2nd Neurosciences Foundation Seminar

A synopsis of the work that will be covered.

Three projects currently or recently supported by the Foundation

1. A feasibility study exploring connections in the brain in schizophrenia.

The aim of this work is to get a better understanding of schizophrenia. The Scottish Health Public Information Office describes schizophrenia as '*a serious mental health problem….. a difficult disease to understand and difficult or sometimes impossible to diagnose'*. This study, led by Dr Rajiv Krishnadas, a Glasgow psychiatrist, sets out to explore whether a new type of MRI scanning could be of value. It's called 'MRI connectivity'. Instead of producing pictures of structures in the body, it produces diagrams of the network of connecting fibers in the brain. Scans of brain structure are generally normal in subjects with schizophrenia. The behavioural patterns could perhaps be explained by abnormalities in the connections between different parts of the brain.
To investigate this the researchers have to recruit patients who have never been on medication for schizophrenia – otherwise they might just be looking at effects of the drugs. That makes the study particularly challenging. However, the team has now managed to obtain scans on 8 of the 10 subjects that they proposed to investigate in this preliminary study, and they will soon be able to start to analyse the results. Several groups around the world have the technical expertise to undertake studies like this, but few have the clinical infrastructure to enable patients to be recruited.

2 Whole brain Human Ischaemic Stroke Perfusion and Extended Re-canalisation (WHISPER) -Pilot Study.

'Time is brain' is the slogan used to raise awareness of the need for rapid treatment following a stroke. This CT scan shows the problem. The part shown in red is at the centre of the region affected by the blockage in blood supply. It will not recover. However, the part in green still has some blood flow, but this is significantly reduced. This section of the brain is at risk if it is not treated with a clot-busting drug.

Current guidelines are that treatment has to be administered within 4.5 hours, otherwise it's too late, but specialist neurologists suspect that this time window could be extended in some cases. That's what is being explored in this study. The research team is led by stroke specialist Professor Keith Muir.

Preliminary results suggest that up to 40% of stroke patients who reach hospital between 4.5 and 24 hours after onset might benefit from clot-busting treatment. The Neurosciences Foundation supports small studies that explore what should be researched on a larger scale. This is shaping up to fit into that category. Considering that there are around 133,000 strokes of this type in the UK every year, the benefit to patients could be considerable.

3 Early detection of deterioration in children who have had a head injury.

This project is led by consultant neurosurgeon Mr Roddy O'Kane and clinical scientist Dr Ian Piper. Supported initially by the Neurosciences Foundation, and then by the EU, Ian established a European network called BrainIT. This has enabled bedside monitoring measurements on adults in neurological intensive care units from around Europe to be standardised so that research studies can include a much larger patient population than would otherwise have been possible. Research findings will therefore be much more rigorous. The network is investigating why patients often develop unexpected complications after head injuries. These are generally the result of a rise in pressure in the brain, but why this happens in some patients and not others is not clear. Our recent funding was to enable the researchers to set up a similar network for children's intensive care units because a child's brain does not always behave in the same way as an adult one. This network has been established and has Centres in Glasgow, Edinburgh, Birmingham, Liverpool, Oxford, Nottingham, Newcastle, Barcelona, Leuven (Belgium) and Iasi (Romania) plus Bristol, London (St George's), Manchester, Riga in Latvia, and Bucharest in Romania.

The project has now been completed, and has helped the research team to secure further grant income. This includes an **EU Grant of 600K Euro's** from the EU ERA-NET-NEURON programme to undertake specific studies using the network infrastructure. This demonstrates that the leading European scientists in this field consider that the work is extremely valuable and is likely to lead to improved care of children in intensive care units.

The Miss MJM Smith's Trust has made contributions towards these three projects.

The work in the five studentships supported by the Foundation will be described by our students.

4.The Multiple Sclerosis project – Tim Morgan

Two of the students are working to develop materials for use with positron emission tomography – a medical imaging technique that detects specific molecular substances in the body. Tim was our first NSF student. He is being supervised by Dr Andrew Sutherland, an organic chemist who has the skills necessary to develop these materials. Tim is producing novel chemical compounds that could be used to assess drugs that are being developed to treat patients with multiple sclerosis. Faults develop in particular molecular processes in the body and this leads to MS. Drugs could counteract this, but we need to be able to see whether or not they are doing so. Just waiting to see if the symptoms improve isn't good enough. This would take time and other factors could affect symptoms. We need direct measurements of drug action. PET could do that if appropriate materials can be developed.

5. The Brain Tumour project - Maria Clara Liuzzi

Maria is the second student. She is being supervised by Professor Anthony Chalmers – a brain cancer specialist at the Beatson. Her project is similar to Tim's but the target is very different. The aim is to develop materials to study glioma, an aggressive form of brain cancer. Sadly, effective treatments for glioma are still elusive, but the group at the Beatson have made some exciting discoveries and their work is held in high regard internationally.

They are studying irregularities within a protein called PARP that has a role in the repair of breaks in DNA strands.

6. The Parkinson's Disease project - Callum Smith

Callum is the third student. He is working with Dr Donald Grosset who is an expert in Parkinson's Disease. Some PD patients develop dementia, and one of the big challenges for doctors is to determine whether the dementia is due to PD or is another type, such as Alzheimer's Disease. Callum has access to a large dataset from a national UK study on PD. He has sifted through that to look for patterns that might help to characterise the dementia. The research team is now conducting a prospective study to test the findings on a group of patients in the west of Scotland.

7. The head injury project - Katerina Pappa

Katerina is student number four. The title of her project is *'Development and evaluation of a novel treatment intervention for people with acquired brain injury'.* The objective is to explore ways of reducing the impact of cognitive deficits. Currently patients who have damage to the brain resulting from a head injury or stroke often receive physiotherapy to help to restore physical function but therapies for mental function are not in widespread use. This is often a rate-limiting step in the quest for independent living. Katerina is working with Professor Jonathan Evans and colleagues at the Institute of Health and Wellbeing at the University of Glasgow. They will develop a novel intervention by combining two approaches: goal management training based on mental strategies, and working memory training based on core cognitive processes. The difficulty of the training programme increases as the patient progresses. So far this type of rehabilitation hasn't been subject to rigorous scientific evaluation. Now it will be. Matched funding is being provided by the Theresa and Mortimer Sackler Foundation.

8. The stroke project - Fraser Snedden

Fraser is the fifth student. His project has a nifty title - Magnetic resonance imaging to Assess Carotid- Brain interactions in people with stroke (MAC-Brain). This is a programme of work led by Dr David Alexander Dickie at the stroke unit at the Queen Elizabeth University Hospital in Glasgow. MRI scans of the neck are used just now on stroke patients to help to identify the cause and predict the likelihood of mental deterioration, but the scan reporting depends on the experience of the doctors and is very subjective. Fraser is working in David's team on the development of computer image analysis software to automate the process. This should make it more reliable and enable these measurements to be used in large research studies. Matched funding is being provided by the British Heart Foundation Cardiovascular Research Centre at Glasgow University.

The last two of these studentships are being supported by the Margaret Murdoch Charitable Trust.