Cognitive impairment in COPD: a systematic review*

Comprometimento cognitivo em pacientes com DPOC: uma revisão sistemática

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Abstract
The objectives of this study were to characterize and clarify the relationships between the various cognitive domains affected in COPD patients and the disease itself, as well as to determine the prevalence of impairment in the various cognitive domains in such patients. To that end, we performed a systematic review using the following databases: PubMed, Scopus, and ScienceDirect. We included articles that provided information on cognitive impairment in COPD patients. The review of the findings of the articles showed a significant relationship between COPD and cognitive impairment. The most widely studied cognitive domains are memory and attention. Verbal memory and learning constitute the second most commonly impaired cognitive domain in patients with COPD. The prevalence of impairment in visuospatial memory and intermediate visual memory is 26.9% and 19.2%, respectively. We found that cognitive impairment is associated with the profile of COPD severity and its comorbidities. The articles reviewed demonstrated that there is considerable impairment of the cognitive domains memory and attention in patients with COPD. Future studies should address impairments in different cognitive domains according to the disease stage in patients with COPD.

Keywords: Pulmonary disease, chronic obstructive; Mild cognitive impairment; Hypoxia, brain.

Introduction
The hallmark of COPD is chronic airflow obstruction that has a systemic impact and a progressive evolution. It is an important health problem that is estimated to become the fifth leading cause of disability and the third leading cause of death worldwide by 2020. The prevalence of COPD in the global population is close to one percent and increases with age. Among individuals 40 years of age or older in the city of São Paulo, Brazil, its prevalence ranges from 6 to 15.8%.

The typical profile of patients with COPD includes multiple comorbidities, such as heart...
Table 1 - Characteristics of the articles selected.

| Study          | Design       | Objective                                                                 | Sample size and COPD severity | Characteristics of COPD participants                  | Intervention | Results/Conclusions                                                                                     |
|---------------|--------------|----------------------------------------------------------------------------|--------------------------------|-------------------------------------------------------|--------------|--------------------------------------------------------------------------------------------------------|
| Dodd et al.   | Observational| To assess neuropsychological performance in COPD patients hospitalized after an acute exacerbation and recovery, compared with patients with stable COPD and with healthy control subjects | 110 participants: 30 COPD inpatients hospitalized following an exacerbation; 50 outpatients with stable COPD; 30 healthy control subjects | Mean age, 70 ± 11 years; 15 (50%) were female; Mean age, 69 ± 8 years; 28 (56%) were female | -            | In patients hospitalized with an acute COPD exacerbation, impaired cognitive function is associated with worse health status and longer length of hospital stay. Cognitive function might not improve with recovery. |
| Chang et al.  | Cohort       | To determine the extent to which the co-occurrence of COPD and cognitive impairment leads to adverse health outcomes in older adults | 3,093 patients: 431 with COPD only; 29 with COPD and cognitive impairment; 114 with cognitive impairment only; 2,519 with neither COPD nor cognitive impairment | Mean age, 68.84 ± 8.43 years; 29 (64%) were female | None         | Patients with COPD and cognitive impairment had the highest rates of respiratory-related and all-cause hospitalizations and death. |
| Villeneuve et al. | Observational | To evaluate whether there are significant differences between COPD patients and control subjects, in terms of white matter integrity and communication between gray matter resting-state networks, and to test the observed differences related to disease severity, comorbid cerebrovascular disease, and cognitive dysfunction | 45 patients with moderate-to-severe COPD; 50 healthy control subjects | Mean age, 68.84 ± 8.43 years; 29 (64%) were female | None         | In stable, non-hypoxemic COPD, there is reduced white matter integrity throughout the brain and widespread disturbance in the functional activation of gray matter, which might contribute to cognitive dysfunction. White matter microstructural integrity is independent of smoking and comorbid cerebrovascular disease, but gray matter functional activation is not. The mechanisms remain unclear but could include cerebral small vessel disease caused by COPD. |
| Martin et al. | Clinical     | To determine the effect of hypoxia on cognitive performance in COPD patients with PaO2 < 6.6 kPa | 10 patients with moderate-to-severe COPD | Mean age, 64 years; 3 (30%) were female | For a short period of time, patients breathed 21% O2 when PaO2 was < 6.6 kPa | Short-term exposure to hypoxia had no adverse effect on cognitive function. |
| Pereira et al. | Clinical     | To evaluate the effect of a multidisciplinary pulmonary rehabilitation program on cognitive function in COPD patients, adjusting for potential confounders | 34 patients with moderate-to-severe COPD | Mean age, 65.2 ± 7 years; 17 (50%) were female | A 3-month program of pulmonary rehabilitation | Even after adjusting for the sociodemographic factors that might affect cognitive function, the authors found that pulmonary rehabilitation improved cognitive performance in COPD patients. There were gender- and age-related differences in cognitive scores that persisted after rehabilitation. |
| Klein et al.  | Cohort       | To explore the influence of COPD on attentional functions, learning, and logical thinking | 60 COPD patients; 60 control subjects | Mean age, 63.2 ± 9.8 years; 24 (40%) were female | None         | In COPD patients, there was global impairment in cognitive functions that was negatively influenced by advancing age and increased in proportion to the degree of disease severity. |
| Thakur et al. | Cohort       | To elucidate the association between COPD and the risk of cognitive impairment, in comparison with control subjects without COPD | 1,202 COPD patients; 302 control subjects | Mean age, 58.2 ± 6.2 years; 691 (57.4%) were female | None         | COPD is a major risk factor for cognitive impairment. In COPD patients, hypoxemia is a major contributor to cognitive impairment and regular use of home oxygen is a protective factor. Health care providers should consider screening COPD patients for cognitive impairment. |
Table 1 – Continued...

