Volume One –Research Papers:

THE DEVELOPMENT OF NEUROPSYCHOLOGICAL ASSESSMENT AND REHABILITATION FOR INDIVIDUALS WITH DEMENTIA

by

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Thesis Overview

This thesis consists of a research volume (one) and a clinical volume (two). Volume one makes up of three papers that are concerned with the development of neuropsychological assessment and rehabilitation for individuals with dementia. The first paper is a systematic review on the evidence base of everyday action rehabilitation in dementia. The second reports an empirical study of the utility of the Birmingham Cognitive Screen (BCoS) assessment in differentiating the neuropsychological profile between early onset Alzheimer's disease and vascular dementia. The third is a summary of the above findings for dissemination to stakeholders in the research.

Volume two comprises five clinical practice reports (CPRs). CPR1 presents two formulations of a 42 year-old woman presenting with low mood and hoarding behaviour, using cognitive-behavioural and psychodynamic approaches respectively. CPR2 is a report evaluating a text messaging reminder service for psychology appointments in a community psychiatric liaison service. CPR3 details a single case experimental study of a selective mutism intervention for a 5 year-old boy. CPR4 describes the key aspects of work with a 72 year-old female presenting with persistent depression, based on an attachment narrative therapy framework. Finally, the abstract of CPR5, an oral case presentation of a 50 year-old woman with chronic post stroke fatigue, is presented.

For

Pa Pa

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1. Systematic Review: The cognitive rehabilitation of activities of daily living in dementia

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Abstract

Background. It has been shown that cognitive decline alters individuals' ability to engage in daily routine activities. Rehabilitation that enables continuous participation in activities of daily living (ADL) helps maintain personal dignity, meaning and independence. This paper reviews current evidence regarding strategies and efficacy of direct ADL intervention in dementia.

Method. A systematic search of PsycINFO, MEDLINE and CINAHL from inception dates to March 2016 was conducted. Methodological quality of the identified studies was examined. The relative efficacy of the different interventions identified was appraised with reference to the quality of the included studies.

Results. Thirteen studies were identified (5 RCTs and 8 non-RCTs), that examined the impacts of the use of personally meaningful activities in ADL training (1 study), errorless learning methods (5 studies), and errorful practice methods (7 studies) respectively. Whilst the majority of the studies showed positive treatment effects, the details of the study designs, interventions and study quality varied greatly.

Discussion. Aspects of person-centred approach in dementia rehabilitation are adopted in a number of studies but the effects are yet to be investigated more systematically. Whilst studies of errorful interventions reported more consistent evidence of benefits, the category represents diverse approaches and there is a lack of direct comparisons of techniques to evaluate the relative merits. The limitations in the studies quality and in the current review impacted on the generalizability of the results.

Introduction

The Importance of Maintaining ADL in Dementia

Diagnostic and prognostic factor. Dementia is a degenerative condition that impacts on cognitive functioning including memory. It affects 46.8 million people worldwide (7.45 millions in Western Europe) with an annual incidence of 1.6 million cases in Western Europe (Prince et al., 2015). A deterioration in everyday actions (or activities of daily living, ADL) is one of the diagnostic criteria for dementia alongside cognitive decline and behavioural changes (American Psychiatric Association, 2013; McKhann et al., 2011). The varying level of ADL functioning is also indicative of the disease progression (Verlinden et al., 2016), hence a key outcome measure for pharmaceutical efficacy (Desai, Grossberg, & Sheth, 2012). Importantly, beyond the diagnostic label and prognostic factor, ADL holds significance for its direct impact on the quality of life of an individual through the inherent meaning of such activity to the person (Roach & Drummond, 2014).

Personal meaning. Cognitive decline alters the individual's ability to engage in the daily routine activities that one would previously take for granted. The awareness of such change can be distressing for the individuals with dementia and caregivers (Hamilton, Fay, & Rockwood, 2009; Maki, Amari, Yamaguchi, Nakaaki, & Yamaguchi, 2012) and lower quality of life (Woods et al., 2014). Support for continuous engagement in routine everyday actions can therefore help maintain an individual's sense of self and dignity and prevent "excessive dependency" i.e. the decline in ADL can be greater than is justified by the underlying neuropathology (Engelman, Mathews, & Altus, 2002; Tappen, 1994). It is no wonder that the participation in such activities is often expressed by individuals with Alzheimer's disease as their rehabilitation goal (Clare, Evans, Parkinson, Woods, & Linden, 2011a). Lam and colleagues emphasised the importance of maintaining and "relearning" of such behaviours in

rehabilitation as it may be more accessible and gratifying for individuals who are experiencing cognitive decline (Lam et al., 2010). The current review examines the development and efficacy of interventions that enable performance of ADL in individuals with dementia.

Cognitive Interventions for ADL Performance

For cognitive changes in dementia, there has been a growing interest in the development of non-pharmaceutical interventions (Olazaran et al., 2010). Commonly known approaches include cognitive stimulation (CS), reality orientation (RO), cognitive training (CT) and cognitive rehabilitation (CR)(Bahar-Fuchs, Clare, & Woods, 2013; Woods, Aguirre, Spector, & Orrell, 2012) . CS and RO provide non-specific stimulation of cognitive functioning for individual with dementia, using a range of enjoyable social activities. A Cochrane review concluded that there were positive effects particularly for those with mild to moderate dementia (Woods et al., 2012). In describing the more targeted approaches, CT and CR are often used interchangeably (Bahar-Fuchs et al., 2013; Bottino et al., 2005). Based on the WHO (2001) classification, Bahar-Fuchs (2013) differentiated CT as impairment focused whereas CR, participation focused. CT interventions focus on isolated cognitive abilities such as memory and reasoning, using paper and pencil tasks or computerised training. Despite emerging evidence base of the efficacy of CS and CT on cognition, mood and quality of life, their direct links with ADL performance are less clear (Bahar-Fuchs et al., 2013; Olazaran et al., 2010; Willis et al., 2006). The current review concerns the impact of participation focused CR on ADL performance.

Procedural Learning in Dementia Rehabilitation

In considering rehabilitation for individuals with dementia, there is also the issue of differential decline across different memory and learning processes, particularly between procedural and declarative memory.

Two memory processes. *Procedural memory* (Eichenbaum & Cohen, 2004) involves learning through establishing sensori-motor "habits" with repeated exposure. The learning of the knowledge and the knowledge itself are not available to conscious access, hence they form part of the "implicit" memory process. On the other hand, *declarative memory* is defined as learning about facts ("semantic knowledge") and events ("episodic knowledge"). It represents the conscious (hence "explicit") learning and retrieval of arbitrary relationships of information (Eichenbaum & Cohen, 2004). The two memory processes, when intact, interact and complement each other in skills acquisition (Ullman, 2004), for example, learning dance movements with an instructor could possibly utilise both procedural and declarative process to practice and memorize the steps.

Differential declines. For individuals with dementia, e.g. Alzheimer's disease, the two memory systems appear to be affected in different ways. Often, impairment in episodic memory is noted first, followed by impairment in semantic memory and deficits in daily living skills, these occurring prior to the deterioration in executive functions (Bouchard & Rossor, 2007). The different rates of deterioration is supported by the consistent finding that individuals with Alzheimer's disease (AD) appear to be able to learn motor skills implicitly through the procedural memory process but not to learn words through the declarative/lexical memory processes (Heindel, Salmon, Shults, Walicke, & Butters, 1989; Libon et al., 1998; Sabe, Jason, Juejati, Leiguarda, & Starkstein, 1995).

Implications for interventions. Grinstead and Rusted (2001) have proposed that the knowledge of functional information is not degraded in individuals with AD in the mild-moderate range but that retrieval of such information is impaired. They therefore suggest that retrieval through motorical means, as corresponding to the mode with which such information was encoded, is the most effective as a rehabilitation strategy. Similarly, Zanetti et al. (1997) argue that often memory training in AD is ineffective due to the reliance on cognitive effort and skills (declarative learning) that are impaired in AD. Again, they suggest that interventions are more likely to be effective if they target the relatively well-preserved skills i.e. implicit and procedural knowledge. Such a proposal would seem to have significance for the rehabilitation of activities of daily living. However, whilst rehabilitation approaches have been developed for AD using such implicit learning principles, for example, using errorless learning and (ELL) method (van Tilborg, Kessels, & Hulstijn, 2011a), these have mainly been applied to the learning of face-name and word list (Clare et al., 2000; Haslam, Gilroy, Black, & Beesley, 2006; Hopper, Drefs, Bayles, Tomoeda, & Dinu, 2010), or simple motor reaction-time tasks in the laboratory such as the Maze test, or rotor pursuit (van Tilborg, Scherder, & Hulstijn, 2007). Errorless method was initially developed for individuals with severe memory impairment, particularly impairment of explicit, episodic memory (Baddeley & Wilson, 1994; Wilson, Baddeley, Evans, & Shiel, 1994). Errorless learning (ELL) was based on the idea that explicit memory was required to differentiate errors from correct responses in learning. The elimination of error enables individuals with impaired explicit memory to better learn new skills using the relatively intact implicit memory (Page et al. 2006). In errorless training, an individual is given the target information to learn and immediately reproduce, thus preventing his/her active retrieval of information from long term memory (Wilson et al 1994). Whilst Jones and Eayrs (1992) questioned the suitability of errorless

method for the rehabilitation of the more complex skills of daily living, relative to straightforward discrimination tasks such as name learning, such evidence is yet to be established. The current review will therefore draw together current literature regarding strategies specifically for the improvement of ADL performance in order to determine the current state of the field.

Focus of Review

Targeted techniques. The notion that individuals with dementia can improve in their daily living skills through supported practice is not new (McEvoy & Patterson, 1986). Trials that encompass a "package of care" from goal-setting to delivering a person-centred programme of cognitive rehabilitation or occupational therapy have also shown promising results for improving ADL functions (Clare et al., 2010; Clare, Evans, Parkinson, Woods, & Linden, 2011; Kim, 2015; Schmid et al., 2015). However, the relative effectiveness of each element of these programmes can be concealed within such multifaceted approach, particularly in relation to the varied profiles and levels of cognitive deficits of the individuals (Giovannetti, Schmidt, Gallo, Sestito, & Libon, 2006). We cannot always assume that well-used everyday strategies (e.g. checking/active task monitoring) are necessarily effective in error prevention. This is illustrated in Balouch and Rusted's (2013) study. They compared the tea making under a standard and a dual-task condition, in younger (aged 19-35) and older (aged 57-80) adults, and found that in both groups, the use of verbal or non-verbal task monitoring did not impact on the performance accuracy. With growing economic constraints, the importance of developing effective *targeted techniques* to maximise individual independence and well-being cannot be underestimated (Tappen, 1994).

Direct assessment. It has been argued that the development of targeted cognitive rehabilitation techniques requires direct observations and analysis of performance (Colheart, Bates, & Castles, 1994). Such methods have contributed to the understanding of dementia related action disorganisation (Giovannetti, Schmidt, et al., 2006; Humphreys & Forde, 1998; Schwartz, 2006; Stamenova, Roy, & Black, 2014) through error analysis (see Crutch, Rossor, & Warrington, 2007b; Giovannetti et al., 2008). For example, object use difficulty was shown to be qualitatively different when triggered by degraded ADL knowledge in semantic dementia (Giovannetti, Sestito, et al., 2006), compared with the frequent problem of object misplacement experienced in Alzheimer's disease (Hamilton et al., 2009). On the other hand, self-reported or caregivers' reported changes in abilities can be underspecified and prone to informant bias (Doble, Fisk, & Rockwood, 1999; Rueda et al., 2015). It is unfortunate that *direct assessment* of performance is reported to be lacking in dementia research (Giebel, Challis, & Montaldi, 2015).

The current developments of interventions using assistive technology for complex ADL (e.g. the CogWatch Project for tea-making, www.cognwatch.eu) are in their infancy. Such procedures may not be available for immediate adoption in clinical practice. The reasons were highlighted in Bharucha and colleagues' (2009) extensive review of assistive technology applications to dementia care. They identified 58 types of assistive technologies with potential applications to dementia care. The range of technologies included a few that monitor and detect activities or behaviours. Out of these, only one offers prompting for a specific activity - hand washing. A minority of studies (N=3) involved individuals with dementia, using small sample size. The review identified the need to investigate acceptability even for cognitively intact older adults. Moreover, the authors highlighted the demands of such technological development, including heterogeneous sensor networks and

artificial intelligence, to produce sophisticated predictive computation models of complex human activity and behaviour. The resulting daunting costs and knowledge gaps were prohibiting factors in the developments. Lastly, the authors also raised ethical concerns for the ubiquitous monitoring technologies required in the process. The current review will therefore exclude studies in this area.

In summary, motivated by the importance of maintaining ADL skills for individuals with dementia, and the need to develop targeted rehabilitation approaches, this review will focus on studies of cognitive rehabilitation of ADL using direct observational measures and direct intervention methods. The objectives are:

1) to describe the range of targeted rehabilitation strategies that have been reported for daily living skills in people with Alzheimer disease or vascular dementia;

2) to evaluate the effectiveness of these strategies, and the quality of available evidence from controlled trials;

3) to consider future directions of research and rehabilitation practice.

Method

Search Strategy

Three electronic bibliography databases including MEDLINE, CINAHL and PsycINFO from the inception dates to March 2016 were searched. Relevant key concepts were combined utilizing database-specific search terms and subject headings. These were: concepts related to dementia of the Alzheimer or vascular types:(dement* OR Alzheimer* OR vascular dement* OR multi-infarct dement*), combined with concepts related to rehabilitation (*rehabilitation OR remediation* OR *intervention* OR *skill training OR learning OR cognitive therapy),* combined with terms related to activities of daily living (*activities of*

daily living OR naturalistic action OR everyday action* OR action disorgani*ation syndrome OR apraxia).*

Study Selection

The study applied the following a priori inclusion and exclusion criteria:

Participants. Participants with a medical diagnosis of dementia.

