Review Article

Dementia
and Geriatric
Cognitive Disorders

Dement Geriatr Cogn Disord 2012;33:189–203
DOI: 10.1159/000338233

Accepted: March 9, 2012
Published online: May 10, 2012

Executive Function and Activities of Daily Living in Alzheimer's Disease: A Correlational Meta-Analysis

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Key Words
Dementia · Attention · Working memory · Functional ability · Driving · MMSE

Abstract
Background: The assessment of executive function (EF) and activities of daily living (ADL) are important elements in the diagnosis of Alzheimer's disease. ***Methods:*** Following a comprehensive search in three databases, a random-effects meta-analysis was used to investigate the association between ADL ability and seventeen tests of EF, three tests of attention and working memory and the Mini-Mental State Examination. The association between EF and ADL ability was further investigated in relation to four different methods of assessing ADL, and one specific ADL, driving. ***Results:*** Forty-nine studies met the inclusion criteria, and a total of 3,663 participants were included, the majority of whom were diagnosed with Alzheimer's disease. Most of the individual tests, including commonly used tests of EF such as the Clock Drawing Test, Letter Fluency and the Trail Making Test Part B, showed a significant moderate association with ADL. Associations between EF and ADL ability were similar for all four methods of assessing ADL ability. Driving ability was also moderately associated with EF. ***Conclusion:*** The meta-analysis suggests a consistent moderate association between ADL and EF, supporting the growing evidence for a link between ADL and executive dysfunction in early dementia.

Introduction

Alzheimer's disease, at least in the early stages, is typically characterised primarily by impairments in memory; however, for a diagnosis of Alzheimer's disease to be made other deficits also have to be present [1, 2]. One area of cognition that may be affected is executive functioning (EF), an umbrella term for a number of distinct high-level cognitive processes that control everyday actions and thoughts, including working memory, attentional control, planning, inhibition, rule discovery and concept generation [3–5]. There is a large and growing body of research indicating that executive impairments are present even in the earliest stages of Alzheimer's disease [6–9]. Longitudinal studies investigating pre-diagnostic symptomatology and staging of Alzheimer's disease report that executive dysfunction is present before diagnosis, with declining EF occurring between 2 and 3 years before diagnosis [10, 11]. This evidence has even led some authors to suggest that executive function may be the core underlying dysfunction associated with Alzheimer's disease [12, 13], while others have proposed that there may be a subgroup of Alzheimer's disease patients with a specific dysexecutive pattern of impairment [14–17]. Therefore, the available evidence suggests that there is a significant proportion of people with Alzheimer's disease who have discernible executive deficits.

A diagnosis of Alzheimer's disease also requires evidence of impairments in everyday functioning [1, 2]. Ac-

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tivities of daily living (ADL) vary in complexity and difficulty and are typically divided into 'basic' and 'instrumental' (iADL) categories [18]. Basic ADLs – such as bathing, toileting, feeding and dressing – tend to be preserved in early-stage Alzheimer's disease, with links to motor rather than cognitive difficulties [19]. In contrast, iADLs – such as handling finances, shopping, using the telephone, and managing medication – are vulnerable to the effects of early Alzheimer's disease, with evidence for a direct link with cognitive status [20, 21]. A recent review of studies with older people found that EF explains at least three times as much of the variance in iADL as memory [22], while studies of people with Alzheimer's disease have also linked executive dysfunction with declining skills and abilities in ADL [23, 24], suggesting that executive dysfunction may contribute significantly to functional difficulties. A longitudinal study investigating functional impairment found that 2 years before a diagnosis of Alzheimer's disease there was a noticeable decline in iADL ability [25]. This decline occurred during the same approximate pre-diagnostic timeframe in which executive functions begin to decline [10, 11], suggesting the possibility that these contemporaneous declines may involve related mechanisms.

Two previous reviews have briefly discussed the association between declining EF and functional impairment in Alzheimer's disease [26, 27], though at the time of publication little empirical evidence was available. The evidence for a relationship presented in these reviews was mostly based upon clinical observations, an assumed relationship between everyday tasks and underlying cognitive mechanisms and a growing literature in other conditions, such as schizophrenia [28]. Since these reviews were published, a number of studies have investigated the relationship between ADL and EF in Alzheimer's disease using various tests and measures, the present meta-analysis draws on these findings to investigate the nature and strength of the association between tests of EF and everyday ability in people with Alzheimer's disease.

Method

Literature Search Strategy

To identify studies investigating the relationship between executive function and everyday functioning in Alzheimer's disease PubMed, Web of Knowledge and CINAHL were searched on the 28th July 2010. Date of publication was not limited and no specific limit was imposed on the search other than the language of publication had to be English. In total, 33 searches were conducted in each of the three databases. Alzheimer* was included as the first term in all searches, and search terms focussed on three areas: ADL (activities of daily living, daily functioning, disability, driving, functional ability, functional status, telephon* and financ*), executive function (attention, dysexecutive, executive, monitoring, planning, response inhibition, set shifting, self-regulation, purposive action, effective performance, flexibility, volition and working memory), and specific tests of executive function (Behavioural Assessment of the Dysexecutive Syndrome, BADS, Delis-Kaplan Executive Function System, D-KEFS, Stroop, The Hayling Test, Stockings of Cambridge, Tower of Hanoi, Tower of London, Tower of Toronto, Trail Making Test and Wisconsin Card Sorting Test). Reference sections of included articles were examined for any additional studies not identified by the original search. Authors researching the area were contacted for in press/pre-publication journal articles or additional correlational data, including nonsignificant findings that were not included in relevant articles. An identical, updated search was carried out in the same three databases on the 5th July 2011 for articles published since the first search.

Inclusion Criteria

Studies were included if (a) they had recruited participants with a diagnosis of Alzheimer's disease or probable Alzheimer's disease only, or if at least half of the included participants had a diagnosis of Alzheimer's disease or probable Alzheimer's disease and the remainder had other dementia diagnoses; (b) at least one executive function test and at least one measure of ADL were used, and (c) analysis included either a correlation or regression, or data that could be converted to a correlation, that examined the association between the EF and the ADL measures. Any studies not meeting these criteria, including studies that presented data for any participants without dementia, were excluded from the review.

