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RESEARCH ARTICLE

Is Common Denominator Lead to Misdiagnosis of Dementia and Late-Life Depression

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Abstract

Significant cognitive impairments are found in late life depression. This situation brings to mind the question of what are the common and distinct mechanisms of late life depression and dementia. In this review, neural and psychological mechanism are discussed within the scope of denominator and hallmark for both disorders. It is searched several databases e.g. MEDLINE, Web of Science Core Collection from 1974 to 2024 by using variant terms for the focal epilepsy subtypes and social cognition constructs. The pathology of dementia was correlated with late-life depression Studies indicate that depression may be an etiological factor for dementia as well as an increased risk. Also, many life-related stressors can lead to results such as increased reactive oxygen species, inflammatory responses, suppression of neurogenesis, and apical dendritic atrophy and altered functional connectivity in the medial prefrontal cortex. Based on this, it is possible to say that psychological stress factors increase the incidence of the disease in the development of dementia, just like in depression. Late depression should not be labeled as dementia because of they share similar symptoms and should be evaluated clinically correct so that it is not misdiagnosed. Besides, it is substantial to comprehend the relationship between the aging population and the risk of depression and dementia for current and future studies, especially in terms of prevention and treatment.

Keywords: late-life depression, dementia, Alzheimer disease, mild cognitive impairment, biological aging, imaging, hippocampus volume, gray matter, stress hormones

INTRODUCTION

Major depressive disorder (MDD) (American Psychiatric Association, 2013) which is accepted as a serious public health problem, is a common disease (Cassano& Fava, 2002). While depression has a chronic feature it also ranks 4th in terms of disability among all medical diseases with its negative consequences such as causing dysfunction in the work and social areas, and inability to maintain daily life (Işık et al., 2013). The one-year prevalence of Major Depressive Disorder was found to be 7%. This rate varies significantly depending on the age range of the individual. or example, it is three times more common in people aged 1-29 than in those aged 60 and over. It is known that the disorder begins in early adolescence in female gender and is 1.5 to 3 times more common than male gender (McLeod et al., 2015). Etiologically, early negative experiences, presence of major depressive disorder in first-degree family members, and challenging life events predispose to the development of depression. Feelings of worthlessness or guilt that accompany a major depressive episode may cause the person to make negative self-evaluations or to focus on ruminative thoughts about past events (Köroğlu, 2008). Many people say that they cannot make even the smallest decisions because they have trouble focusing. This brings about dysfunctions such as difficulty in carrying out daily tasks and problems in interpersonal relationships (Karamustafalıoğlu& Yumrukçal, 2011).

Late life depression (LLD), on the other hand, is characterized by the presence of multiple minor depressive symptoms that occur mostly in an elderly person over 50 or 60 years of age (Blazer, 2003). Although the overall percentage of depressed older people is lower (8%), the growing elderly population draws attention to a greater need for health professionals to act consciously of the special needs of older people compared to younger people suffering from the same illness. Otherwise, the consequences of untreated or partially treated late-life depression are appalling (Regier et al., 1988; Aziz & Steffens, 2013). As it is known, depression is a common psychiatric disorder in patients with neurological disorders such as Alzheimer's disease (AD) and other types of dementia, stroke, multiple sclerosis (MS), and Parkinson's disease (PD). Based on this, it is possible to say that depressive symptoms play a role in the pathogenesis of these neurological disorders (Wang et al., 2022). How explain abit more. For this reason, understanding late-life depression is clinically key to early detection of

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preventable risk factors and appropriate intervention in order to slowing or preventing the onset of dementia (Diniz et al., 2013).

Although dementia is a very common and increasing disease today, according to 2015 data, there are 47.47 million people diagnosed with dementia in the world. (Prince at al., 2014). The most basic criterion when diagnosing dementia is that there are significant disorders in memory, thinking and behavior. The individual experiences dysfunction in the capacity to maintain daily life (Meichsner et al., 2018). Dementia is also characterized by impairment in cognitive functions such as memory, perception, speech, calculation, abstract thinking, ratiocination, judgment and problem solving as a result of a decrease in cognitive and intellectual functions (Rossor, 1996). Many factors such as low education and income level, frequency of alcohol and cigarette use, hypertension, coronary heart disease, stroke and sedentary living habits constitute risk factors for the development of dementia (Gatz et al., 2007). In other respects, microtraumas and previous head trauma can cause Dementia through neurofibrillary tangle and amyloid accumulation in the brain (Salib & Hiller, 1997). The risk of developing dementia doubles every five years between the ages of 65 and 85. In addition, the rate of developing dementia in elderly patients who are hospitalized for any reason is 6 times higher than the normal population. Epidemiological studies have detected Alzheimer's type dementia in women and multi-infarct dementia in men in a significant rate of dementia cases (Dişcigil, 2013).

