NEURAL REPAIR: THE FUTURE OF STROKE MEDICINE? (Dr. M. Banovic)

Introduction

- Current standard of care for stroke is primarily based on reperfusion therapy on a select few patients who meet criteria for reperfusion and have access to the treatment facilities. Most stroke patients worldwide cannot access this kind of treatment as much of the world does not have access to CT scans, let alone specialist neuroradiological intervention for reperfusion therapy.
- The availability of treatments which encourage neural repair after a stroke has occurred has the potential to lead to more people accessing treatment, albeit in a different form, days or even months after a stroke has occurred, resulting in less disability in stroke patients.
- Drug and cellular treatment will be focused on as it has the potential to be disseminated to a wider patient base than other forms of treatment like robotics.

Stem Cell Treatment [1]

- Stem cell research holds great promise for the future because of the potential to regenerate neural tissue. It still attracts controversy due to the origin of the cells used for treatment (fetal, placental or adult mesenchymal cells).
- Least controversial is the use of autologous or allogenic mesenchymal stem cells of adult origin which have been shown to differentiate into neural tissue. Angiogenesis, neurogenesis and formation of new neural circuitry have been shown at an experimental level. Current limitations include significant side effects (seizures, thrombosis, cancer development and death), and uncertainty of timing of treatment, number of cells to give and optimum route of delivery

HIV drug for stroke treatment?[2]

- The CCR5 antagonist Maraviroc has shown promise in use post-stroke to encourage recovery. Its use was spurred on by the discovery that there was a large upregulation of CCR5 levels in patients brains post-stroke. It has been shown to preserve dendritic spines and has been associated with the formation of new neural projections to the contralateral premotor cortex thus resulting in greater improvement in motor function in the epoch post stroke as compared with placebo.

C3a Peptide[3]

- Still in the experimental stage, induced stroke in mice followed by daily intranasal C3a peptide a week after the stroke led to a greater clinical improvement than those not on C3a. It is suggested that this therapy encourages post ischemic neuroplasticity.

Growth Factors and monoclonal antibodies [4]

- Growth factors have been suggested for trials in neural repair as it was shown that erythropoietin, beta-hCG and epidermal growth factor led to clinical improvements, possibly by neuronal stem cell proliferation. Not enough data is available on growth factors at the moment though.
- Monoclonal antibodies have the potential to provide a permissive environment within which neurons can regenerate by blocking inhibitory proteins within the CNS such as myelin associated glycoprotein, oligo-myelin glycoprotein and Nogo-A. Conflicting results have been obtained with their use in several trials and this underpins the need for larger and more robust trials in the use of these molecules.

Perispinal Etanercept [5]

- Peri-spinal Etanercept (an anti-TNF molecule) is being used by a clinic in the USA for stroke patients long after an ischemic event. No placebo-controlled trials have been done and its use is currently not approved by the American Academy of Neurology. Observational studies have been done showing rapid improvement in post-stroke patients. Unfortunately no corroborating evidence has been obtained by doctors outside the group of authors for the supporting paper.
- Randomized controlled trials are being carried out in Australia on this treatment and is currently in phase I/II.

References

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