

ASSOCIATION BETWEEN ANXIETY, DEPRESSION AND COGNITIVE IMPAIRMENT IN COMMUNITY-DWELLING OLDER ADULTS: A SYSTEMATIC REVIEW

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ABSTRACT

The mental health of a population is the result of complex interactions between different parameters at individual and population levels. Few studies have investigated the potential association between symptoms of anxiety, mild depressive symptoms and cognitive performance in community-dwelling older adults. The objective of the present study was to evaluate the correlation between anxiety, depression and cognitive impairment in community-dwelling older adults by conducting a systematic literature review. Six papers were included in the present study. According to this systematic literature review, symptoms of anxiety and depression in community-dwelling older adults do not represent a consistent risk factor for dementia. Although depression and anxiety affect specific aspects of cognitive domains, such symptoms may not result in impaired cognition in general. Further studies with appropriate designs are clearly required to fill this gap in current knowledge, focusing on socio-environmental variables and on aspects related to individual resilience in order to clarify the role of depression and anxiety in cognitive performance.

Keywords: Depression; anxiety; Cognitive impairment; Comorbidity; Depression and anxiety.

INTRODUCTION

The mental health of a population is the result of complex interactions between different parameters at individual and population levels¹. Depression has been associated with cognitive impairment in two different ways: (1) depression as a risk factor for dementia; and (2) depression leading to mild cognitive impairment as the result of a possible negative effect of mood symptoms on cognition^{2,3,4}. Conclusions on the increased risk of mild cognitive impairment in depressed individuals and its consequent progression to dementia are conflicting^{2,5}. Eysench's theory of efficiency (Eysench, 1992) suggests that anxiety interferes with cognitive performance by exploiting some of the processing and storage resources of the working memory system, which has a limited capacity to store and process. Nevertheless, the differences detected between studies may be related to differences in the follow-up periods, in the study designs, the characteristics of the population samples or the different methodologies used^{2,5}.

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Most of the studies conducted to investigate the association between depression, anxiety and cognitive impairment have been carried out with clinical populations⁶, while few studies have been performed to evaluate this potential association in community-dwelling older adults³. Symptoms of anxiety and depression are common⁷; however, it is not known whether these symptoms, in community-dwelling older adults, lead to the occurrence of cognitive impairment or, assuming that mild cognitive impairment could be an initial stage of dementia, whether symptoms of depression could constitute an early manifestation rather than a risk factor for dementias and Alzheimer's disease^{5,8}.

Determining a correlation between these conditions could shed light on the primary cause and/or predict the outcome of patients affected by these dysfunctions. The objective of the present study was to evaluate the correlation between anxiety, depression and cognitive impairment in community-dwelling older adults by conducting a systematic review of the literature.

METHODS

The CAPES platform was initially used to conduct the literature review for the study, followed by searches of the Web of Science; MEDLINE/PubMed; Directory of Open Access Journals (DOAJ); ScienceDirect (Elsevier BV); SpringerLink; Science & Business Media BV; Gale Academic OneFile; Karger; Oxford Journals; SAGE (Journals online); Annual Reviews; Social Services Abstracts (ProQuest); Pollution Abstracts; Engineering Research Database; Hindawi Journals; PLoS; ERIC (U.S. Dept. of Education); Nature Publishing Group (CrossRef) and Future Science Medicine. The terms used were “*depressive symptoms*” or “depression” “and” “*anxiety symptoms*” or anxiety “and” “*cognitive symptoms*” or impairment cognitive “and” community-dwelling. The search was limited to articles in English.

