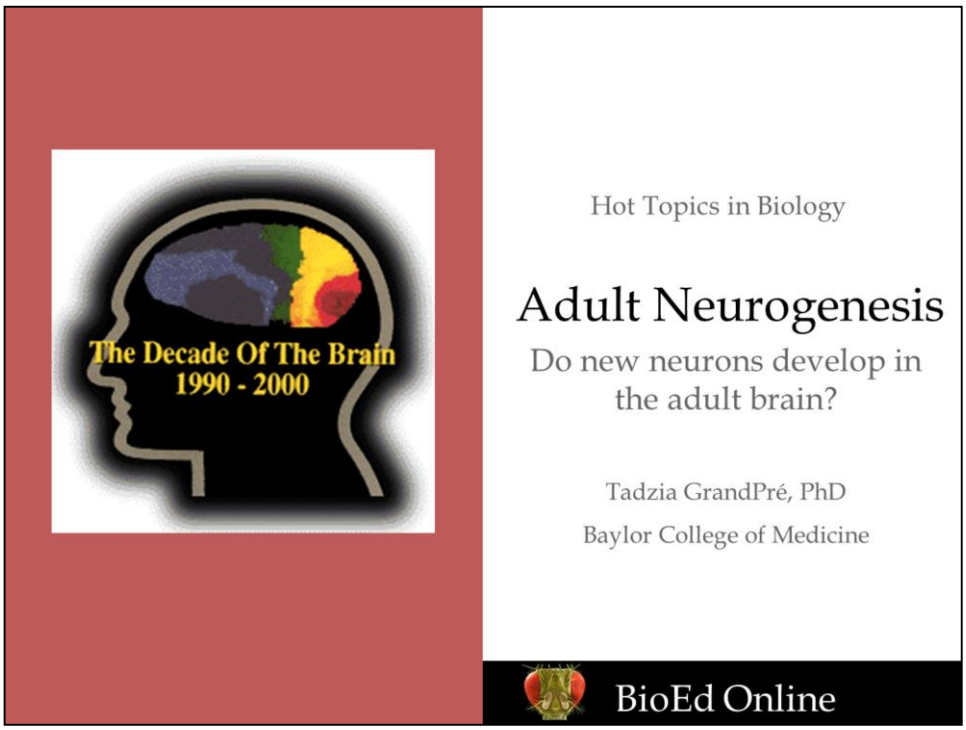

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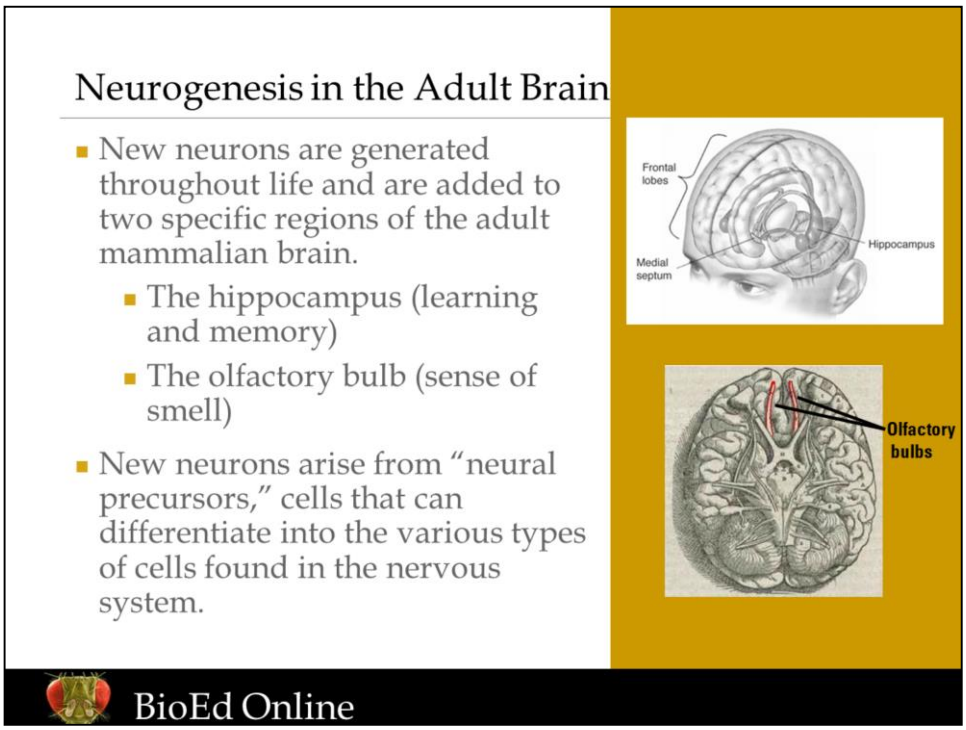

