### What Role Do Executive Functions Play in the Etiology of Behavioral and Psychological Symptoms of Dementia? An Integrative Review

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**Summary**

The aim of our study was to review the literature on the relationship between executive dysfunction (EDF) and the behavioral and psychological symptoms of dementia (BPSD).

**Material/Methods:**

We searched for papers that addressed one or both of two questions: a) is there a causal relationship between EDF and BPSD?; b) What are the main hypotheses or theoretical models that explain this relationship? A systematic search was made to identify all possibly relevant papers on the Scopus - Elsevier and PubMed databases, using an algorithm with the keywords most often used to search for references on EDF and BPSD.

**Results:**

We found 112 works in Scopus-Elsevier and 59 in PubMed; 20 were repeated, resulting in 151 distinct publications. We excluded 143 of these because they did not consider EDF as an independent variable and BPSD as a dependent variable. Five more works came out of a reverse search on the bibliography from the 8 remaining papers, resulting in 13 works for our review. Two groups were formed according to their investigative design to establish the relationship between EDF and BPSD.

**Conclusions:**

The studies generally found an association between EDF and BPSD, but few of them have investigated the nature of this relationship, with little clarification of the mechanism through which the former contributes to the emergence of the latter.

**Key words:** executive dysfunction (EDF), neuropsychiatric symptoms of dementia, instrumental activities of daily living (IADL), personality changes
INTRODUCTION

Dementia is characterized by a decline in nervous system functions, with a close relationship between neuronal loss, memory and the impairment of other cognitive processes. These changes affect the functional performance of the subject and hinder the execution of his/her daily activities (DSM IV, 1994).

Cognitive symptoms are crucial for the characterization of dementia and the differential diagnosis between different types of dementia, and constitute the prime therapeutic targets for pharmacological or non-pharmacological interventions. Furthermore, different patterns of cognitive decline are associated with distinct functional consequences. For example, some authors suggest that measures of executive function (EF) would be better indicators of performance in instrumental activities of daily living (iADL), while measures of memory would be more sensitive to changes in the social functioning of patients with compromised cognitive abilities (Plehn, Marcopulos & Mclain, 2004; Lim, Chong & Sahadevan, 2007).

Alongside the cognitive changes, alterations in patient personality and behavior during the dementive process also contribute to the worsening of their functional difficulties (Sauvager et al., 2002). Relatives and caregivers suggest that behavioral changes are crucial determinants for functional loss, and that they contribute to their overload and stress. They are also an important indicator of the decrease in the quality of life of patients (Hoe et al., 2005).

Behavioral and Psychological Symptoms of Dementia (BPSD) are defined as changes in perception, thought content, mood or behavior, which frequently occur in dementia patients. Behavioral symptoms are identified through the observation of the patient and include aggressiveness, agitation, wandering, culturally inappropriate behavior and sexual disinhibition. Psychological symptoms, on the other hand, are evaluated primarily through interviews with the patients themselves, their families and caregivers, and include anxiety, depressive symptoms, apathy, hallucinations and delusion (Finkel et al., 1996).

A number of studies have investigated the contribution of EF and BPSD to the characterization and differentiation of dementias. Back-Madruga et al. (2002), for example, compare the neuropsychological profile, neuropsychiatric symptoms, activities of daily living (ADL) and caregiver burden in patients with the typical variant of Alzheimer dementia (tvAD) and with the frontal variant of the disease (fvAD), matched for global cognitive performance. The authors found that the group with fvAD showed worse performance on neuropsychological measures of EF, higher frequency of neuropsychiatric symptoms, greater ADL impairment and increased stress on the caregiver, when compared with the group with tvAD (Back-Madruga et al., 2002).

Perri et al. (2005) investigated whether a brief battery of neuropsychological assessments coupled with a behavioral assessment could be a reliable protocol for the differential diagnosis between the frontal variant of frontotemporal dementia (fvFTD) and AD. The authors found that scores on executive tasks, a copy of the Rey figure and a phonemic fluency test (FAS), coupled with meas-
ures of apathy, were able to distinguish patients with AD from patients with fvFTD with over 80% accuracy (Perri et al., 2005).