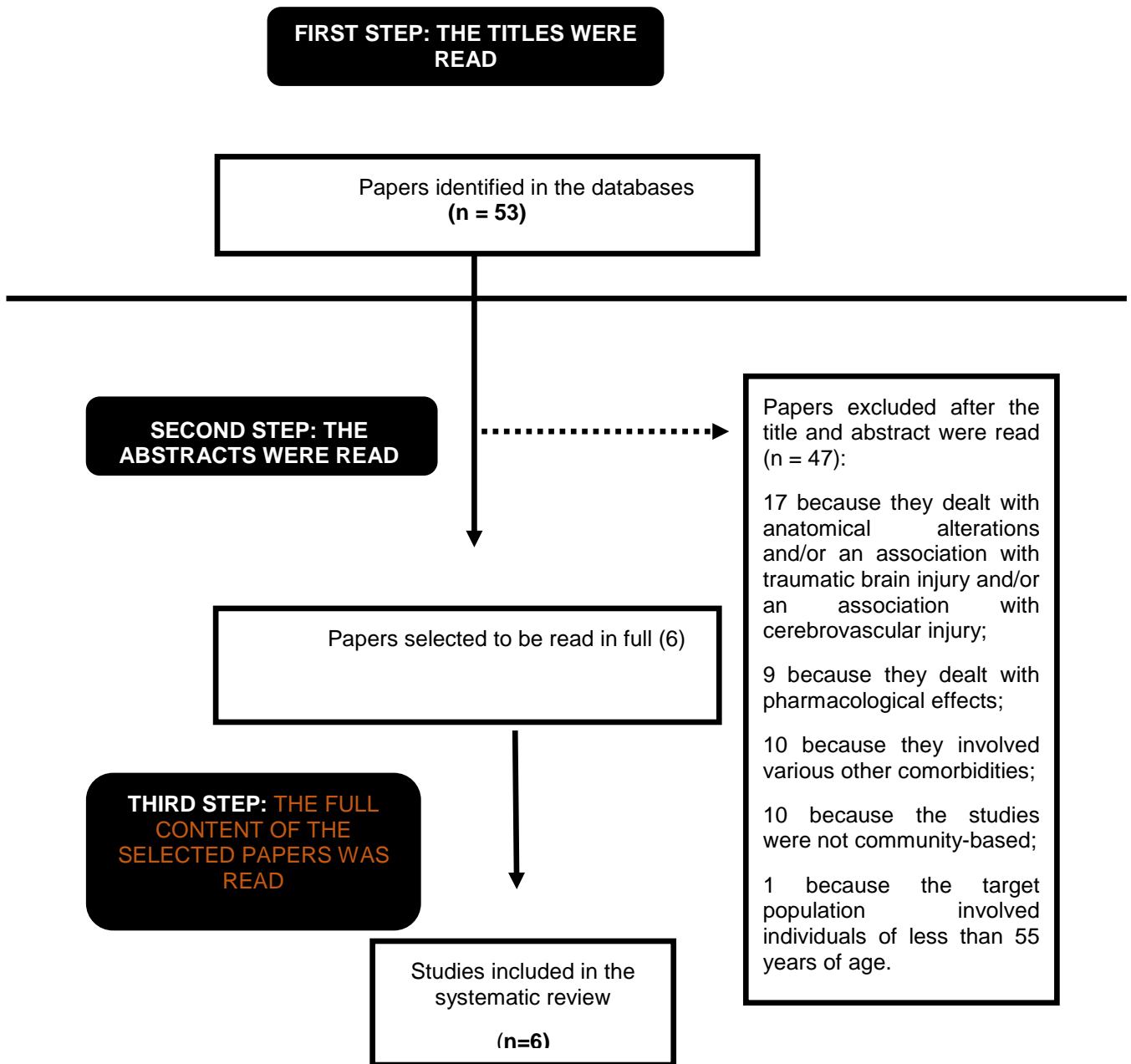
All the papers retrieved were included in the present review as long as the studies had been conducted in human beings, included participants over 55 years of age, were community-based and had been published in the preceding 15 years. Studies in which the patients had psychiatric comorbidities other than anxiety and depression, participants with neurological disorders, study populations of individuals under 50 years of age, studies conducted in outpatient clinics or with hospitalized patients and studies involving cognitive, depressive and anxiety syndromes secondary to the use of psychoactive substances or clinical conditions were excluded from the study.

