OBJECTIVE: Late-life depression is an under-diagnosed and under-treated disease that reduces the well-being of older adults. Executive dysfunction is another critical impairment in elderly depressed individuals which further disrupts their everyday functioning. This systematic review aims to analyze the association between executive function and depression severity in elderly individuals diagnosed with major depressive disorder.

METHOD: The studies were retrieved from MEDLINE/PubMed, ISI Web of Knowledge and PsychInfo, after a search strategy combining the terms "depression", "executive function", "neuropsychological assessment", "elderly" and "late life". Study selection, data collection and quality ratings was performed by two independent raters.

RESULTS: A total of 1,130 articles were found but only 8 studies met the defined eligibility criteria and evaluated the association between depression severity and executive functioning. Six out of 8 studies found an association between depression severity and executive function, with correlations ranging from small to large (r = -0.15 to -0.53). The included reports had several methodological limitations such as selective data reporting, non-comprehensive executive function assessment and not controlling potential biases.

CONCLUSION: Depression severity may be more strongly correlated with a specific set of executive abilities although it also seems to be a broad-based association with executive functioning as a whole. Future high-quality prospective studies are recommended in order to understand the causal relationship between depression severity and executive functioning taking into account possible mediators such as age-related or neurodegenerative cognitive impairment, educational level and other clinic characteristics (e.g. age of onset, medication).

KEYWORDS: Late-life Depression, Major Depressive Disorder, Executive Function.
Over the last decades, several authors have explored the relationship between clinical variables and neuropsychological performance, including the severity of depressive symptoms. Lichtenberg et al.\(^7\) found that the severity of depressive symptoms accounted for approximately 8% of cognitive functioning variance in older adults. There have also been reports in adult patients with major depressive disorder (MDD) describing an association between poor executive functioning and severe depressive symptoms.\(^{15,16}\) However, data regarding the association between cognitive deficits and depression severity have been quite contradictory, which is most likely explained by several confounding factors such as antidepressant medication, history of electroconvulsive therapy (ECT), education levels, types of neurocognitive tests applied, status of depressed patients, age of onset, among others.

Executive functioning impairment is normally present in elderly patients with depression but there is a need to further understand how these deficits are related to clinical outcomes. Thereby, this systematic review aims to analyze the association between executive function and depression severity in elderly individuals diagnosed with MDD.

This review is part of a program\(^{17,18}\) to systematically review themes of interest to the field of geriatric psychiatry.

### METHODS

#### Eligibility criteria

The present review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.\(^{19}\) Studies were included if they met the following eligibility criteria: (i) full-text articles in English presenting data from observational (cross-sectional or case–control), longitudinal, retrospective, and prospective studies; (ii) reports describing any kind of association between executive functioning tests scores and depression severity scores (e.g. bivariate correlations, univariate or multivariate regression analyses); (iii) studies including elderly subjects 60 or more years old diagnosed with MDD; (iv) data on standardized neuropsychological measures of executive functioning and validated scales of depressive symptom severity.

Studies were excluded if the sample had other comorbid mental illness or neurological disorders, if the authors did not provide detailed information regarding the statistical procedure applied or did not provide adequate description of the executive functioning assessment procedures.

#### Sources

The studies were retrieved from MEDLINE/PubMed, ISI Web of Knowledge and PsychInfo. Experts on the topic were also contacted to provide relevant reports. Included reports and previous systematic reviews references were also manually screened for additional relevant studies. Searches were closed on February 10th 2016.

#### Search

The search was performed combining the following terms: depression, executive function, neuropsychological assessment, elderly, late life.

#### Selection of studies

Study selection was performed by two independent raters who established consensus regarding study selection. A third rater was also called to address any disagreements between the initial raters. After database searching, the reports were screened based on title and abstract, and were excluded if they did not clearly meet eligibility criteria. Finally, full-text analysis was completed on the remaining studies in order to assess them based on the defined eligibility criteria.

