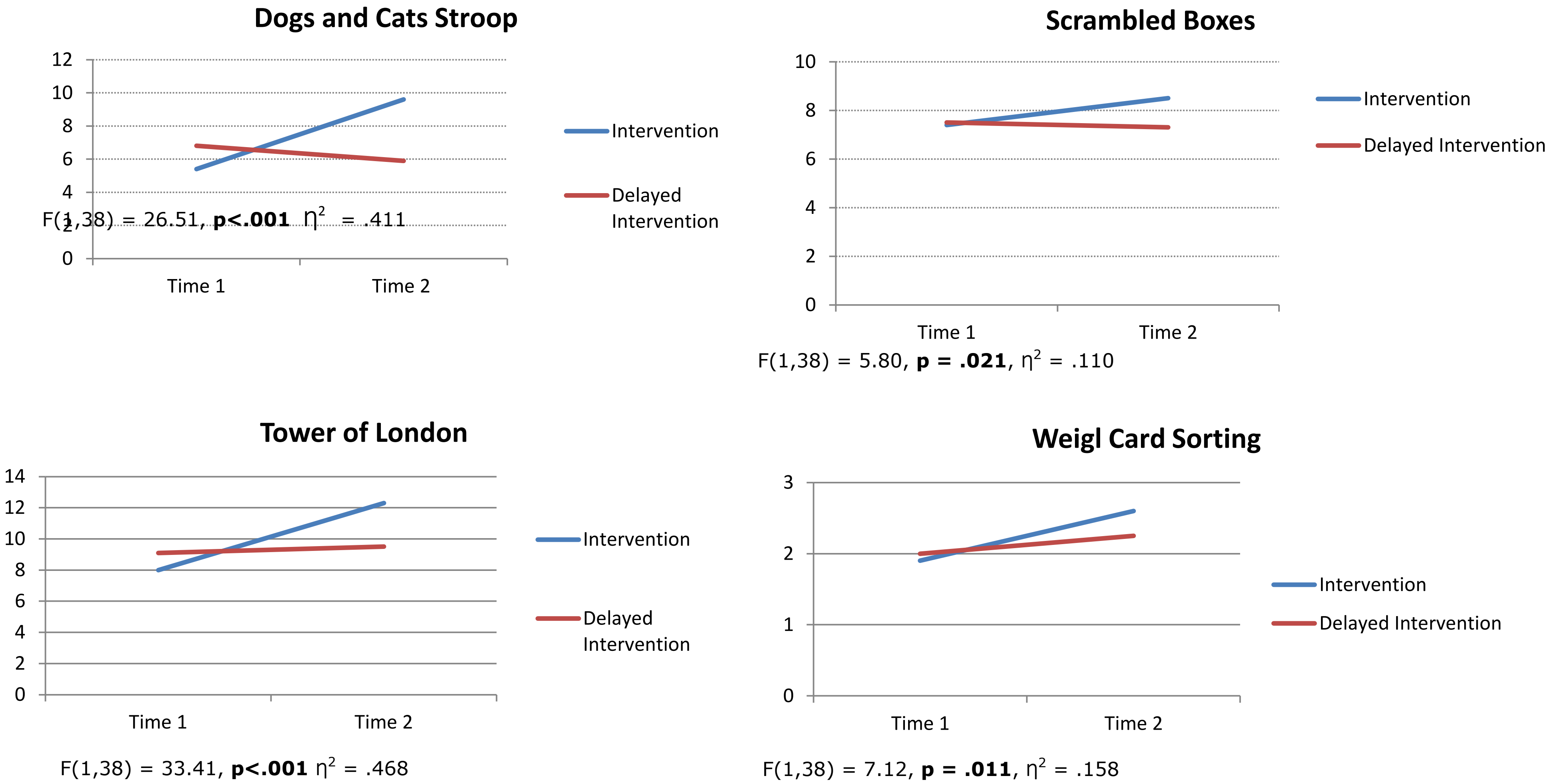
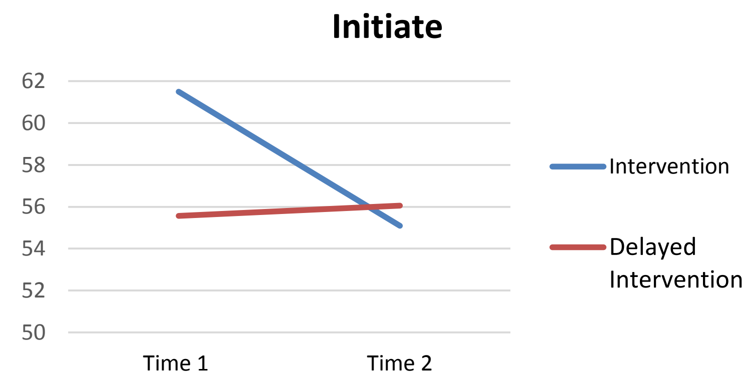
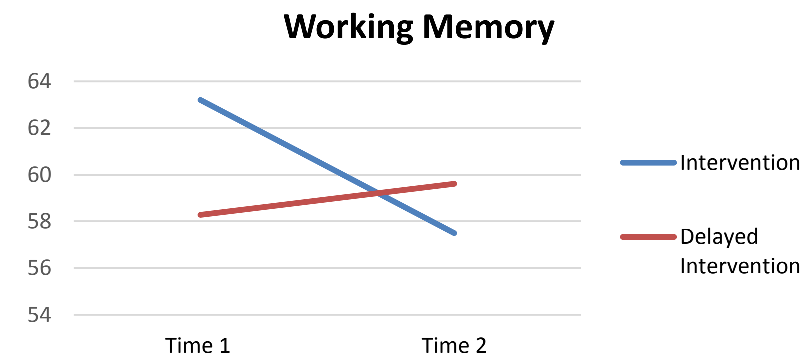


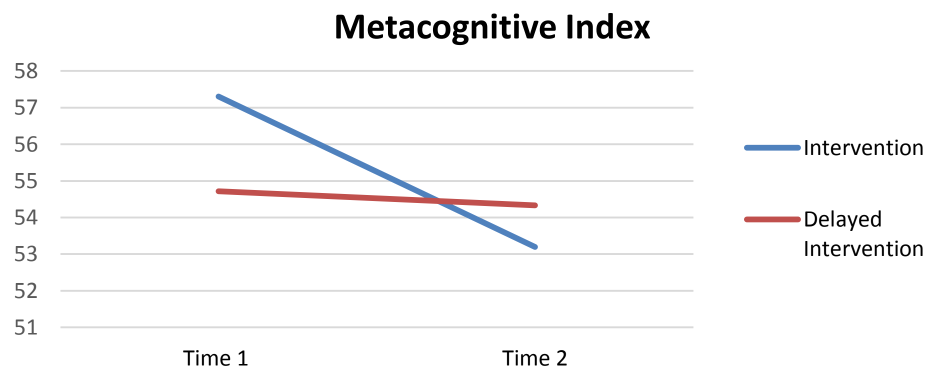
Figure 5-2: Graph of significant interaction effect between group and time for neuropsychological assessments



F(1,38) = 8.61, **p = .006**, η^2 = .181



F(1,38) = 5.29, **p=.027**, η^2 = 119



F(1,38) = 4.58**, p = .034**, η^2 = .116

Figure 5-3: Graph of significant interaction effect between group and time for behaviours of executive function*

***Lower score indicates lower level of dysfunction**

Table 5-7: Interaction effects between group and time

Neuropsychological Assessments of Executive Function					
	F	**df**	**p-value**	**Sig to .001**	**Partial η^2**
Cats and Dogs	**26.51**	**(1,38)**	**<.001**	**Yes**	**.41**
Tower of London	**33.41**	**(1,38)**	**<.001**	**Yes**	**.47**
Scrambled Boxes	**5.80**	**(1,38)**	**.021**	**No**	**.11**
Spatial Reversal	1.11	(1,38)	.298	No	.03
Weigl Card Sorting	**7.12**	**(1,38)**	**.011**	**No**	**.16**

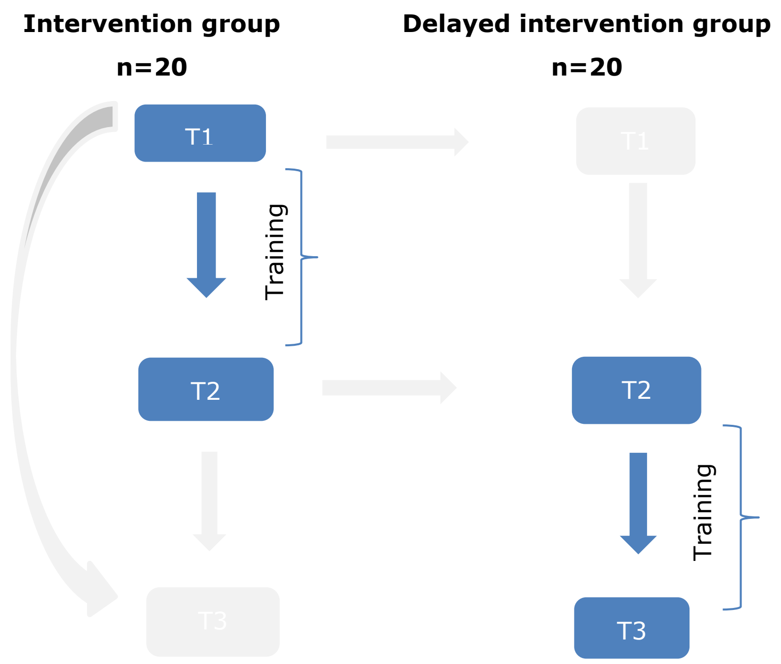
Behaviours of Executive Function					
	F	**df**	**p-value**	**Sig to .001**	**Partial η^2**
Inhibit	1.14	(1,38)	.292	No	.03
Shift	1.63	(1,38)	.209	No	.02
Emotional Control	0.26	(1,38)	.613	No	.01
SelfMonitor	2.65	(1,38)	.112	No	.07
Behavioural Regulation Index	0.19	(1,38)	.669	No	.01
Initiate	**8.61**	**(1,38)**	**.006**	**No**	**.18**
Working Memory	**5.29**	**(1,38)**	**.027**	**No**	**.12**
Plan/Organise	0.38	(1,38)	.542	No	.04
Task Monitor	0.77	(1,38)	.386	No	.03
Organise materials	1.10	(1,38)	.301	No	.02
Meta Cognitive Index	**4.58**	**(1,38)**	**.034**	**No**	**.12**
Global Executive Composite	1.02	(1,38)	.320	No	.02

5.4.3 Changes in executive function scores post intervention

A paired samples t-test was conducted to examine the difference in pre intervention scores and post intervention scores of executive function, for both neuropsychological and behavioural assessments in the intervention group first, and then in the delayed intervention group. This determined whether the mean scores on all executive function assessments post cognitive training compared to pre cognitive training was statistically different to zero.

Overall both groups showed a significant improvement in neuropsychological assessments following the cognitive training program. As was found with the interaction effect, the change from pre to post intervention was not as apparent for the behaviours of executive function.

Detailed results from both the intervention and delayed intervention groups are displayed below for the neuropsychological assessments and for the behaviours of EF as measured by the BRIEF-A.



5.4.3.1 Neuropsychological Assessments

For the intervention group, it was found that scores on the "Cats and Dogs Stroop", t(19) = -5.0, p<.001, *d* = -1.15 and "Tower of London", t(19)= -8.3, p<.001, *d*=-1.90 assessments were significantly higher post intervention even at the more stringent alpha level, both with large effect sizes. The "Weigl card sorting" assessment appeared to show an improvement, t(19) = -3.2, p=.006, *d* = -.73 but was not significant at the more stringent level, and had a medium effect size. The "Scrambled Boxes" assessment showed a trend towards significance (.030), but did not reach significance at the adjusted alpha level. It also showed a medium effect size. There was no significant difference in mean scores for the "Spatial Reversal" assessment for the intervention group post intervention (p= .183).

The delayed intervention group showed a significant improvement post intervention on all scores of the neuropsychological assessments of EF; Tower of London t(19) = -8.6, p<.001, *d* =-1.9 "Cats and Dogs Stroop" t(19) = -5.7, p<.001, *d* =-1.4, "Scrambled Boxes" t(19) = -5.0,p <.001, *d* =-1.1, "Spatial Reversal" t(19) = -4.3, p<.001, *d* = -0.9 and "Weigl Card Sorting" t(19) = -5.8, p<.001, *d* = -1.4.

All assessments for the delayed intervention group showed a large effect size as measured by Cohen's *d*.

5.4.3.2 Behavioural Executive Functions

For the intervention group, significant changes were seen for Emotional Control, with a large effect size t(19) = 3.95, p ≤.001, *d*= 1.01 and a significant improvement was seen in the Global Executive Composite scores with large effect size t(19) – 4.14, p<.001, *d* = 1.02. Changes were seen also in initiation and in the metacognitive index of behavioural executive function, although not at the more stringent alpha level; initiation t(19) = 3.07, p = .006, *d* – 0.73; metacognitive index t(19) = 3.28, p = .004, *d* =-0.80.

In the delayed intervention group, no significant changes were seen in behavioural executive function when using the stringent alpha level of .001. Both emotional control and the behavioural regulation index approached this stringent significant level; Emotional Control t(19) = 3.73, p = .002, *d* = -0.85; Behavioural Regulation Index t(19) = 3.21, p = .005, *d* = -0.76, both showing a large effect.

Tables 5.8 and 5.9 display the pre and post intervention assessment scores for the intervention group and the delayed intervention group, respectively.

Table 5-8: Pre and post intervention scores for intervention group

	T1		T2					
	Neuropsychological Assessments of Executive Function							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Cats and Dogs	**5.7**	**5.6**	**10.11**	**5.7**	**4.86**	**<.001**	**Yes**	**-1.15**
Tower of London	**8.2**	**3.6**	**12.3**	**3.8**	**8.26**	**<.001**	**Yes**	**-1.90**
Scrambled Boxes	7.6	2.6	8.6	2.1	2.36	.030	No	-0.55
Spatial Reversal	3.1	2.9	4.1	3.1	1.39	.183	No	-0.32
Weigl Card Sorting	**2.0**	**1.4**	**2.5**	**1.6**	**3.15**	**.006**	**No**	**-0.73**
	Behaviours of Executive Function*							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Inhibit	49.4	7.1	47.2	7	1.94	.067	No	0.45
Shift	62.8	11.5	59.7	9.1	1.26	.225	No	0.29
Emotional Control	**52.6**	**8.9**	**48.2**	**7.0**	**3.95**	**.001**	**Yes**	**1.01**
SelfMonitor	55.4	8.9	53.5	5.6	0.89	.385	No	0.22
Behavioural Regulation Index	54.7	8.4	51.8	5.5	2.31	.033	No	0.60
Initiate	**61.5**	**11.7**	**55.1**	**10.1**	**3.07**	**.006**	**No**	**0.73**
Working Memory	63.2	12.1	57.5	10.8	2.70	.015	No	0.62
Plan/Organise	56.5	10.7	53.4	10.0	1.96	.065	No	0.42
Task Monitor	60.0	11.3	58.6	9.0	0.57	.576	No	0.14
Organise materials	45.0	8.1	43.0	5.7	1.51	.148	No	0.24
Meta Cognitive Index	**57.3**	**9.6**	**53.2**	**8.1**	**3.28**	**.004**	**No**	**0.80**
Global Executive Composite	**56.6**	**8.3**	**52.9**	**7.0**	**4.14**	**<.001**	**Yes**	**1.02**

*Lower score denotes lower level of dysfunction;

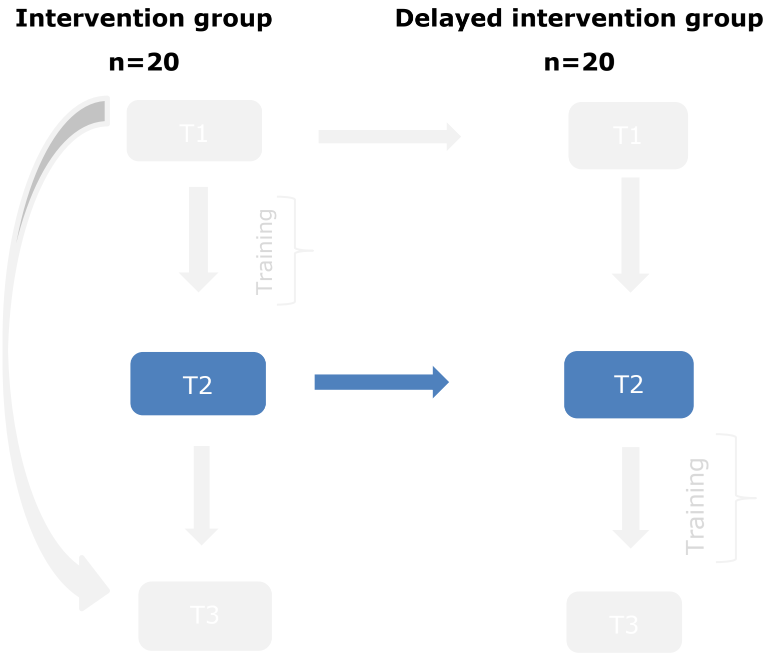
Table 5-9: Pre and post intervention scores for delayed intervention group