The methodology of the papers selected was evaluated according to the 22 methodological criteria defined in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement. In this initial step, the articles selected were evaluated and classified as: completely in compliance with each item, partially in compliance with each item or not in compliance with a given item. Following analysis and classification of the papers, their compliance with each item was evaluated and scored according to the following criteria: items completely in compliance were awarded a score of 1; those partially in compliance received a score of 0.5 and those for which the item evaluated was not in compliance were given a score of 0. The papers completely in compliance with at least half + 1 of the items (12 features) were considered to be of good quality.

RESULTS

A total of 53 articles were retrieved from the available databases using the search strategy described above. There was no repetition of papers. Following perusal of the titles and abstracts of these papers, 47 were excluded based on the pre-established inclusion and exclusion criteria. Of these, 17 dealt with anatomical abnormalities and/or an association with traumatic brain injury and/or an association with a cerebrovascular accident; 9 studies dealt with pharmacological effects; and another 10 studies dealt with various comorbidities (schizophrenia, chronic obstructive pulmonary disease, asthma, heart failure, hypothyroidism). Ten papers were excluded because the studies were not community-based and one study was excluded because the target population consisted of individuals of less than 55 years of age (Figure 1).

Figure 1 - Flowchart depicting the process used to select the studies.



After reading the entire contents of the remaining six papers, all were found to comply satisfactorily with more than half the items defined in the STROBE checklist, with the minimum percentage of compliance being 77.27% (Table 1).

Table 1 - Comparison of STROBE scores

Authors	Number of items fully complied with	Number of items partially complied with	Number of items not complied with	%
Gale et al. (2011) ⁶	21	1	0	95.45%
Beaudreau and O'Hara (2009) ³	18	4	0	81.81%
Salthouse (2012) ¹¹	20	2	0	90.90%
Wetherell et al. (2002) ¹⁰	18	4	0	81.81%
Dotson et al. (2014) ⁹	17	5	0	77.27%
Sinoff and Werner (2003) ⁵	19	3	0	86.36%

Depression and cognitive impairment

In a longitudinal, population-based study conducted in England, Gale et al. (2012) evaluated the association between symptoms of depression and cognitive ability in older adults⁶. The analyses were based on a sample of 8,611 individuals divided into three groups according to age: 50-60 years (n = 2,552), 60-80 years (n = 5,070) and 80-90 years (n=989). The symptoms of depression were evaluated at 4 different moments between 2002 and 2009 using a version of the Center for Epidemiologic Studies - Depression Scale (CES-D) that evaluates symptoms of depressed mood in the preceding week. Cognitive function was evaluated at four moments during the study using tests of immediate and delayed recall, prospective memory, verbal fluency and attention. The authors, however, failed to mention the actual scales used. The principal cognitive functions deteriorated as a function of age, particularly after 60 years of age; however, there was no tendency for the symptoms of depression to worsen with aging, with the size of the effect being 0.01 in the 50-60-year age group, 0.01 for the 60-80-year age group and 0.10 for those over 80 years of age. There was a weak association between depressive symptoms and poorer cognition only in patients in the 60-80-year age group, with the size of the effect being 0.26.

Beaudreau and O'Hara (2009) conducted a cross-sectional, population-based study involving 102 individuals of 60-80 years of age in California, USA to evaluate the association

between symptoms of anxiety and depression and cognitive function³. Depressive symptoms were evaluated using the Geriatric Depression Scale – Long Form, a self-report instrument validated for use in older adults. This 30-item scale consists of five factors: mood, psychomotor agitation, social retraction, despair and lack of vitality. All the questions involve yes/no answers. The neuropsychological tests were performed using the following scales: (1) The Rey Auditory Verbal Learning Test (RAVLT) to evaluate episodic memory; (2) The Stroop Color and Word Test to evaluate inhibition; (3) The Symbol Digit Modalities Test (SDMT) to evaluate processing speed / shifting attention; (4) The Controlled Oral Word Association Test (COWAT) to evaluate verbal fluency; and (5) The Boston Naming Test (BNT-II) to measure of confrontation naming. The authors concluded that symptoms of depression were not associated with cognitive impairment if symptoms of anxiety were not present. A correlation was found between an increased number of symptoms of depression and poorer episodic memory (RAVLT) alone; however, this association was not statistically significant ($p = 0.06$).