Recently, another study tested the hypothesis that fvAD could be clinically identified by difficulties related to EDF (Woodward et al., 2010). Individuals with this disease variant would be similar in terms of their behavioral and neuropsychological profile to FTD patients, and both would differ from AD patients in the degree of cognitive impairments, behavioral symptoms and functional decline. Their results showed that fvAD patients have higher levels of executive deficits, increased frequency of BPSD and more functional loss than patients with classic AD (Woodward et al., 2010).

Some authors using functional neuroimaging techniques have found bilateral hypoperfusion of the dorsolateral prefrontal cortex in AD patients with psychotic symptoms compared with those with AD without psychotic symptoms, and decreased metabolism in the posterior orbitofrontal cortex in fvFTD patients with apathy and disinhibition symptoms (Mega et al., 2000; Peters et al., 2006).

Despite the existence of a series of works reporting the coexistence of EDF and BPSD, few studies have set out to investigate the nature of this relationship. In particular, it is important to know if EDF is a predictor of the emergence of BPSD, understood as a syndrome, or if specific components of EDF are related to an equally specific behavioral or psychological symptom. The general objective of this study, then, was to conduct an integrative review of the literature on the relationship between EDF and BPSD. The integrative review, like a systematic review, uses a specific standardized methodology for searching and reviewing the works found. It is distinguished from a systematic review because it allow the inclusion of different methodologies (experimental and non-experimental) and data sources (primary and secondary) contributing to a presentation that integrates multiple perspectives on a single phenomenon of shared interest. It incorporates a wide range of purposes, ranging from concept definition, review of evidence and theories to the analysis of the methodological problems involved in a particular topic (Broome, 1993). In general the method summarizes the empirical or theoretical results available in the literature on a particular topic, providing a better understanding of it (Whittemore & Knaff, 2005).

Our specific goal was to summarize the studies that proposed a causal relationship between EDF and BPSD. Our hypotheses were that subjects with EDF would present: 1) a greater chance of having BPSD, and 2) specificity of the relationship between different components of EDF and BPSD.

**METHOD**

In order to perform the integrative review, the following procedures were employed:
1) Development of guiding questions for the search:
   a) Is there a causal relationship between EF and BPSD. If the answer is positive?
**b) What are the main assumptions or theoretical models that explain this relationship?**

2) Determination of databases and terms and keywords to be used for the systematic search;

3) Systematic search in databases indexed for the terms and keywords;

4) Organization and description in a table of the studies found in step 3, summarizing and interpreting work components of the review;

6) Discussion of findings.

The search done in the PubMed and Scopus-Elsevier databases was restricted to papers that were written in English. On the Scopus-Elsevier database, the search was restricted to the title, abstract, keywords and author fields (TITLE-ABS-KEY-AUTH).

The terms and keywords used to refer to the BPSD and EDF do not seem to occur systematically in the literature. There are several terms related to each of the two concepts. For example, the expression in English “behavioral and psychological symptoms of dementia” can be described with the acronym BPSD, as neuropsychiatric symptoms, or as behavioral disturbance. Similarly, EDF may also be referenced as executive function deficits, frontal lobe dysfunctions, or dysexecutive syndrome.

To overcome this difficulty in choosing the terms and keywords that would be used in the search, the terms most commonly found in the literature were chosen. These terms and keywords were grouped into an algorithm, respecting the command rules used in the advanced search section of each of the databases.

