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Working Memory and Cognitive Flexibility Mediates Visuoconstructional Abilities in Older Adults with Heterogeneous Cognitive Ability

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Abstract

Previous studies suggest that executive functions influence the performance on visuoconstructional tasks. This study aims to investigate whether the relationship between planning ability and the copy of complex figures is mediated by distinct components of executive functions (i.e., working memory, inhibitory control and cognitive flexibility). We included a 129 older adults with Alzheimer's disease (n = 36, AD), mild cognitive impairment (MCI, n = 67), and with no evidence of cognitive impairment (controls, n = 26). We evaluated the mediation effect of planning abilities, working memory, cognitive flexibility and inhibitory control on visuoconstructional tasks using a multiple mediation models. We found a significant direct effect of planning on visuoconstructional abilities and a partial mediation effect of working memory and cognitive flexibility on visuoconstructional abilities. The present results indicate that the performance on visuoconstructional task is mediated by multiple interrelated executive functions components, in particular working memory and cognitive flexibility. (*JINS*, 2015, *21*, 392–398)

Keywords: Planning, Executive functions, Neuropsychological test, Elderly, Alzheimer disease, Mild cognitive impairment

INTRODUCTION

Planning is the ability to establish the best way to achieve a particular goal, considering the hierarchy of steps necessary to achieve it. The planning process involves a "look-ahead" strategy. The subject need to generate multiple sequences of hypothetical events, appraise their potential consequences, start the necessary steps to implement the required actions and monitor continuously the outcomes (Carlin et al., 2000). Thus, planning can be viewed as a "higher-order" executive function, involving the interaction of core executive functions, for example, working memory, inhibitory control, and cognitive flexibility (Diamond, 2013; Miyake, Friedman, Emerson, Witzki, & Howeter, 2000).

Several tasks evaluate planning ability in clinical and research settings. The Tower of London (TOL) is one of the most used paradigms (Shallice, 1982). In this task, the subject has to plan a series of movements on a wooden tower to achieve a particular goal (i.e., copy a target stimulus shown on a card). Other assessment paradigms included the copy of complex figures (e.g., the Rey-Osterrieth complex figure test and the Taylor Complex Figure Test). These are well-validated measures of planning, visuospatial abilities, and episodic memory (Rabin, Barr, & Burton, 2005; Shin, Park, Park, Seol, & Kwon, 2006). There are many adaptations of these tests, including versions designed and validated for older adults with mild cognitive impairment (de Paula et al., 2012; Portella et al., 2003).

Visuoconstructional ability requires the interaction of cognitive processes that transform mental representation into motor commands (Smith, 2009). The capacity to plan and monitor the execution of drawing's copy are essential to the performance on this task. Previous studies reported significant associations between different measures of executive functions and accuracy on the copy of Complex Figure Tests. A study of patients with traumatic brain injury found that executive functions explained 11% to 16% of the variance in the scores of the Rey-Osterrieth Complex Figure

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(Schwarz, Penna, & Novack, 2009). Impairment of planning can lead to difficulties on drawing's copy (Guérin, Ska, & Belleville, 1999; Ogino et al., 2009; Schwarz et al., 2009). Studies with healthy subjects and patients with dementia demonstrated that elderly with better planning abilities reproduce the figure elements more accurately (Elderkin-Thompson et al., 2004; Freeman et al., 2000). Preserved working memory functioning is also important during the copy of complex figures (Freeman et al., 2000).

Despite these studies suggest an important association between executive functions and visuoconstructional abilities, there is scarce information about how specific executive function domains mediate visuoconstructional abilities in older adults. As executive functions encompasses both core and complex processes, it is important to assess how they mediate the performance on visuoconstructional tests. Thus, the aim of the present study is to evaluate how distinct components of executive functions (i.e., working memory, inhibitory control and cognitive flexibility) mediate the relationship between planning ability and copy of complex figures.

METHODS

Participants

The subjects included in the current analysis were recruited at a geriatric outpatient unit at the Clinics Hospital of the Federal University of Minas Gerais. All participants underwent a comprehensive clinical and neuropsychological assessment. After the clinical and neuropsychological assessment, the final diagnosis was adjudicated at consensus meeting with a panel of experts in the diagnosis and management of neuropsychiatric disorders in the elderly. We evaluated 129 consecutive subjects (68 women). They were divided into four groups: amnestic mild cognitive impairment subjects (aMCI; $n = 38$), multiple domains aMCI (mdaMCI; $n = 29$), patients with mild probable Alzheimer's disease (AD; $n = 36$). Older adults with no evidence of cognitive impairment or current psychiatric disorders were included in the control group ($n = 26$). We used the Winblad and Colleagues (Winblad et al., 2004) criteria for the diagnosis of aMCI and mdaMCI, and the NINCDS-ADRDA (McKhann et al., 1984) criteria for AD. All participants with dementia had scores of 0.5 and 1 on the Clinical Dementia Rating scale (CDR) (Morris, 1993) while MCI participants had scores of 0.5 on the CDR. Controls had scores of 0 on the CDR.