| Study | Design | Objective | Sample size and COPD severity | Characteristics of COPD participants | Intervention | Results/Conclusions |
|-------|--------|-----------|-------------------------------|--------------------------------------|--------------|---------------------|
| Antonelli-Incalzi et al. (14) | Observational study | To assess whether certain neuropsychological patterns are associated with various limitations to physical independence in COPD patients | 149 COPD patients | Mean age: 68.5 ± 8.0 years; 11 (64%) were female | None | COPD is associated with slight decreases in mood and cognition. Severe COPD is associated with chronic systemic inflammation and subtle cognitive deficits (e.g., digit symbol coding tasks). Levels of oxygen desaturation appear to mediate specific changes in brain neurochemistry and structure that suggest sustained brain damage. |
| Borson et al. (15) | Observational study | To model the relationship between respiratory failure and domains related to brain function, including low mood, subtly impaired cognition, systemic inflammation, and structural/neurochemical brain abnormalities | 9 healthy control subjects | None | COPD patients are more likely to cause a traffic accident. Impaired driving performance in COPD patients cannot be predicted on the basis of the severity of the disease. There might be subclinical encephalopathy in COPD, characterized by subtle impairment of global cognitive ability. |
| Orth et al. (16) | Observational study | To analyze driving performance in COPD patients and healthy control subjects | 17 COPD patients | Mean age: 66.7 ± 2.5 years; 14 (44%) were female | None | Cognitive function in COPD patients with hypoxemia might not be impaired despite their poor quality of life status. |
| Pinto de Lima et al. (17) | Observational study | To test the hypothesis that clinically stable COPD patients without overt cognitive symptoms can nonetheless have subtle cognitive impairment | 30 COPD patients | Mean age: 65 ± 8 years; 10 (33%) were female | None | Cognitive impairment was more prevalent in patients with congestive heart failure or COPD than in those with cancer. |
| Salik et al. (18) | Observational study | To determine the relationship between cognitive function and quality of life in COPD patients with mild hypoxemia and moderate airway obstruction | 149 COPD patients | Mean age: 68.7 ± 8.5 years; 22 (16.4%) were female | None | Impaired drawing ability is a risk factor for mortality and its testing might improve the assessment of hypoxemic COPD patients. |
| Antonelli-Incalzi et al. (19) | Observational study | To evaluate the prognostic role of cognitive impairment in patients with severe COPD | 49 newly diagnosed, untreated OSA patients | None | A minority of newly diagnosed OSA patients had distinct neuropsychological impairment. The greater body mass index of cognitively impaired OSA patients indicates that the metabolic syndrome might also be causally related to the cognitive dysfunction. |

MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MCI: mild cognitive impairment; kPa: kilopascal; CHF: congestive heart failure; and OSA: obstructive sleep apnea.
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We systematically searched the following databases: PubMed, Scopus, and ScienceDirect. Searches were limited to studies in humans published in the last ten years in order to focus on the recent interest and scientific evidence in this area. The inclusion criteria were being a clinical trial, epidemiological study, observational study, cohort study, or case-control study; and providing information on the subject at hand (i.e., cognitive impairment in COPD patients). We excluded articles that dealt with subjects unrelated to this topic, those that were not available in full text, and those that were review articles or simple case reports, as well as those published in languages other than English, Spanish, or French. The article selection process is depicted as a flowchart in Figure 1.

