

# New Developments in Clinical Trials in Neuroscience & Psychiatry

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Translational neuroscience offers enormous potential, but has yet to deliver really substantial benefits for patients with the disorders of the nervous system that cause such a large burden of disability: stroke, dementia, neurodegenerative diseases and the major psychiatric disorders. This meeting sought to take a step back to examine the strengths and weaknesses of translational research in the field, to identify key barriers and potential solutions. Gordon Murray, Professor of Medical Statistics at The University of Edinburgh gave the opening lecture which set the scene. He drew a sharp contrast between cardiology and neuroscience. In cardiology, the availability of useful and reliable surrogate markers (coronary artery patency, left ventricular function, blood pressure) had underpinned the development of large-scale trials able to detect effects on major clinical outcomes. These trials then established the benefits of aspirin, beta blockers, angiotensin converting enzyme inhibitors and thrombolysis, just to name a few. By contrast, in acute stroke, thrombolysis had skipped the translational pathway and was developed in stroke 'on the back of' experience in cardiology. Neuroprotection, which had shown so much promise in animals, has yet to show benefits in man. Very presciently, Professor Murray outlined the themes that many of the speakers would return to during the afternoon. The most important of these was the need for careful methodological development of better surrogate markers, both of the underlying biological processes, but also of the clinical outcomes those processes were mostly likely to influence. Professor Joanna Wardlaw then went on to outline the rather chequered history of imaging as a surrogate outcome in acute stroke research. One illustrative example which she drew on, was the use of advanced neuroimaging to outline cerebral tissue that was ischaemic but potentially rescueable by therapy. Whilst it is relatively straightforward to produce attractive colour-rendered pictures of cerebral perfusion it has become clear that the use of different measurement algorithms can produce radically different results. In brief, there is a need for much greater methodological rigour in the development and application of such techniques and the research community needs to reach consensus on an optimal and standardised approach. Several of the themes of her talk are reflected in a recent editorial in the journal 'Stroke'.

Next on the podium was Professor Stephen Lawrie, Professor of Psychiatry and Neuroimaging at The University of Edinburgh, who outlined the promises and challenges of



neuroimaging in major psychiatric disorders. His talk ran along the theme that although there were undoubtedly structural and functional changes in the brain in people at risk of, or with established psychotic disorders, there were many challenges in measuring these changes precisely or understanding their underlying biological substrate. Multicentre imaging studies, offer greater statistical power to help detect and clarify the nature of the subtle structural and functional changes that occur in the brain. Neurogrid, Neuropsygrid and the Scotland-wide SINAPSE collaboration certainly seem to be forging ahead, developing the technological advances needed that will facilitate multicentre imaging studies to help take the field further forward.

Dr Roger Staff from the University of Aberdeen showed results of work in progress on the use of SPECT and PET imaging in dementia and Alzheimer's disease. The techniques do seem to show promise as useful surrogate outcomes and the promising results in a small phase II trial are now being tested on a larger scale in a phase III trial of a therapeutic agent for this major group of diseases.

Dr Carl Counsell moved away from imaging to consider how to improve the clinical assessment of outcome in Parkinson's Disease and neurodegenerative disorders. His talk was a reminder that while biomarkers (imaging, molecular biology and genetic) have some role in the assessment of new treatments for Parkinson's Disease and in neurodegeneration, in parallel with those developments, the science of clinical measurement needs to be applied to assess the impact of disease on the patient and their life. He outlined the path forward that developments in clinimetrics would need to take to achieve this goal.

This exciting and fruitful symposium was rounded off by a lecture from Dr Walter Koroshetz, Deputy Director of the National Institute of Neurologic Disorders and Stroke, at the National Institutes of Health, Bethesda, USA. He outlined themes that were all too familiar to the audience: the difficulties of moving successfully from identifying a potential therapeutic target, selecting an agent that might act on that target and then establishing its effects in animals and subsequently in humans. In parallel with the challenges of scientific development of agents, there is also a difficulty – on both sides of the Atlantic – of developing the careers of the next generation of clinical trialists. They will need stamina to overcome the bureaucratic and organisational hurdles to clinical trials and combine it with the scientific vision and charisma that are needed to lead the large collaborative groups to undertake multicentre international clinical trials. He ended on a note of optimism. Whilst these problems are significant, they are all potentially soluble and we must work on them one step at a time.

This well-attended meeting was supported by the following academic institutions, research groups and NHS research networks: The University of Edinburgh Centre for Clinical Brain Sciences, Edinburgh Neuroscience, the Edinburgh Clinical Trials Unit Collaboration, the Scottish Collaboration of Trialists, the Scottish disease-specific research networks in stroke, mental health and neuro-degenerative disorders, the SFC Brain Imaging Centre and a grant from The Royal Society of Edinburgh. ♦

The lectures are available on-line at  
<http://www.cbs.ed.ac.uk/bcm.html>