Procedure

A summary of the process used to identify articles for inclusion is shown in figure 1. After the search was conducted all unique abstracts were screened to identify those articles that matched the inclusion criteria. Full text articles were obtained for abstracts that appeared to meet criteria and to include the necessary statistical comparisons. Using these methods, 55 journal articles, one conference abstract and one PhD thesis were identified that contained the necessary correlations or regression coefficients to be included in the meta-analysis. The majority of studies included in the meta-analysis were cross-sectional; only baseline data was included if longitudinal articles were identified. One article, although it indicated possible significant associations between an ADL measure and both Category Fluency and the Stroop [29], was excluded as it did not present data and details of correlations could not be obtained. Four studies were excluded as the data presented included data from people without dementia [30–33]. One study utilised a composite executive function score and individual test scores could not be obtained [34]; however, this article was included in secondary analysis that investigated different methods of assessing ADL. Another study that utilised a composite EF score [35] was included in the main analysis as the necessary correlational data were available in the lead author's PhD thesis [36]. Therefore, 52 articles were included in the meta-analysis.

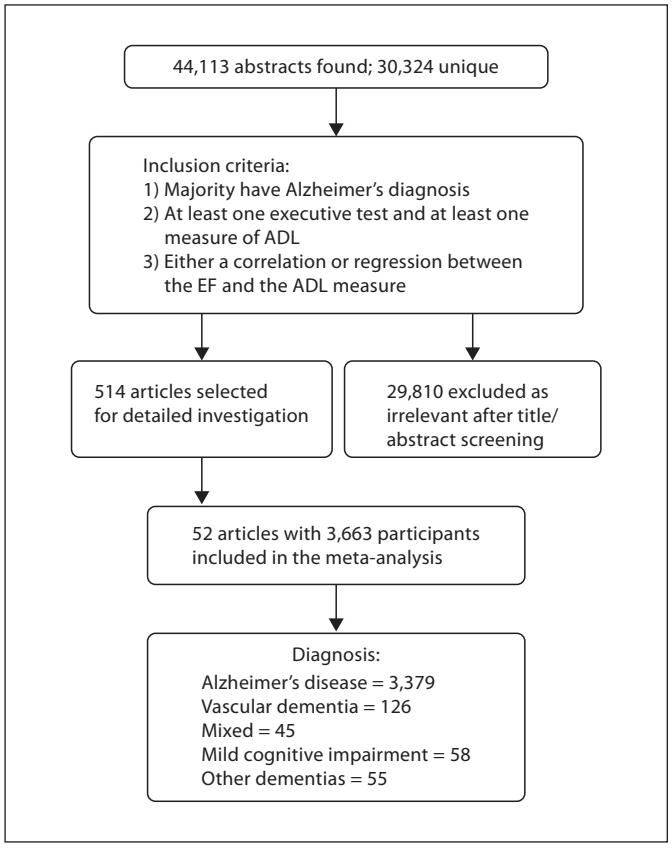

Fig. 1. Flow chart of procedure.

Statistical Analysis

The effect size *r* was used and the procedure outlined by Borenstein et al. [37] was followed. A standardized correlation direction was used, and where necessary the direction was changed to facilitate cross-study comparisons. If a relevant study reported regression analyses, odds ratios, *t* or *F* statistics, these were converted to correlations. One study [38] reported standardized betas, and these were converted to correlations using the formula $r = \beta + 0.05$ [39] which it has been suggested accurately estimates correlations from beta coefficients. Two studies each contributed two independent samples to the meta-analysis; one study included an English-speaking and a Spanish-speaking sample [38] while another included two separate samples of people with dementia [40]. In four cases, pairs of studies reported the same samples and hence they were combined in the meta-analysis. The first pair investigated different aspects of driving ability [41, 42], though the later article included one further participant. The second pair investigated simulated driving ability [43, 44], with the latter study amalgamating data from both studies. The third pair employed the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset and reported data for different tasks [45, 46]. The final pair reported data for different tasks from the Memory Impairment and Dementia Awareness Study (MIDAS) [47, 48].

Effect sizes were calculated using the random effects model since the included studies employed different methods of assessing ADL and EF and included heterogeneous samples of people with Alzheimer's disease. The random effects model estimates and incorporates the magnitude of heterogeneity into the overall estimated effect [49]. Random effects meta-regression analyses were used to investigate moderator variables; these examined the effect of age and Mini-Mental State Examination (MMSE) [50] score on the estimated effect sizes. Between-study heterogeneity for each cognitive measure was assessed using an index of inconsistency (I^2). This calculates a percentage of heterogeneity resulting from study differences that is not due to chance; therefore, larger values indicate greater heterogeneity [51]. All computations were based on Fisher's *z* transformations and were conducted using the Comprehensive Meta-Analysis 2 [52] software package which calculated average *z* scores and *p* values, weighted effect *r* values and 95% confidence intervals for the collective effect sizes. All but six of the included studies presented multiple correlations, typically between one measure of ADL and many executive tests, although 15 studies used more than one ADL measure. The software package was instructed to average the multiple within-study correlations to correct for violations of independence so that all available data could be included in the analysis. Forest Plot Viewer [53] was used to create the forest plot. Holm-Bonferroni correction for multiple comparisons at the 5% level was applied to all analyses.

To address the risk of possible publication bias, where studies of nonsignificant findings are less likely to be published than those with significant findings, 18 authors were contacted for additional information not included in relevant articles. Six responded, with five able to provide the necessary information; three of these provided details of statistically nonsignificant analyses.

