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Engineering a smarter treatment for Parkinson's disease

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SUMMARY

Parkinson's Disease is a neurodegenerative disease that affects parts of the brain that control the movement of muscles, and can result in the person having 'shakes' or tremors and experience difficulty walking and speaking. One treatment for these symptoms is Deep Brain Stimulation (DBS), which implants an electrode into the brain to calm muscle tremors and other motor symptoms.

Professor Madeleine Lowery is using computer models to build a better understanding of how DBS affects brain tissue, how it stimulates the nerves that carry signals to muscles and how it impacts the muscles themselves.

Ultimately the aim is to develop a 'smart' Deep Brain Stimulation system that can figure out what the person needs and can automatically deliver the correct level of timely stimulation, thereby reducing symptoms effectively and with longer battery life.

"We are building computer models of electrodes, of brain tissue, of the nerves that convey signals to muscles and of the muscles themselves."

Research to model and understand Deep Brain Stimulation

Parkinson's Disease affects more than six million people worldwide.

The neurological condition affects parts of the brain that help us to control our movements, and this means that people with Parkinson's disease typically develop tremors or 'shakes', they may stoop, sway, fall. They may have trouble speaking clearly and their muscles may 'freeze' when they want to walk. As the disease progresses, the symptoms typically get worse, and there is currently no way to reverse the changes within the brain.

For some people with Parkinson's Disease though - and particularly those for whom medicines no longer control the tremors or gait 'freezing'- one treatment option to manage symptoms is Deep Brain Stimulation (DBS).

This involves surgically implanting an electrode into an affected brain region. The electrode is powered by a battery, which is in turn implanted into the person's chest cavity, and the implanted electrode delivers small electrical pulses or stimuli to brain cells which are involved in the control of muscles.

More than 100,000 people around the world have received Deep Brain Stimulation to date, and for many it effectively eases the symptoms of Parkinson's Disease.

However, DBS has some downsides and can have side-effects. Motor symptoms may actually worsen until the 'dosage' is optimised for the person, and the dosage required can change as the disease progresses. The helpful effects of DBS may wane for an individual over time, and the battery typically needs to be replaced every few years, which requires an invasive surgical procedure.

Professor Madeleine Lowery leads a major project at UCD School of Electrical and Electronic Engineering to model and understand Deep Brain Stimulation and inform 'smarter' systems that sense the needs of the person and automatically alter accordingly.

The research, which is funded through a prestigious European Research Council Consolidator Grant takes a whole-system approach.

"We are building computer models of electrodes, of brain tissue, of the nerves that convey signals to muscles and of the muscles themselves," explains Professor Lowery. "We are also recording signals from muscle of the healthy volunteers and from people with Parkinson's Disease to inform our models."

Models will inform more effective treatments for Parkinson's Disease

By using computer models to simulate how Deep Brain Stimulation works in people with Parkinson's Disease, Professor Lowery's group plans to **design smarter and more efficient ways to control Deep Brain Stimulation** treatment and make it more effective.

Professor Lowery's group is using computer science and mathematics to take a whole-system approach to modelling the nervous system, muscles and Deep Brain Stimulation. It's an approach that has attracted considerable **scientific interest**, and Professor Lowery has published widely in **peer-reviewed journals** and her research is presented at **international conferences.**

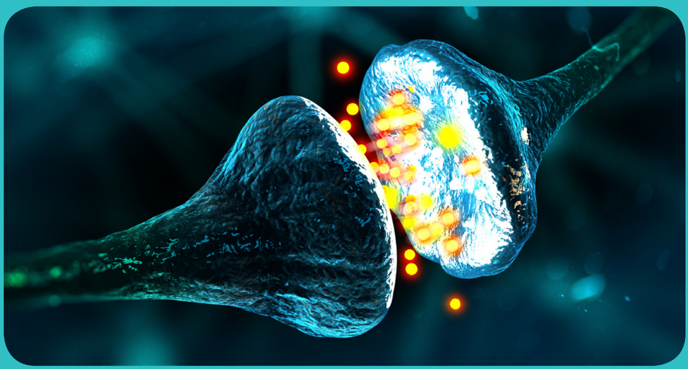
In 2014 she was awarded a **prestigious European Research Council (ERC)** grant to lead a five-year project on Deep Brain Stimulation. A relatively small number of researchers in Europe win ERC funding each year for 'blue-sky' research with the potential for large societal impact.

"One output of the project will be a computer model of the entire neuromuscular system which captures the electrode in DBS and how it affects surrounding brain tissue and the muscles it controls," says Professor Lowery. "This will help scientists and clinicians to understand how electrical signals of different strengths (amplitude), lengths (duration) and rates (frequency) are conducted through the brain tissue and the effect that they have on networks of neurons in the brain that are responsible for movement. Understanding these characteristics will help to **inform what stimulation 'dosages' are likely to be effective."**

Her group at UCD is also building computer models of the motor nerves that run between the brain and muscle (carrying the signal to move or stop) and of the muscle itself, measuring how it responds to signals from the brain. "We are particularly interested in modelling muscles in the hand, because these muscles have strong connections to the brain, are very important in the controlling fine hand movements and are often the site of tremors and disrupted movement in Parkinson's Disease," explains Professor Lowery.

By building and combining these computer models, by running simulations of Deep Brain Simulation pathways on the models and by taking measurements from healthy volunteers and people with Parkinson's Disease, Professor Lowery's findings will tell us more about the **specific changes in muscle co-ordination in Parkinson's Disease** and how different 'dosages' of Deep Brain Stimulation can affect those movements.

