EDITORIAL
GLIAL CONTROL OF SYNAPTIC FUNCTION

Our view of glial function has undergone dramatic changes in recent years. For much of the past century, glial cells were believed to have little influence on neuronal responses. Glia were thought to provide structural and metabolic support to neurons, but not to interact actively with them.

Recent studies have demonstrated just how misleading was this classical view. Robust bidirectional communication between glial cells and neurons has been documented in numerous investigations. These breakthrough studies were made possible when optical signals, such as those generated by elevations in intracellular Ca\(^{2+}\), were monitored in addition to electrical signals. Many transmitters released from neurons have been shown to activate glial receptors, resulting in Ca\(^{2+}\) increases and other glial responses. Glial cells, in turn, release a number of transmitters and modulators that activate neurons and regulate the efficacy of synaptic transmission. These recent studies demonstrate that glial cells can directly influence neuronal excitability and synaptic transmission and suggest that glia play a significant role in information processing in the nervous system. Many important new studies related to glial control of synaptic function will appear in *Glia* and in other journals in the coming year, a good indicator of the vivacity of the field.

This special issue of *Glia* highlights recent advances in glial control of synaptic function. Glial control of synaptogenesis is discussed by Ullian et al., while Marcaggi and Attwell describe glial amino acid transporters and their effect on synaptic transmission. Schipke and Kettenmann describe neuronal activation of glial cells and Evanko et al. review mechanisms of glial release of chemical messengers. Several papers in this issue then describe glial modulation of synaptic transmission in different regions of the nervous system, including the hippocampus (Volterra and Steinhäuser), the supraoptic nucleus (Oliet et al.), the retina (Newman), and the neuromuscular junction (Colomar and Robitaille), as well as in cell culture (Araque and Perea). Glial release of D-serine and modulation of transmission at N-methyl-D-aspartate (NMDA) synapses is discussed by Miller. Finally, Lin and Bergles describe recent work on direct synaptic signaling from neurons to glia.

Owing to space constraints, additional important topics related to glial signaling are not covered extensively in this special issue. Among these are the demonstrations that glial cells: (1) modulate synaptic transmission in a molluscan cell culture model by release of an acetylcholine-binding protein (Smit et al., 2001); (2) send modulatory inputs to neurons in response to an intrinsic excitability that generates spontaneous Ca\(^{2+}\) oscillations (Parri et al., 2001); and (3) modulate vascular tone by release of cyclooxygenase products in response to neuronal stimulation (Zonta et al., 2003).

As the articles in this special issue demonstrate, our understanding of active interactions between neurons and glia has advanced remarkably in recent years, supporting the view that glia regulate synaptic function and are integral elements of nervous system circuitry. These studies make it equally clear, however, that much remains to be learned. Do the same synaptic interactions seen in brain slices occur in vivo? What role do glia-neuron interactions play in information processing, learning, and memory in the brain? These questions will be addressed in the coming years, using powerful new techniques, including in vivo recording and transgenic animal lines. It is our hope that many of these questions will be
answered in time for the publication of the next special issue of *Glia* devoted to glial control of synaptic function.

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**REFERENCES**