Three analyses were conducted. The first analysis investigated the relationship between ADL and individual tests of executive function. Additionally, data from four tests which are not typically viewed as assessing EF were included. Three tests of working memory or attention were included; Trail Making Test Part A, Digit Span Forwards and Digit Span, a combined score for Digit Span Backwards and Digit Span Forwards that was reported in seven studies. Working memory and attention were specific search terms in the meta-analysis and are viewed as related to or as important elements of EF [54, 55]. The fourth test, the widely used MMSE, allowed for a comparison between cognitive status and ADL. Data from these four tests was only included in the first analysis. The second analysis investigated the effects of using different methods of assessing ADL by examining whether informant ratings, clinician ratings, performance-based measures or self-reports of ADL differed in the strength of association with executive function; this analysis included data from one additional study [34] which was excluded from the executive test analysis due to the use of a composite EF score. The second analysis also included data from three tests of EF that were each used in only one study: the D-KEFS Tower and Sorting tests (used in [56]) and the Letter-Number Sequencing test (used in [57]). A final analysis investigated the association between driving ability (see Dickerson et al. [58] for discussion) and executive function and included informant-rating questionnaire studies and observational studies of practical driving ability.

Table 1. Study details

Authors	Participants and demographics	Tests included	ADL measure
Alzheimer's disease-only studies			
Alva et al. [59], 2011	AD = 782 (mean age 73.6, mean MMSE = 16.5)	CDT, TMT-A	Informant: Alzheimer's Disease Assessment Scale-Activities of Daily Living
Back-Madruga et al. [14], 2002	AD = 20 (executive AD = 10, mean age 73.6 (9.6), mean MMSE = 22.2 (3.6); typical AD = 10, mean age 79.9 (6.1), mean MMSE = 23.7 (3.1))	Letter Fluency[a], Similarities, Stroop[a], TMT-B[a]	Informant: IADL
Bassett [60], 1999	AD = 20 (mean age 75.3 (9.87), mean MMSE = 21.95 (4.14))	Digit Span, MMSE, Similarities, TMT-A, TMT-B	Self: 5-item Financial Competency Questionnaire devised for the study
Boyle et al. [61], 2003	AD = 45 (mean age 76.7 (7.7), mean MMSE = 22 (3.2))	DRS Initiation	Informant: IADL, PSMS
Bracco et al. [62], 1990	AD = 143 (mean age 60.8 (5.9), mean MMSE = 22 (3.2))	Digit Span Forwards, MMSE, Set Test (Category Fluency), Token Test	Informant: BDS
Breen et al. [63], 1984	AD = 35 (AD = 21: mean age 75.14 (7.08), mean MMSE = 20.19 (4.42); AD with unipolar depression = 14: mean age 73.64 (8.67), mean MMSE = 17.50 (6.24))	Block Design, Digit Span, Digit Symbol, MMSE, Similarities	Informant: BDS
Brown et al. [45], 2011 Marshall et al. [46], 2011	AD = 193 (mean age 75.33 (7.48), mean MMSE = 23.34 (2.06)) AD = 178 (mean age 75.6 (7.4), mean MMSE = 23.4 (2.0))	Brown et al.: Digit Symbol (n = 189)[a], TMT-A (n = 191)[a], TMT-B (n = 183)[a] Marshall et al.: MMSE	Informant: FAQ
Cahn-Weiner et al. [64], 2003	AD = 24 (mean age 75.3 (7.1), mean MMSE = 24.2 (2.0))	Letter Fluency	Informant: combined modified IADL and PSMS
Čechová et al. [65], 2009	AD = 34 (mean age 78.5 (7.3), mean MMSE = 22.5 (2.04))	Category Fluency	Informant: combined Bristol Activities of Daily Living Scale, DAD, FAQ
Chen et al. [66], 1998	AD = 31 (mean age 69.9, mean MMSE = 17.6)	Letter Fluency, DRS Conceptualization DRS Initiation, MMSE, WCST	Informant: BDS-Activities
Dawson et al. [67], 2009	AD = 40 (mean age 75.1 (7.7), mean MMSE = 26.5 (2.9))	Letter Fluency, TMT-A, TMT-B	Performance: driving errors
Earnst et al. [57], 2001	AD = 20 (mean age 71.9 (7.2), mean MMSE = 20.5 (4.8))	Digit Span Backwards, Digit Span Forwards, Letter-Number Sequencing[b]	Performance: Financial Capacity Instrument total score
Farias et al. [35], 2003 Tomaszewski [36], 2000	AD = 42 (mean age 71.67 (8.52), mean MMSE = 22.02 (5.11))	From paper [35]: Digit Span From dissertation [36]: Letter Fluency, MMSE, Similarities, TMT-A, TMT-B (n = 17)	Informant: IADL Performance: DAFS (plus Misplaced Objects and Spatial Orientation Tests included in total score)

