

## Psychiatric Neurostimulation in Singapore

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Psychiatric conditions are estimated to account globally for 21.2% of years lived with disability (YLD) and 7.1% of disability-adjusted-life-years (DALYs),<sup>1</sup> although the actual figure may be even higher.<sup>2</sup> In Singapore, 12% of the population will have at least one lifetime affective, anxiety or alcohol use disorder.<sup>3</sup> Treatment for psychiatric conditions is broadly divided into talking therapies, pharmacotherapies and neurostimulation. For more severe psychiatric conditions, the latter two therapies are often required. However, investment in psychiatric pharmacotherapies has diminished in recent years with most major pharmaceutical companies pulling out of or scaling back investment into psychiatric drug development.<sup>4</sup> Psychoactive drug development is now the preserve of small- and medium-sized companies.

The implication is that future advances in psychiatric treatment will depend increasingly on the development of neurostimulatory techniques. Neurostimulation is defined as modulation of the central or peripheral nervous system by electrical or magnetic impulses and has novel mechanisms distinct from the typical monoamine or dopamine pathways that the majority of psychiatric drugs are thought to function. The good news is that there have been rapid advances in the field of neurostimulation over the past 20 years that portends hope for psychiatric treatment advances. We will describe briefly the major psychiatric neurostimulation modalities currently available and on the horizon for Singapore.

### Current Psychiatric Neurostimulation in Singapore

The oldest psychiatric treatment still in active use is electroconvulsive therapy (ECT).<sup>5</sup> ECT is essentially the induction of a brief medically controlled seizure by passing an electrical current through the brain. ECT is one of the most effective acute treatments for depression,<sup>6</sup> bipolar disorder,<sup>7</sup> treatment resistant schizophrenia,<sup>8</sup> catatonia and affective disorders with high suicidal risk.<sup>9</sup> This effectiveness is also evident in the child and adolescent population.<sup>10</sup> It

is also effective in the treatment of neuroleptic malignant syndrome, Parkinson's disease, self-injurious behaviour in intellectual disability and catatonia in autism. It is a highly safe treatment with a mortality rate of less than 2 per 100,000 treatments<sup>11</sup> with the most common side effects being mild headache and muscle ache. The most worrying side effects of ECT are possible cognitive side effects like delirium, anterograde and retrograde amnesia which are more common with the older forms of ECT, like sine wave and high fixed dose bitemporal ECT.<sup>12</sup> Over the past 25 years, ECT techniques have moved from a "one-size-fits-all" approach to an individualised seizure titration method with different electrode placements (bitemporal, bifrontal, right unilateral),<sup>13</sup> dosages relative to individual seizure threshold and different electrical current parameters<sup>14</sup> to customise the efficacy versus side effect profile of various types of ECT to the individual patient's needs.

Our institution runs a large ECT service and we conduct more than 2000 ECT treatments a year for about 400 patients. We have recently revamped our ECT services to provide modern ECT with an 83% remission rate for patients with depression, an improvement on clinical global improvement (CGI) score from "severely ill" to "mildly ill" for patients with schizophrenia and most significantly of all, a 76% rate of cognitive improvement on the Brief ECT Cognitive Scale (BECS)<sup>15</sup> for our patients after just 3 sessions of ECT. The observed cognitive improvement after ECT underscores the pernicious effects of severe mental illness on our patient's cognition and the effectiveness of ECT in treating these psychiatric conditions.

Despite the strong evidence base for the efficacy of ECT, it remains an underused and highly stigmatised treatment due to the misconceptions of ECT from the media and the possible cognitive side effects of ECT. Partly in response to the difficulty of prescribing ECT, new neurostimulation techniques like repetitive transcranial magnetic stimulation (rTMS) have been developed in the past 2 decades and is

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now part of standard treatment for depression in many developed countries, including Singapore where the College of Psychiatrists endorses the use of rTMS in treatment-resistant depression.<sup>16</sup> Modern rTMS started when Anthony Barker and his colleagues in Sheffield developed a practical high performance rTMS machine that could deliver powerful and focal magnetic pulses to stimulate the brain. Since that seminal work, extensive research has demonstrated the efficacy of rTMS in the treatment of depression<sup>17</sup> and it has been United States FDA approved for use in treatment-resistant depression since 2008. There is also increasingly convincing data of its efficacy in treating auditory hallucinations in schizophrenia, anxiety and possibly addictive disorders. While rTMS is not as efficacious as ECT, it has much higher patient acceptability due to the lack of anaesthesia, benign side effect profile (typically a mild and transient headache) and high safety profile. There are also less exclusions to treatment compared to ECT, with the main two being a history of seizures or ferromagnetic material in the brain. At this time, rTMS therapy is available in the private sector and in our institution. Other public healthcare institutions are also in the process of setting up rTMS programmes.

### The Future of Psychiatric Neurostimulation in Singapore

An exciting new neurostimulatory technique called transcranial direct current stimulation (tDCS) is also rapidly gathering evidence as a unique neurostimulatory modality for depression,<sup>18</sup> auditory hallucinations in schizophrenia and possibly cognitive disorders. As compared to ECT or rTMS, tDCS does not cause neuronal depolarisation and instead seems to cause a sustained change in resting neuronal stimulatory threshold and may have a pro-cognitive effect independent of its antidepressant effects. The side effect and safety profile is even more favourable than rTMS and it carries the promise of possible self-administration of treatment which would be a significant advantage over ECT and rTMS, both of which require the patient to travel to a treatment site. Researchers in Singapore General Hospital and National University Hospital are currently conducting trials in our local population and the results are highly anticipated by the local psychiatric community.

Non-ablative (e.g. deep brain stimulation, DBS) neurosurgeries for psychiatric conditions like obsessive compulsive disorders (OCD)<sup>19</sup> and depression<sup>20</sup> are tantalising future treatment options. Local neurosurgeons have been trained and conversant in using DBS in the treatment of OCD and depression and active discussions about offering this treatment modality are in progress to offer the most treatment-resistant patients a chance of improvement.

Techniques aside, a key future development will be the heartware (i.e. training future doctors and psychiatrists about current and future neurostimulation modalities), local research, development and implementation of neurostimulation programmes to give our patients access to the full menu of treatment options for psychiatric conditions. One key step will be the establishment of a Section for Neurostimulation under the College of Psychiatrists to establish local treatment standards, drive education and research as well as serve as an expert body for local psychiatric neurostimulation. The future will indeed be stimulating for neurostimulation in psychiatry.

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