
Neurocognitive decline in familial caregivers of Alzheimer disease patients: A Systematized Review

Disminución neurocognitiva en los cuidadores familiares de pacientes con enfermedad de Alzheimer: Una revisión sistematizada

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Abstract

Alzheimer's disease (AD) is the most prevalent among all dementias. The assistance to AD patients is primarily provided by familial caregivers, who play an important role in the management of the patient's basic needs. Some studies suggest that these caregivers suffer from chronic stress, which may imply significant changes in important brain structures responsible for cognitive processes. The purpose of this review is to synthesize the literature that examined the Neurocognitive Functions (NF) of familial caregivers of AD patients. This review has three objectives: 1) identify which NF are affected the most in familial caregivers of AD patients, 2) identify the tests that the reviewed studies used to measure NF, and 3) identify whether there are studies conducted in Puerto Rico that examined the NF of familial caregivers of AD patients. A review search was carried out through EBSCOhost, ScienceDirect, PubMed, and Google Scholar databases. Through the evaluation process of judges, the articles for the final sample were determined. Descriptive and frequency analyses were conducted. A total of 10 articles met the inclusion criteria; from these, 7 identified that the NF affected in familial caregivers most reported in this review were attention, working memory, and processing speed. The instruments most frequently used to detect these deficits were the Trail Making Test, Stroop Test and Mini Mental State Examination. We suggest conducting research on the NF of informal caregivers of AD patients in Puerto Rico in order to provide information for the development of interventions for this population.

Keywords: Caregivers, Alzheimer's disease, Neurocognitive decline, and Neurocognitive Functions

Resumen

La enfermedad de Alzheimer (EA) es la más común entre las demencias. La asistencia a los pacientes con EA es brindada principalmente por familiares. Algunos estudios sugieren que los cuidadores sufren de estrés crónico, lo que puede implicar cambios significativos en estructuras cerebrales responsables de procesos cognitivos. El propósito de esta revisión fue sintetizar la literatura que examinó las Funciones Neurocognitivas (FN) de los cuidadores familiares de pacientes con EA. Esta revisión tiene tres objetivos: 1) identificar qué FN se ven más afectadas en los cuidadores familiares de pacientes con EA, 2) identificar las pruebas que los estudios revisados utilizaron para medir la FN, y 3) identificar si existen estudios realizados en Puerto Rico. Se realizó una búsqueda en bases de datos EBSCOhost, ScienceDirect, PubMed y Google Scholar. A través del proceso de evaluación de jueces se determinaron los artículos para la muestra final. Se realizó análisis descriptivo y de frecuencia. Un total de 10 artículos cumplieron los criterios de inclusión; de estos, 7 identificaron que las FN afectadas en los cuidadores familiares más reportadas en esta revisión fueron la atención, la memoria de trabajo y la velocidad de procesamiento. Los instrumentos utilizados con más frecuencia para detectar estos déficits fueron el *Trail Making Test*, el *Stroop Test* y el *Mini Mental State Examination*. Sugerimos realizar investigaciones sobre las FN de los cuidadores informales de pacientes con EA en Puerto Rico con el fin de brindar información para el desarrollo de intervenciones para esta población.

Palabras claves: Cuidadores, Enfermedad de Alzheimer, Deterioro Neurocognitivo y Funciones Neurocognitivas

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Alzheimer's disease (AD) is the most common cause of dementia among older adults. The disease is characterized by a progressive decline of cognitive and functional abilities. According to the World Health Organization (WHO, 2015), 47.5 million people have dementia, with 7.7 million cases every year, expected to increase to 75.6 million by 2030. In Puerto Rico, there are 20,910 cases diagnosed with AD of which 64.8% are women (DSPR, 2019). The National Institute of Health (NIH, 2019) indicates that AD currently ranks as the third leading cause of death in the United States, while in Puerto Rico, AD ranks as the fourth cause of death (DSPR, 2019).

