FALL 2019

SYNERGIES

DEPARTMENT OF PSYCHIATRY

Anxiety in Late-Life

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Introduction

Worry is a universal part of human experience. Although worry may have some evolutionary advantages by detecting threat and planning strategies to avoid harm, excessive worry perturbs everyday activities and reduces quality-of-life. Generalized anxiety disorder, characterized by excessive and persistent worry, is one of the most prevalent anxiety disorders in the United States and worldwide. Our team investigates anxiety disorders, particularly among older adults, because of its high prevalence and its pronounced impact on health conditions. For example, anxiety has been tied to increased cardiovascular burden and worsening cognitive decline. Despite severe health implications, late-life anxiety is underdiagnosed and undertreated in clinical practice, and the neural mechanisms underlying anxiety are understudied.

Background

Severe worry is defined as intense and uncontrollable worry associated with an interruption in functioning and reduced quality-of-life. In the United States, it is estimated that 31.1% of adults suffer from severe worry (with or without a diagnosis of anxiety disorder) at some point in their life, and anxiety disorders have a higher prevalence in females than males.[1] With the exception of specific phobias, generalized anxiety disorder (GAD) is the most common form of anxiety disorder. GAD is characterized by severe worry about everyday activities and life events. Interestingly, the prevalence of many anxiety disorders appears to decrease in late-life, although GAD maintains similar prevalence rates in young and old.[2-4] Compared to other anxiety disorders, GAD has a relatively late-onset, and almost half of older patients with GAD report the onset of their disorder after age 50.[5] In community samples, one study suggests that 20% of older adults report severe worry.[6] The prevalence of anxiety disorders in late-life, however, is believed to be underestimated due to the challenges of assessing and diagnosing anxiety in the elderly, which we will discuss in detail later in this paper.

(Continued on Page 2)

CME Credit

Disclosures: *Drs. Mizuno and Andreescu report receiving grant support from the National Institute of Mental Health.*

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The high prevalence of late-life anxiety is emerging as a significant public health burden in an aging population. According to the 2013 State of Health report in the United States, anxiety disorders were one of the four diseases with the largest number of years-lived-with-disability in 2010 following low back pain, other musculoskeletal disorders, and major depressive disorder.[9] Large longitudinal studies of late-life anxiety also reported the high risk of relapse, with recurrence and chronicity rates up to 39 to 52% after three to six years.[10-12]

Late-onset anxiety disorder risk factors in older adults are often age-related and include life events/stressors such as bereavement, chronic illness and disability, caregiver status, and social isolation.[6] Late-onset GAD also is distinguished from early-onset GAD by a more frequent association with medical comorbidities (e.g., hypertension), greater disability, and poorer health-related quality-of-life after controlling for medical burden and depressive symptoms.[7,8]

Relevant Comorbidities

Late-Life Anxiety and Depression

Comorbidity of anxiety and depressive disorders has been reported for all age groups. This comorbidity is partially a result of the transdiagnostic quality of worry, a symptom present in both anxiety and depressive disorders. In addition, both classes of disorders share other symptoms, including irritability, decreased concentration, restlessness, sleep changes, and fatigue. Among older adults with anxiety disorders, 13 to 23% of them also met criteria for major depressive disorder[7,8] and 26.1% met criteria for any depressive disorder.[9] Likewise, 48% of patients with a major depressive disorder also had a current anxiety disorder diagnosis,[9] and 28% of depressed elderly patients would meet diagnostic criteria for GAD.[10]

Late-life anxiety is associated with unfavorable outcomes in health and age-related cognitive functions, and comorbidity of anxiety and depressive disorders further increases negative outcomes, including greater risk for chronicity,[11] lower social functioning, and higher severity of anxiety symptoms.[12] Likewise, the presence of anxiety symptoms among depressed older adults has been associated with greater suicidal risk, greater somatic symptoms, and an increased risk of cognitive impairment.[10,13,14]

Comorbidity of depression and anxiety negatively affects response to treatment.[15] Older adults with depression and concurrent anxiety symptoms required 50% more time to respond to antidepressants, the first-line pharmacological treatment for late-life anxiety disorders. Also, older adults with both anxiety and depressive disorders are more likely to discontinue treatment.[15,16] Anxiety symptoms often persist after remission of depression and increase the risk for depressive relapse.[15,17,18]

Late-Life Anxiety and Risk of Dementia

Late-life anxiety is frequently comorbid with declining cognitive functions. In general, age is the strongest predictive factor of cognitive impairment and Alzheimer's disease (AD), and older adults with a clinically relevant level of anxiety have an increased risk of cognitive decline.[19] For example, individuals with late-life GAD show deficits in multiple cognitive domains, including language, processing speed, immediate and delayed memory, and executive function.[20] Cross-sectional studies and observational research have shown that anxiety symptoms in the elderly may increase the risk of cognitive decline.[14,21-23]

The association between dementia and anxiety symptoms is still a matter of debate, with some studies reporting no significant difference in the prevalence of anxiety symptoms in the elderly with dementia compared to nondemented subjects,[24] while others report a positive association.[25,26] The wide range of reports may result from diagnostic difficulties in patients with dementia, as well as methodological differences between the studies. The symptoms that are seen in both anxiety disorders and dementia, such as restlessness, fatigue, and poor concentration, make it difficult to distinguish anxiety in the context of dementia.[27] Additionally, AD participants may have difficulty relaying information about themselves, prompting researchers to rely on caregiver reports with limited ability to assess internal symptoms such as worry and rumination.[28]

The causal relationship between anxiety and cognitive decline may be bidirectional. Chronic anxiety may contribute to cognitive decline through various stress-related pathways that increase allostatic load.[29-34] Conversely, worsening cognition may trigger increased anxiety and worry.[35-37] Anxiety-induced chronic stress may increase cerebrovascular burden, chronic inflammation, and unopposed glutaminergic excitotoxicity in vulnerable brain regions (e.g., the hippocampus and prefrontal cortex).[38-41] Stress-induced neurotoxic injury may result in neurodegeneration and cognitive decline. On the other hand, more evidence is becoming available to support that declining cognition may precipitate late-life anxiety. For example, a higher amyloid burden, the most established biomarker of AD, is suspected of playing a role in late-life anxiety. Several groundbreaking recent studies have reported an association between anxiety/worry and amyloid burden; in particular, anxiety may moderate the association between beta-amyloid burden and cognitive decline.[42-45] Furthermore, anxiety may represent an early manifestation of preclinical AD.[43]