Fox et al. [68], 1997	AD = 19 (mean age 74.3 (6.4), mean MMSE = 21.3 (2.75))	Block Design, Digit Symbol, TMT-A, TMT-B	Clinician: driving predictions Performance: driving test
Fukui and Lee [69], 2009	AD = 57 (mean age 78.0 (6.1), mean Hasegawa Dementia Scale-Revised = 16.0 (5.9))	CDT	Informant: modified IADL, modified PSMS
Giovannetti et al. [70], 2008	AD = 70 (mean age 79.0 (6.7), mean MMSE = 20.08 (3.8))	Animal Naming-Association Index (Category Fluency; n = 54), CDT (n = 68), Letter Fluency (n = 60), Mental Control (n = 56), MMSE (n = 70)	Performance: NAT
Hall et al. [71], 2011	AD = 202 (males = 91: mean age 74.36 (8.21), mean MMSE = 21.53 (4.59); females = 111: mean age 76.95 (7.74), mean MMSE = 20.95 (4.47))	CDT, Letter Fluency (n = 91), TMT-A, TMT-B (n = 91)	Informant: IADL, PSMS
Heinik et al. [72], 2002	AD = 49 (mild: mean age 77.88 (7.16), mean MMSE = 20.53 (2.80); moderate: mean age 80.65 (6.13), mean MMSE = 13.21 (4.47))	CDT (two scoring methods)	Informant: IADL (n = 40), PSMS dressing subscale (n = 47)
Loewenstein et al. [73], 1992	AD = 33 (mean age 77.1 (6.3), mean MMSE = 18.69 (4.74))	Block Design, Letter Fluency, MMSE, Similarities	Performance: individual DAFS items
Loewenstein et al. [38], 1995	AD = 183 (English (n = 127): mean age 77.29 (6.6), mean MMSE = 20.75 (3.9); Spanish (n = 56): mean age 73.00 (5.8), mean MMSE = 19.11 (4.7))	Block Design, Digit Span, Letter Fluency, MMSE	Performance: individual DAFS items
Mahurin et al. [74], 1991	AD = 18 (mean age 66.9 (5.4), mean MMSE = 19.4 (3.4))	Letter Fluency, MMSE, TMT-A, TMT-B	Performance: Structured Assessment of Independent Living Skills
Matsuda and Saito [75], 2005	AD = 73 (mean age 74.75 (8.94), mean MMSE = 18.42 (6.26))	Digit Span Forwards, Digit Symbol, Similarities	Informant: 27-item combined ADL/IADL questionnaire devised for the study
Monaci and Morris [76], 2012	AD = 34 (mean age 76.4 (7.4), mean MMSE = 19.6 (5.3))	CAMCOG-EFS, MMSE, Similarities	Informant: Katz index, IADL
Nussbaum et al. [77], 1995	AD = 19 (mean age 75.47 (9.11), mean MMSE = 21.95 (2.04))	DRS Conceptualization, DRS Initiation	Informant: Dementia Behavior Rating Scale
Ott et al. [78], 1996	AD = 26 (mean age 72.5 (7.5), mean MMSE = 21.1 (3.9))	CDT, Digit Span Backwards, Digit Span Forwards, Letter Fluency, Mazes, MMSE, TMT-A, TMT-B	Informant: 19-item combined ADL/IADL questionnaire devised for the study
Ott et al. [79], 2000	AD = 79 (mean age 74.7 (7.9), mean MMSE = 19.6 (4.9))	CDT	Informant: 4-point informant-rated driving questionnaire
Ott et al. [40], 2003	AD = 27 (mean age 74.9 (5.9), mean MMSE = 21.8 (2.9))	Porteus Maze, TMT-B	Informant: 4-point informant-rated driving questionnaire

Table 1 (continued)

Authors	Participants and demographics	Tests included	ADL measure
Ott et al. [80], 2008	AD = 88 (mean age 75.8 (6.9), mean MMSE = 24.0 (3.5))	5 Computer Mazes, MMSE, TMT-A, TMT-B	Performance: Driving test
Pereira et al. [81], 2008	AD = 26 (mean age 73.8 (6.7), mean MMSE = 20.4 (6.0))	EXIT25	Performance: DAFS
Perry and Hodges[34], 2000[b]	AD = 24 (mean age 69.75 (7.6), mean MMSE = 21.0 (3.6))	Composite score (Dual performance test, TEA-Elevator counting with distraction, TEA-Map Search, Stroop, WCST), MMSE	Informant: 25-item combined ADL/IADL questionnaire devised for the study
Razani et al. [82], 2011	AD = 49 (mean age 74.41 (8.53), mean MMSE = 23.60 (5.24))	Category Fluency[a], Letter Fluency[a], WCST[a]	Performance: DAFS
Rebok et al. [83], 1994	AD = 10 (mean age 75.4 (3.5), mean MMSE = 22.5 (2.4))	Category Fluency, MMSE	Performance: Driving Advisement System, Driver Performance Test
Rizzo et al. [43], 1997 Rizzo et al. [44], 2001	AD = 21 (mean age 71.5 (8.5)) no MMSE information provided AD = 18 (mean age 73.0 (7)) no MMSE information provided	Block Design, Digit Span, Letter Fluency, TMT-B	Performance: Virtual driving test
Senanarong et al. [84]. 2005	AD = 73 (mean age 70.28 (8.10), mean Thai MMSE = 18.42 (6.60))	Category Fluency, CDT, Letter Fluency, MMSE	Informant: FAQ, Thai ADL
Teri et al. [85], 1989	AD = 56 (mean age 71.0 (6.3), mean MMSE = 23.0 (3.29))	DRS Conceptualization, DRS Initiation	Informant: OARS-IADL, OARS-Self Care
Uc et al. [41], 2004 Uc et al. [42], 2005	AD = 32 (mean age 75.9 (6.2), mean MMSE = 26.3 (2.9)) AD = 33 (mean age 76.1 (5.9), mean MMSE = 26.1 (3.0))	Block Design, Letter Fluency, TMT-B	Performance: Driving test Performance: Landmark test
Verhey, et al. [86], 2003	AD = 283 (mean age 75.4 (6.3), mean MMSE = 19.4 (4.4))	CAMCOG-EFS	Clinician: Nurses' Observation Scale for Geriatric Patients-IADL subscale
Willis et al. [87], 1998	AD = 65 (mean age 73.87 (8.63), mean MMSE = 19.83 (4.08))	Block Design, Digit Symbol, MMSE, TMT-A, TMT-B	Clinician: PSMS; Informant: IADL Performance: Everyday Problem Test for Cognitively Challenged Elderly; Self: IADL
Mixed dementia studies			
Bettcher et al. [88], 2008	n = 53 (mean age 79.5 (5.4), mean MMSE = 20.9 (3.6)); AD = 29, VaD = 20, Mixed = 4	CDT (n = 50), Letter Fluency (n = 50), MMSE	Performance: NAT
Brennan et al. [89], 2009	n = 44 (mean age 76.39 (9.42), mean MMSE = 22.64 (3.42)); AD = 22, VaD = 9, Mixed = 7, FTD = 4, PD/DLB = 2	CDT (n = 43), Letter Fluency (n = 38), Mental Control (n = 35), MMSE	Performance: NAT

