CITATION: Dementia and Geriatric Cognitive Disorders (2015) 40:178-185
DOI:10.1159/000433523

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The association of specific executive functions and falls risk in people with mild cognitive impairment and early stage dementia

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Short Title: Specific executive functions and falls risk

Abstract

Background/Aims: Impairment in executive function is associated with a hightened risk for falls in people with mild cognitive impairment (MCI) and dementia. The purpose of this study was to determine which aspects of executive function are associated with falls risk. Methods: Forty-two participants with a mean age of 81.6 years and a diagnosis of MCI or mild dementia completed five different executive function tests from the computerized CANTAB test battery and a comprehensive falls risk assessment. Results: A hierarchical regression analysis showed that falls risk was significantly associated with spatial memory abilities and inhibition of a pre-potent response. Conclusion: The concept of executive function may be too general to provide meaningful results in a research or clinical context, which should focus on spatial memory and inhibition of a pre-potent response.

Keywords:

Memory impairment, Falls, Cognition, Inhibition of a pre-potent response, Executive function, Attention switching, Spatial Memory

Introduction

Falls in older people are a major health concern and people with dementia are twice as likely to fall compared to people without dementia [1]. Deficits in executive function have been identified as a particular risk factor related to an increase in falls rates [1-3]. Two systematic reviews showed that most studies had used the Trail Making Test (TMT) to assess executive function [1,2]. The TMT examines scanning, visuo-motor tracking, divided attention and cognitive flexibility [4], and is regarded as a standard measurement of executive function [5]. Furthermore, processing speed, abstract reasoning and attention, which are related to executive function [1-3], have been associated with the fate of falls. Cognitive training with a focus on executive function has recently been included in exercise studies for people with dementia [6].

It is generally assumed that there are three separate executive functions that are moderately related but distinct: cognitive flexibility, information updating and monitoring, and inhibition of a pre-potent response (readily available response due to recent evocation, repetition with reinforcement or great emotional charge) [7,8]. Executive function is not a unitary process but refers to a range of cognitive processes that moderate and use information from the cortical sensory systems to produce a behavioural response, such as movement. These cognitive processes involve several cortical areas such as the dorso-lateral prefrontal cortex to encode the plan for movement, the supplementary motor area to decide the sequence of movement, the hippocampus and parahippocampal regions to support spatial planning and working memory, and the primary motor cortex with simultaneous processing in the basal ganglia and the cerebellum to prepare the execution of the movement. While walking itself might be a routine process, the incoming sensory information (e.g. from uneven surfaces) and its use to adapt the movement requires executive function processes [9].

Executive function includes a wide range of different cognitive abilities such as working memory, reasoning, self-regulation, visual search abilities, planning and perseverance [4,10]. . Not all of these cognitive abilities deteriorate at the same rate during the development of mild cognitive impairment (MCI) and dementia [11,12]. For example, Lefleche and Albert [13] showed that in people with mild Alzheimer's disease (AD), the ability to complete mental set shifting, self-monitoring or sequencing tasks was significantly impaired in comparison to people without AD, while the ability to solve verbal problem tests was not impaired. Executive function is associated with prefrontal cortex activity and, depending on executive function task, different neural subsystems are involved [14,15].

Executive functions are often assessed using the Trail Making test, Stroop test, the Go No Go task, clock drawing tasks and abstract reasoning tasks but measurements differ across studies and only a small selection is usually included [2]. It would be helpful for clinicians who are treating people with mild cognitive impairment (MCI) and dementia to know which dimensions of executive function are related to the risk of falling. They would then be able to target these people with fall prevention interventions.

The purpose of this study was to determine which cognitive abilities related to executive function are associated with an increased falls risk in people with MCI and early stage dementia. As part of a study to test the feasibility of a falls intervention programme for people with MCI and early stage dementia, we assessed cognitive abilities using a computerized cognitive test battery to include a range of executive function tests. The aim of this analysis was to investigate, which particular executive function abilities are related to the falls risk parameters within this sample population.