	T2		T3					
	Neuropsychological Assessments of Executive Function							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Cats and Dogs	**5.9**	**5.6**	**10.10**	**4.0**	**5.7**	**<.001**	**Yes**	**-1.4**
Tower of London	**9.5**	**2.6**	**13.1**	**3.0**	**8.6**	**<.001**	**Yes**	**-1.9**
Scrambled Boxes	**7.25**	**1.7**	**8.95**	**1.9**	**5.0**	**<.001**	**Yes**	**-1.1**
Spatial Reversal	**3.2**	**2.0**	**4.8**	**2.3**	**4.3**	**<.001**	**Yes**	**-0.9**
Weigl Card Sorting	**1.95**	**1.7**	**3.2**	**1.2**	**5.8**	**<.001**	**Yes**	**-1.4**
	Behaviours of Executive Function*							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Inhibit	49.6	7.2	47.7	6.0	0.60	.556	No	0.30
Shift	61.0	9.8	61.1	9.8	0.02	.981	No	0.01
Emotional Control	**49.1**	**5.4**	**45.8**	**5.5**	**3.73**	**.002**	**No**	**0.85**
Self-Monitor	60.8	9.0	59.4	9.1	.841	.412	No	0.20
Behavioural Regulation Index	**54.5**	**6.3**	**52.4**	**6.0**	**3.21**	**.005**	**No**	**0.76**
Initiate	56.1	8.3	54.0	6.6	1.45	.165	No	0.36
Working Memory	59.5	10.0	57.3	9.3	1.71	.104	No	0.39
Plan/Organise	50.6	6.1	49.7	5.6	0.81	.431	No	0.22
Task Monitor	61.6	8.5	62.1	8.0	0.34	.740	No	0.08
Organise materials	44.9	5.0	42.9	4.5	2.38	.030	No	0.58
Meta Cognitive Index	54.3	5.7	52.7	5.2	1.60	.130	No	0.36
Global Executive Composite	53.1	6.3	52.8	4.6	0.18	.862	No	0.05

*Lower score denotes lower level of dysfunction;

5.4.4 Difference between treatment and delayed intervention group at T2

The changes that were noted within the groups post intervention have been examined in the previous section. Also of interest, was the difference between the groups at T2; at this point the intervention group have received the intervention, while the control group have not.



5.4.4.1 Neuropsychological Assessments

Using the more stringent alpha, no significant differences were found between the treatment and control groups at T2. Using a less conservative significance level of .05, difference in the mean scores could be seen for the "Tower of London", "Cats and Dogs Stroop" and "Scrambled Boxes" (Table 5.10).

Scores on the "Cats and Dogs Stroop" assessment were higher for the intervention group (10.1±5.6) than the delayed intervention group (5.9±5.6), $t(38) = 2.33$, $p = 0.26$. $d = 0.19$.

Scores on the “Tower of London” assessment were higher for the intervention group (12.8±3.8) than the delayed intervention group (9.5±2.6), $t(31.34) = 3.12$, $p = 0.004$, $d = 1.00$.

Score on the “Scrambled Boxes” assessment were higher for the intervention group (8.8±2.1) than the delayed intervention group (7.3±1.7), $t(38) = 2.59$, $p = 0.14$, $d = 0.85$.

5.4.4.2 Behavioural Executive Functions

Using the stringent alpha level, no significant differences were found between the treatment and delayed intervention groups at T2. The scores on the Self Monitor assessments were significant to .005, where scores for the intervention group were higher (53.5±5.6) than the delayed intervention group (60.8±8.9), $t(38) = 2.3$, $p = .005$, $d = 0.98$.
Table 5.10 below displays results for all assessments

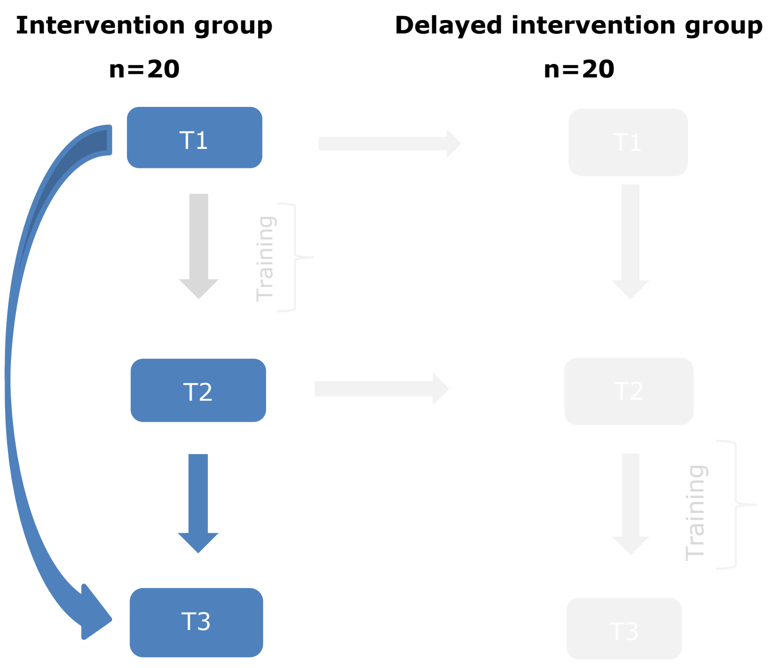
Table 5-10: Executive function scores in treatment and control group at T2

	Treatment (n=20)		Delayed Control (n=20)					
	Neuropsychological Assessments of Executive Function							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Cats and Dogs	**10.11**	**3.84**	**9.5**	**2.59**	**2.33**	**.026**	**No**	**0.19**
Tower of London	**12.79**	**3.84**	**9.5**	**2.59**	**3.12**	**.004**	**No**	**1.00**
Scrambled Boxes	**8.84**	**2.01**	**7.25**	**1.74**	**2.59**	**.014**	**No**	**0.85**
Spatial Reversal	4.32	3.16	3.2	1.96	1.32	.198	No	0.43
Weigl Card Sorting	2.68	1.6	1.95	1.67	1.40	.170	No	0.45
	Treatment (n=20)		Delayed Control (n=20)					
	Behaviours of Executive Function*							
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Sig to .001**	**Cohen's *d***
Inhibit	47.21	6.95	49.56	7.23	1.006	.321	No	0.33
Shift	59.74	9.14	61.00	8.21	.441	.662	No	0.14
Emotional Control	48.26	6.98	49.17	5.36	.440	.663	No	0.14
Self-Monitor	**53.47**	**5.60**	**60.78**	**8.95**	**2.99**	**.005**	**No**	**0.98**
Behavioural Regulation Index	51.79	5.50	54.50	6.35	1.39	.173	No	0.46
Initiate	55.11	10.07	56.06	8.29	.312	.757	No	0.10
Working Memory	57.47	10.82	59.61	10.01	.623	.538	No	0.21
Plan/Organise	53.42	10.01	54.28	6.51	.307	.761	No	0.10
Task Monitor	58.63	9.04	61.56	8.54	1.01	.319	No	0.33
Organise materials	43.00	5.70	44.89	5.03	1.07	.293	No	0.04
Meta Cognitive Index	53.21	8.13	54.33	5.67	.485	.631	No	0.16
Global Executive Composite	52.84	7.02	53.11	6.31	.122	.903	No	0.04

*Lower score denotes lower level of dysfunction;

5.5 Maintenance of effects for intervention group

As detailed above, the intervention group completed all assessments, completed the 8 week training program and then completed all EF assessments again. Following this, participants returned to normal care and executive function assessments were then completed again 8 weeks later. During this 8 weeks break, participants did not have access to the cognitive training program. This allowed investigation into maintenance effects.



Maintenance effects were measured (between T2 and T3), and the final EF scores were compared to baseline scores of EF (T1 and T3). These were conducted for intervention group only. See Table 5.11 below.

There were no significant change in scores on any of the EF assessments between T2 and T3, indicating that changes in EF that occurred between T1 and T2 were maintained over the 8 week period where participants were no longer using the cognitive training program, as verified by the program software.

When changes in EF scores were examined for the intervention group, from baseline, T1 to T3, significant improvements were seen for 3 of the assessments in the neuropsychological assessment; "Cats and Dogs Stroop" ($p<.001$), "Tower of London" ($p<.001$) and the "Weigl Card Sorting" ($p < .001$).

None of the components of the BRIEF-A reached statistical significance using the stringent alpha level, however a number showed improvement with a trend towards significance; metacognitive index ($p=.001$), plan/organise ($p=.004$), inhibit ($p=.005$), global executive composite ($p=.005$), emotional control, ($p=.016$), behavioural regulation index ($p=.040$), working memory ($p=.045$).

Table 5-11: Maintenance effect of cognitive training for intervention group

Neuropsychological Assessments (n=18)

	T2		T3				T1		T3				
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**t statistic**	**p-value**	**Cohen's *d***
Cats and Dogs	9.78	5.62	9.06	5.30	1.37	.190	**5.11**	**5.18**	**9.06**	**5.30**	**-4.89**	**<.001**	**-1.15**
Tower of London	12.50	3.73	12.44	4.18	.142	.889	**7.89**	**3.32**	**12.44**	**4.18**	**-6.87**	**<.001**	**-1.69**
Scrambled Boxes	8.72	2.08	8.50	2.07	.524	.607	7.39	2.50	8.5	2.07	-2.01	.061	-0.48
Spatial Reversal	4.17	3.19	4.17	2.71	0	>.999	2.89	2.90	4.17	2.71	-1.71	.106	-0.40
Weigl Card Sorting	2.56	1.54	2.83	1.43	2.05	.056	**1.89**	**1.37**	**2.83**	**1.43**	**-4.59**	**<.001**	**-1.06**

Behavioural Executive Functions (n=18)

	T2		T3				T1		T3				
	Mean	**SD**	**Mean**	**SD**	**t-statistic**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**t statistic**	**p-value**	**Cohen's *d***
Inhibit	47.94	6.85	47.00	5.54	.824	.423	**50.94**	**6.67**	**47.00**	**5.54**	**3.284**	**.005**	**0.83**
Shift	58.88	9.34	61.69	6.85	-1.272	.223	63.44	12.32	61.70	6.85	.578	.572	0.15
Emotional Control	49.50	6.88	50.13	7.24	-.598	.558	**53.70**	**9.29**	**50.13**	**7.24**	**2.713**	**.016**	**0.73**
Self-Monitor	54.69	4.56	54.38	6.52	.238	.815	56.94	9.15	54.38	6.52	.963	.351	0.25
Behavioural Regulation Index	52.63	5.30	53.06	5.26	-.699	.495	**56.06**	**8.44**	**53.06**	**5.26**	**2.246**	**.040**	**0.68**
Initiate	57.00	9.63	57.69	11.2	-.639	.532	62.06	10.82	57.70	11.21	2.020	.062	0.50
Working Memory	58.81	10.55	59.13	9.80	-.183	.857	**64.56**	**11.42**	**59.13**	**9.80**	**2.187**	**.045**	**0.55**
Plan/Organise	54.88	10.24	52.75	12.39	1.382	.187	**58.50**	**10.43**	**52.75**	**12.39**	**3.424**	**.004**	**0.89**
Task Monitor	57.81	9.22	58.44	9.06	-.273	.789	60.94	11.82	58.44	9.06	.986	.340	0.25
Organise materials	43.94	5.74	44.00	6.04	-.041	.968	47.44	7.97	44.00	6.04	2.70	.017	0.72
Meta Cognitive Index	54.44	8.15	54.38	8.20	.102	.920	**59.31**	**8.98**	**54.38**	**8.20**	**4.413**	**.001**	**1.05**
Global Executive Composite	54.00	6.83	54.75	6.89	-1.103	.287	**58.38**	**8.20**	**54.75**	**6.89**	**4.143**	**.005**	**0.82**

Figure 5.4 below displays data throughout the intervention process at T1, T2 and T3. Four of the neuropsychological assessments that reached significance are shown in the figure. It can be seen that there was an increase in scores in the intervention group between T1 and T2 (post training), with no increase in the delayed intervention group. Scores for the delayed intervention group then increased between T2 and T3 (upon completing training), while scores in the intervention group were maintained between T2 and T3.

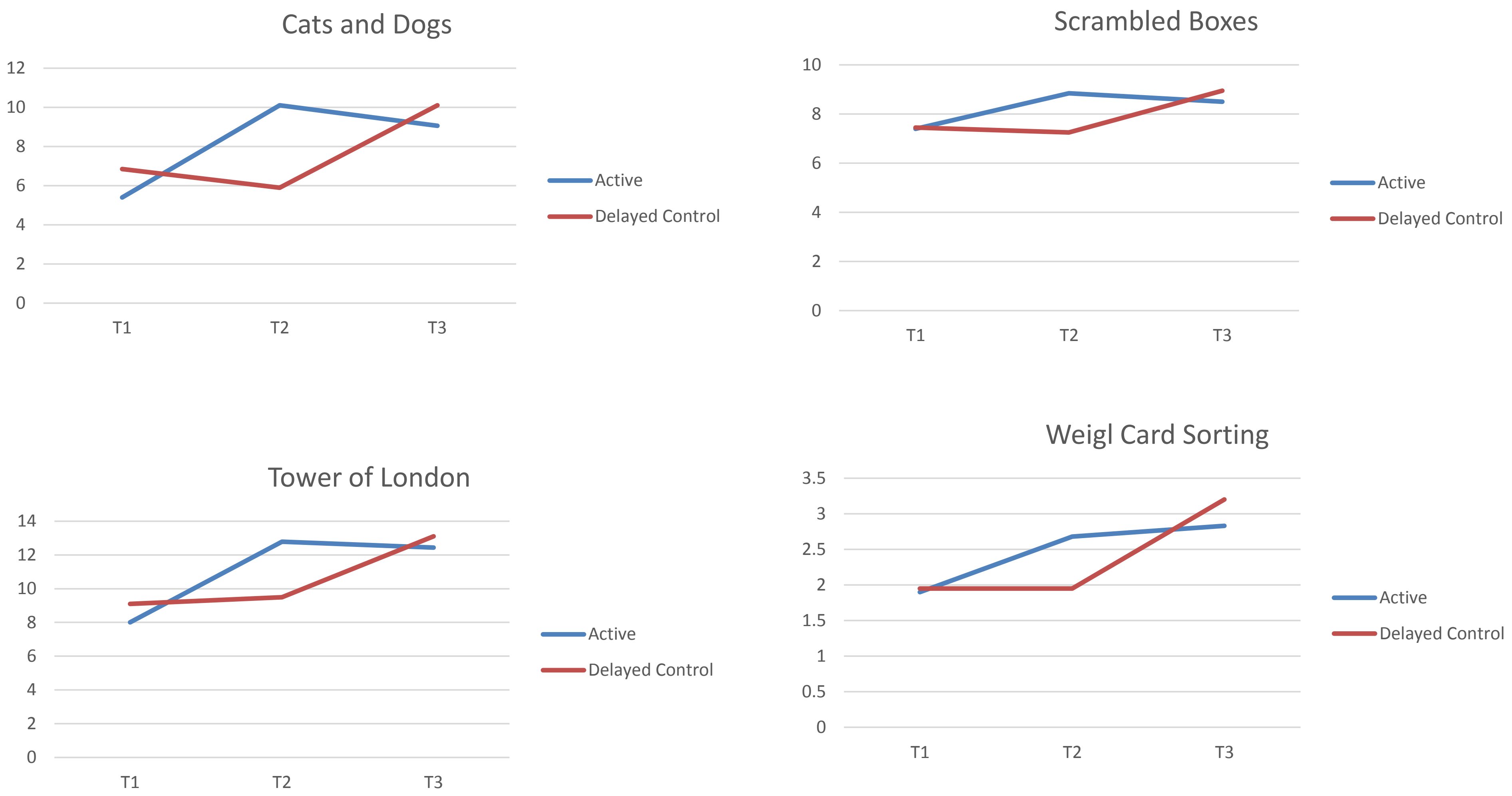


Figure 5-4: Scores for treatment and delayed control at T1 T2 and T3

5.6 Effects of age, IQ, cog ability and minutes spent

The descriptive statistics for age, IQ, cognitive ability and the number of minutes spent on the training program are below in Table 5.12.

