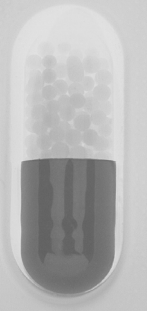


Cognitive Enhancers for Treatment of Alzheimer's Disease and Other Forms of Dementia



Aricept (donepezil)
Cognex (tacrine)
Exelon (rivastigmine)
Namenda (memantine)
Reminyl (galantamine)

Overview

Alzheimer's disease is the most common and well-known form of degenerative dementia. More than 50% of people who develop dementia have Alzheimer's disease, and it affects approximately 2.5 million Americans. By definition, dementia is a syndrome—a cluster of symptoms—of impaired **cognition** affecting the individual's intellectual abilities, particularly memory, problem solving, judgment, awareness, and behavior. Alzheimer's disease is a progressive, irreversible brain disease involving a deterioration of brain cells that results in loss of intellectual functioning.

The cause of Alzheimer's disease is unknown, but symptoms of the disease may be associated with the selective loss of brain cells known as **cholinergic neurons** in affected areas of the brain. There are certain pathological hallmarks of Alzheimer's disease that are found at autopsy, including **senile plaques** (degenerating neurons twisted around a waxy protein-polysaccharide substance known as **amyloid**) and **neurofibrillary tangles** (helical thread-like tangles within neurons).

Cognitive enhancers are medications used for treating dementia. Commonly, they are used to treat mild-to-moderate dementia of Alzheimer's disease, with the exception of Namenda (memantine), which has an indication for treatment of moderate-to-severe Alzheimer's disease. Deterioration of cognition and memory in Alzheimer's disease, and perhaps in other forms of dementia, may be due to degeneration of **cholinergic neurons**. Cognitive enhancers improve function by inhibiting the breakdown of the neurotransmitter **acetylcholine**, thereby increasing brain acetylcholine levels and optimizing the function of intact cholinergic neurons. By blocking the **cholinesterase enzyme** that breaks down acetylcholine and thus inhibiting its destruction, these agents (except for Namenda), known as **cholinesterase inhibitors**, can improve memory and overall function.

Namenda (memantine) is distinct from the other cognitive enhancers. It represents a new class of medication with a mechanism of action that is quite different from the other cognitive agents for the treatment of Alzheimer's disease. Namenda works by blocking the receptors for the neurotransmitter **glutamate**. It is believed that glutamate plays an important role in the neural pathways associated with learning and memory. In brain disorders such as Alzheimer's disease, overexcitation of neurons produced by abnormal levels of glutamate may be associated with neuronal cell dysfunction (resulting in cognitive and memory deficits) and

eventual cell death (leading to deterioration and collapse of intellectual functioning). By selectively blocking a type of glutamate receptor (the **NMDA receptor**) while allowing for normal neurotransmission, Namenda may help reduce the destructive, excitotoxic effects associated with abnormal transmission of glutamate. In addition, because Namenda works differently from other cognitive enhancers, it may be combined with other agents such as Aricept.

As research into new treatments for Alzheimer's disease continues, it is expected that new medications similar to Namenda may be introduced. Both Namenda and the cholinesterase inhibitors (Aricept, Reminyl, Exelon, and Cognex) may improve the patient's overall function and delay worsening of symptoms, but neither class of medications can prevent the underlying progression of Alzheimer's disease. Research into the cause of Alzheimer's disease is as important as looking for new treatments. If the cause of the disease may be understood, then new measures to prevent it may also be discovered.