Late-Life Anxiety and Medical Comorbidity

Across age groups, individuals with anxiety disorders have increased mortality both from natural and unnatural causes.[46] Late-life anxiety is associated with greater disability and poorer health-related quality-of-life.[47] Late-life is often accompanied by health challenges, and anxiety is associated with several medical conditions, such as gastrointestinal problems, hypo- or hyperthyroidism, diabetes, cardiovascular disease, and respiratory disorders.[48-51]

More recently, the link between anxiety and cardiovascular disease has been the focus of several studies. Thus, anxiety has been reported as a significant risk factor for mortality after coronary bypass surgery.[52] A recent meta-analysis reported that anxiety was associated with a significantly elevated risk of cardiovascular mortality [relative risk 1.41], coronary heart disease [relative risk 1.41], stroke [relative risk 1.71], and heart failure [relative risk 1.35].[39] In a prospective longitudinal study, higher anxiety symptom levels were associated with increased risk for incident stroke independent of other risk factors, including depression.[53] Another study reported that anxiety symptoms predicted major cardiovascular events at five years in patients following coronary artery bypass surgery.[52]

Late-Life Anxiety and Substance Use Disorders

Another type of disorder that is highly comorbid with anxiety is substance use disorder (SUD). According to the National Comorbidity Survey Replication in 2005, one in five individuals with SUD also meets the criteria for an anxiety disorder. SUD in older adults is an emerging

public health concern that is associated with aging in populations around the world.[53] However, research is scarce in this area. There have been increases in treatment admissions for illicit and prescription drug abuse in older adults in the United States.[54,55] Among prescription drug misuse, opioid and benzodiazepine misuse is a particular concern due to high rates of fatal overdosing.[55,56] Older patients are more likely to receive opioid and benzodiazepine prescriptions, and they are more likely to have side effects such as increased risk of falls and cognitive impairment.[57-60] More recently, interest in the medicinal use of cannabis has been increased. The use of cannabis/cannabinoids is particularly relevant for older individuals due to the increased frequency of symptoms such as chronic pain, insomnia, and mood symptoms.[61] However, so far, there is very little evidence of its efficacy in older adults, and the potential of side effects and drug-drug interactions should not be underestimated.

The comorbidity between anxiety and SUD complicates treatment and worsens the prognosis of SUD. Although the mechanisms underlying the relationship between anxiety and SUD are unclear, there are several hypotheses: self-medication hypothesis (substances used to self-treat anxiety), substance-induced anxiety (anxiety caused by intoxication or withdrawal), and common factors theory (shared personality/ neurobiological vulnerabilities between anxiety and SUD).[62,63]

Treatment

Adequate treatment of late-life anxiety disorders is particularly important given the morbidity and mortality risks associated with untreated anxiety.[65] However, treatment of late-life anxiety disorders is generally less successful than in younger adults. Late-life anxiety disorders are more likely to be chronic, with frequent relapses and uncommon remission.[30] The treatment of late-life anxiety disorders raises several specific challenges. For instance, older adults are less likely to seek help from mental health professionals.[65] They also are more likely to drop out of treatment due to perceived stigma related to mental health.[66] The preference of treatment types appears to be different between older and younger adults. One study reported that older adults tend to be willing to participate in psychoeducational classes but are more reluctant to join group therapies.[67] In another study with a community survey, the majority of older adults reported psychotherapy as the preferred treatment.[68]

Pharmacotherapy

A meta-analysis of 32 studies concluded that pharmacotherapy is more effective than psychotherapy for late-life anxiety.[69] However, pharmacotherapy for older adults requires a comprehensive assessment that may not be necessary for other age groups. Elderly patients have several pharmacokinetics and dynamics changes related to reduced glomerular filtration and hepatic metabolization, lower cardiac output, and decreased activity of target receptors.[70] These physiologic changes increase the risk of medication-related side effects, such as anticholinergic (urinary retention, constipation, delirium, cognitive difficulties), antiadrenergic (orthostatic hypotension), and antihistaminergic (drowsiness, dizziness, confusion) effects.[71-73]

As seen in other age groups, the most common pharmacological treatment for anxiety in late-life is benzodiazepines.[74-76] Some studies have found benzodiazepines efficacious in reducing anxiety symptoms in older adults.[77,78] However, the mass-scale use of benzodiazepines in late-life anxiety remains problematic because of well-known risks such as falls, cognitive impairment,[60,61] and the risk for misuse.[55-57]

Antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), are considered the first-line treatment for late-life anxiety disorders. The effectiveness of SSRIs in late-life anxiety (predominantly GAD) has been reported in three randomized controlled trials.[79-81] SNRIs (venlafaxine XR and duloxetine) have also been found to be equally efficacious in older and younger adults.[82,83] Although SSRIs and SNRIs are relatively well-tolerated, several risks that are specific to late-life need to be monitored, including an elevated risk of falls,[84-86] gastrointestinal bleeding,[87] bone loss,[88] and hyponatremia.[89] Closely monitoring blood pressure is particularly recommended for higher doses of SNRIs (especially venlafaxine).[90] Other classes of antidepressant drugs, such as tricyclic antidepressants (TCA) and irreversible monoamine oxidase inhibitors (MAOI) may be efficacious. However, they should be considered only for cases resistant to other treatment options due to their side-effect profiles and safety concerns.

