3. Other somatic therapies

a. Electroconvulsive therapy

Electroconvulsive therapy has the highest rates of response and remission of any form of antidepressant treatment, with 70%-90% of those treated showing improvement (234, 236). Although the remission rate with ECT appears to be lower when it is used in community settings than when it is used in clinical trials (237), the proportion of patients with major depressive disorder who respond to ECT is still greater than the proportion who respond to antidepressant medication. In addition, ECT has been associated with significant improvements in health-related quality of life (238). Consequently, ECT should be considered for patients with severe major depressive disorder that is not responsive to psychotherapeutic and/or pharmacological interventions, particularly those with significant functional impairment who have not responded to numerous medication trials (239). Electroconvulsive therapy may be particularly beneficial and can be considered as a first-line treatment option for severe major depressive disorder when it is coupled with psychotic features (240, 241), catatonia (239, 242), suicide risk (243), or food refusal leading to nutritional compromise, as well as in other situations when a particularly rapid antidepressant response is required (240), such as with severely ill inpatients (239). Electroconvulsive therapy is also indicated as a first-line treatment for patients who have previously shown a positive response to this treatment modality or who prefer it (239).

1. Side effects of electroconvulsive therapy

Electroconvulsive therapy is a very safe treatment, and there are no absolute contraindications to its use (239). Risks of morbidity and mortality, in general, do not exceed those associated with anesthesia alone (239, 244, 245). However, the presence of some medical conditions may necessitate modifications in anesthesia or ECT administration.

Electroconvulsive therapy may have cardiovascular side effects, mediated by changes in the autonomic nervous system with the initial stimulus and subsequent seizure activity (239). More specifically, ECT typically causes a transient rise in heart rate and blood pressure, with associated increases in cardiac workload and intracranial pressure. These effects can be managed by optimizing blood pressure control prior to ECT and administering anti- hypertensive agents (e.g., short-acting beta-blockers or calcium channel blockers) at the time of ECT (239). Arrhythmias, which are usually transient, can also occur in conjunction with ECT and can be managed with usual antiarrhythmic therapies if they do not resolve spontaneously (239).

Electroconvulsive therapy can also be associated with cognitive effects, the most common of which is a period of confusion following the ECT and associated anesthesia that generally lasts between 30 and 60 minutes (246). Electroconvulsive therapy also is associated with antero- grade amnesia, which typically resolves soon after the last ECT treatment (247). Some degree of retrograde amnesia, particularly for recent memories, may continue for a longer period of time after the end of the ECT course (247) but is less pronounced for autobiographical memories than for impersonal memories (248). These cognitive effects of ECT are related to electrode placement, stimulus dosage, age, and premorbid cognitive status (249-253). Retrograde amnesia also improves over time, typically resolving within 6 months (248, 252), although some patients report incomplete recovery of memories, particularly for events around the time of the treatment (247, 254). Rarely, patients report more pervasive and persistent cognitive disruption, the basis of which is uncertain (252, 255). For many individuals, however, subjective memory (256) and quality of life (238) is improved following ECT with the resolution of the major depressive episode and its associated deficits in memory or executive functioning (257, 258).

2. Implementation of electroconvulsive therapy

The evaluation preceding ECT consists of a psychiatric history and examination to verify that ECT is indicated, a general medical evaluation (including medical history and physical examination with cognitive assessment, vital signs, and any specifically indicated laboratory, radiologic, or imaging studies) to define factors that may influence the risk of ECT, and an anesthesia evaluation to identify and address the nature and extent of anesthetic risk and the need for modification of medications or anesthetic technique (239). This evaluation should include a summary of treatment indications, treatment risks, and a suggestion of any indicated additional evaluative procedures, alterations in treatment, or modifications in ECT technique (239). In assessing indications for caution (e.g., recent myocardial infarction, cardiac arrhythmias, intracranial space-occupying lesions), the relative risks and benefits should be carefully weighed in collaboration with an anesthesiologist, a general medical physician, and other specialists, as necessary. Once completed, the pre-ECT evaluation will serve as the basis for a specific, individualized discussion of the risks and benefits of ECT relative to other therapeutic options as part of the informed consent process. With the patient's permission, it is helpful to educate the patient's family about ECT and involve them in discussions relating to consent.