Due to the loss of cognitive and functional abilities, AD patients require caregiving. *Caregiving* refers to the attendance of another person's health needs, including daily living activities, emotional support, and other forms of help (Alzheimer's Association, 2019). The caregiving of AD patients is an effortful task that demands strict commitment, particularly in Latino families with a high level of familismo (Borsje et al., 2016; Correa et al., 2015). *Familismo* refers to an umbrella of values, attitudes, beliefs, and norms that Latinos have regarding the importance of family loyalty, closeness, maintaining good relationships, contributing to the well-being of the family nucleus, and the extended family. (Guillermo-Ramos et al., 2007; Ayón, Marsiglia, & Bermudez-Parsai, 2010). The values of familismo are instilled from childhood. Reyes-Blanes and Vazquez-Montilla (2000) interviewed 250 Mexican and Puerto Rican parents to learn the expected values of children in general. Their content analysis revealed that parents expected their children to inhere the value: "to be close or his or her family". That is, parents expected children to prefer spending time with family than friends, to share confidences with family, and to show signs of affection such as kisses and hugs.

Guillermo-Ramos and colleagues (2007) explain that Latino caregivers grow up with a high level of familismo that has been introjected throughout their life from their family of origin. This high level of familismo can create a sense of commitment to care for the AD patient family member, or it could create increased pressure on the Latino caregiver. This could arise if the caregiver feels obligated to take care of the patient 24 hours a day. As a consequence, the failure to comply with this obligation may result in self-induced feelings of blame.

Neurocognitive Decline in Familial Caregivers

The familial caregivers are exposed to psychological distress that includes symptoms of burnout, depression, and anxiety disorder (Borsje et al., 2016; Dassel et al., 2017; Vitaliano et al., 2009). The mean age of caregivers is 63 (Administration on Aging, 2004). Due to the advanced age of the caregivers and the chronic stress and condition associated with the caregiving of AD patients, the familial caregivers are at risk of neurocognitive decline including dementia and other health complications (Correa et al., 2015; Vitaliano et al., 2009). High levels of cortisol seem to impact the prefrontal and hippocampal areas which may lead to impairments in the neurocognitive functions (NF) such as attention, working memory, processing speed and different types of storage memory (e.g., short term memory, long term memory; Correa et al., 2018). Studies suggest that cortisol levels in dementia caregivers impact the regulation of the hypothalamic-pituitary-adrenal (HPA) axis leading to hypercortisolemia (Vugt et al., 2006). The negative effect of hypercortisolemia can be related to the neurocognitive decline in caregivers (Correa et al., 2015).

Lathan and colleagues (2016) carried out a study to examine the relationship between psychosocial factors and cognitive

performance among caregivers of dementia patients. The authors found, that when comparing cognitive performance between dementia caregivers and controls, dementia caregivers perform worse than non-caregivers on tests of attention, information processing, processing speed, and short-term working memory. Furthermore, the authors found that caregivers of dementia patients reported high levels of stress and difficulty sleeping.

Similarly, Mackenzie and colleagues (2009) examined learning and memory in caregivers of cognitively impaired older adults. The authors found that caregivers reported significant levels of burnout and exhibit significantly higher levels of distress in comparison with non-caregivers. Also, the caregiver's performance was significantly poorer in learning and memory tasks. Previous studies also suggest that, in addition to physical and mental health problems, caregivers also exhibit cognitive deficits. However, little is known about caregiver's neurocognitive decline despite the impact that could have on effective self-functioning and the care of the AD patient. Most studies with familial caregivers are mainly focused on the effects of emotional distress and a minority of studies focused on the neurocognitive decline.

The purpose of this review is to synthesize the literature that examined the NF of familial caregivers of AD patients. This review has three objectives: 1) identify which NF are affected the most in familial caregivers of AD patients, 2) identify the tests that the reviewed studies used to measure NF, and 3) identify whether there are studies conducted in Puerto Rico that examined the NF of familial caregivers of AD patients.

The exact NF most affected in familial caregivers of AD patients is unknown. Additionally, it is important to identify the instruments used to measure the NF, since

the use of different instruments to measure the same NF may affect the studies comparisons and the interpretation of the data. The use of instruments not designed to evaluate NF such as general intelligence tests, screening, or behavioral scales, can affect the proper identification of deficits in these functions.