#### Data collection

The following data was extracted from the articles: sample size, participants sociodemographic characteristics (age, gender, and educational level), clinical information (clinical status, age of first onset, length of episode, symptom severity, and medication), global cognitive functioning (e.g. Mini-Mental State Examination - MMSE), depression severity scales, neuropsychological instruments used to assess executive functioning, and main significant findings. These procedures were performed by two independent investigators, who reached a consensus in case of disagreement. Only articles that used at least one neuropsychological test of executive function and evaluated late life depression severity were selected. Mean weighted averages were also calculated for age, gender, education, MMSE score, age of onset and length of episode, based only on studies which provided clear information regarding these topics.

#### Risk of bias in studies

For assessing the risk of bias within each included trial we developed the following 5-point quality scale based on the following criteria: 1 point for gold standard diagnosis procedures (e.g. DSM-IV, SCID, ICD, etc); 1 point for complete description of critical clinical information (medication status, age of onset, etc); 1 point for exclusion of major potential cofounders (comorbid mental or neurological disorders, ECT, etc); 1 point for absence of selective reporting; 1 point for comprehensive assessment of executive functioning. The quality scale was completed independently by two raters to ensure reliability of extraction of study characteristics. No discrepancies were found between them.
**RESULTS**

Based on the defined strategy, a total of 1,130 articles were found in the search (682 in Pubmed, 202 in ISI Web of Science, and 246 in PsychInfo); 212 articles were duplicates and 40 articles were not in English language and were therefore excluded, reducing the collection to 918 articles. After the screening, 908 articles were excluded as they were not related to the defined research question. Ten reports were screened for full-text and two were excluded as they did not analyze any kind of association between symptom severity and executive functioning, leaving a total of 8 included studies, as illustrated in figure 1.

A summary of the participants’ clinical and sociodemographic characteristics is presented in Tables 1 and 2. Regarding the characteristics of the reviewed studies, participants were mainly outpatients with MDD (n=557; 84.5%). Sexton et al.21 mainly included remitted patients (n=27), although they also included patients with mild and moderate symptoms (n=9). Alexopoulos et al.9 included 43 remitted patients, although 15 had recurrence during the follow-up period. The sample from Jungwirth et al.25 included 13 patients with MDD but the authors performed their analyses using pooled data from patients with subsyndromal (n=9) or minor depressive disorder (n=23). Sample sizes ranged from 21 to 157 participants.

Seven of the studies diagnosed MDD based on the criteria from Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV), while only one used DSM-III-R. Two studies combined DSM-IV and Research Diagnostic Criteria. Five of the studies used the Structured Clinical Interview for DSM to determine MDD, while one study opted for the National Institute of Mental Health interview. Baudic et al. used a non-standardized clinical interview and a cut-off point of the Montgomery and Asberg Depression Rating Scale (MADRS) (>20). Murphy et al. used the DSM-IV criteria but assessed included subjects using the Schedule for Affective Disorders and Schizophrenia.

Regarding gender, there was a total of 294 female and 189 male subjects, with a mean proportion of 60.87% of females across studies, although two studies did not report information regarding gender. Age means ranged from 61.4 to 75.8 years, with an average of 70.6, while education level ranged from 9.6 to 14.9, averaging 13.8 years. Jungwirth et al. did not report mean education level but most participants had completed either secondary or vocational school.

Regarding the participants clinical characteristics, the included trials reported several relevant indicators. Only three studies reported mean age of depression onset, ranging from 45.4 to 54.51, with a 51.38 years average. Only two studies reported data regarding mean

---

**Figure 1** - Flowchart for selection of reviewed articles.
### Table 1: Participants' sociodemographic and clinical information