Methods

Participants

In total, 42 participants (55% female) with a mean age of 81.6 years (range: 67-94; SD 6.59) completed falls risk assessments as well as a battery of computerised cognitive tests. The participants were recruited from memory clinics (76%), falls services (14%), Community geriatricians (7%) and a rehabilitation clinic (2%) in Nottingham(shire)/UK. Of those, 21% had a fall within the last 6 months. Inclusion criteria were over 65 years of age, a diagnosis of mild cognitive impairment or mild dementia (Mini Mental State Examination (MMSE; [16]) 21-26, Montreal Cognitive Assessment (MoCA, [17]) 15-25 or Test Your Memory (TYM; [18]) 30-45; test depending on service through which participant was recruited), resident of Nottingham City or Nottinghamshire county and available and willing carer. Exclusion criteria were lacking mental capacity to consent to participate, inability to speak or understand good English, MMSE scores affected by visual or hearing impairment, physical disabilities or uncorrected sensory impairment that prevents undertaking of tests, such as being unable to see, to hold a pen or to walk without human help.

Ethics

The study had ethical approval from the NHS Health Research Authority Committee East Midlands. Information letters for participants and, if applicable their consultees (family member or friend), were sent ahead of the first assessment to the participant to give them sufficient time to consider the study. Consent was signed prior to the first assessment.

Procedures

The assessments were completed in two stages: first, research assistants with experience in the assessment of people with cognitive impairments and using the CANTAB test battery visited the participant at their home and recorded demographic characteristics, completed a health questionnaire (including the MoCA) and administered the cognitive test battery. The second part of the assessment evaluating falls risk was completed at an out-patient rehabilitation unit by two experienced registered physiotherapists.

Cognitive assessment

Cognitive abilities were assessed using the computerised CANTAB test battery [19] including the Motor Screening Task (MOT; to familiarise the participant with the touch screen computer), the Spatial Span test (SSP; to assess spatial working memory), the Attention Switching Task (AST; to assess response time for attention switching and inhibition of response), the simple and complex Reaction Time test (RTI), the Stockings of Cambridge test (SOC; to assess spatial planning/reasoning) and the Rapid Visual Processing task (RVP; to assess sustained attention). The tests were administered in the order above. Prior to each test, the research assistant explained the test to the participant. Each test started with practice items. Only if the research assistant was confident that the participant understood the task, they would proceed with the assessment. The total assessment took about one hour.

With exception of the Motor Screening Task and the simple Reaction Time test, all the tests required executive functioning abilities. Working memory, decision making, inhibition, planning and perseverance are part of executive function and required for the Spatial Span test, the Choice Reaction time test, the Attention Switching Task, the Stockings of Cambridge test and the Rapid Visual Processing task [4,9,20]. The tests and scores are explained in table 1. Test validity and reliability have been established in people with mild cognitive impairment and dementia [20-22].

[Table 1 to be inserted here]

According to the three dimensions model of executive function outlined above [8,9], the AST switch and SOC scores would reflect inhibition of a pre-potent response, the SSP, RTI and RVP scores indicate information updating and monitoring, and the AST congruency cost score represents cognitive flexibility.

Assessment of falls risk

The falls risk assessment was a combination of three assessments. The Physiological Profile Assessment (PPA; [23]), the Timed Up And Go test (TUAG; [24]) and the Berg Balance test (BERG; [25]). While the PPA assesses vision, peripheral sensation, muscle force, reaction time and postural sway [23], the TUAG assesses functional mobility [24] and the Berg Balance test static and dynamic balance [25]. These are commonly used as clinical tools. Participants performed the tests in the same order and were allocated sufficient rest periods between activities to prevent fatigue.

Statistical Analysis

Descriptive statistics were computed and normality assumptions checked. As all three falls risk scores were significantly related and might cover different contributors to the risk, a composite falls risk score was calculated based on the average of the z-scores for each test (with Berg Balance scores reversed). Pearson's correlations between raw executive function test scores (SSP, AST, complex RTI, SOC and RVP) and the falls risk composite scores were calculated. Significant executive function scores were entered into a hierarchical regression analysis controlling for sex and age. P-value levels for significance are reported for all significant results. All analyses were completed in SPSS 22.0.

Results

Participants had an average MoCA score of 20.81 out of 30 (SD 3.26; range: 15-28; higher scores indicate less impairment) and completed one or more of the cognitive and falls risk tests (see table 2). Nineteen participants completed all tests.

[Table 2 to be inserted here]

Pearson's correlations between the three falls risk scores were significant (see table 3).

[Table 3 to be inserted here]

There were significant correlations between the composite falls risk score and AST switch cost scores (r = .34; p = .04; n = 37) as well as AST percentage correct (r = -.39; p = .02; n = 37), and scores on the Spatial Span test (r = -.39; p = .02; n = 37). For scores on the SSP test, this was confirmed using a Spearman's rank correlation due to the limited range of scores (Spearman's r=-.37; p=.03; n=37). None of the other cognitive tests scores were significantly related to falls risk.