Table 5-12: Descriptive statistics for age, IQ, cognitive ability and minutes spent

	n	Mean	SD	Min	Max	Median
Age	39	36.72	5.66	30	49	35
IQ	37*	43.38	7.81	32	63	43
Cognitive Ability	39	21.90	21.9	7	24	23
Minutes spent	39	954.05	848.50	339	5353	711.29

*if participant scored at baseline on Leiter 3, IQ was deemed indeterminate and not calculated, this occurred for n=2

The effects of age, IQ, cognitive ability and number of minutes spent on the program were investigated to see if there was any effect on the outcome of EF across the neuropsychological and behavioural EF. An analysis of covariance (ANCOVA) was conducted to examine these effects.

None of these covariates appeared to be predictive of change, with no significant effect observed. This suggests that age, IQ level, cognitive ability or the number of minutes spent on the training program do not have a significant effect on whether a change in EF scores would be observed

Due to the large variation in number of minutes spent, this element was examined also where times spent was categorised: 0-400 minutes, 400-800 mins; 800-1200 minutes and +1200minutes. A Kruskall-Wallis test showed that number of minutes spent did not appear to be a statistically significant predictor of change in post scores when categorised.

5.7 Relationship between cognitive reserve and executive function

This section will focus on the relationship between level of cognitive reserve and executive function, thus addressing study objective 5. The null hypothesis was that there is no relationship between cognitive reserve and level of executive function.

Levels of cognitive reserve for the whole sample were presented in the previous chapter, where it was found that the mean cognitive reserve score was 84.63 (SD=15.58), indicating a medium level of cognitive reserve.

This section examined the relationship between baseline level of cognitive reserve and baseline level of executive function, and also examined whether level of cognitive reserve was predictive of a change in scores of EF after the cognitive training intervention.

The relationship between levels of cognitive reserve and executive function were examined using Pearson's bivariate correlation. A stronger relationship was observed between level of cognitive reserve and neuropsychological assessments of EF than behavioural EF (Table 5.13).

A significant relationship with cognitive reserve was found in all 5 neuropsychological EF assessments ("Cats and Dogs Stroop", p<.001, "Tower of London", P<.001, "Scrambled Boxes", p<.0001, "Spatial Reversal", p=.003, "Weigl Card Sorting", p<.001).

Six of the 12 components of the BRIEF-A showed a significant relationship with cognitive reserve; shift (p=0.39), initiate (p=.001), plan/organise (p=.013), task monitor (p=.010), metacognitive index (p=.001) and the global executive composite score (p=.003) were all significantly related to levels of cognitive reserve.

Table 5-13: Relationship between cognitive reserve and executive function

Neuropsychological Assessments		
	r	p-value
Cats and Dogs	**.690**	**<.001**
Tower of London	**.680**	**<.001**
Scrambled Boxes	**.562**	**<.001**
Spatial Reversal	**.459**	**.003**
Weigl Card Sorting	**.575**	**<.001**
Behavioural Executive Function Assessments		
	r	p-value
Inhibit	-.276	.088
Shift	**-.332**	**.039**
Emotional Control	-.290	.074
Self-Monitor	-.305	.059
Behavioural Regulation Index	-.128	.436
Initiate	**-.494**	**.001**
Working Memory	-.211	.198
Plan/Organise	**-.395**	**.013**
Task Monitor	**-.407**	**.010**
Organise materials	-.177	.282
Meta Cognitive Index	**-.514**	**.001**
Global Executive Composite	**-.467**	**.003**

A bivariate analysis was conducted to determine whether level of cognitive reserve was predictive of change in EF scores from pre to post intervention. A difference score was calculated for all EF scores using pre and post scores. There was no significant relationship between level of cognitive reserve and a change in EF scores from pre to post intervention across any of the EF assessments. Again, this suggests that pre-existing level of cognitive reserve does not have an impact on whether there will be a change in EF score post intervention

5.8 In Sum

A 2-way mixed ANOVA was completed in order to examine the interaction effect between the factors 'group' and 'time'. A significant interaction effect was seen for "Cats and Dogs Stroop" and for "Tower of London", with "Weigl Card Sorting" and "Scrambled Boxes" approaching significance. Initiation showed the strongest interaction effect for behavioural executive functions but it did not reach significance, while working memory and the metacognitive index also trended towards significance.

Both the intervention and the delayed intervention group improved following the cognitive training. Improvements were seen most clearly in the neuropsychological assessments rather than in the everyday behaviours of executive function. The intervention group improved significantly on the "Cats and Dogs Stroop" and "Tower of London", showing a large effect, with "Weigl Card Sorting" showing a trend towards significance at p value of .006 but not reaching the stringent .001 alpha level. There was a significant improvement in scores of emotional control and in the Global Executive Composite score with a large effect size, and with changes in initiation and the metacognitive index coming close to significance. The delayed intervention group then improved significantly on all 5 neuropsychological measures of executive function post training also with large effect sizes. None of the behavioural executive function scores reached significance, however emotional control and the behavioural regulation index approached the stringent alpha level, and again appeared to show a large effect in the delayed intervention group.

When the intervention group completed the intervention, they returned to normal care, and were no longer using the cognitive training program. This was verified by the Scientific Brain Training Pro program record. After 8 weeks, executive function assessments were completed again. There were no significant changes in EF scores at T3 as compared to T2, indicating that any effects gained from the training were maintained after the training had discontinued. Table 5.14 below gives a summary of all significant results found across all comparisons along with effect sizes.

There was no significant baseline difference between the treatment and delayed intervention group in terms of age, gender, IQ, cognitive ability or previous use of and iPad. Similarly, no significant differences were found at baseline between the treatment and delayed intervention group in any of the EF assessments, neuropsychological or behavioural. The delayed intervention group also did not show any significant changes in scores on any EF assessments when these assessments were repeated but without any intervention given.

No significant relationship was seen between age, IQ, cognitive ability or number of minutes spent on the program and an improvement in scores of EF.

Finally, a relationship was observed between level of cognitive reserve and baseline levels of executive function across all 5 neuropsychological assessments of EF, and in shift, initiate, plan/organise and self-monitor and in the metacognitive index and the global executive composite score as assessed by the BRIEF-A. However, level of cognitive reserve was not found to be predictive of a change in EF score following the cognitive training intervention.

Table 5-14: Summary of significant changes in executive function following intervention

	Neuropsychological Assessments			
	Within Participants		**Between Groups**	**Interaction**
	Intervention group	Delayed Control		
Cats and Dogs	✓	✓	.026	✓
Tower of London	✓	✓	.004	✓
Scrambled Boxes	.030	✓	.014	.021
Spatial Reversal		✓		
Weigl Card Sorting	.006	✓		0.11
	Behaviours of Executive Function			
	Within Participants		**Between Groups**	**Interaction**
	Intervention group	Delayed Control		
Inhibit				
Shift				
Emotional Control	✓	.002		
Self-Monitor			.005	
BRI	.033	.005		
Initiate	.006			.006
Working Memory	.015			.027
Plan/Organise				
Task Monitor				
Organise Materials		.030		
MCI	.004			.034
GEC	✓			

BRI=Behaviour Regulation index; MCI = Meta Cognitive Index; GEC = Global Executive Composite

✓ = $p<.001$

Boxes marked in green indicate a large effect size; boxes marked in grey indicate medium effect size

CHAPTER 6

DISCUSSION

6 Discussion

6.1 Introduction

This chapter will discuss the findings of the study in relation to the feasibility of conducting a cognitive training program with a population of adults with DS and the effect that cognitive training had on level of executive function. As discussed in the introduction and literature review chapters, individuals with DS are at increased risk of developing AD, and also show increased levels of executive dysfunction compared with people with ID from other aetiologies and compared to the general population. Furthermore, early signs of AD in people with DS include frontotemporal changes associated with behaviours of executive function. A number of research studies have been conducted to examine the effects of cognitive training on levels of executive function in the general population, yet despite the increased risk with people with DS, little research has been done to date on attempting to modulate early changes in EF through cognitive intervention in this population. The primary aim of the study was to determine the feasibility of conducting a cognitive training intervention with a population of adults with DS; essentially to answer the question 'Can this be done?'. The secondary aim was to examine the effects that the training had on levels of executive function, and whether external factors may modulate these effects.

This chapter is divided into 4 sections. Section 1 will discuss the study as a whole in order to lay down the context in which the results will be discussed. This will include discussion on the scope of the study and on the methodology used. Section 2 will discuss demographics of the sample and the baseline scores in order to gain an understanding of the population. Section 3 will discuss the feasibility of conducting a cognitive training intervention study with this population. Section 4 will discuss the effect of the training on levels of executive function.

6.2 Context of the study

This section will discuss the nature and scope of the study and will set the context in which further results will be discussed. In order to discuss the feasibility of this current study, the nature of feasibility studies must first be considered along with the broader framework of intervention research. Feasibility research and intervention research are distinct paradigms, however in this case, both are relevant and will be discussed as this study is examining the feasibility of an intervention.

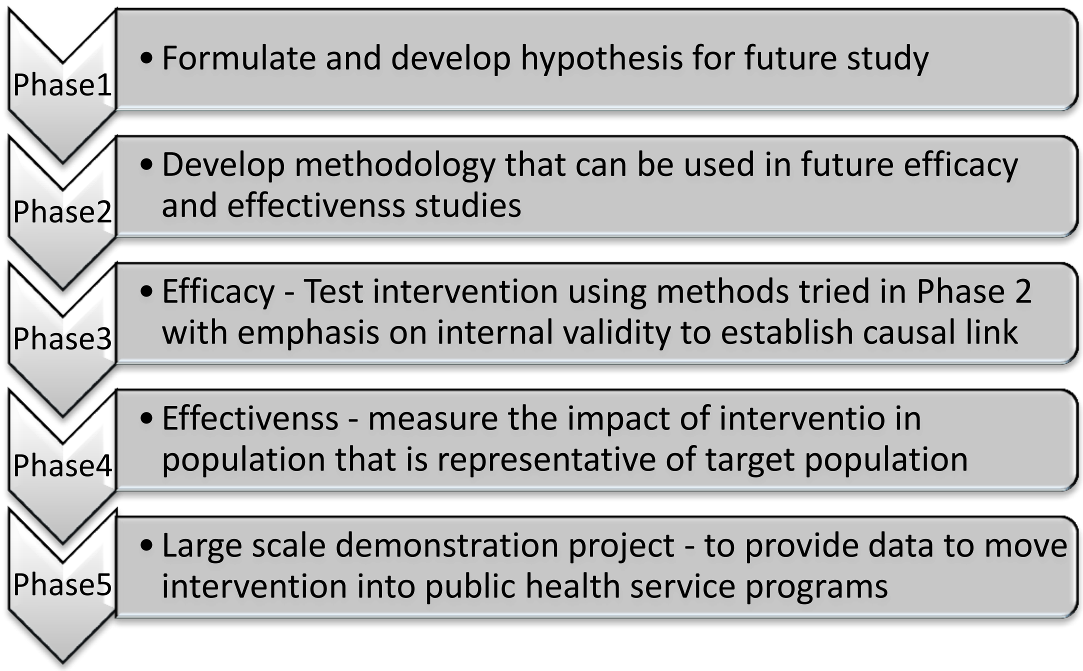
6.2.1 Feasibility Studies

In the literature, there is no universally adopted definition of what constitutes a feasibility study, and there are no set parameters that must be adhered to in order to satisfy the classification of a feasibility study. The distinction between a feasibility study and a pilot study is often blurred also, with Thabane et al. (2010) stating that the goal of a pilot study is to assess feasibility, and that the terms 'pilot study' and 'feasibility study' are used interchangeably throughout the paper. Whitehead et al. (2014) similarly discussed the ambiguity of differentiating pilot studies and feasibility studies, noting that while a study may claim to be either a pilot or feasibility study, this may not be the case under another definition. In a recent systematic review of the literature, it has been concluded that a distinction between the two is ineffectual and not desirable (Eldridge et al., 2016), and that all preliminary work could be described as 'feasibility' work (Whitehead et al., 2014). The Medical Research Council (MRC) guidelines also present pilot and feasibility studies as interchangeable concepts, in that both fall under 'preparatory work' (Craig et al., 2008).

As was noted in Chapter 4, in a definition used by the National Institute of Health Research the main focus of a feasibility study is on the question 'Can this study be done?'. As with the definition of feasibility studies and its distinction from pilot studies, there is incongruity in what the scope of a feasibility study should be, with one theory suggesting that a feasibility study of a randomised controlled trial need not itself be randomised, and that a feasibility study should not evaluate the outcome of interest (Arain et al., 2010). In contrast, Orsmond and Cohn (2015) propose that a preliminary evaluation of participant responses to the intervention is required in order to see if the intervention shows promise of being successful with the intended population. In the current study, an evaluation of the effect of the intervention was included, to evaluate whether the intervention showed sufficient promise of having a positive effect on EF, to satisfy the ethical concern with a vulnerable population of not proposing an onerous larger trial for people with ID without there being some evidence that the outcomes had the potential to be beneficial. As is made clear throughout the literature, strong preparatory work as occurred here ensures proper consideration is given to the practical implementation of the intervention (Craig et al., 2008).

6.2.2 Intervention Research

The 5 stages of intervention research were outlined by Greenwald and Cullen (1985), (see Figure 6.1 below) progressing from development of hypothesis, developing methodology to efficacy testing to effectiveness testing and finally to a large scale introduction of the intervention to broader populations, including entire communities.



(Greenwald and Cullen, 1985)

Figure 6-1: Five stages of intervention research

In terms of evaluating intervention studies, there is a continuum that progresses from efficacy to effectiveness. Efficacy shows how the intervention works under ideal and controlled conditions and effectiveness shows how the intervention will work in real world conditions (Singal et al., 2014). Efficacy trials are characterised by strict standardisation and strong control (Glasgow et al., 2003). In contrast, effectiveness studies account for external factors that may moderate the effect of an intervention (Singal et al., 2014). As effectiveness trials more closely represent real world conditions, level of implementation and levels of participation can vary. The distinction between efficacy and effectiveness has important consequences in the translation of health promotion research to practice.

As the current study is a feasibility study, there are certain limitations to the conclusions that can be drawn as regards efficacy or effectiveness, and results must be taken in context. Although the resulting conclusions may be limited, the implementation of the intervention in this study more closely resembled the real world conditions of an effectiveness study. The delivery of the intervention varied among participants, with some completing the cognitive training at home, and others completing the training within the day service, with variation also in levels of support needed and used. Training was also completed at a time convenient to the participant, and was flexible, depending on existing schedules. This helped to ensure that the training was integrated into daily routine as much as possible. The results yielded can be taken as a promising indication that results for the intervention on appropriate outcome measures in a large scale study would be significant (Mcgrath, 2013), however final conclusions on the efficacy or effectiveness cannot be made here due to the preliminary nature of the study.

The results from this study will therefore be discussed in this context and while conclusions as to effectiveness cannot be reached, the results yielded in terms of change in levels of EF are nevertheless central to the study as they allow an understanding of impact of the training on levels of executive function and on the appropriateness of further study.

Section 2 – The Sample

6.3 Recruitment of the Sample

According to the Central Limit Theorem, a sufficient number of independent observations is needed for the means of those observations to follow a normal distribution (Fischer, 2010); 30 has been used as a rule of thumb as big enough to suffice, provided the distribution is not overly skewed (Corder and Foreman, 2009). With this as a guide, the aim from the outset was to recruit approximately 40 individuals. As noted in section 3.9.1, response rates were low with an overall response rate of 35.8%.

This response rate, however, reflects the responses obtained from the initial letter of invitation. As this yielded a sufficient number of participants for this study, no effort was made to increase the rate. Initial letters of invitation were sent to the participants via the gatekeepers, and no further follow up was done to ensure that these letters of invitation reached the target individuals.

It was noted that 85% of those who attended the accessible information session continued to participate in the study, suggesting that this was an effective recruitment process. As with the letters of invitation to the study, however, it was not established whether others knew about the information session and chose not to attend, or simply did not know about it. For future studies, it would be recommended to send a follow up letter to notify or remind people again of the information session.

6.4 Demographics of the Sample

This section will discuss the demographics of the participants who took part in the study. In this, the focus will be on age, level of IQ and level of cognitive function, and will discuss how these demographics related to the results yielded in the study. Level of cognitive reserve measured at baseline will be discussed, and subsequently baseline levels of executive function. As a result of inclusion criteria, all participants with DS were between the ages of 30 and 49 with a mild or moderate level of ID. It was found that four individuals scored within the 'severe' range of ID using the Leiter-3, and this issue will be discussed further in relation to the IQ scores.