The exclusion criteria for inclusion in the study was the presence of other neurologic or psychiatric disorders, and the absence of severe sensory or motor disabilities. All MCI participants and healthy controls showed Mini-Mental State Examination scores above the Brazilian cutoff for dementia, according to educational level (Brucki, Nitrini, Caramelli, Bertolluci, & Okamoto, 2003). All participants and their caregivers, when necessary, signed the informed consent for participation. The study was approved by the Federal University of Minas Gerais Institutional Review Board.

Neuropsychological Assessment

All participants underwent a comprehensive neuropsychological assessment for the definition of cognitive status (de Paula et al., 2013). After the neuropsychological evaluation, all participants did the "Simplified" Taylor Complex Figure Test (sTCFT), Tower of London (TOL), Five Digit test, Corsi Blocks Span (backward component). These tests were administered by a trained neuropsychologist blinded to the results of the neuropsychological assessment. With the exception of the complex figure, none of the other tests involved the manipulation of pencil.

The sTCFT is an adaptation of the Taylor original figure where some graph-elements were excluded, reducing from 18 to 12 specific elements. The task is a valid measure of visuoconstructional and non-verbal memory for older adults with few years of formal education. The copy was followed by immediate recall (3 min) and delayed recall (25–30 min) tasks. The scoring criteria is based on the original Taylor figure, considering the element accuracy and precision, ranging from 0 to 2 points. The total score of the test ranges from 0 to 24, and higher scores indicate better performance on the task.

The TOL (Portella's version; Portella et al., 2003) was used as a measure of planning abilities. The test consists of 12 problems with growing complexity in which a subject need to match different balls' configurations showed by an examiner. This version is valid for Brazilian older adults (de Paula et al., 2012). The total score ranges from 0 to 46. Higher scores indicate better planning abilities.

We used the backward component of the Corsi Blocks Span to assess working memory (Kessels, van den Berg, Ruis, & Brands, 2008). We used the product score between the maximum span achieved and the total of correct trials as proposed by Kessels et al. (2008), with scores ranging from 0 to 144. Higher scores indicate better working memory efficiency. The task was validated for this population (de Paula et al., 2013).

We used the Five Digit Test (FDT) (Sedó, 2004) as a measure of inhibitory control and cognitive flexibility. It is a stroop-like paradigm involving figures from 1 to 5 and quantities from 1 to 5, divided into four trials. In the first trial, the subject must read the number shown on stimulus. In the second trial, the subject must count how many symbols are depicted in the stimulus. In the third trial, the subject need to tell how many digits are written and must not read the number shown on the stimulus (e.g., the stimulus 3-3-3-3, the correct answer is "four"). This trial assesses selective attention, an important aspect of inhibitory control (Diamond, 2013). In the fourth trial, the participant must shift the responses (what number and how many digits) in the stimulus, assessing cognitive flexibility.

Statistical Procedures

As data distribution was predominantly non-parametric, group differences in demographic and scores on neuropsychological tests were analyzed by the non-parametric test Kruskal-Wallis. The effect size of these comparisons was estimated by the *r* coefficient ($r = Z/\sqrt{N-1}$) when appropriate. Bivariate correlations between planning, working memory, cognitive flexibility, inhibitory control, and sTCFT Copy were tested using Spearman correlation analysis. This analysis was conducted with the whole sample.

Prior the mediation analysis, the scores on the neuropsychological tests were normalized with log-transformation. We performed a mediation analysis to estimate the direct and indirect effect of planning through mediators on sTCFT copy. The objective of mediation analysis is to evaluate how a predictor (X) influences an outcome (Y) directly and indirectly through one or more mediator variables (Hayes, 2013; Preacher & Hayes, 2008). In the present study we assessed the direct effect of planning (X) and the indirect effect of mediators working memory (M_1), cognitive flexibility (M_2), and inhibitory control (M_3) on sTCFT Copy (Y). We used the macro PROCESS for SPSS to carry out the mediation analysis (Hayes, 2012).