An additional aspect of decision-making prior to ECT relates to the use of psychotropic medications during the ECT course. There is growing use of ECT combined with antidepressant medication. Although data supporting this practice are still few, it does not appear to increase side effects and may augment response (259, 260). An additional goal of combination treatment is to minimize the risk of relapse between the end of the ECT course and the attainment of full antidepressant effectiveness. Antipsychotic medications are typically continued during the ECT course (239, 261), although most data on this practice come from studies of patients with schizophrenia who are receiving ECT. The safety of combining lithium and ECT has been questioned, although there are conflicting data (239, 262). Medications that have anticonvulsant properties are often discontinued or

given at decreased doses during the ECT course to minimize effects on seizure induction (239, 261). With benzodiazepines, there is some evidence that concurrent use may diminish ECT effectiveness, particularly when right unilateral electrode placement is used (263).

Electroconvulsive therapy may be administered either unilaterally or bilaterally (using a bitemporal or bifrontal electrode placement). Compared with patients who receive bilateral treatment, most patients who receive right unilateral electrode placement with low stimulus intensities experience fewer cognitive effects but less therapeutic benefit (253). Stimuli of higher intensity (i.e., 500% above seizure threshold) are associated with antidepressant effects more comparable to those seen with bilateral electrode placements, although such stimulus intensities are not always achievable with existing ECT devices (264). Regardless of what electrode placement is chosen, stimulus dosing should be individualized and stimulus parameters adjusted to induce an adequate generalized seizure, which is typically at least 20 seconds or greater in motor duration and 30 seconds in EEG duration (239). Failure to induce an adequate seizure should be followed immediately by restimulation at higher energies until an adequate seizure is elicited.

Electroconvulsive therapy is typically administered 2-3 times/week; less frequent administration has been associated with less cognitive impairment but also a longer lag in the onset of action (265). In clinical practice, the need for ECT to be administered at this frequency could produce logistical barriers for some patients who would either require hospitalization or transportation after ECT sessions. The acute course of ECT treatment typically consists of six to 12 treatments and generally does not exceed 20 treatments (239, 266). It is important that treatment continue until symptoms have remitted or clearly reached a plateau, since relapse rates appear to be greater and overall prognosis worse if ECT is discontinued prematurely (237). Use of a formal rating scale may be helpful in assessing symptom response as well as the cognitive side effects of treatment, permitting adjustments in the treatment parameters or frequency (239, 267).

For more detail on the administration of ECT, see APA's *The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging (A Task Force Report of the American Psychiatric Association)* (239).

b. Transcranial magnetic stimulation

Transcranial magnetic stimulation (TMS) uses a specifically designed magnetic coil that is placed in contact with the head to generate rapidly alternating magnetic-resonance- imaging-strength magnetic fields and produce electrical stimulation of superficial cortical neurons. Based on the results of a multisite randomized sham-controlled clinical trial of high-frequency TMS over the left dorsolateral prefrontal cortex (268), TMS was cleared by the FDA in 2008 for use in individuals with major depressive disorder who have not had a satisfactory response to at least one antidepressant trial in the current episode of illness. However, another large randomized sham-controlled trial of TMS added to antidepressant pharmacotherapy showed no significant benefit of left dorsolateral prefrontal cortex TMS (269). In comparisons of actual TMS versus sham TMS, most (270-272) but not all (273) recent meta-anal- yses have found relatively small to moderate benefits of TMS in terms of clinical response. Although the primary studies used in these meta-analyses are highly overlapping and the variability in TMS stimulus parameters and treatment paradigms complicates the interpretation of research findings, these meta-analyses also support the use of high-frequency TMS over the left dorsolateral prefrontal cortex. Lesser degrees of treatment resistance may be associated with a better acute response to TMS (274).

In comparison with ECT, TMS has been found in randomized studies to be either less effective than ECT (275) or comparable in efficacy to ECT (276-278), but in the latter studies TMS was more effective and ECT was less effective than is typically seen in clinical trials. A fewer number of studies have compared cognitive effects of TMS and ECT. One randomized trial found no significant difference between TMS and non-dominant unilateral ECT on performance on neuropsychological tests at 2 and at 4 weeks of treatment (276), although a small open-label trial reported a greater degree of memory difficulties with ECT than with TMS shortly after the treatment course (279).

Across all studies, TMS was well tolerated and was associated with low rates of treatment dropout (270, 280). Transient scalp discomfort and headaches were the most commonly reported side effects (280).

In clinical practice, the need for daily TMS could produce logistical barriers for some patients.

c. Vagus nerve stimulation

Vagus nerve stimulation is approved for use in patients with treatment-resistant depression on the basis of its potential benefit with long-term treatment. There is no indication for the use of VNS in acute phase treatment of depression, as data showed no evidence for acute efficacy (281, 282). Further information on the use of VNS as an adjunct to other antidepressive treatments is provided in Section II.B.7.c.