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New research perspectives in the treatment of bipolar disorder in older adults

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In Cade's pioneering work on using lithium for the treatment of manic-depressive illness, 30% of patients were elderly (1). Unfortunately, this inclusiveness has not continued, and the extensive subsequent literature on the treatment of bipolar disorder lacks systematic studies of elderly patients (2). But in fact, elderly patients with mania constitute 5–20% of all patients in need of acute treatment for affective disorders, and the prevalence of bipolar disorder among individuals aged 65 years and older is estimated at 0.10–0.40% (3). Further, the elderly appear to have a distinct pattern of mental health service utilization, in that they are higher users of case management programs (4) and need more prolonged inpatient psychiatric services (5) than younger patients. Bipolar disorder was also a predictor of rehospitalization among elders treated in a geropsychiatric program (6). The limited research focused on geriatric bipolar patients has meant that there are no guidelines for their treatment that are based on controlled medication treatment studies. Prescription patterns for the treatment of bipolar disorders in the elderly have changed without clear evidence concerning tolerability and efficacy differences (7).

It has been usual practice in the pharmacotherapy of bipolar elders to be guided by evidence derived from data on younger patients. However, this extrapolation may not be valid because of age-related pharmacodynamic and pharmacokinetic factors, and psychosocial constraints that may affect management in the elderly (2). Late-onset bipolar disorder in elders is often associated with medical and neurological conditions (8, 9), and these may diminish tolerability and efficacy (10). Elders may also have different drug concentration/dose ratios compared to younger patients (2).

Bipolar disorder can be associated with neuronal and glial cell loss (11). The possibility of enhancing neuronal regeneration with treatments is supported by findings that lithium may increase neuronal cell growth in the adult brain (12). In fact, lithium may also be helpful in the prevention of dementia in bipolar patients (13). Considering that bipolar disorder in the elderly is associated with structural and cognitive abnormalities, understanding the

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biochemistry of neuronal damage and regeneration has particular relevance to their treatment.

We present here four clinical research papers related to aspects of bipolar disorder in older adults. These reports reflect salient research trends and provide new findings in the context of the current literature.

In the first paper, **Sajatovic et al.** (14) have performed a *post hoc* analysis of combined data of two industry-sponsored studies in which the efficacy and tolerability of quetiapine in the treatment of mania was assessed in mixed-aged patients. They focused on the results obtained in patients aged 55 years or older. Quetiapine was effective and rather well tolerated in the older patient cohort. Among known adverse reactions, somnolence and postural hypotension occurred more frequently in the older age group than in the younger cohort. Atypical antipsychotic medications are frequently used in the elderly (15), and this study offers further support for careful use of these medications in older adult and elderly bipolar patients.

One of the difficulties in the treatment of the elderly is effective service delivery (16). Additionally, functional impairments (17) can present a barrier. The elderly may have difficulties in accessing treatment facilities and obtaining appropriate social support (18). These problems may be compounded by effects of medical comorbidities (18, 19).

Kilbourne et al. (20) present findings concerning the development, implementation, and initial results of a new service delivery model targeted at the needs of medically ill bipolar elders. The model emphasizes increased efficiency in delivering treatment resulting from clinician-assisted self-management and increased evidence-based interventions. The model was well received by the patients, who were found to be highly compliant.

Cognitive impairments may be associated with poor function (21) and may limit the benefits of treatment. **Depp et al.** (22) found cognitive impairment in middle-aged and elderly patients with bipolar disorder compared to healthy control subjects. Using the strategy of longitudinal assessment, they found that patients with bipolar disorder had more variability in their cognitive functioning than either healthy controls or patients with schizophrenia. Since the observation period was only 1–3 years and intensity of mania was not specifically measured, the authors encourage more specific investigations over a longer period of time.

The paper of **Forester et al.** (23) illustrates the strategy of examining mechanisms of treatment effects of lithium using neuroimaging. They found an association between brain lithium level and *N*-acetyl-aspartate (NAA) and *myo*-inositol levels in a small group of patients with bipolar I disorder aged 56–85 years. Consistent with other studies on younger adults, lithium increased NAA levels, suggesting that it may have caused neuronal regeneration. The elevated *myo*-inositol level is surprising, and may reflect increase in activity of the inositol-monophosphatase. These early findings signal the utility of *in vivo* biochemistry in elders with bipolar disorder.

This collection of important papers points to the need for further research in bipolar elders. This need was recognized in a report by the National Institute of Mental Health (NIMH) and the Depression and Bipolar Support Alliance (19) and in recent NIMH funding, including a

double-blind clinical trial for treatment of mania in older adults (24). We thank *Bipolar Disorders* for helping to bring attention to the needs and research opportunities in this underserved patient population.

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