Results

The search yielded 478 articles. After the abstracts had been reviewed, only 16 articles were selected for inclusion in the review. The characteristics of the selected articles are shown in Table 1. Our review of those studies revealed a significant relationship between COPD and cognitive impairment. It is important to point out that there is as yet no consensus regarding the definition of cognitive impairment in patients with COPD. Different operational definitions of such impairment among the studies reviewed made it difficult to evaluate that aspect across those studies.

Methods

In this review of the literature, we adopted the classification of cognitive domains devised by Lezak,\(^{18}\) According to that author, who is the current reference in neuropsychological assessment, the cognitive domains correspond to five key areas: perception; attention; memory and learning; executive function; and language. We adopted a systematic approach using the following search strings (comprising terms related to COPD and to the Lezak classification of cognitive domains): “cognitive impairment” AND “COPD”; “cognitive decline” AND “COPD”; “cognitive dysfunction” AND “COPD”; “hypoxia” AND “cognitive impairment” AND “pulmonary disease”; “cognitive impairment” AND “hypercapnia” AND “pulmonary disease”; “cognitive attention” AND “COPD”; “memory and learning” AND “COPD”; “memory learning” AND “COPD” AND “cognitive”; “perceptive function” AND “COPD”; “verbal language” AND “COPD”; and “executive functions” AND “COPD”.

Discussion

Various controlled studies have investigated the prevalence of cognitive impairment in

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COPD,\(^\text{21,25,28}\) showing that prevalence to be higher in COPD patients than in healthy control subjects.\(^\text{10,31}\) According to such studies, mild cognitive impairment is present in 36% of COPD patients and in 12% of subjects without COPD. In a study conducted by Antonelli-Incalzi et al.,\(^\text{30}\) the prevalence of cognitive impairment and severe cognitive impairment in COPD patients was found to be 32.8% and 10.4%, respectively.

The prevalence of cognitive impairment in patients with COPD was found to be associated with the severity of the disease,\(^\text{20,25}\) being 3.9% among patients with mild COPD, 5.7% among patients with moderate COPD, and 7.7% among patients with severe COPD. In fact, a relationship has been found between the Mini-Mental State Examination score and the severity of COPD \((r = -0.49, p < 0.001)\).\(^\text{30}\) However, the study conducted by Salik et al.\(^\text{29}\) showed that cognitive function in COPD patients with mild hypoxemia was similar to that observed for healthy subjects. According to those authors, cognitive function is affected by hypoxemia only when the latter is severe. In addition, Grant et al.\(^\text{17}\) reported a 77% prevalence of cognitive impairment in patients with hypoxemic COPD. The reasons for this variation across studies include differences in the degree of COPD severity and in the age of the patients included in the studies, as well as the use of different diagnostic criteria for cognitive dysfunction and different cognitive tests.

The studies included in our review had large sample sizes and included a great variety of patients, which reduces any bias in prevalence rates. It is known that COPD is associated with an increased risk of impaired cognitive function,\(^\text{26}\) even when the data are adjusted for age, gender, smoking history, and level of education.\(^\text{19,25}\) Villeneuve et al.\(^\text{10}\) reported that level of education was the only variable for which there were significant differences among COPD patients with mild cognitive impairment, COPD patients without cognitive impairment, and healthy control subjects.\(^\text{10}\) The authors ruled out strokes and

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**Figure 1** - Selection of the articles analyzed in this review.
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Lezak, refers to skills involved in formulating

variables more commonly impaired in the main

subtypes of mild cognitive impairment found in

patients with COPD.

Learning implies acquiring information and

therefore changes the state of memory. Verbal

memory is one of the cognitive domains that

are most frequently impaired in patients with

COPD.10 According to Villeneuve et al.,10 verbal

memory and learning is the second most commonly

impaired cognitive domain in patients with COPD.