Neurogenesis in the Adult Brain

The long-standing dogma that the brain of adult mammals is incapable of producing new neurons recently has been overturned. We now know that while most cells in the brain are born during the embryonic and early postnatal period of development, new neurons are generated throughout life and are added to at least two areas of the brain: the hippocampus (which is involved in certain types of learning and memory) and the olfactory bulb (which is involved in the sense of smell). These newly generated neurons arise from populations of cells known collectively as "neural precursors," which can differentiate into the various types of cells that make up the nervous system. Adult neurogenesis (the birth of new neurons) has been demonstrated in a number of animals, including rodents, monkeys, and humans.

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Regulation of Adult Neurogenesis

Neurogenesis is a dynamic process. A variety of conditions have been shown to regulate the rate at which new neurons are generated, and also their migration, integration into the existing circuitry of the brain, and likelihood of survival. For example, many factors that enhance sensory, cognitive, and motor stimulation, such as physical exercise, increase the number of adult-generated neurons in the hippocampus (which is involved in certain types of learning and memory). Newly generated neurons in the olfactory bulb (which is involved in the sense of smell) have an increased chance of survival when mice are exposed to an odor-enriched environment. It has also been shown that certain kinds of learning can increase the survival rate of new neurons in both the hippocampus and the olfactory bulb. In contrast, virtually any type of stress can inhibit the production of new neurons in the hippocampus. The rate of neurogenesis in both the hippocampus and the olfactory bulb also naturally decreases with age.

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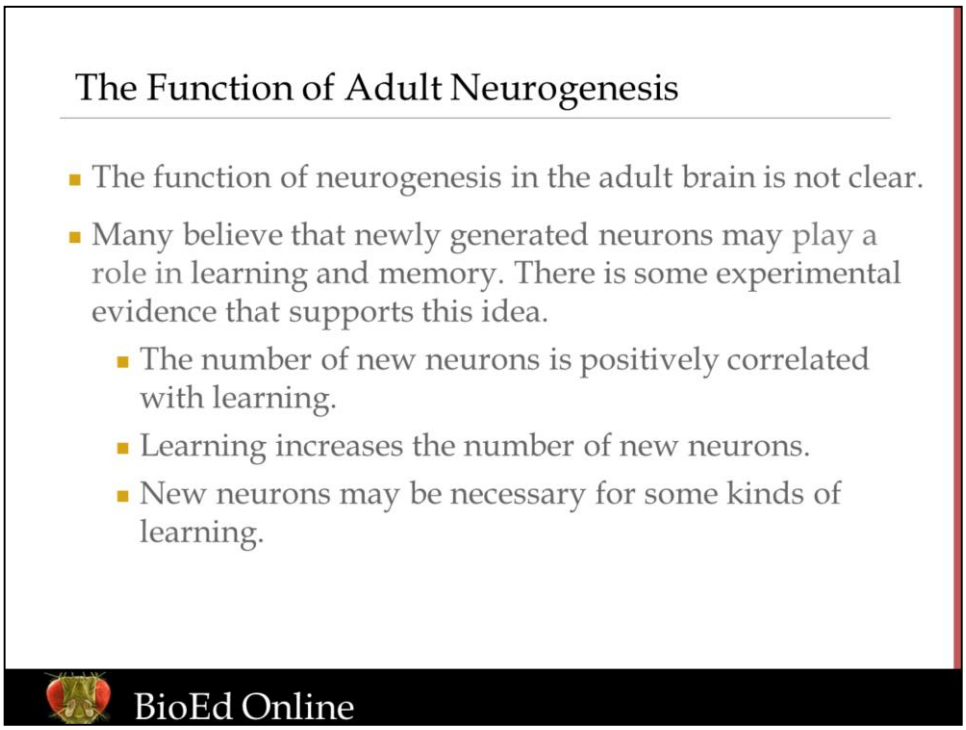

