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CLINICAL CONUNDRUM

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Is ECT a viable option to treat depression in older adults with bipolar disorder who are vulnerable to cognitive side effects?

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1 | BACKGROUND

First used over 80 years ago, electroconvulsive therapy (ECT) is the oldest of the currently used biological treatments in psychiatry. ECT is indicated for severe depression, mania, treatment-resistant schizophrenia psychosis, catatonia, and comorbid depression in dementia. ECT delivers a unilateral or bilateral electrical stimulus to the brain of an anesthetized patient to induce a generalized seizure. Response and remission rates of ECT in depression are high (73%–90% and 67%–73%, respectively).[1] In bipolar disorder (BD) the effectiveness of ECT has been shown for manic, depressive, and mixed episodes. For treatment-resistant bipolar depression, ECT is the treatment option with the most supporting evidence.[2] Nevertheless, in most guidelines for BD, ECT is advised only as a last-resort option and in life-threatening cases. This is possibly due to the stigma of ECT and concern for complications such as a switch to mania and neurocognitive side effects.

To date, data on safety and efficacy of ECT in older age bipolar disorder (OABD) are lacking, given that prior research has focused on mixed-age cohorts. OABD is a specific group with special needs due to somatic and psychiatric comorbidity, cognitive vulnerability, as well as age-related brain changes, life issues, and psychosocial functioning. The presence of somatic comorbidity limits pharmacotherapeutic options due to drug interactions and altered drug metabolism.[3] Therefore, ECT may become a viable option for OABD earlier than in adult BD.

In current guidelines ECT is mostly advised as second- or third-line therapy for adults with BD, but these are not further specified for OABD, given the lack of evidence from large clinical trials of OABD patients treated with ECT. Expert consensus suggests, however, that ECT is a safe and effective treatment in OABD.[3]

As an example of ECT effectiveness in OABD despite risk factors for neurocognitive side effects, we present in the current case report a patient with vascular hyperintensities in the brain and a previous history of ECT-related cognitive impairment, who recovered with ECT.

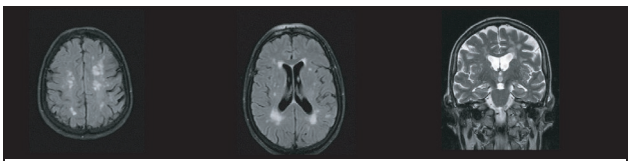
2 | CASE

A 72-year-old woman had been treated for bipolar II disorder at our outpatient clinic since 2010. The age of onset of her first mood symptoms was 19 years old, when she had depressive symptoms. In 1975, 6 months after her first child was born, she had a depression with a suicide attempt. She jumped from a balcony, which led to a fracture of her first lumbar vertebra and irreversible cauda

equina syndrome (CES) for which she has a sacral neurostimulator. In 2010, financial stressors precipitated a depressive episode which was treated with nortriptyline 70 mg daily. Then she had an episode of hypomania, which was treated adding lithium 600 mg daily. In retrospect, between her suicide attempt and 2010 she had several episodes of hypomania, especially in the summer. The diagnosis of recurrent depressive mood disorder was changed to bipolar II disorder. From 2010 till 2014 she was euthymic and treated with lithium 600 mg daily with therapeutic serum levels around 0.60 mmol/L. In 2014, she had an episode of hypomania. Overall, depressive episodes predominated the clinical picture. Other than the CES, her medical history showed hypothyroidism for which she used levothyroxine 88 micrograms daily. Her family history was notable for depressive disorder (mother), bipolar disorder (son), and Alzheimer's dementia (grandfather).

In 2017, despite the use of 800 mg of lithium daily, with serum levels of 0.82 mmol/L, she had a severe depressive episode with reduced sleep, inner tension, reduced appetite and psychotic symptoms. Because of the urgency of the situation, due to severity of the depression and suicidal thoughts, she was admitted and referred for ECT. She received four right unilateral treatments resulting in complete remission of her depression, reported subjectively as well as objectively with an improvement of the Montgomery–Åsberg Depression Rating Scale (MADRS) score from 40/60 to 0/60 in 2 weeks. In 2018, 11 months after her previous ECT course and in spite of the daily use of 800 mg lithium and nortriptyline 75 mg, she was admitted to a psychiatric hospital for a severe depressive episode with psychotic symptoms. Her MADRS score was 37, and neurocognitive symptoms were prominent with a Montreal Cognitive Assessment (MoCA) score of 16/30 (compared to a MoCA of 27/30 the year before) and autobiographical memory loss. The patient and her partner reported that these symptoms of autobiographical memory loss started in 2017, after the first course of ECT, and were static. Magnetic resonance imaging (MRI) of the brain was performed as part of the work-up of her neurocognitive deficits and showed white matter hyperintensities (Fazekas grade 2 of 3) and hippocampal atrophy (medial temporal atrophy grade 2 of 4) (Figure 1).

