Treatment-resistant depression

First line treatment includes pharmacotherapy, psychotherapy, and forms of non-invasive brain stimulation such as transcranial magnetic stimulation and electroconvulsive therapy. Patients who fail conservative therapy may be candidates for functional neuromodulatory procedures.

Initial attempts at surgical treatment for chronic depression or major depressive disorder (MDD) included nonspecific destructive surgeries such as the prefrontal leucotomy (lobotomy). After these procedures fell out of favor, more selective ablative procedures targeting the orbitofrontal cortex and the medial prefrontal cortex were attempted. Recently, DBS targets investigated for treatment of medically intractable depression include: the subcallosal cingulate gyrus, inferior thalamic peduncle, nucleus accumbens, and ventral capsule / striatum. [1) 2) 3)]

Several of these targets gained interest after patients undergoing DBS for OCD noted improved mood as a side effect [4)]. Vagus nerve stimulation (VNS) has also been explored as an option after patients receiving VNS for seizures were noted to have an improvement in depressive symptoms independent of seizure control [5)]

Treatment

see Treatment resistant depression surgery.

Outcome

Thirty percent of patients with treatment resistant depression (TRD) attempt suicide at least once during their lifetime. However, it is unclear what the attempted and completed suicide incidences are in TRD patients after initiating a treatment, and whether specific treatments increase or decrease these incidences.

Bergfeld et al.,searched PubMed systematically for studies of depressed patients who failed at least two antidepressant therapies and were followed for at least three months after initiating a treatment.

They estimated attempted and completed suicide incidences using a Poisson meta-analysis. Given the lack of controlled comparisons, they used a meta-regression to estimate whether these incidences differed between treatments.

They included 30 studies investigating suicidality in 32 TRD samples, undergoing deep brain stimulation (DBS, n = 9), vagal nerve stimulation (VNS, n = 9), electroconvulsive therapy (ECT, n = 5), treatment-as-usual (n = 3), capsulotomy (n = 2), cognitive behavioral therapy (n = 2), ketamine (n = 1), and epidural cortical stimulation (n = 1). The overall incidence of completed suicides was 0.47 per 100 patient years (95% CI: 0.22-1.00), and of attempted suicides 4.66 per 100 patient years (95% CI: 3.53-6.23). No differences were found in incidences following DBS, VNS or ECT.

Suicidality is poorly recorded in many studies limiting the number of studies available.

The completed and attempted suicide incidences are high (0.47 and 4.66 per 100 patient years

respectively), but these incidences did not differ between three end of the line treatments (DBS, VNS or ECT). Given the high suicide risk in TRD patients, clinical trials should consider suicidality as an explicit outcome measure [6].

1)
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