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Population</th>
<th>Criteria</th>
<th>Tool</th>
<th>Age</th>
<th>Gender (F/M)</th>
<th>Education</th>
<th>MMSE</th>
<th>Age of Onset</th>
<th>Length of Episode</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexopoulos et al.</td>
<td>43 (remitted)</td>
<td>DSM-IV; RDC</td>
<td>SCID / SADS-L HRDS-24 ≥ 18</td>
<td>73.3 (7.6)</td>
<td>27 / 16</td>
<td>13.7 (2.9)</td>
<td>28 (2.7)</td>
<td>67.6% with one or more previous episode</td>
<td>No info</td>
<td>Maintenance antidepressant treatment (51.2%) Placebo (48.8%)</td>
</tr>
<tr>
<td>Baudic et al.</td>
<td>21 (currently depressed)</td>
<td>DSM-IV</td>
<td>Clinical Interview MADRS &gt;20</td>
<td>71.8 (8.8)</td>
<td>No info</td>
<td>9.6 (3.3)</td>
<td>28.1 (1.4)</td>
<td>No info</td>
<td>No info</td>
<td>Unmedicated</td>
</tr>
<tr>
<td>Boone et al.</td>
<td>73 (currently depressed)</td>
<td>DSM-III-R</td>
<td>SCID</td>
<td>61.4 (6.6)</td>
<td>38/35</td>
<td>14.9 (3.2)</td>
<td>No info</td>
<td>47.7 (19.72)</td>
<td>26.3 (37.27)</td>
<td>Unmedicated (≥ 2 weeks)</td>
</tr>
<tr>
<td>Jungwirth et al.</td>
<td>45 (currently depressed)</td>
<td>DSM-IV</td>
<td>SCID</td>
<td>75.78 (0.42)</td>
<td>36/9</td>
<td>88.9% completed secondary or vocational school</td>
<td>No info</td>
<td>No info</td>
<td>No info</td>
<td>Antidepressants (33%) Benzodiazepines (24.4%)</td>
</tr>
<tr>
<td>Murphy et al.</td>
<td>157 (currently depressed)</td>
<td>DSM-IV</td>
<td>SADS HRDS-24 ≥ 19</td>
<td>72 (6.9)</td>
<td>93 / 64</td>
<td>13.21</td>
<td>27.61</td>
<td>No info</td>
<td>No info</td>
<td>No information</td>
</tr>
<tr>
<td>Sair et al.</td>
<td>129 (currently depressed)</td>
<td>DSM-IV</td>
<td>SCID</td>
<td>73.4</td>
<td>76/53</td>
<td>14.2</td>
<td>27.51</td>
<td>No info</td>
<td>No info</td>
<td>No information</td>
</tr>
<tr>
<td>Sexton et al.</td>
<td>36 (mainly remitted)</td>
<td>DSM-IV</td>
<td>SCID</td>
<td>71.8 (7.7)</td>
<td>24/12</td>
<td>13.9 (3.7)</td>
<td>29.9 (1.4)</td>
<td>45.4 (19)</td>
<td>No info</td>
<td>Antidepressants (92%) Unmedicated (6%) Other medications (2%)</td>
</tr>
<tr>
<td>Sheline et al.</td>
<td>155 (currently depressed)</td>
<td>DSM-IV</td>
<td>SCID</td>
<td>68.72 (7.28)</td>
<td>No accurate info</td>
<td>14.04 (3.12)</td>
<td>≥21 No info on mean</td>
<td>54.51 17.05</td>
<td>No info</td>
<td>Unmedicated</td>
</tr>
</tbody>
</table>

MDD: Major Depressive Disorder; DSM: Diagnostic Statistics Manual; RDC: Research Diagnosis Criteria; SCID: Structured Clinical Interview for DSM; HRDS: Hamilton Depression Rating Scale; MADRS: Montgomery and Asberg Depression Rating Scale; ssD: Subsyndromal Depression; mD: Minor Depressive Disorder; NIMH: National Institute of Mental Health.

* Demographic and clinical data is regarding the pooled sample including MDD, ssD and mD participants.

