Medical Co-Morbidity, Brain Disease, and The Future of Geriatric Psychiatry

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The co-occurrence of psychiatric and medical illness and the complex bi-directional relationship of disorders of the aging brain and body is the rule, rather than the exception, in geriatric psychiatry. Psychiatric illnesses ranging from affective disorders to anxiety and cognitive disorders are common in the geriatric population, and often co-occur with medical illness, which is likewise prevalent in this population. Medical illness may hasten the initial presentation of psychiatric illness, affect its course, and influence response to treatment and prognosis, and psychiatric illness and its treatment may predict greater severity and poorer outcome of medical illness. Adding to this complexity, the symptoms of psychiatric and medical illness frequently overlap in the geriatric population, and are influenced by medication burden and side effects, as well as age-related biological and environmental factors, all of which necessitate the need for increasing diagnostic vigilance and collaboration with medical providers in the care of geriatric patients. This special edition of the Journal addresses the complex relationship between psychiatric and medical illness in the elderly. In this editorial we highlight examples of medical and psychiatric syndromes that are co-occurring, interrelated, and mechanistically linked, thereby providing a mounting argument for a changing standard of research and clinical practice in geriatric psychiatry.

GERIATRIC BIPOLAR DISORDER: AN EXAMPLE OF THE ROLE OF MEDICAL CO-MORBIDITY IN PSYCHIATRIC ILLNESS

Contrary to widely held clinical lore, bipolar disorder does not "burn out" with advancing age, and it represents a substantial proportion of older adults with mood disorders treated in inpatient (5%–10%) settings.[1] Furthermore, older patients with bipolar disorder use more outpatient mental health services, including day hospital and case management, than older adults with unipolar depression.[2] Treatments for bipolar disorder in later life, however, remain understudied despite persisting functional impairment and increasing recognition of the medical complexity and risk for cognitive impairment with advancing age. Two articles in this issue of the Journal highlight medical co-morbidity in older adults with bipolar disorder and the impact of lithium on renal function.

The findings by Dols et al.[3] add to the literature on medical co-morbidity in bipolar disorder with advancing age. This cross-sectional descriptive study includes demographic and clinical data on 101 older individuals with bipolar disorder (mean age, 68.9 years; 53% female). Although the prevalence rates of psychiatric co-morbidities such as anxiety disorders (10%) were low, lifetime alcohol dependence and abuse (38.7% in total) were substantial and study subjects had on average 1.7 medical co-morbid conditions (including hypertension [27.8%] and metabolic syndrome [28.7%]). Previous studies have also reported considerable rates of medical co-morbidity in geriatric bipolar disorder including comparable levels of cardiovascular disorders and greater burden of endocrine dysfunction, metabolic syndrome, and obesity than older adults with depression.[4] Furthermore, the Dols et al. study points out high rates of polypharmacy, with 31.7% of patients in this sample treated with more than one psychotropic medication.

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Polypharmacy not only increases the risk of drug–drug interactions and adverse effects, but the specific medications used to treat the various phases of bipolar illness are associated with medical consequences including renal (lithium) and liver toxicity (anticonvulsants) and metabolic syndrome (atypical antipsychotics).

The study by Rej and colleagues[5] provides an important contribution to our understanding of the consequences of lithium, and, in particular, the vexing dilemma of the risk of renal disease in older lithium users with bipolar disorder who continue to have significant recurrences of bipolar depression, mania, and mixed states with advancing age. Lithium use has been declining in older adult cohorts despite its low cost and superior efficacy in preventing mood episode relapse and suicide and reducing use of psychiatric services.[5] Clinicians often cite concern for cognitive side effects or risk of renal toxicity as primary reasons for avoiding or discontinuing lithium treatment in older adults. The population-based cross-sectional study by Rej et al. examined prevalence rates and clinical correlates of renal disease among 2,480 lithium users 70 years and older from an administrative health database in Ontario, Canada. The 6-year prevalence rates of chronic kidney disease (CKD), acute kidney injury (AKI), and nephrogenic diabetes insipidus (NDI) were 13.9%, 1.3%, and 3.0%, respectively. Furthermore, the clinical correlates independently associated with chronic kidney disease included hypertension (odds ratio [OR], 2.05), diabetes mellitus (OR, 1.86), ischemic heart disease (OR, 1.65), NDI (OR, 2.54), AKI (OR, 11.7), lithium duration greater than 2 years (OR, 1.71), loop diuretic (OR, 1.74), hydrochlorothiazide (OR, 1.48) and atypical antipsychotic use (OR, 1.49). The authors note that the definition of CKD had high specificity but low sensitivity, thereby likely underestimating the true prevalence of CKD in lithium users by a factor of nearly three. Regardless, the risk of CKD in lithium users over the age of 70 years is considerable and escalates in those individuals with a history of hypertension, diabetes, and/or ischemic heart disease particularly if the duration of lithium use exceeds 2 years.

Rej and colleagues provide guidelines for monitoring serum lithium level and renal function (estimated glomerular filtration rate [eGFR]) every 3–6 months and encouraging referral to nephrology based upon absolute eGFR measurements or yearly rates of eGFR decline. Tapering an individual off lithium after years of successful use can be associated with high risk of mood episode relapse and should be exercised with caution. Careful monitoring and treatment of medical co-morbidity in close collaboration with primary care, and specialty nephrology consultation when indicated, may reduce the risk of chronic kidney disease in geriatric lithium users.

FRAILTY AND DEPRESSION IN THE GERIATRIC POPULATION: OVERLAP OF PHYSICAL AND PSYCHIATRIC SYNDROMES

Physical and psychiatric syndromes can interact in a synergistic fashion, as is the case with depression and frailty—a complex syndrome of fatigue, weakness, weight loss, slowed gait, and reduced physical activity. Although frailty may be less well recognized than depression by geriatric psychiatrists, similar to depression it is highly prevalent (up to 18% of community dwelling elders over the age of 80 years of age)[6] and associated with increased morbidity, mortality, and disability. Further, depression and frailty may each influence the severity and expression of the other. To explore this relationship, Brown et al. measured the prevalence of frailty and the interaction between individual frailty characteristics and depression on mortality risk in 1,027 older adults (age 75) from the Nordic Research on Ageing Study (NORA). The authors found all frailty characteristics (gait speed, physical activity, grip strength, fatigue) enriched in depressed versus nondepressed older adults. Similar to other recent findings of sex differences, frailty characteristics, particularly gait speed, were associated with faster progression to death in elderly depressed women, but not in depressed men (hazard ratio [HR], 1.84; 95% confidence interval [CI], 1.05–3.21).[6,7] These accumulating data support the interrelatedness of the two syndromes and raise key questions: do depression and frailty co-occur; is one a prodrome or risk factor for the other; and are there common underlying mechanism(s), including sarcopenia, hyperglycemia, and changes in sex and growth hormone levels, that give rise to each? An integrated clinical and research approach to the