6.4.1 Age

From the inception of the study, age was a fundamental component. From the literature on DS and AD, it has been established that the risk of developing AD increases sharply from the age of 40 to 60 (Holland et al., 1998, Tyrrell et al., 2001, Coppus et al., 2006). It has also been established that by the age of 35, the neuropathological features of AD are present in virtually all people with DS (Holland and Oliver, 1995). In addition to this, there is much evidence that some of the early symptoms of AD in people with DS, such as behavioural changes, are more typical of dementia of the frontal type (Ball et al., 2006b) and can result in executive dysfunction. It has been noted also, that while the neuropathological symptoms will appear, not everyone with DS will display clinical symptoms of AD, although the risk will increase with age. The prodromal period, where AD has not yet reached the clinical stage has been identified by Belleville et al. (2001) as a key period in which to provide interventions to promote brain plasticity.

This information from previous research guided the study in two ways. The first was in identifying the age group of interest for the study of 30-49. This age range would likely have some neuropathological features of AD, and may be in the prodromal stage, but without yet clinical symptoms. A dementia screening was conducted to ensure that clinical dementia was not already present. The second way in which previous research guided the study was in matching the intervention group and the delayed intervention group on age. From the literature, it was noted that within the age range selected, the risk of increased neuropathology would likely increase with age; thus the neuropathology of those in the higher age range e.g. aged 45-49 would likely be different to those in the lower age range e.g. aged 30-35. Due to the sample size, the risk of a mismatched treatment and control group was large, and to compare a predominantly >40 group with a predominantly <40 group would threaten the internal validity of the study. As a result of this, simple randomisation was not undertaken but rather stratified randomisation.

Of the total sample, the majority (65%) were between the ages of 30 and 39. As was noted, prior to consent, concern was raised at the information session from both carers and potential participants about lack of previous experience with an iPad. This concern may have been greater for those in the older age category and may have prevented some individuals aged over 40 from participating in the study.

Another possibility is that some of those in the older age category (40-49) who received information on the study had already been given a diagnosis of dementia, thus precluding them from participation.

As discussed, age had been identified at the beginning of the study as a possible extraneous variable, thus stratified randomisation was done to ensure that the treatment and control groups were matched on age. When analysis was conducted at baseline to compare the treatment and control groups on demographics, it was found that the groups were indeed equal in terms of mean age.

Of further interest was whether age did in fact have an effect on scores of executive function following the cognitive training intervention, on either the neuropsychological assessment or behaviours of executive function as measured by the BRIEF-A. Age was not found to be a predictor of a change in EF scores following the intervention. Indeed no relationship was observed between age and scores of EF.

The fact that no relationship was observed could suggest that matching groups on age may not be necessary for future studies, as it appears unlikely to have an effect on scores of EF. Due to the small sample, however, it is possible that some relationships went undetected.

6.4.2 IQ

Level of IQ was measured using the Leiter-3, a nonverbal IQ assessment. In line with the inclusion criteria for the study, participants had a mild or moderate level of ID. When the IQ assessment was conducted it was found that there was some incongruence between scores on IQ test and level of ID. The WHO defined classifications of ID, with 50-69 indicating mild, 35-49 as moderate, and 20-34 as severe and under 20 as profound. Ten participants yielded an IQ score that would place them in an ID category other than was given. Subsequent analysis in the study used the IQ scores yielded by the Leiter 3 assessment.

There are a number of possibilities for this inconsistency. As was discussed in the literature review, while DS does not determine IQ, it does affect the distribution of IQ and in contrast to children in the general population, after the first year of life, a downward trajectory in IQ is seen in those with DS (Pennington et al., (2003). In addition to this, the IQ trajectory in those with DS in adulthood is also different to the general population, with a decline in IQ seen in those with DS earlier than in the general population (Epstein et al., 1989). Another possibility for the discrepancy seen is the lack of information on the process in which the ID classification was first established. In this study, non-verbal IQ was measured, whereas performance IQ could have yielded a different overall score, where discrepancies of up to 15 IQ points have been cited between the two (Kaufman, 1976). This could have placed some individuals within a different ID classification bracket. Similarly, if an IQ test was conducted in order to establish level of ID initially for participants, a different test battery would likely have been used. A difference of ±10 points in the results of different IQ tests batteries can be expected (Floyd et al., 2008).

Thus, while there was discrepancy in some cases between the non-verbal IQ score yielded in this study and the classification of ID that was taken from the records, those who scored in the 'severe' range were still included in the study. As discussed above, there are a number of reasons why the scores on the Leiter-3 could have differed from the IQ range in which individuals had previously been classed; the most obvious being that score in IQ assessments can fluctuate depending on the assessment used. So, the scores yielded were used for further analysis as an indicator of non-verbal IQ, but were not intended, and would not be sufficient to 'reclassify' those individuals into a different ID category. Therefore, while it was acknowledged that participants were recruited dependent on the inclusion criteria of mild/moderate ID, those who scored in the severe range on this particular assessment were not excluded. No significant difference was found between the change scores for those four who scored in the severe range and those who scored in the mild/moderate range on the IQ test.

There is some controversy over the usefulness of IQ testing, and indeed over the definition of intelligence, which is beyond the scope of this discussion, however the measure was included in the study as a general measure of cognitive ability. The purpose was to investigate whether level of ability, including cognitive, attentional and neuropsychological ability, would impact on change scores in EF following cognitive training intervention.

Non-verbal IQ scores ranged from 32 to 63, with no significant differences observed between the treatment and control groups. Non-verbal IQ scores were not found to be associated with a change in EF scores from pre intervention to post intervention. This suggests that IQ level does not have an impact on whether cognitive training will lead to an increase levels of executive function, in which case those with lower level of IQ would be as likely to benefit from cognitive training as those with a higher IQ score.

6.5 Cognitive Reserve

As noted in the literature review, a lot of research on cognitive reserve has focused on the connection between cognitive reserve and dementia, with evidence that a higher level of cognitive reserve may be protective against early clinical symptoms of dementia (Stern, 2006). High levels of cognitive reserve are associated with higher levels of education, high occupational achievement, enriched social environments (Stern et al., 1995a) and early childhood intelligence (Richards and Sacker, 2003).

The interaction between cognitive reserve and cognitive training is reciprocal. It is thought that cognitive reserve would have an impact on the effect of cognitive training and also that cognitive training would have an effect on level of cognitive reserve. In a recent study it was found that the pre-existing level of cognitive reserve was predictive of change following cognitive training (Mondini et al., 2016). Studies using fMRI have also shown that following cognitive training, increased activation was found in the frontal, temporal and parietal areas of the brain (Belleville et al., 2011). Increased activation creates more efficient cognitive networks thus resulting in higher cognitive reserve (Scarmeas and Stern, 2003). In order to discuss change in neural activation following cognitive training, it would be necessary to include a brain imaging component that would enable recording of neural change pre to post intervention. The initial application for ethical approval sought to complete a neuroimaging component, however this was rejected. As a result, any discussion on neural change was beyond the scope of this study.

In this study, cognitive reserve was measured using the CRIq (Nucci et al., 2012), which gathers information based on data on education, employment and leisure activities. This data is collected based on past information, and consequently there was no way to measure change in cognitive reserve following the intervention. Therefore, in this case, no comment is possible on the effect of training on cognitive reserve. What is of interest, however, is the relationship between pre-existing levels of cognitive reserve and levels of executive function, and in particular whether level of cognitive reserve is a predictor of change in executive function following cognitive training.

Overall, participants in the study ranged from having low to medium-high cognitive reserve, with 70% of participants either in the low-medium or medium categories. In this study, a significant relationship was found between level of cognitive reserve and all five neuropsychological assessments of EF ; "Cats and Dogs" "Tower of London", "Scrambled Boxes", "Spatial Reversal". "Weigl Card Sorting", where higher cognitive reserve was associated with higher level of EF. This was found previously in the literature, where higher cognitive reserve is associated with better performance on tests of EF (Roldan-Tapia et al., 2012).

However, in this study, level of cognitive reserve did not show a significant relationship between the difference in pre and post EF intervention scores. This differed from a recent study in which a relationship was seen between pre-existing cognitive reserve and change scores on a global measure of cognition. In a study conducted by Mondini et al. (2016), implications of cognitive reserve for cognitive training were examined among a population of people with mild to moderate dementia. It was found that those with lower cognitive reserve benefited more from a cognitive training program than those with higher cognitive reserve, as measured by the MMSE. As was discussed in the literature review, Stern (2009) noted that cognitive reserve modulates the neuropathology of dementia, whereby those with high reserve may have the neuropathology of dementia, and not display clinical symptoms for a longer period of time. Thus, in the Mondini et al. (2016) study, if participants with high cognitive reserve had mild to moderate symptoms of dementia, it was likely that the neuropathology was more advanced than for those with low cognitive reserve. This could explain the effect seen, as advanced underlying pathology would prevent new learning and improvement; in fact, the results may have been showing that the stage of neuropathology is what modulates change, and that cognitive reserve was a proxy for this.

This creates an interesting comparison with the current study. An important difference between the Mondini (2016) study and the current study is that in the current study, none of the participants had a diagnosis of dementia. Crucially, however, as this study is with a population of adults with DS, it would be expected that neuropathology of AD would be present in participants, particularly in the older age group. However no association was found either for age or level of cognitive reserve in relation to observed improvements in EF scores post training. This could also have been due to the fact that the majority of participants (70%) were either in the low-medium or medium level of cognitive reserve and thus there was not a large amount of variation within the sample. For future research, a larger sample size could allow better scope for a wider variation in levels of pre-existing cognitive reserve and allow for further investigation into its impact on cognitive training.

6.6 Measures of executive function at baseline

As was discussed in Chapter 2, there is ambiguity around the accepted definition of executive function, which leads to certain challenges of EF measurement, as a construct that is not clearly defined and is difficult to measure. At present, assessments that measure frontal lobe activities are the most commonly used and reliable measures of EF but their use in people with DS can be challenging. The measures used in the current study were, however, successfully used in samples with DS in a number of previous studies, most notably Ball et al. (2008). In addition to measuring EF using neuropsychological assessments, the behaviour component of EF was also assessed using the BRIEF-A. This allowed for an examination of real world changes that would have an effect on the day to day life of the participant.

Due to the fact that EF is highly effortful, in order for it to be assessed, a certain amount of complexity is needed in the task to preclude automated responses (Suchy, 2009). In previous literature, one of the difficulties in measuring EF with a population of people with DS was that the individual may not have understood the rules of the EF task, and thus failure on the task may have been as a result of this rather than a failure of EF. In order to address this issue, extra time was taken in explaining the rules of all five games clearly, and it was ensured as far as possible that participants understood these prior to assessment. Also, in accordance with instructions from Ball et al. (2008) a practice trial was given on the neuropsychological assessments. All assessments were successfully completed by the lead researcher and by the blind assessor in a standardised manner. This further supports the use of these assessments in the measurement of EF in a population with DS.

Scores on the five neuropsychological assessments were compared to scores in the study conducted by Ball et al., (2008), with the demographics of both samples being comparable. Scores were found to be comparable, where 2 assessments scored slightly higher ("Tower of London", "Weigl Card Sorting") in the current study and 3 assessments scored slightly lower ("Cats and Dogs", "Scrambled Boxes", "Weigl Card Sorting") than in the study conducted by Ball et al., (2008). Spatial Reversal showed the highest percentage of participants scoring at floor level, although this was comparable to results found in Ball et al., (2008) at 37.5%. For the "Weigl Card Sorting task" 22.5% scored at floor level, which was lower than was found in the 2008 study, where 53.6% scored at floor level. The average score on "Cats and Dogs Stroop" was slightly lower in the current study, but with comparable levels scoring at floor level as in Ball et al., (2008). Overall, the assessments were found to be useful with this population, with similar baseline findings from the previous report.

It has been reported in several studies that individuals with DS are at higher risk of executive dysfunction than individuals with ID from other aetiologies and also the general population (Ball et al., 2008, Lanfranchi et al., 2010, Rowe et al., 2006). Working memory has been noted as being particularly impaired in individuals with DS (Conners et al., 2001). Results from this study corresponded to these findings, where it was found that a third of participants scored above 65 in the BRIEF-A, indicating abnormally elevated scores and clinical level of dysfunction in this domain.

The issue of EF is thus critical to adults with DS, and this study has contributed to further standardising the measurement of EF, and also in identifying measures that are sensitive to change.

6.6.1 Relationship between neuropsychological assessments of executive function and BRIEF-A

The relationship between the neuropsychological assessments of EF and the behavioural aspect of EF was examined. This was done to address the issue raised by Chaytor et al., (2006) of the need to understand the relationship between cognitive testing and real world performance. It had been noted previously that performance on assessments of EF are sometimes inconsistent with everyday EF abilities (Wilson, 1993). The ecological validity of EF assessments has important implications for clinical relevance, as deficits seen only in neuropsychological assessments, but not in everyday life carry little meaning. The BRIEF-A was developed as a reliable and valid tool to address these issues.

In this study, it was possible to correlate results from the neuropsychological assessments with their related behaviours as measured by the BRIEF-A, to examine whether deficits as measured by neuropsychological assessments were also seen in day to day behaviour.

The arrows in Figure 6.2 below show the correlations that would be expected, as both assessments are measuring the same executive process. The arrows in red show the significant correlations that were seen, while the blue arrows were not significant. Poor correlation was seen between working memory as measured by the BRIEF-A and three neuropsychological assessments ('Tower of London', 'Scrambled Boxes', 'Spatial Reversal') that were also related to working memory. This was most notable for 'Scrambled Boxes' where working memory would have been hypothesised to be the main cognitive process involved. As was discussed in the literature review, there are certain challenges in measuring executive processes, due to their complex and dynamic nature. The structured nature of a neuropsychological assessment in a clinical environment may not place sufficiently high demands on an executive process such as working memory, particularly due to its short time frame. This may reduce the opportunity to observe deficits in certain domains (Holmes-Bernstein and Waber, 1990), whereas the BRIEF-A gives the opportunity to rate frequency of behaviours in the preceding month, which may capture the broader range of functioning (Roth and Gioia, 2005).

For the remaining 4 neuropsychological assessments, there was good correlation with the assessments in the BRIEF-A that were measuring the same cognitive process; "Cats and Dogs Stroop" was significantly correlated with 'Inhibit', both measuring inhibition; "Tower of London" and 'Plan' were significantly correlated, both measuring planning; "Spatial Reversal" was significantly correlated with 'Inhibit', again both measuring inhibition and "Weigl Card Sorting" and ''Shift' were significantly correlated and were both measuring set shifting. Again, these findings contribute to supporting the fact that these assessments are in fact measuring the targeted domain.

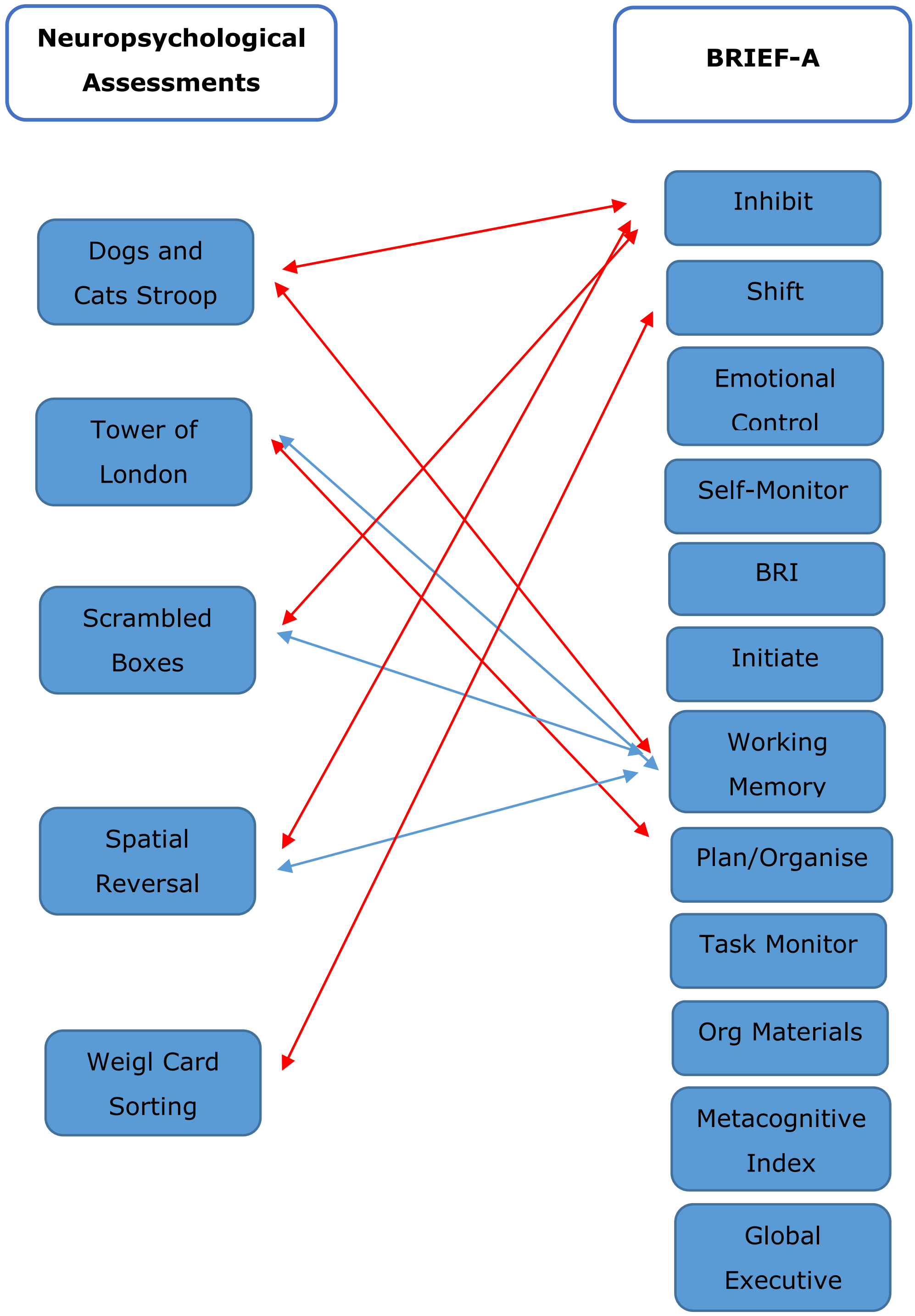


Figure 6-2: Common executive functions measured by neuropsychological assessments and BRIEF-A

*Red arrows show significant correlations; Blue arrows show non-significant correlations

Section 3 – Feasibility of the Study

This section will discuss the feasibility of the study, in relation to the parameters of feasibility set out in Chapter 3 and reported in Chapter 4. The intervention was delivered using a cognitive training program on an iPad. Technology use among adults with ID is low, with barriers such as cost, ease of use and lack of access, support and training named as the biggest reasons for underutilisation. (Carey et al., 2005).