Intervention. The review included studies with an identifiable element of intervention which addressed specific activities of daily living (ADL) task(s), performed by the individual with dementia. Limits were applied to studies with sufficient details of intervention and with outcome measures based upon *observed* performance of daily living tasks targeted for the intervention. The key characteristics of ADL tasks were 1) goal-directed 2) routine 3) involving sequential actions, and 4) involving the use of familiar objects (Ramsden, Kinsella, Ong, & Storey, 2008; Zacks et al., 2001)[1]. Examples of these tasks include grooming, dressing, tea-making, meal preparation. Interventions that were of pharmaceutical or assistive technological natures were excluded (see exclusion criteria below).

Comparator interventions. These included no treatment/standard treatment, or alternative therapeutic method(s).

Outcome. Studies that include, as primary outcome, direct observation of activities of daily living performance, rather than self-reported or caregivers' reported changes in abilities.

Type of studies. As everyday action rehabilitation in dementia is an emerging area of research, there have been few randomised controlled trials (RCTs) conducted, this review therefore will also include non-randomised studies (NRSs). The NRS that were eligible for

[1] On the basis of the criteria, examples of the exclusions are: 1) repetitive non-purposeful behaviours with/without objects e.g. checking, banging, and throwing of objects, 2) regular activities but without the use of objects e.g. navigation to familiar places 3) activities that do not require sequential actions e.g. checking the time.

this systematic review of complex interventions included: quasi-randomised controlled trials, controlled before-and-after studies (CBAs) and interrupted time series (ITS) (Ryan et al., 2013).

Exclusion criteria were employed for the elimination of articles:

1) Papers with no report of an intervention.
2) Interventions that did not directly target ADL performance or the ADL intervention and evaluation were inadequately specified.
3) Interventions that were pharmaceutical in nature, or those that target primarily the emotional, physical or sensory aspects of dementia.
4) Theoretical, descriptive or review papers.
5) Studies in which it was impossible to differentiate the results for individuals with dementia.
6) Studies only presenting data from participants with Korsakoff's syndrome, frontotemporal or Lewy body dementias, due to the potential atypical presentation of their functional deficits.
7) Participants with other neurological or psychiatric comorbidity.
8) Case reports with no empirical data.
9) Non-peer reviewed articles and book chapters.
10) Non-English language papers.
11) Studies that examined the use of specialist assistive technology.

The search results were reviewed, relevant studies were identified and full texts retrieved.

Quality Assessment

The risk of bias criteria was adapted from those reported by Higgins (2011) to meet the specific requirements of this review. Alongside the relative strength of the design (i.e. RCTs in general are rated higher than NRSs), the quality/conduct of the study was also an important element to consider, when the level of bias was assessed. Due to the range of study designs included, the quality assessment in this paper was informed by several guidelines. In particular, Higgins' (2011) guidelines were adapted with additional criteria from Downs and Black's (1998) guidelines on external validity and treatment fidelity to enable quality assessment for both randomised and non-randomised studies of health care intervention. The resulted criteria covered domains relevant for both RCTs and non-randomised controlled studies, that is 1) unbiased *selection* of comparison groupings/conditions, 2) procedures to minimize *performance bias*, 3) *adherence to treatment*, 4) procedures to minimize *detection bias*, 5) appropriate application of *statistics* and adjustments for between groups confounding factors, 6) unbiased and clear *reporting*, and 7) *representative*ness of participants and settings (Table 1.1). Studies were rated as high risk (0 point), low risk (2 points) or unclear risk (1 point) in each of these domains. Where inadequate information is given in the report for a certain domain, the risk of bias of that study will be rated as "unclear".

Results

Description of Studies

The review and discussion process yielded 14 papers (representing 13 studies from 8 countries). Figure 1.1 details the elimination of excluded papers. The included studies comprised 5 randomised controlled trials (RCTs)(Coyne & Hoskins, 1997; Lam et al., 2010; Lin et al., 2010; Tappen, 1994; Thivierge, Jean, & Simard, 2014), and 8 non-RCTs (Bettcher, Giovannetti, Klobusicky, et al., 2011a; Bier et al., 2008; Dechamps et al., 2011; Giovannetti

Table 1.1 Tool for the assessment of risk of bias and other quality issues

Domain	Requirement	Low risk/desirable (2 points)	Unclear risk or quality (1 point)	High risk/inadequate (0 point)
Selection bias	Unbiased allocation of comparison groupings/conditions at baseline	Use of randomisation, allocation concealment, or within-subject designs	Inadequate details of randomisation or other strategies	Evidence of allocation bias that may alter results seriously e.g. alternation approach
Performance bias	Procedures to minimise systematic differences between groups in the exposure to factors other than the intervention of interest	Effective blinding of participants/trainer of intervention received, counterbalance presentation of conditions	Not described or no evidence of serious bias within the reported method	Evidence of bias that may alter results seriously e.g. knowledge of participants of their intervention allocation.
Fidelity of treatment (Hildebrand et al., 2012)	Steps to ensure therapist's adherence to intervention protocol e.g. therapist training, supervisions, and monitoring procedures in place	Treatment fidelity protocol, or well reported standardised treatment methodology	Poorly described or absence of treatment protocol and/or potential/mild threat of validity e.g. author acted as therapist	Poorly described non-standard treatment protocol or significant confound from concurrent interventions, or the use of third party therapist without steps taken to attain treatment fidelity
Detection bias	Procedure to minimise systematic differences between groups in how outcomes are determined	Blinding of independent assessors, use of multiple assessors, minimise subjectivity of measure	Absence of active element to control but without evidence of serious bias within the reported method	Author/trainer/investigator as assessor
Statistical bias	Appropriate statistics with controls for confounding factors across groups e.g. unequal attrition rates	Valid statistical test given the study aim and sample, use of statistical control for differences between groups	An acceptable analytical strategy, though superior and available strategy not adopted.	Inappropriate test of hypothesis and evidence/reporting of confounds between comparison groups shown without statistical or methodological control
Reporting quality/bias	Key aspects of study clearly described. All pre-specified and relevant outcomes are reported with no bias.	Clear and complete reporting of participants characteristics, interventions, outcome measures and follow ups across groups	Elements of unclear or incomplete reporting that raise some doubt about the results	Bias reporting data that may alter results seriously. Evidence of systematic difference between findings that are reported and those that are not hence results are likely to be distorted.
External validity	Representative participant and settings for the population of interest	Large sample drawn from representative characteristics and settings	Moderate sample in a typical treatment setting	Small sample in a laboratory or non-representative setting

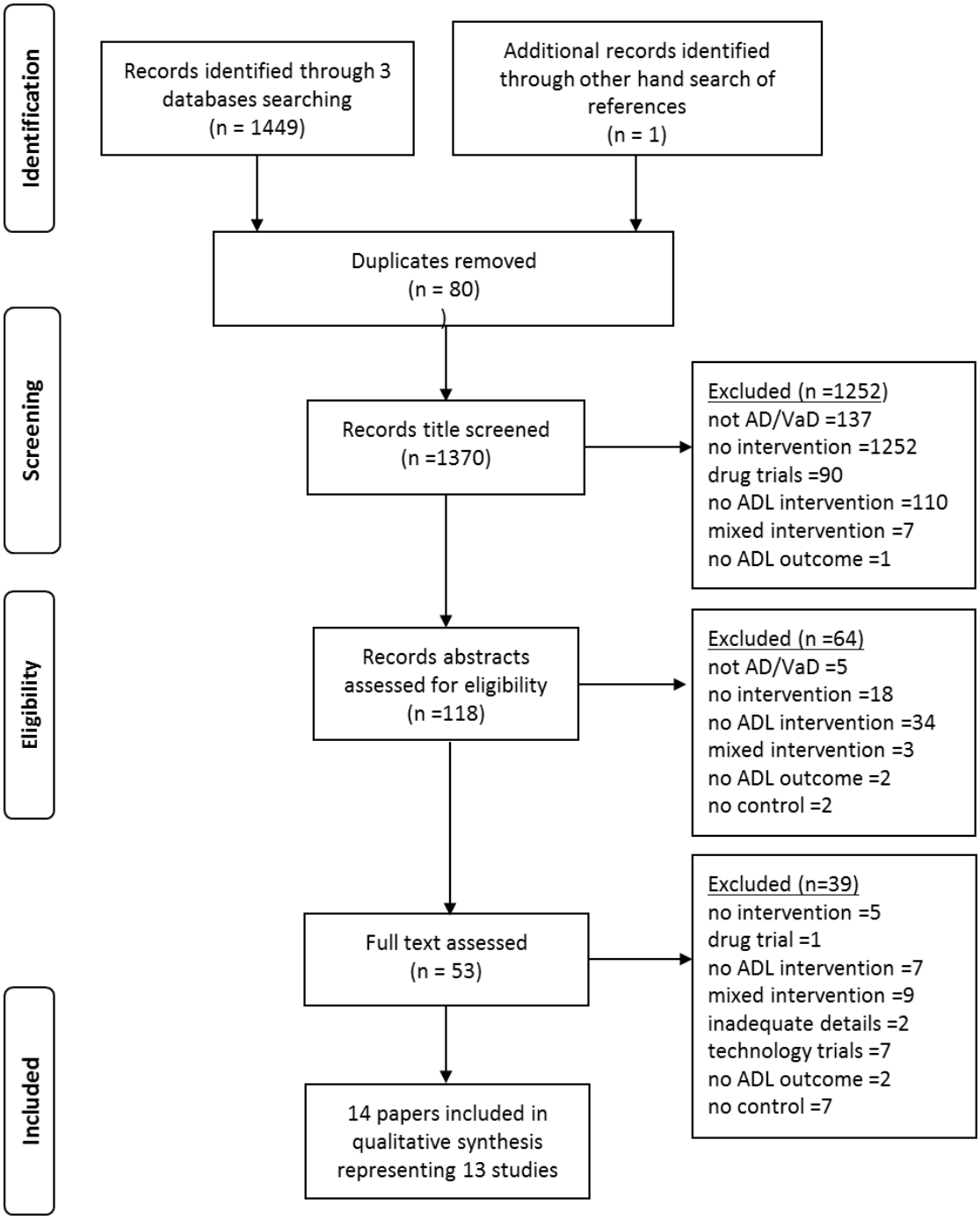

Figure 1.1 Search process and result

et al., 2007; Giovannetti, Seligman, Britnell, Brennan, & Libon, 2015; van Tilborg, Kessels, & Hulstijn, 2011; Zanetti et al., 1997; Zanetti, Zanieri, Giovanni, et al., 2001). The latter included a range of designs: within-subject cross over trials (3 studies), clinical controlled trials (2 studies), controlled before and after trial (1 study), interrupted time series (1 study), or a combination of all of the above (1 study). There was also significant diversity on other aspects concerning study characteristics or intervention details (Table 1.2).

Setting. Half of the studies (7/13) were conducted in the participants' own living environments. These included nursing/residential care homes or their own homes. Two studies were conducted at a day care facility. One study used a combination of the above. Three studies investigated the effects of intervention at their specialist clinical laboratory.

Characteristics of the participants. The number of participants in the RCTs ranged from 24 to 85 (mean (SD)=55.4 (30.9). Apart from the single case study (Bier 2008), the number of participants in the non-RCTs ranged from 10 to 87 (mean (SD)=30.4 (28.7). These are comparable with other studies of rehabilitation for individuals with dementia (Bahar-Fuchs et al., 2013) Eight studies only included individuals with Alzheimer's disease (AD), one study (Bettcher 2011a) also included a small proportion (7/87) of other dementia types. Four out of the 5 RCTs used a less specific criteria of "a diagnosis of dementia" (Coyne 1997, Lin 2010, Tappen 1994), or "DSM-IV diagnosis of dementia" (Lam 2010). All but one study (Coyne 1997) indicated the severity of the dementia with MMSE scores (mean ranged from 6.4 to 25.0). The scores suggested wide ranging differences across studies. Within some studies (e.g. Lin 2010 and Dechamps 2011), the whole severity spectrum of dementia was found in the participants. In contrast, the age range of the participants was more consistent across the included studies with the mean ranging from 76 to 86 years of age.

