Depression and the Aging Brain

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Impact of Aging on the Epidemiology of Depression

Depressive disorders among the elderly are a disabling illness that can result in death and need to be properly diagnosed and treated by clinicians. Although the rates of depressive disorders are lower in the elderly than in younger cohorts, prevalence rates are still high and accounts for nearly two percent of all disability in those over 60. Recent data shows that the 12-month prevalence of **major depressive disorder (MDD)** from ages 65-74 is 3.1% and the lifetime prevalence is 11.7%.[1] Similar to depressive disorders in the younger population, females are at higher risk for MDD with a 4.5% 12-month and a 16.9% lifetime prevalence from ages 65-74; whereas, men have a 1.4% 12-month and a 5.1% lifetime prevalence. The prevalence of MDD is highest among non-Hispanic white individuals with a lifetime prevalence of 13.2%, and lowest among African-American elderly, 5.1%.[2]

The lower rates of MDD among the elderly are perplexing to many clinicians. There are several factors to suggest why these rates are lower compared to younger cohorts: 1) older persons may have greater difficulty remembering past symptoms; 2) they may be less psychologically oriented in responding a mental health interview; 3) there may be a cohort effect in younger generations of an increased rate of MDD; and 4) persons who have had MDD may be less likely to live until older age, more likely to be institutionalized, and have more medical comorbidities precluding their participation in epidemiological surveys. Despite these lower rates among the elderly in the community, rates of MDD in primary care settings are high (five percent) and even greater among the nursing home population, 15-25%, and those in acute care hospitals, as high as 12%.[3]

Impact of Aging on the Risk Factors for Depression

Many stressors common to late life serve as important risk factors for developing major depression: physical illness, limited mobility, sensory deprivation from deafness or blindness, retirement, economic deprivation, poor living conditions, social isolation, rejection by children, as well as loss of spouse. A prior history of depression places elderly patients at substantial risk. It has also been hypothesized that the elderly may have specific physiologic changes that place them at particular risk; these include decreased acetylcholine, dopamine, and norepinephrine as well as increased monoamine oxidase. In addition, there are changes in the hypothalamic-pituitary-adrenal axis with increased levels of cortisol.

Other risk factors include commonly prescribed medications such as analgesics, antihypertensives, antibacterials, anti-parkinsonian drugs, cancer treatments, cardiovascular medications, estrogens, progestational agents, hypoglucemic agents, sedatives and steroids. There are many medical conditions that are frequently associated with depression such as stroke, Alzheimer's Disease, Parkinson's disease, cancer as well a chronic pain and many others.

Impact of Aging on the Clinical Presentation of Depression

The majority of elderly individuals who have MDD have suffered from early onset depressive disorder; only a minority have late-onset depression, first episode after the age of 50. Personality abnormalities, positive family history, family dysfunction, and guilt are more likely to be seen in early rather than late-onset depression. Anxiety, apathy, hypochondriasis, apathy, loss of interest, cognitive impairment and psychosis are associated more often with late-onset depression. Structural changes in the brain's subcortical structures, leukoencephalopathy, frequently seen in the elderly with MDD are more severe in late-onset depression and independently predict worsening of quality of life and disability.[4] Due to the association with leukoencephalopathy and cardiovascular risk factors, the vascular depression hypothesis has been proposed to explain the etiology of late-onset depression.[5] The clinical presentation of late-onset depression proposed by the vascular depression hypothesis include: reduced depressive ideation, greater psychomotor disturbance, apathy, executive dysfunction on neuropsychological testing, and neuroimaging abnormalities in the basal ganglia and white matter. Regardless of age of onset, the most important risk factors for developing depression in later age are being female, experiencing lack of satisfaction with life, feelings of loneliness, smoking and bereavement in the last six months of life.

