MODULATION OF TRANSMISSION AND EXCITABILITY IN SYMPATHETIC GANGLIA BY ANAESTHETICS AND OTHER DRUGS. A PRIMER ON GRANT AND MANUSCRIPT WRITING.

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Sympathetic ganglia are important physiologically for their role in regulating arteriolar tone, blood pressure and heart rate. They also provide excellent model systems for evaluating mechanisms of synaptic transmission and drug action. I shall discuss two examples of experimental findings relevant to anaesthetic action, and one of relevance to the development of analgesic and anti-epileptic drugs. In so doing, I shall describe the processes of publication, of obtaining research grant support and of setting up collaborative studies with academic and industrial colleagues.

1. In the early days of anaesthesia it was noted that some then-used barbiturates produced an undesirable fall in blood pressure. This was traced to a blockade of the nicotinic acetylcholine receptors responsible for transmission through the ganglia, through a hitherto-unknown mechanism of drug action, open ion-channel block.

2. Experiments on sympathetic ganglia were among the first to show that barbiturates and many other anaesthetics strongly potentiated the action of the inhibitory neurotransmitter γ-aminobutyric acid (GABA), an important component of anaesthetic action in the brain.

3. During intense sympathetic ganglionic discharge the released acetylcholine activates a second set of acetylcholine receptors, the muscarinic receptors, which can facilitate or even generate high-frequency postganglionic discharges. This turns out to result from the inhibition of a hitherto-unknown potassium current initially termed the “M-current” (now known to be carried by Kv7 potassium channels). The current is present in many neurons and axons in the central and peripheral nervous systems, and drugs that enhance the current are now in use or under development as anti-epileptic and analgesic agents.