In this study, as discussed, initial apprehension, from both participants and carers was apparent for those who had no previous experience with using a tablet. Perceived ability to manually copy information was observed as a main barrier to technology use in a study conducted with 83 adults with intellectual disabilities. This was deemed to be more important than reading ability as a key threshold skill in accessing technology (Carey et al., (2005). In the current study, all participants were able to navigate to the cognitive training program, with two participants needing prompting and support to do so. Similarly all participants successfully used the 'username' and 'password' features to access the training program. At the beginning of the program, the touch screen challenged some participants who had no previous experience with this. Common difficulties included pressing down too hard on the screen, or using the tip of the fingernail to touch the screen, which does not work. For those who did not have experience, the initial training session focused on this aspect. The researcher demonstrated the use of the touch screen, and showed the level of pressure needed on the palm of the hand. The game that relied heavily on this was the *Tower of Hanoi*, and this was used as a training game for getting used to the touch screen, where necessary. Fifty five percent had previously used a tablet, however after initial training, lack of experience did not present as a barrier to completing the training, or to navigating to the program. The easy use and features of the iPad have been found useful in research with individuals with disabilities (Linder et al., 2013).

As was noted above, access to technologies has been identified as a barrier to use, and this includes access to Wi-Fi. In this study a 3G connection was used to ensure that all participants were able to access the program whether Wi-Fi was available or not. This was crucial, as Wi-Fi was not available either in the day services or in community group homes, and thus participants living in a community group setting would have been excluded from the program. This flexibility meant that participants were able to continue the training even when outside the home, whether on a short break, or completing the program in the day service. This also highlighted the limited availability of Wi-Fi and internet access for many adults with ID, and corresponds with the findings from Carey et al., (2005) which documents lack of technology resources for people with ID.

Based on the experiences of the participants in this study, it appears that with a little support people with mild/moderate level of ID can quickly adapt to the use of technology. In order for this to happen, however, access to technology is vital. This has already been identified as a challenge, and is an issue that needs to be addressed.

6.7 Feasibility for Participant

This section will examine the feasibility of conducting the cognitive training program in relation to the participants. In line with the feasibility parameters set out in this regard, the issue of ability to play and progress in the games, adherence to the program and level of enjoyment throughout the program will be discussed. The feasibility parameters are also linked to training induced learning and brain plasticity as was discussed in the literature review. Green and Bavelier (2008) outlined recommendations for learning transfer including task difficulty, motivation, feedback and flexible learning, and these aspects will be discussed within the feasibility parameters.

6.7.1 Ability to progress

One of the feasibility parameters set out was the measurement of whether participants were able to progress in the program. As discussed, it was ensured that all participants would be familiar with accessing the program, and that the rules and mechanics of each game would be explained. This included training and demonstration at the beginning of each session, if necessary, on the goal of the games and how to achieve this goal. In addition to this, however, the ability of participants to progress in the games was also integral. This was measured remotely by the training program, which recorded progression on each game, and monitored the scores achieved.

Task difficulty was identified as a factor for training induced learning by Green and Bavelier (2008). An algorithm in the training program adjusted the level of difficulty as necessary. Once a participant twice achieved a score of 80% or higher, they would advance to the following level. If a score of 50% or below occurred, they would go back to the previous level. This meant that participants were constantly at a level that was challenging, but was not unobtainable. The only cases where task difficulty was an issue was where a participant found the baseline level too difficult. This only arose with two participants, who struggled to understand the concept of a game. Even in these cases, however, with support from the researcher, the participants were able to complete part of the task, and so reached an acceptable level of challenge. There were no instances where the participants were unable to complete any game at all. In the case of one participant, in the *Tower of Hanoi*, the researcher talked through the rules of the game at each session, and would assist the participant with each move. This continued for 5 weeks, where it appeared the participant was not successfully learning. At one session in week 5, however, the participant successfully completed the game, and spoke aloud the thought process involved. In that session, the participant moved to level 3 and showed a clear understanding of the rules. For the remainder of the program, the participant ranged from level 1 to 3, and was most comfortable at level 2, but continued to display an understanding of the goal of the game and what was needed to achieve the goal, but was sometimes not able to follow this through to completion.

Overall, the progression observed in the training program suggested that participants were engaged with the program, and were learning and adapting to the increasing difficulty of higher levels. It was seen that 20-30% of participants advanced to level 7 out of 9 levels in three of the most played games; *Tower of Hanoi*, *Private Eye* and *Objects Where Are You?*.

Flexible learning was another concept noted by Bavelier and Green (2008), and was also related to the ability of participants to progress through the program. As part of progression in the games, the number of games that were played was of interest. Participants generally began with 3 games at the beginning of the program. Depending of level of ability with these games, extra games were added the following week. All decisions were made on an individual basis, depending on the ability and wishes of the participant, in order to achieve a balance and to ensure that the participant was challenged by a variety of games but not overwhelmed by too many rules and options. Overall 82.5% of participants played between 4 and 8 games, which allowed for training of a variety of cognitive processes. Of those remaining, 12.5% played more than 9 games and 5% played 3 or less. This showed that 95% of the sample were able to both progress in the games and learn the distinct rules of at least 4 games, and adapt to the increased task demands that came with increasing levels. Again, this shows that, when given the opportunity, individuals with DS can progress in previously untried endeavours. It would be recommended that future research would similarly decide on the number of games used on an individual basis, and to be flexible and adaptable to individual needs.

6.7.2 Adherence

Adherence to the program was a key aspect in examining the feasibility of conducting a cognitive training program, without which, no possible gain could be expected. Overall adherence to the program was high, with 90% of participants completing the full 8 weeks of the program, and 97.5% completing at least 6 weeks, and completing the follow up executive function assessments. In the literature, there is no consensus on the number of minutes that should be spent on cognitive training, after which an improvement would be expected. Furthermore, even if there were a recommended dosage for the general population, this would not necessarily be suitable or feasible for a population with DS. For example, in one of the largest studies on cognitive training in the general population, the ACTIVE trial, involving 2832 individuals, training sessions lasted 75 minutes (Wolinsky et al., 2006). Based on feedback from both participants and carers in the current study, the suggested training time of 30 minutes was sufficient and, above which would not have been feasible.

The dosage of 800 minutes, made up of 20 minutes a day, 5 days a week for 8 weeks, was chosen for this study based on previous studies. As this dosage was not definitive, participants were not excluded from subsequent assessment and analysis if the recommended 800 minutes was not fully completed. The range of completed training was 339 minutes to 5353 minutes, with a mean of 930 and a median of 711. The large range is reflected in the extremely large standard deviation of 848, which shows that the data points are spread far from the mean. What was of interest also was whether there was a minimum number of minutes in which an individual could complete the training, while still seeing effects. In this study, no relationship was found between number of minutes and change in scores pre to post intervention, and thus this study was unable to address this issue. This could have been due to the large standard deviation coupled with the small sample size. A high standard deviation will increase the minimum detectable effect and thus a larger sample size is needed in order to find small statistically significant differences. More research is needed in this area in order to determine the minimum number of minutes needed in order to observe an effect.

The high level of adherence was also linked to one of the principles of training induced learning proposed by Bavelier and Green (2008); motivation. Motivation is linked to successful learning, with emphasis on intrinsic, rather than extrinsic motivation, where intrinsic motivation has been linked with high quality learning and creativity (Ryan and Deci, 2000) . Task difficulty is intertwined with this idea, and, as was discussed above, the training program successfully monitored task difficulty so that the games were not at too difficult or too easy a level. No external incentives, or rewards were used in the study.

The BEADS booklet was used, as a visual representation of the training timeline, and was also aimed at motivating the participant to complete the recommended 5 days a week of training. The BEADS booklet was quite divisive among participants. Those who used the BEADS booklet (70%) were enthusiastic about its use. In contrast, of those that did not use it, more than half were quite opposed to its use, with the remaining participants indifferent. As a motivational tool, it appeared effective for those that used it, and had no negative effect on those that didn't use it, and thus overall was a positive addition to the study. It would be recommended that future research would have the option of a similar aid, as for those who wanted to use it, it appeared to be a valuable resource.

The BEADS booklet also facilitated discussion when the research was coming to an end, when the iPad would have to be returned and the researcher would no longer be visiting. Returning the iPad at the end of the training program had been a major concern to ethics committees at the beginning of the study. This proved not to be an issue after all, however, with no one overly concerned with returning the iPad on completion of the program. This could have been that, in response to earlier concerns raised by ethics committees, it was strongly emphasised at the beginning of the study, and again coming towards the end of the study, that the iPad would be returned, and thus participants were prepared for this.

When participants did not complete the training on any given day, a reason for this was noted. Two of the most common reasons were that the individual was too busy, or that they simply did not want to. The fact that participants felt comfortable giving these responses was encouraging, as it showed that participation was indeed a conscious choice. This would suggest that, on the days that training was completed, it was done through a desire to complete the training, rather than out of a sense of obligation.

The second most common reason for not completing the training was that there was a lack of support to do so. As was reported in the results, 50% of participants required some support for the duration of the training program. Support was given by the researcher on 2/3 days during the week. For the remaining days, a support person, either a family member or support staff was involved in support of the individual with DS. As was recorded in field notes, in these circumstances, support staff were enthusiastic overall about giving support, however more barriers existed for support staff than for family carers, including administrative duties, change of staff/roster, and lack of extra staff which meant one to one attention was not always possible. The integration of a cognitive training program into a day service program would be a useful way to promote its use, and thus there would no longer be a reliance on staff in the community group homes to complete the training.

Completing the training was a novel situation for all participants for a number of reasons; using an iPad, playing games on a computer, being part of a research project and working with a researcher biweekly. The fact that the research project was associated with Trinity College Dublin was also an important factor, and a number of participants stressed this factor;

"I'm working on a project with Trinity"

"I'm doing this for my course in Trinity"

(Two different participants, taken from Field Notes)

These factors were novel, and could have contributed to the interest and enthusiasm that was reflected in the high adherence levels. Conversely, in cases where the training was not completed, two participants expressed a preference for completing the training with the researcher. Completing the training may have been associated with the novel and unusual experience, where individuals would have received one to one attention from the researcher when completing the training. For participants living in a community group setting, there may not be many opportunities for similar one to one attention in other aspects day to day. This could have increased enthusiasm for the cognitive training program. This did not appear to be a significant factor, however, as no difference was noted in terms of adherence between those living with family and those living in a community group setting.

6.7.3 Level of Enjoyment

Using an accessible structured questionnaire, participants were asked to rate their level of enjoyment each week on a 3-point Likert scale. The vast majority of participants consistently rated the training program as enjoyable throughout. The highest percentage of 'did not enjoy' was seen in week 1, but was still very low at 7.5%. As discussed above, participants appeared at ease to express when they did not want to complete the training, thus strengthening the findings of the weekly structured questionnaire. In addition to the weekly structured questionnaire, the researcher was in regular contact with participants, and the findings in the questionnaire were reflected in the behaviour of the participants, and in the levels of adherence seen in the program.

Despite the high levels of enjoyment, a number of participants indicated that 8 weeks of training was long enough, and two carers expressed this view also. However, despite this assertion, all participants who completed an exit interview said that they would like to be involved in a similar program again. One of the issues that was highlighted when discussing the length of the program was difficulty in arranging a time for the researcher to visit, as this occurred 2-3 times a week, often in the evening. If the program were conducted in the day service, and was integrated into the schedule, there would be no scheduling conflicts, and thus would reduce the pressure on the individual.

6.8 Feasibility for Staff/Carer

The feasibility of the training program was examined from the perspective of the support person, and the amount of support needed to successfully complete the training.

6.8.1 Amount of support needed

The support that was needed in order to complete the training was of interest in the study. After the first training session 17.9% were able to complete the training program independently. While this was encouraging, it meant that support was needed for over 80% of the sample, and this training was conducted with both the participants and the support person at the first training session. During the course of the program, the level of support needed dropped, as participants became more familiar with the program, with less than half (40%) needing support for the duration. The support needed initially included support with turning on the iPad, accessing the program, username and passwords, explanation of the rules of the games, encouragement during training, time keeping and reminders to complete the training.

For those who needed support for the duration of the program, the type of support needed was in navigating through the games within the training program, and encouragement during the training, and with time keeping. The support that was needed was thus an important part of the feasibility of conducting a cognitive training program, as for some participants, it was vital for successful use of the program.

6.8.2 Training for support persons

The amount of training needed for support staff was of interest in relation to the feasibility of the overall study, in order to estimate what resources would be needed to conduct a large scale study, and how much time, outside of the support given during training would staff need to invest.

At the first training session, staff were asked to sit in on the training with the participant. At the end of the session, the researcher would repeat the steps involved with the support person, and the username and password were noted by both participant and support person. The support person was able to contact the researcher at any point if necessary in relation to the training if any problems arose. This single training session was sufficient for support persons. The only instances where subsequent contact was made with the researcher were when there was a problem with accessing the program and that was as a result of a difficulty with the internet connection.

This suggests that one training session for the support person is sufficient. This further addressed the issue of feasibility from the perspective of the support person, where time spent outside supporting the actual training was minimal and was not arduous.

6.9 Effect of Training on levels of executive function

As discussed above, there are certain limitations to the conclusions that can be drawn from the hypothesis testing conducted in the study, due to the sample size limitations, and the scope of a feasibility study. The results yielded, however, are an important preliminary evaluation of the effect of cognitive training on levels of executive function. This is particularly crucial for this population where little research has been done to date on the effects of cognitive training, despite the increased risk for people with DS for both high levels of executive dysfunction and onset of AD.

This section will discuss the findings, using the results yielded from both the treatment and delayed intervention groups to examine the effect of cognitive training on scores of EF as measured by both neuropsychological assessments and proxy rated behaviours of EF as measured by the BRIEF-A.

6.9.1 Alpha level and effect size

The use of the .05 alpha level in order to determine statistical significance was first mentioned in Fisher’s book (1925) *Statistical Methods for Research Workers* (Cowles and Davis, 1982). It has since been adopted as the level at which statistical significance is decided and is part of the cornerstone of evidence based decision making. If multiple comparisons are made within the one dataset, however, the chances of making a Type I error increase. This risks placing too much importance on a single significant result, when in fact that result may have been the 1 in 20 that would have been expected by chance alone, according to the 5% significance level (Bland and Altman, 1995). In this study comparisons were made for neuropsychological assessments and for all components of the BRIEF-A, both within participants and between groups at different time points. An adjusted level was calculated, and the alpha level of .001 was used.

The p value was intended to be part of a fluid non-numerical process, that used not only data, but also background knowledge and expertise in order to lead to scientific conclusions (Nuzzo, 2014). In an account of the application of statistics to psychology entitled "Things I have Learned (So Far)", Jacob Cohen (1990) cautioned on the over reliance and interpretation of the significance level of .05 and "its arbitrary and unreasonable tyranny" (Cohen, (1990) pg. 1310). Another criticism of the p value, is the lack of information it yields on the size and relevance of the effect (Nuzzo, 2014). Nonetheless, the use of significance level is still prevalent in science, and a useful reference point on the possibility-probability continuum (Cohen, 1990) and to understand whether the results were the same or different to what random choice might produce. The results in this study will thus be discussed both in terms of level of significance, (both adjusted and unadjusted) but also in relation to the effect size that was observed.