On the other hand, it is important to identify literature from Puerto Rico because, at the moment, individualized interventions addressing NF in familial caregivers were not identified. Although support groups were reported, these groups only address the emotional aspects related to caring for the patient with AD and not necessarily the NF of familial caregivers. This is an important issue due to the high levels of chronic stress that the familial caregiver experiences, which may lead to a neurocognitive decline. Thus, having a decline in their NF can compromise their quality of life and could affect the adequate care of the patient (Dassel et al., 2011).

Methods

Design

This is a Systematized Literature Review (De León-Casillas & Moreno-Torres, 2020) that included elements of PRISMA (Liberati et al. 2009). This Systematized Literature Review consisted of five phases. Phase I and II were conducted systematically following the preestablished protocol. Phase III and IV were conducted unsystematically (traditional). A Risk of Bias assessment of the literature was not conducted.

Table I
Phases of this Systematized Literature Review

Phases	Description	Systematization
Pre-Phase	Protocol Preparation	
Phase I	Article Identification and Search	Systematic
Phase II	Article Screening	Systematic
Phase III	Data Extraction	Unsystematic
Phase IV	Literature Synthesis	Unsystematic

Sources and Search Strategy

The literature review was conducted in four databases: EBSCOhost, ScienceDirect, PubMed, and Google Scholar databases. These databases were distributed amongst the reviewers by the first author. The following keywords were used for the literature search: Cognitive* Deficit OR (Cognitive* Function) OR (Neurocognitive* functions) OR (Neurocognitive* deficits), Caregivers* and Alzheimer's. The combination of such terms was applied in each of the databases. The filters applied were: Peer-Review, Full-Text and published between 2005-2019.

Inclusion/Exclusion Criteria

The selected articles had to meet the following inclusion criteria: 1) studies that administered a cognitive test or battery to caregivers of patients with AD; 2) the studies should have measured at least one NF: attention, memory, working memory or executive functions, 3) empirical studies.

Procedures

Identification and Search of the Literature. The literature review began with the initial searches in each database.

Firstly, each reviewer independently searched the assigned database using the preestablished search strategy previously mentioned. Secondly, each reviewer documented the search information (e.g., total of initial results).

Articles Screening. After the identification and search of the literature, the screening process began. Firstly, duplicates were removed. Secondly, each reviewer independently examined the eligibility of each article, starting with the Titles, Abstracts, and then the Full-Texts. The articles that did not meet the inclusion criteria were excluded. Thirdly, to minimize the bias, a second reviewer double-checked the included articles of each database.

Data Extraction. After the article screening, the data extraction was conducted independently by each reviewer. The data extraction was carried out using an Excel spreadsheet document. The information to extract from each article was: 1) title, 2) author(s), year of publication, 3) study's purpose, 4) study's objectives, 5) country where the study was carried out, 6) demographic characteristics of the sample, 7) study design, 8) cognitive assessment instruments used, 9) analysis 9) neurocognitive deficiencies identified and 10) limitations to determine its eligibility. Table I shows the selection process.