"We are already using our measurement systems on people with Parkinson's Disease," she notes. "We are **analysing changes in their muscle co-ordination** as they go through a specific programme of physical rehabilitation exercises at the Royal Hospital in Donnybrook. This means we can measure the progress of these patients as they move through the physical therapy, and we can use the readings to inform the computer model we are building of the nervous system and muscles. "



The UCD researchers will soon include more people with Parkinson's Disease (as well as healthy volunteers) on their wider study to model nervous system changes.

As the project develops, Professor Lowery's group aims to design a new **closed-loop Deep Brain Stimulation** system. This will monitor signals from muscles and 'tell' the implanted electrode the strength and length of electrical stimulus that is needed.

This smarter closed-loop system stands to offer several benefits to people with Parkinson's Disease, according to Professor Lowery. "It could work more effectively for the individual, and it would **'know' to adjust the stimulus** if the disease progresses, potentially making **DBS more effective for longer,**" she says. "It would also **use battery power more efficiently**, meaning that batteries will last longer and need to be replaced less frequently."

What Professor Lowery is discovering about the nervous system and how it can be controlled with electrical stimuli is also informing the wider field of 'neuromodulation', a form of therapy that uses electricity to manage symptoms such as pain, muscle spasms and hearing loss.

Research References

Publications

Schmidt C., Dunn E., Lowery, M., van Rienen, U. Uncertainty Quantification of Oscillation Suppression during DBS in a Coupled Finite Element and Network Model. IEEE Transactions on Neural Systems and Rehabilitation Engineering (In Press)

McManus L., Hu X, Rymer W.Z., Suresh N., and Lowery M.M. "Muscle fatigue increases beta-band coherence between the firing times of simultaneously active motor units in the first dorsal interosseous muscle," Journal of Neurophysiology, ;115(6):2830-9. 2016.

Davidson C.M., de Paor A.M, Cagnan H., and Lowery M.M, Analysis of Oscillatory Neural Activity in Series Network Models of Parkinson's Disease During Deep Brain Stimulation, IEEE Transactions on Biomedical Engineering, Special Edition on Brain Jan;63(1):86-96, 2016.

McManus LM, Hu X, Rymer WZ, Lowery MM, Suresh NL, Changes in motor unit behavior following isometric fatigue of the first dorsal interosseous muscle, Journal of Neurophysiology, J Neurophysiol. May 1;113(9):3186-96. 2015.

Minogue CM, Caulfield BM, Lowery M.M. An Energetic Model of Low Frequency Isometric Neuromuscular Electrical Stimulation. Annals of Biomedical Engineering. Aug;43(8):1865-76. 2015

Minogue CM, Caulfield BM, Lowery MM. Whole body oxygen uptake and evoked torque during a single 30 minute session of sub-tetanic isometric electrical stimulation of the quadriceps muscles, Archives of Physical Medicine and Rehabilitation, 2014 Sep;95(9):1750-8.

Budini F., Lowery M.M., Conroy L. and De Vito G . Dexterity Training Improves Manual Precision in Patients Affected by Essential Tremor. Archives of Physical Medicine and Rehabilitation, 2014 Apr;95(4):705-10.

Kang G. and Lowery, M.M. Effects of antidromic and orthodromic activation of STN afferent axons during DBS in Parkinson's disease: a simulation study, Frontiers in Computational Neuroscience, 2014 Mar 19;8:32.

Davidson C.M., de Paor A.M, and Lowery M.M, Application of Describing Function Analysis to a Model of Deep Brain Stimulation, IEEE Transactions on Biomedical Engineering, 61: 957 - 965, 2014.

Minogue CM, Caulfield BM, Lowery MM. Whole Body Oxygen Uptake and Evoked Knee Torque in Response to Low Frequency Electrical Stimulation of the Quadriceps Muscles. Journal of Neuroengineering and Rehabilitation, 2013 Jun 28;10(1):63.

Schmidt, C. Grant, P., Lowery, M. van Rienen U. 'Influence of Uncertainties in the Material Properties of Brain Tissue on the Probabilistic Volume of Tissue Activated', IEEE Transactions on Biomedical Engineering, 2013 May;60(5):1378-87.

Kang G. and Lowery, M.M. 'Interaction of Oscillations, and their Suppression via Deep Brain Stimulation, in a Model of the Cortico-Basal Ganglia Network', IEEE Transactions on Neural Systems and Rehabilitation Engineering, 2013 Mar;21(2):244-53.

Grant P.F. and Lowery M.M. Simulation of cortico-basal ganglia oscillations and their suppression by closed loop deep brain stimulation. IEEE Transactions on Neural Systems and Rehabilitation Engineering, 2013 Jul;21(4):584-94.

Grant P.F. and Lowery M.M. Effect of dispersive conductivity and permittivity in volume conductor models of deep brain stimulation. IEEE Transactions on Biomedical Engineering, 57(10):2386-93, 2010.

Grant P.F. and Lowery M.M. Electric field distribution in a finite-volume head model of deep brain stimulation. Medical Engineering & Physics, 31(9):1095-103, 2009.

Awards

European Research Consolidator Grant 2014 "Multiscale Modelling of the Neuromuscular System for Closed Loop Deep Brain Stimulation" Royal Academy of Medicine in Ireland Conway Medal, 2015.

Delsys Prize for Innovation in Electromyography 2010

Conferences

Chair of International Society of Electrophysiology and Kinesiology Congress 2018, University College Dublin (http://www.isek.org/congress-2018/)