The resulting algorithm used in both Scopus-Elsevier and PubMed, according to the description above, was as follows

```plaintext
(((neuropsychiatry symptoms AND dementia) OR (behavioral AND psychological AND symptoms AND dementia) OR (behavioral disturbance AND dementia) OR (BPSD)) AND ((executive function) OR EF OR (executive AND functions AND disorders) OR (frontal cortex AND dysfunctions) OR (frontal lobes AND dysfunctions) OR (Executive and Control)))
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**Table 1.**

<table>
<thead>
<tr>
<th>General feature</th>
<th>Specific feature</th>
<th>Amount</th>
<th>Percentage (%)</th>
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</thead>
<tbody>
<tr>
<td><strong>Not an original article</strong></td>
<td>Review</td>
<td>37</td>
<td>25.90</td>
</tr>
<tr>
<td></td>
<td>Case Study</td>
<td>10</td>
<td>7.00</td>
</tr>
<tr>
<td></td>
<td>Conference paper</td>
<td>8</td>
<td>5.60</td>
</tr>
<tr>
<td><strong>Does not use EF and / or BPSD as variable</strong></td>
<td>Psychometric validation</td>
<td>9</td>
<td>6.30</td>
</tr>
<tr>
<td></td>
<td>Pharmacological efficacy</td>
<td>8</td>
<td>5.60</td>
</tr>
<tr>
<td></td>
<td>Do not be with elderly</td>
<td>4</td>
<td>2.80</td>
</tr>
<tr>
<td><strong>Does not have in its design EF as independent variable and BPSD as dependent variable.</strong></td>
<td>EF not like IV</td>
<td>23</td>
<td>16.10</td>
</tr>
<tr>
<td></td>
<td>BPSD not like DV</td>
<td>21</td>
<td>14.70</td>
</tr>
<tr>
<td></td>
<td>BPSD as IV</td>
<td>7</td>
<td>4.90</td>
</tr>
<tr>
<td></td>
<td>paradigm reverse (BPSD&gt;EF)</td>
<td>6</td>
<td>4.20</td>
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<tr>
<td></td>
<td>Work not available in full</td>
<td>10</td>
<td>7.00</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td>143</td>
<td>100.00</td>
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</tbody>
</table>
Moreira et al., Executive dysfunction and BPSD

We found 112 works in Scopus-Elsevier and 59 on PubMed. Of these, 20 were repeated, resulting in 151 distinct works.

Based on the guiding questions, we selected all works that attempted to identify the role of EDF in BPSD, hypothesizing some sort of relationship between the two symptoms. We therefore used the following criteria for exclusion:

- not an original article;
- does not use EDF and / or BPSD as variables;
- does not aim to investigate the association between EDF and BPSD;
- does not have EDF as independent variable and BPSD as dependent variable in its design.

Of the total number of articles, 143 were excluded. Table 1 summarizes the process.

In order to identify works that may not have been included in the first stage of the search, a reverse search was conducted on the references from the 8 selected studies, using the same inclusion and exclusion criteria mentioned above. After this procedure, 5 more works were included, totaling 13 studies that comprised the study population for this review.

RESULTS

We found few studies that set out to investigate the nature of the relationship between EDF and BPSD, considering the first as independent variable and the second as dependent variable.

We looked for specific responses to the guiding questions of our study.

a) Is there a causal relationship between EF and BPSD?

Even considering the different types of study design and data analyses used, this relationship seems to appear consistently. Some considerations, however, must be stated:

- I) The association between EDF and BPSD occurred either as general or specific measures, that is, even if global EF measurements showed an association with BPSD, the relationship appeared to be some impairment between an EDF – specific symptom and a specific feature of BPSD. Verbal fluency, for example, was the EDF parameter that was most frequently associated with symptoms of delirium and hallucination (Chen et al., 1998; Silveri et al., 2004; Hopkins & Libon, 2005; Nagata et al., 2009; Gallagher et al., 2011). This interpretation should be taken with caution, however, since the investigation of specific hypotheses in each study tended to restrict the EDF measurement used.

- II) Some variables appear to alter the relationship between EDF and BPSD, making it necessary to consider them according to the investigated hypothesis. In some studies where the global measure of cognition was controlled, the association between the two symptoms was weakened (Gallo, Schmidt & Libon, 2008), suggesting that changes were associated more with disease severity than with the general measure for EDF, although this relationship did not change in cases where the EDF measure was specific, such as verbal fluency (Hopkins & Libon, 2005; Gallagher et al., 2011).
### Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Assessment instruments for BPSD</th>
<th>Assessment instruments for EF</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chen et al., 1998</td>
<td>Tests the hypotheses that: 1) Deficit in EFs are associated with greater severity of functional impairment and BPSD and 2) Deficit in EF are related to specific BPSD.</td>