Data Analysis

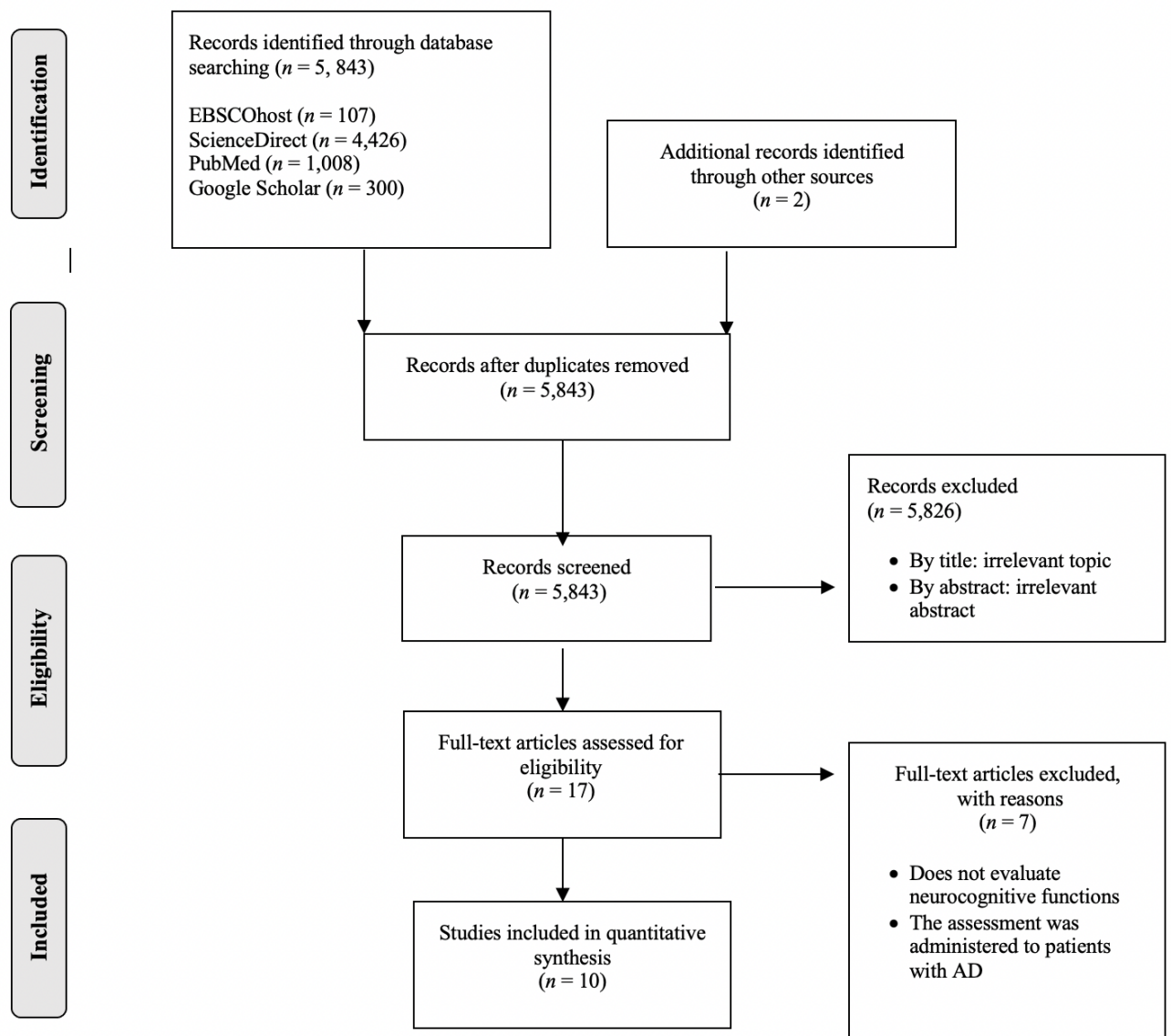
Before conducting the final analyses, data preparation was carried out. The extracted data that was on the Excel Spreadsheet was converted into Statistical Package for the Social Sciences (SPSS) variables. To calculate the Total Sample Number, the samples of each study were summed. Then, the same procedure was carried out but by sex to calculate the Total Number of Women Familial Caregivers. The Total Sample Age Range consists of the lowest age and the highest age reported

across studies. To calculate the Total Sample Mean Age, the mean sample age of each individual study was entered in SPSS and then descriptive analyses were conducted.

To achieve our objectives, three nominal variables were constructed in SPSS: 1) “NF of Caregivers”, 2) “Instruments used to

measure the NF of Caregivers” and 3) “Country of Study”. These nominal variables were developed based on the characteristics of each included study. The final analyses consist of frequency analyses conducted in SPSS for each of these nominal variables.

Figure I
PRISMA Flowchart



Results

Table II

Studies about neurocognitive performance in familial caregivers of Alzheimer's disease patients.