Table 1.2 Characteristics of the included studies arranged by intervention types

Study rating	Study design/setting	Participants with dementia	Intervention /no. of sessions	Comparator	Task(s)	ADL measure	Intervention effects
10	**Single blind cluster RCT/ 3 dementia care facilities**	**74**, 66, then 57 **Dx**= dementia **Age**=83.5±6.9 **Female**=74% **MMSE**=13.8±4.4	**Person-centred activity choice /14**	**ADL matched to ability only**	**Varied ADLs, number not specified**	**Assessment of Motor and Process Skills (AMPS)**	**Post training: NS improvement across I&C** **FU (4 months): NS deterioration across I&C**
11	**Single blind RCT with block randomisation and cross-over design/ Participants' own home**	**20,** 17 analysed**.** **Dx=** AD **Age=**80.0±5.4 **Female=**71% **MMSE** =21.8±2.4	**ELL and SR /8**	**No training**	**One ADL chosen with participant**	**Direct Measure of Training: observation tool for steps of the chosen ADLs.**	**Post training:** ***p*=.01* (I1) *p*=.001** (I2)** **FU (3 months): maintained**
10	Within-subject, cross over trial/ 4 nursing homes	**14** **Dx=**AD **Age=** 86.0±5.7 **Female=**86% **MMSE=**15.2 (mild to severe)	ELL /6	LM, TEL	3 ADL tailored to participants	Observation rating for each step performed	Post training: LM *p*=.01; ELL *p*=.003** TEL *p*=.015* FU (3 weeks): LM *p*=.009**; ELL *p*=.002** TEL *p*=NS Time x methods LM>TEL *p*=.002** ELL>TEL *p*=.09 LM>ELL *p*=.55

Table 1.2 Characteristics of included studies arranged by intervention types (cont'd)

ID	Study rating	Study design/setting	Participants with dementia	Intervention /no. of sessions	Comparator	Task(s)	ADL measure	Intervention effects
Errorless Learning (cont'd)								
Bier 2008	9	Multiple baseline interrupted time series/ Client's own home	**1** **Dx**=mixed dementia **Age**=76 **Gender**=Female **MMSE**=25.0±1.0	ELL and VC /8 and 10	No training	Cassette radio, VCR	% of steps done without help and errors	Post training: $p<.001$*** No transfer of training FU (9 weeks): deterioration trend $p=0.052$
Lin 2010	**7**	**Single blind cluster RCT/ 3 dementia care facilities**	**85**, then 82 **Dx**=dementia **Age**=81.2±6.4 **Female**=53% **MMSE**=11.8±6.1	**"SR training" /24**	**TAU**	**Eating**	**1) fed by caregiver 2) verbal assistance 2) physical assist. 3) self-eating time**	**Post training fed by caregiver NS *verbal assistance* $p<.05$* physical assistance NS self-eating time NS**
van Tilborg 2011[a]	6	Controlled, repeated measures and cross over trial/ A care home	**12**, 11, then 10 (vs. 16 controls) **Dx**= Dementia **Age**=79.8±4.4 **Female**=not reported **MMSE** =20.4±3.5	ELL with LM /5	Explicit step learning	coffee making, water warming	Number of correct steps	Post training: $p=.16$ FU (1 week) $p=.04$* (ELL deteriorated more)

Table 1.2 Characteristics of included studies arranged by intervention types (cont'd)

ID	Study rating	Study design/setting	Participants with dementia	Intervention /no. of sessions	Comparator	Task(s)	ADL measure	Intervention effects
Errorful Learning								
Giovannetti 2007 (Bettcher 2011b)	11	Within-subject, cross over trial / An outpatient neurological clinic	**46**; **38**[b] **Dx=** AD **Age=**80.0±6.1; 79.9±5.6 **Female=**not reported, 81% **MMSE =**21.5±4.4; 22.6±2.9	Cues by objects arrangement /1	Standard mixed layout	3 standard NAT ADLs	Naturalist Action Test coding for: 1) completed steps 2) error score 3) error detection 4) error correction	Post training: step completion *p*=.002** error reduction *p*<.001*** error detection *p*=.23 error correction *p*=.08
Tappen 1994	**10**	**Single blind RCT/ A nursing home**	**72,** 63 analysed **Dx=** dementia **Age=**84±8.5 **Female=** 75% **MMSE=** 6.4±6.6	**Least and graded verbal and physical assistance /100**	**1) Cognitive stimulation 2) TAU**	**7 basic ADLs**	**Physical and Self Maintenance Scale: independence ratings of trained tasks.**	**Post training: vs. cog stimulation NS vs. TAU *p*=.01***
Bettcher 2011a	10	Non-randomised controlled trial[a]/ 3 outpatient clinics	**87** **Dx**= AD (80), other dementia types (7) **Age**=77.0±6.0 **Female**=not given **MMSE** =22.0±3.2	Training on task objects and actions knowledge /1	No training group	3 standard NAT ADLs	Naturalist Action Test coding for: 1) total error 2) error detected 3) error corrected	Post training: error reduction *p*=.002** error detection *p*=.001** error correction *p*=.76
Giovannetti 2015	8	Controlled before and after study/ A University affiliated specialist clinic	**20** AD vs. PD, PDD **Dx=** AD **Age=**75.6±4.9 **Female**=not reported **MMSE =**22.0±3.4	Goal cue given at the end of each NAT task /1	PD group PDD group	3 standard NAT ADLs	Naturalist Action Test coding for: 1) corrected errors 2) additional errors 3) checking behaviour	Post training: 1) AD > PDD *p*=.02* 2) *p*=.46 3) AD > PDD *p*=.05

Table 1.2 Characteristics of included studies arranged by intervention types (cont'd)

ID	Study rating	Study design/setting	Participants with dementia	Intervention /no. of sessions	Comparator	Task(s)	ADL measure	Intervention effects
Errorful Learning (cont'd)								
Coyne 1994	**7**	Single blind RCT with repeated measures/ A 230-bed nursing facility	**24** **Dx**= dementia **Age**=84.2 (range 68-96) **Female**=100% **SPMSQ**=9.55 (7-10) (>7=severe impairment)	**Verbal prompts and positive reinforcement /9**	**TAU**	**Eating and drinking**	1) Independence rating per step 2) self-feeding frequency	**Post training:** **1) Eating** *p*=.011* **Drinking** *p*=.007** **2) NS for both eating and drinking** **FU (1 week)** **NS i.e. no deterioration**
Zanetti 1997	6	Within-subject control trial/ A day hospital for dementia	**10** **Dx=** AD **Age=**77.2±5.3 **Female=**90% **MMSE =**19.8±3.5	Verbal support/15	Untrained tasks	20 ADLs	Task completion time standardised with 10 healthy controls	Post training Improvements at p<0.05 on both trained and untrained tasks
Zanetti 2001	6	Non-randomised controlled study/ A day hospital for dementia	**18** **Dx=**AD **Age=**76.4±9.8 **Female=**89% **MMSE=**19.6±3.6	Verbal and physical support and modelling/15	No training group	13 ADLs	Mean completion time	Post training: not reported FU (4 months) Training group improved at p<0.025* NS for control group

Note. RCTs are in bold font. ELL=errorless learning; C= control group; Dx= diagnosis; I= intervention group; LM=learning by modelling; NAT=Naturalistic Action Test; MMSE= Mini Mental State Examination; NS=no significant difference between intervention and comparator; PD=Parkinson's disease; PDD=Parkinson's disease dementia; SPMSQ=Short Portable Mental status Questionnaire, SR=spaced retrieval; TAU=treatment as usual; TEL=trial and error learning; VC=vanishing cues.

[a]These two studies (Dechamp 2011, van Tilborg 2011) also represent Errorful Learning studies as they contrasted between ELL and Errorful Learning methods

[b]Bettcher 2011b represented a retrospective analysis of the Giovannetti 2007 study data with exclusion of 8 participants with MMSE<15.

*p<0.05, ** p<0.01, *** p<0.001

Interventions. Whilst all studies focused on improving specific ADL tasks, important variations were noted. With regard to therapeutic approaches, apart from one study (Lam 2010) which evaluated the effects of personal meaning in activity, all studies looked at techniques to enable procedural learning or practice (Zanetti et al., 1997). The basis of the intervention can be broadly divided into errorless approaches or errorful approaches. Errorless learning (ELL) method (described in 5 studies) represents a more *coherent* approach as the trainer directs the individual to the correct action prior to initiation of each step (Bier 2008, Dechamps 2011, Lin 2010, Thivierge 2014, van Tilborg 2011). Two of the five studies above (Dechamps 2011, van Tilborg 2011), plus seven others studies included errorful training practices (Table 1.2). Errorful approaches enabled the participants to retrieve the task step from their long-term memory to complete the task (Middleton & Schwartz, 2012), and represented a more diverse range of techniques (described further below). The duration of interventions varied considerably from a one-off trial (Bettcher 2011a, Giovannetti, 2007; Giovannetti 2015) to highly intensive practices (e.g. 100 sessions in Tappen 1994).

ADL assessments. For outcome measures, five studies used standardised ADL assessments[2]. Five studies derived their own performance rating; and three measured task completion time. Seven of the 13 studies applied follow up measures from 1 week to 4 months post intervention (Table 1.2).

Due to the significant diversity in the sample characteristics, study methods, as well as nature of intervention, meta-analysis was not carried out for the synthesis of the data.

[2] Three studies used the Naturalistic Action Test (ACT)(Schwartz, Segal, Veramonti, Ferraro, & Buxbaum, 2002); one study used the Assessment of Motor and Processing Skills (AMPS)(Fisher, 2006); and one study used the Physical and Self Maintenance Scale (PSMS)(Hokoishi et al., 2001).

Risk of Bias in Included Studies

The assessments of the methodological and reporting quality of the papers are detailed in Table 1.3. The table positions the RCTs at the highest level of evidence, followed by the non-RCTs. As described in the methodological section and Table 1.1, all studies were appraised for their risk of bias and other quality issues. The rationale of the quality ratings for each study is given in the quality assessment forms (Appendix A).

Table 1.3 Risk of bias and validity assessment for all included papers

	Selection bias	Performance bias	Fidelity of treatment	Detection bias	Statistical bias	Reporting bias	External validity
RCT							
Coyne 1997							
Lam 2010							
Lin 2010							
Tappen 1994							
Thivierge 2014							
Non-RCT							
Bettcher 2011a							
Bettcher 2011b[a]							
Bier 2008							
Dechamps 2011							
Giovannetti 2007							
Giovannetti 2015							
van Tilborg 2011							
Zanetti 1997							
Zanetti 2001							

Note. Explanation for the individual quality rating are provided in Appendix A
Green=low risk; Amber=unclear risk; Red=high risk
[a]Bettcher 2011b was the report of further analysis from the data collected in Giovannetti 2007's study.

RCTs. None of the RCTs applied concealment of allocation, with 3/5 studies offering little detail of the randomisation process. Blinding of the assessor was employed in 100% of the RCTs and the majority (80%) incorporated appropriate methods to ensure treatment

fidelity. However, most (80%) of the studies were overall lacking in clarity, completeness and consistency of reporting and all presented some risk of statistical bias. For example, three studies did not control for demographic differences across groups (Coyne 1997, Lam 2010, Lin 2010), two used no statistical correction for multiple comparisons (Coyne 1997, Lin 2010) and three did not adequately account for outcome bias due to data loss to follow up (Lam 2010, Lin 2010, Tappen 1994).

Non-RCTs. Whilst the non-RCTs were inferior in their robustness in selection bias, risk for treatment contamination or infidelity, as well as their detection bias, there appeared to be stronger controls for performance bias (using within subject and counterbalanced strategies in 5/8 studies), statistical bias and reporting quality, when compared to the RCTs.

All the above studies, more so for the non-RCTs, were limited in their external validity due to the modest sample sizes.

Findings as a Function of Intervention Type

Table 1.2 presents detailed characteristics of the studies within each intervention type in the order of their quality of evidence ratings.

Use of activities of personal significance. The study by Lam et al. (2010) was a well thought out RCT with the intervention group and the control group participated in the same occupational therapy group training. The only difference between the two groups was that the tasks given to the intervention group were of personal significance to them, whereas tasks for the control group were randomly selected. The activities of personal significance were identified through a pre-trial questionnaire. However, no difference was found in ADL abilities between the two groups post intervention.

Errorless learning (ELL) with or without other strategies. Two RCTs and 3 non-RCTs employed the errorless method with a variety of supplementary strategies. One RCT (Thivierge, 2014) incorporated ELL with spaced retrieval (SR), i.e. gradually increasing the interval of retrieval during practice (Camp, Foss, O'Hanlon, & Stevens, 1996), compared this with no training using a cross-over design. The investigators used a sophisticated design to reduce risks of bias (Appendix A). In their training, "ELL" was introduced through graded support: involving firstly, the trainer modelling, then step by step verbal instruction, then trainees reciting steps during execution alongside support from the trainer, then fully independent execution. Such gradual and systematic reduction of support, can also be described as a vanishing cues (VC) approach (Glisky, Schacter, & Tulving, 1986). Spaced retrieval periods were applied within each level of support. The findings showed superior performance in two groups of participants, comparing their training vs. no training periods, retained after 3 months. However, spontaneous improvement was also observed during the initial no training period measured in one group. This puts into question whether other extraneous factors at play that could potentially account for the observed improvements.

SR method was also reported in another RCT (Lin 2010) for feeding independence of individuals with moderate to severe dementia in a care setting. However, no theoretical underpinning was provided nor details of the training beyond the label "SR" with "ELL". Even without statistical correction for multiple comparisons, no significant improvement of self-feeding was reported in the SR training group. This was despite a relatively large sample size (n=32) and session number (24) amongst the included studies.

In contrast, a detailed description of the intervention was given in a single subject intervention study by Bier (2008) of an individual with mild dementia. During the training, the participant was given complete verbal and physical assistance for every step, then

gradually reduced support (VC). Using multiple baseline time series measures of completed steps, the authors revealed significant improvement in the participant's use of a cassette radio and a video cassette recorder, but there was no transfer of training (to recording, rather than listening with the same cassette radio), nor maintenance of improvement during the follow up phase. This is despite a very intensive training of 141 trials for one task and the participant's mild degree of dementia.

Two non-RCTs directly contrasted ELL and errorful learning (EFL) methods. Including participants with all severities of dementia, a study in four nursing homes (Dechamps 2011) compared ELL, two EFL methods: *learning by modelling (LM*), and *trial and error learning (TEL).* Here, ELL was defined as verbal, written and pictorial prompting prior to participants performing each step in the action sequence to prevent errors occurring. LM consisted of trainer demonstrating and describing each steps for participants to copy. The trainer demonstrated progressively longer step sequences as participants produced more correct steps and errors were corrected after occurrence. Finally, TEL was limited to cues given only after 3 failed attempts by participants. After training, all methods showed significant improvement. While LM resulted in significantly greater improvement than TEL, ELL did not differ from either LM or TEL in effect. The improvements were maintained after 3 weeks only in the ELL and LM groups.