<td>A convenience sample of 31 patients (mean age = 69.9, educational = 13.91; MMSE = 17.6) with AD probable, who underwent a neuropsychological evaluation protocol of EF. The assessment of neuropsychiatric symptoms occurred throughout the 2 weeks in which the neuropsychologic protocol was applied. In a first moment correlations were performed to evaluate the association of EF deficits with BPSD, after this the global cognition was controlled and partial correlations were performed.</td>
<td>Neurobehavioral Rating Scale (NRS)</td>
<td>Phonemic Verbal Fluency (FAS), Mattis Subscales of Conceptualization and P/I, Stroop, TMT B and WCST</td>
<td>All measures of EF correlated with Agitation / Disinhibition and the total score of the NRS. The FAS test and WCST were the only measures that correlated significantly with psychoses. After controlling for global cognition, all associations found were changed: the association between verbal fluency test and Agitation/Disinhibition was lost, and psychotic symptoms ceased to associate with measures of both verbal fluency and cognitive flexibility.</td>
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<tr>
<td>1</td>
<td>Nagata et al., 2009</td>
<td>To investigate the relationship between delusional thoughts and EF deficits in patients with Alzheimer’s dementia.</td>
<td>48 elderly patients (women = 32, mean age = 77.2 ± 7) with probable AD (CDR = 0.5 or 2; MMSE &gt; 18) were divided into two groups, those with delusional thoughts (N = 19) and those without (N = 29). Comparisons were made between groups, both of sociodemographic variables and of behavioral and EF measures. Then a logistic regression was conducted to examine the contribution of clinical measures, EF, and general cognition for delusional thoughts.</td>
<td>BEHAVE - AD: Delusional scale.</td>
<td>FAB</td>
<td>The delusional patients group presented a worse FAB performance: total score, similarity, motor sequence and conflicting instructions. The logistic regression showed that the FAB total score, but not MMSE, independently influenced the manifestation of delusional thoughts.</td>
</tr>
<tr>
<td>Study</td>
<td>Hypothesis/Method</td>
<td>Cognitive Measure</td>
<td>Outcome Measures</td>
<td>Results</td>
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<tr>
<td>Moreira et al., 2010</td>
<td>Investigates the hypothesis that both white matter and executive dysfunction are associated with BPSD in patients with stroke.</td>
<td>Behavioral Inhibition Scale (BIS), Trail Making Test A (TMT-A), Verbal Fluency Test (VFT)</td>
<td>Global cognitive function, executive function, and behavioral inhibition</td>
<td>The BPSD group showed worse performance on all cognitive measures compared to the control group.</td>
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<tr>
<td>Negati et al., 2010</td>
<td>To investigate the association between EF and BPSD in Alzheimer’s disease.</td>
<td>Trail Making Test A (TMT-A), Stroop Color-Word Test (Stroop), Wisconsin Card Sorting Test (WCST)</td>
<td>Global cognitive function, executive function, and behavioral inhibition</td>
<td>The BPSD group showed worse performance on all cognitive measures compared to the control group.</td>
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<tr>
<td>Rosengren et al., 2010</td>
<td>To evaluate whether the presence of EF deficits in MCI patients with BPSD is associated with a greater severity of depressive symptoms.</td>
<td>Stroop Color-Word Test (Stroop), Verbal Fluency Test (VFT), Digit Span Test (DST)</td>
<td>Global cognitive function, executive function, and behavioral inhibition</td>
<td>The MCI group showed worse performance on all cognitive measures compared to the control group.</td>
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</table>

The BPSD patients presented with worst performance in both the general cognition and EF measures, and EF had a higher correlation with global cognitive function, executive function, and behavioral inhibition. The MCI group showed worse performance on all cognitive measures compared to the control group. In a multiple regression analysis, the FAB total score was responsible for 27% of the variance in the assessed symptoms.
<table>
<thead>
<tr>
<th>No.</th>
<th>Study</th>
<th>Objective</th>
<th>Methodology</th>
<th>Executive Function Variables</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Garcia-Alberca et al., 2011</td>
<td>To evaluate the involvement of specific cognitive functions, including EF, and its association with BPSD frequency and intensity in AD patients.</td>
<td>A sample of 125 outpatients (Mean Age = 76.4 ± 6; education = 6.34 ± 2.7), with AD diagnosis were assessed with a neuropsychological and behavioral protocol. The cognitive variables which best predicted the BPSD frequency and intensity were investigated, even after having controlled sociodemographic and clinical characteristics.</td>
<td>NPI</td>
<td>All executive function variables proved to be significant in the final regression model for linear frequency and total NPI, the only exception was semantic verbal fluency, which did not enter the model for symptom severity.</td>