We used a parallel multiple mediator model analysis using ordinary least squares (OLS) regression-based path analysis, once the mediators are supposed to be in the same hierarchical level. The significance of indirect effects was assessed by bootstrapping (K = 5000). Bootstrap confidence intervals respect the irregularity of the sampling distribution of the indirect effect. This procedure also reduces the bias of a predominantly non-parametric data. We also conduct a percentile-based bootstrap confidence interval (CI) for the indirect effect. If the confidence interval does not contain the number zero, it provides evidence of a significant indirect effect. A pairwise comparison between specific indirect effects was used to test whether one indirect effect is statistically different from another. The criterion for statistical significance was *p*-value <.05.

RESULTS

Table 1 shows demographic characteristics and the scores on the neuropsychological tests according to each diagnostic group. The groups significantly differed in age and education, and on all neuropsychological measures. Pairwise comparison showed no significant differences in demographic variables and scores on the sTCFT, TOL, Five Digit test, Corsi Blocks Span (backward component) between the controls and aMCI groups. Controls and aMCI subjects performed better than mdaMCI and AD subjects on the neuropsychological tests. Subjects with mdaMCI had statistically significant higher scores on the MMSE, and the TOL compared to AD subjects.

The parallel multiple mediation analysis using the ordinary least square method assessed the direct influence of planning on visuoconstructional ability and the indirect effect of the proposed mediators. The direct effect in the initial model (c = 0.225; $t = 4.449$; $p < .001$) was larger than the direct effect of planning on visuoconstructional ability in the model

Table 1. Participants' description and group comparisons

	NC (1)		aMCI (2)		mdaMCI (3)		AD (4)		Group comparisons			
	n = 26		*n* = 38		*n* = 29		*n* = 36					
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	K-W	*p*-Value	Post-hoc*	r
Age	70.58	7.17	73.03	7	77	7.43	76.17	7.11	13.59	.004	1 < 3, 1 < 4, 2 < 3	−0.41, −0.36, −0.26
Education	6.23	4.38	6.97	5.53	3.97	3.65	3.75	3.19	16.36	.001	1 < 3, 1 > 4, 2 > 3, 2 > 4	−0.32, −0.34, −0.35, −0.37
MMSE	26.85	3.04	26.58	2.03	23.52	3.17	21.33	3.25	53.02	<.001	1 > 3, 1 > 4, 2 > 3, 2 > 4, 3 > 4	−0.52, −0.67, −0.47, −0.72, −0.32
TOL	21.54	9.14	25.79	8.85	22.28	9.78	16.28	8.13	17.35	.001	1 > 4, 2 > 4, 3 > 4	−0.26, −0.47, −0.32
sTCFT Copy	19.23	5.53	19.84	4.47	15.41	5.63	14.81	6.2	23.45	<.001	1 > 3, 1 > 4, 2 > 3, 2 > 4	−0.40, −0.38, −0.46, −0.43
CSB	16.31	12.29	17.32	10.3	11.21	8.19	10.44	8.63	11.83	.008	2 > 3, 2 > 4	−0.31, −0.35
FDT Inhibition	3.19	5.11	3.05	3.63	7.21	7.54	5.86	7.09	8.82	.032	1 < 3, 2 < 3	−0.29, −0.28
FDT Switching	6.88	6.97	5.42	5.06	11.03	5.88	11.28	6.44	26.2	<.001	1 < 3, 1 < 4, 2 < 3, 2 < 4	−0.40, −0.37, −0.47, −0.49

MMSE = Mini-Mental State Examination; TOL = Tower of London Test; sTCFT = "Simplified" Taylor Complex Figure Test; CSB = Corsi Span Backward; FDT Inhibition = Five Digit Test Inhibition errors; FDT Switching = Five Digit Test Flexibility errors; NC = Normal Controls; aMCI = amnestic mild cognitive impairment; mdaMCI = multiple domain amnestic mild cognitive Impairment; AD = Alzheimer's disease; k-w = Kruskal-Wallis.* *p*-Values corrected for multiple comparisons with Bonferroni method (*p* = .008).

