NEURONS, GLIA, AND THEIR SYSTEMIC INTERACTIONS

For decades, scientists thought that all of the missing secrets of brain function resided in neurons. However, a wave of new findings indicates that glial cells, formerly considered mere supports and subordinate to neurons, participate actively in synaptic integration and processing of information in the brain.

VESCE, BEZZI, AND VOLTERRA (2001)

The past decade of studies has changed our view of the integrative capacities and roles of glia. A picture is emerging in which neurons and astrocytes, a subtype of glial cell, are in a continuous regulatory dialogue. . . . It is likely that the results of these recent studies will signal a new way of thinking about the nervous system, in which the glial cell comes to the forefront of our attention. MAZZANTI, SUL, AND HAYDON (2001)

Glial cells are active partners of neurons in processing information and synaptic integration. The active properties of glia, including long-range signaling and regulated transmitter release, are beginning to be elucidated. Recent insights suggest that the active brain should no longer be regarded as a circuitry of neuronal contacts, but as an integrated network of interactive neurons and glia. BEZZI & VOLTERRA (2001)

Development of microelectrode and sensitive electrophysiological recording devices has made neurophysiology the dominant paradigm for the study of biological communication. Robert O. Becker (1990, 1991) attempted to draw attention to the importance of the perineural system in a pair of classic papers. A decade later, researchers in a number of laboratories began to make a series of discoveries that confirmed and expanded upon Becker's insights.

The nervous system consists of an astronomical number of neurons, but there are some five to ten times more supporting cells, collectively called the *neuroglia* (from the Greek, meaning "nerve glue"). These cells include the astrocytes, oligodendroglia, and microglia. Outside the brain, in the peripheral nervous system, there are other cells that can be included in this supportive category: Schwann cells, satellite cells of peripheral ganglia, and ependymal cells. The latter are epithelial cells that line the ventricles, choroid plexus, and central canal of the spinal cord.

Nerve cells have always seemed to be the primary actors in exchanging information. The relatively tiny glial cells (in contrast to the very long neurons) were never considered to have any major or direct role in communication, although they have been studied extensively for their roles in development and repair of nerve damage (Matsas & Tsacopoulos 1999; Vernadakis & Roots 1995). For a description of the structure of these fascinating cells, see a histology textbook such as Fawcett (1994).

The recent revolutionary discovery is that the perineural connective tissue is also a dynamic communication system with multiple interactions with the neurons. Researchers are exploring the roles of these cells in neuronal-glial, neuronal-neuronal, and glial-glial interactions (McGrath et al. 2001; Miykata & Hatton 2002; Morale et al. 2001; Vesce, Bezzi & Volterra 2001; Watanabe 2002). Neuron-glial signaling cascades are being described (Morale et al. 2001).

Figure 15-3 shows a scheme for nonsynaptic communication within the brain through the astrocytic syncytium. The dotted line denotes a calcium wave that can propagate through this network (Cornell-Bell et al. 1990; Ventura & Harris 1999). Astrocytes have a repertoire of neurotransmitter receptors that mirror those of the neighboring neural synapses (Vesce, Bezzi & Bolterra 1999).

Glia now appear to play a key role in the pathophysiology of pain (Watkins, Milligan & Maier 2001) and in Parkinson's disease, mental illnesses, the action of psychotropic drugs, and learning, to name a few (Hertz, Hanson & Ronnback 2001).

It even has been proposed that fully differentiated glial cells can serve as stem cells that can give rise to cortical neurons (Alvarez-Buylla, Garcia-Verdugo & Tramontin 2001).