### Table 2: Summary of sample characteristics (mean weighted average)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>N studies</th>
<th>Studies</th>
<th>N participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70.65</td>
<td>8</td>
<td>9, 20-26</td>
<td>659</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>60.87</td>
<td>6</td>
<td>9, 20,21,23,25,26</td>
<td>483</td>
</tr>
<tr>
<td>Education (number of schooling years)</td>
<td>13.78</td>
<td>7</td>
<td>9, 20-24,26</td>
<td>614</td>
</tr>
<tr>
<td>Mini Mental State Examination</td>
<td>27.86</td>
<td>5</td>
<td>9, 20,21,24,26</td>
<td>386</td>
</tr>
<tr>
<td>Age of Onset (years)</td>
<td>51.38</td>
<td>3</td>
<td>21-23</td>
<td>264</td>
</tr>
<tr>
<td>Length of Episode (weeks)</td>
<td>25.60</td>
<td>2</td>
<td>20,23</td>
<td>202</td>
</tr>
</tbody>
</table>
length of illness with values ranging from 25.2 to 26.3 years.\textsuperscript{20,23} Sair et al.\textsuperscript{9} also reported a mean of 5.6 MDD episodes within their sample, while Alexopoulos et al.\textsuperscript{26} noted that 67.6% of the sample had at least one previous episode of MDD.

Regarding pharmacological treatment three studies included only unmedicated patients\textsuperscript{22-24} and two had no information regarding medication status.\textsuperscript{20,26} Jungwirth et al.\textsuperscript{25} included a total of 33.3% of patients on antidepressants,\textsuperscript{25} while the sample collected by Sexton et al. was mainly on antidepressants (92%).\textsuperscript{21} In the study by Alexopoulos et al.\textsuperscript{9} patients completed a continuation (16 weeks) and maintenance nortriptyline treatment during the 2 year prospective study, although 21 patients had placebo during the maintenance treatment.\textsuperscript{9} Moreover, five studies also reported mean MMSE score, with values ranging from 27.51 to 29.9 and an average score of 27.86.

Assessment procedures, methodological considerations and major findings are presented at table 3. Depression severity was assessed with several different scales including the MADRS, the 17 and 24 item version of the Hamilton Depression Rating Scale (HRDS-17 and HRDS-24) and/or the long and short version of the Geriatric Depression Scale (GDS-30 and GDS-15, respectively). Mean MADRS score ranged from 22.33 to 33.3, HDRS-17 from 4.2 to 19.6, HDRS-24 from 25.79 to 26.7 and GDS-15 from 3.8 to 4.4. Only one study reported data regarding the full version of GDS, with a mean score of 22.1.

Executive functioning assessment encompassed the Trail Making Test B (TMT-B) in half the studies, while three also applied the Wisconsin Card Sorting Test, the Stroop test, Verbal Fluency Tasks and/or the Initiation and Preservation Domain of the Matis Dementia Rating Scale (DRS-IP). Other applied executive functioning tasks included the Controlled Oral Word Association Test (COWAT), the Cognitive Estimates Test (CET), the Hayling Test, the Graphic Sequences of Luria, the Auditory Consonant Trigrams, the Ascending Digits Task and the Digit Span.

Finally, regarding the association between depression severity and executive functioning there were also different analysis procedures from the included studies. Four studies performed correlation analysis,\textsuperscript{21-24} two completed regression analysis\textsuperscript{20,25} and two used mixed-effects models.\textsuperscript{9,26} Moreover, half the studies used the composite score from executive function tests,\textsuperscript{51-23} while the other half evaluated the association with each sub score.\textsuperscript{20,23,25} Six out of 8 studies found an association between depression severity and executive function performance in elderly patients with MDD.\textsuperscript{21-24} The correlations between depression severity and executive function measures ranged from small to large (r=-0.15 to -0.53).