Clare et al. [47], 2012 Martyr et al. [48], 2012	n = 96 (mean age 78.68 (7.84), mean MMSE = 24.22 (2.78)); AD = 50, VaD = 29, Mixed = 17	Clare et al.: Category Fluency Martyr et al.: Letter Fluency, MMSE	Informant: FAQ; Self: FAQ
Hill et al. [90], 1995	n = 81 (mean age 85.4 (5.58), mean MMSE = 17.9 (5.26)); AD = 45, VaD = 20, Mixed = 1, Alcohol dementia = 5, unspecified dementia = 10	Block Design, Digit Span Backwards, Digit Span Forwards, MMSE	Informant: Cambridge Mental Disorders of the Elderly Examination Family Interview Schedule, Katz index
Norton et al. [91], 2001	n = 30 (mean age 73.1 (8.5), mean MMSE = 22.0 (4.0)); AD = 20, VaD = 3, DLB = 2, alcohol dementia = 1, dementia due to multiple etiologies = 2, dementia of unknown etiology = 2	DRS Initiation	Informant: IADL
Ott et al. [40], 2003	n = 24 with mild or very mild dementia. Smaller sample excluding people with no dementia. No specific demographic information was provided.	10 Computer Mazes	Informant: 4-point informant-rated driving
Razani et al. [56], 2007	n = 33 (mean age 73.82 (8.76), mean MMSE = 22.27 (5.13)); AD = 21, Mixed = 10, FTD = 2	Letter Fluency, MMSE, D-KEFS-Sorting[b], D-KEFS-Stroop, D-KEFS-TMT-B, D-KEFS-Tower[b], WCST	Informant: IADL Performance: DAFS
Sabbagh et al. [92], 2007	AD/MCI = 124 (mean age 83.9 (7.6), mean MMSE = 21.1 (8.7)); AD = 66, MCI = 58	Category Fluency (n = 89), CDT (n = 85), Digit Span (n = 91), Letter Fluency (n = 90), Stroop (n = 74)	Clinician: Functional Assessment Staging
Stokholm et al. [93], 2005	n = 33 (mean age 76.3 (6.2), mean MMSE = 24.2 (2.1)); AD = 22, VaD = 4, mixed = 4, FTD = 2, other = 1	EXIT25[a] (n = 23), MMSE[a] (n = 23)	Informant: DAD
Vallotti et al. [94], 2001	AD = 44 (mean age 79.0 (7.0), mean MMSE = 18.9 (5.2)) VaD = 41 (mean age 79.0 (6.0), mean MMSE = 18.7 (4.5))	Category Fluency, Letter Fluency, MMSE, Token Test	Informant: Barthel Index

[a] Not reported in the paper but included in the meta-analysis. [b] Articles or tests included in the secondary analysis only.

ADL test abbreviations: Blessed Dementia Scale (BDS), Direct Assessment of Functional Ability (DAFS), Disability Assessment in Dementia (DAD), Functional Activities Questionnaire (FAQ), Instrumental Activities of Daily Living (IADL), Naturalistic Action Test (NAT), Older Americans Resource Scale (OARS) and Physical Self-Maintenance Scale (PSMS).

Executive and cognitive test abbreviations: Cambridge Cognitive Examination-Executive Functioning Scale (CAMCOG-EFS), Clock Drawing Task (CDT), Delis-Kaplan Executive Function System (D-KEFS), Executive Interview (EXIT25), Mini-Mental State Examination (MMSE), Mattis Dementia Rating Scale (DRS), Test of Everyday Attention (TEA), Trail Making Test-Part A (TMT-A), Trail Making Test-Part B (TMT-B), Wisconsin Card Sorting Test (WCST).

Patient group abbreviations: Alzheimer's disease (AD), Dementia of Lewy body (DLB), Frontotemporal dementia (FTD), Mild cognitive impairment (MCI), Mixture of Alzheimer's disease and vascular dementia (Mixed), Parkinson's disease (PD), Vascular dementia (VaD).

Table 2. Effect sizes, CIs and heterogeneity for individual tests

	n	k	Effect size	95% CI	p	Heterogeneity		
						Q	Q p	I^2
Executive test								
Block Design	464	9	0.370	0.286 to 0.448	**<0.001**	6.267	0.617	0.00
Category Fluency	630	9	0.542	0.360 to 0.684	**<0.001**	59.89	<0.001	86.64
Clock Drawing Task	1,505	11	0.347	0.267 to 0.423	**<0.001**	19.17	0.038	47.83
Digit Span Backwards	127	3	0.181	0.003 to 0.348	0.047	1.05	0.593	0.00
Digit Symbol	381	5	0.466	0.250 to 0.638	**<0.001**	18.48	0.001	78.35
DRS Conceptualization	106	3	0.232	−0.205 to 0.592	0.298	8.72	0.013	77.06
DRS Initiation	181	5	0.395	0.259 to 0.515	**<0.001**	2.83	0.587	0.00
Executive Functioning Scale	317	2	0.419	0.107 to 0.656	0.009	3.52	0.061	71.55
Executive Interview (EXIT25)	49	2	0.455	−0.408 to 0.889	0.298	9.52	0.002	89.50
Letter Fluency	1,128	22	0.335	0.266 to 0.400	**<0.001**	30.54	0.082	31.24
Mazes	165	4	0.448	0.305 to 0.571	**<0.001**	3.19	0.364	5.88
Mental Control	89	2	0.230	0.022 to 0.419	0.031	0.00	0.981	0.00
Similarities	257	7	0.467	0.361 to 0.561	**<0.001**	1.84	0.934	0.00
Stroop	127	3	0.033	−0.146 to 0.211	0.716	0.10	0.950	0.00
Token Test	228	2	0.599	−0.114 to 0.904	0.093	34.92	<0.001	97.14
Trail Making Test Part B	697	15	0.315	0.227 to 0.398	**<0.001**	18.29	0.194	23.44
Wisconsin Card Sorting Test	113	3	0.509	0.282 to 0.685	**<0.001**	3.90	0.142	48.68
Attention and working memory								
Digit Span Forwards	343	5	0.214	−0.131 to 0.512	0.223	35.04	<0.001	88.58[a]
Digit Span	386	7	0.415	0.323 to 0.499	**<0.001**	2.21	0.899	0.00
Trail Making Test Part A	1,398	11	0.365	0.292 to 0.434	**<0.001**	14.20	0.164	29.56
Cognitive status								
Mini-Mental State Examination	1,397	25	0.451	0.376 to 0.520	**<0.001**	59.91	<0.001	59.94

[a] Removing Bracco et al. [62] reduced I^2 to 0.00% (n = 200, k = 4; effect size of 0.070; 95% CI −0.073 to 0.210, p = 0.335).
Bold indicates significant after Holm-Bonferroni correction for multiple comparisons.