6.10 Intervention Group Vs Delayed Intervention Group

Cognitive training was first delivered to the intervention group, and the scores following this intervention were then compared to the delayed intervention group, who had not yet received the intervention. The delayed intervention group acted as a passive control group at this time, in that those in this group continued with normal care. The delayed intervention group controlled for objective practice effects that may be seen from repetition of EF assessments, but importantly, also to control for the Hawthorne effect (Jones, 1992). The Hawthorne effect describes how positive changes in behaviour can be seen simply as a result of being observed and of participating in research.

6.10.1 Passive control group

As discussed in the literature review, studies on cognitive training in the general population have shown some promising results. Mixed results have been found in those studies that compared the active training group to an active control group (Martin et al., 2011, Kelly et al., 2014). Active control groups received interventions such as educational DVDs, health-promotion training or computer game training that was not directed at cognitive functioning (Kelly et al., 2014). In the study conducted by Martin et al., (2011) an improvement was seen for the active control group when compared to the passive control group, but improvements did not exceed those of the active control group. In a systematic review and meta-analysis of 31 studies on the impact of cognitive training, Kelly et al., (2014) found that cognitive training was effective when compared to active control groups on the executive function measures and on composite measures of cognitive function. This meta-analysis suggests that improvements seen in executive function scores following cognitive training were as a result of the cognitive training, and not due to other factors that also influenced those who were in the active control group.

In the current study, a passive control group was used, due to logistics, time and resource constraints. The passive control group refers to the status of the delayed intervention group prior to receiving the intervention. This refers to the fact that the group were not completing any activity in place of the intervention, but rather were continuing with normal care. In order to successfully include an active control group, the study would have needed the active training group, an active control group and a passive delayed intervention group. Apart from time and resource constraints, a third group would have reduced the number of participants in each group, which would have limited the statistical analysis that would have been possible. Also, as was discussed above, the primary goal was to establish the feasibility of conducting a cognitive training intervention, and thus the inclusion of a third group was beyond the scope of the study.

6.11 Did cognitive training have an effect on executive function?

In order to examine the changes in scores following cognitive training, this study made a number of comparisons.

1. Between intervention group and delayed intervention group at baseline to ensure comparability
2. Repeat EF measures for delayed intervention group when no cognitive training had been given to modulate practice effects
3. Comparison between treatment and control group on EF measures when intervention group had received the intervention and delayed intervention group had not
4. Within group comparisons for both the treatment and control groups following receipt of cognitive training intervention
5. Maintenance of EF scores for the intervention group following an 8 week period when cognitive training had stopped.

6.11.1 Baseline comparison and practice effects

As was reported in chapter 5, and regarding comparison 1, the treatment and control group were comparable at baseline across all demographic factors (age, IQ, cognitive, reserve, cognitive ability), previous experience with iPad, and across neuropsychological measures of EF and proxy rated behavioural measures of EF; no statistical differences were observed between the groups at baseline. With both groups being comparable at the beginning of the study, the only measureable difference between them when measured at T2 was that the intervention group had received the cognitive training intervention while the delayed intervention group had not.

Practice effects refer to changes observed in test scores that can be attributed to familiarity with the test instrument, and are not as a results of any external intervention given (Goldberg et al., 2015) and may obscure changes occurring in neuropsychological function (Basso et al., 1999). Practice effects raise the risk of misinterpreting outcomes, and increase the level of 'noise' in a clinical trial (Goldberg et al., 2015). The risk of misinterpretation is two-tailed; 1) there is a risk that an intervention is deemed effective, but rather the change seen is simply due to practice effects, 2) however there is also the risk that scores for the control group are in fact decreasing, but that this decrease is being masked by practice effects. This is a challenge, in particular, for longitudinal trials for people with MCI or AD, and also in repeated neuropsychological testing for AD in clinical practice.

A number of solutions were suggested by Goldberg et al. (2015) for practice effects, including alternate forms, pre baseline mass practicing, reliable change index and control groups. The use of alternate forms has been controversial, in that there is a risk of non-equivalence and difference in task difficulty (Goldberg et al., 2015). The aim of massed practice pre baseline is to reach a plateau of practice effect prior to testing, however the number of trials needed differs for different assessments. This would not have been suitable in this study, as it increases the likelihood of ceiling effects. The reliable change statistic gives information on change seen in individuals beyond practice effects, however it cannot be used for group means. Control groups were the final suggestion for modulating practice effects. While control groups do not fully obviate practice effects, no treatment control groups can yield an estimate of practice effect, with any change seen attributable to either practice effects, measurement error, or variation associated with disease course (Basso et al., 1999).

There has been some evidence that repeated measures of executive function may be particularly sensitive to practice effects. From the literature on EF and as discussed in the literature review, EF cannot be activated if a task needs only an automated response; the task must demand a high level of effort and this effort must preclude this automated response (Suchy, 2009). The research that has been conducted on practice effects in EF, however, has been with a healthy, well-educated adult population of average or above average intelligence (Basso et al., 1999), and thus may not be as relevant to a population of adults with DS. Some research has suggested that practice effects diminish with age, and thus older adults are less likely to show an improvement due to practice effects (Horton, 1992).

In this study, no practice effects were observed in any of the five neuropsychological assessments. Likewise, no change was observed in the proxy rated scores on the BRIEF-A assessment either when it was repeated at time 2 for the delayed intervention group. In the study above conducted by Basso et al (1999), it was suggested that practice effects may have been seen as participants were able to remember the previous assessments, and adjust decision making or problem solving based on this memory of the previous test. This did not appear to be relevant in the current study. The independent assessor who conducted the blind assessment reported the need to repeat instructions and rules for the assessments in many cases.

The data collection strategies, including the use of the independent assessor appeared to be implemented as intended, thus increasing confidence in the findings.

6.11.2 Impact of Intervention

In order to examine the effects of cognitive training on levels of EF, changes in EF scores post intervention were reported for the intervention group, and also for the delayed intervention group post intervention. A comparison was also made between the groups at time 2, when the intervention group had received the intervention and the delayed intervention group had not. Finally the interaction effect between group and time was examined.

In examining the within participants effects, "Tower of London" which measured planning and working memory and "Cats and Dogs Stroop", which measured inhibition and working memory showed the most improvement, with both the treatment and delayed intervention groups showing a significant increase in scores and with a large effect size as measured by Cohen's d. The "Tower of London" task resembled a game previously played in the cognitive training program *Towers of Hanoi* that and where the object of the game was to move blocks to match a target configuration. It was observed in post assessment that some participants noted this similarity, and indicated that the same method was needed to complete the assessment as was needed when doing the cognitive training program. The "Tower of London" was also the assessment in which the largest effect size was seen (d = 1.9 for both groups). None of the other games in the cognitive training program bore any resemblance to the assessments that were used to measure EF.

The "Weigl Card Sorting Task", which measures set shifting, also showed an improvement post intervention with a medium effect size for the intervention group and a large effect size for the delayed intervention group. "Scrambled

Boxes", which measures working memory and attention, showed an improvement in both groups, however this did not reach the adjusted significance level in the intervention group, but did show a medium effect size for both groups. "Spatial reversal", which measures set shifting and inhibition failed to show a significant improvement for the intervention group post intervention, but did for the delayed intervention group. "Spatial reversal" measured set shifting, inhibition and attention. Each of these cognitive processes were also measured by other assessments; "Weigl Card Sorting" measured set shifting, "Cats and Dogs Stroop" measured inhibition and "Scrambled Boxes" measured attention. This could indicate that perhaps "Spatial Reversal" is not as sensitive to change as the other measurements.

As was shown in Chapter 4, the most played games in the training program were *Tower of Hanoi*, measuring planning; *Find Your Way*, measuring visual attention; *Private Eye* measuring attention and *Objects Where Are You?*, measuring working memory

These results suggest that cognitive training does show promise for improvements in EF as measured by neuropsychological assessments. The areas in which improvement was most seen was in planning, inhibition, set shifting, working memory and attention, as these were the cognitive processes measured by "Tower of London", "Cats and Dogs", "Weigl Card Sorting" and "Scrambled Boxes". These findings are consistent with the cognitive processes that were targeted by the games in the cognitive training program.

It was noted in the literature review that in previous studies on cognitive training, there had been little research into the effects of the training on day to day life. It was also suggested in the systematic review by Kelly et al. (2014), that in order to target changes in day to day life, the focus should be on executive functions. Ball et al. (2008) also suggested that interventions that are aimed at positive changes in everyday life may help to improve the quality of life for people with DS (Ball et al., 2008). This study aimed at addressing this gap in the literature by including a measure of executive function in an everyday environment, using the BRIEF-A. In the BRIEF-A, all of the components combine to form two indices – the Behavioural Regulation

Index and the Meta Cognitive Index, and also an overall Global Executive Composite Index. The Behavioural Regulation Index comprises inhibit, shift, emotional control and self –monitor scales; it represents the ability of the individual to appropriately regulate behaviour and emotion. The Metacognitive Index comprises initiate, working memory, plan/organise, task monitor and organisation of materials; it represents ability for systematic problem solving while engaging working memory.

The changes in scores on the BRIEF-A within participants were not as marked for behaviours of executive function as was seen for the neuropsychological assessments. There is research to suggest that transfer between different cognitive processes may be seen, for example, training on working memory could lead to improvement on inhibition tasks, as both processes activate areas of the ventrolateral prefrontal cortex (Thorell et al., 2009). As shown above in Figure 6.2 (pg 237), the BRIEF-A measured the same processes as were measured by the neuropsychological assessment, although a correlation was not seen between all of these processes. For example, "Scrambled Boxes" primarily assessed working memory, however this did not correlate significantly with the working memory component of the BRIEF-A. As discussed in the literature review, the measurement of EF has certain challenges, one of which is that neuropsychological assessments that aim to measure a specific cognitive process inherently attempt to separate integrated functions into component parts. Similarly, it was noted that some individuals with frontal lobe damage performed well on EF assessments, whereas others failed at EF assessments while showing no apparent frontal lobe damage (Damasio et al., 1994, Andrés, 2003, Baddeley and Wilson, 1988). Neuropsychological assessments also measure executive functions over a short period of time, and thus do not capture the integrated, multifaceted decisions that form the executive process in real life situations (Goldberg and Bougakov, 2000, Burgess, 1997). These challenges help to explain why an improvement in an executive process as measured by a neuropsychological assessment may not be seen in a behavioural measure of EF that assesses EF in real life situations.

The within participants comparison examined the change that was seen in participants from pre intervention to post intervention. A comparison was also made between the groups at time 2, when the intervention group had received the intervention and the delayed intervention group had not. The trend for both comparisons was similar, which showed that following the intervention, an improvement could be seen in "Tower of London", "Scrambled Boxes" and "Cats and Dogs Stroop" and "Weigl Car Sorting Task". This suggested that completed the intervention had a positive impact on these neuropsychological assessments.

The two-way mixed ANOVA gives perhaps the most complete picture as it examines the interaction effect between the groups (treatment and delayed intervention group) and time (pre and post intervention). As above, similar trends were seen with this interaction, which strengthens the earlier findings. Examining this interaction effect showed similar results to those found in previous comparisons, with the largest effect seen for "Tower of London" and "Cats and Dogs Stroop". These two assessments, which primarily measure planning and inhibition were found to have shown the largest improvement across all comparisons. In the case of "Tower of London", as noted above, although the assessment was different to the game in the training program *Tower of Hanoi*, a similarity between training game and assessment could account for the improvement seen.

An interaction effect was found also for "Scrabbled Boxes and "Weigl Card Sorting", however this was not as strong as for "Tower of London" and "Dogs and Cats Stroop". For all comparisons, "Spatial Reversal", which primarily measured set shifting and inhibition showed the least improvement of the 5 neuropsychological EF assessments used.

As was found with previous comparisons, the interaction seen for behaviours of EF, as measured by the BRIEF-A was not as strong as for the neuropsychological assessments. None reached significance to the adjusted alpha level, suggesting that improvements seen from cognitive training may not have translated to positive changes in day to day behaviour.

As earlier stated, caution is needed in relation to the interpretation of the above results due to the feasibility nature of the study and the small sample size.

6.12 Maintenance effects

Maintenance effects were investigated for individuals in the intervention group. There was an opportunity to examine this as participants in the intervention group no longer had access to the cognitive training program between T2 and T3. No significant differences were found in the scores from T2 to T3, indicating that any improvements seen in EF between T1 and T2 remained after 8 weeks without any training. During this 8 week break it was established that participants did not continue with the training program, as the program records any activity. Unfortunately, there was no opportunity to examine longer term maintenance effects in this study. The ACTIVE trial examined effects of training and found that after 10 years, less decline in self-reported IADLs was seen in those who had completed the training, with some additional booster sessions (Rebok et al., 2014), suggesting that cognitive training does have the potential to maintain effects from initial training even after cessation of training. Including longitudinal follow up in future research would be beneficial, particularly with respect to monitoring the onset of dementia with this population.

6.13 In Sum

This chapter discussed the main findings of the study, both in terms of feasibility and on the impact that cognitive training had on levels of executive function. The most salient points are summarised below.

6.13.1 Feasibility

The feasibility parameters that were set out for the study; ability to progress, adherence, level of enjoyment and support needed, were discussed with reference to the principles of training induced learning and brain plasticity put forward by Green and Bavelier (2008). These principles related to task difficulty, motivation, feedback and flexible learning. Through the use of these parameters, it was found that conducting a cognitive training program using an iPad with this population was feasible.

6.13.2 Cognitive training and executive function

A statistically significant correlation was found between the EF constructs measured by neuropsychological assessments and the BRIEF-A, suggesting that both instruments were measuring the same constructs, apart from the 'working memory' component, where a significant correlation was not found.

Improvements were seen more clearly in the neuropsychological assessments of executive function rather than in the everyday behaviours of EF, which suggests that transfer to everyday behaviours is more difficult, and corresponds to previous research.

While these results are promising in relation to the benefits of cognitive training, conclusions are limited due to the feasibility nature of the study and the sample size.

CHAPTER 7

CONCLUSIONS AND RECOMMENDATIONS

7 Conclusions and Recommendations

7.1 Introduction

The preceding chapters have dealt with a number of key issues, methodology of the study and findings. This chapter will synthesise all these facets of the study and draw final conclusions. The contribution made to the field will also be outlined, along with the limitations of the study. Finally, recommendations will be made for future research along with recommendations for policy and practice based on the findings.

7.2 Premise of the study

This study aimed to examine the feasibility of cognitive training with a population of adults with Down syndrome (DS), and also to examine the effect that this training had on levels of executive function. In Chapter 1, the issue of dementia in people with DS was considered. It has long been established that the risk of Alzheimer's disease (AD) in people with DS is far greater than in the general population, with prevalence of clinical symptoms apparent in 15% to 40% of the population (Prasher and Krishnan, 1993), and neuropathology of AD present in almost all of the population by age 40, as shown by neuroimaging studies (Roizen and Patterson, 2003, Schupf et al., 2010a, Royston et al., 1996, Lamar et al., 2011). In the general population, it has also been shown through neuroimaging studies that neuropathology of AD does not on its own determine the presence of clinical symptoms of AD, where it was reported by Esiri et al. (2001) that a quarter of the older population met neuropathological symptoms for AD, but did not show deficit in cognitive function. Cognitive reserve is a theory to explain this disparity, where a person with high cognitive reserve will be better able to withstand a brain insult, whether through trauma or disease, such as AD. Years in education, level of occupation, and level of social engagement have been used as proxies to estimate levels of cognitive reserve in individuals. It is hypothesised that these life experiences may determine the efficiency of cognitive networks, with increased education, occupation, leisure activities resulting in more efficient cognitive networks, and thus presenting a higher threshold for clinical symptoms. This neural network efficiency can be measured using functional imaging (Stern, 2013). In an imaging study conducted by Belleville et al. (2011) it indicated that cognitive training had a significant impact on neural activity in adults with mild cognitive impairment (MCI), thus also showing that the brain remains very plastic, even in those with MCI.

From the aforementioned literature on dementia and cognitive reserve, both of these concepts were integral in creating the context on which this study was based. It was beyond the scope of this study to investigate effect of training on dementia as longitudinal follow-up was not possible. Brain imaging was not possible either, due to logistic constraints, ethical issues relating to the fact that cognitive training had not previously been shown to be feasible with this population. In these circumstances, brain imaging was seen as unduly burdensome, and thus neural activity could not be measured. Thus, while dementia and cognitive reserve are central themes in the study, it was not possible to measure the effect of training on either dementia or cognitive reserve. As cognitive reserve is built up throughout the lifetime, it was, however, possible to examine whether existing level of cognitive reserve at the beginning of the study would impact on cognitive training success.

