Neurostimulation Devices for the Treatment of Neurologic Disorders

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Abstract

Rapid advancements in neurostimulation technologies are providing relief to an unprecedented number of patients affected by debilitating neurologic and psychiatric disorders. Neurostimulation therapies include invasive and noninvasive approaches that involve the application of electrical stimulation to drive neural function within a circuit. This review focuses on established invasive electrical stimulation systems used clinically to induce therapeutic neuromodulation of dysfunctional neural circuitry. These implantable neurostimulation systems target specific deep subcortical, cortical, spinal, cranial, and peripheral nerve structures to modulate neuronal activity, providing therapeutic effects for a myriad of neuropsychiatric disorders. Recent advances in neurotechnologies and neuroimaging, along with an increased understanding of neurocircuitry, are factors contributing to the rapid rise in the use of neurostimulation therapies to treat an increasingly wide range of neurologic and psychiatric disorders. Electrical stimulation technologies are evolving after remaining fairly stagnant for the past 30 years, moving toward potential closed-loop therapeutic control systems with the ability to deliver stimulation with higher spatial resolution to provide continuous customized neuromodulation for optimal clinical outcomes. Even so, there is still much to be learned about disease pathogenesis of these neurodegenerative and psychiatric disorders and the latent mechanisms of neurostimulation that provide therapeutic relief. This review provides an overview of the increasingly common stimulation systems, their clinical indications, and enabling technologies.

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Neurostimulation devices provide much needed therapeutic relief to an unprecedented number of people affected by debilitating neurologic and psychiatric disorders worldwide. The rise of modern-day neuromodulation therapies extends over half a century, which are rich with serendipitous discoveries and technological advances that have led to different types of neurostimulation strategies. Within the past 2 decades, innovation in medical device technology has begun to drive the evolution of these neurostimulation systems at a more accelerated pace.

Neurostimulation therapies include invasive and noninvasive approaches that apply electromagnetic energy to specific anatomical targets to induce neuromodulation of the corresponding neural circuitry. In particular, invasive neurostimulation therapies have emerged as an effective treatment for a growing number of medically resistant neurologic and neuropsychiatric disorders. As such, this review will focus on the following established invasive neurostimulation strategies used clinically to modulate disordered circuitry to restore functionality: deep brain stimulation (DBS), motor cortex stimulation (MCS), responsive neurostimulation (RNS), spinal cord stimulation (SCS), and vagus nerve stimulation (VNS) (Figure 1). All these implantable neurostimulation systems include 3 primary components: stimulating electrode(s), an internalized pulse generator (IPG) that serves as a battery pack, and electrode extender(s) to subcutaneously connect the electrode(s) to the pulse generator. The surgical placement of the components depends on the type of neurostimulation system device, the anatomical location of the targeted dysfunctional neuronal circuitry, and the patient's medical history.

DEEP BRAIN STIMULATION

Historical Perspective

The earliest history of what became neuromodulation therapy started with ablative procedures in stereotactic and functional neurosurgery in the mid-20th century to treat neuropsychiatric disorders. At that time, without pharmaceutical options for psychiatric disorders, desperate measures were taken to mitigate debilitating symptoms. The American neurophysiologist John Farquhar Fulton observed that modulation of regions of the cerebral cortex affected behavior in nonhuman primate studies.[1] These studies found that lesioning the prefrontal cortex reduced anxiousness and inspired the Portuguese neurologist Egas Moniz to develop a frontal lobotomy procedure for which he received a Nobel Prize in 1949. For over a decade, until the mid-1950s, tens of thousands of lobotomies were performed in the United States to treat severe psychiatric disorders such as schizophrenia; however, these procedures often led to severe adverse effects, including extreme personality changes. With the introduction of the first antipsychotic drug chlorpromazine in 1952, along with the devastating adverse effects of lobotomies, these controversial procedures were largely abandoned by the late 1960s. Meanwhile, the Spanish neuroscientist Jose Delgado observed that implantable stimulating intracranial electrodes could aid in diagnosis and possibly provide therapeutic effects for neurologic disorders such as schizophrenia and epilepsy.[2] Furthermore, Robert G. Heath conducted clinical studies that leveraged intracranial electrodes to modulate brain activity to understand and treat intractable psychiatric disorders.[3-5]

During these clinical studies to modulate pathological behavior related to neuropsychiatric disorders, it was observed that stimulation of specific deep brain structures induced analgesia.[6] This serendipitous discovery ushered in decades of clinical studies to explore different neurostimulation targets to provide relief from intractable neuropathic and nociceptive pain.[7-9] Deep brain stimulation targets included the sensory nuclei of the thalamus, periaqueductal/periventricular gray, anterior cingulate cortex, internal capsule, posterior hypothalamus, and nucleus accumbens (NAc).[10] For decades to follow, rather than treating neurologic movement disorders, DBS