A hierarchical regression analysis controlling for sex and age confirmed that falls risk was significantly associated with SSP scores and AST switch cost scores (see table 4).

[Table 4 to be inserted here]

Assumptions for normality, multicollinearity, homoscedasticity, linearity, residual statistics were checked and results confirmed that these were met.

A post-hoc power calculation using an online power calculator [26] for hierarchical regression analyses indicated an observed power of 0.86 for step 3.

The results of the regression analysis indicated that an increased falls risk is related to a decreased ability to retain spatial information and to a longer response time to inhibit a pre-potent response. These results were found when controlling for sex and age.

Discussion

The findings indicated that falls risk might not be related to all aspects of executive functions in people with mild cognitive impairment and early stage dementia. In this study only spatial memory abilities and inhibition of a pre-potent response were related to falls risk; other aspects of executive function such as complex reaction time, planning, cognitive flexibility, reasoning and sustained attention were not significantly associated with falls risk in this study. The spatial span test assessed spatial working memory abilities and the attention switching task (AST switch score) examined the ability to inhibit responding in the same manner as for the previous trial. Following the three dimensions of executive function model [8,9], these two tasks reflect the dimensions of 'updating and monitoring of working memory representations' (SSP) and the dimension of 'inhibition of a pre-potent response' (AST switch cost). However, other scores representing these two concepts (RTI, RVP and SOC) were not significantly associated with falls risk. The third dimension, 'cognitive flexibility', which was reflected in the AST congruency score, was not related to falls risk. While the results showed that not all cognitive abilities accredited to executive function are associated with falls risk, the findings also confirmed that cognitive tasks cannot be contributed homogeneously to the different dimensions of executive functions [9]. Each task might tap into different dimensions or cover only selected aspects of one dimension. For this study, the cognitive abilities measured in the CANTAB were attributed to the executive function dimensions based on literature; a factor analysis should confirm the structure of dimensions for this population.

Strength and limitations

The CANTAB test battery provides precise and reliable measurements with no floor or ceiling effects [19]. Therefore, small differences and a low level in impairment in cognition can be assessed. However, only a limited number of aspects of executive function were assessed and not all dimensions of executive functions were evenly covered by the selected tests; only the AST congruency score tested cognitive flexibility and the relation with verbal working memory, for example, was not examined in this study.

While the findings indicate that working memory ability and attention switching are associated with falls risk, the sample size was too small to rule out other cognitive abilities might be contributing to a risk of falling.

Given the large number of factors affecting falls risk in people with dementia [27,28,29], it is important to keep in mind that the contribution of the impairment of cognitive abilities to the overall falls risk will be limited. This was reflected in the moderate correlations between working memory or attention switching ability and falls risk. The type of dementia, which might have an effect on falls risk [27] was not recorded and therefore not included in the analysis. However, while different etiologies might affect different executive function processes, there is no evidence that executive function processes involved in movement and falls risk do not remain the same across different types of dementia.

A composite score for falls risk was computed to form a more reliable and encompassing measure than a single falls risk measurement score [30]. All three tests are used as measures of falls risk in a clinical context but assess different aspects contributing to the risk of falling. The composite score therefore includes more risk factors than a single falls risk measure.

Context

Magnetic resonance imaging studies have confirmed the association between different aspects of executive function, brain measures and falls. Kievit, Davis, Mitchell et al. [15] demonstrated that multitasking and fluid intelligence, which are both considered part of executive function [7] are distinguishable cognitive abilities with fluid intelligence but not multitasking related to grey matter volume in one particular area of the prefrontal cortex (Brodmann Area 10). In addition, performance in multitasking but not fluid intelligence was related to white matter intensities in the Anterior Thalamic Radiation area. A lower density of grey matter in the bilateral middle frontal gyrus and superior frontal gyrus has been shown to be associated with a history of falling in older adults [31].

The concept of executive function might therefore be too general, in particular if measured with only one test, to provide meaningful results in a research or clinical context. Research and rehabilitation programmes concerned with reducing falls risk in people with MCI and dementia should therefore use a series of cognitive tests to identify the different cognitive abilities related to executive function and falls risk. While the relationship between cognitive scores and real life difficulties is not straight forward, the information gained from the test results can inform development and delivery of rehabilitation programmes, as well as support the communication with the participants.