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<td>1</td>
<td>Silveri et al., 2004</td>
<td>To investigate whether specific patterns of cognitive impairment are predictors of different types of BPSD, especially mood disorders and psychotic symptoms.</td>
<td>A sample of 40 elderly patients with AD diagnosis (Mean age = 75.6 ± 6.5, education = 7.2 ± 4.5 and MMSE = 17.8 ± 6.4) and fvFTD (Mean age = 76.1 ± 8.9, education = 9.6 ± 5.2 and 19.7 ± MMSE = 6), underwent a neuropsychological assessment protocol of mood changes and psychotic symptoms. Comparisons were made between groups and a linear regression to examine the predictive value of standard neuropsychological deficits in measures of BPSD, especially psychotic and mood symptoms.</td>
<td>Survey Psychiatric Assessment Schedule – SPAS; NPI - Depression, anxiety, delusion and hallucination; Wartegg Completion Task - WCT</td>
<td>Both scales correlated only in the group with fvFTD, either mood change as psychosis symptoms. The linear regression results showed executive measures had predictive value, but only in the fvFTD group and in relation to psychotic symptoms, with the model composed of the Digit Span reverse, Rey Figure Copy, Phonemic Verbal Fluency Test, Raven and nomination. Some cognitive variables showed differential predictive value depending on the behavioral assessment scale used: low scores in the figure copying tasks (Rey), nomination and fluency showed up as predictors of psychotic symptoms when these were assessed by both SPAS and NPI, but the memory test showed value only in relation to psychotic symptoms assessed by the NPI. High scores on Raven were predictors of psychotic symptoms as assessed by the SPAS while high scores on the naming task were predictive when assessed by NPI.</td>
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<td>1</td>
<td>Swamb et al., 2004</td>
<td>Test the hypothesis that AD patients with executive dysfunction would show: 1) worse general cognitive functioning, 2) increased progression of measures of cognitive impairment 12 months from baseline, 3) greater ADL impairment and 4) more BPSD.</td>
<td>A sample of 131 subjects with AD probable (mean age = 72.9 ± 8.4 and education = 13.3 ± 2.8) and a control group of 64 healthy volunteers (age = 70.3 ± 8.8 and education = 13.8 ± 2.9) underwent a neuropsychological protocol of global cognition, EF, and BPSD at first (base line) and after 12 months (follow-up). A performance cutoff of EF assessment tasks was used based on performance of the control group at baseline to define executive dysfunction. Within the experimental group those with and without executive dysfunction were compared in all variables obtained at baseline and on follow-up.</td>
<td>- Cohens-Mansfield Agitation Inventory (CMAI); Behavior Rating Scale of Dementia (BRSD)</td>
<td>Cancellation letters Task and the time to complete the first threeADAS - Cog mazes. Using a Cancellation letters Task cutoff (37.2 / 40), 84 (64%) AD patients were classified as having deficits in EF. AD patients with EF deficit had significantly higher dementia severity (CDR), worse global cognitive functioning (MMSE), the worst scores for ADL's and higher frequency of psychosis symptoms. These subjects also showed significant worsening in dementia severity and overall cognitive functioning when evaluated 12 months after the baseline.</td>
</tr>
<tr>
<td>1</td>
<td>Tsol et al., 2008</td>
<td>Determining whether EF impairment in a population with dementia presents predictive value for the emergence of BPSD in a longitudinal study.</td>
<td>A sample of 42 patients (Mean age = 67.3 ± 7.9) diagnosed with dementia (24 = AD; 14 = VD, 1 = DM, and 3 = FTD), and their caregivers, were evaluated and re-evaluated between 3 to 6 years after the baseline assessment. The measures of global cognition and EF at baseline were tested in a regression model to investigate how much it would explain the BPSD evaluated in Follow-Up. The time variable (baseline to follow-up) and the deterioration degree that occurred in the period were used as covariates.</td>
<td>- Baseline: structured interview; - Follow-up: NPI, CMAI and Dementia Apathy Interview and Rating (DAI-R). None of the global cognition measures were predictive for BPSD at follow-up, on the other hand, CAMCOG-R EF measures showed association with higher levels of BPSD and caregiver stress at follow up. Among the behavioral measures, Apathy was the symptom most strongly associated with difficulties in EF at baseline.</td>
<td>- Baseline: CAMCOG-R, Phonemic Verbal Fluency; - Follow-Up: CAMCOG-R and Phonemic Verbal Fluency</td>
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<tr>
<td>2</td>
<td>Gokalsingh et al., 2000</td>
<td>To test the hypothesis that disinhibition and irritability, defined as loss of behavioral and emotional control, are disorders associated with changes in the control of cognitive processes, suggesting a general executive dysfunction of the Supervisory Attentional System (SAS).</td>
