Encyclopedia of Health & Aging

Neurobiology of Aging

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The 1990s were designated the “decade of the brain,” and we have in fact learned much about this most mysterious of the human bodily organs over the past few years. As we have gained knowledge about the brain, we have also learned much about the dynamics of the brain as it develops over time—changes that have a profound impact on the aging process overall.

The brain shrinks (the term used is*atrophy*, designating both the shrinking of brain tissue and the widening of spaces or sulci between the lobes of the brain) for both men and women at about the same rate. For example, the average brain weight for a healthy man at 65 years of age is approximately 1,360 grams, and this decreases to approximately 1,290 grams by 90 years of age. The frontal and temporal cortex gradually atrophies in 30% to 50% of normally aging individuals, but the parietal and occipital cortices do not atrophy. In addition, the cerebral ventricles enlarge in size roughly threefold (i.e., the pockets of fluid at the base of the cortex). These changes are usually exaggerated in dementing disorders. Individuals vary significantly, and these individual differences rarely reflect cognitive capacity, although there is a loose association between brain size and cognitive function. Older adults with brains that appear to be markedly reduced in size at autopsy may perform perfectly normally up until the times of their deaths.

The adult brain contains approximately 20 billion neurons. Neurons are the key cells for transmitting information through the brain. A number of small protrusions from the main body of the neuron collect information from neighboring cells. A long single projection transmits this information to other cells. There is debate as to the extent of neuronal loss in the cortex with aging. Most agree, however, that neurons do not usually reproduce during late life (as compared with, e.g., liver cells) and that the numbers of neurons gradually decrease throughout life. Neurons may decrease in size with aging, yet this varies from one part of the brain to another (e.g., less decrease in the brain stem nuclei, much greater decrease in the hippocampus). Although the neuron is generally no longer able to divide after formation, it is continually changing its synaptic connections. This action permits the brain to recover from destruction of some parts such as from a stroke. Such neuroplasticity has been recognized to be a most important characteristic of the aging brain. As nerve cells die off, there is a compensatory lengthening and an increasing number of dendrites in the remaining nerve cells.

Neurons cluster together in networks or nuclei, such as the dentate nucleus located in the cerebellum, and project their axons often to distant portions of the brain. The brain is not like most other organs such as the kidney and heart; in the brain, precise anatomical connections are extremely important. Therefore, the axons of a particular nucleus will project to specific regions of the brain to provide networks for complex signal transduction.

In addition, there are numerous supportive cells, such as astrocytes and glial cells (an abnormal proliferation of which can lead to a cancers such as an astrocytoma or a glioblastoma). These cells may actually increase in number with aging in areas where neurons decrease in size and number.

With aging, deposits of materials increase in the brain, and these deposits are frequently associated with brain diseases. Senile plaques composed of amyloid (they are immunoreactive for β-amyloid) first begin to appear in the cortex with normal aging.

If diffuse, they are generally considered to have no pathological significance. When they mature, pieces of neurons filled with β-amyloid and crosslinked protein begin to accumulate around a central amyloid core, forming the plaque that is considered to be the primary pathology of Alzheimer's disease. Neurofibrillary tangles are normally limited to the entorhinal cortex and the inferior temporal lobe. By the time when neurofibrillary tangles spread to the cortex, cognitive impairment is usually apparent—another pathological sign of Alzheimer's disease. Lipofuscin, a brown “wear-and-tear” pigment, begins to accumulate in neuronal bodies with aging but is not associated with any specific disease process. Lewy bodies are composed of ubiquitin or α-synuclein cytoplasmic inclusions that are the defining histological lesions in the substantia nigra in Parkinson's disease. Lewy bodies outside the substantia nigra are present in people with late-onset dementia who do not have typical Parkinson's disease. They are found in the limbic and neocortical areas of the brain.

Chemical messengers or neurotransmitters are the key connections between neurons. These chemicals, produced in the neuron, are exuded from the axon of one neuron and attach to receptors in another neuron. They are released into the synaptic cleft (the space between neurons), and once they attach to receptors, they create a physiological response (e.g., increasing the flow of sodium across the cell membrane). Some neurotransmitters, such as norepinephrine and serotonin, are produced by nerve cells predominantly in the midbrain. The axons from these cells extend to the fore-brain in pathways that are specific to one another. In other words, neurons that produce different neurotransmitters are selective as to the areas of the brain to which they project. Acetylcholine, in contrast, is produced in many areas of the brain, although the long projection neurons that use acetylcholine as a neurotransmitter are found only in a few discrete places in the midbrain.