In such patients, the prevalence of impairment

in visuospatial memory and intermediate visual

memory is 26.9% and 19.2%, respectively.14 In

patients with COPD and sleep apnea, verbal

memory and visual memory are the most commonly

affected cognitive domains,28 although processing

speed, working memory, and executive function

are also affected (p = 0.01, p = 0.02, and p ≤ 0.001,

respectively).23

The term “executive functions”, coined by

Lezak, refers to skills involved in formulating

goals, planning their achievement, and effectively

performing behaviors.18 The assessment of

executive functions in patients with COPD

has shown that such patients tend to have

slower processing speeds.19 Twenty percent of

patients with exacerbated COPD exhibit a loss in

processing speed that is significant enough to be

considered pathological. Slower processing speed

has been related to the duration of hospital stay,

quality of life measured with the Saint George's

Respiratory Questionnaire, and the number of

COPD exacerbations.19

The ability to understand and communicate

is determined by language. This mental process

enables structured thinking, allowing an individual
to make connections between ideas and mental

representations. There have been studies evaluating
cognitive function in a number of diseases,20

including sleep apnea and COPD. Patients with

COPD and sleep apnea have been found to

perform more poorly on tests of verbal fluency

and deductive thinking than do COPD patients

without sleep apnea. There are data indicating

that only 3% of COPD patients have a completely

normal cognitive profile.19

We made cognitive impairment the focus of

the present review because it is a common
cosorbidity in patients with COPD. The strength

of our review is that it explored the relationship

between COPD and cognitive impairment in the

various cognitive domains over the last ten years,
during which time a number of relevant clinical

studies on this subject have been conducted. In

addition, the studies included had large sample

sizes. There have been a number of reviews of

cognitive impairment in elderly people and

COPD patients.13-16 The review conducted by

Schillerstrom et al.23 addressed the impact of

medical illness on executive function. In another

review, Dodd et al.11 explored the mechanisms

that cause injury and dysfunction in the brain,
discussing the methods used in order to evaluate
cognition, gathering evidence on the nature

and level of cognitive impairment in COPD. Another

recent review, conducted by Schou et al.,17

investigated the occurrence and severity of
cognitive dysfunction in COPD patients, exploring

the relationship between the severity of COPD

and the level of cognitive function. In our review,

we included nine new studies about COPD and
cognitive impairment, conducted between 2009

and 2013, which were excluded from the review

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Table 2 - Tests or batteries of tests used in the assessment of the cognitive domains under study in the articles selected.