Off-label use of antipsychotic drugs in the treatment of late-life anxiety is common in the community. The only antipsychotic with some evidence of efficacy in anxiety disorder is quetiapine, with doses between 50-150 mg being as efficacious as 20 mg of paroxetine or 10 mg of escitalopram.[91] Quetiapine has demonstrated efficacy and tolerability both as a monotherapy and as an adjunctive to SSRIs.[92] In a large study (N=450), quetiapine XR monotherapy (50-300 mg/day) was efficacious in treating late-life anxiety in the elderly (number needed to treat = 8).[93] The study reported multiple side effects such as drowsiness, dry mouth, dizziness, headache, and nausea.[93] One small study of risperidone showed its efficacy as an augmentation strategy.[94] Importantly, clinicians need to balance the potential benefits of second-generation antipsychotics in the elderly with substantial metabolic side effects, including weight gain, hyperglycemia, and increased cholesterol,[95-97] as well as the increased risk of sudden death and cardiovascular events.[98] Mirtazapine (Remeron®) is a popular choice for the treatment of anxiety in late-life mainly because of its effects on sleep and appetite, but the evidence for its efficacy is limited and inconsistent.[99]

Few studies have focused on second-line pharmacological strategies. Pregabalin was found efficacious in late-life anxiety, although it is difficult to assess the clinical impact of pregabalin (i.e., pregabalin was associated with a two-point greater reduction on the Hamilton Anxiety Scale than placebo).[100] A recent study found that buspirone was as effective and well-tolerated as sertraline for the treatment of late-life anxiety.[101]

Psychotherapy

The efficacy of cognitive-behavioral therapy (CBT) has been demonstrated in numerous studies for various psychological disorders. Although CBT is a type of psychotherapy that has been studied extensively in late-life anxiety, the results remain mixed. Some trials and meta-analyses have shown moderate efficacy of CBT in late-life anxiety,[101,102] while others have failed to prove the superiority of CBT over supportive therapy or waiting lists.[103-105]

Since CBT targets modification of maladaptive cognition and behaviors, one study investigated the ability to learn new cognitive skills among older adults with anxiety. The study reported that patients

with late-life anxiety were able to acquire new cognitive skills and use them effectively.[105] Another study reported that patients with late-life anxiety who received CBT maintained gains up to one year after CBT treatment.[102] Furthermore, another study reported that CBT remained more beneficial at one-year follow-up than immediately following treatment in patients who received at least three months of pharmacotherapy prior to receiving CBT.[106] These results indicate that CBT in older adults brings long-term benefits.

Late-life specific challenges in CBT may be accounted for by diminishing cognitive ability, particularly the cognitive reappraisal.[107-109] One study has reported that relaxation therapy may be the most efficacious kind of CBT for older patients with anxiety.[104] To accommodate late-life specific needs, some modifications can provide better outcomes, such as between-session reminder phone calls, a weekly review of concepts, in-home assignments with relatively easy instruction components, and a more simplified approach.[110] Also, more group-specific adjustments can be implemented to facilitate the impact of psychotherapeutic interventions. Incorporating religion and/or spirituality for older African American subjects were proven to be effective.[110] Telephone-delivered CBT for rural populations was superior to telephone-delivered nondirective supportive therapy in late-life anxiety.[111] Older adults were more likely to complete Internet-delivered CBT than younger adults, although younger adults had a more robust response.[112] Overall, psychotherapy is not proven to be more effective than pharmaco-therapy; however, it might be clinically relevant to question whether combining CBT and medication would be more effective. Augmenting SSRI treatment with CBT improved worry symptoms and reduced relapse rates in older adults with late-life anxiety.[113]

Different innovative psychotherapeutic approaches are actively being examined. For example, modular CBT uses a personalized protocol that considers the specific symptoms of the patients and allows flexibility to tailor the treatment components to individual patient needs.[115] Mindfulness-based stress reduction (MBSR) is proven to reduce anxiety symptoms in older adults.[116] MBSR for anxious elderly patients with cognitive dysfunction also has shown promising preliminary results.[117] Acceptance and Commitment therapy also has shown improvement in worry severity in elderly patients.[118] These promising results suggest the need for further investigation and validation on larger samples.

Conclusion and Current Research at the University of Pittsburgh

Late-life anxiety is highly prevalent and causes significant functional impairment and distress. While it has long been known that late-life anxiety is comorbid with mood and substance use disorders, recent studies support further links between late-life anxiety with both cognitive decline and cardiovascular disease. Aging populations and the increased prevalence of cardiovascular disease and Alzheimer's disease heighten the significance of these links. In clinical practice for anxiety disorders, a challenge specific to late-life anxiety disorder is to identify anxiety symptoms based on self-reporting that may be hampered by impaired cognitive function.

Antidepressants remain the first-line treatment for late-life anxiety; however, benzodiazepines continue to be the most common pharmacological treatment. The treatment options are the same for every age group, but older patients tend to need extra consideration and monitoring of the side-effects. Although SSRIs are more effective than psychotherapy in late-life anxiety, many elderly anxious subjects prefer psychotherapeutic interventions. These interventions appear to work best when tailored to the needs, expectations, and cultural backgrounds of older anxious individuals.

The Geriatric Psychiatry Neuroimaging (GPN) lab is currently conducting several studies exploring the neural mechanisms of late-life anxiety, as well as experimental interventions with transcranial magnetic stimulation (TMS) for severe worry in late-life. One of these studies aims to identify neural mechanisms of late-life anxiety and its relationship with the neuropathologic changes of aging (e.g., neurodegeneration and white matter disease). In particular, we focus on severe worry as a transdiagnostic symptom that manifests in several mood and anxiety disorders. This study uses neuroimaging to measure the functional connectivity during "rest" and during worry induction and regulation (i.e., reappraisal). We further investigate how brain age (measured by white matter hyperintensity burden) moderates the relationship between worry severity and functional connectivity of the brain network. This project will allow us to develop effective interventions targeting aberrant neural networks that are specific to older individuals with severe worry.

Although the association between late-life anxiety and cognitive impairment has been reported in several recent studies, we still do not know the mechanistic pathways connecting anxiety/worry with cognitive decline. We are examining a model in which chronic and severe worry augment the risk of cognitive decline through increased chronic stress markers. In this study, we measure beta-amyloid via Pittsburgh Compound B Positron Emission Tomography (PiB-PET) as a measure of AD neuropathology, as well as three types of chronic stress markers (proinflammatory cytokines, cortisol level, and stressor-evoked blood pressure reactivity). No modifiable risk factor has been established to change the course of AD, and identifying such a factor is a common goal of much AD research. Our study proposes that severe worry is a modifiable risk factor that can possibly change the trajectory of cognitive decline or AD progression and, consequently, reduce the enormous socioeconomic burden associated with AD.