To sum up, by definition, dementia is a progressive cognitive impairment syndrome which resulting in health problems, change of behavior and personality, deprivation of independence, and death principally (Borsje et al., 2015). Two hypotheses are put forward regarding on the coexistence of depression and dementia. The first argues that depression occurs as a response to the early cognitive decline of dementia. Therefore, depression is considered a prodrome of dementia. The second considers depression as a risk factor for dementia. Subsequent theory has been supported by biological, neurological and psychological mechanisms (Hayley et al., 2016). Additionally, results from a meta-analysis showing depression is associated with a twofold increased risk of dementia (Livingston et al., 2017).

In this systematic review, it is aimed to best answer the following research questions by gathering existing data from various clinical and neuropsychological domains: Are there common pathologies underlying depression and dementia? Is it possible to think of a continuum including depression, Mild Cognitive Impairment (MCI), and dementia in older age? Are there enough data to think of a causal direction between depression and dementia in older age? Does depression mediate the link between MCI and Dementia? Moreover, it is thought to be subsidiary questions would be listed as; what are the psychosocial predictors of late life depression? Do these predictors overlap with the predictors of dementia? What are the protective factors against late life depression? Do these protective factors also buffer against conversion of MCI to dementia? ‟

Depression tops the list of mental disorders seen in the elderly. However, this situation is overlooked for various reasons and is associated with physical or other mental disorders related to old age. In this study, we aimed to discuss the overlapping common points of late-life depression and dementia, their specific symptoms, their relevance in daily life, what is missed when making a diagnosis, and the possible consequences of misdiagnosis for both the hospital and the health centers and the patient. In this way, it is thought that patients will be treated more questioningly when diagnosing, more attention will be paid and a correct treatment plan will be applied to the patient. Based on this, it is anticipated that the burden on patients and hospitals will be reduced and more lives will be touched with correct diagnosis and intervention.

METHODS

Search results and analyzes are obtained from multidisciplinary databases where we can find and track them in the best possible way that is searched several databases from 1974 to 2024 including PsycINFO and MEDLINE (via EBSCOhost), Embase, and Web of Science Core Collection (via Clarivate Analytics). Literature review; it was carried out using abstract, title or keyword filters in specified databases. It is constructed a comprehensive search strategy using variant terms for the focal epilepsy subtypes and social cognition constructs. The search strategy developed for articles is presented below;

(("depress*" OR "mood") AND (‟elderly″ OR ‟aging″ OR ‟old″ OR "late life") AND ("imaging" OR "fMRI" OR "PET" OR "functional magnetic resonance imaging″ OR "Positron emission tomography" OR "thickness")) OR (("dement*" OR "mild cognitive impairment" OR ‟ MCI″ OR "Alzheimer" OR "Alzheimer′s disease") AND OR ‟gray matter″ OR ‟functional connectivity″ OR ‟amygdala″ OR ‟hippocampus″)).

In order to scan the gray literature, as recommended in the PRISMA guide, manual scanning was carried out by entering keywords into Google Scholar and Google internet search engines to capture unpublished studies or studies that could be overlooked during database review. After identifying the sought records by searching the databases with keywords, all data were transferred to ZOTERO, a resource management program. Duplicate records were removed, and in the second step, the articles were examined and eliminated according to the exclusion criteria. The inclusion-elimination process of studies was carried out by the researcher and author. In this section, inclusion and exclusion criteria are clearly presented, and each study meeting the criteria was found suitable for review.

Inclusion Criteria: Articles presenting original research results published in peer-reviewed journals in Turkish and English.

Exclusion Criteria: Publications in languages other than Turkish and English, measurement tool development studies, studies not published in peer-reviewed journals, studies that do not include the basic components of depression, late-life depression and dementia (neuropsychological and clinical) were not included in the review.

