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Cognitive reserve in elderly: neuropsychological aspects and the education role in the latest findings

Reserva cognitiva no idoso: aspectos neuropsicológicos e o papel da educação nas últimas descobertas

João Gabriel Magalhães Dias^{1*}, Pablo Rodrigo Andrade da Silva^{1*},
Tânia Corrêa de Toledo Ferraz Alvez²

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ABSTRACT: The elderly population is growing worldwide, and therefore cognitive decline and dementia is a major problem for healthcare system. However, many elders do not develop dementia or significant cognitive impairment even though present brain lesions, such as cortical atrophy and/or lesions, leading to the concept of Cognitive Reserve (CR). The main objective of this review is to establish the recent findings of CR in elderly cognition and explore some of the cognitive markers related to CR. In order to accomplish that we carried out a search for papers published either in English or Portuguese language in the last 5 years in the Medline database using as keywords *cognitive reserve, elderly* and *aging/ageing*. We filtered 14 studies that specifically approached the neuropsychological aspects (e.g. memory, attention, orientation, executive function) and reviewed them in detail. Based on these papers regarding old-aged individuals, education appears to have several implications on CR by strengthening cognitive abilities, however does not appear to impact on cognitive decline. Besides, we realized that cognitive performance is one of the form to measure CR, even though the methods cannot be standardized, which may be the cause of some varied conclusions. Regarding CR, education was the most prevalent measure, and CR seems to have a beneficial effect on

executive function and episodic memory and it seems to act by both neural reserve and neural compensation. Print exposure appears as a potential variable positively related to cognitive performance and CR.

Keywords: Cognitive reserve; Aged; Aging.

RESUMO: A população idosa está crescendo mundialmente e, portanto, declínio cognitivo e demência são um grande problema para o sistema de saúde. Contudo, muitos idosos não desenvolvem demência ou algum prejuízo cognitivo significativo, mesmo que apresentem lesões cerebrais, como atrofia e/ou lesões corticais, levando ao conceito de Reserva Cognitiva (RC). O principal objetivo dessa revisão é estabelecer as descobertas recentes da RC na cognição dos idosos e explorar alguns dos marcadores cognitivos relacionados à RC. Com o intuito de conseguirmos nosso objetivo, nós realizamos uma pesquisa por artigos publicados tanto em língua inglesa quanto portuguesa, nos últimos 5 anos, na base de dados Medline usando como palavras chave: reserva cognitiva, idoso e envelhecimento. Nós filtramos 14 estudos que abordavam especificamente aspectos neuropsicológicos (p.e, memória, atenção, orientação, função

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1. Universidade de São Paulo, Faculdade de Medicina, São Paulo, Brazil. E-mails: joao.gabriel.dias@usp.br, pablo.silva@usp.br.

2. Universidade de São Paulo, Faculdade de Medicina, Departamento de Psiquiatria, São Paulo, Brazil. E-mail: tania.ctfalves@hc.fm.usp.br

Corresponding author: Pablo R. Andrade. University of São Paulo, São Paulo Medical School, Brazil. Av. Dr. Arnaldo, 455. Cerqueira César - São Paulo, SP, Brasil. CEP: 01246-903. E-mail: pablo.silva@usp.br

executiva) e os revisamos em detalhes. Baseados nesses artigos em relação a idosos, educação parece ter várias implicações na RC por fortalecer habilidades cognitivas, contudo não parece impactar no declínio cognitivo. Além disso, notamos que performance cognitiva é uma das formas de se medir RC, embora os métodos não possam ser padronizados, o que pode ser a causa de conclusões diversas. Em relação à RC, educação foi

INTRODUCTION

The elderly population is growing worldwide. The decrease of mortality rates in whole world has implications in increase of life expectancy. According to World Health Organization (WHO), there are 764,852 people over 60 years at 2010¹. Furthermore, the projections indicate 1.2 billion of elderly individuals at 2025², which may reach 2 billion at 2050³. In Brazil, both life expectancy and age structure has undergone profound changes with progressive increase of the life expectancy at birth⁴ and most elderly participation in demographic distribution⁵. Therefore, cognitive decline and dementia is and will be a major problem for health system worldwide.