In this study executive functions were the measurable outcome of interest. Executive function is related to the other key concepts, of cognitive reserve and dementia in a number of ways. Individuals with DS have been shown to have higher levels of executive dysfunction when compared to individuals in the general population and adults with ID from other aetiologies (Rowe et al., 2006). Roldan-Tapia et al. (2012) found that those with higher cognitive reserve performed better on tasks of EF. Similarly, one of the key tenets of cognitive reserve is the usage of flexible strategy, an ability associated with EF and assessed by EF tasks (Tucker and Stern, 2011). An improvement in levels of EF, or the maintenance of levels of EF despite MCI would have significant positive implications on quality of life for individuals. As was discussed in the literature review, EF impacts on numerous aspects of day to day life from going to the shop, to making future plans to emotional reactions to situations. Otero et al., (2014) compared EF to the driver of a car whereby the driver has control and use of all the component parts of the car, with all parts being necessary for driving. Maintenance of level of function means that the same level of independence previously experienced by the individual can be continued for as long as possible.

Thus, while the outcome of interest was in levels of EF both as measured by neuropsychological assessments and in behaviours of executive function, it was necessary to understand the reciprocal and interrelated connections between EF, cognitive reserve and dementia for adults with Down syndrome.

7.3 Principal Study Findings

This section will outline the principal study findings relating to the sample, the feasibility of the study and the effect of training on levels of EF.

7.3.1 Cognitive reserve

Cognitive reserve was measured using the CRIq (Nucci et al., 2012), which calculates a cognitive reserve score based on years in education, years in type of occupation and social factors. The mean IQ score placed participants in the 'medium' cognitive reserve category.

A significant relationship was found between cognitive reserve scores and baseline scores of EF. The relationship between cognitive reserve and EF was investigated further. No significant relationship was found between level of cognitive reserve and change in EF scores following cognitive training. This was contradictory to a study by Mondini et al (2016) where it was found that scores from the CRIq were significant predictors of change in cognitive performance as measured by the MMSE following cognitive training.

7.3.2 Executive function baseline

Executive function was measured using neuropsychological assessments from the Cambridge Executive Function Assessment (Ball et al., 2008) and the Behavioural Rating Inventory of Executive Function – Adult version (BRIEF-A). This allowed for examination of EF both in terms of neuropsychological assessment and also real life application of EF.

The neuropsychological assessments "Tower of London", "Cats and Dogs", "Scrambled Boxes", "Spatial Reversal" and "Weigl Card Sorting" measured a range of cognitive processes; planning, inhibition, working memory, attention, and set shifting. Scores on these assessments were comparable to EF scores using the same measures in a study conducted by Ball et al. (2008).

Scores on the BRIEF-A indicated that approximately a third of participants had abnormally high deficits in working memory when compared to the normative sample. Dysfunction was also seen in shift – the ability to move freely from one situation/problem to another, task monitoring and initiation.

The neuropsychological assessments and the BRIEF-A measured different aspects of EF. Overall there was high correlation between the neuropsychological assessments and the corresponding measurement of the same process as measured by the BRIEF-A. Working memory was an exception to this, where no significant relationship was found between "Scrambled Boxes" and the "Working Memory" component in the BRIEF-A, whereas both are measuring aspects of working memory. The challenges in measuring EF processes were highlighted previously where the measurement of EF processes to the exclusion of others is almost impossible due to the highly complex and interconnected nature of EF (Suchy, 2009).

7.3.3 Feasibility

The feasibility of conducting a cognitive training program with a population of adults with DS was the principal aim of the study. Feasibility was assessed based on a number of parameters which are summarised below.

7.3.3.1 Adherence

Adherence to the program was high, with 97.5 completing at least 6 weeks of the training and 90% completing the full 8 weeks. Participants completed an average of 930 minutes and a median 711 minutes of where the recommended dosage was 800 minutes. The range was extremely large;

from 339 minutes to 5353 minutes. In additional analysis using ANCOVA, the number of minutes spent on the training program was not found to be a predictor of change in EF scores following cognitive training. The extremely large range and standard deviation coupled with the small sample size may have precluded the observation of a detectable effect.

When training was not completed, the most frequent reason given was that the participant was too busy. This highlights the idea that individuals with DS have a number of commitments in the weekly schedule and that this should be taken into account when planning a training program. Other reasons given included 'no support', 'did not want to', 'forgot' or 'would only complete with researcher'.

7.3.3.2 Enjoyment

Overall level of enjoyment was high throughout the program with highest levels of enjoyment observed between weeks 3 and 6. The highest percentage of 'did not enjoy' was seen in week 1, but was still very low at 7.5%.

In the exit interviews it was indicated that completing the training for 8 weeks was long enough, however all of those who were asked said they would compete the program again if it was on offer, after a break.

7.3.3.3 Support

As mentioned above, not having support was indicated as the second most frequently given reason (18.8%) that training was not completed. The level of support needed throughout the program declined throughout the course of the program, where 82.1% required support at the beginning of the program and this dropped to 40% who required support at week 8.

7.3.3.4 Environment

The majority of participants (62.5%) completed the training at home, with a further 30% completing the training both at home and at the day service and 7.5% completing the training solely in the day service.

The environment in which the training was completed did not have an effect on the number of minutes spent on the training program.

7.3.4 Effect of training

The treatment and delayed intervention group were comparable at baseline and no practice effects were evident as there were no significant differences in the delayed intervention group between time 1 and time 2, where no intervention had yet been given.

The cognitive training program appeared to have a positive effect on scores of EF as measured by the neuropsychological assessments.

Overall there was a trend towards improvement following the training for "Tower of London", "Cats and Dogs Stroop", "Scrambled Boxes" and "Weigl Card Sorting". Improvement in scores on "Spatial Reversal" were weaker.

These results from the neuropsychological assessments were promising as an indication that cognitive training may have a positive impact on levels of executive function.

The effect of cognitive training on behaviours of executive function as measured by the BRIEF-A was not as clear as the neuropsychological assessments.

An improvement was observed for the 'emotional control' at post assessment for both the treatment and delayed intervention groups. The Behavioural Regulation Index (BRI) comprises inhibit, shift emotional control and self – monitor scales; it represents the ability of the individual to appropriately regulate behaviour and emotion. An improvement was also observed in the BRI in both treatment and delayed intervention groups at post assessment.

As noted previously, due to the small sample size, effects may have been undetectable. Further investigation is needed into the effects of cognitive training on everyday behaviours.

7.4 Contribution to the Field

The biggest contribution the study has made to research with regard to people with Down syndrome was to lay the ground work for further research into the effects of iPad based cognitive training within this population. While issues such as poor executive functioning and risk of early onset of AD for adults with DS have been known for a long time, there has been little work done to date on interventions to attempt to tackle these issues. This study has shown that it is feasible to conduct a cognitive training program using an iPad with adults with DS with a mild or moderate level of ID.

Prior to conducting a large scale trial, there is a need to first examine the important parameters and to assess whether it is possible to conduct such a study on a smaller scale. It was thus necessary to first complete this assessment, as failure to do so would risk not only time, resources and funding, but it would be unethical to recruit a large number of people with no prior evidence to suggest that the study is worthwhile. This is an even bigger issue when dealing with a vulnerable population such as adults with DS, as it would be unethical to propose this task without some evidence that the outcome may be beneficial.

Results from the study suggest that cognitive training can have a positive effect on levels of executive function. Further investigation is needed in this area, particularly in relation to the transfer to behaviours of EF.

Since very little previous research had been done in this area with this population, the study presented an opportunity for people with ID to be involved in its development from its inception. Focus groups were conducted at the very beginning of the study, where people with ID had an input into the development of the accessible material for the study. The games that were chosen for inclusion were chosen based on the advice from those in the focus group. All aspects of the study were inclusive, from initial information, consent, participation and included recommendations for future research from participants and their families/carers.

This study was able to identify potential barriers to successful implementation of a cognitive training program. It was identified early in the study that reassurance was needed in relation to the use of technology for those who did not have previous experience with iPads or similar tablets.

Providing evidence on the possibility of integration of technology into the lives of people with ID was an additional contribution. This study has shown that, despite preconceptions, technology is not a barrier to be overcome for people with ID, but rather a useful and underutilised resource that provides an opportunity to develop new skillsets. While initial support may be needed, as was shown in this study many people with ID can independently use technology to increase mental stimulation.

The study provided further information on executive function in adults with DS prior to the onset of clinical dementia. This study provided corroboration that these neuropsychological assessments are useful and suitable for a population of adults with DS. The BRIEF-A was also found to be a useful assessment to provide information on the everyday behaviours of EF.

This study has also added to the understanding of cognitive reserve with a population with DS. The cognitive reserve index questionnaire (Nucci., 2012) proved suitable for use with this population. While adults with DS in the age group of interest in this study may not have had the opportunity for much education or job prospects, leisure and social activities also contribute to level of cognitive reserve and the CRIq was able to capture these experiences to give an estimate of cognitive reserve.

Due to the increased levels of executive dysfunction and due also to the risk of early onset of AD, this study focused on adults with DS. However, the outcomes of this study, from the methodology and program used, the use of the EF assessments, to findings in relation to feasibility may also be applicable to individuals with ID from other aetiologies.

7.5 Limitations

7.5.1 Sample size

The relatively small sample size was a limitation of the study in terms of the conclusions that can be made from the statistical analysis, however this was a necessity to manage the study. Prior to this study, very little research had been conducted on the use of an iPad to deliver a cognitive training program and thus it was necessary to investigate whether a training program would be used by adults with DS, whether it would be adhered to, whether it would be enjoyed, how it would be integrated into a schedule, how much support would be needed. These issues needed to be addressed, and it was possible to do so with the sample size used.

The study was focused on the effects of cognitive training in relation to executive function. It was therefore also necessary to investigate whether cognitive training showed promise in improving executive functioning. According to the Central Limit Theorem, a sufficient number of independent observations is needed for the means of those observations to follow a normal distribution (Fischer, 2010); 30 has been used as a rule of thumb as big enough to suffice, provided the distribution is not overly skewed (Corder and Foreman, 2009). The sample in this study therefore was suitable for assessing feasibility and it was possible to conduct statistical analysis, however it was necessary to exercise caution in interpreting or overstating the results yielded.

A further larger scale study would be needed in order to examine the effects with higher statistical power. In conducting a large scale study, it would be necessary to ensure that positive aspects of this study are not lost due to increase in sample size.

7.5.2 No brain imaging component

As was discussed above, since little previous research had been conducted, ethical approval was not given to include a neuroimaging component to this study. It was considered that this would place too much burden on the participants, without any previous evidence that individuals with DS would use and complete the training program. The study findings may now be used as evidence base to justify the inclusion of a neuroimaging component in future research on cognitive training with individuals with DS.

7.5.3 Passive control group

A passive control group was used in the study rather than an active control group. This refers to the status of the control group prior to receiving the intervention, where no alternative intervention was offered, but rather this group continued with normal care prior to completing the cognitive training. In health research the use of active controls is often employed due to the fact that it would be unethical to have a passive control. The issue has been highlighted in psychological studies, as the use of a passive control does not account for placebo effects; the participant in the intervention group knows that they are participating in a program/intervention and so they expect to improve (Boot et al., 2013).

In previous studies on cognitive training it has been found that the active intervention group showed improvement when compared to the passive control group, but that differences were not found when compared to the active control group (Martin et al., 2011), with other studies showing an improvement compared to both active and passive controls.

In this study, there were a number of barriers to including an active control group. With only one researcher, it would have been logistically impossible to meet with those completing the intervention and also those engaged in the active control task. Without the same level of contact with the researcher a comparison with an 'active control' group would have been insufficient. Another prohibitive obstacle to the use of an active control group in the context of this study, was the type of program that would have to be used by the active control group. For a realistic comparison, it would have been necessary to use a computer based program that was similar, but that did not target cognitive training. Due to both time and resource constraints this was not possible.

This study addressed the concern by using a delayed intervention group with partial crossover design to allow for the hypothesis to be tested twice – once with the active group and once with the delayed intervention group.

7.5.4 No inclusion of people with severe or profound ID

It was not possible to develop a training program specifically for people with DS for the purposes this study. The program used was initially developed and mainly used with individuals with traumatic brain injury. It was suitable for use with people with DS with a mild or moderate level of ID, but it would not have been suitable for people with severe or profound ID.

7.6 Recommendations

This section will outline recommendations, based on the findings from this study. Firstly, the recommendations from the participants and support staff/family for future programs will be outlined. Subsequently recommendations for future research, policy and practice will be presented.

7.6.1 Recommendations from participants and support persons

The recommendations below emerged from a thematic analysis conducted from exit interviews with participants and support persons.

7.6.1.1 Recommendations from Participants

- Include games that are more similar to action video games
- Include musical challenges
- More animation that indicates progress throughout the game

- More contact with the researcher
- More accessible instructions
- More accessible demonstrations of the games and rules
- Better graphics

7.6.1.2 Recommendations from Support Persons

- Integrate training into day service program
- Clearer graphics in the program
- Clearer instructions with less writing in the program

7.6.2 Research

The following are recommendations for future research emerging from this study

7.6.2.1 Larger sample

As this study found that cognitive training was feasible with a population of adults with DS, and also showed improvements in EF, a cognitive training study with a larger sample size is recommended.

7.6.2.2 Brain imaging component

Cognitive training studies in the general population have used neuroimaging to examine changes in neural activity following training. This would have an advantage over using EF assessments alone, but would present certain challenges. A study has been conducted using PET scans with adults with DS, and this was found to be feasible and well tolerated (d'Abrera et al., 2013). An fMRI would present additional challenges, due to the need to stay very still, but these would not necessarily be insurmountable. Alternative options such as functional near red spectroscopy (fNRS) could be investigated also, which allows monitoring of brain activity through the recording of blood flow. This offers an alternative non-invasive, portable option to traditional functional neuroimaging. Regardless, a future study could include this measurement option.

7.6.2.3 Randomised Control Trial

A study with a large sample size was recommended above. With a larger sample, a randomised controlled trial would be recommended.

7.6.2.4 Information sessions

Information sessions were found to increase the response rate, and allowed an opportunity for potential participants and support persons to discuss any concerns about level of ability in relation to technology. The use of similar information sessions is recommended for future research.

7.6.2.5 Development of a specific program for people with ID

The cognitive training program used in this study was found to be suitable for use with people with DS, however it was not developed specifically with this population in mind, and thus was not perfectly designed to meet specific needs. While games were chosen where literacy was not necessary, there were nevertheless a lot of written instructions in the program, which was not ideal. It would be useful to develop a more accessible program specifically for people with DS, using the accessible information guidelines with respect to language used and font size.

7.6.2.6 Evaluation of future research

This study has provided the basis from which future studies can develop the area of cognitive training with a population of adults with Down syndrome, or indeed with a population of individuals with ID from other aetiologies. As discussed in the methodology (Figure 3.7, pg 134) , there were a number of elements in the study that had the potential to be active components in the outcome above the cognitive training itself. The active input of the researcher, in engaging with the participant one on one, while using an iPad, could be addressed with the use of an active control group. In an active control group, a researcher would continue to have one to one contact with all participants while using an iPad in both the training component and in the control group component. Greater resources would be needed to facilitate this. The outcome measures used in the current study were suitable and would be recommended, with the exception of 'Spatial Reversal'.

The results of the current study can also be used in determining the ideal sample size for future studies of its kind with this population. Based on the hypothesis that there is a difference from baseline measures to post intervention with the effect sizes noted in this study, a sample of 300 would be recommended.

7.6.2.7 Further investigation into effects of IQ, cognitive reserve on training

As related to above, a larger sample would allow further examination of the effects of IQ and cognitive reserve on training to determine whether baseline levels of IQ and cognitive reserve have an impact on change following the training.

7.6.2.8 Further investigation into effect of dosage on training

There is no consensus, either in the general population or in this population as to the minimum dosage at which an effect would likely be seen. Further investigation of this issue is needed, where a larger sample size would be better able to identify the minimum dosage needed to yield a change.

7.6.3 Policy

7.6.3.1 National Dementia Strategy

The Irish National Dementia Strategy (2014) highlighted the fact that people with DS are at greater risk of developing AD at an earlier age. It also acknowledges that cognitive activity can impact on dementia. In future national strategies, the role of cognitive reserve and cognitive training should be highlighted.

7.6.3.2 New Directions Policy

Including cognitive training in the day service program would lend itself to the underpinning philosophy of the 'New Directions' policy (Health Service Executive, 2012), which recommends moving away from the old day programs to person centred approach that focuses on quality and personal outcomes.