Glial cells are emerging from the background to become more prominent in our thinking about integration in the nervous system. Given that glial cells associated with synapses integrate neuronal inputs and can release transmitters that modulate synaptic activity, it is time to rethink our understanding of the wiring diagram of the nervous system. It is no longer appropriate to consider solely neuron-neuron connections; we also need to develop a view of the intricate web of active connections among glial cells, and between glia and neurons. Without such a view, it might be impossible to decode the language of the brain. HAYDON (2001)

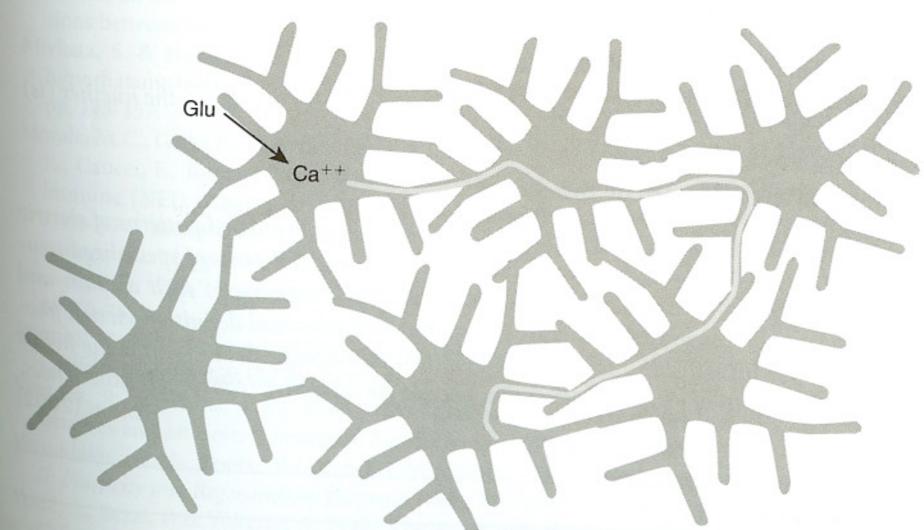

Figure 15-3 Astrocytes form an interconnected system called a *syncytium*. The astrocytic syncytium allows a nonsynaptic means of communication within the brain. (From Ventura, R.E. 'Astrocytes in the hippocampus', Synapse Web, Boston University, *http://synapses.bu.edu/*)

WAVE ASPECT OF CONSCIOUSNESS

Memory and consciousness cannot be understood without a better picture of the energetics of cells and tissues. As an interesting example, Charman (1997) logically views what we refer to as *mind* as a brain-generated neuromagnetic field. To paraphrase:

When the mosaic of neurons resonates at preferred frequencies, so will their associated microfields. These will interact with each other to form a complex neuromagnetic whole that permeates through the magnetically transparent physical structure of the brain as if it was not there.

Add to this concept of mind the biomagnetic fields of the peripheral neurons and the cell and tissue structures associated with them, and we begin to see a dynamic picture of the biomagnetic body as a whole.

Freeman described the situation as follows:

Pulses coming into a set of neurons are converted into synaptic currents which we call waves. These currents are filtered and integrated over time and space in the wave mode. The wave activity reaching trigger zones is converted back into the pulse mode. The pulse is then transmitted from one place to another across the synapse. This involves further delay, dispersion in time, etc.

FREEMAN, QUOTED BY PRIBRAM IN BULSARA AND MAREN (1993)

That a deeper level of analysis would be required for understanding consciousness was recognized long ago by Max Planck:

We must assume behind this force (in the atom) the existence of a conscious and intelligent mind. This mind is the matrix of all matter. MAX PLANCK

The idea has been developed formally by Pearson:

Mind is a property of the "nuether," a sub-quantum level of reality. . . . the nuether (is) structured like a neural network. PEARSON (1997)

Romijn also has elaborated on these ideas:

. . . [T]he hypothesis is put forward that the fleeting, highly ordered patterns of electric and/or magnetic fields, generated by assemblies of dendritic trees of specialized neuronal networks . . . encode for subjective (conscious) experiences such as pain and pleasure, or perceiving colors. Because by quantum mechanical definition virtual photons are the theoretical constituents of electric and magnetic fields . . . it is the highly ordered patterns of virtual photons that encode for subjective (conscious) experiences.

ROMIJN (2002)

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