Publishing original research results in peer-reviewed journals is considered a mechanism that ensures reliability and reduces the concern for bias, especially in terms of the accuracy of statistical testing findings (Kelly et al., 2014). For this reason, publication criteria in peer-reviewed journals were applied in this systematic review. The reason why we do not go much beyond concepts other than late-life depression and dementia is to avoid going out of context and distracting the topic. The resulting PRISMA flow diagram is given in Figure 1

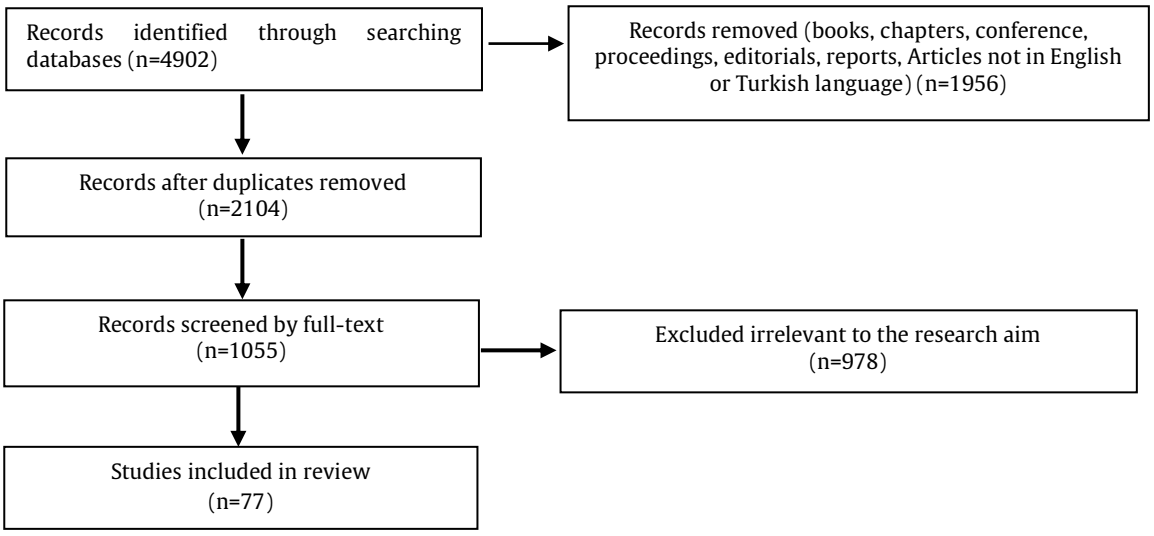

Figure 1. PRISMA flow diagram

RESULT AND DISCUSSION

Neurological Mechanism of Dementia and Depression

Dementia

Dementia which redounds on 5-6% of those aged 65 and over and 30% of those aged 85 and over (Hebert et al., 2013) is a progressive neurodegenerative disease (Schneider et al., 2007). It primarily affects limbic, paralimbic and neocortical areas (Jonker et al., 2000) that results in irreversible degeneration of the cerebral cortex and hippocampus (Wenk, 2003). Many types of dementia are characterized by confusion, disorientation, and memory loss, among other symptoms of the disease (Wais et al., 2006; West et al., 1994).

Studies conducted to date have found that episodic memory impairment, such as amnesia, is often the first and most prominent part of the dementia syndrome. Neuropathological studies support that dementia pathology is earliest observed in medial temporal lobe (MTL) structures, which are involved in the processing of episodic memory (Hyman et al., 1984). Cognitive deficits mainly affect memory, visuospatial and executive functions (Brown et al., 1990; Zgaljardic et al., 2004).

It is now widely accepted that neuroinflammation has an important pathogenetic effect in dementia. Gray matter atrophy, which is one of the main signs of neurodegeneration, is one of the factors that should be examined in the course of dementia, including cognitive decline (Fereshtehnejad et al., 2017). On the other hand, while aging is vital for many neurodegenerative diseases, a more detailed understanding of age-related white matter pathology and associated cellular responses is needed (Prinz et al., 2019). About white matter, focal lesions seen on magnetic resonance imaging (MRI) do not only explain tissue shrinkage. There are hyperintensities associated with the increased risk of stroke and dementia (Prince & Scheltens, 2015).

Serotonin is one of the most detailed and comprehensively studied neurotransmitters in the Central Nervous System (CNS), known to regulate many physiological functions (Arreola et al., 2015). Biogenic monoamine serotonin acts as both a neurotransmitter and neuromodulator, which has been linked to cognitive decline and multiple areas of behavioral and psychological symptoms of dementia (Dillon et al., 2013). Serotonin dysfunction characterized by decreased metabolites and serotonin in the brain, decreased serotonin 2A receptors in the cortex and hippocampus, and loss of serotonin neurons in the raphe nucleus are seen in elderly dementia patients (Göthert, 2013).