Word count: 2125

Funding:

This article presents independent research funded by the National Institute for Health Research (NIHR) under its Programme Development Grant Programme (Reference Number RP-DG-0611-10013). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Conflict of Interests:

None of the authors have any conflicts of interest that might bias this work

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Table 1: Description of executive function test scores included in the assessment

Name	Description
Spatial Span (SSP)	Participant is shown a sequence of coloured blocks on screen and asked to recall the sequence afterwards SSP length refers to the longest sequence successfully recalled by the participant.
Attention Switching Task (AST)	Participant is asked to press arrows on the keyboard corresponding to arrows pointing left or right on the screen. In the congruent condition, arrows on the screen are at the same side of the screen they are pointing at (arrows pointing left are on the left), in the incongruent condition the arrows are positioned at the opposite side of the screen (arrows pointing left are on the right side of the screen). AST congruency cost refers to the difference in completion time between congruent and incongruent trail condition. AST switch cost refers to the difference in completion time between those trials where the trial type was the same as the previous one (e.g. both trials congruent) and those trials where the trial type was different to the previous one (e.g. congruent followed by an incongruent trial). AST percentage correct refers to the percentage of correct responses.
Complex	Participant is asked to press a button and release it once a yellow dot

Reaction Time test (complex RTI)	appears on the screen to touch the dot. In the complex RTI condition the participant has to choose between five locations where the dot might appear. Complex RTI movement time refers to the time (in milliseconds) it takes to touch the dot after a press pad button has been released. Complex RTI movement time refers to the time (in milliseconds) it takes to release the press button.
Stockings of Cambridge (SOC) number of problems solved in minimum moves	Participant is shown two displays each containing three coloured balls in pockets. The participant is asked to re-arrange the balls in the lower display to create a copy of the pattern on the upper display. SOC number of problems solved in minimum moves refers to the number of successful completions of a display in minimum moves.
Rapid Visual Information Processing (RVP) sensitivity to target	Participant is shown a white box on screen in which digits from 2 to 9 appear in a pseudo-random order at the rate of 100 digits per minute. The participant is asked to press a button on a press pad every time one of three particular series of three digits appears on screen (357, 246, 468). RVP sensitivity to target refers to the participant's ability to detect the target sequences.

Table 2: Descriptive statistics for cognitive and falls risk raw scores

test	N	Minimum	Maximum	Mean	SD
SSP[a] length	41	2	6	4	.92
AST[b] congruency cost	40	-194.40	406.50	131.86	118.33
AST[b] switch cost	40	-241.69	326.63	-10.75	108.05
AST[b] percentage correct	40	20.00	93.75	65.30	15.99
Complex RTI[c] movement	38	285.25	1702.12	553.47	253.22
Complex RTI[c] reaction time	38	321.50	1117.50	496.94	159.99
SOC[d] number of problems solved in minimum moves	24	3	10	6.29	2.05
RVP[e] sensitivity to target	28	.64	.96	.80	.07
PPA[f] (risk score)	39	-.63	4.99	2.56	1.62
TUAG[g] (sec)	38	6.99	34.30	14.27	6.74

Berg Balance test	39	24	56	46.44	10.10
composite falls risk	38	-.1.33	1.75	-.033	.80

[a]Spatial Span; [b]Attention Switching Task; [c]Complex Reaction Time test; [d]Stockings of Cambridge; [e]Rapid Visual Information Processing test; [f]Physiological Profile Assessment; [g]Timed Up And Go test

Table 3: Pearson's correlations between falls risk scores

	TUAG	BERG[c]
PPA[a]	.40 p=.02	-.42 p=.01
TUAG[b]		-.77 p=.00

[a] Physiological Profile Assessment, [b] Timed Up And Go test, [c] Berg Balance scale

Table 4: Hierarchical regression analysis predicting falls risk

	B	SE B	β
Step 1			
constant	-1.85	1.74	
age	0.02	0.02	0.18
sex	0.06	0.28	0.04
Step 2			
constant	-0.58	1.71	
age	0.02	0.02	0.19
sex	-0.08	0.27	-0.05
SSP[a]	-0.35	0.14	-0.40 (p=.02)
Step 3			
constant	0.04	1.63	
age	0.02	0.02	0.13
sex	0.08	0.26	0.05
SSP[a]	-0.35	0.13	-0.40 (p=.02)
AST[b] switch cost	0.00	0.00	0.35 (p=.03)

Note $R^2 = .19$ for Step1; $\Delta R^2 = .15$ for Step 2 ($p < .05$); $\Delta R^2 = .11$ for Step 3 ($p < .05$);
[a] Spatial Span; [b] Attention Switching test