\section*{DISCUSSION}

The aim of this systematic review was to analyze the association between depression severity and executive functioning. Eight studies were included in the analysis and four of them reported statistically significant associations between these two variables. Across the included studies it is possible to identify associations with several depression severity scales, including HRDSD-17 and 24, MADRS and GDS-15. Boone et al.\textsuperscript{23} found worse executive functioning on moderately depressed subjects (HRDS-17>19) in comparison to mildly depressed elderly (HRDS≤18). Interestingly, Baudic et al.\textsuperscript{24} found several significant correlations with MADRS but did not find any association to the GDS-30 score. When applying MADRS the examiner him/herself evaluates symptom severity, in contrast to GDS-30 which is a self-administered test. Patients may not be able to accurately assess themselves or may underestimate their depressive disorder, which may explain why there were no significant associations.

As most included studies provided cross-sectional data on elderly patients with MDD, one cannot assume a causal relationship between symptom severity and executive functioning. Current neurobiological models of depression postulate that the frontostriatal neural pathways are compromised during depressive episodes, which may possibly explain the relationship between symptom severity and executive impairment.\textsuperscript{27} Executive functions are heavily dependent on the frontostriatal circuitry\textsuperscript{20,29} and may be a strong indicator of the degree of frontostriatal compromise.\textsuperscript{30} Neuroimaging studies suggest that neuropsychological deficits in depression may be considered within a framework of frontostriatal disruption. There is evidence of significantly reduced regional cerebral blood flow in the medial prefrontal cortex of depressed patients with severe cognitive impairment. Although these circuits seem to play a role in the interaction between depression and executive functioning a question still remains: does impaired executive performance result from frontostriatal abnormalities induced by a depressive state or does a persistent frontostriatal dysfunction which underlies executive impairment influence the course of depressive symptoms? To this day, there is not enough evidence to validate the direction of the causal relationship between these constructs.

Two of the included studies used prospective designs and add interesting findings to this debate.\textsuperscript{9,26} The one-year prospective study by Murphy et al.\textsuperscript{35} also found that improvement in executive function was associated with amelioration of depression, although subjects received uncontrolled treatment according to clinical indication which can act as a potential cofounder. Alexopoulos et al.\textsuperscript{9}
found that initiation and preservation deficits significantly predicted depressive symptom severity, even in patients that did not relapse during the two years of follow-up. However, this study only followed patients which initially achieved remission after an antidepressant treatment, which does not allow us to understand the proposed association in treatment-resistant patients. There is preliminary evidence about the association of depression severity and executive functioning across time although the studies have significant biases. Future research should take into account several factors which can mediate this association. We can even consider that executive impairment may result from the interaction between depressive symptoms and secondary brain changes related to aging or to subclinical dementia. The executive dysfunction observed in patients over 60 years may be related to frontal neurodegeneration or malfunction of the frontal pathways, displayed by their inability to be activated or to be inhibited.11 The mechanisms that further explain these changes are unknown but the association between neurodegenerative processes and dysexecutive syndrome is widely accepted. Maybe there are several degrees of interaction between depressive symptoms and subclinical dementia, which lead to higher or lower associations between depression severity and executive performance.