Different neurotransmitters have been associated with different disease processes. Dopamine depletion is associated with many of the functions that decrease with aging, such as locomotion and cognitive function, which involve dopamine and dopamine receptors. There is a loss of receptor binding in the frontal, temporal, and cingulated cortices associated with age. Overall cholinergic function declines with normal aging (but this is not necessarily directly associated with memory loss and aging). Acetylcholine regulation is severely and adversely affected in Alzheimer's disease. γ-Aminobutyric acid (GABA) is a widespread neurotransmitter that is thought to be associated with the inhibition of neuron excitability. The antianxiety drugs, such as the benzodiazepines, interact with GABA to enhance this inhibition.

There may be a 10% to 20% loss of serotonin receptors with aging (but only to middle age); however, the significance of these findings is not known. Serotonin is thought to be associated with both sleep and depression; many of the new-generation antidepressant drugs are selective serotonin reuptake inhibitors, meaning that they increase the concentration of serotonin in the synaptic cleft by reducing the reuptake of the neurotransmitter into the cell of origin. Norepinephrine is another neurotransmitter thought to be associated with mood because blockage of neuro-transmission can lead to severe depressive episodes. Age-related changes in norepinephrine circuits, such as those of serotonin, are not as clear as those in dopamine circuits.

In addition to neurotransmitters, the brain contains many hormones such as cortisol, opioids, estrogen, and thyroid-releasing hormone. Much of the neuroendocrine activity in the brain takes place in the hypothalamus as it releases both stimulating and

inhibiting factors that reach the pituitary gland, which in turn releases a variety of hormones that target different organs throughout the body. For example, adrenocorticotropin hormone (ACTH) is released from the pituitary gland and targets the adrenal gland, which in turn produces cortisol. Cortisol concentrations in the blood subsequently feed back information to the brain on the concentrations of these hormones via the hypothalamus; therefore, they control the secretion of hormones by modulating the secretion of corticotropin-releasing hormone from the hypothalamus.

Hormones can affect the brain in a number of ways. For example, chronic elevated levels of cortisol, which may result from chronic stressors in the environment, can lead to permanent dysfunction of some brain regions such as the hippocampus. Some have speculated that people who have experienced considerable stress throughout their lives may be at risk not only for late-life depression but also for atrophy of the hypothalamus and memory loss.

Vascular changes in the brain, such as small strokes (microinfarcts) and stroke, increase in frequency with aging. These small infarctions can lead to cognitive dysfunction and depression. There is emerging evidence that these vascular changes are associated with inflammatory mechanisms. Vascular occlusion derives from the development of vascular plaques and thrombosis (blood clots). Brain amyloid plaques show many indications of inflammatory processes, as evidenced by increased activation of microglia. This is associated with increased production of inflammatory markers such as IL-6. The interest in nonsteroidal anti-inflammatory agents (e.g., aspirin) as a preventive for Alzheimer's disease derives from the possibility of lowering risk by reducing the potential for inflammation.

The brain has many compensatory mechanisms to counteract these brain changes with aging. When speech centers in the dominant hemisphere are damaged, the nondominant hemisphere may compensate and speech function may return gradually. Areas of the cerebellum may be destroyed by a stroke, and other motor systems will take over. Compensation is greater in the higher cortical centers and decreases in the peripheral nervous system. Therefore, it is much more difficult to recover from a spinal cord injury than from a brain injury.

We are now only at the threshold of understanding the mechanisms by which the brain works and how these mechanisms change with age. However, these mechanisms do not inevitably determine what humans think and how they feel. Cognitive psychology adds an additional and necessary dimension to our understanding of mood and behavior.

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See also

- Alzheimer's Disease
- Anxiety Disorders
- Apolipoprotein E
- Behavioral Disorders in Dementia
- Calcium Disorders of Aging
- Delirium and Confusional States
- Depression and Other Mood Disorders
- Imaging of the Brain

- Lewy Body Dementia
- Memory
- Mild Cognitive Impairment
- Neurological Disorders
- Pseudodementia
- Schizophrenia, Paranoia, and Delusional Disorders
- Stroke
- Vascular Dementia
- Vascular Depression

Further Readings and References

Burns RA., Abou-Saleh MT. Neuroendocrinology of ageing. In: Copeland JRM, Abou-Saleh MT, Blazer DG, eds. Principles and Practice of Geriatric Psychiatry. London: Wiley; 2002: 51–55.http://dx.doi.org/10.1002/0470846410.ch9

Byrum CE, Moore SD, Hulette CM.Neuroanatomy, neurophysiology, and neuropathology of aging. In: Blazer DG, Steffens DC, Busse EW, eds. American Psychiatric Press Textbook of Geriatric Psychiatry. Washington, DC: American Psychiatric Press; 2004: 53–81.

Powers RE. Neurobiology of aging. In: Coffey CE, Cummings JL, eds. Textbook of Geriatric Neuropsychiatry. Washington, DC: American Psychiatric Press; 1994: 35–70.