| Neuropsychological assessment instrument or function assessed | Cognitive domain |
|--------------------------------------------------------------|-------------------|
|                                                              | Perception | Attention | Memory and learning | Abstract thinking and executive function | Language | Intelligence | General (global screening) |
| Wechsler Test of Adult Reading(19,22) | X          | X          |                       |                       |          |              |                       |
| Mini-Mental State Examination(10,19,21,25,28-30) | X          | X          |                       |                       |          |              |                       |
| Rey Complex Figure Test-Copy and Rey Complex Figure Test-Recall(19,22) | X          | X          |                       |                       |          |              |                       |
| Wechsler Memory Scale-III UK Word Lists(10) | X          | X          |                       |                       |          |              |                       |
| Delis-Kaplan Verbal Fluency test(19) | X          | X          |                       |                       |          |              |                       |
| Delis-Kaplan Trail Making Test(10,19,21) | X          | X          |                       |                       |          |              |                       |
| Wechsler Adult Intelligence Scale-III UK Letter-Number Sequencing(19,21) | X          | X          |                       |                       |          |              |                       |
| Wechsler Memory Scale-III UK Spatial Span(19,21) | X          | X          |                       |                       |          |              |                       |
| Wechsler Adult Intelligence Scale-III Digit Symbol(19,21) | X          | X          |                       |                       |          |              |                       |
| Wechsler Adult Intelligence Scale-III Symbol Search(19,21) | X          | X          |                       |                       |          |              |                       |
| Montreal Cognitive Assessment(10) | X          | X          |                       |                       |          |              |                       |
| Digit Span Test (Wechsler Adult Intelligence Scale-III)(19,21) | X          | X          |                       |                       |          |              |                       |
| Digit Symbol coding test (Wechsler Adult Intelligence Scale-III)(19) | X          | X          |                       |                       |          |              |                       |
| Semantic Verbal Fluency(19) | X          | X          |                       |                       |          |              |                       |
| Letter verbal fluency (P, F and L)(19) | X          | X          |                       |                       |          |              |                       |
| Rey Auditory Verbal Learning test(19,21) | X          | X          |                       |                       |          |              |                       |
| Block Design(19) | X          | X          |                       |                       |          |              |                       |
| Bells Test(19) | X          | X          |                       |                       |          |              |                       |
| Word Lists Learning, Delayed Recall, and Delayed Recognition (Wechsler Memory Scale-III)(20) | X          | X          |                       |                       |          |              |                       |
| Verbal Fluency-FAS task (Delis-Kaplan Executive Function System)(19,21) | X          | X          |                       |                       |          |              |                       |
| Stroop Color-Word Test(19,21) | X          | X          |                       |                       |          |              |                       |
| Attention Network Test(19) | X          | X          |                       |                       |          |              |                       |
| Standard Progressive Matrices(23) | X          | X          |                       |                       |          |              |                       |
| Verbal and Nonverbal Learning Test (part of the Vienna Test System)(24) | X          | X          |                       |                       |          |              |                       |
| Raven’s Colored Progressive Matrices(19) | X          | X          |                       |                       |          |              |                       |
| Phonemic verbal fluency test(19) | X          | X          |                       |                       |          |              |                       |
| Corsi Block-Tapping task (visuospatial span)(19) | X          | X          |                       |                       |          |              |                       |
| Verbal word span(19) | X          | X          |                       |                       |          |              |                       |
| Rey Auditory 15-Word Learning test(19) | X          | X          |                       |                       |          |              |                       |
| Albert’s test (visual exploration)(19) | X          | X          |                       |                       |          |              |                       |
| Copying geometrical drawings with or without landmarks(19) | X          | X          |                       |                       |          |              |                       |
| Immediate Visual Memory Test(19) | X          | X          |                       |                       |          |              |                       |
| Sentence construction(19) | X          | X          |                       |                       |          |              |                       |
| The Computer-Aided Risk Simulator (driving simulator test)(27) | X          | X          |                       |                       |          |              |                       |
| Dementia Rating Scale(19,28) | X          | X          |                       |                       |          |              |                       |
| Wide Range Achievement Test-3(24) | X          | X          |                       |                       |          |              |                       |
| Logical memory subtest of the Wechsler Memory Scale-III(21) | X          | X          |                       |                       |          |              |                       |
| Mental Deterioration Battery(16) | X          | X          |                       |                       |          |              |                       |
| 10-item Hodkinson Abbreviated Mental Test(20) | X          | X          |                       |                       |          |              |                       |
Conducted by Schou et al., because they were not published within the date range set for the search of the literature in the latter.

One of the limitations of the present review is the great variety of outcome measures evaluated. However, our review of the literature clearly showed the existence of a relationship between COPD and cognitive impairment. That relationship appears to be determined by the severity of COPD and by its comorbidities.

The most widely studied cognitive domains are memory and attention, both of which have been explored with specific assessment tools and found to be considerably impaired in patients with COPD. Evidence suggests that a structured assessment of cognitive function should be a routine component of the evaluation of COPD patients. Future studies should explore impairment in the various cognitive domains in COPD patients at different stages of the disease.