Dotson et al. (2014) evaluated the effects of depressive symptoms on the cognitive function of 71 healthy individuals in Florida, USA. The symptoms of depression were evaluated using the CES-D, a 20-item, self-report instrument used to assess the frequency and severity of depressive symptoms experienced in the preceding week. The State-Trait Anxiety Inventory was used to evaluate anxiety symptoms. Neuropsychological tests were applied to evaluate episodic and working memory, attention and executive functions. Measurements of episodic memory included the immediate recall trial of the Hopkins Verbal Learning Test – revised (HVLT-R) and the Brief Visuospatial Memory Test – revised (BVM-T-R). The total scores obtained in Digit Span and Letter-Number Sequencing (LNS), which are sub-tests of the Wechsler Adult Intelligence Scale, were used as a measurement of working memory and executive functions. Parts A and B of the Trail Making Test (TMT-A and TMT-B) were also used. Processing speed was slower in older adults with depressive symptoms and these individuals tended to perform more poorly with respect to working memory (TMT-A $F = 4.61$; $p = 0.04$ and LNS $F = 6.19$; $p = 0.02$).

Anxiety and cognitive impairment

Evaluating a sample of 100 older adults followed up for three years in the state of Israel, Sinoff and Werner (2003) found a statistically significant association between high anxiety symptom scores and cognitive decline. Symptoms of anxiety were evaluated using

Sinoff's Short Anxiety Screening Test, while cognition was evaluated using the Mini Mental State Examination. Individuals with anxiety symptoms had a relative risk of 3.96 for cognitive impairment. For "path analysis", a more parsimonious statistical model was used. In this case, the results showed that, with anxiety, there is both a direct and an indirect effect on cognitive decline ($p < 0.01$).

In the previously mentioned study conducted by Beaudreau and O'Hara (2009), anxiety symptoms were evaluated by applying the Beck Anxiety Inventory, a short self-report instrument that has been recommended for use in community-based studies. This inventory evaluates the presence of 21 different symptoms of anxiety over the preceding week. The linear regression results show that severe anxiety (a high score in the Beck scale) was positively associated with a poor performance in two of the three tasks of executive function: processing speed / shifting attention (SDMT) $R^2 = .11$ ($p < 0.01$) and inhibition (Stroop) $R^2 = .12$ ($p < 0.01$).

Wetherell et al. (2002) studied the association between anxiety and cognition in a sample of 704 healthy older adults with a mean age of 63 years, in California, USA. The cognitive tests used were the Wechsler Adult Intelligence Scale Synonyms, WIT III Analogies, Koh's Block Design, two measures of visual learning (Names and Faces and Thurstone's Picture Memory) and the CVB-Scales Digit Span Test and Card Rotations. Anxiety was evaluated using the 10-item subscale from the State-Trait Personality Inventory (STPI). The tests were performed on three different occasions, with a 3-year interval between each interview. Higher states of anxiety were associated with a statistically significant impairment for synonyms ($\beta: 6.4$), analogies ($\beta: 9.0$), in the block test ($\beta: 12$), names and faces ($\beta: 4.8$) and in Thurstone's Picture Memory Test ($\beta: 8.5$) ($p < 0.05$).

Anxiety, depression and cognitive impairment

Dotson et al. (2014) evaluated the effects of symptoms of depression and anxiety on cognitive function in 71 healthy individuals in Florida, USA. Individuals with moderate depression and anxiety scored better in cognitive tests compared to individuals with depression alone, suggesting a beneficial effect of moderate symptoms of anxiety on cognition.

In the aforementioned study conducted by Beaudreau and O'Hara (2009), comorbid anxiety and depression was positively associated with impairment in various cognitive domains: processing speed / shifting attention (SDMT), $R^2 \Delta = .03$, $p = 0.05$; episodic memory

(RAVLT), $R^2 \Delta=.05$, $p<0.05$; and semantic memory (BNT), $R^2 \Delta=.05$, $p<0.05$. The only cognitive task associated with anxiety was inhibition, with anxiety being associated with lower scores for inhibition (Stroop), $R^2=.12$, $p<0.01$; however, no such association was found when both anxiety and depression were present.