The Function of Adult Neurogenesis

A central focus of current investigations is to increase understanding of the functional significance of newly generated neurons—what they do and how they contribute to the brain's activities. While many answers remain unknown, new insights are emerging at a stunning rate. Experimental studies of neurogenesis suggest that new neurons are not only generated throughout life, they also integrate into the circuitry of the brain and actively participate in its functions. The hippocampus is known to play a critical role in learning and memory, and many have hypothesized that newly generated neurons within the hippocampus contribute to these processes. Although currently limited, there is support for this idea. For example, conditions that decrease adult neurogenesis, such as stress, seem to impair learning. In contrast, conditions that enhance the generation of new neurons, such as physical exercise, often are associated with improved learning on tasks that rely on the hippocampus. Studies also have shown that learning promotes the survival of new neurons. In fact, better learners seem to retain more new neurons, especially when trained on difficult tasks. These findings suggest an intriguing link between neurogenesis and learning. There also is evidence that neurogenesis is not only correlated with learning but that it may actually be required for learning. By using an experimental approach to decrease the number of new neurons in the hippocampus, one study has shown that animals perform poorly on some types of learning tasks when neurogenesis is reduced. Unfortunately, the methods used in this study, and in fact all methods currently available to selectively reduce neurogenesis, are likely to have additional affects on brain function, making results less than conclusive. Nevertheless, these and other studies provide initial support for the hypothesis that newly generated neurons participate in at least some forms of hippocampal learning and memory.

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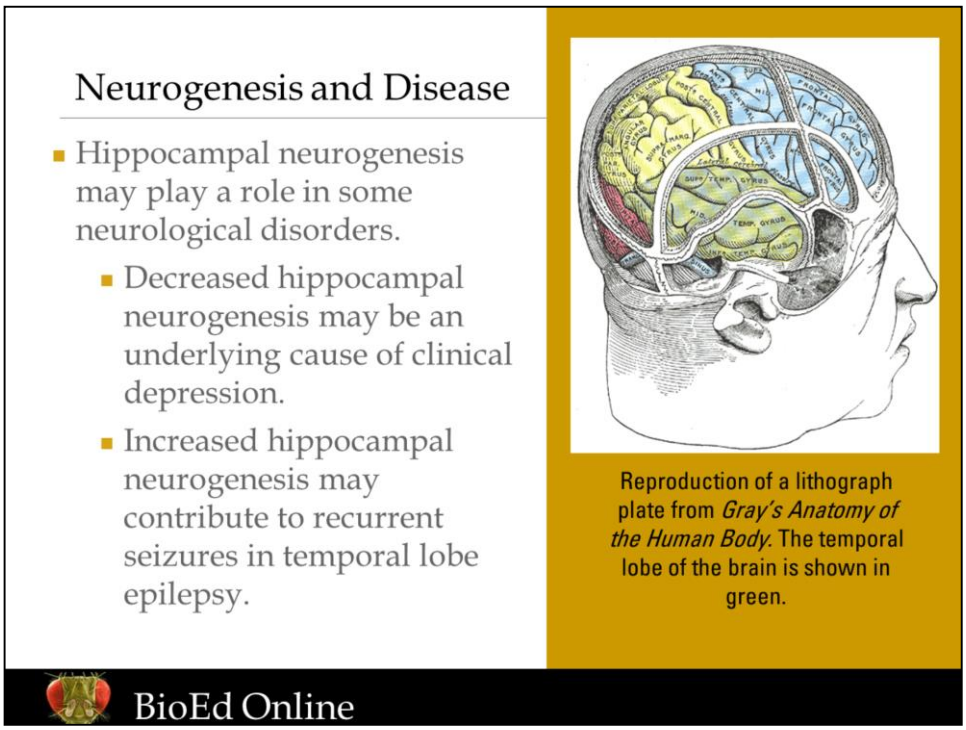

Neurogenesis and Disease

The birth of new neurons in the hippocampus also may play a role in various neurological disorders and diseases, including epilepsy and depression. Studies have shown that many therapies and medications used successfully to treat individuals suffering from depression can cause an increase in the production of new hippocampal neurons. Others have demonstrated that the beneficial effects of some antidepressants are blocked when neurogenesis is prevented. These and other observations suggest that a reduction of neurogenesis could be an underlying cause of depression. If this hypothesis is correct, it may be possible to help people who are suffering from depression by developing ways to increase the production of new neurons in the hippocampus. In contrast, by using animals to study temporal lobe epilepsy, scientists have shown that neurogenesis increases in response to prolonged seizure activity. However, in this case, the production of new neurons is not beneficial because those neurons develop, migrate, and integrate inappropriately and seem to contribute to recurrent seizures. Although the functional significance of abnormal neurogenesis in these and other medical conditions is not yet understood, it is an intense area of research that may one day yield new treatments for these disorders.