Another study (van Tilborg 2011) presented a slight variation of the above techniques. They contrasted implicit learning (combined ELL *with* LM), when participants copying trainer step by step with no verbal instruction given and "all errors were prevented" (no details as to how), with explicit learning (comparable to TEL above), when participants were given full verbal instruction of the ADLs to memorise and act on. In the explicit learning condition, errors were corrected immediately after

occurrence. Significant improvements were resulted with both methods, with no difference in positive effects between the methods.

In summary, five studies of varying quality ratings (from 6 to 11, Table 1.2), examined errorless method. Two studies compared errorless with errorful methods yielding no difference in outcomes. Superior outcomes from errorless learning were reported in two of the five studies (Bier 2008, Thivierge 2014) when compared with no training. Retention of effects was reported in only one of the studies (Thivierge 2014). However, the same study did not rule out element of spontaneous recovery observed in the baseline period.

Errorful practice/interventions. Two RCTs and 5 further non-RCTs examined various errorful methods for the procedural practice of ADLs.

Verbal and/or physical prompting during the task was adopted by both RCTs and 2 non-RCTs. With no rationale given for the choice of the strategies, one RCT (Coyne, 1997) found that highly structured verbal prompting and positive reinforcement/praise significantly improved independence in eating and drinking at mealtimes in the trained group, compared to the untrained group, both groups having severe cognitive impairment and residing in a large nursing home. The effects were maintained after one week. Nevertheless, high risks of bias in the reporting and statistical process were noted (see Table 1.3 and Appendix A). A higher quality RCT (Tappen, 1994) adopted "least and graded" verbal and physical prompting for a range of basic ADLs. The rationale was the concept of excess disability (from a lack of engagement) in dementia. Tappen (1994) found significant improvement in overall ADL performance in the trained group as compared to a cognitive stimulation group or a no-training group. Two non-RCTs (Zanetti 1997, 2001) investigated effects of combining different strategies to support errorful practice: from verbal cues, prompts, answers to questions (Zanetti 1997), to the combination of verbal cue, reinforcements, verbal and

physical prompts and modelling (Zanetti 2001). The first study, using a within-subject design, found no difference between the trained and untrained activities. The subsequent study, using control participants, demonstrated a positive effect on completion time in the trained group compared to non-trained group, measured at 4 months post training. As both studies employed small numbers of participants (n=10, and n=11 in the trained groups), the generalisability of these results is uncertain.

Three further non-RCTs represented targeted cognitive-model led investigations in a laboratory setting. Two (Giovannetti 2007, Bettcher 2011a) adopted Cosentino et al's (2006) two-component model of action script deficits in dementia. They examined the executive component (Giovannetti, 2007) and the semantic component (Bettcher, 2011a), respectively. A third (Giovannetti, 2015) aimed to compensate for episodic memory deficit identified in dementia.

The use of environmental adaptation in promoting error monitoring through reduced *executive demands* of the task was reported by the first study (Giovanetti 2007). In the intervention condition, the everyday tasks objects (for making toast with butter and jam, and making coffee with cream and sugar) were arranged in order, from left to right, according to the order of the task steps. In the control condition, the objects were laid out in a relatively unstructured fashion. The effects on task steps completion and error scores were examined and further analysis on error detection and correction were reported by Bettcher et al. (2011b).

The effects of action semantic knowledge training on error monitoring, targeting the *semantic component*, was investigated by the second study (Bettcher 2011a). Ten minutes training of the knowledge of task-relevant objects and steps were given via verbal, pictorial and video presentations, prior to execution of each ADL task.

A reminder of the task goal was used by the third study (Giovannetti, 2015), given *after* participants' self-report completion of each task, to compensate for episodic memory deficit through. Any error correction after the goal cue was recorded.

The design and implementation of all the above studies were elegant and analyses thorough, which yielded significant and specific positive effects for all studies in all conditions (Table 1.2). However, as the studies were conducted in a clinical laboratory, the ecological validity of the finding would require further investigations.

In summary, nine studies examined various errorful intervention methods. Two (from the ELL group of studies above) contrasted errorful learning with ELL and showed no significant effect. Six studies showed superior outcomes when compared with no training (2 studies), treatment as usual (3 studies), or clinical controls (1 study) (Table 1.2). These included two RCTs (Coyne 1997, Tappen 1994) for individuals with severe dementia. Retention of intervention effects were reported in two studies at 1 week post training (Coyne 1997) and 4 months post training (Zanetti 2001) respectively.

Summary of Findings

The current review aimed to identify emerging targeted rehabilitation strategies for ADL performance in people with dementia, and the evidence of effects. Thirteen studies were included from 1449 records identified from the search criteria. Apart from one RCT evaluating the use of personally meaningful activities with no reported significant effect on ADL outcomes, all studies were categorised into investigations of techniques based on errorless intervention or errorful intervention. The contrast between errorless and errorful methods showed that RCTs were equally distributed across the two categories, yielding no

difference in overall quality ratings (Fisher's exact p=0.88). Two studies compared errorless and errorful methods directly and found no difference in effects (Table 1.2).

Errorless learning (ELL) methods. When compared with no training, two ELL studies yielded positive effects. These included one RCT of quality rating of 11 and a single case experimental study with a rating of 9 (maximum score=14). No significant effect was found when compared with treatment-as-usual (1 study).

Errorful methods. Significant positive effects were found in six studies when compared to no training, treatment-as-usual, or across clinical controls. These positive results were found in two RCTs, and four non-RCT with comparable quality ratings to those in the errorless learning category.

Maintenance of training effects were also equally distributed across the two categories, lasting similar time periods (i.e. 3 weeks and 3 months respectively after ELL interventions; 1 week and 4 months after errorful interventions). The effects will be further discussed in the light of the quality of the evidence.

Discussion

Strength of Study Designs and Quality

The focus of the current review, that is ADL, constitutes complex behaviours. The complexity imposes demands on investigators to adequately define the behaviour, interventions and means of monitoring, given the vast array of possible performances for meaningful comparison. Such demands might have related to the finding that many of the included studies had insufficient quality of reporting (Table 1.3).

Sample size and generalizability. Implementation of cognitive intervention and evaluation of ADL can be time consuming (Tappen, 1994) which may have led to the small

sample size in 9/13 of the studies, that is 20 or less, which will have limited the statistical power and external validity. Whilst four studies provided larger sample sizes, including two RCTs (Lam 2010, Lin 2010), these showed no effect of treatment (Table 1.2). The other two studies presented one-off training and evaluation in a laboratory setting with no follow up, hence offering limited generalisability. A large proportion (8/13) of the studies, however, adopted within subject designs to limit the variability of the data. The implementation in participants' natural environments to improve ecological validity of the findings was also a strength of some included studies.

Choice of ADL outcome measures. The use of direct observation, for example, of types of errors committed (Bettcher, Giovannetti, Klobusicky, et al., 2011b; Bettcher, Giovannetti, Libon, et al., 2011; Giovannetti et al., 2007), allowed investigators to closely monitor the nature of difficulties and aspects of improvement post training. For example, Giovannetti et al. (2007) reported that arranging task objects according to the task step sequence improved individuals' completion of relevant steps, using the correct objects, but did not reduce perseverations or step reversal errors. However, other studies offered no elaboration of the ways individuals failed to accomplish the task steps, except for an overall rating of ADL independence. Such lack of details limited the analysis of the possible cognitive deficits that underlay the performance difficulty. The phenomenon indicated a lack of explicit translation between the theoretical advances on the cognitive neuropsychology of everyday action and dementia (Crutch, Rossor, & Warrington, 2007a; Giovannetti et al., 2010; Humphreys & Forde, 1998; Schwartz, 2006), and the current evidence base.

Lack of reported rationale for methodological decisions. Whilst positive effects were found in nine studies (Table 1.2), seven compared the interventions with treatment as usual or no training conditions. While five of the reviewed studies reported maintenance of

effect at different periods (Coyne 1997, Dechamps 2011, Thivierge 2014, van Tilborg 2011, Zanetti 2001), the rationale of the choice of follow up period was not clear. Similarly, there was a lack of informed decisions in the intensity, and length of intervention in all the reported study procedures.

These findings suggest that the evidence base on direct ADL intervention in dementia is in its infancy. Nevertheless, the included studies have revealed the growing emphasis on person-centred care in dementia (Brooker, 2003), as well as the interests in the relative effectiveness of errorless method and errorful method of interventions. These will be discussed below.

Developing Person-centred Investigation and Intervention

A person-centred approach (Brooker, 2004, Kitwood, 1997) refers to the extent that individual differences and values are respected, and whether activities are delivered in a positive social environment. Such an approach is generally accepted as best practice in dementia care (National Institute for Health and Clinical Excellence, 2006).

Intervention that targeted person-centred care. Only one study formally investigated the benefits of the use of personally meaningful activities in ADL training (Lam 2010). The investigators highlighted that, while they found no difference in abilities across the intervention and control groups on follow up, only the group trained on personally meaningful activities experienced significant deterioration in MMSE scores. This suggests that the use of meaningful activities in practice might have mediated the effects of cognitive decline. Perhaps further analysis, partialling out the effects of MMSE changes, could help verify such hypothesis. Whilst there was no high risk to bias found in this study (Table 1.3 and Appendix A), there were inadequate details for the randomisation process, and a lack of

control for the higher level of education in the intervention group relative to the control group. Both factors may have impacted on the validity of the negative finding.

Elements of person-centred care in included studies. Whilst person-centred care was not the focus of the other investigations, three included studies adopted the principles of *personal choice and/or interest* in the selection of ADL to be trained. For example, in Thivierge et al.'s (2014)'s study, the activity "was chosen in collaboration with the patient and his/her cargiver in order to target…needs and interests" (p1191). Such process, with the emphasis on respecting personal ability and relevance was also reported in two other studies (Dechamps 2011, Bier 2008). All three studies showed positive treatment effects.

The effect of *positive social environment* on the intervention outcome was not directly explored in the reviewed studies. Nevertheless, in Lam et al's (2010) well-controlled RCT, both intervention and control groups participated in the same group training, and gained equivalent improvements, regardless of the *personal significance* factor. In other reviewed studies with superior intervention effects (Bettcher 2011, Bier 2008, Coyne 1997, Tappen 1994, Thivierge 2014, Zanetti 2001), 6/9 involved additional social inputs in the trained group but not the controlled group/condition. The possible effects of the social interactions with the research team on the observed improvement in functions were acknowledged in one study (Thivierge 2014), and should be taken into account in future studies.

Considerations of dementia severity in person centred approach. In studies targeted for individuals with more severe dementia residing in nursing homes, basic personal care ADL tasks (e.g. eating, drinking) were chosen (Coyne 1997, Lin 2010, Tappen 1994). Studies targeting individuals with mild to moderate levels of dementia adopted a more sophisticated range of tasks (e.g. preparing hot drinks). Nevertheless, personal choice was not typically given. Within this constraint, a more person-centred approach would be in the form

of tailored support to the specific needs of the participants in the prescribed task. The importance of this was illustrated in Balouch and Rusted's (2015) 5-year longitudinal study contrasting strategies in promoting error monitoring for individuals with Alzheimer's disease. Across participants, different methods of recall (performance vs. verbal recall) benefited different participants with mild/moderate AD; and within individuals, the effects of methods varied across stages of dementia. Balouch and Rusted argued, that cognitive capacity must inform behavioural strategies for everyday task performance in people with dementia. Even when learning simple motor skills, a tailored approach to individual's particular needs and abilities was recommended (van Tilborg et al., 2007). Where details were given, such tailored support was noted amongst some included studies. For example, Tappen (1994) adopted "least and graded verbal/physical assistance" given according to the participant's online performance. This contrasted with Coyne (1997)'s highly standardised, hence less person-centred, verbal prompting scripts delivered at fixed 1-minute intervals.

Errorless or Errorful Intervention?

Within the included studies, and ruling out other variability, efficacy was reported in a larger proportion of studies using errorful methods relative to those that used errorless methods (see above).

Relative efficacy. Evidence that errorful methods were no worse or better than errorless methods, for individuals with mild to moderate memory impairment including those in the early stage of AD, was found in the rehabilitation literature (see review by Middleton and Schwartz, 2012). The wealth of the current evidence lies in the training of a single behaviour component using discrete tasks requiring no flexibility of response e.g. word-list learning, stem completion or face-name association tasks (Clare and Jones, 2008), whereas

the applicability of the findings from the above tasks to everyday actions has been questioned (Evans et al., 2000; Jones & Eayrs, 1992; Kessels, Loon, & Wester, 2007).

The current review identified 12 studies that investigated errorful or errorless methods directed for ADL practice in dementia. There were common and discrete issues across studies employing the two approaches. In the included studies, some "errorless learning" (ELL) procedures incorporated spaced retrieval (Thivierge 2014), vanishing cues (Bier 2008) or copying (van Tilborg 2011). These are recognised errors *reduction/minimising* methods with evidence of differing effectiveness (Clare and Wilson, 2004). The lack of report of resulting error rates makes it difficult to interpret the observed effect of the error reduction methods. Moreover, the learning by steps copying (modelling) was classified as ELL in one study (van Tilborg, 2011) but not ELL in another (Dechamps, 2011). With variable details reported, it was also not clear if techniques given the same name, for example, SR (in Thivierge 2014 and Lin 2010), were applied in the same way across studies. Moreover, in everyday actions practice, the application of implicit EL method, for example, action modelling, does not prevent participants' use of covert verbal strategies (hence explicit learning process) in support of their task performance (van Tilborg et al., 2011). The ability to use explicit memory is in part, dependent on the severity of memory impairment and might over-ride the benefit of ELL (Metzler-BaddEley & Snowden, 2005). This is consistent with the idea that ELL is more effective for individuals with severe cognitive impairment (Cohen et al 2010; Clare and Jones, 2008, Page et al. 2006). However, this proposal cannot be confirmed based on the current review, as only two included studies targeted participants with severe dementia and employed errorful methods with positive effects. ELL studies in the review included individuals with mild or a mixed group of mild to severe dementia.