Again, she was referred for ECT. Due to the severity of her depressive episode she received 30 bitemporal treatments. She experienced many cognitive side effects mainly postictal confusion and a persistence of autobiographical memory loss. She achieved complete remission with a MADRS score of 0.



1.A. Deep white matter hyperintensities (WMHs), transverse T2 fluid-attenuated inversion recovery (FLAIR) image

1.B. Periventricular and deep WMHs, Fazekas grade 2, tranverse T2 FLAIR image

1.C. Medial temporal atrophy grade 2, coronal T2 image

FIGURE 1 MRI images

Key message

Extrapolating results from older patients with depression and younger adults with BD suggests that ECT is a safe and effective treatment in OABD. Further research is a necessary step to include recommendations on ECT in OABD clinical guidelines.

Learning points

- In OABD, somatic comorbidities may limit pharmacotherapeutic options, leading to ECT as the next step in the treatment algorithm earlier than in younger adults.
- White matter hyperintensities have been shown to be associated with cognitive side effects during ECT, but these effects are often transient, do not affect efficacy, and therefore should not be a reason to withdraw a patient from ECT.
- ECT is a good option for OABD even in those vulnerable to cognitive side effects.

Three months after her treatment course a full neuropsychological examination, consisting of neurocognitive tests covering all cognitive domains, was performed to examine her neurocognitive complaints. The outcome was compared to previous scores from 2013. The examination showed no neurocognitive deficits. Except of an increase in the number of errors she made on a test for prolonged planning, cognitive domains including attention, concentration, fluency, recall, memory, and executive function were within age and education adjusted norms and did not represent a decline from her premorbid function, despite the persistence of her autobiographical memory complaints. Because of the abnormal MRI in combination with the persistent cognitive complaints, the patient was referred to a neurologist, who concluded that there were no signs of cognitive decline or dementia.

In sum, our patient was referred for ECT twice in a short period of time and fully recovered both times, despite hippocampal atrophy and the presence of white matter hyperintensities on MRI. The cognitive side effects that appeared during the second course were severe, but transient, as measured by repeated full neuropsychological examinations. However, the patient reports persistent autobiographical memory problems, albeit improved compared to 2017.

Importantly, autobiographical memory was not objectively measured in her neurocognitive assessment. Ultimately, the patient thought that the tradeoff of better mood with worsened autobiographical memory was favorable, and that she would consider future ECT if necessary.

For the past 2 years since her last ECT course, the patient is euthymic with maintenance medication of nortriptyline 50 mg daily

(with a serum level of 0.02 mg/L) and lithium 600 mg daily (with a serum level of 0.82 mmol/L).

3 | DISCUSSION

The majority of BD treatment guidelines published in the last decade do not provide specific recommendations on OABD, reflecting the scarcity of original research specifically focused on older patients (60+). Extrapolating from results of ECT in adults with BD and older adults with unipolar depressive disorder (OAUD), a favorable effect of ECT in OABD can be expected. Indications for treatment with ECT in OABD are cases of treatment resistance, previous ECT response, or urgent safety concerns (severe suicidality, physical exhaustion or refusal of all foods and fluids).[3]

Older patients may experience more pronounced cognitive side effects during an ECT course, although research on this topic is sparse. The evidence available suggests that most ECT patients experience some degree of transient post ECT confusion after an individual ECT session. Furthermore, bitemporal ECT treatment is associated with a higher risk to develop transient cognitive impairment directly after ECT compared to right unilateral ECT. Moreover, older patients may be more vulnerable to cognitive problems because older age itself or age-related comorbidities such as hypertension, cerebrovascular disease, dementia, and Parkinson disease may lead to cognitive frailty.

Furthermore, patients with BD are more likely to have white matter hyperintensities than healthy controls. White matter hyperintensities, particularly deep white matter hyperintensities, seem to correlate with illness severity and poorer outcomes including poorer cognitive performance.[4] Interestingly, although older adults with white matter hyperintensities who receive bilateral ECT are at increased risk of transient cognitive impairment, this cognitive impairment improves with continuation of ECT and clinical recovery of the patient as in our patient presented here.[5]

Our case shows that OABD can be treated safely and effectively with ECT, even in patients with some brain atrophy and vascular hyperintensities or a history of ECT-related cognitive impairment. Although often reassuring and inspiring, case reports are inadequate as an evidence base to guide treatment decisions. Research on predictors of efficacy and safety is warranted to formulate clinical guidelines on ECT in OABD.

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