The non-detection of major depression poses significant consequences including higher rates of nursing home placement, increased burden on caretakers, increased visits to physicians, and increased risk of physical disability. Some investigators believe that there may be increased mortality among the elderly who have depression, but this remains controversial. Unfortunately, detection of depression poses a challenge for many; nursing home staff recognize depression in only in 37%-45% of patients, and primary care physicians only diagnose half and treat less than half of those with MDD.

Impact of Aging on the Course of Depression

Clinical characteristics of depression may differ among the elderly and may manifest with more somatic complaints, anxiety, apathy and anhedonia. There may be unexpected functional decline and a resistance to care. Clinical screening scales, such as the Geriatric Depression Scale and PHQ-9, are helpful for clinicians to improve detection of depression among their elderly patients. Screening for suicide is also necessary, as suicide increases with age among men. For women, suicide rates do decrease slightly after age 55. Suicide attempts in the elderly need to be taken extremely seriously, as suicide lethality is exponential with age.[6]

Although, the median time to recovery from a MDD episode is no different among older and younger patients, the elderly are much more likely to experience

recurrence.[7] Unlike younger individuals with MDD, there are no good predictors for recovery or recurrence among the elderly, including medical comorbidity.

Impact of Aging on Treatment of Depression

Treatment of depression in the elderly must take into account pharmokinetic and pharmacodynamic changes in late life. Pharmacokinetic changes include decreased absorption, increased volume of distribution, decreased metabolism, and decreased excretion. Patients in later life may have age-related changes in drug sensitivity. Elderly patients may have pharmacodynamic changes that make them more vulnerable to anticholinergic and noradrenergic side effects of medication, due to age-related receptor sensitivity and age-related changes in cholinergic and monoaminergic neurotransmission.[8] Dosing, therefore, should start low doses and titrated slowly. If administration is a challenge, many antidepressants come in liquid form or have soluble tablets. Despite these concerns, clinicians should be attentive not to undertreat these patients and fail to provide adequate trials at therapeutic dosages.

Acute treatment of depression in the elderly frequently begins with a trial of a **selective serotonin reuptake inhibitor (SSRI)** for four to twelve weeks with the goal of remission. SSRIs are generally well tolerated in the elderly and have limited drug-drug interactions and less likely to be discontinued. A good trail is one that has achieved a therapeutic dose in at least eight weeks and about 60-70% of patients will respond. Once there is resolution of depressive symptoms, maintenance treatment should be continued for at least four to six months in order to consolidate remission and recovery. Compared to placebo, continued treatment with antidepressants is more efficacious in preventing relapses and recurrences.[9] In absence of maintenance treatment, 30-90% who achieved recovery will experience recurrence in eight to 48 months.

Unfortunately failure of response to SSRIs may be as high as 77%. Therefore, augmentation of the SSRI with buproprion, lithium or nortryptiline could be considered. For lithium, drug levels and renal function should be closely monitored. In addition, augmentation using other antidepressants, such as mirtazapine and venlafaxine, may be effective. There are several atypical antipsychotics that are FDA approved as augmentation strategies. The data on treatment of non-remission of depressive symptoms is limited and results are not optimal; this will hopefully be an area of greater clinical investigation in the future.

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First line treatment for concomitant psychotic symptoms is with antipsychotic medications with careful monitoring of extrapyramidal syndromes and tardive dyskinesia. Avoiding anticholingeric agents, monitoring QT interval, and the need to assess for Parkinson's symptoms, as well as for metabolic syndrome, should be considered in selecting an agent.

Electroconvulsive therapy (ECT) remains an effective treatment of for MDD in the older population, and a consideration among those with pharmacological treatment resistant disorders, concomitant psychotic symptoms, high suicide risk, and rapidly physically declining due to neurovegetative symptoms. There are few absolute medical contraindications to ECT. In addition, non-pharmacological interventions with emphasis on increased socialization, activity and exercise as well as psychotherapy have proven to be effective treatments for milder cases of depression in the elderly population.

Aging does affect the epidemiology, risk factors, clinical presentation, course, and treatment of depression in the elderly. Depression, however, remains the most treatable psychiatric disorder of late life.[10]

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