

## **Memory and Memory Enhancement**

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Recent news reports that an electrical brain-stimulation technique improved human memory draws attention to the extraordinary progress that neuroscience has made in understanding the structure and organization of memory. We have learned that memory is not a single faculty of the mind and that different brain systems support different kinds of memory. The main distinction is between our capacity for conscious memory for facts and events (called declarative memory) and several kinds of unconscious memory, such as for habits and skills, (collectively called nondeclarative memory). Declarative memory is what we mean when we use the term memory in everyday language. In the case of nondeclarative memory, performance does change as the result of experience and in that sense deserves the term memory, but the change happens without requiring any conscious memory content and in some cases without awareness that memory is being used. For example, when we learn to ride a bicycle or hit a golf ball, we have a very limited ability to report what we have learned. Declarative memory is the kind of memory that is most vulnerable to being weakened by aging and disease and is the kind of memory that was improved by brain stimulation.

We also know that particular structures in the brain, including the hippocampus and entorhinal (pronounced en-toe-rine-ol) cortex, are essential for the formation of enduring declarative memory and that damage within these structures results in severe forgetfulness. The most common, and best known, cause of this condition is Alzheimer's disease, a debilitating and catastrophic condition that occurs in the aged. The disease affects only about 10 percent of people between the ages of 65 and 85 but as many as 40 percent of people over the age of 85. The first target of Alzheimer's disease is the entorhinal cortex, which explains why the disease typically begins with memory problems.

In contrast to Alzheimer's disease, which primarily affects the elderly, weakening of memory ability is a universal feature of normal aging, detectable as early as the fourth or fifth decades of life. This difficulty with memory is sometimes called benign senescent forgetfulness, though it is not completely benign and, as noted, it does not begin in senescence. In the case of age-related memory impairment, changes also occur in the brain regions important for memory formation, though the changes are in different locations and involve different processes than those that occur in Alzheimer's disease. It should be emphasized that the memory problems experienced during normal aging are much less severe than in disease, and they are not a prelude to Alzheimer's disease. It is sometimes said that if you forget who the guests were at your daughter's wedding—that's normal aging. If you forget the wedding itself, that's Alzheimer's disease.

With these points in mind, it is understandable why efforts to improve memory, and to prevent or arrest memory decline, have focused on the entorhinal cortex and hippocampus. In 1998, two groups independently showed that activity in a brain region that included entorhinal cortex was related to how well people would later remember the material they studied. The more active the region was during learning, the better memory was on a later test. Earlier this year, researchers found that stimulation of this same cortex during learning facilitated later retention. That is, low levels of stimulation helped retention. Participants learned a series of locations in a virtual environment, and stimulation was applied in 5-second on-off bursts while half of the locations were being learned. Later, the participants remembered the locations that had been accompanied by stimulation better than the locations that had not. It is thought that the stimulation worked by resetting the electrical rhythm of brain cells in the hippocampus, immediately downstream from entorhinal cortex, thereby creating a brain state optimal for learning.

It is important to note that this study was carried out in patients with drug-resistant epilepsy, who had intracranial electrodes surgically placed within entorhinal cortex. This is a standard clinical procedure to determine the location of seizure activity and to assess the prospects for surgical removal of epileptic tissue. Thus, the procedure is invasive, involving neurosurgery to place the electrodes. One does not imagine that a person with age-related weakening of memory would choose to undergo such a procedure. The prospect of improving the ability to

remember a new name, a new face, a new location, or a new fact seems appealing enough, but implanting electrodes deep in entorhinal cortex so that an individual can deliver pulses to his or her brain at opportune learning moments seems rather extreme.

On the other hand, in the case of a debilitating and deteriorating condition like Alzheimer's disease, the possibility of improving memory, even by extreme methods, has more to recommend it. Yet here any benefits of stimulation would likely be limited to the disease's early stage when the condition is usually limited to memory problems. At later stages, the disease inevitably progresses to involve language, problem solving, and judgment. At that point, the judgment as to when something should be remembered, and the decision to stimulate, might require a caretaker. Furthermore, as the condition worsens and the entorhinal cortex suffers neuronal loss, the beneficial effects of stimulation would diminish.

There is also an important cautionary note that should go with any discussion of memory-enhancing treatments. Forgetting is an important part of remembering. We need to forget and pass over the details in order to comprehend the main points, and we need to set aside the details in order to form general concepts. Indeed, our memories are built to generalize and assemble general knowledge, not to retain a literal record of particular events. Accordingly, the search for memory enhancers is not a simple matter of wanting to improve retention. An improved memory is not necessarily an optimal memory. Nevertheless, for individuals with severe memory impairment, as occurs in Alzheimer's disease, identifying treatments that could combat the forgetfulness would be an important and valuable achievement.

At the present time, drugs are not available that can improve memory selectively and reliably. It has been known for decades that drugs like amphetamine and caffeine can improve memory a little but these drugs have side effects and they improve memory by increasing arousal and counteracting fatigue rather than working directly on memory. There has been widespread popular interest in assorted herbs and vitamins for improving memory, but the effects are modest and unreliable. The main thrust of pharmaceutical companies currently is to develop compounds that work preferentially on the hippocampus or entorhinal cortex, for example, by targeting molecules that are particularly enriched in these structures. There are also attempts to influence directly mechanisms and processes that are unique to these structures. In this way, one hopes to influence memory without affecting other neural functions. In the meantime, great strides are being made in understanding memory and diseases of memory like Alzheimer's, and we can look forward to the possibility of drugs that will prevent the disease or halt its progression, not just drugs that slow down the process by treating memory impairment for a period of time.

**Fonte: The Dana Foundation, June 2012. [Portal] Disponível em: <[http://www.dana.org/news/features/detail\\_rop.aspx?id=38824](http://www.dana.org/news/features/detail_rop.aspx?id=38824)>. Acesso em: 19 June 2012.**