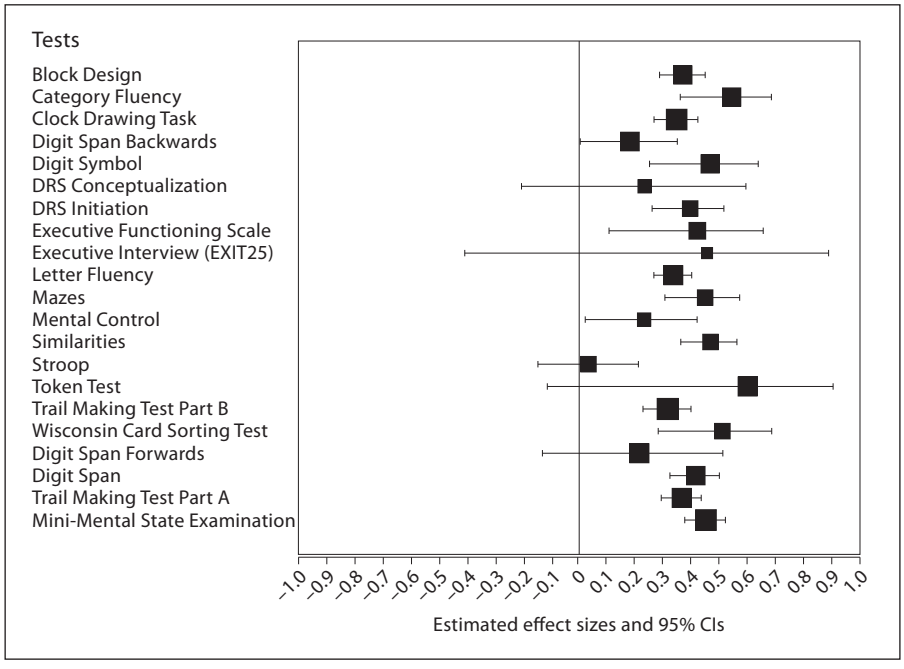

Fig. 2. Forest plot of executive and other cognitive tests.

Table 3. Effect sizes, CIs and heterogeneity for individual tasks for Alzheimer's disease-only and mixed dementia samples

	Alzheimer's disease-only samples					Mixed dementia samples				
	n	k	effect size	p	I^2	n	k	effect size	p	I^2
Executive test										
Block Design	383	8	0.377	**<0.001**	0.00					
Category Fluency	360	6	0.585	**<0.001**	87.26	270	3	0.456	**<0.001**	77.16
Clock Drawing Task	1,328	8	0.348	**<0.001**	30.39	177	3	0.305	0.062	77.83
Digit Span Backwards	46	2	0.188	0.240	4.24					
DRS Initiation	151	4	0.386	**<0.001**	0.00					
Letter Fluency	737	16	0.365	**<0.001**	0.00	391	6	0.269	**0.001**	59.14
Mazes	141	3	0.406	**<0.001**	0.00					
Stroop						107	2	0.029	0.768	0.00
Trail Making Test Part B	664	14	0.322	**<0.001**	28.90					
Wisconsin Card Sorting Test	80	2	0.564	**0.003**	68.18					
Attention and working memory										
Digit Span Forwards	262	4	0.234	0.296	89.90					
Digit Span	295	6	0.402	**<0.001**	0.00					
Cognitive status										
Mini-Mental State Examination	982	18	0.484	**<0.001**	53.18	415	7	0.364	**<0.001**	70.51

Bold indicates significant after Holm-Bonferroni correction for multiple comparisons.

Results

In the first search 40,790 references were found, with 27,704 of those being unique; in the second search a further 3,323 references were returned of which 2,620 were unique. Thus, there were 44,113 abstracts found in total, of which 30,324 were unique; 514 abstracts were investigated in more detail, and 49 studies reported in 52 articles met inclusion criteria. Table 1 describes the studies in more detail. Thirty-nine studies featured a sample consisting solely of people with Alzheimer's disease while a further 10 studies included people with a range of dementias, with Alzheimer's disease the most commonly reported. In total, data from 3,663 people with dementia were included in the meta-analysis; of those 3,379 were diagnosed with Alzheimer's disease, with 3,060 in Alzheimer's disease only studies. Those that remained had either vascular dementia (n = 126), mild cognitive impairment (n = 58), mixed dementia (n = 45), frontotemporal dementia (n = 8), Parkinson's disease (n = 1), Lewy body dementia (n = 3), or alcohol dementia (n = 6). Twenty-four were unspecified, and 13 had other dementias.

Analysis of Associations between ADL Ratings and Scores on Individual Cognitive Tests

The analysis examined the assessment between ADL ratings and scores on 21 different tests (table 2). Random effects meta-analysis found significant estimated effect sizes for all tests used in four studies or more, with the exception of Digit Span Forwards, a test of working memory. Block Design, Category Fluency, Digit Symbol, Similarities, Mazes and the Wisconsin Card Sorting Test showed the strongest associations with ADL. However, the estimated effect sizes for Mazes and the Wisconsin Card Sorting Test should be viewed as preliminary due to the small number of studies and the small sample sizes included in these analyses. Similarly, of the seven tests that were used in three or fewer studies all but one showed nonsignificant effect sizes after Holm-Bonferroni correction. Of note, the large but nonsignificant estimated effect sizes for the Executive Interview (EXIT25) [95] and The Token Test were due to one study reporting a large correlation and the other study reporting a small correlation; which is indicated by the large confidence intervals in figure 2. The findings from these seven tests should be viewed as preliminary since only with more studies will the eventual effect sizes for these less-commonly used tests be established. There was a moderate to large degree of between-study estimated heterogeneity, as indicated by the inconsistency indices (I^2) in table 2 especially for Category Fluency, Digit Symbol, and most of the tests used in only a small number of studies, supporting the choice of a random effects model.