Therefore, no conclusion can be drawn regarding effectiveness of different practices in relation to the severity of dementia (Dechamps 2011).

Concerning other potential mechanisms for the observed improvements, two studies noted that training effects were not associated with neuropsychological changes (Lam 2010, Thivierge 2014). Based on the concept of excess disability, Tappen (1994) argued that the training brought about improvement by enabling the full expression of the participants' *existing* functional resource. Thivierge et al. (2014) identified improvement even *before* training, but after the first assessment and selection of ADL tasks. This might reflect the affective impact of the opportunity, after a period of non-use, to re-connect with activities that brought personal meaning (Cohen-Mansfield & Jensen, 2006).

Within the errorful practice category, a group of studies (Giovanetti 2007, Bettcher 2011b, Giovanetti 2015) focused on the issue of error monitoring – a domain related to attention and executive functions, also known to be affected in AD alongside memory. The use of environmental adaptation and goal cues to reduce attention and memory loads were investigated. These interventions differed from the other errorful methods in the included studies, in the lack of online reinforcement and prompting from the trainer (Coyne 1997, Tappen 1994, Zanetti 1997, Zanetti 2001), hence reducing the confounding social factors. Whilst significant effects of the intervention were obtained in their laboratory, the findings applied only to individuals with less severe impairment, the investigators also questioned the transferability of the findings in a home environment.

Limitations of the Review

The current review included only published results and may reflect a publication bias (Easterbrook, Gopalan, Berlin, & Matthews, 1991). As studies with statistically significant

positive results are more likely to be published, by reviewing only the published papers, the positive effects of the interventions might be over-represented. The inclusion of only English language papers would also lead to language bias. Nevertheless, cultural diversity is reflected as the studies were conducted across 8 countries. Moreover, a combination of RCT and non-RCTs were included. According to the hierarchy of evidence (Higgins & Green, 2011), this would suggest a compromise on quality. However, the assumption of the hierarchy of evidence has recently been challenged (Walach & Loef, 2015). In the review of dementia rehabilitation, the inclusion of non-RCT, for example, single case studies was recommendation due to the diversity of participant's characteristics, outcomes, and the early stage of evidence development (Bahar-Fuchs et al., 2013). As the development of research in cognitive rehabilitation for activities of daily living is limited relative to other types of cognitive rehabilitation for dementia e.g. word list learning, face-name learning, the inclusion of RCT and non-RCT would be appropriate. This requires consideration of the multifaceted study quality criteria, that are relevant across both RCT and non-RCT studies. Walach and Loef (2015) suggested the matrix analytic approach for evidence synthesis, an approach also adopted in this review (Table 1.3). The author's use of non-standardised quality criteria through combining multiple quality criteria (from those of Downs and Blacks (1998) and Higgins (2011)), would increase the risk of bias of the quality assessment itself. Moreover, the results of the current review would be less helpful for future comparisons with other reviews of the same area that use standardised criteria. Finally, none of the included RCTs reported allocation concealment, which has been shown empirically to substantially influence RCT study results (Ryan 2013). Given the above limitations, the findings of this review should be viewed with caution.

Future Directions

The current review on the cognitive rehabilitation of everyday actions for dementia revealed preliminary evidence for diverse approaches to support functional abilities. The emphasis of person-centred approach in the research process of such personally meaningful activities is gathering desirable momentum, its benefits need to be more formally and widely investigated. Whilst the current reviewed evidence seems to be in favour of errorful interventions, given the above limitations, no firm conclusion can be drawn. To advance current evidence, further refining and clarity of the concepts of errorless vs errorful methods in ADL is required. Thereafter, more quality studies directly comparing the two methods, and amongst the array of errorful methods would inform the relative efficacy of the approaches. The next stage of the evidence development could focus on efficacy relative to the disease progression (Bouchard & Rossor, 2007) and neuropsychological profile (Libon et al., 1998) of the individuals. More evidence is also required to establish the optimum period, intensity of training, and the sustainability of the training effect. The current review also raised the need to investigate the potential of the social as well as the physical environments as enabling factors in rehabilitation. Meaningful contribution to individualised targeted therapy would require more details of techniques applied, better descriptions of participants' cognitive profile and ADL deficits.

Conclusion

ADL improvement is possible in the context of cognitive decline. There is a greater need for a finer grained person-centred approach to ADL rehabilitation to inform investment in longer term tailored support. Whilst errorful approaches seem to present more consistent evidence for benefits than errorless approach, they represent a diverse group of techniques.

Further evidence is required to confirm findings of all studies. A stronger theory-practice link would help better refine and define the rehabilitation techniques.

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2. Empirical Report: Differentiating cognitive profiles in younger people with Alzheimer's disease and subcortical ischaemic vascular cognitive impairment: A validation of BCoS

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Abstract

Background. The classification of the common types of early onset dementia is challenging. Neuropsychological profiling has been an important diagnostic criterion that implicates on treatment strategies. Assessments need to be more reliable in identifying the key cognitive differences between Alzheimer's Disease (AD) and vascular dementia. This study examines the utility of the Birmingham Cognitive Screen (BCoS) in classifying cognitive impairment from AD pathology and subcortical vascular pathology.

Method. BCoS profiles were obtained from individuals under the age of 75. In the current study, these were 28 individuals with basal ganglia/thalamic stroke, 47 healthy controls (both group took part in a previous study), and 30 individuals with Alzheimer's disease (from the current study). Seventeen BCoS measures were entered into three logistic regression models to differentiate between each pair of the groups. Missing values (1.05%) were estimated with single imputation procedure. Goodness of fit statistics were obtained using the Receiver Operating Characteristic (ROC) analyses.

Results. Three significant models were obtained when contrasting the controls and the stroke group, the controls and the AD group; and the stroke group and the AD group (all $p<0.001$). The models explained 85-89% of the variances, and correctly classified 90.7-93.1% of the cases. The areas under the ROC curve demonstrated good fit of the models. Key measures that characterised the stroke group and the AD group were identified.

Discussion. The findings of the current study correspond to the existing understanding of the specific cognitive profiles of the two disease pathologies. In particular, the two clinical groups differed in terms of executive functions. Limitations and future research directions were discussed.

Introduction

The rapid growing numbers of individuals with dementia has been well documented both in the UK (Prince et al., 2014) and world wide (Ferri et al., 2005). The most common dementia pathologies reported are Alzheimer's disease (AD) (McKhann et al., 2011) and cerebrovascular disease. The latter includes stroke (Leys, Hénon, Mackowiak-Cordoliani, & Pasquier, 2005; Román et al., 1993) and subcortical ischaemic vascular disease (Chui, 2007), both of which can progress to vascular dementia (VaD). Alzheimer's Disease and vascular dementia differ in terms of disease progression, preventative factors and clinical features. Therefore, an accurate and timely diagnosis would help targeted treatment (National Institute for Health and Clinical Excellence, 2006) and functional rehabilitation (Giovannetti, Schmidt, Gallo, Sestito, & Libon, 2006). Nevertheless, the process of diagnosis for the two dementias remains problematic with multiple challenges in the differentiation of the two dementias.

Challenges in the diagnosis process. For early onset (before 65) dementia, the challenge relates to the low relative prevalence of dementia in comparison with other mental disorders causing cognitive impairment in younger people such as schizophrenia (Mendez, 2006); the more varied differential diagnosis and clinical features, as well as the more frequent non-memory type cognitive deficits e.g. apraxia, language deficits (Snowden et al., 2011). On the other hand, with an aging brain, small vessel disease commonly co-occurs with the Alzheimer disease pathological markers such as neurofibrillary tangles and neuritic plaques (Reed et al., 2007), leading to similarity in clinical presentation and related risk factors (Mathias & Burke, 2009; Reed et al., 2007). It is acknowledged that the validation of cognitive profiles to distinguish between the two pathologies (subcortical vascular ischaemia vs Alzheimer's disease) would be clinically and scientifically invaluable in advancing diagnostic certainty (Reed et al., 2007).

The use of cognitive profiling in diagnosis. Efforts to differentiate the cognitive profiles between AD and Vascular Dementia (VaD) have also been fraught with challenges. Graham, Emery and Hodges (2004) observed that, across studies, inconsistencies in interpreting cognitive profiles between AD and VaD was in part due to the diverse pathology and diagnostic categories covered in the existing VaD diagnositic guidelines (Román et al., 1993; Román et al., 2004). When broad diagnostic categories are used, a wide range of associated functional deficits in the study samples is shown, so the differential power and utility of the results in the studies are reduced (Braaten, Parsons, McCue, Sellers, & Burns, 2006) have been well recognised (see Lopes et al., 2012; Reed et al., 2007; Schmidtke & Hüll, 2002). Furthermore, the reliance on memory impairment as the diagnostic criteria for VaD has been questioned (Looi & Sachdev, 1999), as individuals with significant decline due to vascular causes might not display the memory impairment but other types of cognitive deficits may be revealed (Moorhouse & Rockwood, 2008). This is particularly true for the young-onset group (Rossor, Fox, Mummery, Schott, & Warren, 2010), which has led to Hachinski's (1994) proposed term "vascular cognitive impairment" (VCI), rather than "dementia", for cognitive decline resulting from a vascular cause.

The development of diagnositic criteria for vascular cognitive impairment. The concept of vascular dementia (VaD)/vascular cognitive impairment (VCI) continued to be developed and refined, with increasing emphasis on the subcortical ischemic changes that lead to symptoms of vascular cognitive impairment (Chui, 2007). Executive dysfunction has also been raised as the defining feature of VaD (Chui, 2007; Looi & Sachdev, 1999; Román et al., 2004). Moreover, in predicting cognitive decline, a systematic review and meta-analysis of post-stroke dementia (cohort size=7511 in 73 papers) (Pendlebury & Rothwell, 2009) has indicated the central causal role of stroke itself, rather than the underlying vascular risk

factors, in the subsequent development of dementia. This finding is consistent with an autopsy study (Troncoso et al., 2008). However, it has been suggested that, due to the wide range of vascular lesion risk factors, extent and locations in stroke, studies addressing vascular cognitive impairment need to target a more homogenous subgroup with lesions particularly relevant to the onset of vascular dementia (Bowler & Gorelick, 2009; Desmond, 2004; Jokinen, 2006). There has been growing evidence of the key role of thalamus and basal ganglia involvement in the onset of cognitive impairments (Benisty et al., 2009; Bowler & Gorelick, 2009; Gold et al., 2005) and dementia progression (Benjamin et al., 2014; Lopes et al., 2012); as the two structures are the most vulnerable to global ischemia, relative to the cortex, corpus callosum and subcortical cortical u-fibers (Chui, 2007). Once such ischaemia occurs, the resulting disruption of the frontal-basal ganglia – thalamic circuit also leads to executive function deficits which are the more recent proposed diagnostic feature for subcortical ischaemic vascular dementia (SIVD, Chui, 2007) as well as vascular dementia (VaD, Román et al., 2004). However, further evidence is called for to demonstrate the sensitivity and specificity of dysexecutive function as the diagnostic criteria for vascular dementia (Chui, 2007). These findings inform the importance of targeting basal ganglia and thalamus lesions in the study of vascular cognitive impairment.

Considerations in sample selection. Recent studies have demonstrated a correspondence in profiles between post stroke cognitive impairment (no dementia) and vascular dementia (VaD)(Bowler & Gorelick, 2009; Nyenhuis et al., 2004; Sachdev et al., 2004). The highlighted profile of more impaired executive functions, slow processing speed and motor control, with relatively spared long term memory, are the features that typically distinguish vascular dementia (VaD) from Alzheimer's disease (AD)(Looi and Sachdev, 1999). Often when differentiating the cognitive profiles of decline due to AD pathology or

VaD related pathology, studies have recruited individuals with post-stroke ischaemia (and no dementia) and those with early stage AD (De Jager, Hogervorst, Combrinck, & Budge, 2003; Jokinen, 2006). Such sampling has been advocated to allow the identification of the more subtle frontal and other related symptoms in vascular cognitive impairment, without the contamination of the more global memory impairment that are apparent in both vascular and AD groups (Desmond 2004; Looi and Sachdev, 1999). The approach rules out the masking of the subtle symptoms of executive dysfunction - a possible reason for the lack of difference across AD and VaD, reported in some studies (McGuinness, Barrett, Craig, Lawson, & Passmore, 2009; Voss & Bullock, 2004). The variability in findings of the cognitive profiles of AD and vascular cognitive impairment across studies, could also be the result of the use of different cognitive tests with dissimilar focus, sensitivities and specificities.

Cognitive screening tests. Commonly used cognitive screening tests such as the Mini-Mental State Examination (MMSE, Folstein et al 1975) are known to be relatively insensitive to mild and atypical forms of cognitive impairment (Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010; Webb et al., 2014). The memory items are not sufficiently demanding to detect an early amnestic state in AD (Trzepacz, Hochstetler, Wang, Walker, & Saykin, 2015). More detailed assessments (e.g. the Repeatable Battery for the Assessment of Neuropsychological Status, RBAN, Randolph 2012) often do not isolate the frontal or visuo-motor deficits found in early vascular cognitive impairment Bowler & Gorelick, 2009; Nyenhuis et al., 2004) due to the lack of inclusion of executive and praxis measures. Other instruments such as the MoCA (Nasreddine et al., 2005), ACE-R (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) and more recently ACE-III (Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013) have better discriminatory ability. However, the visuospatial and language demands inherent in the instruments confound the assessment process for individuals who

have visuospatial and language processing difficulties (as in Vascular Dementia, VaD)(Looi and Sachdev, 1999) or word finding difficulties (as in AD and VaD). Thus, not infrequently, patients require more lengthy and expensive, detailed neuropsychological assessments which can cause delay in diagnosis.

