The Edinburgh Parkinson's Lecture, Monday 17 September 2018

The Road to New Treatments for Dementia and Parkinson's

Professor Giovanna Mallucci

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An audience of around 200 people, predominantly members of the Edinburgh Branch of Parkinson's UK, but including also many health professionals and researchers, came to the Queens Medical Research Institute, University of Edinburgh, to hear Giovanna Mallucci deliver the seventh annual Edinburgh Parkinson's Lecture. Professor Mallucci was introduced by Professor Siddarthan Chandran, Director of the Anne Rowling Regenerative Neurology Clinic, who highlighted two ways in which Professor Mallucci differed from her six predecessors in that role: firstly, by being the first female scientist to deliver our lecture, and secondly, by her broad canvas approach in her research, which is less Parkinson's specific than that of her predecessors, but has sought common themes which might help to unlock treatments for the five neurodegenerative conditions: Alzheimers, Parkinson's, the Tauopathies, ALS and Prion disease.

Since the video of Professor Mallucci's lecture is available for viewing on our website, this report offers only an outline of her talk. Her initial motivation for undertaking research in prion disease after her medical training was her awareness of how little could then be done for the five neurodegenerative conditions, which have now become the most common cause of death in the developed world. She stressed the importance of the tracking the loss of synapses, which are important both for the transmission of information between brain cells, and for the maintenance of the health of the neurons. She noted a common mechanism in the five conditions: as the number of synapses in a cell goes down, the accumulation of misfolded proteins (in the case of Parkinson's, alpha-synuclein) goes up, leading eventually to the loss of the brain cell. Slowing the process of protein misfolding could slow down the development of the disease. In her study of prion disease, she had established that reducing the number of cells about to misfold reversed the decline and restored memory, function of brain cells and motivation in the mice being treated. This meant that the process must be reversible for the other conditions, including Parkinson's. Mapping of mouse brains had showed that cells have a defence mechanism built in to reduce the stress in the cell and refold the misfolded protein.

She next discussed the use of drugs to stimulate the process of recovery, by reactivating the 'broken thermostat', which had caused protein production to shut down. GSK2606414, a PERK inhibitor used for cancer had been used successfully on mice with prion disease and with Parkinson's, but it could not be used on humans because it rots the pancreas, and ISRIB had also been used on mice but was not suitable for humans. Instead of developing new drugs from scratch, a slow and extremely expensive process, her colleague Mark Halliday had identified two existing drugs, Trazodone and DBM, which were suitable for repurposing and their plans for clinical trials were now well underway.

To conclude, she returned to the question of accelerated loss of synapses, which are so important for keeping brain cells alive. Plasticity of the brain is important for recovery from injury. She explained how animals disconnect their synapses when they hibernate and reconnect them when rewarmed. Experiments with prion mice have shown how cooling leads to production of the protein RBM3, which provides neuroprotection, preserving plasticity and the ability to regenerate synapses. There are lots of ways of protecting brain cells that leave the misfolded proteins alone and go to the core of how to protect your synapses and your neurons. Therapeutic hypothermia has some limited use for humans, but research with those who swim in very cold water has shown that they boost their RBM3. Now the research teams are looking for ways of protecting the brain without cooling people. It will not be a cure, but if people can be kept at the early stage of the disease and slow its progression, that will be well worth achieving. A five or ten year delay will be a great help.

After acknowledging the contribution of many colleagues, Professor Mallucci answered questions from the audience, in a lively session chaired by Dr Conor Maguire. Themes included the importance of sleep in the maintenance of synaptic health and repair; the desirability of early intervention, although more will be known when clinical trials are underway about whether it is ever too late for treatment; the role of exercise in boosting synapses; and optimism about the future as new ways of slowing progress of dementia and Parkinson's are developed.

After closing remarks from Dr David Dexter, from Parkinson's UK, the evening ended with a vote of thanks from Professor Dario Alessi, University of Dundee. The Parkinson's UK Scottish Team collected donations from the audience as they left, which will be used to support further Parkinson's research.