Salthouse (2012)¹¹ evaluated the effects of symptoms of anxiety and depression on cognitive function in a sample of 3,781 healthy adults aged 18-97 years in Virginia, USA between 2001 and 2009. The symptoms of depression were evaluated using a 20-item version of the CES-D. Cognition was evaluated using the WAIS-IV and WMS-VI tests. Anxiety symptoms were evaluated using the 20-item Spielberger State-Trait Anxiety Inventory. A positive correlation was found between symptoms of anxiety and depression and many of the cognitive variables, particularly when the effects of age and sex were controlled. The analyses showed a correlation between symptoms of depression and a poorer performance in reasoning (β : 0.16), impaired visuospatial memory (β : 0.12); impaired episodic memory (β : 0.9); processing speed (β : 0.11) and vocabulary (β : 0.11); $p<0.01$). A correlation was found between symptoms of anxiety and a poorer performance at reasoning (β : 0.12); impaired visuospatial memory (β : 0.12); impaired episodic memory (β : 0.6); processing speed (β : 0.8) and vocabulary (β : 0.7); $p<0.01$. The cognitive domains that worsened as the symptoms of depression increased were the same as those that worsened as symptoms of anxiety increased (Table 2)

Table -. Correlation between anxiety, depression and cognitive impairment

Author and Year of Publication	Study Design	Sample Size and Age	Cognitive Impairment
Gale et al. (2011) ⁶	Longitudinal study	8,611 adults over 50 years of age	Evidence of an association with depressed individuals (60-80 years of age).
Beaudreau and O'Hara (2009) ³	Cross-sectional study	102 adults over 60 years of age	Decrease in cognition in individuals with depression and anxiety.
Salthouse (2012) ¹¹	Longitudinal study	3,781 healthy adults of 18 to 97 years of age.	Decrease in cognition in individuals with depression and in those with depression and anxiety.
Sinoff and Werner (2003) ¹⁰	Longitudinal study	100 adults over 60 years of age	Decrease in cognition in individuals with anxiety

Wetherell et al. (2002) ⁹	Longitudinal study	704 adults over 50 years of age	Decrease in cognition in individuals with anxiety
Dotson et al. (2014) ⁵	Cross-sectional study	-----	Decrease in cognition in individuals with depression

DISCUSSION

Some studies have suggested a potential association between symptoms of anxiety, symptoms of depression and cognitive performance in community-dwelling older adults (Beaudreau and O'Hara, 2009). However, conclusions regarding an increased risk of mild cognitive impairment in depressed individuals and progression to dementia are conflicting. Dotson et al. (2014) suggests a statistically significant correlation between depression and cognitive impairment; however, since that was a cross-sectional study, no conclusions can be drawn in relation to the progression of symptoms due to its small sample size. The findings of Salthouse (2012) indicate that the higher the scores for the symptoms of depression, the poorer the individual's performance in cognitive tests. On the other hand, although the results of the study conducted by Gale et al. (2011) were similar to those found by Salthouse (2012) in individuals of 60 to 80 years of age, no such correlation was found between symptoms of depression and cognitive impairment in individuals of 50-60 years of age or in those over 80 years of age. None of the other studies reviewed here adopted the strategy used by Gale et al. (2011) of creating three different age groups. Furthermore, the latter two studies were conducted in different countries and used different versions of the same scale to evaluate the symptoms of depression. Beaudreau and O'Hara (2009) concluded that symptoms of depression in the absence of anxiety were not associated with cognitive impairment. A correlation was found between an increased number of depressive symptoms and poorer episodic memory alone; however, this association was not statistically significant ($p=0.06$). Nevertheless, Beaudreau and O'Hara's study was cross-sectional, used different scales from those used in the previously mentioned studies and had a small sample size.