Table 2. Regression coefficients, standard errors, and model summary information for the parallel Multiple Mediator Model

		Consequent														
		M_1 (Working Memory)				M_2 (Cognitive Flexibility)				M_3 (Inhibitory Control)				Y (sTCFT Copy)		
Antecedent		Coeff.	SE	*p*		Coeff.	SE	*p*		Coeff.	SE	*p*		Coeff.	SE	*p*
X (Planning)	a_1	0.413	0.09	<0.001	$\mathbf{a_2}$	−0.178	0.06	0.003	$\mathbf{a_3}$	−0.137	0.06	.016	**c’**	0.108	0.05	.025
M_1		—	—	—		—	—	—		—	—	—	$\mathbf{b_1}$	0.107	0.05	.022
M_2		—	—	—		—	—	—		—	—	—	$\mathbf{b_2}$	−0.270	0.07	<.001
M_3		—	—	—		—	—	—		—	—	—	$\mathbf{b_3}$	−0.180	0.08	.021
Constant		4.940	2.06	0.018		12.445	1.38	<0.001		7.74	1.32	<.001		16.701	1.42	<.001
		$R^2 = 0.15$				$R^2 = 0.07$				$R^2 = 0.04$				$R^2 = 0.37$		
		F(1,127) = 22.17, *p* = <.001				F(1,127) = 9.24, *p* = .003				F(1,127) = 5.96, *p* = .016				F(4,124) = 18.46, *p* <.001		

Note. Mediation model using OLS regression. 1 = Corsi Blocks Span Backward; 2 = Five Digits Test Flexibility errors; 3 = Five Digits Test Inhibition errors; X = Tower of London; Y = Simplified Taylor Complex Figure Test.
Coeff = coefficient; SE = standard error.

including the 3 mediators (c’ = 0.108; $t = 2.262$; $p = .025$) (Table 2 and Figure 1). The mediation model found that planning was also significantly associated with all mediators variables (working memory, cognitive flexibility, and inhibitory control) (Table 2 and Figure 1). As the direct effect did not decrease to zero when the mediators were included in the model, we have evidence of partial mediation effect.

Planning was positively associated with working memory, and negatively associated with cognitive flexibility and inhibitory control (Figure 1, paths a). It should be noted that these negative associations are due the fact that scores used as measure of cognitive flexibility and inhibitory control were in different metric in relation to the others. Each mediator predicted the sTCFT copy when controlling for planning and the others mediators (Figure 1, paths b). We further tested which variables were significant mediators of the effect of planning on visuoconstructional abilities by assessing the confidence interval of the indirect effect of working memory, cognitive flexibility and inhibitory control on visuoconstructional abilities. We used a 5.000 resampling approach and found a significant positive indirect effect of working memory (point estimate = 0.044, 95% percentile CI = 0.012 to 0.082), and cognitive flexibility (point estimate = 0.048, 95% percentile CI = 0.014 to 0.094). However, the indirect effect of inhibitory control was not significant (point estimate = 0.025, 95% percentile CI = –0.0003 to 0.062). We performed a pairwise comparison between the indirect effects of planning through working memory and cognitive flexibility to test which mediator have a stronger indirect effect on visuoconstructional ability. There was no significant differences between them (point estimate = –0.004; 95% percentile CI = –0.059 to 0.0489).

DISCUSSION

The aim of this work was to investigate whether core components of executive functioning mediate the relationship between planning and the performance of a complex figure copy test. We found that working memory, and cognitive flexibility exerts partial mediation effects on the relationship between planning and the copy of the sTCFT. Our results helped to parse out the mediating effect of working memory and cognitive flexibility and support the hypothesis that working memory, and cognitive flexibility are critical to the adequate performance of visuoconstructional tasks (Diamond, 2013; Guérin et al., 1999)

We tested the effect of aspects of executive functioning as mediators of the relationship between planning and visuoconstructional ability from a hierarchical perspective (Diamond, 2013). We found that working memory and cognitive flexibility, but not inhibitory control, were partial mediators of this relationship. Our results are in line with the literature (Freeman et al., 2000; Guérin et al., 1999). Moreover, we can hypothesize that the “online” interaction between working memory and cognitive flexibility allow a subject to change the spatial perspective and to adopt