The ageing population is directly linked with dementia prevalence leading to a great impact on health costs due to functional impairment and a consequent dependence condition of patients. However, many elders do not develop dementia or significant cognitive impairment even though present brain lesions, such as cortical atrophy and/or lesions. Those issues fit into the concept called Cognitive Reserve (CR). Actually, CR is the hypothesized capacity of the mature adult brain to compensate for the effects of a disease or injury that would be sufficient to cause clinical dementia in an individual with less CR^{6,7,8}. Applying this hypothesis to dementia, CR predicts that older adults with higher CR will have a lower risk of developing overt features of dementia than individuals with less CR. Neuropsychological aspects, as educational life, are seen as one of the most relevant elements in an active model of CR, as well as brain structure, which directly implies a more quantitative concept of reserve: a brain (or passive) reserve⁷.

Nevertheless, studies focus on specific neuropsychological domains implicated in CR and the comparison about the intrinsic relationship between the various domains are rare. About cognitive functions, it is possible to list several related aspects, including attention, executive function, memory, learning and intelligence. The last studies have shown some of these aspects are associated to age-related cognitive development and/or for their decline^{9-13,15-22}. Therefore, the main objective of our paper is to establish the recent findings on CR in elderly cognition as well as how certain cognitive markers are related with CR in elderly individuals. In other words, our

a medida mais prevalente e RC parece ter um efeito benéfico em função executiva e memória episódica, de forma que parece agir através tanto da reserva neural quanto da compensação neural. Exposição a textos impressos parece ser uma variável em potencial relacionada com a performance cognitiva e RC.

Descritores: Reserva cognitiva; Idoso; Envelhecimento.

work exposes and discusses the relationship between CR and Elderly Cognition.

Search strategy and selection criteria

This work is an academic and scientific production which comprises a didactic nature. All our results were finally selected for the relationship between Cognitive Reserve and Elderly, more specifically about Neuropsychological Aspects and its last findings. Firstly, we carried out a meticulous research into the Medline database - The National Research Register via Pubmed, using as keywords some medical subject heading terms: *cognitive reserve*, *elderly* and *aging/ageing*. We selected only the papers written in the last five years, covering the period between 2009 and 2014. This strategy led us to get a total of 173 papers. The flow chart 1 resumes the selection process of the papers reviewed here.

Inclusion criteria

For inclusion in this review, we selected the papers that could give us the needed substrates to better understand the latest findings about how cognitive reserve and ageing in humans are associated. Initially, we filtered the articles using the Pubmed filter for humans and language; We solely chose the papers written in English or Portuguese language. The next step was to filtered the relevant papers by excluding reviews and by reading the title and excluding those that were not directly related to this review, for example the articles about animal experiments that eventually passed through the previous filter. If the title were relevant to the theme, we included the article for posterior analysis. This preliminary scan resulted in 80 papers selected. Subsequently, we screened independently the abstracts and selected potentially relevant articles. At this stage we excluded reviews, aside from original papers that we have not access using the Open Access Medline, VPN USP, ResearchGate and Google Scholar. Those articles were considered not relevant papers for this review.

At the end of this stage, we reached 64 original studies that we can download. After carefully reading those

papers, we excluded six papers, four articles were not relevant at the final reading and two were about studies in progress. Our next step was to study the original articles compiled and set up a table with the following topics: author and year of publication; sample characteristics; study methodology; results; relevant observations and CR markers. Besides at this point, we organized the papers in many categories in order to facilitate the analysis and then we filtered 14 studies that specifically approached

the neuropsychological aspects (e.g, memory, attention, executive function). Thus, the others studies that approached “categories” as Brain Structure, Life Habits and Events were do not included in this review. However, we also included education to understand its role on the interface between CR and the neuropsychological aspects of cognition.

The flowchart below resumes the selection process and retrieving articles.