Authors	Purpose	Design	Sample	Neurocognitive Instruments	Results
Vitaliano et al. (2005)	Evaluate the neurophysiological correlation of cognitive deficits in family caregivers of patients with AD.	Quasi-experimental/ Cross-sectional/ Correlational	$n = 96$ (caregivers) $n = 95$ (non-caregivers)	Shipley Institute of Living Scale (SILS).	Caregivers and non-caregivers did not differ in Vocabulary or Abstract Reasoning scores ($p > .05$).
Vugt et al. (2006)	Examine the cognitive functioning of spousal caregivers of patients with dementia and explore the consequences for patient and caregiver functioning.	Quasi-experimental/ Longitudinal/ Comparative analysis	$n = 119$ (caregivers) $n = 108$ (non-caregivers)	Mini-Mental State Examination (MMSE), The delayed recall score of the Auditory Verbal Learning Test (AVLT), Letter Digit Coding Test (LDCT), Stroop Color-Word Test, A shortened form of the Groninger Intelligence Test	Control subjects performed better than caregivers on tasks measuring global cognitive functioning, memory recall delay, and information processing speed ($p \leq .05$). However, they did not show significant differences for cognitive flexibility ($p = 0.083$).
Dassel & Schmitt (2008)	The goal of this study was to examine the degree to which mild, nonclinical differences in the Executive Functions influence the accuracy and reliability of functional reports by spousal	Quasi-experimental/ Correlational	$n = 20$ (MCI caregivers) $n = 20$ (AD caregivers)	Mini-Mental State examination (MMSE), Adult Lifestyle Functional Interview (ALFI-MMSE), National Adult Reading Test-Revised (NART-R), WASI (Wechsler), Measures of executive	The results suggest no significant group differences in the total frequency of abnormal EF test scores ($p = .92$). However, the results revealed that caregiver EF (problem solving, attention, sequencing, and cognitive flexibility) composite score were significant impact the accuracy of caregiver reports of the performances of activities of daily living in persons with MCI or mild to moderate AD ($p = .04$).

caregivers of persons with mild cognitive impairment (MCI) or mild to moderate AD.

functioning Similarities (Wechsler), Block Design (Wechsler), Matrix Reasoning (Wechsler), Letter-Number Sequencing (Wechsler), Self-Ordered Pointing Task (SOPT), Letter-Number Sequencing (Wechsler), Verbal Fluency, Wisconsin Card Sorting Test (WCST), Trail Making Test - Part B.

Vitaliano et al. (2009)	We evaluated the relationship between caregiver status and decline on the digit symbol test and whether this relationship was mediated by depressed mood.	Quasi-experimental/ Longitudinal/ Comparative analysis	$n = 122$ (caregivers) $n = 117$ (non-caregivers)	DST (Wechsler), Mini Mental State Examination (MMSE)	Caregivers had lower DST scores and higher Hamilton depression scores at T1, T2, and T3 than non-caregivers (all $p < .05$). although caregivers started well below non-caregivers, they experienced a more rapid rate of decline than non-caregivers ($p = .047$). Caregivers declined 4.5 times faster than non-caregivers.
Mackenzie et al. (2009)	The primary purpose of this study was to determine whether caregivers perform more poorly than matched controls on neuropsychological measures	Quasi-experimental/ Cross-sectional/ Comparative analysis	$n = 16$ (caregivers) $n =$ (non-caregivers)	California Verbal Learning Test (CVLT-II), Working Memory Index (WMI) from the Wechsler Adult Intelligence Scale (WAIS-III).	Caregiver performance was significantly poorer than that of controls on the learning outcomes ($p = .03$). Also, demonstrate poorer learning on the CVLT-II and total number of words recalled. In the same way, caregivers performed significantly more poorly than controls on the episodic memory outcomes ($p < .01$).

of learning, episodic memory, and working memory.