Table 4. Effect sizes, CIs and heterogeneity for different methods of assessing everyday functioning

ADL method	n	k	Effect size	95% CI	p	Heterogeneity		
						Q	Q p	I^2
Clinician rating	452	4	0.350	0.217–0.471	**<0.001**	5.08	0.166	40.96
Informant rating	2,415	30	0.372	0.312–0.430	**<0.001**	58.88	0.001	50.75
Performance-based	815	19	0.390	0.316–0.459	**<0.001**	23.10	0.187	22.19
Self-rating	181	3	0.351	0.214–0.475	**<0.001**	1.14	0.564	0.00
Alzheimer's disease only studies								
Clinician rating	367	3	0.332	0.148–0.494	**<0.001**	8.89	0.143	48.55
Informant rating	2,043	23	0.394	0.324–0.459	**<0.001**	48.42	0.001	55.41[a]
Performance-based	694	16	0.414	0.334–0.488	**<0.001**	19.46	0.193	22.94[b]
Self-rating	85	2	0.419	0.222–0.583	**<0.001**	0.223	0.637	0.00
Mixed dementia studies								
Informant rating	372	7	0.294	0.177–0.403	**<0.001**	7.82	0.252	23.24
Performance-based	121	3	0.259	0.079–0.422	**0.005**	1.10	0.577	0.00

[a] Removing Bracco et al. [62] reduced I^2 to 38.74% (n = 1,900, k = 22; effect size of 0.368; 95% CI 0.303–0.428, p < 0.001).
[b] Removing Pereira et al. [81] reduced I^2 to 0.00% (n = 668, k = 15; effect size of 0.387; 95% CI 0.318–0.452, p < 0.001).
Bold indicates significant after Holm-Bonferroni correction for multiple comparisons.

Moderator Variables and Heterogeneity

Moderator variables were investigated to see whether age or MMSE score influenced the estimated effect sizes. Age was found to be a significant moderator variable for three tests, Category Fluency (z = –2.172, p = 0.030), Trail Making Test Part A (z = –2.073, p = 0.038) and MMSE (z = –1.986, p = 0.047), though after correcting for multiple comparisons these association were no longer significant. Meanwhile, MMSE score was not a significant moderator variable for any test. A further area of heterogeneity could arise from including multiple dementia diagnoses; consequently the meta-analyses were rerun excluding these 10 studies. In the original meta-analysis scores for Digit Symbol, the Cambridge Cognitive Examination-Executive Functioning Scale [96], the Dementia Rating Scale (DRS) [97, 98] Conceptualization subscale, Similarities and Trail Making Test Part A were available only for people with Alzheimer's disease so the analysis with regards to these tests was unchanged. For a further three tests (EXIT25, Mental Control and The Token Test) analysis could not be rerun as the data came from one study with Alzheimer's disease and one study with a mixed dementia sample in each case. Table 3, therefore, shows data for the remaining 13 tests. The estimated effect sizes and significance remained relatively unchanged after excluding studies with mixed samples of people with dementia, although the degree of inconsistency for many of the tests was greatly reduced; this was especially so for the Clock Drawing Test and Letter Fluency. The analysis was repeated with five tests where significant data from studies with mixed dementia samples could be included (table 3). This shows that for all five tests the estimated effect sizes were slightly reduced, with the Clock Drawing Test no longer statistically significant. The inconsistency for three of the tests was higher than that seen in both the full analysis and the Alzheimer's disease only analysis, suggesting that there is generally more variability in the findings from studies conducted with mixed dementia samples, though it should be noted that the analysis with these studies had small sample sizes.

Associations between EF Scores and Ratings Based on Different Methods of Assessing ADL Ability

The next stage of the analysis investigated the association between EF test scores and each of the four different methods of assessing ADL: performance-based, clinician rating, informant rating or self-rating. Of the four methods, informant rating was the most commonly used, with performance-based being the next most commonly employed method. As table 4 shows, similar estimated effect sizes were found for all four methods, and these did not differ statistically, suggesting there was little difference in the results obtained for the four measurement approaches.

Moderator Variables and Heterogeneity

A moderate degree of within-test heterogeneity was found, especially for informant ratings. Age was found to be a moderating variable for informant ratings of ADL ($z = -2.579$, $p = 0.010$) and approached statistical significance as a moderator variable for performance-based tests of ADL ($z = -1.910$, $p = 0.056$). MMSE score was not a significant moderator variable for any of the different methods of assessing ADL. Heterogeneity from the 10 studies with mixed dementia samples was also investigated. As table 4 shows, the heterogeneity indices increased marginally when only people with Alzheimer's disease were included in the analysis, suggesting that the inclusion of participants with other dementias had little impact on heterogeneity. Interestingly, in the Alzheimer's disease only analysis, after the Bracco et al. [62] study was removed from the informant rating analysis and after the Pereira et al. [81] study was removed from the performance-based analysis, the estimated effect sizes and the heterogeneity for both was reduced (see note in table 4), suggesting that these two studies which found large effects were slightly inflating the estimated effect sizes.

Driving Ability

A final analysis was conducted on the nine studies that investigated whether EF was related to driving ability. This analysis included a combined sample size of 337 people and reported an effect size of 0.404 (95% CI 0.266–0.526, $p < 0.001$, $I^2 = 39.84$) suggesting that EF is moderately related to driving ability in people with Alzheimer's disease. The effect sizes after separating the studies into those using either performance-based ($n = 207$, $k = 6$; effect size of 0.355; 95% CI 0.224–0.473, $p < 0.001$, $I^2 = 0.00$) or informant/clinician ratings ($n = 149$, $k = 4$; effect size of 0.500; 95% CI 0.216–0.706, $p = 0.001$, $I^2 = 68.22$) indicated that the two different methods of assessing driving ability were relatively comparable in their associations with EF. There was a moderate degree of within-test heterogeneity, with the informant/clinician rated studies increasing the amount of between-study variance; however this was due to one study [79] and after this study was removed no inconsistency was found for informant/clinician ratings ($n = 70$, $k = 3$; effect size of 0.612; 95% CI 0.431–0.746, $p = 0.001$, $I^2 = 0.00$). Neither age nor MMSE score was a significant moderating variable between driving ability and EF. Due to the small number of studies, moderation analysis could not be conducted in relation to the different methodologies used to investigate driving.

