Neurophysiology

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Title of project or programme

Neurophysiology

Principal Investigators of project/programme grant

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Source of funding information

Medical Research Council

Total sum awarded (Euro)

1637013.08

Start date of award

01-04-2006

Total duration of award in months

48

The project/programme is most relevant to

Parkinson’s disease

Keywords
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The overall aim of our research is to provide a more detailed understanding of the anatomy and physiology of midbrain dopamine neurons and their associated neural networks. In addition, we examine the effects of drugs of abuse on the brain, in an attempt to gain insight into the molecular basis of addiction. We use a combination of high-resolution in vitro and in vivo electrophysiological

and neuroanatomical techniques in rats and mice. Dopamine neurons play key roles in processing and learning about rewards. Dopamine neuron dysfunction is implicated in a range of disorders: for example, selective degeneration of substantia nigra pars compacta (SNpc) dopamine neurons underlies Parkinson's disease; classical anti-psychotics are dopamine receptor antagonists, implicating dopamine hyperfunction in schizophrenia; and drugs of abuse elevate dopamine levels and induce long-term molecular changes in the dopamine system that underlie compulsive addictive behaviour. We have recently shown that a sub-population of presumed dopamine neurons in the ventral tegmental area (VTA) are, in fact, not dopaminergic. Because these neurons were previously assumed to be dopaminergic, little is known about their anatomy and physiology and how that differs from dopamine neurons. One important difference concerns their responses to aversive stimuli. We found that dopamine neurons are uniformly inhibited by an aversive stimulus, which is consistent with reward theories of their function. In contrast, the non-dopamine neurons were typically excited by the aversive stimulus, which suggests that they may encode information about motivationally-important stimuli in a manner distinct from dopamine neurons. Part of our current research is focused on characterizing the in vivo physiology and anatomy of these non-dopamine neurons. In particular we wish to know which neurotransmitters they release, where they project to, what information they encode and whether a similar population exists in the SNpc. We are also carrying out quantitative anatomical studies of neuron distribution within the VTA and SNpc. In addition, we continue to address fundamental questions about dopamine neurons. For example, although there are distinct subgroups of dopamine neurons (e.g., those that co-release neuropeptides and express calcium binding proteins such as calbindin) it is not known if they have distinct in vivo physiology. This may be of clinical relevance because these subgroups of dopamine neurons show differential vulnerability to Parkinson's disease. In the near future, we will extend this combined physiological and anatomical approach to include dorsal raphe dopamine and serotonin neurons.

Lay Summary