

In normal functioning the degree of neuronal synchronization is highly controlled. From experiments that record the neuronal activity in different brain areas simultaneously in animals, it is known that correlation of spike activity between neurons (measured by the correlation level of synchronization) changes depending on the stage of behavior, motivation, attention, or activation of the memory processes. However, under some conditions, such as physical stress, heat shock, or strong emotional stress, the level of synchronization may become higher, involving nonspecific large populations of brain neurons and the synchronization may become uncontrollable.

Depending on at which frequency the synchronization rhythm occurs and how many neurons are involved, it may produce different physical effects; muscle weakness, involuntary muscle contractions, loss of consciousness, or intense (tonic) muscle spasms. The higher level of synchronization takes place in persons affected with epilepsy when they experience periodic seizures since they have a pathologic source (e.g., from injury to the brain) of rhythmic synchronization. Because the neurophysiological mechanisms of epileptiform synchronization are better documented, this incapacitating technology is described in terms of epileptogenesis.

The neurophysiological mechanisms active in epileptogenesis involve changes in membrane conductances and neurotransmitter alterations as they affect neuronal interaction. In the process of epileptogenesis, either some neurons are discharging too easily because of alterations in membrane conductances or there is a failure of inhibitory neurotransmission. The actual discharges have been recognized to result from a neuronal depolarization shift with electrical synchrony in cell populations related in part to changes in membrane conductances. The ionic basis and biochemical substrate of this activation have been areas of considerable study but still leave many questions unanswered. What are the basic cellular properties, present in normal cells and tissue, that could contribute to the generation of abnormal activity? What parts of the systems are low threshold and function as trigger elements?

One of the current hypotheses is involved with microcircuitry, particularly local synaptic interactions in neocortical and limbic system structures. In the hippocampus, the role of the trigger element has been long attributed to the CA3 pyramidal cells--a hypothesis based on the fact that spontaneous synchronous burst discharge can be established in CA3 neurons. Some studies describe an intrinsically bursting cell type in the neocortex that plays a role similar to that of CA3 cells in the hippocampus and that of deep cells in the pyriform cortex. The intrinsic nature of these cells appears to be an important contributor to the establishment of synchronized bursting in these regions. Another apparent requirement in such a population is for a certain degree of synaptic interaction among neurons, such that discharge of even one cell enlists the activity of its neighbors. Given the presence of these bursting cells and the occurrence of excitatory interactions among them in normal tissue, it may actually be the morphologic substrate for epileptiform discharges.

Another hypothesis has focused particularly on the role of N-methyl-D-aspartate (NMDA) receptors. Various factors regulate the efficacy of NMDA receptors: their