The majority of the studies reviewed here reported cognitive impairment in patients with symptoms of anxiety. Eysench's theory of efficiency (Eysench, 1992) suggests that anxiety interferes with cognitive performance by exploiting some of the processing and storage resources of the working memory system, which has a limited capacity to store and process. Therefore, having to simultaneously perform tasks that depend on the same component of working memory tends to result in greater impairment. Indeed, anxiety creates

preoccupation and other intrusive thoughts that compete for the resources of the working memory (Eysenck, 1992), hence anxiety interferes with verbal tasks and with tasks that demand attention and complex coordination. For visuospatial tasks, anxiety exerts a potentially negative effect on the efficiency of the executive process. Therefore, the effects of anxiety on visuospatial tasks may depend on the complexity of the task and as a consequence the results may be less consistent than for verbal tasks. On the other hand, the presence of cognitive impairment may increase the risk of developing and preserving states of anxiety (Beaudreau et al., 2009).⁹ Generalized anxiety may lead to cognitive impairment, particularly in late adulthood, and in older adults anxiety and cognitive impairment may affect each other mutually, with one condition exacerbating the other.

The impact of comorbid anxiety and depression on cognition has been described by Beaudreau and O'Hara (2009) and by Salthouse (2012). DeLuca et al. (2005) showed that individuals over 55 years of age with major depression and generalized anxiety or panic disorder suffered a greater decline in memory compared to those with depression alone. Dotson et al. (2014) reported conflicting results, suggesting that individuals with moderate states of depression and anxiety had better cognitive evaluation results compared to individuals with depression alone. Those authors suggested an inverted-U function in relation to the association between anxiety and cognitive performance in that moderate levels of anxiety would be associated with a better performance in cognitive tests, while mild and severe anxiety symptoms would be associated with impaired performance in cognitive tests. Nevertheless, as already mentioned, that was a cross sectional study with a small sample size and its results failed to confirm the original hypothesis put forward by the authors, since they were unable to show that symptoms of mild and severe anxiety are associated with performance deficits in cognition tests.

It is not known how the presence of anxiety and depression symptoms affects cognitive function; whether the effect would be because of the mood states themselves, improving with the remission of the psychiatric symptoms, or whether the mood symptoms would represent a risk factor for dementia in older adults. According to Kessler et al. (1999), individuals suffering from major depression and generalized anxiety are more likely to perceive their mental health as regular or poor. In addition, their work and social functioning are more likely to be affected compared to individuals with major depression but without anxiety. We would like to offer the following hypotheses to explain the different results found in the medical literature in relation to depression, anxiety and cognitive impairment in

older adults: (1) Symptoms of depression and anxiety interfere with specific aspects of cognitive domains, as suggested by the majority of the longitudinal studies reviewed here; however, they may not cause clinically identifiable general cognitive impairment in community-dwelling older adults; therefore, it is the cross-sectional cohort studies with small sample sizes that present most of the conflicting results. (2) Non-biological factors such as poor physical environment and poor social conditions, known to be producers of chronic stress and highly stressful life events (Brown et al., 1987), may be more important insofar as cognitive performance is concerned than the presence of anxiety and depression per se, and none of the studies listed here evaluated the effect of these variables on cognition. (3) The capacity to manage stress using appropriate coping strategies leads to better adaptation and has a positive impact on health (Bandura, 2002; Lazarus and Folkman, 1984). None of the studies reviewed evaluated the individual's ability to manage stress using appropriate strategies, nor did they evaluate whether resilience would lead to better adaptation and if this would be important in preventing cognitive decline in older adults with symptoms of anxiety and depression.

The present study was based on a systematic review of the literature; therefore, it cannot be used to test hypotheses. Nevertheless, the discrepancies between the findings suggest that whereas studies focus scientific interest on psychiatric disease and its consequences for cognition, variables such as the physical environment, poor social conditions and the individual's ability to manage stress through the use of appropriate strategies may also exert an important impact on cognitive performance. This systematic review of the literature shows that symptoms of anxiety and depression in community-dwelling older adults were not consistently found to represent a risk factor for dementia. It is clear that further studies with appropriate designs need to be conducted to fill this gap in currently available knowledge, focusing on socio-environmental variables and aspects related to resilience to clarify the role of depression and anxiety on cognitive impairment.

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