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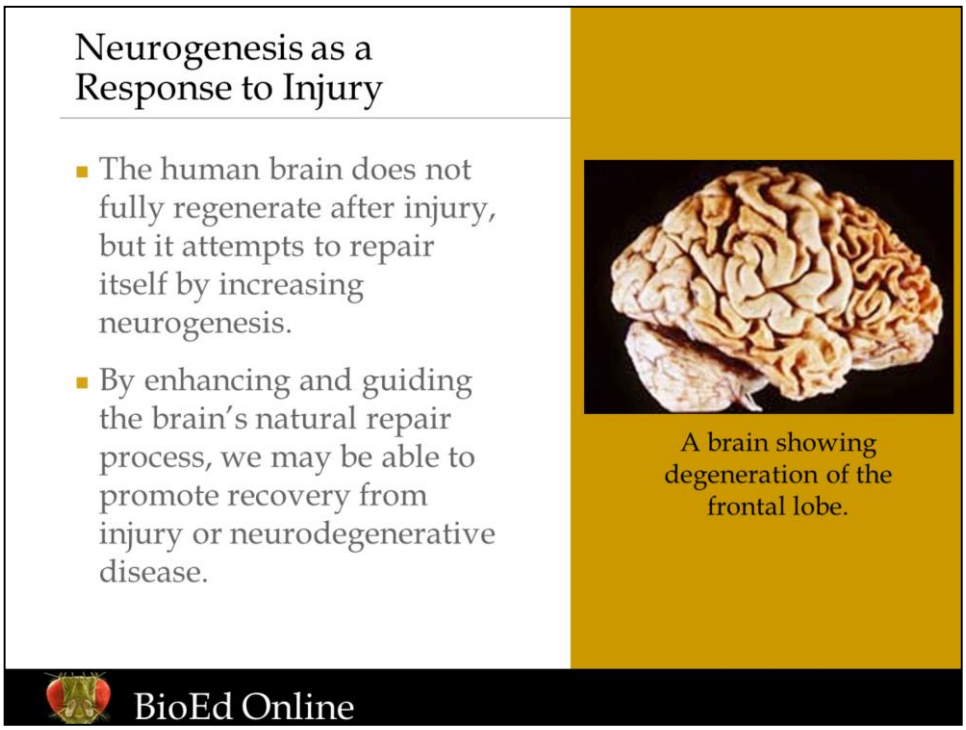

Neurogenesis as a Response to Injury

The discovery of adult neurogenesis also has uncovered the exciting potential for novel approaches to treating brain and spinal cord injuries. Some animals, such as lizards and goldfish, can regenerate entire segments of their injured nervous systems. While the human brain clearly does not have this capacity, it does appear to have greater regenerative ability than was previously believed. In fact, many studies have shown that neurogenesis is stimulated in the mammalian brain in response to injury and disease. For example, experiments in rodents have demonstrated that new cells are generated in response to brain injury caused by a stroke. Those new cells can migrate to the site of the injury in the cerebral cortex (where neurogenesis does not normally occur) and differentiate into mature neurons that form connections with neighboring cells. There are also reports of enhanced neurogenesis in the human brain in response to stroke as well as Huntington's disease and Alzheimer's disease. This injury-induced neurogenesis does not lead to recovery, but many scientists believe it represents the brain's attempt to repair itself. This creates hope that we can learn how to enhance and guide the brain's existing repair process. Naturally, this will not be an easy undertaking. It will require an understanding of how to stimulate the generation of new cells, direct their migration to areas that require repair, and control their differentiation into the appropriate kind of neuron. It may also be necessary to manipulate the natural environment of the adult brain to make it more conducive to regeneration. In addition, problems may arise if new neurons do not integrate properly into the existing network of nerve cells. Still, these discoveries raise the hope that we will one day learn how to guide the brain's natural response to injury for therapeutic use.

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