

Nutrition and stem cells as emerging therapies for neurodegenerative disease

Neurodegenerative disease represents an ever-increasing burden to the UK, measured both in decrease in the length and quality of life for patients, and in rising economic cost to the NHS and social care. For example, the prevalence of Parkinson's disease (PD) in the UK is predicted to almost double between 2018 and 2065, from approximately 145,000 to over 256,000 cases. Like PD, dementia (including Alzheimer's disease), Huntington's disease (HD), multiple sclerosis (MS) and other neurodegenerative disorders continue to challenge researchers and clinicians alike; with little in the way of curative therapies in the pipeline.

Research into the treatment of neurodegenerative disorders is currently focusing on key areas: prevention of onset, neuroprotection, delaying or halting disease progression, and cell replacement. The role of nutrition, both during neural development and throughout life, is now being widely investigated; and nutritional supplementation is being evaluated as a neuroprotective therapy. With the discovery of stem cells, cell replacement therapies are now more widely considered to be a realistic option for patients with specific neurodegenerative diseases.

Nutrition

Essential nutrients, and in particular vitamins, have been linked widely with neurodegenerative disease. For example, it is well established that levels of vitamin D decline in older individuals and are generally lower in populations living in northern latitudes. Vitamin D deficiency has been linked with multiple sclerosis and more recently PD, and this vitamin is currently being tested as a neuroprotective therapy in clinical trials for MS.

Conversely excess nutrients might also be damaging to the central nervous system and there are emerging theories that modern diets may expose neurons to toxic levels of metab-

olites. Nicotinamide is one such compound. Found in large quantities in red meat, nicotinamide is a precursor to NAD⁺ the metabolite, integral to the production of energy (ATP) within mitochondria. NAD⁺ levels need to be tightly regulated for normal cellular function, and mitochondrial dysfunction is a key hallmark in multiple neurodegenerative diseases.

There is a plethora of evidence that nutrients and vitamins play a critical role in neural development. For example: retinoic acid (vitamin A), ascorbic acid (vitamin C) and 2 nicotinamide can all influence the conversion of stem cells to neural cells and subsequently neurons.

Thus, there is a clear need to balance nutrient levels both in the developing brain and throughout life. Working at the subcellular level, essential nutrients influence energy supply to neurons, mitochondrial function, and many other cellular processes. There is evidence to suggest that these nutrients may also act on non-neuronal cells within the CNS, including astroglia and immunomodulatory microglia. Therefore, adapting the nutritional balance of those suffering from a neurodegenerative disease may provide a simple yet effective therapy, potentially to slow disease progression or enhance quality of life.

Stem cells and cell replacement therapies

More than four decades of research has been conducted on identifying a suitable cell source for replacement therapies for neurodegenerative disorders, particularly for PD and HD. Indeed, founding editor of ACNR, Professor Roger Barker, currently leads an EU consortium conducting clinical trials in foetal tissue transplants for PD.

Since the early 1990s stem cells have been proposed as a sustainable, reliable and safe source for neuronal replacement. Following extensive laboratory research across the globe,

this work is reaching a critical juncture with the launch of two clinical trials involving transplantation of neural progenitors derived from human pluripotent stem cells: at Kyoto University, Japan; and through the New York Stem Cell Consortia, USA.

Key to success in converting stem cells to functional mature neurons that could be used for cell replacement is the recreation of an optimal environment for stem cell differentiation in the laboratory, i.e. mimicking the developing brain in the culture dish.

This creates the unique opportunity to merge nutritional neuroscience and stem cell technology.

The "nutrition and stem cells" series for ACNR will explore key issues and latest research into nutritional neuroscience and stem cells, as emerging therapies for neurodegenerative disease. Focus will be on current research, including: nicotinamide, vitamin D and other essential nutrients; their roles in neuronal development, stem cell differentiation, immune modulation, neuroprotection and potential for clinical application.

The series will also feature updates from ongoing clinical trials using stem cell transplants and will explore the future of this emerging therapy for neurodegenerative disease.

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Cancer anti-sickness drug could offer hope for hallucinations in Parkinson's

Parkinson's UK is partnering with UCL, and investing £1 million in a pioneering phase II clinical trial to explore if the drug ondansetron is safe and effective against hallucinations.

Visual hallucinations are when people see things that aren't there and may affect up to 75% of people with Parkinson's at some point during the condition.

The 12-week trial is set to recruit 216 people over two years in 20-25 NHS clinics across England, Scotland and Wales. Participants will either receive drug or placebo tablets, to take at home for 12 weeks.

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