We also are testing two additional pathways of how severe worry may affect AD and AD-related risks. These two pathways are hippocampal atrophy and vascular burden. Hippocampal atrophy is one of the earliest and most validated markers of AD, but the mechanisms of degeneration in the hippocampus are still unknown. We hypothesize that stress-induced glutamate excitotoxicity associated with severe worry contributes to hippocampal atrophy. As another pathway, this study measures cerebrovascular burden (both peripheral vascular disease and cerebral small vessel disease.) Several studies suggest that severe worry is a risk factor for cardiovascular disease and stroke. We posit that an increased risk of cardiovascular disease increases the risk for AD.

Currently, available treatments for late-life anxiety have moderate efficacy. However, longitudinal observations indicate that up to half of patients relapse in three to six years in geriatric populations. Commonly used pharmacological and psychotherapeutic interventions in late-life anxiety are particularly ineffective for reducing worry severity. Our fMRI-directed TMS treatment study aims to modulate cortical plasticity in the regions that are associated with severe worry. This project uses inhibitory TMS (low-frequency TMS at 1 Hz) to induce neural modulation and, consequently, reduce worry severity. Details regarding these projects can be found at www.gpn.pitt.edu.

References

1. Harvard Medical School. National Comorbidity Survey (NCS). Data Table 1: Lifetime Prevalence DSM-IV/WMH-CIDI Disorders by Sex and Cohort. 2017.
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime Prevalence and Age-of-Onset Distributions of DSM-IV Disorders in the National Comorbidity Survey Replication. *Arch Genpsychiatr*. 2005; 62: 593-602.
3. Flint AJ. Epidemiology and Comorbidity of Anxiety Disorders in Later Life: Implications for Treatment. *Clin Neurosci*. 1997; 4: 31-6.
4. Beekman AT, Bremmer MA, Deeg DJ, Van Balkom AJ, Smit JH, De Beurs E, et al. Anxiety Disorders in Later Life: A Report From the Longitudinal Aging Study Amsterdam. *Int J Geriatr Psychiatry*. 1998; 13: 717-26.
5. Goncalves DC, Byrne GJ. Sooner or Later: Age at Onset of Generalized Anxiety Disorder in Older Adults. *Depression and Anxiety*. 2012; 29: 39-46.
6. Bryant C, Jackson H, Ames D. The Prevalence of Anxiety in Older Adults: Methodological Issues and a Review of the Literature. *J Affect Disorders*. 2008; 109: 233-50.
7. Van Balkom AJ, Beekman AT, De Beurs E, Deeg DJ, Van Dyck R, Van Tilburg W. Comorbidity of the Anxiety Disorders in a Community-Based Older Population in the Netherlands. *Acta Psychiatr Scand*. 2000; 101: 37-45.
8. Cairney J, Corna LM, Veldhuizen S, Herrmann N, Streiner DL. Comorbid Depression and Anxiety in Later Life: Patterns of Association, Subjective Well-Being, and Impairment. *Am J Geriatr Psychiatry*. 2008; 16: 201-208.
9. Beekman AT, De Beurs E, Van Balkom AJ, Deeg DJ, Van Dyck R, Van Tilburg W. Anxiety and Depression in Later Life: Co-Occurrence and Communality of Risk Factors. *Am J Psychiatry*. 2000; 157: 89-95.
10. Lenze EJ, Mulsant BH, Shear MK, Schulberg HC, Dew MA, Begley AE, et al. Comorbid Anxiety Disorders in Depressed Elderly Patients. *Am J Psychiatry*. 2000; 157: 722-728.
11. Schoevers RA, Beekman AT, Deeg DJ, Jonker C, Van Tilburg W. Comorbidity and Risk-Patterns of Depression, Generalised Anxiety Disorder and Mixed Anxiety-Depression in Later Life: Results From the AMSTEL Study. *Int J Geriatr Psychiatry*. 2003; 18: 994-1001.
12. Hopko DR, Bourland SL, Stanley MA, Beck JG, Novy DM, Averill PM, et al. Generalized Anxiety Disorder in Older Adults: Examining the Relation Between Clinician Severity Ratings and Patient Self-Report Measures. *Depression and Anxiety*. 2000; 12: 217-25.
13. Jeste ND, Hays JC, Steffens DC. Clinical Correlates of Anxious Depression Among Elderly Patients With Depression. *J Affect Disorders*. 2006; 90: 37-41.
14. Deluca AK, Lenze EJ, Mulsant BH, Butters MA, Karp JF, Dew MA, et al. Comorbid Anxiety Disorder in Late Life Depression: Association With Memory Decline Over Four Years. *Int J Geriatr Psychiatry*. 2005; 20: 848-854.
15. Flint AJ, Rifat SL. Anxious Depression in Elderly Patients. Response to Antidepressant Treatment. *Am J Geriatr Psychiatry*. 1997; 5: 107-115.
16. BH M. In: BA W, Editor. Psychological Treatment of Older Adults: An Introductory Text. New York: Plenum Press; 1996. P. 91-101.
17. Andreescu C, Lenze EJ, Dew MA, Begley AE, Mulsant BH, Dombrovski AY, et al. Effect of Comorbid Anxiety on Treatment Response and Relapse Risk in Late-Life Depression: Controlled Study. *Br J Psychiatry*. 2007; 190: 344-349.
18. Dombrovski AY, Lenze EJ, Dew MA, Mulsant BH, Pollock BG, Houck PR, et al. Maintenance Treatment for Old-Age Depression Preserves Health-Related Quality of Life: A Randomized, Controlled Trial of Paroxetine and Interpersonal Psychotherapy. *J Am Geriatr Soc*. 2007; 55: 1325-1332.