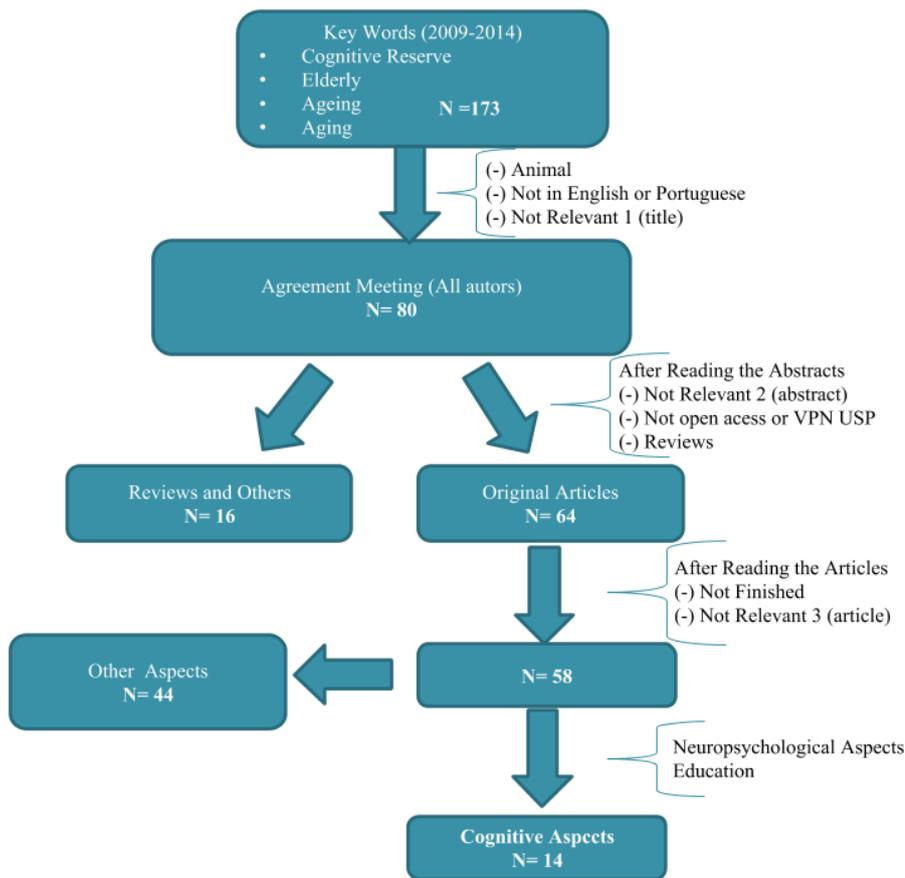


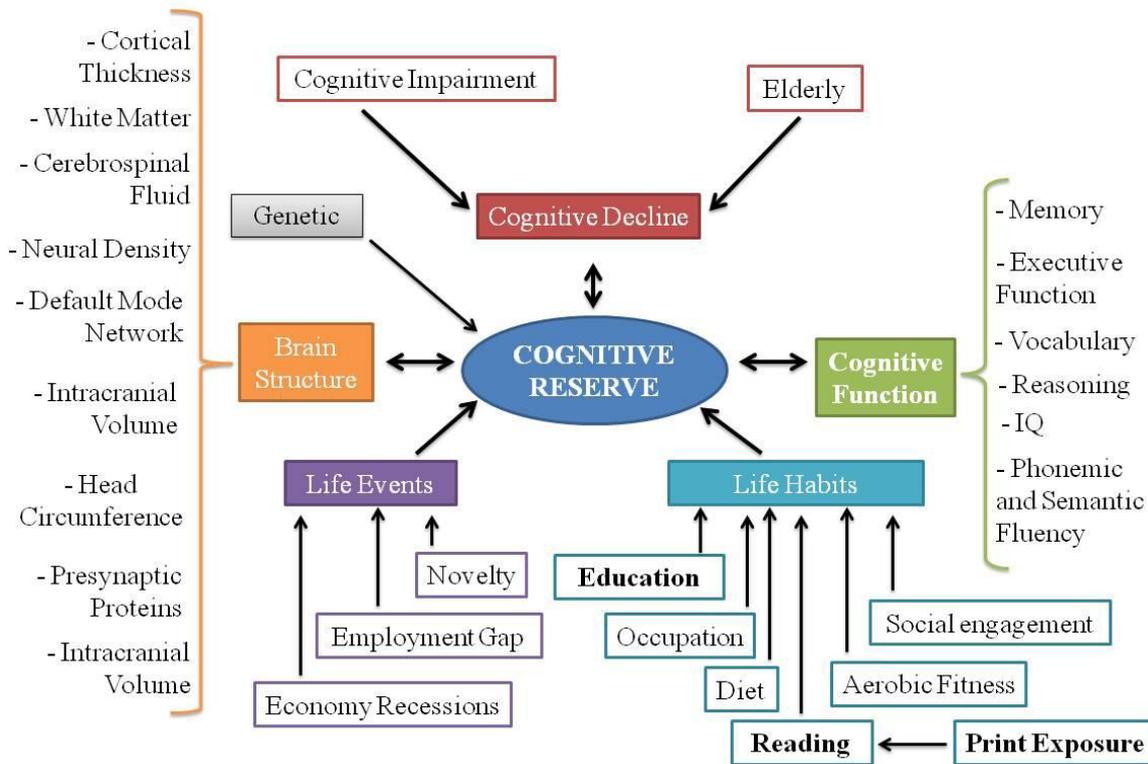
Figure 1. Selective process and retrieved papers regarding Cognitive Reserve

RESULTS AND DISCUSSION

We propose to study the neuropsychological aspects of Cognition in three approach axes: the relationship between CR and its markers, the evaluation for cognitive performance and the interface with education, which was the most recurrent component of CR found in our review.