Oken et al. (2011)	Evaluate whether the stress of being the primary caregiver of a person with dementia produces cognitive dysfunction.	Quasi-experimental/ Cross-sectional/ Correlation	$n = 31$ (caregivers) $n = 25$ (non-caregivers)	Stroop Color Test and Word Test, Attention Network Test (ANT), Consortium to Establish a Registry for Alzheimer's Disease (CERAD) word list Recall test.	Caregivers performed worse than non-caregivers on the 2 attention tasks but not on the word list memory test. The 2 groups were different in ANT performance ($p = .006$), borderline different in the Stroop conflict condition time ($p = .03$) but not different on the CERAD delayed word-list memory task ($p = .51$).
Correa et al. (2015)	Analyze the effects of chronic stress of family caregivers of AD patients on cognition, cortisol/DHEA ratios and BDNF levels and investigate the relation between these variables.	Experimental/ Predictive analysis	$n = 17$ (caregivers) $n = 18$ (non-caregivers)	The Forward and Backward Digit Span Tests, subtests of the Wechsler Adult Intelligence Scale (WAIS III), The Trail Making A and B Tests, The Logical Memory Tests I and II, subtests of the Wechsler Memory Scale III.	Caregivers showed more stress, depression and anxiety symptoms than non-caregivers, as well as significantly worse performances on attention, working memory and executive function tests ($p < .05$).
Correa et al. (2016)	Compare the effects of chronic stress related to caregiving activities on the cognition of younger and older caregivers and to investigate physiological parameters that may be	Quasi-experimental/ Comparative analysis	$n = 34$ (caregivers) $n = 35$ (non-caregivers)	The Digit Span Test (Wechsler). Trail Making A and B tests. Stroop test. Logical Memory Test, Mini Mental	The results suggest a significant age effects on working memory, attention, processing speed and inhibitory response capacity ($p < .05$). Further investigations of these results suggest that older controls had lower performances than younger controls for all tasks (all $p < 0.01$).

modulated by stress and related to cognitive performance

Dassel et al. (2017)	Examine whether dementia compared to non-dementia spousal caregiving is related to cognitive health.	Quasi-experimental/Longitudinal/Comparative analysis	$n = 192$ (caregivers) $n = 1,063$ (non-caregivers)	Modified Telephone Interview for Cognitive Status (mTICS)	Results revealed that dementia caregivers had significantly greater cognitive decline ($p < .01$) compared to nondementia caregivers.
Correa et al. (2018)	Investigate the reversibility of the cognitive impairments of familial caregivers of AD patients during their caregiving-related chronic stress condition.	Correlational	$n = 33$ (caregivers) $n = 34$ (non-caregivers)	Digit-span tests (Wechsler), Trail Making A and B tests, The Logical memory test version II (Wechsler), The word/color (III) version of the Stroop test	Caregivers' performance was worse than controls on all neuropsychological tests ($p < .001$).

Study's Samples Demographics

The descriptive analyses revealed that from a total of 612 caregivers across studies, 60% were women. The Total Age Range ranged from 46 to 86 years, with a Total Sample Mean Age of 69.5 ($SD = 6.3$) years.

Neurocognitive Functions of Familial Caregivers

The reviewed studies measured a diverse range of NF. These NF were: attention, working memory, processing speed, immediate and recent memory, declarative memory, episodic memory, executive functions, ability to inhibit response, memory recovery, cognitive

flexibility, learning, visuospatial processing, problem-solving, judgment, intricate attention psychomotor speed and cognitive-motor translation (Table III). The majority of the reviewed studies ($n = 9$) reported that the NF of familial caregivers of AD patients can be compromised. Only the study of Vitaliano et al., (2005) showed no difference between caregivers and non-caregivers' groups. In this specific study, the instrument used was a unique scale that did not measure specific NF (Shipley Institute of Living Scale). Instead, this study measured verbal IQ (verbal knowledge & general reasoning), a measure of general intelligence, and not NF.