19. Schultz SK, Moser DJ, Bishop JR, Ellingrod VL. Phobic Anxiety in Late-Life in Relationship to Cognition and 5HTTLPR Polymorphism. *Psychiatr Genet*. England 2005. P. 305-306.
20. Butters MA, Bhalla RK, Andreescu C, Wetherell JL, Mantella R, Begley AE, et al. Changes in Neuropsychological Functioning Following Treatment for Late-Life Generalised Anxiety Disorder. *Br J Psychiatry*. 2011; 199: 211-218.
21. Sinoff G, Werner P. Anxiety Disorder and Accompanying Subjective Memory Loss in the Elderly as a Predictor of Future Cognitive Decline. *Int J Geriatr Psychiatry*. 2003; 18: 951-959.
22. Andreescu C, Teverovsky E, Fu B, Hughes TF, Chang CC, Ganguli M. Old Worries and New Anxieties: Behavioral Symptoms and Mild Cognitive Impairment in a Population Study. *Am J Geriatr Psychiatry*. 2014; 22: 274-284.
23. Palmer K, Berger AK, Monastero R, Winblad B, Backman L, Fratiglioni L. Predictors of Progression From Mild Cognitive Impairment to Alzheimer Disease. *Neurology*. 2007; 68: 1596-1602.
24. Forsell Y, Winblad B. Anxiety Disorders in Non-Demented and Demented Elderly Patients: Prevalence and Correlates. *J Neurol Neurosurg Psychiatr*. 1997; 62: 294-295.
25. Hwang TJ, Masterman DL, Ortiz F, Fairbanks LA, Cummings JL. Mild Cognitive Impairment Is Associated With Characteristic Neuropsychiatric Symptoms. *Alzheimer Dis Disorders*. 2004; 18: 17-21.
26. Geda YE, Smith GE, Knopman DS, Boeve BF, Tangalos EG, Ivnik RJ, et al. De Novo Genesis of Neuropsychiatric Symptoms in Mild Cognitive Impairment (MCI). *Int Psychogeriatrics*. 2004; 16: 51-60.
27. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety Disorders in Older Adults: A Comprehensive Review. *Depression Anxiety*. 2010; 27: 190-211.
28. Seignourel PJ, Kunik ME, Snow L, Wilson N, Stanley M. Anxiety in Dementia: A Critical Review. *Clin Psychol Rev*. 2008; 28: 1071-1082.
29. Schulkin J, McEwen BS, Gold PW. Allostasis, Amygdala, and Anticipatory Angst. *Neurosci Biobehavior Rev*. 1994; 18: 385-396.
30. Lenze EJ, Wetherell JL. A Lfespan View of Anxiety Disorders. *Dialogues Clin Neurosci*. 2011; 13: 381-399.
31. Mantella RC, Butters MA, Amico JA, Mazumdar S, Rollman BL, Begley AE, et al. Salivary Cortisol Is Associated With Diagnosis and Severity of Late-Life Generalized Anxiety Disorder. *Psychoneuroendocrinology*. 2008; 33: 773-781.
32. Narita K, Murata T, Hamada T, Kosaka H, Sudo S, Mizukami K, et al. Associations Between Trait Anxiety, Insulin Resistance, and Atherosclerosis in the Elderly: A Pilot Cross-Sectional Study. *Psychoneuroendocrinology*. 2008; 33: 305-312.
33. Simon NM, Smoller JW, McNamara KL, Maser RS, Zalta AK, Pollack MH, et al. Telomere Shortening and Mood Disorders: Preliminary Support for a Chronic Stress Model of Accelerated Aging. *Biol Psychiatry*. 2006; 60: 432-435.
34. Sibille E, Su J, Leman S, Le Guisquet AM, Ibarguen-Vargas Y, Joeyen-Waldorf J, et al. Lack of Serotonin1b Receptor Expression Leads to Age-Related Motor Dysfunction, Early Onset of Brain Molecular Aging and Reduced Longevity. *Mole Psychiatr*. 2007; 12: 1042-1056, 975.
35. Ballard C, Neill D, O'Brien J, McKeith IG, Ince P, Perry R. Anxiety, Depression and Psychosis in Vascular Dementia: Prevalence and Associations. *J Affect Disorders*. 2000; 59: 97-106.
36. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, Dekosky S. Prevalence of Neuropsychiatric Symptoms in Dementia and Mild Cognitive Impairment: Results From the Cardiovascular Health Study. *JAMA*. 2002; 288: 1475-1483.
37. Starkstein SE, Jorge R, Petracca G, Robinson RG. The Construct of Generalized Anxiety Disorder in Alzheimer Disease. *Am J Geriatr Psychiatry*. 2007; 15: 42-49.
38. Bisht K, Sharma K, Tremblay ME. Chronic Stress as a Risk Factor for Alzheimer's Disease: Roles of Microglia-Mediated Synaptic Remodeling, Inflammation, and Oxidative Stress. *Neurobiol Stress*. 2018; 9: 9-21.
39. Emdin CA, Odutayo A, Wong CX, Tran J, Hsiao AJ, Hunn BH. Meta-Analysis of Anxiety as a Risk Factor for Cardiovascular Disease. *Am J Cardiol*. 2016; 118: 511-519.
40. Delvecchio G, Stanley JA, Altamura AC, Brambilla P. Metabolic Alterations in Generalised Anxiety Disorder: A Review of Proton Magnetic Resonance Spectroscopic Studies. *Epidemiol Psychiatr Sci*. 2017; 26: 587-595.

[41] Schulkin J, McEwen BS, Gold PW. Allostasis, Amygdala, and Anticipatory Angst. *Neurosci Biobehavioral Rev*. 1994; 18: 385-396.

[42] Pietrzak RH, Lim YY, Neumeister A, Ames D, Ellis KA, Harrington K, et al. Amyloid-Beta, Anxiety, and Cognitive Decline in Preclinical Alzheimer Disease: A Multicenter, Prospective Cohort Study. *JAMA Psychiatry*. 2015; 72: 284-291.

[43] Donovan NJ, Locascio JJ, Marshall GA, Gatchel J, Hanseeuw BJ, Rentz DM, et al. Longitudinal Association of Amyloid Beta and Anxious-Depressive Symptoms in Cognitively Normal Older Adults. *Am J Psychiatry*. 2018; Jun 1; 175(6): 530-537.

[44] Pietrzak RH, Scott JC, Neumeister A, Lim YY, Ames D, Ellis KA, et al. Anxiety Symptoms, Cerebral Amyloid Burden and Memory Decline in Healthy Older Adults Without Dementia: 3-Year Prospective Cohort Study. *Br J Psychiatry*. 2014; 204: 400-401.

