Nitric oxide can alter brain function

November 26 2008

Research from the Medical Research Council (MRC) Toxicology Unit at the University of Leicester shows that nitric oxide (NO) can change the computational ability of the brain. This finding has implications for the treatment of neurodegenerative diseases such as Alzheimer's Disease and our understanding of brain function more generally.

The research is led by Professor Ian Forsythe and is reported in the journal *Neuron* on 26th November.

Professor Forsythe, of the MRC Toxicology Unit, explains: "It is well known that nerve cells communicate via the synapse – the site at which chemical messengers (neurotransmitters such as acetylcholine or glutamate) are packaged and then released under tight control to influence their neighbours.

"Nitric oxide is a chemical messenger which cannot be stored and can rapidly diffuse across cell membranes to act at remote sites (in contrast to conventional neurotransmitters which cannot pass across cell membranes).

"It is broadly localized in the central nervous system, where it influences synaptic transmission and contributes to learning and memory mechanisms. However, because it is normally released in such minute quantities and is so labile, it is very difficult to study.

"We have exploited an in vitro preparation of a giant synapse -called the calyx of Held, developed here at the University of Leicester in the

1990s- and its target in the auditory pathway to explore nitric oxide signalling in the brain.

"We show that NO is made in response to incoming synaptic activity (activity generated by sound received by the ear) and that it acts to suppress a key potassium ion-channel (Kv3). Normally these ion-channels keep electrical potentials very short-lived, but nitric oxide shifts their activity, slowing the electrical potentials and reducing information passage along the pathway, acting as a form of gain control.

"Surprisingly, the whole population of neurons were affected, even those neurons which had no active synaptic inputs, so indicating that nitric oxide is a 'volume transmitter' passing information between cells without the need for a synapse. Such a function is ideal for tuning neuronal populations to global activity. On the other hand, too much nitric oxide is extremely toxic and will cause death of nerve cells; so within the kernel of this important signaling mechanism are the potential seeds for neurodegeneration, which if left unchecked contribute to the pathologies of stroke and dementias."

In the future Professor Forsythe's research group will be trying to understand how these signalling mechanisms are applicable elsewhere in the brain and will investigate how aberrant signalling contributes to neurodegenerative disease processes such as in Alzheimer's disease..

Source: University of Leicester