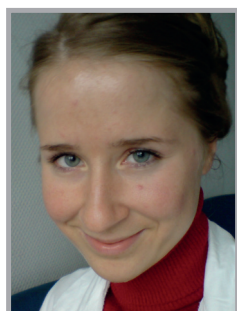


# Should electroconvulsive therapy be more routinely used in the treatment of depression in elderly patients with cognitive disturbances?



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The Central Institute of Mental Health is a reference center for electroconvulsive therapy (ECT) and we have extensive experience in the application of the procedure to geriatric patients with severe or drug treatment-resistant affective disorders and/or pre-existing cognitive impairment. This article will give a short update of current knowledge about the use of ECT in geriatric psychiatric patients and in particular in depressed patients with pre-existing cognitive disturbances. The practical intention is to deliver systematic information on the indications for ECT in clinical practice, with particular emphasis on its application in depressive patients with pre-existing cognitive impairment.

### Depression in late life & in the course of dementia

Depression in the elderly is a serious illness and may lead to impaired physical function, increased mortality and unwarranted

use of healthcare resources. In particular in patients over 65 years of age, it remains underdiagnosed and undertreated. The prevalence is fairly high and varies depending on the population, affecting up to 9% of the community-dwelling elderly, but 25% of the institutionalized and recently hospitalized elderly [1,2]. Patients with late-onset depression (first episode after 65 years of age) are less likely to have a family history of depression and frequently have significant medical comorbidities, especially cardiovascular diseases [3]. Three important conditions complicate antidepressant drug treatment in this population: polypharmacy, side effects and drug resistance. The elderly are at higher risk of suffering from clinically relevant drug–drug interactions under treatment with antidepressants and treatment of medical comorbidities, and, in addition, they are more sensitive to side effects of tricyclic antidepressants (e.g., anticholinergic

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“Elderly patients may be more vulnerable to cognitive side effects of ECT because of pre-existing neurodegenerative disorders.”

delirium) [4]. Less than half of older adults with depression achieve remission with antidepressant medications, and rates of remission are even poorer for those with comorbid conditions.

Patients with late-onset depression often present with cognitive complaints or cognitive deficits. These cognitive changes may occur as a consequence of depression or may indicate a coexisting condition such as Alzheimer’s dementia (AD) or Parkinson’s disease. Establishing whether depression is the primary cause of cognitive change or whether a concomitant dementing illness exists is important in the management of the disease. In addition to depression with coexisting AD, the term ‘vascular depression’ has emerged from imaging findings of white matter hyperintensities indicating cerebrovascular disease associated with late-onset depression and greater neuropsychological impairment on testing [5,6]. It is hypothesized that cerebrovascular ischemia disrupts brain circuitry and results in depression as well as neuropsychological impairment.

In the course of AD, noncognitive symptoms (e.g., depressed mood, apathy or social withdrawal) may be among the first clinical symptoms even before major cognitive and functional impairment emerge [7]. In addition, depression is a significant behavioural aspect of the symptomatology of AD that affects the cognitive and functional status of patients with AD [8]. Recently, new research criteria for the diagnosis of AD were defined and the established National Institute of Neurological and Communicative Disorders and Stroke (NINCDS)–Alzheimer’s Disease and Related Disorders Association (ADRDA) criteria were revised [9]. By these criteria, the diagnosis of AD is no longer a diagnosis of exclusion. Both clinical evidence of episodic memory impairment and *in vivo* biological evidence of Alzheimer’s pathology demonstrated by a set of biomarkers is now needed for diagnosing AD, even in the earliest stages of clinical manifestation [10]. Even in the case of very early clinical manifestation (i.e., for patients who do not yet fulfil the criteria of dementia but only show isolated episodic memory impairment), the term ‘prodromal AD’ has been coined as a diagnostic classification [11]. This allows for attributing the clinical phenotype of depression more often to a diagnosis of AD than by using the earlier NINCDS–ADRDA criteria of AD.

Despite this, disentangling late-onset depression from early dementia can be especially challenging. Whether cognitive changes in the

setting of late-onset depression signal a coexisting illness or are simply an effect of the depression is complex. Although pseudodementia can be caused by late-onset depression, it is relatively uncommon and depression commonly coexists with dementing illnesses, including 40% of Parkinson’s disease, 20–30% of AD and 30–60% of stroke patients [12].

### Indications for electroconvulsive therapy in depressed elderly patients

Electroconvulsive therapy is a highly effective treatment for severe major depression, [13] and it is also frequently used in the elderly [14,15]. The procedure is carried out under general anesthesia for muscle relaxation and induces a generalized seizure by the application of a brief electric pulse by electrodes positioned to the skull. Because of the invasive nature of this treatment and some misperceptions regarding the mechanisms of action, the use of ECT is controversial and it is held in reserve for severe depression accompanied by psychotic features, treatment resistance and/or self-harm. Potential side effects of ECT mainly consist of transiently impaired cognitive functioning [16,17].

Electroconvulsive therapy can be used as first-line treatment in delusional depression/depression with psychotic symptoms. In cases of drug therapy-resistant affective disorder, it is also indicated as second-line treatment. Moreover, studies reveal that ECT may be more efficacious in elderly compared with younger patients [18] and may also be more efficacious than drug treatment in the elderly population [17].