Since the middle of the 20th century, it has been known that the dopaminergic system has a major role in behavioral control and causes serious neurological and psychiatric diseases in dysfunctions that occur (Schultz, 2007). Studies have found that cognitive dysfunction in dementia patients is closely correlated with dopaminergic depletion in the associative striatum. Disinhibition of the basal ganglia pacemaker in the outer globus pallidus-subthalamic nucleus network as a result of dopaminergic depletion is another possible scenario explaining the mechanism (Burkhardt et al., 2009). Dopamine-dependent synaptic plasticity is also observed in physiological conditions such as aging. A recent study found that dopaminergic innervation of the striatum changes with age, leading to slower cognitive functions (Li et al., 2020).

Signaling pathways through various neuroactive compounds and their various receptor types are important for brain homeostasis. GABA and glutamate are among the subjects. The imbalance between excitation and inhibition causes changes in the activity of neural populations, which is claimed to point to a potential mechanism of cognitive dysfunction that contributes significantly to the pathomechanism of dementia (Giovannetti & Fuhrmann, 2019).

Risk factors

In dementia, there are neurobiological and environmental risk factors rather than a single etiological factor or factors. Risk factors are listed as cerebrovascular pathology and events, closed skull fracture, hypotension and hypertension, heart diseases, smoking, obesity (Samieri et al., 2018), diabetes, thyroid disorders and depression (Yüksel, 2009). For instance, it has been determined that clinical trials associated with vascular risk factors provide minimal benefit in preventing cerebral small vessel disease lesions and related dementia (Weber et al., 2012). Sporadic dementia has been correlated with impaired calcium homeostasis, oxidative stress, and age-related breakdowns in energy production (Dorszewska et al., 2016).

Therebesides, treatable disorders such as atypical presentations of other neurodegenerative defectiveness, neoplasms and autoimmune encephalopathies are among the most common causes of dementia.

There are many causes associated with the increased risk of Alzheimer's disease including genetic risk, infection, and protein unfolding. Two of the major theories that attract attention for the cause of AD is the existing of pathological β-amyloid (Aβ) and Tau protein (Glenner & Wong, 1984). Intracellular neurofibrillary tangles formed by hyperphosphorylated tau protein are the greatest indicator of neural processes in dementia pathology (Hanger et al., 2009). A quantitative proteomic map reflecting multiple isoforms of tau shows heterogeneous findings in disease progression and critical targets at each stage of the disease while working with Alzheimer's patients. A small number of Aβ production is not considered toxic and may even be assumed to have a physiological function, but amyloid plaques consisting of a large number of highly aggregated Aβ fibrils represent an abnormal pathological lesion (Takahashi et al., 2004). Increased Aβ level correlates with the alteration of synapses seen in dementia (Mucke et al., 2000).

Late life depression

Depression has been found to progress biological aging, which has been reported with a reduction in telomere length to a critical length, rapid aging of the brain, and epigenetic aging (Thieme, 2018). It is particularly marked by disruption of the "cognitive control network" to include the dorsolateral prefrontal cortex, the dorsal and rostral regions of the anterior cingulate, and the parietal junctional regions. Neuroimaging studies of major depression reveal a reduction in both the volume of the anterior cingulate cortex and functional connectivity in the medial prefrontal cortex (Wise, et al., 2017). Inadequate prefrontal perfusion in the mentioned regions caused a decrease in problem solving skills and an increase in the tendency to act on negative emotions. This is thought to play a role in suicidal behavior (Desmyter et al., 2011).

The amygdala, hippocampus and dorsomedial thalamus, which are the main subcortical limbic brain regions where structural and functional abnormalities are detected, act a part in depression (Lorenzetti et al., 2009). There is an opinion that depression in adults is associated with the destruction of synaptic connections between hippocampal neurons (Campbell & MacQueen, 2003). In the hippocampus, damage to plasticity has been observed with chronic exposure to stress and sustained reductions in neuroprotective factors that foster neuronal atrophy and reduce synaptic number and function (Duman et al., 2016). Videlicet, hippocampal volumetric changes, hippocampal neurogenesis and apoptosis of hippocampal neurons are found in depression (Dellarole et al., 2004).