[45] Krell-Roesch J, Lowe VJ, Neureiter J, Pink A, Roberts RO, Mielke MM, et al. Depressive and Anxiety Symptoms and Cortical Amyloid Deposition Among Cognitively Normal Elderly Persons: The Mayo Clinic Study of Aging. *Int Psychogeriatrics.* 2018; 30: 245-251.

[46] Meier SM, Mattheisen M, Mors O, Mortensen PB, Laursen TM, Penninx BW. Increased Mortality Among People With Anxiety Disorders: Total Population Study. *Br J Psychiatry*. 2016; 209: 216-221.

[47] Porensky EK, Dew MA, Karp JF, Skidmore E, Rollman BL, Shear MK, et al. The Burden of Late-Life Generalized Anxiety Disorder: Effects on Disability, Health-Related Quality of Life, and Healthcare Utilization. *Am J Geriatr Psychiatry*. 2009; 17: 473-482.

[48] Byrne G, Rosenfeld G, Leung Y, Qian H, Raudzus J, Nunez C, et al. Prevalence of Anxiety and Depression in Patients With Inflammatory Bowel Disease. *Canadian J Gastroenterol Hepatol*. 2017; 6496727.

[49] Lustman PJ, Griffith LS, Clouse RE, Cryer PE. Psychiatric Illness in Diabetes Mellitus. Relationship to Symptoms and Glucose Control. *J Nervous Mental Dis*. 1986; 174: 736-742.

[50] Todaro JF, Shen BJ, Raffa SD, Tilkemeier PL, Niaura R. Prevalence of Anxiety Disorders in Men and Women With Established Coronary Heart Disease. *J Cardiopulm Rehab Prevent*. 2007; 27: 86-91.

[51] Ittermann T, Volzke H, Baumeister SE, Appel K, Grabe HJ. Diagnosed Thyroid Disorders Are Associated With Depression and Anxiety. *Soc Psychiatr Psych Epidemiol*. 2015; 50: 1417-1425.

[52] Tully PJ, Baker RA, Knight JL. Anxiety and Depression as Risk Factors for Mortality After Coronary Artery Bypass Surgery. *J Psychosomatic Res*. 2008; 64: 285-290.

[53] Lambiase MJ, Kubzansky LD, Thurston RC. Prospective Study of Anxiety and Incident Stroke. *Stroke*. 2014; 45: 438-443.

[54] Simoni-Wastila L, Yang HK. Psychoactive Drug Abuse in Older Adults. *Am J Geriatr Pharmacother*. 2006; 4: 380-394.

[55] Wu LT, Blazer DG. Substance Use Disorders and Psychiatric Comorbidity in Mid and Later Life: A Review. *Int J Epidemiology*. 2014; 43: 304-317.

[56] Wu LT, Blazer DG. Illicit and Nonmedical Drug Use Among Older Adults: A Review. *J Aging Health*. 2011; 23: 481-504.

[57] Schulden JD, Lopez MF, Compton WM. Clinical Implications of Drug Abuse Epidemiology. *Psychiatr Clin North Am*. 2012; 35: 411-423.

[58] Maree RD, Marcum ZA, Saghafi E, Weiner DK, Karp JF. A Systematic Review of Opioid and Benzodiazepine Misuse in Older Adults. *Am J Geriatr Psychiatry*. 2016; 24: 949-963.

[59] Airagnes G, Pelissolo A, Lavallee M, Flament M, Limosin F. Benzodiazepine Misuse in the Elderly: Risk Factors, Consequences, and Management. *Curr Psychiatry Reports*. 2016; 18: 89.

[60] Markota M, Rummans TA, Bostwick JM, Lapid MI. Benzodiazepine Use in Older Adults: Dangers, Management, and Alternative Therapies. *Mayo Clin Proc*. 2016; 91: 1632-1639.

[61] Bogunovic OJ, Greenfield SF. Practical Geriatrics: Use of Benzodiazepines Among Elderly Patients. *Psychiatr Serv*. 2004; 55: 233-235.

[62] Minerbi A, Hauser W, Fitzcharles MA. Medical Cannabis for Older Patients. *Drugs Aging*. 2019; 36: 39-51.

[63] Smith JP, Randall CL. Anxiety and Alcohol Use Disorders: Comorbidity and Treatment Considerations. *Alcohol Res Curr Rev*. 2012; 34: 414-431.

[64] Pasche S. Exploring the Comorbidity of Anxiety and Substance Use Disorders. *Curr Psychiatry Reports*. 2012; 14: 176-181.

[65] De Beurs E, Beekman AT, Van Balkom AJ, Deeg DJ, Van Dyck R, Van Tilburg W. Consequences of Anxiety in Older Persons: Its Effect on Disability, Well-Being and Use of Health Services. *Psychol Med*. 1999; 29: 583-593.

[66] Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Friedman SJ, Meyers BS. Stigma as a Barrier to Recovery: Perceived Stigma and Patient-Rated Severity of Illness as Predictors of Antidepressant Drug Adherence. *Psychiatr Serv*. 2001; 52: 1615-1620.

[67] Arean PA, Alvidrez J, Barrera A, Robinson GS, Hicks S. Would Older Medical Patients Use Psychological Services? *Gerontologist*. 2002; 42: 392-398.

[68] Mohlman J. A Community Based Survey of Older Adults' Preferences for Treatment of Anxiety. *Psychology Aging*. 2012; 27: 1182-1190.

[69] Pinquart M, Duberstein PR. Treatment of Anxiety Disorders in Older Adults: A Meta-Analytic Comparison of Behavioral and Pharmacological Interventions. *Am J Geriatr Psychiatry*. 2007; 15: 639-651.

[70] Pollock B, Forsyth C, Bies R. The Critical Role of Clinical Pharmacology in Geriatric Psychopharmacology. *Clin Pharmacol Therapeutic*. 2009; 85: 89-93.

[71] Mugdha E. Thakur, Dan G. Blazer, David C. Steffens, Editors. *Clinical Manual of Geriatric Psychiatry*. Washington DC: American Psychiatric Publishing, Inc; 2014.