Discussion

This random effects meta-analytic study investigated the relationship between executive function and activities of daily living in Alzheimer's disease. The first analysis found significant associations between ADL and 13 of 21 tests, including 10 of 17 tests of executive function. The tests with the largest effect sizes also had relatively large confidence intervals and large indices of inconsistency, suggesting wide variability, though generally heterogeneity tended to be reduced once studies that included mixed dementia samples were excluded. For the seven tests where a significant relationship between EF and ADL was not found, all tests were used in three or fewer studies involving smaller sample sizes, suggesting that reduced power may have contributed to the nonsignificant finding. The findings therefore support the conclusions of previous reviews that proposed a relationship between EF and ADL [26, 27], but demonstrate that the relationship is moderate in size; consequently, people with Alzheimer's disease who present at memory clinics with executive dysfunction are likely to have difficulties with everyday functioning. However, further research is needed to clarify the association between less frequently used tests of EF and ADL in people with Alzheimer's disease.

Analyses investigating different methods of assessing ADL indicated that all four methods were moderately correlated with EF, to a roughly similar degree. This indicates that if the primary question of interest is the relationship between EF and ADL, then an ADL questionnaire may be just as informative as a more costly and time-consuming performance-based measure of ADL. Finally, the nine studies that investigated the association between driving and EF also found a moderate estimated effect size, as would be expected since driving is a complex, cognitively-demanding ability. The finding supports and partially updates a previous meta-analysis where neuropsychological test scores, including executive functioning, were related to driving ability in dementia [99]. One difference, however, is that informant ratings of driving ability, albeit with only four studies, were largely comparable with performance-based tests of driving ability, whereas previously performance-based tests of driving ability have been seen as more strongly related to EF [99]. The association between driving ability and tests of EF may indicate that people with early-stage Alzheimer's disease who present with discernible executive deficits may need a full driving assessment, especially those diagnosed at a younger age; tests of EF may provide a preliminary screening.

Surprisingly, the random effects meta-analysis suggests a relatively consistent moderate association between EF and ADL ability. An important caveat, however, is that few of the EF tests included in the meta-analysis have established ecological validity and this may have important implications for the relationship between EF and everyday functioning. It could be expected that due to increased face validity or acceptability to people with Alzheimer's disease, ecologically valid tests of EF would have stronger associations with ADLs than more traditional neuropsychological tests of EF such as those included in this meta-analysis. However, a review of six studies, none of which included people with Alzheimer's disease, suggests that the relationship between ecologically valid tests of EF and ADL may also be in the moderate range [100]. The strength of this relationship should be clarified through further research employing more ecologically valid tests of EF in Alzheimer's disease.

The current meta-analysis suggests that EF plays an important role in influencing functional ability in Alzheimer's disease. However, the moderate effect size indicates that tests of executive function explain only some of the variance in ADL ability in people with Alzheimer's disease. Other cognitive functions such as memory or visual perception may also affect everyday functioning in people with Alzheimer's disease [101, 102]. The moderate association between ADL and cognitive status (MMSE) indicates that cognitive status is also important for independent living, especially as the estimated effect size was relatively large; however, as a moderator variable MMSE had no impact on the association between executive function and ADL. Conversely, informant ratings of ADL were found to be significantly influenced by increasing age and a similar trend was seen for performance-based tests of ADL, suggesting that functional ability reduces with age [48, 85]; though interestingly, EF was unaffected by age. However, the negative association between MMSE score and age may have implications for the clinical interpretation of cognitive test scores. Clinical assessments and research investigating Alzheimer's disease and ADL should therefore take age into account as this is likely to impact on both informant ratings and actual performance.

While it is important clinically to know that there is a consistent moderate association between ADL and EF, it would also be important to know which specific ADLs are more susceptible to executive dysfunction. However, studies that present data for individual ADLs are rare, so it is difficult to relate specific everyday functions to EF or to determine which ADLs are more strongly related to executive functioning. It is likely that more complex ADLs place higher demands on executive functions than simpler ADLs, but this information is lost when presenting total scores. Future studies could investigate the association between specific ADLs and EF; to date few studies have investigated individual ADLs [35, 38, 56, 73, 82]. These authors, coincidentally, used the same performance-based measure of ADL; perhaps the nature of performance-based measures of ADL encourages presentation of data from individual ADLs, although recently studies have begun to investigate the association between executive function and specific ADLs using questionnaires [48, 71].

Conclusions

The meta-analysis supports the clinical observation that executive functioning is associated with everyday functional ability, including driving, in Alzheimer's disease though the association was found to be moderate. The findings also show that cognitive status, as indexed by MMSE score, is associated with functional ability in people with Alzheimer's disease, indicating that while executive function is an important component of everyday functioning in Alzheimer's disease, other elements including cognitive status also affect everyday activities and tasks. Older age was found to impair functional ability, though age had little impact on executive function test performance. Thus, a person with Alzheimer's disease who is older, has an impaired MMSE score and evidence of executive dysfunction is likely to have greater functional disability. It is recommended that clinicians should conduct a detailed functional assessment and consider rehabilitation techniques designed to improve executive function, as this is likely to assist in improving or maintaining functional ability, which in turn supports independence and contributes to an increased quality of life. Any intervention approach should be tailored to the age of people with Alzheimer's disease since it is likely that older people with Alzheimer's disease will have different rehabilitation needs from younger people with Alzheimer's disease.

Acknowledgments

We are grateful to Carla Back-Madruga, Patrick Brown, Gad Marshall, Jill Razani and Jette Stokholm for providing additional data that could be included in the meta-analysis. This research is funded by a National Institute for Social Care and Health Research PhD studentship awarded to Anthony Martyr.

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* References marked with an asterisk indicate studies included in the meta-analysis.