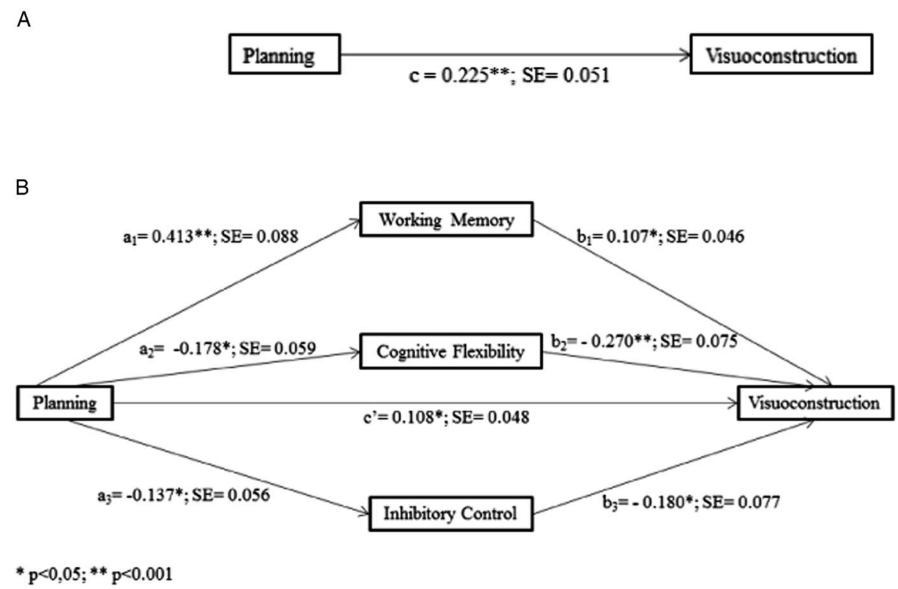

Fig. 1. A: Total effect of planning on visuoconstruction. B: Direct and indirect effects of planning on visuoconstruction through mediators. *Legend.* Planning: Tower of London, Visuoconstruction: sTCFT copy, Working Memory: Corsi Blocks Span Backward, Cognitive Flexibility: Five Digits Test Flexibility errors, Inhibitory Control: Five Digits Test Inhibition errors.

different strategies to perform adequately on visuoconstructional tests. However, as these executive function aspects are partial mediators of the relationship between planning and visuoconstructional abilities, additional studies are necessary to understand fully how planning and visuoconstructional abilities are interrelated. The central component of inhibitory control of our task is cognitive inhibition. Cognitive inhibition is essential for performance on working memory tasks (Diamond, 2013). The lack of specificity of our inhibitory control task can partially explain why inhibitory control was not an indirect mediator of the relationship between planning and visuoconstructional.

Previous studies also found a significant association between inefficient planning and inaccurate drawing performance in older adults. Elderkin-Thompson et al. (2004) assessed older adults with depression and found an association between poor planning and a more inefficient organization of complex figure copy, compromising its quality. Freeman et al. (2000) found a relationship between planning and quality of copy of a complex figure test in a study with healthy elderly and demented patients. They have found that healthy elderly had better planning, reproducing better the elements of the figure, having better performance on copy of a complex figure.

The influence of executive functions in cognitive performance is not restricted to visuoconstructional ability. Theories have been defined executive functions as a manager of metacognition of other cognitive processes and behavior (Goldberg, 2001; Prencipe et al., 2011). Studies have demonstrated the importance of executive functions for efficient episodic memory encoding and retrieval, and for adequate performance in complex activities of daily living in older adults (Bouazzaoui et al., 2013; Craik & Rose, 2012; Pereira, Yassuda, Oliveira, & Forlenza, 2008; Unsworth, Brewer, & Spillers, 2011). Altogether, executive functions and its components seem to be higher-order metacognitive processes that influence the performance of several cognitive domains such as episodic memory and visuoconstructional ability. Within this perspective, executive functions can be viewed as a cognitive hub that controls and manipulate several processes leading to optimal performance of other cognitive domains.

The present should be viewed in light of its limitations. First, we included a relatively small sample of subjects what might limit the power of the analysis. However, our sample size is powered to detect a moderate or large effect size, but may not be sensitive to small effects. The participants were recruited from a convenience sample, and the current findings may not be generalized to other populations. We did not control the analysis for age and premorbid intelligence. As these variables can influence planning abilities, they might have had some impact on the current results (Gallagher & Burke, 2007; Köstering, Stahl, Lenhart, Weiller, & Kaller, 2014; Strauss, Sherman, & Spreen, 2006; Zook, Davalos, DeLosh, & Davis, 2004; Zook, Welsh, & Ewing, 2006). We need to acknowledge that all of the executive functions tasks have a significant visuospatial component in addition to its core measurement. Therefore, the association found between visuoconstruction and executive functions may reflect, in part, shared method variance between the tests, that may have influenced and partially explain the present results. Finally, we could not state whether the direct effect is larger or smaller than the indirect effects, because there is no consensus as to which method is the most appropriate to measure the effect sizes on multiple mediators model (Hayes, 2013; Preacher & Kelley, 2011). Therefore, additional studies including larger samples recruited from community-based studies are necessary to confirm the present results.

In conclusion, we found that cognitive flexibility and working memory are partial mediators of the relationship between planning and visuoconstructional abilities. To our knowledge, our study is the first to attempt to understand how planning exert its effect on a complex figure copy in a heterogeneous sample of elderly subjects. Given the importance of visuoconstructional abilities and the lack of information about its mediators, future studies are necessary to provide a deeper understanding of the factors that influence this cognitive domain.

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