

Neurology Symposium

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DECLARATION OF INTERESTS The author was a member of the organising committee for this symposium.

INTRODUCTION

Neurological disorders are common, yet their diagnosis is often challenging and effective therapies are frequently perceived as limited. This symposium provided an overview of disorders related to muscle, demyelination, sleep and orthopaedic neurology, together with an insight into emerging stem cell technologies. The breadth of topics was matched by a varied audience, which included general practitioners, neurologists, physicians, trainees and medical students.

SESSION 1 FLEXING MUSCLES

Dr Kevin Talbot (Professor in Clinical Neurology, University of Oxford) emphasised the heterogeneity in presentations of motor neurone disease, caused by the convergence of inherited and acquired defects in multiple biological pathways.¹ Recent genetic and pathological advances have contributed to a greater understanding of why motor neurones are vulnerable to degeneration. The diagnosis remains a clinical one with support from paraclinical tests. Investigations are helpful in excluding mimics such as degenerative disease of the cervical spine and multi-focal motor neuropathy with conduction block. An improved understanding of disease pathogenesis has yet to translate into effective disease-modifying therapies, although there has been progress in supportive therapies such as gastrostomy and ventilatory support.

Dr Cheryl Longman (Consultant Clinical Geneticist, Western General Hospital Edinburgh) continued with an insightful summary of inherited muscle disease. These disorders are not uncommon, with a prevalence of one in 2,000 – reflecting approximately 2,500 affected individuals in Scotland. Genetic testing provides prognostic information and may help to begin effective treatments in disorders due to inherited enzyme deficiencies such as Pompe disease. Systemic complications can also be targeted; for example reducing the risk of sudden cardiac death by implanting cardiac defibrillators in laminin myopathies. Detailed clinical evaluation and genetic blood testing allow recognition of the more common muscle diseases. Advancing genetic technologies will expand the range of genes for which testing is readily available.

Dr James Miller (Consultant Neurologist, Royal Victoria Hospital Newcastle) completed the session by considering the diagnosis and treatment of inflammatory myopathies. Key investigations include autoantibodies such as anti-Jo 1, anti-Mi2 and antisignal recognition protein (anti-SRP). Novel myositis-specific antibodies are emerging including anti-155/140-kDa polypeptide (anti-p155/140) and anti-140-kDa-polypeptide (anti-p140). Other useful tests include muscle biopsy, magnetic resonance imaging (MRI) of the muscles and neoplasia screen. Established immunosuppressive therapies, including steroids, intravenous immunoglobulin and plasma exchange, are effective for most patients with dermatomyositis and polymyositis. Azathioprine, methotrexate and mycophenolate mofetil may be used as steroid-sparing agents while more directed monoclonal therapies such as rituximab are also emerging.

SESSION 2 LEARNING FROM OTHER SPECIALTIES

Neuropathic pain caused by injury to peripheral nerves may be exceptionally severe. Professor Rolfe Birch (Professor of Neurological Orthopaedic Surgery, Royal National Orthopaedic Hospital, Middlesex) delivered an update on complex regional pain syndrome. The mechanism of pain and potential therapeutic interventions were discussed.

Dr Paul Reading (Consultant Neurologist, James Cook University Hospital, Middlesbrough) described the range of normal sleep before considering sleep disorders associated with ageing, the investigation and management of excessive daytime sleepiness, insomnia and parasomnias.² Increased fragmentation leads to less robust sleep with normal ageing. Excessive daytime sleepiness is reported by up to 5% of the population and arises secondary to primary sleep disorders, circadian malalignment and chronic medical, neurological and psychiatric disorders. Insomnia is probably the most common sleep disorder, and often arises due to hyperarousal and concerns over reduced sleep. Parasomnias are sleep dysfunctions associated with disturbance, some of which may be normal variants.

SESSION 3 DEMYELINATING DISEASES

Dr Raj Kapoor (Consultant Neurologist, The National Hospital for Neurology and Neurosurgery, London) presented an update on multiple sclerosis. While diagnosis remains based on clinical manifestations, advances in neuroimaging have led to a revision of diagnostic criteria, allowing new brain lesions on MRI to indicate dissemination in time and place after a single attack.³ The recognition that neurodegeneration occurs from disease outset has focused research on disease modification and neuroprotection. First-generation disease-modifying therapies (interferons and glatiramer acetate) have some clinical effect and are generally well tolerated. Oral agents, including fingolimod and cladribine, are emerging although long-term risks of infection, malignancy and autoimmune disease associated with these are uncertain. Meanwhile, supportive treatment is best undertaken in multidisciplinary settings with a focus on mobility, spasticity, pain and bladder dysfunction as well as cognitive impairment and fatigue.

Dr John Winder (Consultant Neurologist, University Hospitals Birmingham) highlighted the broad spectrum of Guillan-Barré syndrome (GBS) currently described. Patients may have axonal or demyelinating neurophysiology, with clinical subtypes including motor, sensory and autonomic involvement, as well as the rarer Miller Fisher and cervico-pharyngeal variants. A spectrum of antiganglioside antibodies have been described, leading to greater understanding of GBS. Intravenous immunoglobulin and plasma exchange effectively accelerate recovery but do not influence the prognosis of the small proportion of patients with severe morbidity. Emerging monoclonal antibody treatments such as eculizumab may be effective in targeting complement response at early stages of illness.

SESSION 4 NEUROSCIENCE MADE POPULAR

When discussing treatment of neurological disease, it is not uncommon for patients to ask: 'What about stem cells, doctor?' Dr Jo Mountford (Senior Lecturer in Stem Cell Technology, University of Glasgow) helped to provide an answer by explaining what stem cells are, where they are derived from, potential applications in treatment of neurological disease, as well as common misconceptions and potential pitfalls with their use.

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- 3 Polman CH, Reingold SC, Edan G et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to 'McDonald Criteria'. *Ann Neurol* 2005; 58:840–6. doi:10.1002/ana.20703
- 4 Greenfield S. *Tomorrow's People: how 21st century technology is changing the way we think and feel*. London: Penguin; 2003

Baroness Susan Greenfield (Professor of Pharmacology, University of Oxford) delivered a thought-provoking consideration of why neuroscience is interesting to all. In considering the plasticity of the developing brain, the effects of an 'enriched environment' on the development of personality and individuality were speculated upon. A changing childhood environment may lead to improved information-processing skills, but are other areas of human cognition likely detrimentally affected in a 'multi-tasking' technological era?⁴ Will individuals develop with shorter attention spans and reduced empathy as a result of decreased social interaction and, as 'sensation seekers', less aware of the consequences of their actions? Consideration was also given to neurodegenerative disease, in particular how advances in research are focussing on pre-symptomatic surrogate markers of degenerative disease and means for arresting and stabilising cell death. The symposium concluded with a reflection that neuroscience is fascinating to all because our brains reflect our individual experiences and by studying the underlying mechanisms we can more deeply appreciate the essence of our individuality.

TAKE-HOME MESSAGE

Substantial progress in basic neuroscience research has helped advance our understanding of the genetic, immunological and degenerative basis of many disorders. While neurology remains a clinical specialty requiring sound bedside acumen, progress in laboratory and imaging investigation techniques has contributed to real advances in achieving accurate diagnoses. Emerging immunomodulatory, enzyme replacement and regenerative therapies, coupled with progress in multidisciplinary supportive treatments, are providing greater promise and expectation for patients and clinicians alike.