Previous studies suggest a role for monoamine neurotransmitters as the cause of pathophysiological changes that occur following chronic stress in depression (Leonard, 1989). Recent studies have found that the endocrine and immune systems play an important role in the pathology of these disorders (Brambilla, 2000). Based on the idea that the hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the coordination of the stress response by Hans Seyle in 1936, researchers of the period concluded that chronic stress had negative effects on mental health. According to the endocrine hypothesis, the secretion of corticosteroid hormones, one of the most important endocrine components, is one of the ways to respond to stress. Thanks to the parallel activity of the autonomic nervous system (ANS) and hypothalamic-pituitary-adrenal (HPA) axis, an appropriate response to acute stress is provided for survival when exposed to life-threatening situations (Herman et al., 2016). For example, as a result of the studies, the neuroendocrinology of depressed patients was compared with chronically stressed rats and it was determined that they share the same HPA axis-oriented features (Checkley, 1996). To this respect it has been concluded that chronic cortisolemia in patients with depression will result in suppression of the immune system. As a result, this situation has been attributed to the decrease in the effect of glucocorticoids on the immune system and the development of glucocorticoid receptor resistance (Maes, 1999).

However, studies over the last 15 years show that a significant paradigm shift has occurred in understanding the function of the immune system in depression. Evidence is presented that activation rather than suppression of the innate immune system occurs (Geerlings et al., 2015). Chronic inflammation has been found to play a central role not only in the pathogenesis of depression, but also in the pathogenesis of many diseases such as cancer, cardiovascular diseases and diabetes, which are often comorbid with major depression (Engelhart et al., 2004). Those developments brought about new discussions. For example, if chronic inflammatory changes are a common feature of major depression, what might be the long-term consequences?

The hippocampus serve a function in stress and mood regulation in addition to cognitive activity in patients with depression. In a stress-ridden person, the individual's hippocampus volume is reduced, while the dendritic complexity of neurons in CA3 is impaired. This affects neurogenesis in the dentate gyrus (Lucassen, 2007). Exposure to too much stress can cause not only hippocampal neuronal damage but also cognitive impairment (Wamsteeker & Bains, 2010). That is to say, apart from the adaptive neuroplastic changes that occur in the face of stress, an increase in neurogenesis is observed to support the preservation of homeostasis in the hippocampus (Krishnan & Nestler, 2008). The neocortex and hippocampus are known to mediate cognitive aspects of depression such as memory impairments and feelings of unhappiness, worthlessness, guilt and sadness, and suicidal ideation (Drevets, 2001). High dysfunctions in several brain regions and circuits that regulate the intercorrelated emotion, reward, and executive function of the limbic system are implicated in depression and antidepressant action (Berton & Nestler, 2006).

Monoamine changes thought to be responsible for many of the symptoms of depression are an important finding in dementia The decrease in brain concentrations of serotonin, noradrenaline, dopamine and GABA with advancing age is presented as a reason that increases the disposition to depression in the elderly (Alexopoulos, 2000). Serotonin neurotransmitter is responsible for modulation of mood, cognitive functions, libido and sleep (Ninan, 1999). Dysregulation of the serotonin system, which is considered central to the etiology of depression, and the view that the main inhibitor, serotonin receptor 5-HT1A (5-HT1AR), plays a key role in depressive neuropathology has been noted for a long time (Hirvonen et al., 2008). Also, it is possible to talk about a deterioration and/or dysfunction in 5-HT1A-FGFR1 heteroreceptor complexes in Raphe-hippocampal serotonin neuron systems in the development of depression (Borroto-Escuela et al., 2021).

The noradrenergic system is involved in controlling responses to the environment and is involved in alertness

as well as mood, learning, memory and attention. It has also been stated that the noradrenergic system is related to impulses and motivations (Leonard, 1997). Corticotropin releasing factor (CRF), defined as the stress hormone, is effective in the regulation of the central norepinephrine (NE) system. Results from both animal models and human studies demonstrate the occurrence of CRF hypersecretion in depression (Nemeroff et al., 1984).

Dopamine is effective in many aspects of brain function, including cognition, affect, and locomotion (Lauder & Bloom, 1975). There is strong evidence that the mesolimbic dopamine system correlates with reward-related motivated and hedonic behaviors. Studies have found causality of midbrain dopamine neurons in both arousal and relaxation of various behaviors associated with stress-related depression, including reduced anhedonia and motivation (Nestler & Carlezon Jr, 2006).

