

14th International ALS/MND Symposium

17-19 November, 2003; Milan, Italy

Each year for the past 14 years the Motor Neurone Disease clinical and research 'community' (and an increasing number of people with MND) have assembled to share the latest research into this most devastating of neurological diseases. In keeping with the difficult nature of the condition, most of the presentations given demonstrate the necessity of international collaboration. In this respect one has to acknowledge the role of the Motor Neurone Disease Association in being a catalyst for change in bringing together basic and clinical researchers on one hand and patients and carers on the other.

MND/ALS remains a clinical diagnosis. The identification of a biomarker for ALS would have the effect of improving the accuracy and speed of early diagnosis, help to dissect out the relationship between different forms of motor neurone disease and provide an objective measure of progression for clinical trials. New technology in the form of protein chips provides the potential to produce a molecular signature of the disease to act as a biomarker. A combined study from Boston and Pittsburgh used CSF from patients with ALS on CIPHERGEN® protein chips which use a novel physical method to profile the protein content of biological material. Using complex statistical algorithms they reported that their method could reliably identify about 80% of patients with ALS, with a few false positives. Sounds marginally less accurate than a clinical neurologist but it is a promising approach in principle.

The search for therapies for MND has recently taken on a high throughput screening approach. Lucy Bruijn, the research director of ALSA (the US ALS Association), described how, under the umbrella of the National Institutes for Neurological Diseases and Stroke (NINDS), 1040 compounds (750 FDA approved) have been screened for efficacy in motor neurone diseases. This has involved approximately 20 centres in the USA and Europe which have some sort of in vitro assay of motor neurone survival (e.g. glutamate toxicity). This work has produced the surprising result that 3 types of cephalosporin seem to have a motor neurone protective effect and that ceftriaxone in particular may be useful. However, it was a little depressing to note this produced a modest survival in G93A SOD1 mutant mice (the archetypal animal model of ALS). Overall, this very expensive and labour intensive enterprise has not been a conspicuous success.

In much of the experimental work on ALS/MND in the past there has been undue focus on the cell body as the seat of the pathophysiology of the disease. Axonal and dendritic processes account for at least 95% of the volume of a motor neurone and it was therefore encouraging to see that increasing attention is now being given to role of axonal degeneration. Chris Miller from Kings College in London reviewed the evidence that axonal protein transport is dysfunctional in transgenic mouse models of ALS.



Dr Letitia Mazzini, who presented the session on stem cell transplants

Glass and colleagues from Emory University in Atlanta presented some elegant longitudinal traditional neuropathological studies in transgenic mice harbouring human SOD1 mutations. Mice were examined at 28, 47, 80 and 120 days post-natally. The first signs of pathological change were evident by day 47 in the motor end plate. This is before the disease is clinically evident in the mice. By day 80 when mice have overt muscle weakness as evidenced by poor performance on a rotarod test, 60% of ventral roots have degenerated. Remarkably motor neurons in the spinal cord are not reduced in number, suggesting that the disease process begins in the periphery. A patient with early MND who died unexpectedly was examined at autopsy and showed similar degenerative changes in the NMJ and ventral roots. On a similar theme Michael Sendtner, working on autosomal recessive Spinal Muscular Atrophy due to mutations in the SMN gene, demonstrated that the specific transport of subclasses of mRNA in the axon may be critical for motor neurone integrity.

Away from the sober world of hard science, two more sensational presentations caused quite a stir. A group of Italian Neurologists from Turin have performed a 'feasibility' study of direct intraspinal implantation of mesenchymal (bone marrow) stem cells (MSCs) in ALS. Seven patients had autologous MSCs which had been expanded in culture for 32 days, implanted by directly surgically exposing the thoracic spinal cord. The best that could be said was that this extraordinary procedure did not seem to hasten the disease. Just because it is feasible does not mean it is justified. Explaining this to patients in the MND clinic, who are understandably desperate, is not easy. Perhaps the most lively session of the whole meeting was from Deborah Annetts who is the chief executive of the Voluntary Euthanasia Society (who incidentally have removed the word Euthanasia from their website and are now known as VES!). She is a lawyer by training and an impressive and professional proponent for the cause of 'choice' in when to end life. This is a profoundly serious and controversial issue and was a brave choice for a platform presentation to an audience including carers and patients. Whatever the legal or moral position surrounding assisted suicide no one can doubt that an open and honest discussion is to be welcomed.



Delegates at the conference

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