References

1. de Batlle J, Romieu I, Antó JM, Mendez M, Rodríguez E, Balcells E, et al. Dietary habits of firstly admitted Spanish COPD patients. Respir Med. 2009;103(12):1904-10. http://dx.doi.org/10.1016/j.rmed.2009.06.001
2. Jemal A, Ward E, Hao Y, Thun M. Trends in the leading causes of death in the United States, 1970-2002. JAMA. 2005;294(10):1255-9. http://dx.doi.org/10.1001/jama.294.10.1255
3. Sociedade Brasileira de Pneumologia e Tisiologia. II Consenso Brasileiro sobre Doença Pulmonar Obstrutiva Crônica (DPOC). J Pneumol. 2004;30(Suppl 5):1-42.
4. de Oliveira JC, de Carvalho Aguiar I, de Oliveira Beloto AC, Santos IR, Filho FS, Sampaio LM, et al. Clinical significance of COPD patients followed in a real practice. Multidiscip Respir Med. 2013;8(1):4. http://dx.doi.org/10.1186/2049-6958-8-4
5. Miravitles M, Muñoz C, Tirado-Conde G, Levy G, Muellerova H, Soriano JB, et al. Geographic differences in clinical characteristics and management of COPD: the EPOCA study. Int J Chron Obstruct Pulmon Dis. 2008;3(4):803-14. http://dx.doi.org/10.2147/COPD.S4257
6. Sin DD, Lacy P, Yong E, Man SF. Effects of fluticasone on systemic markers of inflammation in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2004;170(7):760-5. http://dx.doi.org/10.1164/rccm.200404-5430OC
7. Bolton CE, Ionescu AA, Shiels KM, Pettit RJ, Edwards PH, Stone MD, et al. Associated loss of fat-free mass and bone mineral density in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2004;170(12):1286-93. http://dx.doi.org/10.1164/rccm.200406-7540OC
8. Mannino DM, Thorn D, Swensen A, Holguín F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. Eur Respir J. 2008;32(4):962-9. http://dx.doi.org/10.1183/09031936.00012408
9. Wasswa-Kintu S, Gan WQ, Man SF, Pare PD, Sin DD. Relationship between reduced forced expiratory volume in one second and the risk of lung cancer: a systematic review and meta-analysis. Thorax. 2005;60(7):570-5. http://dx.doi.org/10.1136/thx.2004.037135
10. Villeneuve S, Pepin V, Rahayel S, Bertrand JA, de Lorimier M, Rizk A, et al. Mild cognitive impairment in moderate to severe COPD: a preliminary study. Chest. 2012;142(6):1516-23. http://dx.doi.org/10.1378/chest.11-3035
11. Dodd JW, Getov SV, Jones PW. Cognitive function in COPD. Eur Respir J. 2010;35(4):913-22. http://dx.doi.org/10.1183/09031936.00125109
12. Allen SC, Jain M, Ragab S, Malik N. Acquisition and short-term retention of inhaler techniques require intact executive function in elderly subjects. Age Ageing. 2003;32(3):299-302. http://dx.doi.org/10.1093/ageing/32.3.299
13. Antonelli-Incalzi R, Gemma A, Marra C, Capparella G, Fusco L, Carbonin P. Verbal memory impairment in COPD: its mechanisms and clinical relevance. Chest. 1997;112(6):1506-13. http://dx.doi.org/10.1378/chest.112.6.1506
14. Antonelli-Incalzi R, Corsonello A, Trojano L, Acanfora D, Spada A, Izzo O, et al. Correlation between cognitive impairment and dependence in hypoxemic COPD. J Clin Exp Neuropsychol. 2008;30(2):141-50. http://dx.doi.org/10.1080/13803390701287390
15. Hung WW, Wisnivesky JP, Siu AL, Ross JS. Cognitive decline among patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2009;180(2):134-7. http://dx.doi.org/10.1164/rccm.200902-0276OC
16. Heaton RK, Grant I, McSweeney AJ, Adams KM, Petty TL. Psychologic effects of continuous and nocturnal oxygen therapy in hypoxemic chronic obstructive pulmonary disease. Arch Intern Med. 1983;143(10):1941-7. http://dx.doi.org/10.1001/archinte.1983.00350100121023
17. Grant I, Heaton RK, McSweeney AJ, Adams KM, Timms RM. Neuropsychologic findings in hypoxemic chronic obstructive pulmonary disease. Arch Intern Med. 1982;142(8):1470-6. http://dx.doi.org/10.1001/archinte.1982.00350100121023
18. Lezak MD, Howieson DB, Loring DW. Neuropsychological assessment. 4th ed. New York: Oxford University Press; 2004.
19. Dodd JW, Charlton RA, van den Broek MD, Jones PW. Cognitive dysfunction in patients hospitalized with acute exacerbation of COPD. Chest. 2013;144(1):119-27. http://dx.doi.org/10.1378/chest.12-2099