Table 3: Methodological Considerations and Major Findings

<table>
<thead>
<tr>
<th>Study</th>
<th>Depression Severity</th>
<th>Executive Function Tests</th>
<th>Study Design and Statistical Procedures</th>
<th>Quality Scale (1 to 5)</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexopoulos et al.</td>
<td>HDRS-24 26.7 ± 6.4</td>
<td>DRS-IP</td>
<td>2-Year Prospective Study (Mixed-effects models)</td>
<td>2 Pts: gold standard diagnosis; participants clinical data</td>
<td></td>
</tr>
<tr>
<td>Baudic et al.</td>
<td>MADRS 33.3 ± 6.3</td>
<td>COWAT; CET; Hayling Test; Stroop; TMT-B; GSL; WCST</td>
<td>Cross-sectional (Bivariate correlation)</td>
<td>3 Pts: no potential cofounders; no selective reporting; comprehensive assessment</td>
<td></td>
</tr>
<tr>
<td>Boone et al.</td>
<td>HDRS-17 19.6 ± 5.14</td>
<td>Stroop; ACT; WSCT; COWAT</td>
<td>Cross-sectional (Bivariate correlation)</td>
<td>5 Pts: gold standard diagnosis; participants clinical data; no potential cofounders; no selective reporting; comprehensive assessment</td>
<td></td>
</tr>
<tr>
<td>Jungwirth et al.</td>
<td>HDRS-17 12.71 ± 6.18</td>
<td>TMT; Verbal Fluency</td>
<td>Cross-sectional (Univariate ANOVA)</td>
<td>1 Pt: gold standard diagnosis</td>
<td></td>
</tr>
<tr>
<td>Murphy et al.</td>
<td>MADRS-24 25.79</td>
<td>DRS-IP</td>
<td>1-Year Prospective Study (Mixed-effects models)</td>
<td>1 Pt: no selective reporting</td>
<td></td>
</tr>
<tr>
<td>Sair et al.</td>
<td>MADRS 23.3 ± 7.77</td>
<td>ADT</td>
<td>Cross-sectional (Multivariate regression analysis)</td>
<td>2 Pts: gold standard diagnosis; no selective reporting</td>
<td></td>
</tr>
<tr>
<td>Sexton et al.</td>
<td>HDRS-17 4.2 ± 4.8</td>
<td>Digit Span; Letter Fluency; TMT B</td>
<td>Cross-sectional (Bivariate correlation)</td>
<td>3 Points: gold standard diagnosis; participants clinical data; no selective reporting</td>
<td></td>
</tr>
<tr>
<td>Sheline et al.</td>
<td>MADRS 26.17 ± 4.5</td>
<td>Verbal Fluency; TMT-B; Stroop; DRS-IP; WCST</td>
<td>Cross-sectional (Partial correlation analysis)</td>
<td>3 Pts: gold standard diagnosis; no selective reporting; comprehensive assessment</td>
<td></td>
</tr>
</tbody>
</table>

HDRS: Hamilton Depression Rating Scale; DRS-IP: Initiation and Preservation Domain of the Mattis Dementia Rating Scale Trail Making; COWAT: Controlled Oral Word Association Test; CET: Cognitive Estimates Test; Stroop: Color-Interference subtest; TMT-B: Trail Making Test B; GSL: Graphic Sequences of Luria; WCST: Wisconsin Card Sorting Test; ACT: Auditory Consonant Trigrams; ADT: Ascending Digits Task; CC: Concordance Correlation
Late-life depression severity and executive function
Monteiro S

There were only two studies which did not find any association between depression severity and executive functioning score. Sexton et al. found no significant association between composite executive score and depression severity. However, 75% of the sample was composed by remitted patients (mean HRDS-17 = 4.2; mean GDS-15 = 3.8). Thereby, and because few patients had active symptoms, it would have been difficult to find a connection between depressive severity and executive functioning. However, this study also found impaired executive function in unremitted MDD patients in comparison to healthy controls. It has been reported that elderly depressed patients with symptom remission show more difficulty in executive tasks when compared to healthy subjects. Thus it seems that executive function does not return to pre-illness levels after remission and deficits may be augmented during acute depressive states.

The second study showing no association was developed by Sair et al., who found no relationship between ascending digits task performance and depression severity. The task was developed to assess working memory but this was the first study to use it to evaluate executive dysfunction in depressed elderly patients. Because the authors only applied this specific test it seems reasonable to assume they found no significant association. As previously stated, executive functioning assessment encompasses a wide-range of tests and using only the ascending digits task is a poor approach in comparison to comprehensive evaluation procedures. Furthermore, there are studies that found no relationship between working memory and depression severity.

