



FIGURE 26-2 Neurobiology of Alzheimer's disease. (SOURCE: American Health Assistance Foundation, 2005, with permission. <http://www.ahaf.org/alzdis/about/BrainAlzheimer.htm>)

Neurotransmitters

A decrease in the neurotransmitter *acetylcholine* has been implicated in the etiology of Alzheimer's disease. Cholinergic sources arise from the brain stem and the basal forebrain to supply areas of the basal ganglia, thalamus, limbic structures, hippocampus, and cerebral cortex.

Cell bodies of origin for the *serotonin* pathways lie within the raphe nuclei located in the brain stem. Those for *norepinephrine* originate in the locus ceruleus. Projections for both neurotransmitters extend throughout the forebrain, prefrontal cortex, cerebellum, and limbic system. *Dopamine* pathways arise from areas in the midbrain and project to the frontal cortex, limbic system, basal ganglia, and thalamus. Dopamine neurons in the hypothalamus innervate the posterior pituitary.

Glutamate, an excitatory neurotransmitter, has largely descending pathways with highest concentrations in the cerebral cortex. It is also found in the hippocampus, thalamus, hypothalamus, cerebellum, and spinal cord.

Areas of the Brain Affected

Areas of the brain affected by Alzheimer's disease and associated symptoms include the following:

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| Frontal lobe: | Impaired reasoning ability. Unable to solve problems and perform familiar tasks. Poor judgment. Inability to evaluate the appropriateness of behavior. Aggressiveness. |
| Parietal lobe: | Impaired orientation ability. Impaired visuospatial skills (unable to remain oriented within own environment). |
| Occipital lobe: | Impaired language interpretation. Unable to recognize familiar objects. |
| Temporal lobe: | Inability to recall words. Inability to use words correctly (language comprehension). In late stages, some clients experience delusions, and hallucinations. |
| Hippocampus: | Impaired memory. Short-term memory is affected initially. Later, the individual is unable to form new memories. |
| Amygdala: | Impaired emotions: depression, anxiety, fear, personality changes, apathy, paranoia. |
| Neurotransmitters: | Alterations in acetylcholine, dopamine, norepinephrine, serotonin and others may play a role in behaviors such as restlessness, sleep impairment, mood, and agitation. |

Medications and Their Effects on the Brain

1. Cholinesterase inhibitors (e.g., tacrine, donepezil, rivastigmine, and galantamine) act by inhibiting acetylcholinesterase, which slows the degradation of acetylcholine, thereby increasing concentrations of the neurotransmitter in the brain. Most common side effects include dizziness, GI upset, fatigue, and headache.
2. NMDA receptor antagonists (e.g., memantine) act by blocking NMDA receptors from excessive glutamate, preventing continuous influx of calcium into the cells, and ultimately slowing down neuronal degradation. Possible side effects include dizziness, headache, and constipation.