Excitotoxicity and nerve cell death

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Neural excitotoxicity can be involved in spinal cord injury, traumatic hearing loss and Alzheimer's. The Stressprotect project has gathered data on this often devastating phenomenon at biochemical, genomic and physiological levels.

Excessive stimulation by neurotransmitters such as glutamate causes nerve damage. Overactivation of glutamate receptors allows high levels of calcium ions to enter the cell which in turn activates a number of cell structure destruction routes.

The exceptional significance of excitotoxicity to neuronal degeneration renders this area an important research target. The Sixth Framework Programme (FP6) project Stressprotect focused on a particularly important pathway, c-Jun N-terminal kinase (JNK) to develop new ways

to prevent neurological disorders caused by excitotoxicity.

Project scientists investigated the action of D-JNKI1, a peptide that is a potent inhibitor of cell death prompted by the JNK pathway. A complete characterisation of its interaction as a drug and the effects on nerve tissue was compiled.

One big plus is that D-JNKI1 displays selective action – it is taken into neurons where it is needed. Moreover, using in vitro and in vivo excitotoxicity models, D-JNKI1 was shown to afford protective and beneficial neuroprotection. Damage was averted during ischaemia (loss of blood supply), seizures, severing of a neuronal axon, Alzheimer's and traumatic hearing loss.

Importantly, when D-JNKI1 was applied with pure oxygen at pressure several hours after an episode of cerebral ischaemia, the area of tissue death was reduced by up to 83%. After a stroke, neurological scores and behaviour showed a lasting improvement.

Success of Stressprotect is mirrored in publication of results in some five high-ranking science journals. The Federation of European Neuroscience Societies (FENS) also presented the project's data detailing its significance to the treatment of neuronal death, central to many neurodegenerative diseases.

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