Based on those 58 papers that we categorized, we developed a scheme with the possible domains and associations of CR^{9-22,25-68}. In bold, we highlight the specific topics that will be approached in this review. The scheme 1 represents the major aspects that being investigated in the

past 5 years regarding cognitive reserve. It is noteworthy that this figure does not express a relation necessarily found between CR and these studied topics. At least in the last five years, researches on the Cognitive Reserve orbited around 7 topics: Cognitive Function^{9-12,18-22,56}, Brain Structure^{8,27-29,35,37,39,42,47,49,58,59,65}, New Methods of Measure^{36,48,50,60,66}, Life Habits^{13-17,25,30-32,34,43,46,52,64}, Life Events^{44,45}, Cognitive Decline^{26,33,38,40,41,51,54,55,57,61,63,67} and Genetic Factors^{53,62}.



Scheme 1. Latest topics considered in studies regarding cognitive reserve

Cognitive reserve and its markers

About markers for CR, the most papers use some education measures, which can be a direct measure of years of education, literacy or educational level. Others recurrent forms of evaluate CR are vocabulary and reading performance, which can be related to education in some ways. It is noteworthy that even if certain CR markers are demonstrably related to the CR, they still only being indirect measures, since no one has yet defined the mechanism for CR formation.

Accordingly to our literature review, education is the most studied topic related to CR, being years of studies the most used marker^{10,12,18,21,22}. Nevertheless, others markers could be also associated to education, such as fluid intelligence (IQ measures), specially the subtests that involve vocabulary (fluid intelligence), whereas the crystalized intelligence (evaluated through another part of IQ subtests) is more related to innate capacities and is less influenced by education. Investigating intelligence quoeficient (IQ), Ritchie et al.¹⁶ demonstrated a positive association of education with IQ, mainly among children with lower initial IQ and even into later life. Reading and vocabulary performance are often measured using respectively tests like WAIS-R²³ and NART²⁴ which can be used as IQ indicators. Therefore, the major types of CR

markers found in this review are at least indirect related with education, strengthening our belief that education is one of the most important values associated with CR.

Besides, Giogkaraki et al.¹⁸ reported that CR attenuates the negative impact of ageing on verbal episodic memory and on executive function when they used years of education, vocabulary and reading performance as markers for CR. CR also improves the benefits of executive function and episodic memory against gait speed decline according to Holtzer et al.²⁰, that only used vocabulary performance to evaluate CR. Both studies focus on an elderly populations.

About neural mechanisms (neural reserve and neural compensation), Ansado et al.⁹ evaluated the attention of young and elderly people through a visual activity with two demands of difficulty. In this task, the participants were exposed to different types of visual situations: in one case they needed to indicate if the target letter matched with one of the probe letters; and in the other case if all letters were in uppercase or not. **At the end of the study, they concluded that at low level of task demand, neural compensation was present in elders, whereas at high level both neural compensation and neural reserve were observed.** Futhermore, Steffener et al.¹⁰ found that elderly people maintain their task performance despite the brain changes by possible using both mechanisms of CR, evaluated by years of education and IQ. These findings

suggest that elderly people use both neural reserve and neural compensation mechanisms to cope with increase in task demand.

Among the newest findings, CR was related with initial gait speed, and an association between gait speed decline with higher initial CR in elders, as reported by Holtzer et al.²⁰. On the other hand, Puccioni and Vallesi²¹ measured CR by years of education, occupation, usual activities and they showed an association of CR with speed processing. Yet in the study of Singh-Manoux et al.¹⁹, no correlation was detected between CR and the rate of cognitive decline. They quantified CR by height, education and occupation and each of these markers had three levels: low, intermediate and high. Education and occupation were considered a marker for active reserve, while height was a marker for passive reserve based on Brickman et al.⁸.