<td>28 elderly patients (Mean age = 69.35 ± 6.48 and education = 10.57 ± 3.75), native French speakers, were divided into two groups matched for age, sex and education, one group with and another without disinhibition according to the NPI. All patients underwent a Neuropsychological and BPSD assessment. Furthermore, two experimental tasks to evaluate EF were also used: The sentence arrangement task and four new CPT measures (sustained, selective, preparation and suppressive attention).</td>
<td>NPI, Impulsivity Rating Scale (IRS), BPSD, Montgomery and Asberg Depression Scale (MADRS) and Anxiety Scale COVI.</td>
<td>Trail Making Test - parts A and B, Phonemic and Semantic Verbal Fluency, Continuous Performance Test, Experimental Sentence Arrangement Task</td>
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<p>| 2 | Hopkins et al., 2005 | To examine the hypothesis that psychotic symptoms in dementia are associated with an inability of EF to regulate or put into context visuospatial stimuli. | 24 patients with psychotic symptoms (age = 78.37 ± 6.63 and education = 11.33 ± 2.82) and 24 without symptoms (age = 79.75 ± 7.7 and education = 11.54 ± 2.8) matched for general cognition and depressive symptoms, underwent a neuropsychological assessment protocol, especially for EF and visuospatial processing. The groups were compared on performance of neuropsychological protocol and in the second stage EF measures were used to examine their contribution to the total of psychotic symptoms. | NPI | Boston Revision of the Wechsler Memory Scale - Mental Control subtest (WMS - MC), Phonemic and Semantic Verbal Fluency, Clock drawing task | In comparisons between the groups, psychotic patients had lower scores on WMS - MC. In intra group comparison, subjects with high scores for psychotic symptoms also had poorer performance on WMS - MC and FAS, besides presenting a significantly higher percentage of type All / Part Errors than subjects with low scores on the Boston nomination test. On the linear regression, after controlling for general cognition (MMSE), the performance on WMS - MC was responsible for almost half of the variance, being the main cognitive variable on the predictive model. |</p>
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<td>2</td>
<td>Galet et al., 2008</td>
<td>First, investigate the hypothesis that BPSD expression is not a function of dementia severity but a combination with EF impaired. Second, investigate how BPSD and EF deficits are associated with functional loss. A sample of 48 patients (age = 79 ± 5.44 and education = 13 ± 2.58) underwent neuropsychological and functional assessments. The association between cognitive variables, including EF and BPSD, were examined as well as how much the first one could predict the second. All cognitive scores were standardized in a z-score. The predictive value of both symptoms, behavioral and executive, for the impairment of instrumental activities of daily living were also investigated.</td>
<td>NPI</td>
<td>Phonemic Verbal Fluency (FAS) and Clock drawing task</td>
<td>The total score for MMSE correlated significantly only with NPI total. As for functionality, it was found that the index of EF correlated moderately with ADLs, plus the total NPI and MMSE. In regression analysis, only the total MMSE and NPI proved to be significant in the regression model.</td>
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<td>1</td>
<td>Galagher et al., 2011</td>
<td>To investigate the role of socioeconomic variables, EF, visioperceptual processing and neuroimages for an etiological model of hallucinations in Parkinson’s disease patients. 30 subjects with visual hallucination symptoms (age = 65.5 to 74.3) and 64 without symptoms (age = 59 to 74) underwent an extensive evaluation battery of symptoms related to Parkinson’s disease, sleep disorders, depression, hallucination, EF, global cognition and visual perception. From the medical records of independent sample, a brain histological specimens, a clinical, demographic and the presence of cognitive deficits documented were evaluated. Comparisons were made between groups with and without hallucinations and the contribution of each variable for the presence or absence of visual hallucinations were investigated.</td>
<td>Sleep Scale, Life Apathy Rating Scale, Hamilton Depression Scale, University of Miami Parkinson’s disease hallucinations questionnaire - UMP - HQ</td>
<td>FAB, SCOPA - COG attention and SCOPA - COG executive</td>
<td>There were differences between the groups with and without visual hallucinations in FAB and SCOPA-COG executive measures, but not in SCOPA-COG attention measures. In the binary logistic regression analysis as well as measures of sleep disturbances, vision and global cognition, the SCOPA-COG executive score was also included in the final model.</td>