7.6.4 Practice

The recommendations below are related to cognitive training in practice.

7.6.4.1 Introduce to day service

It is recommended that cognitive training be integrated into a day service program. In the present study, training was conducted on an individual basis, but for logistical reasons, it could be adopted in a group setting in the day service. It was noted previously by Kelly et al. (2014) that cognitive training in group sessions may give additional benefits than individual training.

There are a number of activities that are currently repeated frequently in the day service, particularly table top activities and arts and crafts. It would be possible to introduce a cognitive training session in place of some of these activities during the week. Training could be conducted in a group setting with support staff and would be recommended to last between 20 and 30 minutes.

7.6.4.2 Increase access to technology

This study has shown that using technology is not a barrier for people with ID, and that those with ID should be offered all the opportunities afforded by technological advances. There is a need to ensure that individuals with ID have increased access to technology, to accessible apps and have support from staff in familiarisation with new technology. In today's society, people with ID will be excluded from the community if there is no access to IT. In order to ensure this, it is essential that there is a focus in gaining IT literacy, not just for the younger generation, but for all people with ID.

7.7 Conclusion

As was observed by Cohen (1990), the aim of a successful piece of research is not to definitively settle an issue, but rather to make a theoretical proposition more likely, and to use this to guide future research and replication.

This study aimed to examine the feasibility of conducting a cognitive training program with adults with DS using an iPad. Based on a number of parameters to determine feasibility, from the point of view of both the person with DS and those caring for the person with DS, it was found that it was feasible to conduct such a program. The study also aimed to examine whether a cognitive training program could have an effect on levels of executive function. While, conclusions are limited due to small sample size, improvement was seen in neuropsychological assessments of executive function following cognitive training. Positive effects reflected in everyday behaviours were not as promising. These findings need further investigation with a larger sample size. Previous experience with an iPad was not necessary, which serves as an important reminder not to leave people with ID behind in technological advances that have the potential to be beneficial to all.

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9 Appendices

9.1 Appendix 1 Ethical approval letter

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Ms. Eimear McGlinchey
School o Nursing and Midwifery
University of Dublin, Trinity College
24 D’Olier Street
Dublin 2

REF:140510

Title of Study: Utilising technology in assessing the feasibility of cognitive training to influence executive function in adults with Down syndrome.

Dear Eimear,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in February 2015, we are pleased to inform you that the above project has been approved without further audit.

Yours sincerely,

pp Siobhan Brown

Dr Ruth Pilkington

Chairperson

Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2, Ireland.

www.healthsciences.tcd.ie

9.2 Appendix 2 Accessible Quiz

Quiz

	True	False
I have to take part in this study	☐	☐
I will do some tests at the start of the study and at 2 other times	☐	☐
I will be given games to play on a computer	☐	☐
I will keep the i-pad after the study	☐	☐
My name will be written in a report	☐	☐

9.3 Appendix 3 Accessible Information Booklet

Information Leaflet

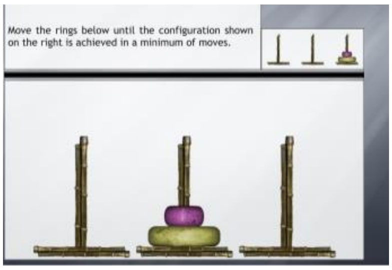
Brain Exercises for Adults with Down Syndrome

The BEADS Study

Down Syndrome Ireland

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

What is a brain training program?



A brain training program is a set of puzzle games. These are exercises for the brain.

What is this project?

This project wants to see if doing a brain training program will help to keep the brain healthy.

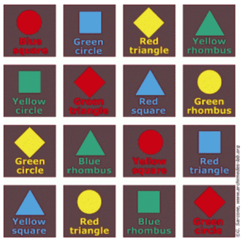
To do this, we will do some tests at the start of the study and also another 2 times. We want to see if the brain training program made a difference.

Why is it important?

As people get older our brains can start to change.

If we can keep our brain active then it can help to protect us from diseases like Dementia.

What would I have to do?



At the start of the program you would do some tests. These tests are like puzzles. We will do these again 2 more times.

You would be given an I-pad for the 8 weeks you would be doing the study. This will have games on it.

You would play these games for 20 minutes, 5 days a week for 8 weeks.

We would then compare the tests to see if they were different.

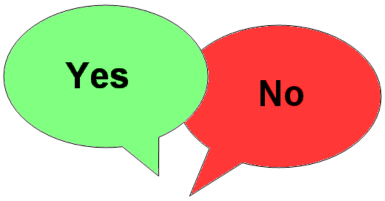
How long will I be doing the training for?

The training program will last for 8 weeks

If I start the program, do I have to finish it?

No, you can stop at any time you want

Do I have to take part?



No, it is your choice whether you want to take part or not

Who do I ask if I have any questions?

If you have any questions, you can

call Eimear on 01 8963332

or

e-mail Eimear at nicloine@tcd.ie

or

write to Eimear at
School of Nursing and Midwifery
24 D'Olier Street
The Gas Building
Trinity College Dublin
Dublin 2

9.4 Appendix 4 Accessible Consent Form

Consent Form

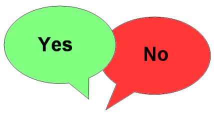
Please read the information below and sign this consent form if you wish to take part in this study.

Please tick

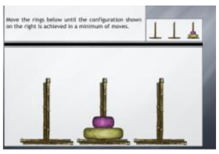
I agree with the following statements:

I have read and understand the information booklet ☐

I know who to call if I have any questions ☐



I know that it is my choice to take part in this study ☐



I know what I will be asked to do in the study ☐

I understand that I will give the I pad back at the end of the study ☐

I understand that all the information I give will be kept private and confidential. My name will never be used ☐

I understand that this consent form will be kept in a safe place for 5 years after the study is finished ☐

I understand that I can stop taking part at any time.
I do not have to give a reason ☐

Your Consent

Your name: ___________________________________

Please tick

 I wish to take part ☐

Your phone number: ____________________________

Your address: _________________________________

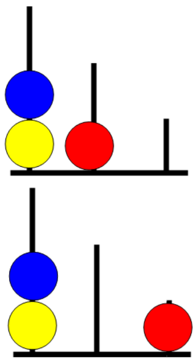
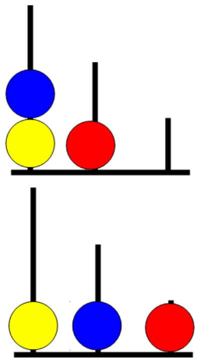
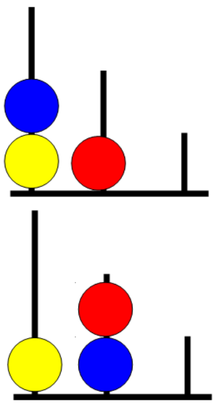
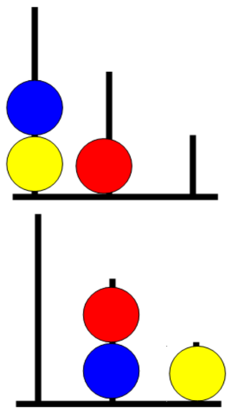
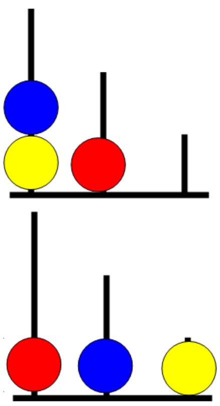
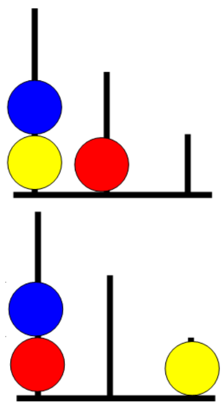
____

____

Your signature: ________________________________

Date: ____

9.5 Appendix 5 Configurations for Tower of London

One Move	Two Move
	
Three Move	**Four Move**
	
Five Move	**Six Move**
	

9.6 Appendix 6 List of Questions in BRIEF-A

1. Has angry outbursts
2. Makes careless errors when completing tasks
3. Is disorganised
4. Has trouble concentrating on tasks
5. Taps fingers or bounces legs
6. Needs to be reminded to begin a task even when willing
7. Has messy closet
8. Has trouble changing from one activity to another
9. Gets overwhelmed by large tasks
10. Forgets his/her name
11. Has trouble with jobs or tasks that have more than one step
12. Overreacts emotionally
13. Doesn't notice when he/she causes others to feel bad
14. Has trouble getting ready for the day
15. Has trouble prioritising activities
16. Has trouble sitting still
17. Forgets what he/she is doing in the middle of things
18. Doesn't check work for mistakes
19. Has emotional outbursts for little reason
20. Lies around the house a lot
21. Starts tasks without the right materials
22. Has trouble accepting different ways to solve problems
23. Talks at the wrong time
24. Misjudges how difficult or easy tasks will be
25. Has problems getting started on his/her own
26. Has trouble staying on topic when talking
27. Gets tired
28. Reacts emotionally to situations
29. Has problems waiting his/her turn
30. People say he/she is disorganised
31. Loses things
32. Has trouble thinking of a different way to solve problem

33. Overreacts to small problems
34.Doesn’t plan ahead for future activities
35.Has short terms attention span
36.Makes inappropriate sexual comments
37.When people are upset, doesn’t understand why
38.Has trouble counting to three
39.Has unrealistic goals
40.Leaves bathroom a mess
41.Makes careless mistakes
42.Gets emotionally upset easily
43.Makes decisions that get him/her into trouble
44.Is bothered by having to deal with changes
45.Has difficulty getting excited about things
46.Forgets instructions easily
47.Has good ideas but cannot get them on paper
48.Makes mistakes
49.Has trouble getting started on tasks
50.Say things without thinking
51.His/her anger is intense but ends quickly
52.Has trouble finishing tasks
53.Starts things at the last minute
54.Has difficulty finishing tasks on own
55.People say he/she is easily distracted
56.Has trouble remembering things
57.People say he/she is too emotional
58.Rushes through things
59.Gets annoyed
60.Leaves room a mess
61.Gets disturbed by unexpected changes in daily routine
62.Has trouble coming up with ideas for what to do in free time
63.Doesn’t plan ahead for future tasks
64.People say he/she doesn’t think before acting
65.Has trouble findings things in closet
66.Has problems organising activities
67.After having a problem, does not get over easily

68. Has trouble doing more than one thing at a time
69. Mood changes frequently
70. Doesn’t think about consequences before doing something
71. Has trouble organising work
72. Gets upset easily over little things
73. Is impulsive
74. Doesn’t pick up after self
75. Has problems completing his/her work

9.7 Appendix 7 Accessible Structured Questionnaire

How much did you like the games this week?

Did not like it	Liked it a little	Really liked it

How hard did you think the games were this week?

hard	A bit hard	Not hard

How excited are you about continuing next week?

Not excited	A little excited	Really excited

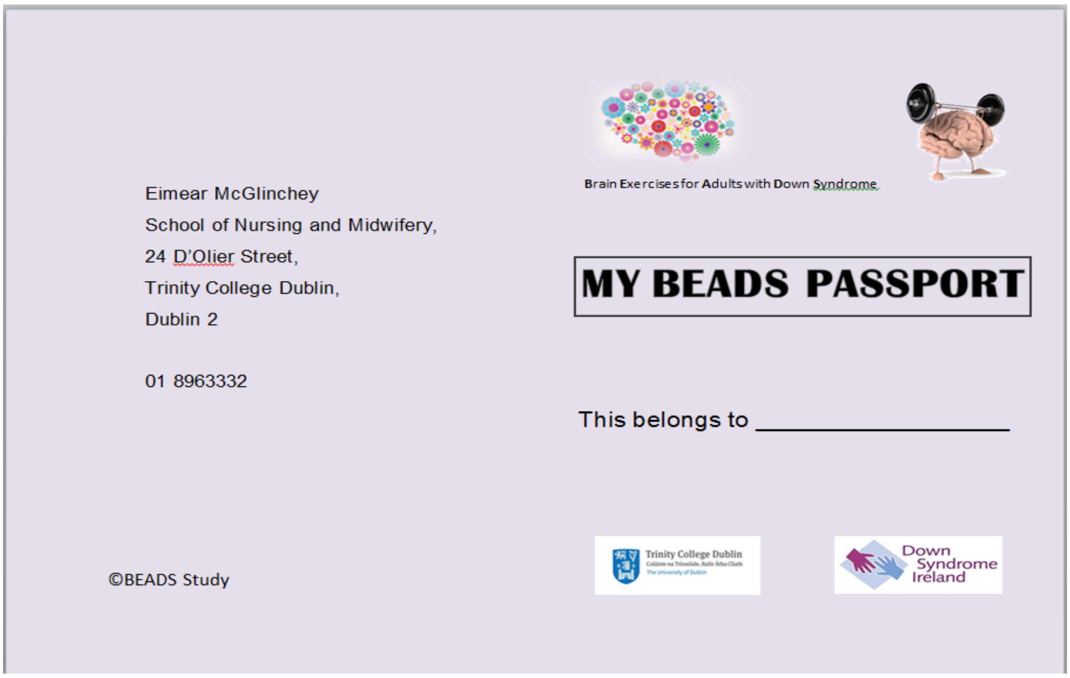
How many days did you do the training……….

	Number of days
At home	
In the day service	
Other	
If Other, please say where	

Did you do the training…..

	Number of days
On your own	
With staff	
With family	
With researcher	

9.8 Appendix 8 BEADS passport



Eimear McGlinchey
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24 D'Olier Street,
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Dublin 2

01 8963332

©BEADS Study

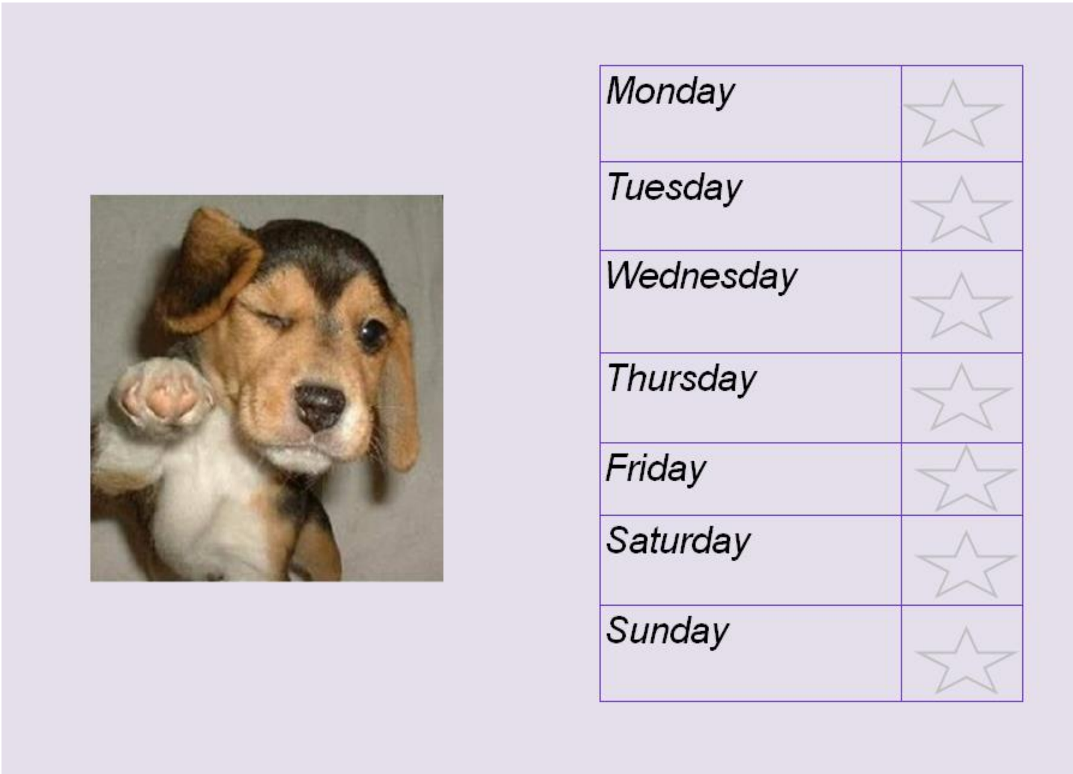
Brain Exercises for Adults with Down Syndrome

MY BEADS PASSPORT

This belongs to ________________

Trinity College Dublin

Down Syndrome Ireland



Monday	☆
Tuesday	☆
Wednesday	☆
Thursday	☆
Friday	☆
Saturday	☆
Sunday	☆

Monday	☆
Tuesday	☆
Wednesday	☆
Thursday	☆
Friday	☆
Saturday	☆
Sunday	☆

Congratulations!

You are finished the training program!

Monday	☆
Tuesday	☆
Wednesday	☆
Thursday	☆
Friday	☆
Saturday	☆
Sunday	☆