Their results indicate that only the high occupation group showed a faster decline on cognition and no difference was noted in the rate of cognitive change among the others occupation groups, neither in the education and height groups. Similar results were noted for Barulli et al.¹², which no found significant interactions between age and the CR (years of education and reading performance) on reaction time, although the study evaluated only 18 participants. Even so, some results can not be extrapolated to the elderly population in general. Puccioni and Vallesi²¹ and Barulli et al.¹² only considered a very small sample, 23 and 18 individuals respectively. Besides, a negative point of Singh-Manoux et al.¹⁹, a 10-year study, was the low mean age at baseline, 56 years old.

The Table 1 below describes the CR markers used by the articles.

Table 1. The CR markers

Paper	CR Markers
Giogkaraki et al. ¹⁸	CR as a latent variable: years of education, vocabulary, and reading performance
Singh-Manoux et al. ¹⁹	CR markers: height, education (highest qualification) and occupation
Holtzer et al. ²⁰	CR marker: vocabulary performance
Puccioni; Vallesi ²¹	CR index questionnaire: years of education, occupation, usual activities
Ansado et al. ⁹	Neural compensation and neural reserve as mechanisms of cognitive reserve
Steffener et al. ¹⁰	CR as a factor score: years of education and IQ (reading and vocabulary performance)
Barulli et al. ¹²	CR proxy: years of education and reading performance
Zahodne et al. ¹⁷	CR indicator: literacy (vocabulary performance)
Zimmerman et al. ²²	CR proxy: reading performance and years of education

Cognitive performance

Cognitive Performance can be understood as an individual performance in cognitive tests at a single time point, which is compared to that of other individuals, may be a control group as healthy youngers or elders. Besides education, others markers can be used to offer a possible measure of CR in elders. These measures include aspects of cognitive performance, as processing speed, response time and the selection strategy accuracy. We found articles that investigated these aspects in performance tests of attention, memory, reasoning, phonemic and semantic fluency. Among these type of tests, the first task measured visual attention⁹, while the last four task results were based on vocabulary measures by reading or education markers¹⁷. Moreover these factors, verbal conflict resolution is also studied in tasks to investigate response time and accuracy²¹. We understand all of these tasks as an indirect predictors of CR.

Comparing 16 healthy youngers to 16 healthy elders in visual selective tests with different levels of attention (low and high), Ansado et al.⁹ found that normal aging affects visual selective attention and causes more slower reaction time and slower accuracy, even though the elderly subjects maintained a good level in the performance test. Albeit elderly participants performed worse than young people at both low and high attentional load levels with regarding both to accuracy and reaction time, older people did not show an exacerbated performance decline at the higher load level with respect to the reaction time.

In other study, Barulli et al.¹², investigated the differences between young and senile performance based on cognitive tasks of mathematical procedures. Among the youngest group, they highlighted verbal IQ apparently did not predict better strategy selection, while among the oldest individuals, higher verbal IQ was associated to better strategy selection. However, the youngest group showed better accuracy than the older group in strategy

selection. In other hand, Puccioni and Vallesi²¹ realized the accuracy level was comparable in the two age groups in a study of verbal conflict resolution, even though older adults were slower than younger ones. In summary, the results of Puccioni and Vallesi²¹ work show that greater verbal intelligence is associated with better verbal conflict resolution.

While the results mentioned have been found in many studies comparing healthy elders to healthy young, we also selected papers that investigated cognitive decline by comparing healthy elderly and elderly with cognitive impairment, such as dementia. Likewise, the conclusions of these worked were based on cognitive performance. It is a consensus the cognition performance decline over the years. The questions are how this happen and what neuropsychological aspects decline. We found a significant number of articles that show no education involvement in age-related cognitive decline: over the years, the slowest decline was observed on verbal fluency domain when the elderly was evaluated for reading performance tasks¹⁷. We also found results that indicate the gait speed decline over the years²⁰. Moreover, while declines in memory, reasoning, phonemic and semantic fluency were also related over the years, vocabulary did not followed this pattern¹⁹. Against what were often hypothesized, those elderly with more grade of schooling completed exhibited the similar or slightly faster decline than those with less grade when the both groups are submitted to tests of verbal learning, short-term memory, executive function, processing speed and expressive language¹³.