Table III

Neurocognitive functions (NF) affected in familial caregivers according to literature

Neurocognitive Function Construct	Number of Studies
Processing speed	$n = 7$
Attention	$n = 7$
Working memory	$n = 7$
Immediate recall	$n = 4$
Delayed recall	$n = 2$
Visuospatial processing	$n = 4$
Executive function	$n = 3$
Inhibitory response capacity	$n = 2$
Episodic memory	$n = 2$
Learning	$n = 1$
Problem solving	$n = 1$
Sequencing	$n = 1$
Cognitive flexibility	$n = 1$
Complex attention	$n = 1$
psychomotor speed	
Cognitive-motor translation	$n = 1$

Notes: As seen, processing speed, attention, and working memory are the most frequently reported affected NF in the literature, with a frequency of seven studies for each one.

The majority of the reviewed studies ($n = 7$) reported that familial caregivers show greater difficulty in specific NF. These NF

were: attention, working memory, and processing speed (table III). Moreover, immediate and delayed recall of declarative memory was also reported as an affected function.

Instruments used to measure the Neurocognitive Functions of Familial Caregivers

The most frequently used ($n = 4$) instruments to measure NF was the Trail Making Test, the Word/Color Stroop Test, and the Mini-Mental State Examination (MMSE). Followed by the Forward and Backward Digit Span Tests and the Logical Memory Tests I and II ($n = 3$). Other instruments used to measure neurocognitive functions can be seen in Table 4. Other instruments were used to measure non-NF constructs such as Level of Caregiver Burnout Symptoms, Caregiver Sense of Competence, Depression, Anxiety, Stress, Sleep Quality, Neuropsychiatric Symptoms, and Physical Health but these results of these tests are beyond the scope of this study. However, it should be mentioned that the authors of different studies decided to apply them either to determine some exclusion criteria (e.g., depression in Dassel & Schmitt, 2008) or to examine whether any alteration in these domains mediated performance in the NF.

Table IV

Instruments used to measure neurocognitive functions

Instrument	Number of Studies
The Forward and Backward Digit Span Tests	$n = 3$
Trail Making A and B Tests	$n = 4$
The Logical Memory Tests I and II	$n = 3$

The word/color (III) version of the Stroop test	<i>n</i> = 4
MMSE	<i>n</i> = 4
AVLT	<i>n</i> = 1
Letter Digit Coding Test	<i>n</i> = 1
Digit Symbol Test	<i>n</i> = 1
A shortened form of the Groninger Intelligence Test	<i>n</i> = 1
mTICS	<i>n</i> = 1
CVLT-II	<i>n</i> = 1
WMI from the WAIS-III	<i>n</i> = 1
ANT	<i>n</i> = 1
Shipley Institute of Living Scale	<i>n</i> = 1
ALFI-MMSE	<i>n</i> = 1
WASI	<i>n</i> = 1
Block Design	<i>n</i> = 1
Matrix Reasoning	<i>n</i> = 1
Similarities SOPT	<i>n</i> = 1
LNS	<i>n</i> = 1
Verbal Fluency	<i>n</i> = 1
WCST	<i>n</i> = 1

Notes: MMSE = Mini Mental State Examination; AVLT = Auditory Verbal Learning Test; mTICS = Modified Telephone Interview for Cognitive Status; CVLT-II = California Verbal Learning Test; WMI = Working Memory Index; WAIS-III = Wechsler Adult Intelligence Scale, 3rd edition; ANT = Attention Network Test; ALFI-MMSE = Adult Lifestyle Functional Interview; NART-R = National Adult Reading Test-Revised; WASI = Wechsler Abbreviated Scale of Intelligence; SOPT = Self-Ordered Pointing Task; LNS = Letter-Number Sequencing; WCST = Wisconsin Card Sorting Test subtests from the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III); subtests of the Wechsler Memory Scale-III; subtests from the WASI

Country of the Reviewed Studies

The identified studies were conducted in the following countries: five (5) in the United States, three (3) in Brazil, one (1) in the Netherlands, and one (1) in Canada. No study was conducted in Puerto Rico.

Discussion

The purpose of this review was to synthesize the literature that examines the NF of familial caregivers of AD patients. It had three objectives, 1) identify which NF are affected the most in familial caregivers of AD patients, 2) identify the tests that the reviewed studies used to measure NF, and 3) identify whether there are studies conducted in Puerto Rico that examined the NF of familial caregivers of AD patients.