The positive associations described in the included studies should also be debated taking into account the executive functioning measures computed for analyzes by the authors. As previously described, the included studies used a wide range of tests to assess executive functioning, making it difficult to objectively compare the reported findings. However, it is interesting to notice that two studies reported small significant correlations between depression severity and composite executive functioning score, which can suggest a broad-based association between both domains. In contrast, Baudic et al. reported moderate to large positive associations between depression severity and several executive functioning subtest (r = -0.44 to -0.53). Taking these data together, it is reasonable to suggest that depression severity may be more strongly correlated with a specific set of executive abilities. This can explain why correlations with composite executive scores were lower or even non-significant. It is also important to highlight that the construct of executive function is very wide and encompasses several subdomains. Patients with depression may display heterogeneous executive profiles, being compromised on one aspect of executive functioning and not on others. In our review, three of the studies did not apply a comprehensive executive functioning assessment which further limits their findings. Future studies should provide further understanding on specific executive function measures, exploring constructs such as cognitive flexibility, inhibitory control, working memory, planning, problem-solving, etc. Moreover, studies should also concurrently address other neurocognitive domains such as language and memory in order to verify if symptom severity is specifically associated to executive functions or if other cognitive functions relevant to effective executive performance also play a role.

There are also several sociodemographic and clinical factors such as age of onset and education levels which can limit the findings reported by the included trials. For instance, the presence of late-life depression symptoms and low levels of education are significant predictors for development of dementia. Several of the included studies lack information regarding MMSE and just one of the studies prospectively assures that the included patients did not develop any kind of dementia. Education levels were also mainly high in the reported samples, which leaves room to speculate whether depression severity and executive functioning in subjects with lower education years follows a different course.

Pharmacological treatment can also act as a potential confounder for the results of some of the reported studies. Out of the four studies which reported a significant association between depression severity and executive functioning, three included only unmedicated patients; the fourth study only included one third of the patients on antidepressants. Conversely, Sexton et al. reported no significant findings and more than 90% of their patients were on antidepressants. There is some evidence suggesting that some antidepressive treatments may attenuate cognitive impairment in MDD patients. A recent trial by Shilyansky et al. suggested otherwise as the authors did not find any cognitive effects of three distinct antidepressants. Regardless, when addressing the relationship between symptom severity and cognitive performance researchers should contemplate the role of pharmacological treatment as it may attenuate depressive state induce deficits. The history of electroconvulsive therapy is another critical factor that should be contemplated by researchers and it was only assessed by two of the included studies. The meta-analysis of Semkovska et al. found that electroconvulsive therapy can induce short-term cognitive abnormalities on executive functioning which return to baseline over the first 3 days and can even improve beyond baseline levels 15 days after the treatment.

Taking into account all the previously described factors, there is a need to develop prospective or retrospective studies with elderly patients in order to understand the causal relationship between executive function and depressive symptoms. Furthermore, these
studies should also make efforts to identify potential moderators of this interaction such as age of onset, length of episode, age-related or neurodegenerative cognitive impairment, education level, among others.

**CONCLUSION**

There is some evidence supporting the relationship between depression severity and executive functioning in late-life depression. This relationship seems to encompass specific executive domains as well as executive function as a whole. Cross-sectional evidence suggests small to large correlations between depressive symptoms and executive performance but there is a need to develop more longitudinal trials which can analyze this relationship over time while controlling for critical confounders such as antidepressant treatment, number of MDD episodes, previous clinical history (age of onset, length of episode, history of ECT), subclinical dementia indicators, among others. Researchers should also make efforts to explore comprehensive executive assessment procedures in order to pinpoint which cognitive domains specifically relate and predict depression severity, so that clinicians can develop more accurate evaluation and treatment procedures to address the needs of these patients.

**CONFLICT OF INTEREST**

Authors report no conflict of interest regarding this study.

**AUTHOR PARTICIPATION**

Monteiro S, Monteiro B, Candida M, Campos C, Paes F and Machado S developed the project, discussed the data, wrote the first draft of the article, and reviewed its final form; Adler N, Rocha NBF, Nardi AE, discussed the data and reviewed the final form of the article.

**REFERENCES**

Late-life depression severity and executive function
Monteiro S