On the other perspective, Payne et al.¹¹ study the relation between CR and Print Exposure. The last concept can be understood as an habitual and lifelong investment in reading and literacy activities^{68,69}. Their found results indicate that higher print exposure has impact in cognitive performance, being associated with more efficient lexical and orthographic processing, greater allocation of attention to clause wrap-up and better sentence recall. Besides, print exposure appeared to buffer against the effects of working memory capacity limitations on sentence recall.

Therefore, it is possible to affirm that cognitive performance is a recurrent form to assess cognitive status in elderly. Know about capacities, as attention or executive function, is an important form to study and to infer conclusions about the influence of CR in aging cognitive development.

The Table 2 below describes the methods used by articles in the investigation of cognitive performance aspects, the direct markers of CR.

Education

We decided to approach education in a exclusive topic due to its relevance and recurrence in papers used in this review. As discussed above, education is a common

measure for CR, still here we focus on analyze by what means education operates in CR.

To start, we find in some results that appear to be contradictory at first glance. While Ritchie et al.¹⁶ did not find significant association between education and processing speed, Zahodne et al.¹⁷ found a relation between this two values, yet regarding the four domains covered in this study (verbal processing speed, working memory, verbal fluency, and verbal episodic memory), processing speed had the smallest relation with education, while verbal fluency was the greatest. This difference may be due to difference in the age groups and in the methodology. Zahodne et al.¹⁷ used individuals ranged 54-94 years, with low mean age for elders, 68.9 years at the beginning, besides lexical decision and sentence verification to measure verbal processing speed. Already Ritchie et al.¹⁶ evaluated using reaction time (RT) and inspection time (IT) in two longitudinal sample, one when the participants were nearly with 83 years and the other with about 70. Thereby, the results of these two papers do not differ much, leading us to a possible conclusion that education does not influence or has small effect on processing speed.

Moreover, Gottesman et al.¹³, and Zahodne et al.¹⁷ found a positive association between education and cognitive performance in two longitudinal studies with large population sample. Already Huang and Zhou¹⁵ were beyond: their findings suggest a causal effect of education on cognition and, despite the large number of participants, 2685, they only had information from individuals living in two provinces of China (Gansu and Zhejiang). One possible issue of Gottesman et al.¹³ and Zahodne et al.¹⁷ is that they used data from individuals under the age of 60 years, which could affect the analysis exclusively for older people. Nevertheless, the facts that in Zahodne et al.¹⁷ the results of individuals with less and more than 70 were quite similar and in Gottesman et al.¹³ was a 20-year longitudinal study attenuates the potential complications of these studies.

In an ethnically-diverse population (Caucasian, African American, Hispanic/White, Hispanic/Black, Asian and others ethnicities) living in Bronx, New York, Zimmerman et al.²² found that elderly individuals with fewer years of education suffer more with the negative impacts of sleep difficulties on verbal fluency than those with more years of study, but no difference between the age groups of individuals without difficulties for sleep was detected. In another study, Farfel et al.¹⁴ demonstrated the importance of the relation between even a few years of education with reduced cognitive impairment on elderly people. A positive point of this Brazilian sample was the high mean age, 74 year. However, as well as described above, a possible problem to expanded the results for the elderly population in general was to included individuals between the ages of 50-60 and another possible complication is that

the data were not obtain directly from the participants but through a informant, since it was a postmortem study, so the measures may not be as accurate. Regarding education and cognitive decline, Gottesman et al.¹³ showed that those with more grade of schooling completed exhibited similar

or slightly faster decline than those with less grade and Zahodne et al.¹⁷ did not find association between education and cognitive decline over the years. These findings suggest that education increases cognitive abilities rather than interfere on cognitive decline in elders.