20. Chang SS, Chen S, McAvay GJ, Tinetti ME. Effect of coexisting chronic obstructive pulmonary disease and cognitive impairment on health outcomes in older adults. J Am Geriatr Soc. 2012;60(10):1839-46. http://dx.doi.org/10.1111/j.1532-5415.2012.04171.x
21. Dodd JW, Chung AW, van den Broek MD, Barrick TR, Charlton RA, Jones PW. Brain structure and function in chronic obstructive pulmonary disease: a multimodal cranial magnetic resonance imaging study. Am J Respir Crit Care Med. 2012;186(3):240-5. http://dx.doi.org/10.1164/rccm.201202-0355OC
22. Martin SE, Bradley JM, Buick JB, Crossan A, Elborn JS. The effect of hypoxia on cognitive performance in patients with chronic obstructive pulmonary disease. Respir Physiol Neurobiol. 2011;177(1):36-40. http://dx.doi.org/10.1016/j.resp.2011.03.007
23. Pereira ED, Viana CS, Taunay TC, Sales PU, Lima JW, Holanda MA. Improvement of cognitive function after a three-month pulmonary rehabilitation program for COPD patients. Lung. 2011;189(4):279-85. http://dx.doi.org/10.1007/s00408-011-9303-6
24. Klein M, Gauggel S, Sachs G, Pohl W. Impact of chronic obstructive pulmonary disease (COPD) on attention functions. Respir Med. 2010;104(1):52-60. http://dx.doi.org/10.1016/j.rmed.2009.08.008
25. Thakur N, Blanc PD, Julian LJ, Yelin EH, Katz PP, Sidney S, et al. COPD and cognitive impairment: the role of hypoxemia and oxygen therapy. Int J Chron Obstruct Pulmon Dis. 2010;5:263-9. http://dx.doi.org/10.2147/COPD.S10684
26. Bonson S, Scanlan J, Friedman S, Zuhr E, Fields J, Aylward E, et al. Modeling the impact of COPD on the brain. Int J Chron Obstruct Pulmon Dis. 2008;3(3):429-34. http://dx.doi.org/10.2147/COPD.S2066
27. Orth M, Diekmann C, Suchan B, Duchna HW, Widdig W, Schultz-Werninghaus G, et al. Driving performance in patients with chronic obstructive pulmonary disease. J Physiol Pharmacol. 2008;59 Suppl 6:539-47.
28. Lima OM, Oliveira-Souza RD, Santos Oda R, Moraes PA, Sá LF, Nasimento OJ. Subclinical encephalopathy in chronic obstructive pulmonary disease. Arq Neuropsiquiatr. 2007;65(4B):1154-7. http://dx.doi.org/10.1590/S0004-282X2007000700012
29. Salik Y, Ozalevli S, Cinrin AH. Cognitive function and its effects on the quality of life status in the patients with chronic obstructive pulmonary disease (COPD). Arch Gerontol Geriatr. 2007;45(3):273-80. http://dx.doi.org/10.1016/j.archger.2006.12.002
30. Antonelli-Incalzi R, Corsonello A, Pedone C, Trojano L, Acanfora D, Spada A, et al. Drawing impairment predicts mortality in severe COPD. Chest. 2006;130(6):1687-94. http://dx.doi.org/10.1378/chest.130.6.1687
31. Corsonello A, Pedone C, Carosella L, Corica F, Mezzei B, Incalzi RA. Health status in older hospitalized patients with cancer or non-neoplastic chronic diseases. BMC Geriatr. 2005;5:10. http://dx.doi.org/10.1186/1471-2318-5-10
32. Antonelli Incalzi R, Marra C, Salvigini BL, Petrone A, Gemma A, Selvaggio D, et al. Does cognitive dysfunction conform to a distinctive pattern in obstructive sleep apnea syndrome? J Sleep Res. 2004;13(1):79-86. http://dx.doi.org/10.1111/j.1365-2869.2004.00389.x
33. Schillerstrom JE, Horton MS, Royall DR. The impact of medical illness on executive function. Psychosomatics. 2005;46(6):508-16. http://dx.doi.org/10.1176/appi.psy.46.6.508
34. Gasquoine PG. Cognitive impairment in common, noncentral nervous system medical conditions of adults and the elderly. J Clin Exp Neuropsychol. 2011;33(4):486-96. http://dx.doi.org/10.1080/13803395.2010.536759
35. Landi F, Pistelli R, Abbatecola AM, Barillaro C, Brandi V, Lattanzio F. Common geriatric conditions and disabilities in older persons with chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2011;17 Suppl 1:S29-34. http://dx.doi.org/10.1097/01.mcp.0000410745.75216.99
36. Corsonello A, Antonelli Incalzi R, Pistelli R, Pedone C, Bustacchini S, Lattanzio F. Comorbidities of chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2011;17 Suppl 1:S29-34. http://dx.doi.org/10.1097/01.mcp.0000410745.75216.99
37. Schou L, Østergaard B, Rasmussen LS, Rydahl-Hansen S, Phanareth K. Cognitive dysfunction in patients with chronic obstructive pulmonary disease--a systematic review. Respir Med. 2012;106(8):1071-81. http://dx.doi.org/10.1016/j.rmed.2012.03.013

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