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INTRODUCTION

Axon-glial interactions in the central nervous system

Axon-glial interactions are critical for brain information transmission and processing. In the CNS, this is a function of the major types of glia – astrocytes, oligodendrocytes and novel NG2-glia. This special issue of the *Journal of Anatomy* comprises contributions arising from a symposium entitled 'Axon-glial interactions in the CNS', held at the University of Portsmouth, UK in July 2010. The aim of the special issue is to bring together an international group of experts to demonstrate the current state of research in the diverse functions of glia in neurophysiology and neuropathology.

A major finding in recent years is that glia can form synapses, a feature once considered the exclusive domain of neurons. These neuron-glial synapses appear to be a unique feature of NG2-glia, and this issue starts with three papers reviewing our current state of knowledge in this field of research. The article by Sakry and colleagues introduces these enigmatic cells and reminds us that it is remarkable to think that we knew nothing of these cells until the generation of antibodies to the NG2 chondroitin sulphate proteoglycan (CSPG) almost 30 years ago by Stallcup and colleagues. It is now well established that NG2-glia, or at least a subpopulation of NG2-glia, serve as a pool of oligodendrocyte precursor cells (OPC) that generate oligodendrocytes throughout life and following demyelination. However, since Bergles and colleagues showed in 2000 that NG2-glia can form synapses, there has been an explosion of interest in these cells. A number of controversies have developed from the findings of different groups; the article by Velez-Fort and colleagues reviews these issues and discusses the relative importance of direct neuron-glial synapses and extrasynaptic modes of transmission between neurons and NG2-glia. A key aim is to determine the functions of neuron-glial synapses. Kukley and colleagues are at the forefront of this research and in their article they review the functional role of neurons in regulating the differentiation of NG2-glia and oligodendrocytes.

The fundamental roles of astrocytes and oligodendrocytes in the CNS are better known than those of NG2-glia. Remarkably, however, far less is known about how these cells interact with each other to maintain axonal function and viability. This is covered by the next two articles in the issue. There is no better illustration of the almost symbiotic nature of neuron-glial relationships than the interdependence between axons and the myelinating cells – oligodendrocytes. When these relationships go wrong, the results are devastating, as reviewed by Edgar and colleagues. Although myelination in the CNS is uniquely the function of oligodendrocytes, it is now becoming clear that astrocytes play a key role in orchestrating axon-oligodendrocyte interactions and myelination. The article by Barnett and colleagues describes their dissection of the interactions between neurons, oligodendrocytes and astrocytes using an exquisite co-culture system.

Synaptic signalling between neurons and glia is now an accepted fact in CNS grey matter. However, it is less appreciated that neurotransmission also occurs in CNS white matter, in the absence of conventional synapses. The physiological functions of neurotransmitters in white matter glia are unresolved, but Matute and colleagues discuss the evidence that they play a key role in white matter pathology. In contrast, Fern and colleagues move away from glial cells to introduce a largely overlooked cell – the pericyte. Pericytes surround blood vessels in the CNS and are believed to be important in regulating local perfusion. Fern and colleagues describe some novel morphological features of pericytes and provide evidence that they may be important in ischemia.

In addition to their key role in synaptic function and maintenance, astrocytes have recently been ascribed a new function: that of neural stem cell. Alzheimer's disease (AD) is the most widespread cause of dementia and is associated with the loss of synapses and neurodegeneration. Rodriguez and Verkhratsky review how the triple transgenic mouse model of AD has begun to provide new insights into the roles of astrocytes and impaired neurogenesis in the early stages of synaptic and cognitive impairment, before gross neurodegenerative changes.

In summary, this special issue touches on some of the recent advances in research on axon-glial interactions. We hope that the articles will stimulate readers to search beyond the neurocentric view of the brain and begin to appreciate how glia are critical for brain function and are central to CNS pathology. We would like to express our thanks to the Anatomical Society for supporting the symposium from which this special issue arose.

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