Table 2: The investigation methods of cognitive performance

Cognitive performance aspects	Method
Attention	Digit Span subtest from the <i>Wechsler Adult Intelligence Scale 3rd edition – WAIS-III</i> ⁷⁰
Visual attention	a. Adaptation of a task developed by Banich ^{71,72} b. <i>Trail Making Test part A - TMTA</i> ⁷³
Verbal processing speed	a. Lexical Decision: speeded word/non-word ¹⁷ ; <i>Components of fluent reading</i> ⁷⁴ b. Sentence Verification: speeded plausible/improbable sentence ¹⁷ ; <i>Information processing correlates of reading</i> ⁷⁵
VerbalWritten fluency	a. Written fluency tests from the <i>Manual for Kit of Factor-Referenced Cognitive Tests</i> ⁷⁶ b. Category Fluency and Letter Fluency tests of <i>Multilingual Aphasia Examination - MAE 2nd ed.</i> ⁷⁷ c. Phonemic and Semantic fluency: Adapted from <i>Word fluency and brain damage</i> ⁷⁸
Verbal learning	Delayed Word Recall Test obtained from <i>A verbal memory test with high predictive accuracy for dementia of the Alzheimer type</i> ⁷⁹
Vocabulary	a. <i>Manual for Kit of Factor Referenced Cognitive Tests</i> ⁷⁶ b. <i>Mill Hill vocabulary test</i> ⁸⁰
Executive function	a. Digit Symbol Substitution Test of the <i>WAIS-III</i> ⁷⁰ b. Word Fluency Test ⁸¹ c. Trail Making Test part B - TMTB ⁷³
Speed of processing	Digit Symbol Substitution Test of the <i>WAIS-III</i> ⁷⁰
Expressive language	Word Fluency Test ⁸¹
Conflict resolution and Conflict adaptation	Stroop task obtained from <i>Sequential congruency effects: Disentangling priming and conflict adaptation</i> ⁸²
Episodic memory	Free and Cued Selective Reminding Test - FCSRT ⁸³
Verbal episodic memory	a. Word list learning and two story memory tasks from <i>The Victoria Longitudinal Study: from characterizing cognitive aging to illustrating changes in memory compensation</i> ⁸⁴ b. Logical Memory Story subtest from the <i>Wechsler Adult Intelligence Scale 3rd edition – WAIS-III</i> ⁷⁰ c. <i>Hopkins Verbal Learning Test - Revised</i> ⁸⁵
Short-term memory	Delayed Word Recall Test ⁷⁹
Working memory	a. Sentence Construction: <i>Memory Change in the Aged</i> ⁸⁶ b. Listening and Computation ¹⁷ c. Adapted from <i>Decomposing adult age differences in working memory</i> ⁸⁷
Mathematical reasoning	a. Modified version of the computational estimation task obtained from <i>Adults' age-related differences in adaptivity of strategy choices: Evidence from computational estimation</i> ⁸⁸ b. Math Reasoning: Heim A. <i>Manual for the AH4 group test of general intelligence</i> . Windsor, UK; 1970. = Alice Heim 4-1 (AH4-I) ⁸⁹
Print exposure	<i>The Author Recognition Test - ART</i> ⁶⁹

The Table 3 below describes the findings results about education accordingly to the articles used in this review.

Table 3: The education role

Paper	Relations of education
Gottesman et al. ¹³ and Zahodne et al. ¹⁷	↑ education ↔ ↑ cognitive performance
Huang; Zhou ¹⁵	↑ education → ↑ cognition
Zimmerman et al. ²²	↓ education and difficulties for sleep ↔ ↓ verbal fluency Education and no difficulties for sleep ↔ verbal fluency
Farfel et al. (2013) ¹⁴	Few years of education ↔ ↓ cognitive impairment
Gottesman et al. ¹³	↑ education ↔ or ↔ ↑ cognitive decline
Zahodne et al. ¹⁷	Education ↔ cognitive decline Education ↔ processing speed
Ritchie et al. ¹⁶	Education ↔ processing speed

FINAL CONSIDERATIONS

In this review, we had selected papers which mostly approached populations that are quite different in socioeconomic aspects compared to Brazilian population. This factor may be a limit to extend the results to countries, such as Brazil or others developing countries, particularly when it approached as education. Furthermore, with an approach on three major topics we noted the existence of many ways to evaluate neuropsychological aspects, both considering cognitive performance tasks and statistical analysis, which may be the cause of some dissonance in results. Besides, several methods to measure CR were also found and the most of them are based on some aspect related to education. In particular, the measure of education is questionable when used only years of (formal) education,

which is just a quantitative variable. Thus, we consider that qualitative aspects of education be necessary to understand in detail how education modulates CR. Based on the results concerning elderly people, education seems to interfere mainly on cognitive abilities than on cognitive decline and CR appears to have a positive effect on executive function and on episodic memory. Both neural reserve and neural compensation are possible mechanisms of CR. Albeit one article approached the relation between Print Exposure and Cognitive Performance, the results suggest that Print Exposure can be a CR marker due to its capacity to buffer against the effects of cognitive decline, as the working memory capacity limitations on sentence recall. We consider this topic needs more investigation in order to evaluate the capacity of Print Exposure measure CR.

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