### Cognitive side effects of ECT

Under ECT, cognitive side effects occur. Studies in younger patients have described confusional states and impairments in concentration, sustained attention, orientation, retrograde memory and short-term anterograde memory impairment and reproduction of autobiographical information immediately after ECT. However, neuropsychological functioning is differentially affected [19–22]. Elderly patients may be more vulnerable to cognitive side effects of ECT because of pre-existing neurodegenerative disorders. To date, research on ECT effects in the elderly is very limited, in particular regarding the frequency and nature of cognitive side effects. More research in this field is urgently needed [23–25]. Methodological concerns that impairments of attention and concentration due to depression

may interfere with neuropsychological memory testing limit the number of investigations on cognitive assessment under ECT. However, the feasibility of pre-ECT cognitive assessment (e.g., Iowa assessment model) and the good adherence to cognitive assessment over a series of ECT has been shown, even in severely depressed populations with psychotic symptoms [26]. For the practice of monitoring ECT effects, the regular administration of brief, focused cognitive tests before, during and after treatment is recommended during the course of ECT [24]. By direct feedback of the neuropsychological results to the individual patient, worries about memory impairments induced by ECT may be relieved [26]. This may also be practised in an elderly population with patients suffering from cognitive impairments before undergoing ECT [14]. When assessing the efficacy of ECT, outcomes valued by patients should be taken into account in order to target the patient's subjective perceptions on effectiveness and treatment satisfaction [27]. Both the procedure of ECT itself and the resulting beneficial effects on depressive core features affect cognitive performance. It has been shown that alleviation of depression is associated with improvement of memory, information processing and executive function in elderly subjects. Thus, several findings provide evidence that ECT may improve cognitive functioning in nondemented elderly undergoing ECT. This has strong clinical relevance concerning the use of index ECT [28].

### **ECT in elderly subjects with pre-existing cognitive impairment**

We have published the first clinical study that examines the use of ECT in elderly patients with depression and pre-existing cognitive deficits (both dementia and mild cognitive impairment). The results of our investigation confirm that ECT is an effective treatment in geriatric depressed patients. In our group of subjects with treatment-resistant depression, depressive symptoms remitted partially or completely in the whole patient sample. Furthermore, ECT did not induce long-term cognitive deficits in any subgroup (patients with or without pre-existing cognitive impairment). ECT was safe and well tolerated irrespective of pre-existing cognitive impairment. Although obtained in an uncontrolled case series, our findings have implications for clinical practice. ECT should not be withheld from or just applied as a last resort treatment in elderly subjects with pre-existing cognitive impairment.

As an interesting additional clinical observation, in five cases we found that there might be a protective effect of acetylcholinesterase inhibitors (ACHE-I) against transient cognitive side effects of ECT [14]. The hypothesis that ACHE-I treatment may protect against cognitive side effects of ECT was also substantiated in a pilot study that applied galantamine to subjects receiving a course of ECT [29]. To give more detail, the impairment in learning new material (delayed recall memory and abstract reasoning) was reduced, and galantamine was well tolerated and safe. In addition, galantamine also appeared to enhance the antidepressant action of ECT. None of the subjects had to discontinue galantamine during the study and no adverse drug reactions were observed. Our group has made a similar observation in a case report [30]. The patient described here remitted completely without any significant deterioration of memory and cognitive abilities while no cholinergic side effects occurred and the ECT treatment was safe and well tolerated. These limited clinical observations warrant further controlled studies in this field. As a practical consequence of these observations, continuation of ACHE-I treatment during ECT is supported, when given for the indication of mild-to-moderate AD. Of course, careful clinical monitoring for known ACHE-I complications (e.g., bronchospasm and/or bradycardia) should be pursued. This is in contrast to the clinical recommendation to interrupt most psychiatric drug treatment during a course of ECT.

Since NMDA antagonists such as memantine may act protectively in the treatment of dementia [31], we decided to reintroduce ketamine (as another NMDA antagonist) as a first-line anesthetic in the ECT routine, when applicable. The first results of our group are promising, since they indicate both higher ECT efficacy under ketamine (since it is not anticonvulsive) and lower cognitive side effects of ECT, which is defined as an acute decline in Mini Mental State Examination scores during the ECT treatment course [32].

### **Conclusion**

Electroconvulsive therapy may be administered to elderly patients when indicated, because it is well tolerated and highly effective. This applies in particular in the case of geriatric depression, which is often drug resistant and complicated by medical comorbidities. The common concern of long-term cognitive side effects appears

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unjustified and is not supported by current data. Nevertheless, there is insufficient evidence and further research with methodologically adequate studies is required.

All geriatric patients should be monitored by cognitive screening tests before index ECT, as well as during and after the ECT course. This has been shown to be feasible even in medically and cognitively impaired patients and this may improve patients' adherence to treatment. Long-term side effects of irreversible cognitive impairment are not proven for ECT.

In particular, antidementia treatment with ACHE-I and/or ketamine anesthesia may have an additional protective effect and might be

administered over the course of ECT. Typical side effects of ACHE-I and ketamine would need to be critically monitored. However, to generalize these observations is as-yet inadequate.

#### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

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