[72] Zubenko GS, Sunderland T. Geriatric Psychopharmacology: Why Does Age Matter? *Harvard Review of Psychiatry*. 2000; 7: 311-333.

[73] Brooks JO, Hoblyn JC. Neurocognitive Costs and Benefits of Psychotropic Medications in Older Adults. *J Geriatric Psychiatr Neurol*. 2007; 20: 199-214.

[74] Benitez CI, Smith K, Vasile RG, Rende R, Edelen MO, Keller MB. Use of Benzodiazepines and Selective Serotonin Reuptake Inhibitors in Middle-Aged and Older Adults With Anxiety Disorders: A Longitudinal and Prospective Study. *Am J Geriatr Psychiatry*. 2008; 16: 5-13.

[75] Olfson M, Marcus SC, Wan GJ, Geissler EC. National Trends in the Outpatient Treatment of Anxiety Disorders. *J Clin Psychiatry*. 2004; 65: 1166-1173.

[76] Olfson M, King M, Schoenbaum M. Benzodiazepine Use in the United States. *JAMA Psychiatry*. 2015; 72: 136-142.

[77] Bresolin N, Monza G, Scarpini E, Scarlato G, Straneo G, Martinazzoli A, et al. Treatment of Anxiety With Ketazolam in Elderly Patients. *Clin Therapeutics*. 1988; 10: 536-542.

[78] Koepke HH, Gold RL, Linden ME, Lion JR, Rickels K. Multicenter Controlled Study of Oxazepam in Anxious Elderly Outpatients. *Psychosomatics*. 1982; 23: 641-645.

[79] Lenze EJ, Mulsant BH, Shear MK, Dew MA, Miller MD, Pollock BG, et al. Efficacy and Tolerability of Citalopram in the Treatment of Late-Life Anxiety Disorders: Results From an 8-Week Randomized, Placebo-Controlled Trial. *Am J Psychiatry*. 2005; 162: 146-150.

[80] Lenze EJ, Rollman BL, Shear MK, Dew MA, Pollock BG, Ciliberti C, et al. Escitalopram for Older Adults With Generalized Anxiety Disorder: A Randomized Controlled Trial. *JAMA*. 2009; 301: 295-303.

[81] Schuurmans J, Comijs H, Emmelkamp PM, Gundy CM, Weijnen I, Van Den Hout M, et al. A Randomized, Controlled Trial of the Effectiveness of Cognitive-Behavioral Therapy and Sertraline Versus a Waitlist Control Group for Anxiety Disorders in Older Adults. *Am J Geriatr Psychiatry*. 2006; 14: 255-263.

[82] Katz IR, Reynolds CF 3rd, Alexopoulos GS, Hackett D. Venlafaxine ER as a Treatment for Generalized Anxiety Disorder in Older Adults: Pooled Analysis of Five Randomized Placebo-Controlled Clinical Trials. *J Am Geriatrics Soc*. 2002; 50: 18-25.

[83] Davidson J, Allgulander C, Pollack MH, Hartford J, Erickson JS, Russell JM, et al. Efficacy and Tolerability of Duloxetine in Elderly Patients With Generalized Anxiety Disorder: A Pooled Analysis of Four Randomized, Double-Blind, Placebo-Controlled Studies. *Hum Psychopharmacol*. 2008; 23: 519-526.

[84] Laghrissi-Thode F, Pollock BG, Miller MC, Mulsant BH, Altieri L, Finkel MS. Double-Blind Comparison of Paroxetine and Nortriptyline on the Postural Stability of Late-Life Depressed Patients. *Psychopharmacol Bull*. 1995; 31: 659-663.

[85] Gebara MA, Lipsey KL, Karp JF, Nash MC, Iaboni A, Lenze EJ. Cause or Effect? Selective Serotonin Reuptake Inhibitors and Falls in Older Adults: A Systematic Review. *Am J Geriatr Psychiatry*. 2015; 23: 1016-1028.

[86] Kerse N, Flicker L, Pfaff JJ, Draper B, Lautenschlager NT, Sim M, et al. Falls, Depression and Antidepressants in Later Life: A Large Primary Care Appraisal. *Plos One*. 2008; 3: E2423.

[87] Yuan Y, Tsoi K, Hunt RH. Selective Serotonin Reuptake Inhibitors and Risk of Upper GI Bleeding: Confusion or Confounding? *Am J Medicine*. 2006; 119: 719-727.

[88] Diem SJ, Blackwell TL, Stone KL, Yaffe K, Haney EM, Bliziotes MM, et al. Use of Antidepressants and Rates of Hip Bone Loss in Older Women: The Study of Osteoporotic Fractures. *Arch Intern Med*. 2007; 167: 1240-1245.

[89] Fabian TJ, Amico JA, Kroboth PD, Mulsant BH, Corey SE, Begley AE, et al. Paroxetine-Induced Hyponatremia in Older Adults: A 12-Week Prospective Study. *Arch Internal Med*. 2004; 164: 327-32.

[90] Baldwin DS, Waldman S, Allgulander C. Evidence-Based Pharmacological Treatment of Generalized Anxiety Disorder. *Int J Neuropsychopharmacol.* 2011; 14: 697-710.

[91] Merideth C, Cutler AJ, She F, Eriksson H. Efficacy and Tolerability of Extended Release Quetiapine Fumarate Monotherapy in the Acute Treatment of Generalized Anxiety Disorder: A Randomized, Placebo Controlled and Active-Controlled Study. *Int Clin Psychopharmacol.* 2012; 27: 40-54.

[92] Kreys TJ, Phan SV. A Literature Review of Quetiapine for Generalized Anxiety Disorder. *Pharmacotherapy.* 2015; 35: 175-188.

[93] Mezhebovsky I, Magi K, She F, Datto C, Eriksson H. Double-Blind, Randomized Study of Extended Release Quetiapine Fumarate (Quetiapine XR) Monotherapy in Older Patients With Generalized Anxiety Disorder. *Int J Geriatr Psychiatry*. 2013; 28: 615-625.

[94] Morinigo A, Blanco M, Labrador J, Martin J, Noval D. Risperidone for Resistant Anxiety in Elderly Persons. *Am J Geriatr Psychiatry*. 2005. P. 81-82.

