Changing the course of Parkinson's disease treatment

THE NEUROSURGEON who pioneered deep brain stimulation for the treatment of movement disorders receives the 42nd Honda Prize.

Alim-Louis Benabid.

In the late 1980s, Alim-Louis Benabid made a discovery that led to the development of deep brain stimulation, a technique used to treat tremors and other symptoms of Parkinson's disease. Today, the technique remains the clinical standard for advanced stages of Parkinson's and has benefitted more than 150,000 patients worldwide. In 2021, the French-Algerian neurosurgeon has been awarded the 42nd Honda Prize.

Deep brain stimulation involves implanting electrodes that stimulate the subthalamic nucleus with adjustable high-frequency pulses. In the days before the technique was developed, treatment for Parkinson's disease meant medication or neuroablative lesion surgery, which involves the targeted destruction of brain tissue. Early in his career, performing lesion surgery in the thalamus was a regular occurrence for Benabid. He would locate the target with electrodes lowered into the brain, set at 20-50Hz, and then burn tissue.

"The problem was that sometimes, tremors would stop during surgery but would recur in a few days time, if the lesion was too small. In contrast, you place patients at risk of having permanent loss of sensitivity with too big of a lesion," explains Benabid. "What would be something strong enough, but without inconvenience? This question was always in the back of my mind."

Benabid believes that a background in both physics and medicine prepared him for the breakthrough. He was curious about the effects of different stimulation frequencies. "My equipment allowed me to stimulate brain tissue at much higher than 100 Hz," he says. Starting from very low frequencies of 1, 5 and 10 Hz, he slowly increased the frequency, until, at 100 Hz, the tremors stopped in the same way as with lesion surgery. "I did not understand what had happened, but it was clear that we had found something that fit our needs," he says. "As soon as the stimulation was stopped, the tremors reappeared. That meant it was reversible as well — everything was good."

Moving the stimulation target from the thalamus to the subthalamic nucleus, in the 1990s, made deep brain stimulation not only capable of suppressing tremors, but also easing rigidity and loss of voluntary movement. Since then, the applications of deep brain stimulation have extended far beyond treatment for Parkinson's disease. The technique is also a treatment option for movement disorders like dystonia, epilepsy, and essential tremor. In addition, the potential to treat other conditions, including depression, Alzheimer's disease, and Huntington's disease are being explored.

"The basic understanding of deep brain stimulation is essentially the same as it was in the 1980s. We still don't understand why it works, but we have come a long way in refining the structure of the device, such that it achieves precision and reduces risk. The electrodes are now a fifth of the size they used to be," says Benabid. He credits this development, achieved in collaboration with industry partners, for making deep brain stimulation the precise, low side-effect treatment that it is today. "Once you give an engineer a reason to innovate, they will do it," he says, chuckling.

Although Benabid retired from full-time work in 2007, he continues the search for new possibilities in movement disorder treatment. "The question now is, can we stop disease progression at the very beginning?" says Benabid. As the co-founder of Clinatec, a biomedical research centre based in Grenoble, he is exploring treatments with light. Instead of electrodes, Benabid's team is using fibre optic cable implants to illuminate the brain's substantia nigra with near infrared light, which is thought to protect dopamine-producing neurons from death.

The new strategy, for which clinical trials are underway, targets patients with few motor problems, but with reduced dopamine levels indicative of early Parkinson's. "There's no reason that only infrared light would bring benefits — it's only a tiny part of the spectrum of light," adds Benabid. "I am pushing strongly that our lab systematically explores the benefits of different ranges of lights." As part of this work, he has asked Australian red and near infrared light specialist, John Mitrofanis, to join him at Clinatec.

The Honda Foundation was established in 1977 with philanthropic contributions from Soichiro Honda, founder of Honda Motor, and his brother Benjiro. The foundation established the Honda Prize in 1980 to honour scientists whose efforts advance 'ecotechnology', technology that works in harmony with complex human needs and the natural environment. Since then, the foundation has recognized the achievements of 41 individuals or groups. The 2021 digital ceremony was broadcast on 17 November. ■

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