

A Retrospective Controlled Study into Memory Complaints Reported by Depressed Patients After Treatment with Electroconvulsive Therapy and Pharmacotherapy or Pharmacotherapy Only

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S100 and Impact of ECT on Depression and Cognition

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**Abstract:**

**Objectives:** The main side effects of electroconvulsive therapy (ECT) are in the realm of cognition. The S100-beta is a calcium-binding protein that is expressed by astrocytes in the central nervous system during depression and has been suggested to modulate the impact of ECT on cognition.

**Methods:** Serum samples of S100-beta were taken before and 1 and 3 hours after each ECT session in 12 depressed patients (mean age, 54 years), treated with bilateral ECT twice weekly (mean, 6 sessions). Measures of depression (Symptom Checklist-90 depression dimension) and a neurocognitive test battery yielding 3 domains of general cognition, memory, and subjective cognitive impairment were administered 1 day before and 5 and 30 days post-ECT.

**Results:** Electroconvulsive therapy was associated with a reduction in depression and subjective cognitive impairment at 5 and 30 days post-ECT. Electroconvulsive therapy was associated with a small but significant rise in S100-beta 1 hour post-ECT (adjusted B = 0.013, P = 0.035), with a directionally similar but reduced effect size at 3 hours post-ECT (adjusted B = 0.010, P = 0.10). Higher level of S100-beta at baseline was associated with poorer memory function at 5 and 30 days of follow-up (adjusted B per tertile group increase, 0.38, P = 0.013) but also with less subjective cognitive impairment (B = -28.2, P < 0.001) and less depression at follow-up (B = -15, P = 0.009).

**Conclusion:** The S100-beta at baseline may be a marker predicting and possibly mediating the differential impact of ECT on cognition and depression.

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Concomitant Use of Vagus Nerve Stimulation and Electroconvulsive Therapy for Treatment-resistant Depression

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## The Cognitive Effects of Electroconvulsive Therapy in Community Settings

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Despite ongoing controversy, there has never been a large-scale, prospective study of the cognitive effects of electroconvulsive therapy (ECT). We conducted a prospective, naturalistic, longitudinal study of clinical and cognitive outcomes in patients with major depression treated at seven facilities in the New York City metropolitan area. Of 751 patients referred for ECT with a provisional diagnosis of a depressive disorder, 347 patients were eligible and participated in at least one post-ECT outcome evaluation. The primary outcome measures, Modified Mini-Mental State exam scores, delayed recall scores from the Buschke Selective Reminding Test, and retrograde amnesia scores from the Columbia University Autobiographical Memory Interview–SF (AMI–SF), were evaluated shortly following the ECT course and 6 months later. A substantial number of secondary cognitive measures were also administered. The seven sites differed significantly in cognitive outcomes both immediately and 6 months following ECT, even when controlling for patient characteristics. Electrical waveform and electrode placement had marked cognitive effects. Sine wave stimulation resulted in pronounced slowing of reaction time, both immediately and 6 months following ECT. Bilateral (BL) ECT resulted in more severe and persisting retrograde amnesia than right unilateral ECT. Advancing age, lower premorbid intellectual function, and female gender were associated with greater cognitive deficits. Thus, adverse cognitive effects were detected 6 months following the acute treatment course. Cognitive outcomes varied across treatment facilities and differences in ECT technique largely accounted for these differences. Sine wave stimulation and BL electrode placement resulted in more severe and persistent deficits.

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**Keywords:** electroconvulsive therapy; major depression; memory; cognitive side effects; amnesia

### INTRODUCTION

Electroconvulsive therapy (ECT) is widely considered the most effective antidepressant treatment, with medication resistance its leading indication (American Psychiatric Association, 2001). However, critics contend that ECT invariably results in substantial and permanent memory loss (Breggin, 1986; Sterling, 2000), with some patients experiencing a dense retrograde amnesia extending back several years (Donahue, 2000; Sackeim, 2000). In contrast, some authorities have argued that, with the introduction of general anesthesia and more efficient electrical waveforms,

ECT's adverse cognitive effects are short-lived, with no persistent effects on memory (Abrams, 2002; Fink, 2004).

Shortly following the ECT course, most patients manifest deficits in retaining newly learned information (anterograde amnesia) and recalling events that occurred in the weeks or months preceding the ECT course (retrograde amnesia) (Sackeim, 1992; Squire, 1986). Randomized-controlled trials have shown more severe short-term memory deficits with sine wave compared to brief pulse stimulation (Valentine *et al*, 1968; Weiner *et al*, 1986), bilateral (BL) compared to right unilateral (RUL) electrode placement (Lancaster *et al*, 1958; Sackeim *et al*, 1986; Sackeim *et al*, 1993; Sackeim *et al*, 2000), and higher electrical dosage (McCall *et al*, 2000; Ottosson, 1960; Sackeim *et al*, 1993). These adverse effects are reduced by the use of RUL ECT with brief or ultrabrief pulse stimulation and electrical dosage titrated to the needs of the individual patient (Sackeim, 2004b). Nonetheless, a minority of US practitioners still use sine wave stimulation, approximately half do not adjust dosage relative to the

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