THE 'FUS' ABOUT BRAIN STIMULATION

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Weighing in at approximately 1.3–1.4 kg, protected by the skull and surrounded by cerebrospinal fluid, our hub of intelligence, interpreter of the senses, controller of behaviour and initiator of movement[1] – ladies and gentlemen, we proudly present the enigmatic crown jewel of the human body: the brain.

Proclaiming success

A proclamation made by United States (US) President George Bush, designated the 1990s as the Decade of the Brain, "to enhance public awareness of the benefits to be derived from brain research" through "appropriate programs, ceremonies, and activities".[2] Although a US-centric proclamation, neuroscience prospered worldwide; between 1991 and 1994 alone, an annual average of 35 570 neuroscience papers were published, with a growth rate of 4%.[3]

Carrying the burden of neurological disorders

The global burden of combined neurological disorders is measured by the absolute number of disability-adjusted life years (DALYs; sum of years of life lost and years lived with disability), as cumulative incidence and prevalence estimates for a collection of diseases are not beneficial.[4] A systematic analysis for the Global Burden of Disease Study 2016 reported a 15% increase in DALYs and a 39% increase in deaths for 15 neurological conditions between 1990 and 2016.[4] Thus, in 2016, these neurological disorders were responsible for 276 million DALYs, comprising 11.6% of global DALYs for all diseases (i.e. the leading cause of global DALYs) and 9 million deaths – that is, 16.5% of total global deaths (the second leading cause of total global deaths), respectively.[4]

Furthermore, the burden of neurological conditions continues to increase as a consequence of a growing and ageing population, along with the rising prevalence of major disabling neurological disorders.[4] The increased recognition of the social and economic burden posed by brain diseases, as well as the growing appreciation that brain disease is a manageable problem, are believed to be two key drivers in the development of effective prevention and treatment strategies in neuroscience.[5]

Focusing on brain stimulation

Deep brain stimulation (DBS) is an approved treatment for multiple neurological conditions, such as dystonia, Parkinson's disease and tremor in the United Kingdom (UK),[6] and additional diseases in the US.[7] Furthermore, DBS is also currently being studied as a potential treatment for disorders such as addiction, chronic pain, dementia, depression (major) and multiple sclerosis.[7] DBS, however, requires invasive surgical implantation of electrodes and lacks cell-type specificity.[8] Although alternative techniques exist, they are also associated with some disadvantages – transcranial magnetic stimulation is non-invasive, but has low spatial resolution, whereas optogenetic-based approaches offer spatial precision but require genetic manipulation.[9]

In the last decade, a new technique for non-invasive brain stimulation has emerged. **Focused ultrasound (FUS)**, has the potential to non-invasively target any area in the brain with a spatial resolution of approximately 2 mm.[8,9] In 2016, it received US Food and Drug Administration approval for the treatment of medication-refractory essential tremor and is currently undergoing trials in the UK.[10]

Combining science and innovation

Yang *et al*. have developed a novel technique, coined 'sonothermogenetics', which builds upon the combined technology of genetics and FUS therapy, to activate specific neurons deep in the brains of mice.[8] They used a viral vector to deliver the thermosensitive transient receptor potential vanilloid 1 (TRPV1) to genetically selected neurons in the striatum. After 3 weeks, a custom-made, miniaturised transducer was fitted onto the mouse head and a FUS beam, only 0.66 mm wide, was delivered 5.8 mm into the brain to reach the striatum. The low-intensity FUS generated a short pulse that increased the tissue temperature to approximately 42°C, which is just a few degrees higher than body temperature, and activated the neurons overexpressing TRPV1 (TRPV1+); neurons in close proximity without TRPV1+ were not affected.[8]

Future 'FUS' for neurological disorders

The cell-type specificity achieved by sonothermogenetics evoked rotational behaviour in a reversible and repeatable manner in the TRPV1+ mice.[8] This means that aberrant motor functioning due to the aforementioned neurological disorders – epilepsy, essential tremor, multiple sclerosis and Parkinson's disease, etc. – have the potential to be alleviated with a non-invasive approach. In the future, sonothermogenetics may not be limited to conditions affected by motor function irregularities; opening up the exciting possibility of non-invasive specific neuromodulation for a plethora of other neurological conditions, such as addiction, depression, headaches, obsessive-compulsive disorder, neuropathy and stroke, among many others.[7]

STOP Multiple Sclerosis

WORLD BRAIN DAY 2021

WFN WORLD FEDERATION OF NEUROLOGY

ms international federation

The World Federation of Neurology celebrated the first World Brain Day, to increase public awareness and promote advocacy related to brain health, on 22 July 2014.[11] This year, World Brain Day is dedicated to ***'stop multiple sclerosis'****, a neurological disease that affects 2.8 million people globally.[12]*

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