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III) The differences in the type of investigation instruments for BPSD should also be considered. Silveri et al. (2004) demonstrated that some results varied depending on the source of data collection, considering both objective instruments, such as the Neuropsychiatric Inventory (Cummings et al., 1994), and subjective ones, such as the Survey Psychiatric Assessment Schedule (Bond et al., 1980), where the lack of correlation between the two scales was interpreted as a consequence of the sensitivity of each instrument to different aspects of the same symptom.

b) What are the main assumptions or theoretical models that explain this relationship?

The examination of the 13 works allowed a division to be made into two groups according to the guiding questions of this study: the first (G1) consisted of 10 works (Chen et al., 1998; Silveri et al., 2004; Swamberg et al., 2004; Hopkins et al., 2005; Tsoi, Baillon & Lindesay, 2008; Nagata et al., 2009; Mok et al., 2010; Nagata et al., 2010; Gallagher et al., 2011; García-Alberca et al., 2011; Rosenberg et al., 2011) that investigated the specificity of the relation between EDF and BPSD, considering changes in EDF as a risk factor for the emergence of BPSD.

The second group (G2) was comprised of three studies (Gokalsing et al., 2000; Silveri et al., 2004; Gallo, Schmidt & Libon, 2008), which tested the relation between EDF and BPSD from the perspective of some theoretical cognitive model. For example, how would specific cognitive changes influence the BPSD at a more basic level of processing and its consequent behavioral response?

A work summary is presented in Table 2, divided into group, work, objective, design, assessment instruments for EF, assessment instruments for BPSD, and results.

**DISCUSSION**

In general, G1 studies show that EDF has a significant association with BPSD, independent of other cognitive functions. In addition, the general measures of EF showed indexes that were more consistent as predictors for emergence of later BPSD, mainly for mood changes (depression and anxiety / agitation). The authors emphasized the importance of using specific instruments for the assessment of EDF, especially in cases that exhibit both cognitive and behavioral changes. The most often used EDF instruments were the Verbal Fluency Test (Chen et al., 1998; Silveri et al., 2004; Hopkins et al., 2005; Gallo, Schmidt & Libon, 2008; García-Alberca et al., 2011) and the Frontal Assessment Battery – FAB (Nagata et al., 2009; Nagata et al., 2010; Gallagher et al., 2011), while the tools used for further evaluating BPSD were the NPI (Chen et al., 1998; Gokalsing et al., 2000; Silveri et al., 2004; Hopkins et al., 2005; Tsoi, Baillon & Lindesay, 2008; Mok et al., 2010; Rosenberg et al., 2011; García-Alberca et al., 2011) and BEHAVE – AD (Nagata et al., 2009; Nagata et al., 2010).
Gokalsing et al. (2000) tested the hypothesis that disinhibition and irritability, defined as a loss of behavioral and emotional control, would be disorders associated with changes in the control of cognitive processes, suggesting a general executive dysfunction of the Supervisory Attentional System - SAS (Shallice & Burgess, 1991). Based on the results, the authors concluded that the subjects with disinhibition symptoms take longer to inhibit the prepotent response of an automatic process, and that this could be related to their reduced ability to “re-focus” attention on alternative response strategies when an automatic routine procedure is available. The difficulty of the experimental subjects was not related to motor impulsivity, but to the difficulty in inhibiting automatic processes according to the SAS model.

Hopkins et al. (2005) examined the hypothesis that psychotic symptoms in dementia were associated with executive control dysfunction in regulating or contextualizing visuospatial stimuli. The authors found differences between the groups with and without symptoms of psychosis in primary EF measures, but did not find these for visuospatial processing measures. In the second stage of analysis, the group with psychotic symptoms was subdivided into subjects with greater and lesser degrees of symptoms. Both executive and visuospatial processing measures were compared in these subgroups, and they presented differences in this analysis. In the last step, we used a multivariate linear regression (stepwise method) to investigate the independent contribution of each cognitive variable (global cognition, executive functions, nomination, visuospatial processing, and memory) for the total measure of severity of psychotic symptoms. Only the measures of global cognition and EDF proved significant in the regression model, with the EDF measure alone being responsible for nearly 50% of the variance in the severity of psychotic symptoms. Since the visuospatial processing measure did not enter in the regression model and since a difference in performance was only found when comparing subjects with greater and lesser severity of psychotic symptoms, the initial hypothesis that visuospatial processing would also be responsible for the severity of psychotic symptoms was only partially upheld, although the authors recognize the limitation of using a non-specific test for visuospatial processing.