It is known that Glutamate or GABA, which acts as a primary excitatory and inhibitory neurotransmitter by controlling the information flow in the brain both internally and externally (Fee et al., 2017), is more vulnerable to stress and depression, and therefore increases the sensitivity to synaptic function and plasticity in the system. Altered glutamate evidence points to impaired GABA neurotransmission, which also puts up in the neurobiology of depression (Ghosal et al., 2017).

Common Denominator of Dementia and Late- Life Depression

In brain autopsy studies, it was determined that the pathology of dementia was correlated with late-life depression. Lifelong episodes of depression cause dementia pathology in the hippocampus to worsen. (Meeks et al., 2006). Reports by Fjell and colleagues (Fjell et al., 2009) stated the existence of a negative correlation between cortical thickness and age, also at the rate of 0.79% and 2.0% indicated annual hippocampal atrophy. Moreover, a direct link was found between the reduction in hippocampal size and impaired memory functionality in older depressed patients (Hickie et al., 2005). Yet, recent studies indicate that there is a profound atrophy of the hippocampus, frontal and parietal cortices in Alzheimer's disease, and there is evidence that depression occurs in approximately 50% of patients with this disorder (Enache ve diğ., 2011). Other clinical studies have also reported that depressed patients with significant cognitive impairment had more than three times the risk of developing dementia compared to those without significant cognitive impairment. Moreover, patients who had major depression before the onset of Alzheimer's disease were found to have higher density of Ab plaques and NFTs in the hippocampus than those with the late-onset form of Alzheimer's disease and a history of depression (Rapp et al., 2005).

Furthermore, white matter abnormalities, which are common in aging, are also frequently encountered in late-life depression. LLD studies have detected impaired microstructural integrity in normal-appearing white matter. Decreased white matter integrity was found in a number of distributed cerebral networks when depressed older adults and controls were compared (Van Uden et al., 2015). Again, Positron Emission Tomography (PET) studies indicate increased cerebral glucose metabolism with depressive symptom severity in LLD patients compared with controls. It is known that the extend of hypermetabolism in LLD is much greater than that observed in middle-aged depressed patients with reduced metabolism or no change observed in these regions. Likewise, it has been reported that LLD hypometabolism areas overlap in individuals with genetic risk for dementia (Smith et al., 2009).

Autem, when the studies examined, in a study lasting more than 3 years, it was found that irreversible dementia developed significantly more frequently in the group of depressed patients with dementia syndrome (DSD) (43%) than in the group with depression alone (12%). As a result of the follow-up, it was determined that the group with dementia syndrome was 4.69 times more likely to develop dementia than the patients with depression alone (Alexopoulos et al., 1993). For example, dementia and depression are quite common and co-occurring in older adults living in sheltered housing (AIHW, 2022). Twenty studies of people aged 70 years and older were reviewed and found the incidence of major depressive disorder was between 0.2 and 14.1 per 100 person-years, while the incidence of clinically significant depressive symptoms was 6.8 per 100 person-years (Büchtemann et al., 2012). Depression is effective in the timing of clinical dementia presentation, regardless of individual sociodemographic characteristics (e.g. education level, lifestyle), nature and content of the pathology (Sweet et al., 2004).

Just like in depression, it is known that psychological stress factors increase the incidence of the disease in the development of dementia. Voluntary or compulsory retirement, caregiving, loss of independence, having economic difficulties, chronic illness, cognitive decline, loss of a loved one and grieving process are known as late-life stressors (Aldwin et al., 1996). The mentioned stressors may cause results such as increased reactive oxygen species, inflammatory responses, suppression of neurogenesis and apical dendritic atrophy in the medial prefrontal cortex and altered functional connectivity (Hall et al., 2015). Low education level and limited life-long cognitive and physical activity are other risk factors. Yet distincly, a 14-year study of 4,922 cognitively sound men in Australia found a correlation between the onset of depression and the incidence of dementia. Rather than assessing depression as a risk factor, the researchers focused on the possibility of it being a marker of new-onset dementia (Almeida et al., 2017).