The Birmingham Cognitive Screen (BCoS) (Humphreys et al., 2012) was developed to screen stroke patients for cognitive problems and takes approximately one hour to complete. It provides a cognitive profile across a range of cognitive processes and indicates whether an individual has a potential impairment, relative to a normative group, in five primary domains of cognition (Table 2.1).

The BCoS has been validated against standard neuropsychological tests that measure similar cognitive functions (Humphreys, Bickerton, Samson, & Riddoch, 2012). It has also been used for prognostic modelling (Bickerton et al., 2015; Bickerton, Samson, Williamson, & Humphreys, 2011), and assessed against measures of cognition and activities of everyday living for patients in the chronic stage (Bickerton et al., 2012). The BCoS has been designed to be aphasia and neglect friendly to overcome the difficulties in assessing individuals with speech and/or visuo-spatial deficits.

Though initially developed to assess individuals with stroke, features in BCoS such as the comprehensive coverage of a range of cognitive domains and subdomains (e.g. action planning, executive functions), while accommodating expressive language or visuospatial deficits which may prove barriers to assessment, suggest that it might also be helpful as an assessment instrument for suspected onset of dementia, particularly for the younger age groups.

Aims

The above review informed the current pilot study, with an aim to explore the utility of BCoS as an assessment to differentiate the cognitive profiles of 1) controls, 2) people with mild AD (AD group) and 3) people with subcortical ischaemic vascular cognitive impairments as a result of a stroke affecting the basal ganglia or thalamus structure (stroke group).

The performance on the BCoS by the above groups of people aged 50-75 will be examined, to determine 1) whether the BCoS measures reveal differential profiles between the groups; 2) how well the profiles discriminate amongst the groups; and 3) whether further investigations are indicated.

Method

Participants

Three groups of individuals aged between 50 to 75 were included: individuals with Alzheimer's disease, individuals with ischemic thalamus and/or basal ganglia infarct as a result of a stroke, and age-matched healthy controls. Informed consent was obtained from all participants. For each group, the exclusion criteria were a) premorbid conditions that could affect cognition (e.g. substance misuse, learning disability, head injury, depression); b) insufficient understanding of English, and c) inability to concentrate for 35 minutes (the time required to perform all memory tests in one session). The U.K. National Research Ethics Committee and the relevant local NHS ethics committee approved the research protocols for the Alzheimer's disease group and the stroke group respectively (see Appendix B for the approval letters).

Participants with Alzheimer's Disease (AD) comprised unselected consecutive patients referred into the study through practitioners of a local memory assessment and

advisory service after their diagnosis (N=14); as well as volunteers with a diagnosis of AD enrolled into the UK National Institution of Health Research Join Dementia Research website, (www.joindementiaresearch.nihr.ac.uk) (N=16). The recruitment period was between February 2015 to April 2016. The diagnosis was made by clinicians in the memory assessment services in the respective care providing health trusts. All subjects in the AD group had an ACE-III score > 60 or MMSE >20 to exclude those with more severe dementia.

Participants from the stroke group. Anonymised data were obtained, according to the UK Medical Research Council's data sharing good practice guidance (Tudur Smith et al., 2015), from the Birmingham University Cognitive Screen Project (BUCS)(www.bucs.bham.ac.uk, Bickerton et al., 2015). The BUCS project was conducted from 2007 to 2011 in the West Midlands, England. Individuals were recruited within three months of their stroke. CT images taken on admission were obtained as part of the data collection process. The subgroup with thalamus or basal ganglia infarct (N=28) was obtained from an original cohort of 727 individuals with a first stroke, assessed within three months post stroke between 2007 and 2011. Additional inclusion criteria were: 1) availability of CT image, and 2) CT image showed clear and confined lesions to the thalamus and/or basal ganglia nuclei but no observable lesion in the cortical areas.

Controls. Anonymised data were also obtained from the BUCS project of age-matched subset of healthy controls assessed in 2007 according to the 2001 UK population census age, sex and education level distribution. The under 75 age groups were selected for the current study (N=47).

Table 2.1 The structure and descriptions of BCoS tasks

Test Domain	Test	Description	Measures
Attention and executive function	Auditory attention	Remember 3 word targets and ignore 3 distractors across 3 blocks of trials	Working memory, accuracy (reflecting response inhibition/sustained attention)
	Rule finding and switching	Find a rule in a visual pattern and switch rule across trials	Rule finding, set shifting
	Apple cancellation	Cancel apples and ignore visually similar distractors	Accuracy, egocentric and allocentric neglect
	Visual extinction	Detection of one or two visual targets	Left or right visual extinction (bilateral trials)
	Tactile extinction	Detection of one or two tactile targets	Left or right tactile extinction (bilateral trials)
Language	Picture naming	Name low frequency pictures	Object recognition and naming
	Sentence construction	Generate sentence to a describe a picture	Syntactic and semantic aspects of speech production
	Instruction comprehension	Ability to understand task instructions	Qualitative measures of verbal comprehension
	Sentence reading	Reading sentence	Different forms of dyslexia, and reading speed
	Read nonwords	Reading nonwords	Phonological dyslexia, and reading speed
	Write words and nonwords	Writing irregular words and nonwords	Different forms of dysgraphia
Memory	Orientation	Personal information, time and place	Memory for current circumstances
	Story recall and recognition	Remember story immediately and after a delay	Immediate and delayed recall and recognition (verbal)
	Task recognition	Remember stimuli from tasks performed	Delayed recognition (non-verbal)
Number processing	Number/price/time reading	Read numbers, prices, clock times	Correct parsing and verbal production of numbers
	Number/price writing	Write numbers, prices	Correct parsing and written production of numbers
	Calculation	Calculate additions, subtractions, multiplication, division	Basic maths abilities
Praxis	Complex figure copy	Copy a complex figure	Constructional apraxia
	Multi-step object use	Carry out a multi-step task with objects	Everyday action object selection, step production, perseveration
	Gesture production	Produce familiar gestures	Gesture production for transitive and intransitive actions
	Gesture recognition	Identify familiar gestures	Gesture recognition for transitive and intransitive actions
	Imitation	Copy meaningless gestures	Gesture imitation

Note: Adopted from Bickerton et al. 2015

Measure

BCoS was designed to detect deficits across a number of critical domains namely, 1) attention and executive function, 2) language, 3) memory, 4) number and 5) praxis (Humphreys et al., 2012). BCoS also differentiates abilities within each of the domains. For example, within the Attention domain, BCoS assesses spatial attention as well as controlled attention; in Language, it distinguishes between written and spoken language; in Memory, immediate and delayed memory, verbal and task memory; in Praxis, perceiving, retrieving and copying actions etc. The hour-long assessment covers a series of 22 short paper and pencil tasks giving 32 measures (Table 2.1). Impairment for each task was determined at the 5th percentile performance of the age-matched controls sample.

The test-retest reliability, inter-rater reliability, content validity, construct validity, correlation with comparable standardized tasks, as well as with general intelligence measures have been demonstrated and reported elsewhere (Humphreys et al., 2012).

Procedure

For the current study, individuals who met the criteria for inclusion in the AD group were given the information sheet (PIS)(Appendix C) and asked for agreement to be contacted by the researcher. Once agreement to be contacted was obtained, the researcher contacted the individuals, explained the project further and (where appropriate) arranged a time and place for the BCoS assessment. A time period of at least 24 hours was given to allow the individual to consider the information in the PIS. On the day of the assessment, signed consent (Appendix C) was obtained from the participant prior to the start of the assessment. The assessment took place at the individual's home. The assessment lasted no longer than 1.5 hours and the participants were informed that they were free to withdraw at any time.

Sample Size Estimate. The BCoS has not been evaluated previously in a dementia population. It has however, been extensively evaluated in stroke patients (Bickerton, Samson, Williamson, & Humphreys, 2011; Bickerton et al., 2012, 2015, Chechlacz et al., 2010, 2013, 2014; Humphreys et al., 2012; Lau et al., 2015; Massa et al., 2015). For logistic regression analysis, the sample size of the smallest group needs to exceed the number of predictor variables. As a "rule of thumb", the minimal acceptable number of events per variable is around 5 (Vittinghoff & McCulloch, 2007). As detailed comparisons across 5 domains was conducted through selected sub-domain measures (see below for details of selection procedures), a sample size of around 100 (with anticipated number of total included measures of no more than 20) was judged to be adequate.

Analysis. Demographic information (age, gender, education level) was compared using ANOVA for continuous data and Chi-square for categorical data; Bonferroni method was used for post-hoc analyses and correction for multiple comparisons.

Descriptive data tables were examined across groups for each of the 32 BCoS measures raw scores using ANOVA and Bonferroni correction for multiple comparisons. This was followed by variable selection procedures prior to the logistic regression analyses. Measures that showed no variability in control participants, and measures that showed no difference in performance across the three groups were removed from further analyses. Variables were also removed due to collinearity identified through correlation analyses (Pearson's r for normally distributed data and Spearman's rho for non-normally distributed data), that is, variables with high correlation ($r>0.80$) with another variable were removed.

Three binomial logistic regressions were conducted to identify cognitive measures that best discriminate between: the controls and the stroke group; the controls and the AD group; as well as the stroke group and the AD group respectively. The empirical validity of

the resulting models (how well they fit the observed data) was assessed using goodness of fit indices. These included: the proportion of variance explained, the percentage of correctly classified cases, as well as the area under the receiver operating characteristic curve (AUC under ROC), where values closer to 1 indicate better fit.

Results

One hundred and five participants were included in the analyses. This comprised 47 healthy controls, 28 participants with basal ganglia/thalamic stroke from the BUCS study, and 30 participants who had a diagnosis of Alzheimer's disease recruited into the current project.

Demographic Characteristics

Demographic details of the participants are shown in Table 2.2. There were significant differences between the control group and the AD group in education, and between the AD and the stroke group in age, gender and years of education. All these factors were therefore controlled for in the key analyses. The presence and severity of cognitive impairment was also examined through the BCoS based on the age-specific cut off scores (5^{th} percentile point of the control range of performance, see Method section above). The number of BCoS measures impaired in each group was examined. This ranged from 2 to 22 measures (mean=9.4, SD=5.9) in the Stroke group, and from 2 to 19 measures (mean=8.9, SD=4.9) in the AD group. Whilst both the stroke group and the AD group had significantly higher numbers of impaired measures than the controls, there was no significant difference in the extent of BCoS impairment across the two clinical groups ($t(56)=0.33$, $p=0.75$). This suggests that the level of cognitive impairment was comparable across the stroke group and the AD group.

Table 2.2 Demographic characteristics of the three groups

	Group						p[a]	Post hoc
	Controls		Subcortical stroke		Alzheimer's disease			
		SD		SD		SD		
N	47		28		30			
Age (years)	65.3	6.0	61.6	9.6	67.6	7.0	0.011	AD>stroke
Gender (% female)	55.5		60.7		33.3		0.037[b]	stroke>AD
Years of education	11.4	2.2	11.5	2.2	13.6	4.3	0.004	AD>controls, AD>stroke
BCoS tasks impaired	3.0	1.2	9.4	5.9	8.9	4.9	<0.001	Stroke>controls, AD>controls

[a]ANOVAs for continuous data and chi-square for categorical data; Bonferroni test for post-hoc comparisons; [b]*p* value for comparison between Stroke group and AD group only

Descriptive Statistics

The mean score and standard deviation of each BCoS task were calculated in each of the three groups (Appendix D). Three measures that showed no variability within the control group (right tactile extinction, instruction comprehension, orientation in time and space) were removed. Two measures showed high collinearity with another measure were also removed. These were: Birmingham rule finding Test *rule detected score* that correlated strongly with the Birmingham rule finding *total accuracy score* (r=0.84, p<0.001); the Sentence reading *accuracy* that correlated highly with Sentence *reading time* (r=0.83, p<0.001). Finally, ten variables were removed as there was no difference in performance across all groups in these measures, based on a significant p value of 0.002 after correction for multiple comparisons. These included: Apple cancellation accuracy, left and right visual extinction, left tactile extinction, nonword reading accuracy, word/nonword writing, personal information, number reading, multiple object use and gesture copy. The descriptive statistics and summary of the reasons for variable exclusions are presented in Appendix D. As a result of the above exclusion processes, 17 BCoS measures were retained for further analyses. These measures are presented in Table 2.3. Across the measures, initial differential profiles between the

Stroke group and the AD group were revealed. The Stroke group obtained significantly lower scores than the control group *and* the AD group in: Auditory attention accuracy, Sentence construction, and Gesture production. There was no difference between the AD group and the control group in these same measures. These measures formed part of the Controlled Attention domain, Language domain and the Praxis domain. Conversely, the AD group obtained significantly lower scores than the Stroke group in Story immediate free recall, Story delayed recognition, and Task recognition, all measuring different forms of episodic memory. The 17 measures were then entered into three binomial logistic regression models to investigate their discriminative abilities across the three groups of participants.

The Discrimination of Control and Patient Types from the BCoS Measures

Missing data analysis. Prior to the logistic regression procedures, missing values analysis was conducted to examine the extent of missing value in the dataset. The result showed that the proportion of values missing was minor (1.05%) and randomly distributed. Therefore, single imputation by SPSS statistics for Macintosh (version 22, 2013) using the Expectation-Maximization Algorithm, was employed. The algorithm estimated the means, variances, and covariances from the individuals with complete data. It adopted the maximum likelihood procedures, using regression equations to relate variables to each other and to estimate values of the missing data, such that the final models predicted the means, variances, and covariances more accurately than any other formulas. This was achieved by repeated computation of the means, variances and covariances through iterative formulation of regression equations as missing data were estimated across variables. By default, SPSS engages in the above process up to 25 times, until the estimates change only negligibly.