The most affected NF of familial caregivers of AD patients are attention, working memory, and processing speed. Furthermore, familial caregivers also presented difficulty in the delayed recall of declarative memory. These results suggest that familial caregivers could show difficulty in these domains. This is consistent with previous studies, which suggest that in addition to mental and physical health difficulties, caregivers also exhibit neurocognitive deficits in areas such as attention, working, and declarative memories (Norton et al., 2010; Richardson et al., 2013). Vitaliano et al. (2009) explain that the chronic stress condition associated with the patient's support in association with their advanced age increases the risk of neurocognitive decline including dementia.

These NF are essential for daily activities. Difficulties in these NF can interfere with the ability to perform more complex mental operations. Moreover, they can directly affect health and quality of life, have an impact on the adequate care of the patient, and even affect the patient's performance in daily life activities (Dassel & Schmitt, 2008). It is important to note that although these NF are reported as the most affected, causal relationships cannot be established because the reviewed studies did not report the effect sizes. Thus, the degree of difficulties in these functions and the severity of the impairment in familial

caregivers of AD patients remains unknown.

As mentioned previously, only one study (Vitaliano et al., 2005) did not find significant differences in NF of familial caregivers of AD patients. Vitaliano et al. used an instrument that measured verbal knowledge and general reasoning. It makes sense that no significant differences were found in NF since the measures of verbal knowledge and general reasoning are not of NF, but measures of general intelligence. Therefore, the instruments used in the study could have affected the results.

Among the instruments reported in the reviewed studies, the most used were the Trail Making Test, the Word/Color Stroop Test, and the Mini-Mental State Examination (MMSE). One of the most widely used tests to measure NF is the MMSE even though it is not a specialized test. The MMSE is a screening test to examine global cognitive functioning which is nowadays widely used to detect dementia. This test is claimed to be imprecise to detect mild cognitive impairment (Cieselska et al., 2016). Thus, the MMSE is not an adequate test to measure NF it is questionable to use this test as an accurate instrument to measure the executive functions of a study sample. Similarly, the subtests of the Wechsler Adult Intelligence Scale (WAIS-III) observed in several of the studies in this analysis, are part of a battery that measures IQ and not the decline of NF. Also, it has been discussed that The Logical Memory subtest of the Wechsler Memory Scale has been characterized by imprecise scoring instructions, which can make data interpretation and study comparisons difficult (Abikoff et al., 1987). This can be quite concerning because since these tests are not specialized, rigorous or accurate performance rates are not necessarily obtained. This also affects the precision to identify neurocognitive deficits in this

population, which, in turn, impacts detection and early interventions.

Additionally, multiple studies examined the same NF constructs with different instruments. This heterogeneous approach to measuring NF may affect the internal validity of the studies because they may not be measuring the intended constructs. Although the availability of various tests to measure NF may increase research viability, it limits the accuracy and agreement between the researchers regarding their findings. Therefore, this heterogeneous approach impedes the advancement of this research field.

Another finding of this review was that no study was conducted to examine the NF of familial caregivers of AD patients in Puerto Rico. That is, the NF of familial caregivers of AD patients in Puerto Rico remains unknown. It is therefore imperative to conduct research that examines this issue in Puerto Rico.

For future studies, we recommend using neuropsychological tests instead of screening tests, to accurately measure the NF. It is crucial for accurate results to measure the NF consistently. Moreover, future studies should examine the potential impact that covariables of burnout, depression, or anxiety symptoms may have on NF of familial caregivers of AD patients (Borsje et al., 2016; Dassel et al., 2017; Vitaliano et al., 2009). Also, it is recommended for future studies to research the NF of familial caregivers of AD patients in Puerto Rico to provide information that facilitates the development of interventions for this population. Studies that examine the NF of familial caregivers of AD patients in Puerto Rico should be conducted.

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Declaration of interest 63

The authors report no conflicts of interest. The authors are responsible for the content and writing of this manuscript.

Approval of the Institutional Board for the Protection of Human Rights in Research

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Consent or Assessment forms

No consent or assent form was distributed for this Systematized Literature Review.

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