Gallo et al. (2008) investigated the hypothesis that the expression of BPSD would not be a unique function of dementia severity, but a combination of this with EDF. Furthermore, executive control would be responsible for much of the variance of BPSD, which would add to the explanation generated by the dementia severity model. Even finding no significant associations between measures of EDF or other specific cognitive measures and BPSD, the authors raised two distinct explanatory hypotheses for the negative result: 1) in the early stages of dementia, the emergence of BPSD and difficulties in specific cognitive functions are relatively independent, or
2) overall measures of BPSD may well require more than a single cognitive factor to be influenced in this presentation.

The works analyzed do not allow us to determine unambiguously the association between EF and BPSD, mainly due to such limitations as sample size, EDF assessment instruments, and the techniques used to analyze the data in each study. This interpretation is more prudent, given the divergence in the literature. While some authors have reported the existence of an association between EDF and BPSD (Mega et al., 2000; Gokalsing et al., 2000; Nakaaki et al., 2008; Butterfield et al., 2010; Monley et al., 2011, Pachalska et al., 2011), others present results suggesting that there is no such relationship (Gallagher et al., 2011; Nagata et al., 2010; Raczka et al., 2010; Senanarong et al., 2005). The argument used by the group that supports the idea of an association is anchored in positive evidence for an association between EDF, BPSD and malfunctions of the frontal brain regions in neuroimaging studies (Morley et al., 2011; Naarding et al., 2007; Pagonnabarraga et al., 2008). The authors who claim there is no relation between both symptoms, on the other hand, argue that while EDF symptoms are related to atrophy of the more dorsal regions of the prefrontal cortex, the BPSD does not present the same anatomical and clinical specificity, with most of these symptoms being related to the involvement of subcortical structures (Migliorelli et al., 1995; White and Cummings, 1996; Kruger et al., 2011).

The purpose of our review was to investigate what is known in the literature about the nature of the relationship between EDF and BPSD. We assume that changes in executive functions cause BPSD. Many of the works found during our search used BPSD as an independent variable and EDF as a dependent variable. In our view, this design restricts the research possibilities by focusing on cognitive descriptive aspects of the patient profile with or without BPSD, but reporting little on the nature of this association.

We could not find a theoretical model that was more frequent or more accepted to cast light on the nature of the relationship between EDF and BPSD. The majority of studies (G1) determined the relationship between the two variables mainly from the work design. Deficits in general executive functions were used as predictors for the emergence of BPSD, but the nature of this relationship was only discussed or hypothesized in the discussion section. The 3 studies that hypothesized and tested in a quasi-experimental design the relationship between EDF and BPSD (G2) used different explanatory models.

Some limitations must be considered:

- 1) the small number of studies that met the inclusion criteria may have limited our knowledge about the variety of models used to explain the relationship between EDF and the prevalence of BPSD.
- 2) The non-systematic use in the literature of keywords and terms related to both EF and BPSD has significantly limited the development of a systematic and efficient search covering the vast majority of works on the theme.

Our option to develop an algorithm that would encompass the largest amount of terms used was a strategy to overcome the difficulty of searching the vast set of works on the topic.
of possible terms associated to both EF and BPSD. The use of indexed terms, like the Mesh terms of PubMed, is a useful proposal to solve this problem, although not all data bases have indexed terms and not all keyword or terms have been indexed.

Future systematic literature reviews that restrict keywords to indexed terms in order to investigate both the consistency and the effect size of the study results with comparable designs may help us to better understand the nature of the relationship between EF and BPSD.

CONCLUSION

Executive dysfunction and the behavioral and psychological symptoms of dementia are among the main factors directly related to functional loss and quality of life in patients with dementia. Knowledge about the role of frontal brain regions for both executive functions and behavioral changes has advanced in recent years. A focus on the mechanisms underlying this association by means of cognitive theoretical models is a potential pathway for understanding the role of EF deficits in neuropsychiatric symptoms.

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Moreira et al., Executive dysfunction and BPSD


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