Depression diagnosed at a later age is more likely to have a poor prognosis and have a higher risk of progression to dementia than depression diagnosed at a younger age (Kok et al., 2012). When depression in young patients is compared with later-stage depression, it was found that the response rate to antidepressants was higher and the rate of response to placebo was similar (Tedeschini et al., 2011). Besides that, it is possible to say that antidepressants are generally ineffective in depression comorbid with dementia (Nelson & Devanand, 2011). On the other hand, one of the most controversial issues nowadays is whether the depression of the elderly individuals progresses with more severe neurovegetative or somatic symptoms compared to the younger ones. It is mentioned that the need for diagnostic tools developed specifically for elderly people is required (Haigh et al., 2018).

CONCLUSION

As a result of the studies carried out to date, many themes and different hypotheses have emerged. These can be listed as follows: the view that depression is an independent risk factor for the development of dementia, the presence of depression affecting the threshold for the development of dementia, dementia or cognitive

impairment as a component of depression, the idea that depression is a prodrome of dementia, and the idea that depression is a response to cognitive decline (Sheline et al., 2006). On the other hand, the fact that dementia and depression share common risk factors, the increasing prevalence of both disorders in the population in question, and the fact that they are comorbid with each other take the discussion to another point (Butters et al., 2008). The aim of this article is to clarify the themes, questions and hypotheses mentioned in the context of late-life depression and dementia.

With neuropsychological evaluation, differential diagnosis of geriatric patients with depression and cognitive impairment can be made (Rushing et al., 2014). Clinicians should be aware of the serious distinction between mild cognitive impairment and dementia when making assessments. Yet, in dementia progressive cognitive decline in daily functioning, describing social or occupational activities are seen (Parmera et al., 2018). In mild cognitive impairment (MCI), mainly functional abilities are preserved, and there is an intermediate state between normal cognition and dementia. Although the individual's efforts to maintain her/his daily life increase, s/he maintains her/his independence in daily activities (Ward et al., 2012). Anyhow, it has been found that patients with mild cognitive impairment associated with depression have twice the risk of developing dementia compared to those without depression (Panza et al., 2010). This suggests that depression may be a prodrome of dementia. Indeed, the mechanisms involved are complex and interconnected, with no single process explaining the relationship. According to the prodromal hypothesis, people presenting with depression in old age should be followed carefully when the first depressive episode occurs at older ages (late-life depression), taking into account the possible, expected cognitive decline in the future (Korczyn &Halperin,2009). On the other hand, research that obtains more reliable data on the underlying neurobiological pathways will pave the way for more effective treatment for both depression and dementia.

However, typical symptoms of "pseudodementia" include psychomotor retardation and passive refusal to respond appropriately to cognitive tests, confusing depression with dementia (Wells, 1979; Jarvik, 1976). Some common features of depression and dementia, such as impaired attention and working memory, changes in sleep patterns, and decreased social and occupational functioning, make it difficult to discuss which disorder comes first. Based on this, it would not be wrong to say that the concept of 'pseudodementia' underlines how blurred the distinction between depression and dementia can be (Özaşkınlı et al., 2005).

Prospective, cross-sectional and meta-analysis studies on late-life depression and dementia in the last decade have found that late-life depression increases the risk of dementia by two to five times, and even an additional depressive symptom increases the risk of dementia by up to 20% (Weiner & Lipton, 2008). Therefore, depression, such as a treatable disorder, needs to be clinically evaluated correctly so that it is not mislabeled as dementia or other chronic medical illness, is not neglected as less important due to medical difficulties, and is not misdiagnosed as a largely incurable problem (Cairney et al., 2018). At the point, it is important to better understand the relationship between the aging population and the risk of depression and dementia, especially in terms of prevention and treatment (Kitching, 2015). For example, it is known that possible biological mechanisms linking depression with dementia include changes in glucocorticoid steroid levels and hippocampal atrophy, increased accumulation of amyloid-β plaques, vascular diseases, inflammatory changes and deficiencies in nerve growth factors. The risk of developing dementia can be eliminated by intervening in these pathways in the treatment of depression. Considering the increasing cases of dementia, the critical importance of cognitive remediation in the treatment of depression will be undeniable (Steffens & Potter, 2008).

Many epidemiological studies evaluate the high prevalence of co-occurrence of depression and dementia as a serious secondary complication that will prevent the recovery of other medical patients. Thus, more serious steps need to be taken in the treatment of LLD and dementia, which are mutually related and share common paths. It is thought that improvements in LLD treatment will help delay or prevent dementia.

DECLARATION

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