Table 2.3 Comparing BCoS tasks performance raw scores across the three groups

	Controls (N=47)			Stroke (n=28)			Alzheimer's Disease (N=30)		
Domain/Test	Mean	SD	Valid N	Mean	SD	Valid N	Mean	SD	Valid N
Attention									
Auditory attention accuracy	52.94_{a}	1.86	47	$\underline{43.78}_{b}$	10.68	27	50.43_{a}	5.66	30
Working memory index	5.96_{a}	0.36	46	5.04_{b}	1.06	27	$5.53_{a,b}$	1.00	30
Rule finding accuracy	10.64_{a}	3.81	44	$8.43_{a,b}$	6.16	28	5.97_{b}	4.68	29
Language									
Picture naming	13.04_{a}	1.04	47	11.57_{b}	1.94	28	11.78_{b}	2.12	30
Sentence construction	7.98_{a}	0.15	47	$\underline{7.43}_{b}$	0.96	28	7.90_{a}	0.31	30
Sentence reading time	15.43_{a}	3.39	47	25.74_{b}	20.66	27	$18.92_{a,b}$	9.00	30
NonWord reading time	7.75_{a}	4.01	47	14.62_{b}	9.55	27	$10.24_{a,b}$	7.24	30
Memory									
Story immediate free recall	9.02_{a}	2.47	47	6.50_{b}	3.19	28	$\underline{4.52}_{c}$	3.00	30
Story immediate recognition	14.13_{a}	0.99	47	12.32_{b}	2.84	28	11.10_{b}	2.52	30
Story delayed free recall	11.62_{a}	1.99	45	6.63_{b}	4.12	27	4.75_{b}	3.46	30
Story delayed recognition	14.69_{a}	0.63	45	13.22_{b}	2.36	27	$\underline{11.70}_{c}$	2.40	30
Task recognition	9.67_{a}	0.64	45	8.83_{b}	1.25	27	$\underline{7.73}_{c}$	1.64	30
Number									
Number writing	4.94_{a}	0.25	46	4.14_{b}	1.51	28	$4.47_{a,b}$	0.94	30
Calculation	3.68_{a}	0.59	47	2.56_{b}	1.37	27	2.93_{b}	1.31	30
Praxis									
Complex figure copy	44.68_{a}	2.40	47	37.56_{b}	8.66	27	39.57_{b}	7.01	30
Praxis gesture production	11.49_{a}	0.83	47	$\underline{10.68}_{b}$	1.63	28	11.67_{a}	0.61	30
Praxis gesture recognition	5.77_{a}	0.48	47	5.14_{b}	0.97	28	$5.43_{a,b}$	0.73	30

Note. Values in the same row not sharing the same subscript are significantly different at $p < 0.05$ in the two-sided test of equality for column means. Scores underlined are significantly lower of the two patient groups. Tests are adjusted for all pairwise comparisons within a row using the Bonferroni correction.

Group classification (Table 2.4).

1) *Control vs stroke group*. The resulting logistic regression model in the discrimination between the control group and the stroke group was statistically significant $\chi^2(7)=73.02$, $p<0.001$. The model explained 85% (Nagelkerke R^2) of the variance and correctly classified 90.7% of the cases, after controlling for the effects of age, gender and number of years in education. Poor performance in *sentence construction*, *working memory* (as measured within the auditory attention test), and *complex figure copy*, as well as longer *nonword reading time* differentiated the control participants with those who had basal ganglia or thalamic lesions due to a stroke. The large area under the ROC curve (AUC) (0.97, CI=0.93 - 1.00) also indicated that the model achieved good fit.

Table 2.4 Classifications of group membership by BCoS tasks using logistic regression

	Control vs Stroke			**Control vs AD**			**Stroke vs AD**		
	B	**Wald**	***p***	**B**	**Wald**	***p***	**B[a]**	**Wald**	***p***
Constant	65.53	8.94	0.003	9.39	2.27	0.132	-102.46	4.34	0.037
Age	-0.22	4.55	0.033	-0.10	1.34	0.246	0.38	3.65	0.056
Gender	0.75	0.34	0.562	-1.96	2.30	0.129	-10.88	4.50	0.034
Education	0.68	4.62	0.032	0.48	7.29	0.007	1.05	4.18	0.041
BCoS Tasks included in the equations									
Working memory index	-3.02	4.69	0.030						
Rule finding accuracy							-0.55	4.65	0.031
Sentence construction	-2.28	5.27	0.022						
Nonword reading time	0.32	4.08	0.043						
Story immed. recognition							-2.90	4.31	0.038
Story delayed recall				-1.01	15.32	0.000			
Complex figure copy	-0.67	7.32	0.007						
Praxis gestures production							7.69	4.93	0.026
% correct classification	*90.7*			*92.2*			*93.1*		
AUC ROC (95% CI)	*0.97*	*(0.93 – 1.00)*		*0.98*	*(0.96 - 1.00)*		*0.99*	*(0.96 – 1.00)*	

Notes. AUC ROC = area under the receiver operating characteristic curve.
[a]A positive B value indicates that AD group obtained higher scores than Stroke group, a negative B value indicates the Stroke group obtained higher scores than the AD group.

2) *Control vs AD group*. A differentiation was also made between the control group and the AD group. The resulting logistic regression model was also statistically significant

$\chi^2(4)=77.57$, $p<0.001$. The model explained 86% (Nagelkerke R^2) of the variance and correctly classified 92.2% of the cases based on the performance in *the verbal memory delayed free recall*, after controlling for the effects of age, gender and years of education. The area under the ROC curve values (AUC) (0.98, CI=0.96 – 1.00) indicated that the model produced excellent fit to the data.

3) *Stroke vs AD group*. More interestingly, when the stroke group and the AD group were compared, controlling for the effects of age, gender and education, the logistic regression model was again statistically significant with $\chi^2(7)=63.18$, $p<0.001$. The model explained 89% (Nagelkerke R^2) of the variance and correctly classified 93.1% of the cases. Classification into the AD group was associated with worse performance in *verbal memory (story) immediate recognition* and in the *Birmingham rule finding and switching test* within the Attention and Executive Functions Domain, but better performance in *gesture production* of the Praxis Domain, compared to the stroke group. The AUC area under the ROC curve again confirmed the goodness of fit of the model (0.99, CI=0.96 - 1.00).

Power consideration. With the current modest sample in mind, the power of the findings was evaluated. Medcalc computation (www.medcalc.org) based on Hanley and McNeil (1982)'s mathematical model was used to identify the minimum area under the curve (AUC) with a desired a power of 0.80, given the current observed sample size of 77, 75 and 58 respectively, and an alpha of 0.05. The minimum area under the curve was estimated at a range of 0.69-0.71 across the three analyses. As the logistic equations in the current study yielded a range of AUCs all greater than 0.90, the sample size is considered sufficient for the desired statistical power.

Discussion

The current pilot study is a preliminary exploration of the utility of BCoS, in differentiating the cognitive profiles of Alzheimer's Disease and subcortical ischaemic stroke, a leading cause of vascular dementia, in younger individuals at an early stage of the disease progress. In selecting the participants for the vascular group, we considered the controversies and challenges in defining and meaningfully comparing the diverse aetiological and clinical presentations of subtypes of vascular dementia. The study adopted the recommendations from the literature, that is,to analyse a well-defined and homogenous group of individuals (Desmond, 2004; Gold et al., 2005; Jokinen, 2006), with pathology that was particularly relevant to the development of vascular dementia, namely, individuals with basal ganglia and/or thalamic infarct as a result of a subcortical ischaemic stroke.

Through ANOVA analyses and logistic regressions modelling of participants' BCoS tasks performance, contrasting patterns of deficits between the subcortical ischaemic stroke group (stroke group) and the Alzheimer's disease group (AD group) were revealed. In particular, ischaemic lesions in the basal ganglia or thalamus areas were associated with more severe deficits in working memory, sentence construction, nonword reading time, gesture production and complex figure copy; whereas individuals with Alzheimer's disease were found to have more deficits in the immediate story recognition, delay story recall, and the Birmingham rule finding test. The ANVOA analysis also suggested that the AD group showed more deficits than the stroke group in other forms of episodic memory as assessed by the task recognition test. The resulting models demonstrated high levels of accuracy in predicting the diagnostic groupings amongst the participants, despite their early and relatively mild stage of cognitive decline. These will be discussed further below.

BCoS Profile Specific to Subcortical Ischaemic Basal Ganglia and Thalamic Pathology

When differentiating between the stroke group and healthy controls, the logistic regression model included tasks that span across a range of cognitive domains (Table 2.3 and 2.4). These tasks were sensitive to impairments resulting from post stroke basal ganglia/thalamus lesions:

The Attention and executive function domain. *The working memory index* (WMI) combines two measures within the Auditory Attention Test (AAT): the proportions of target words correctly recalled or responded to, both after the practice trials and at the end of the Auditory Attention task. It therefore assesses phonological working memory.

The Language domain. *Sentence construction* assesses individual's ability to construct, verbally, two semantically and syntactically correct sentences that describe two given photographs respectively; and *nonword reading speed* measures participants' speed of processing relevant phonological information in reading.

The Praxis domain. The *complex figure copy* requires the participants to copy a complex but meaningless drawing. It therefore involves visuo-spatial analysis, action production and possibly working memory (Massa et al., 2015).

With the extensive and complex connectivity of the basal ganglia-thalamocortical circuits, it is not surprising that lesions in this area can impact on multiple cognitive and neuropsychiatric functioning (Alexander, Crutcher, & DeLong, 1991; Ring & Serra-Mestres, 2002; Schmahmann, 2003), and therefore relate strongly to cognitive decline. It was noted that progressive vascular cognitive impairment often reveals a subcortical profile that is defictis in executive functioning, mental processing speed and motor controls (Bowler & Gorelick, 2009). For the current subcortical stroke cohort, the tasks that were most predictive appeared to be those with more complex demands within their respective domains, for

example, in the language domain, the sentences construction test, rather than the picture naming test; in the praxis domain, the complex figure copy, rather than gesture production or imitation tests. While the profile could be related to the younger age of our participants, their milder and early stage of cognitive decline, it might also reflect the specialism of the basal ganglia-thalamic structure for integrating functional regions (Haber & Calzavara, 2009) to modulate more complex goal directed behaviours (Jahanshahi, Obeso, Rothwell, & Obeso, 2015). The finding that the language difficulty in VaD was more of syntactic nature than of lexicon was also identified in Desmond's review (2004).

The relevance of the thalamic/basal ganglia lesions in processing speed impairment was understood to result from disruption of the subcortical-frontal circuit that involves the prefrontal cortex (Benjamin et al., 2014; Johansen-Berg et al., 2005). Chui's (2007) comprehensive review also related subcortical ischaemic vascular dementia to executive functioning that encompasses: processing speed, working memory and abstract reasoning. However, they cautioned the need for further validation as studies often failed to rule out elements of AD, and their impact on executive functioning. This will be discussed below.

BCoS Profile Specific to AD

The initial comparisons across the three groups have revealed distinctive problems in immediate, and delayed verbal as well as non-verbal episodic memory deficits in AD, suggesting encoding deficits. This is despite the AD group being younger and more educated, factors that are often related to superior memory performance (Crook, Bahar, & Sudilovsky, 1987; Sharp & Gatz, 2011).

Given the current cohort was of younger age and at the early stage of the disease progression, the finding that episodic memory impairment was the only discriminating factor,

perhaps corresponds with it being often reported to be the first sign of cognitive decline, before the development of more extensive cognitive difficulties. A similar finding comes from a study by Johnson and colleagues (2008) who modeled cognitive tests performance that separated 115 autopsy confirmed individuals with AD and 191 older adults without dementia, using confirmatory factor analysis of data from 12 cognitive tasks across five domains. The only structural difference across the two groups lay between the tasks that tap into episodic memory (those that require effortful verbal encoding and immediate recall), with correlations found within the AD group but not the healthy group. This was interpreted to indicate the specific relevance of the impact of episodic memory in the disease process (Johnson et al., 2008). As episodic memory is mediated by posterior cortical structures, such as the temporal and parietal lobes, often affected in young onset AD (Albert et al., 2011), this accounts for the observation that individuals with AD have faster information decay, reduced ability to benefit from retrieval cues, and higher frequency of intrusion errors (Desmond, 2004).

The logistic regression model identified the delayed story recall to be the only subtest which was able to differentiate performance between controls and the AD group. This task assesses delayed retrieval of newly learnt logical verbal information. Studies have often used a range of different memory tasks to improve the diagnostic values for AD (De Jager et al., 2003; Rabin et al., 2009; Silva et al., 2012). Due to the variability in the AD presentation (Lambon Ralph, 2003; Larner & Doran, 2005; Mann, Mohr, Gearing, & Chase, 1992) and the potential atypical features within the early onset cohort (Snowden et al., 2011), it is therefore important, where feasible, to include a wider range of domains to improve the sensitivity of the assessment, particularly when differentiating between two possible dementia pathologies.

Contrasting Profiles Between AD and the Subcortical Ischaemic Stroke Group

The results from the current study have shown the utility of multiple-domain assessment in classifying causes of cognitive decline. Tasks across three domains were included in the regression model to produce the highest classification sensitivity and specificity between the AD and the subcortical stroke group. As discussed above, the more prominent episodic memory deficits in the AD group and the presence of apraxia in the stroke group with basal ganglia/thalamus pathology were well established and have been confirmed by other studies (Graham et al., 2004; Lehéricy et al., 2006; Pramstaller & Marsden, 1996). While individuals in the stroke group also experienced memory deficits when compared with controls (Table 2.3), individuals in the AD group had consistently the lowest scores across the three groups in all memory tasks.

