Neuropharmacology Laboratory

Group Head
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Specific Interests
My laboratory is interested in investigating the role of ionotropic receptor families (e.g., glutamate, GABA and nicotinic receptors) in neurological disorders such as Parkinson’s Disease, Alzheimer’s Disease and Schizophrenia, as well as in the neurodegenerative / neuroadaptive processes that may be associated with these diseases.

Current projects
Nicotinic Receptors, Dopaminergic and Serotonergic Neurotransmission and Schizophrenia:
Schizophrenia is a common and complex disorder with a range of symptoms including auditory hallucinations, delusions and flattened affect. A substantial component of schizophrenic symptomatology appears to arise from deficiencies in an ability to automatically filter or “gate” irrelevant thoughts and sensory stimuli from intruding into conscious awareness. In schizophrenic patients, there is a higher than normal prevalence of tobacco smoking (90%). Several studies have since demonstrated that nicotine, administered either through smoking or gum, transiently normalizes some of the symptoms of schizophrenia, including several sensory gating deficits. Conversely, worsening of symptoms occurs following smoking cessation. We believe the most interesting finding to date is that schizophrenic smokers show a significantly greater clinical response to the atypical antipsychotic clozapine than do schizophrenic non-smokers. The aim of this project is to understand why nicotine potentiates the beneficial actions of atypical antipsychotics such as clozapine.
**APoE, statins cholesterol and Alzheimer's Disease**

The pathophysiology of Alzheimer's disease is thought to be due to the accumulation of beta-amyloid in the brain. Beta-amyloid is derived from APP (amyloid precursor protein). Through different enzymic pathways (alpha, beta and gamma secretases) APP can give rise to APPs, which is neuroprotective and has trophic effects or beta-amyloid; which is neurotoxic and neurodegenerative. There is evidence to suggest an important link exists between beta-amyloid, cholesterol and Alzheimer's disease; the prevalence of Alzheimer's disease is reduced in people taking cholesterol-lowering agents (HMG-CoA reductase inhibitors / statins such as simvastatin). There is now some evidence suggesting that statins reduce beta-amyloid production both in vitro and in vivo; and that this might be due to the shunting of APP towards the increased production of APPs and decreased production of beta-amyloid. ApoE exists in three major forms, ApoE, ApoE, and ApoE, of which ApoE is the most common form, with the ApoE form being much weaker in biological function. ApoE has several functions in the body; it important in cholesterol transport and clearance. Some disease states are associated with the disruption of normal ApoE function. For example, the presence of ApoE form reduces the efficacy in transport and regulation of cholesterol levels, and the presence of this form in humans is a high risk factor for the development of Alzheimer's disease (AD). There is increasing evidence that ApoE has roles in synaptic remodelling, repair, and regeneration after brain injury that are independent of its role in cholesterol transport. Studies have suggested that ApoE may be increased in brain responses to neuronal injury or disease, and its presence has been shown to improve the outcome after brain injury. Mice which are deficient in ApoE, or mice which have ApoE form have been shown to respond poorly to brain injury. The mechanism by which ApoE protects or modifies the outcome of brain injury and the impact of this on ongoing neurodegenerative diseases is not yet understood.

**Inflammatory Processes in Parkinson's Disease**

Parkinson’s disease (PD) is a multifactorial disease and is characterised by a loss of the transmitter dopamine and most animal models try to mimic this loss by the selective destruction of the neurones that contain this transmitter. Recent evidence however suggests that the part of the process of neurodegeneration involves the activation of inflammatory mechanisms. In order to target therapy for PD, the underlying cause for its incidence and progression must be better understood. It is likely that the inflammatory process accompanies the loss of dopamine in PD, but how inflammation effectively kills neurones is unclear. This project use a model of PD that involves inflammatory processes and examines the role and production of reactive oxygen species (ROS) as part of the process that leads to dopaminergic cell death and the development of PD. Specific aspects of the project examine the role of NADPH oxidase (and its isoforms) in the generation of ROS.
Nicotinic Receptors in Parkinson's Disease

There are 2 main types of nicotinic receptor present in brain, the alpha4 and the alpha7 type, although many additional types also exist. Nicotinic receptors are largely localized to basal ganglia structures and thus are of direct relevance to the fine control of movement. Interestingly, in Parkinson's disease there is a loss of nicotinic receptors in these regions. Our studies have focused on whether nicotinic receptor activation can slow the neurodegeneration seen in Parkinson's disease. We have already shown that the activation alpha4 type nicotinic receptor is important in preventing neurodegeneration in animal models of Parkinson's disease. What we don't know is whether these are the only types of nicotinic receptors involved.

Endocannabinoids in Neuroprotection

The endocannabinoid systems comprises the endogenous lipids anandamide and 2-arachidonoylglycerol (2-AG), the proteins responsible for their biosynthesis, uptake and inactivation, and the receptors through which their responses are mediated; the cannabinoid receptors (CB1 and CB2). This system is proposed to be involved in various neurodegenerative diseases such as Parkinson's and Huntington's diseases as well as Multiple Sclerosis. It has been demonstrated that the endocannabinoid system can protect neurons against some forms of neuronal damage.

Members of Laboratory

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Recent selected publications