[95] Finkel S, Kozma C, Long S, Greenspan A, Mahmoud R, Baser O, et al. Risperidone Treatment in Elderly Patients With Dementia: Relative Risk of Cerebrovascular Events Versus Other Antipsychotics. *Int Psychogeriatr*. 2005; 17: 617-629.

[96] Bullock R, Saharan A. Atypical Antipsychotics: Experience and Use in the Elderly. *Int J Clin Practice*. 2002; 56: 515-525.

[97] Gareri P, De Fazio P, Manfredi VG, De Sarro G. Use and Safety of Antipsychotics in Behavioral Disorders in Elderly People With Dementia. *J Clin Psychopharmacol*. 2014; 34: 109-123.

[98] Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Atypical Antipsychotic Drugs and the Risk of Sudden Cardiac Death. *N Engl J Med*. 2009; 360: 225-235.

[99] Schutters SI, Van Megen HJ, Van Veen JF, Denys DA, Westenberg HG. Mirtazapine in Generalized Social Anxiety Disorder: A Randomized, Double-Blind, Placebo-Controlled Study. *Int Clin Psychopharmacol*. 2010; 25: 302-304.

[100] Montgomery S, Chatamra K, Pauer L, Whalen E, Baldinetti F. Efficacy and Safety of Pregabalin in Elderly People With Generalised Anxiety Disorder. *Br J Psychiatry*. 2008; 193: 389-394.

[101] Mokhber N, Azarpazhooh MR, Khajehdaluee M, Velayati A, Hopwood M. Randomized, Single-Blind, Trial of Sertraline and Buspirone for Treatment of Elderly Patients With Generalized Anxiety Disorder. *Psychiatr Clin Neurosci.* 2010; 64: 128-133.

[102] Hofmann SG, Smits JA. Cognitive-Behavioral Therapy for Adult Anxiety Disorders: A Meta-Analysis of Randomized Placebo-Controlled Trials. *J Clin Psychiatry*. 2008; 69: 621-632.

[103] Stanley MA, Beck JG, Novy DM, Averill PM, Swann AC, Diefenbach GJ, et al. Cognitive-Behavioral Treatment of Late-Life Generalized Anxiety Disorder. *J Consult Clin Psychol*. 2003; 71: 309-319.

[104] Wetherell JL, Gatz M, Craske MG. Treatment of Generalized Anxiety Disorder in Older Adults. *J Consult Clin Psychol*. 2003; 71: 31-40.

[105] Thorp SR, Ayers CR, Nuevo R, Stoddard JA, Sorrell JT, Wetherell JL. Meta-Analysis Comparing Different Behavioral Treatments for Late-Life Anxiety. *Am J Geriatr Psychiatry.* 2009; 17: 105-115.

[106] Wetherell JL, Hopko DR, Diefenbach GJ, et al. Cognitive-Behavioral Therapy for Late-Life Generalized Anxiety Disorder: Who Gets Better? *Behav Ther*. 2005: 147–156.

[107] Barrowclough C, King P, Colville J, Russell E, Burns A, Tarrier N. A Randomized Trial of the Effectiveness of Cognitive-Behavioral Therapy and Supportive Counseling for Anxiety Symptoms in Older Adults. *J Consult Clin Psychol*. 2001; 69: 756-762.

[108] Mohlman J, Gorman JM. The Role of Executive Functioning in CBT: A Pilot Study With Anxious Older Adults. *Behaviour Res Therapy*. 2005; 43: 447-465.

[109] Mohlman J. Executive Skills in Older Adults With GAD: Relations With Clinical Variables and CBT Outcome. *J Anxiety Disorder*. 2013; 27: 131-139.

[110] Mohlman J, Price RB, Vietri J. Attentional Bias in Older Adults: Effects of Generalized Anxiety Disorder and Cognitive Behavior Therapy. *J Anxiety Disorder*. 2013; 27: 585-591.

[111] Stanley MA, Wilson N, Shrestha S, Amspoker AB, Armento M, Cummings JP, et al. Calmer Life: A Culturally Tailored Intervention for Anxiety in Underserved Older Adults. *Am J Geriatr Psychiatry*. 2016; 24: 648-658.

[112] Brenes GA, Danhauer SC, Lyles MF, Anderson A, Miller ME. Effects of Telephone-Delivered Cognitive-Behavioral Therapy and Nondirective Supportive Therapy on Sleep, Health-Related Quality of Life, and Disability. *Am J Geriatr Psychiatry*. 2016; 24: 846-854.

[113] Hobbs MJ, Mahoney AEJ, Andrews G. Integrating iCBT for Generalized Anxiety Disorder Into Routine Clinical Care: Treatment Effects Across the Adult Lifespan. *J Anxiety Disorder*. 2017; 51: 47-54.

[114] Wetherell JL, Stoddard JA, White KS, Kornblith S, Nguyen H, Andreescu C, et al. Augmenting Antidepressant Medication With Modular CBT for Geriatric Generalized Anxiety Disorder: A Pilot Study. *Int J Geriatr Psychiatry*. 2011; 26: 869-875.

[115] Wetherell JL, Ayers CR, Sorrell JT, Thorp SR, Nuevo R, Belding W, et al. Modular Psychotherapy for Anxiety in Older Primary Care Patients. *Am J Geriatr Psychiatry*. 2009; 17: 483-492.

[116] Hazlett-Stevens H, Singer J, Chong A. Mindfulness-Based Stress Reduction and Mindfulness-Based Cognitive Therapy With Older Adults: A Qualitative Review of Randomized Controlled Outcome Research. *Clin Gerontol*. 2018.

[117] Lenze EJ, Hickman S, Hershey T, Wendleton L, Ly K, Dixon D, et al. Mindfulness-Based Stress Reduction for Older Adults With Worry Symptoms and Co-Occurring Cognitive Dysfunction. *Int J Geriatr Psychiatry*. 2014; 29: 991-1000.

[118] Wetherell JL, Afari N, Ayers CR, Stoddard JA, Ruberg J, Sorrell JT, et al. Acceptance and Commitment Therapy for Generalized Anxiety Disorder in Older Adults: A Preliminary Report. *Behav Ther*. 2011; 42: 127-134.

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USNW513103 AS/MP 11/19