The attention and executive function domain. Perhaps less expected was the finding that the AD group was more impaired than the subcortical stroke group in the Birmingham rule finding test, one of the executive function tasks. This is surprising, as impaired executive function was often highlighted to be an important diagnostic factor for vascular dementia (VaD) or subcortical ischaemic vascular dementia (SVID)(Chui, 2007; Looi & Sachdev, 1999; Román et al., 2004). Such a discrepancy is possible to explain if we consider the diverse nature of executive functions. Executive functions comprise a range of skills that include: set shifting, switching/updating, monitoring, multi-tasking, inhibition, working memory etc. (Miyake et al., 2000). Therefore, variations in study findings could be a function of different assessment methods and focus. Unlike the working memory index in the executive function domain, which differentiated the stroke group from controls, the Birmingham Rule Finding test measures rule detection and set shifting. The participants were asked to observe and predict the movement of a black marker across a small grid based on a

rule of position, colour or both. The task was designed to minimize confounding factors hence increase specificity: thus working memory load was reduced through keeping the previous marker location in sight; comprehension demand was minimized through task practice and demonstration; language demand was removed by pointing response; and visuospatial demand was reduced by using colour rule and a small centralized visual display.

The approach used in BCoS is not often found in other studies. Studies may adopt an executive function test that incorporates diverse demands. For example, one study of young onset Alzheimer risk factors (Green et al., 2014) used the multi-source interference task (Bush & Shin, 2006) that demands inhibition, monitoring and decision making in one task. Whilst they found that individuals' genetic risk factors influenced the brain activity during executive processing, it was less clear whether one or more of the above processes were affected. Another study used the Addenbrooke Cognitive Examination III (ACE-III, Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013) to differentiate between types of early onset dementia (Elamin, Holloway, Bak, & Pal, 2016). The authors acknowledged that the verbal recall in ACE-III's memory assessment could be biased against individuals with language deficits in their study e.g. those with primary progressive aphasia. Similarly, the specificity of the verbal fluency test (Lezak, 2004) as an indicator for executive functioning deficits was limited by the test's demand on word retrieval and production. The above problem also applies to individuals with vascular cognitive impairment who often have language processing deficit, as studies have used the verbal fluency test or the Stroop test (Perret, 1974) to determine executive functioning in VaD (Desmond, 2004; McGuinness et al., 2009) or subcortical ischaemic vascular disease (Jokinen, 2006). The specificity of test may also be reduced in studies that used the Clock Drawing (Royall, Cordes, & Polk, 1998) or the Trail Making Test

(Reitan, 1955) for executive function assessment (Jokinen, 2006; McGuinness et al., 2009) due to the additional visuospatial and motor control demands of the tasks.

In their comparison between AD and subcortical vascular dementia (SVD) groups, Graham and colleagues (2004) demonstrated a comprehensive approach in executive functions assessment. They used a series of tests, and found no difference between the two groups in the Stroop Test of inhibition (Perret, 1974) and the Wisconsin Card Sorting test of set shifting (Nelson, 1976); but the SVD group was more impaired in the fluency test, the Test of Everyday Attention (Robertson, Ward, Ridgeway, Nimmo-Smith, & McAnespie, 1991) and the digit span tests of working memory; whilst the AD group was more impaired in the dual task test of dividing and attention (Della Sala, Baddeley, Papagno, & Spinnler, 1995). Though the study concluded that overall, the SVD group had more executive dysfunctions, their results also illustrated the different executive dysfunction profiles of the two clinical groups, as revealed in the current study.

Study Strengths and Limitations

The current study has both strengths and limitations. As a research tool, the BCoS applies separate measures for praxis, working memory, attention and executive function that are often omitted in cognitive profiling of dementia (Graham et al., 2004; Johnson et al., 2008; Randolph, Tierney, & Chase, 1998). The value of a multiple domain assessment to improve prognostic and discriminative values for cognitive decline has been recognised (Rasquin et al 2005). Whilst the study sample size was modest relative to the number of measures employed, good measures of fit statistics were obtained. This demonstrated the specificity of the BCoS tasks as intended by the developers, and was achieved through adherence to strong theoretical underpinning in their design of the tasks (Humphreys et al.,

2012). Nevertheless, a larger sample size would be desirable for future investigations that incorporate a wider range of participant characteristics to improve generalizability.

In the recruitment process, the clinical diagnoses of the participants were made independently of the BCoS assessment. Therefore, no circularity occurred where neuropsychological data were used for both allocation of cases to research groups as well as for research outcome. However, there was a lack of blinding of the researcher to the grouping of the participants. Moreover, whilst the extent of impaired BCoS measures was used as a global disease severity measure, there was no other common general measure for severity of cognitive or functional impairment available to compare between the groups. For both the stroke group and the AD group, the diagnoses were not made as part of the research process but in the participants' respective local stroke or memory assessment services, therefore, the diagnostic consistency cannot be assured. However, the national guidelines for stroke diagnosis (https://www.nice.org.uk/guidance/cg68) and Alzheimer's disease diagnosis (https://pathways.nice.org.uk/pathways/dementia/dementia-diagnosis-and-assessment) would typically be followed by the services in the UK. With the time difference (4 to 9 years) in the assessment period between the control/stroke groups, and the AD group, there could be potential bias in the data, as socioeconomic factors that might impact on individual's cognitive performance might have changed over time.

Common to most neurocognitive profile research in dementia, we could not rule out the possibility of other co-occurring pathologies (e.g. vascular lesions, lewy bodies). This common limitation can only be eliminated by autopsy confirmation of diagnosis (employed by Johnson et al., 2008; Reed et al., 2007). These procedures required a costly longitudinal design that is beyond the scope of the current study. Therefore, the current findings are tentative and indicate directions for future research.

Finally, it needs to be considered that the author was involved in developing the Birmingham Cognitive screen, though there was no financial conflict of interest in using the measure or promoting its use to other investigators.

Further Research

With the initial positive findings using a homogenous sample of vascular cognitive impairment against a AD group, further research could explore BCoS's utility for the classification of a different range of vascular lesions and dementia pathologies, which are relevant to younger onset dementia. For example, BCoS's design to overcome communication barriers could facilitate assessments of individuals with frontotemporal dementia or primary progressive aphasias, and since the tests are designed to reduce a visuospatial confound, BCoS could also facilitate the assessment of individuals with posterior cortical atrophy.

The current research took advantage of an existing retrospective database and compromised on the availability of comparable severity and functional measures across study samples. Future research would benefit from a more comprehensive protocol of recruiting individuals using standardised and more refined imaging and diagnostic protocols. The true test for utility of the discriminative function is how well it predicts the course of the disease progression, e.g. stepwise or gradual, from the initial profile (Rittman et al., 2013). Therefore, future studies would also benefit from a longitudinal design to enable monitoring of disease progression and confirmation of the predictive values of the cognitive profile.

The precisions of classification could be further improved by incorporating other relevant factors, such as the effects on cognitive performance of depression (Miranda et al., 2008) and anxiety (Eysenck, Derakshan, Santos, & Calvo, 2007). The inclusion of social

cognition tasks (e.g. emotional recognition) is also recommended as it has also been found to be significant in differentiating between AD and VaD profiles (Mathias & Burke, 2009).

Clinical implications. Though the primary aim of the current study was to identify the utility of BCoS in the diagnosis of dementia, the potential application of BCoS extends beyond the diagnosis. The inclusive, as well as the comprehensive nature of the assessment would potentially help inform individuals, their families and health professionals in the rehabilitation pathway. The BCoS highlights not only an individual's specific performance deficits but also their intact abilities within the general presentation of cognitive decline. Such knowledge would help develop targeted rehabilitation strategies, for example, how to compensate for an area of deficit (e.g. verbal memory) through utilising an area of strength (e.g. visual memory). There is a need for further research into the benefits of BCoS in the rehabilitation of individuals with a diagnosis of dementia.

Conclusion

The BCoS assessment has demonstrated some potential utility in differentiating different types of young onset dementia at an early stage of disease progression, further research with improved methodology is desirable to confirm the findings of the current study.

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3. Public Dissemination Document: The development of assessment and rehabilitation for individuals with dementia

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Introduction

Cognition is the mental action or process of acquiring knowledge and understanding through thought, experience, and the senses (Oxford online dictionary, retrieved from https://en.oxforddictionaries.com/definition/cognition, on 5/11/2016). Cognition therefore, represents a range of abilities, including but not limited to memory. Cognitive decline is one of the diagnostic criteria of dementia, a disease that affects 46 million people worldwide (Prince et al., 2015). The two most common forms of dementia, both for the younger age (under 65) and the older age group are known to be Alzheimer's disease and vascular dementia. Individuals vary in their everyday experiences and rate of disease progression not only across different types of dementia, but also within a group of the same diagnosis (e.g. Alzheimer's disease). Atypical presentations are particularly reported in the younger age group (Snowden et al., 2011). A better understanding of the relationships between diagnostic categories, cognitive profiles and daily living functions would inform future care. This document summarises two research reports concerning the improvements in cognitive assessment and rehabilitation of individuals with dementia. The first is a review of studies for strategies that are effective in supporting individuals in their everyday activities. The second is an evaluation of a cognitive assessment, BCoS, in differentiating the patterns of difficulties between Alzheimer's disease or vascular disease.

Review of helpful strategies that help train people with dementia in everyday activities

Individuals with dementia may experience deterioration in their ability to manage everyday tasks. These range from eating, drinking, to making a coffee, cooking a meal etc. Training that directly works with individuals to maintain their daily living skills would help promote independence, dignity and sense of self. The study reviewed which methods are used to support the training process and the evidence on how effective these methods are.

Method. A search of electronic databases for published papers found 13 studies on strategies of direct training in everyday tasks for people with dementia. These studies were rated according to 1) how well they are designed, 2) how reliable are the results, and 3) how thorough they are reported.

Results. One study found that whether the task to be trained is personally important to the individual (or not) did not seem to make significant difference to the effect of the training. Some elements of person-centred practice were observed in the research procedures of other studies below. Whilst these could potentially improve the benefits of the practice, they were not formally evaluated in these studies.

Five studies looked at whether preventing a person to make errors (errorless) in practice would produce better learning. In these methods, often, a small step is demonstrated at a time then gradually increasing the steps once the person can do the first steps well. If there is a sign of the person not being sure of what to do, they will be shown the correct step straight away.

Seven studies investigated the benefits of various methods that allow errors to occur (errorful). These methods support the individuals' practice in a number of ways. For example to give verbal prompting, using cues in the environment (e.g. way the task objects are arranged), reminding beforehand or after the task is performed, sometimes demonstrating the steps too but individuals are allowed to try and make errors.

Only two studies compared directly between the two training methods and found no difference in effects. When compared with no other training, or usual practice, however, strategies that allowed errors in practice seemed to produce more consistent results. Nevertheless, as suggested above, the actual training techniques are very diverse. In addition, there are also limitations in the quality of the studies. For example, many studies had small

sample sizes. Furthermore, details of the training were often not enough to fully understanding what was meant by "errorless". Some results might be biased, as other factors that caused difference between two groups (e.g. different dementia severity, different age), other than the training itself, were not eliminated in the study procedures.

Conclusion. It is evident that more studies are needed for the person-centred elements of interventions. In addition, more quality studies with better defined techniques, that consider individuals' characteristics and compare methods directly are recommended. As the evidence suggests, at the moment, it seems that maybe allowing errors in everyday activities practice is no worse than not allowing error at all.

Using BCoS to differentiate cognitive characteristics of different types of dementia in younger people

The accurate diagnosis and differentiation between Alzheimer's disease or vascular disease is complex and challenging. Whilst in both conditions, individuals would experience some deterioration in their everyday and cognitive abilities, there are key differences in what abilities are affected and how they would response to treatment. A better understanding of the presentation of each dementia type would help better target treatment and rehabilitation.

Method. BCoS was initially developed for cognitive assessment of stroke survivors. It is relatively short and comprehensive. Whilst most cognitive tests require people to give answers verbally, BCoS is designed to be user friendly for those who struggle with speaking, because of their brain changes after a stroke or dementia. It could therefore, assist in revealing hidden mental skills of those who can't express in words easily, even though they know they answer!

Studies have found that a stroke that affects the deep brain structures called basal ganglia and thalamus (BGT) relates strongly to vascular dementia. This study therefore

compared the BCoS assessments between 28 BGT stroke survivors with 30 individuals with Alzheimer's disease, both with mild cognitive decline and under 75 years old; and 30 healthy individuals of the same age group.

Results. With the BCoS profiles, statistical procedure differentiated, with >90% accuracy, between the all three groups. The BCoS tasks that test memory of verbal information or memory of events, and a task that test abstract problem solving, were more strongly associated with difficulties experienced by people with Alzheimer's disease. At the same time, the tasks that highlighted difficulties in reading accuracy and speed, action control and working memory related more to the BGT group.

Conclusion. This is a preliminary study to determine whether BCoS could be employed for future research in classification of dementia, to support more appropriate interventions. The findings, based on three small and focused samples, corresponded with the existing understanding of the unique cognitive characteristics of the two clinical groups. This indicated that future research with BCoS maybe appropriate to verify the existing findings, and to apply it to wider categories of young onset dementia.

Summary

There is still much to be learnt for the improvement of dementia care. The research and clinical communities can draw from the existing developments in cognitive neuropsychological assessments - as well as the advances in learning and training techniques - in furthering the efficacy and quality of dementia care. Most importantly, the recognition of individual differences (whether it is due to the nature of the dementia, or the person's unique characteristics) is necessary for the translation of theory into person-centred care. Such a principle applies not only in care provisions but also in research practices.

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