Section Contents

Introduction

This section presents 5 articles focused on 3 main diagnostic dilemmas, or "3 *D*s," of Geriatric Psychiatry: depression, delirium, and dementia. The boundaries between depression, delirium, and dementia are often blurred in acute medical and, especially, long-term care settings due to frequently comorbid mood, cognitive, and physical disorders of aging. With the population of adults over the age of 65 years increasing to 22% of the general population by 2040, these 3 disorders will become a challenge for many practicing health care providers. This demographic trend has led to increased scrutiny of effective strategies to predict, prevent, and treat mental, cognitive, and physical disorders of aging. It is becoming more obvious that multiple diseases of aging share common risk factors and may benefit from shared preventive strategies. One avenue of optimizing and personalizing health care is by way of genetic sequencing, which has become more affordable. Relating genetic diatheses to environmental and behavioral stressors on the development of life-limiting syndromes would offer effective individualized medicine. Another way to individualized drug therapeutics is by studying individual pharmacokinetic and pharmacodynamic action of commonly used drugs against target symptoms and adverse effects. Therefore, each article in this section represents a substantial contribution to the field of geriatric psychiatry shedding light on the nuances of diagnosis, management, and outcomes.

The first article, by Drs Scott and Paulson, considers the independent effects of *APOE* on cerebrovascular burden and depressive symptomatology in 3,203 participants from the Wisconsin Longitudinal Study, who were followed for 18 years (1993–2011). Prior research has suggested a dose-dependent effect of *APOE* isoforms on amyloid β peptide clearance, aggregation, and deposition. Among the isoforms, the presence of *APOE*4* puts individuals at significantly higher risk for developing Alzheimer's disease (AD) (ε2/ε4, odds ratio [OR] = 2.6; ε3/ε4, OR = 3.2; ε4/ε4, OR = 14.9).[1] By contrast, ε2 has been shown to reduce risk of developing AD (OR = 0.6). Other vascular and neurodegenerative disorders of aging have shown occasional links to *APOE* isoforms as well supporting the idea of common pathways shared by neurodegenerative disorders of aging. The authors of this article relate the *APOE*-conferred risk to the clinical features of vascular depression. Results suggest that *APOE* is implicated in late-life depression, particularly as adults age into their 70s. Cerebrovascular burden, which is known as a risk factor for geriatric depression, also predicted later-life depressive symptomatology. However, *APOE did not* moderate vascular depression effect, thus linking *APOE* and depressive symptomatology in a way that is independent of cerebrovascular risk.

The second article, by Steiner and colleagues, examined quality of life, functioning, and depression severity in older adults after SSRI treatment using a retrospective secondary analysis of data from the National Institute of Mental Health–funded Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (July 2001–September 2006). They analyzed data for 2,280 nonpsychotic adults (106 older adults aged ≥ 65 years and 2,174 adults < 65) with *DSM-IV-TR*–defined MDD who received citalopram monotherapy. Findings suggested that older adults and younger adults have comparable treatment responses to citalopram monotherapy, with significant improvements in patient-reported depressive symptom severity, functioning, and quality of life. Both older adults and adults < 65 experienced significant improvements and medium to large treatment responses across quality of life, functioning, and depressive symptom severity ($P < .001$). Older adults had smaller treatment effect sizes for all outcomes due to lower severity of depression at baseline. Remitters at exit had significantly better responses to treatment than nonremitters for the majority of outcomes. This study utilizes a relatively large sample and supports the existing literature suggesting that older adults have similar treatment response rates to younger adults.

Given highly comorbid mood and cognitive disorders and the lack of treatments addressing both, the next article, by Wetherell and colleagues, offers the results

of a randomized controlled trial of mindfulness-based stress reduction (MBSR) in 103 older adults diagnosed with depression or anxiety. The authors examined changes in cognitive performance and in mood and anxiety symptoms. The mindfulness group experienced greater improvement on a memory composite score ($P = .046$). Groups did not differ on change in cognitive control. Mindfulness participants also improved more on measures of worry and depression after the acute treatment phase and in the severity of worry, depression, and anxiety at follow-up, and they were more likely to be rated as much or very much improved as rated by the Clinical Global Impressions-Improvement scale. Cortisol level decreased to a greater extent in the mindfulness group only among those participants with high baseline cortisol. The authors concluded that mindfulness-based intervention can improve clinical outcomes such as excessive worry and depression, as well as some forms of immediate memory performance.

The fourth article, by Kim and colleagues, examines perceived stigma and quality of life in a prospective cohort investigation of 128 patients who had recovered from delirium. The subjects were medically ill patients (mostly with cancer) who were referred to the consultation-liaison psychiatric service of a South Korean university-based hospital. Delirium is a common mental illness associated with significant adverse physical and psychological outcomes and partial recovery upon hospital discharge. Patients recovering from delirium might have experienced psychiatric symptoms for the first time and might be vulnerable to continued feelings of shame, depression, hallucinations and delusions, and stigma of psychiatric illness upon discharge. This study found that patients who experienced an episode of delirium reported varying degrees of perceived stigma. Patients' ability to recall their delirium experiences and prior history of depression were associated with a higher stigma and a poorer quality of life. While rarely given sufficient attention, the experience of stigma related to psychiatric illness could be an important symptom after recovery from delirium in older patients, especially in those with a prior history of depression, and require separate postrecovery counseling and management.

The final article, from Reeves and colleagues, explores the use of pharmacokinetic (concentration) and pharmacodynamic (prolactin, $D_{2/3}$ occupancy) data on contributions to symptom reduction and extrapyramidal side effects (EPS) to inform AD-specific dose adjustments. Population pharmacokinetic-pharmacodynamic models were developed by combining pharmacokinetic data from a phase 1 study in 20 healthy older adults, with pharmacokinetic prolactin, [18F]fallypride $D_{2/3}$ receptor imaging, and clinical outcome data from 28 older patients with AD who were prescribed open-label amisulpride (25–75 mg/d) to treat psychosis. Symptom reduction in delusions was associated with amisulpride concentration and $D_{2/3}$ occupancy in the caudate, putamen, and thalamus. Model predictions suggested that across concentrations of 40–100 ng/mL, and occupancies of 40%–70% in caudate and thalamus and 30%–60% in the putamen, there was a 50%–90% probability of response and < 30% probability of extrapyramidal side effects (EPS). Simulations of the data showed that amisulpride 50 mg/d was the appropriate dose to achieve this target range in those aged > 75 years: increasing the dose to 75 mg/d increased the risk of EPS, particularly in those aged > 85 years of low body weight. The authors' findings support clinical consideration of age- and weight-based dose adjustments in older patients with AD-related psychosis, and they indicate that 50 mg/d amisulpride may be the minimal clinically effective dose as well as the maximally tolerated dose in those aged > 75 years.

We hope that our readers will find the information provided in this issue of the *Journal* clinically relevant and helpful in considering treatment options in older adults.

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REFERENCE

1. Farrer LA, Cupples LA, Haines JL, et al; APOE and Alzheimer Disease Meta Analysis Consortium. Effects of age, sex, and ethnicity on the association between apolipoprotein E genotype and Alzheimer disease. A meta-analysis. *JAMA*. 1997;278(16):1349–1356.