‘Never been the same since’

Delirium in older people might have permanent effects on the brain.

If you look up delirium in a medical dictionary, the definition refers to an altered state of consciousness that includes confusion, distractibility, disordered memory, and hallucinations. Causes include diseases that directly affect the brain, like meningitis, and withdrawal from alcohol.

But starting at about age 65, delirium has any number of causes — an infection, a fall, a fracture, dehydration, a surgical procedure — that aren’t so obviously related to the brain. Physically, people can be agitated and restless, or just the opposite, lethargic and listless. Family and friends are often bewildered because people swing from being lucid and seemingly back to their old selves to being utterly confused and “out of it.”

The consolation has been that the condition was temporary, and doctors could assure people that the patient’s thinking would clear. “There is this dogma that delirium is reversible,” said Dr. Sharon Inouye, a Harvard Medical School professor and director of the Aging Brain Center at Hebrew SeniorLife in Boston.

Now Dr. Inouye and other experts on delirium are beginning to question that dogma. The worst may pass, but delirium in older people may leave behind a permanently impaired brain. So they’re investigating whether delirium might accelerate, perhaps even initiate, degenerative processes in the brain.

Delirium-dementia connection

Delirium is often seen in people who are hospitalized or in some other health care setting, such as a nursing home. Medications are frequently a contributing factor, even when people have been taking them for a long time without any trouble.

There’s no lab test or brain scan for delirium. It’s a bedside diagnosis: Doctors make it by observing behavior and evaluating the patient’s mental status. Delirium often goes unrecognized for several reasons: the fluctuating symptoms; lack of a clear-cut treatment so doctors don’t focus on it; other medical problems that may seem more pressing. Dr. Inouye has devised the Confusion Assessment Method to help doctors and nurses know what to look for. We’ve posted a copy on our Web site at www.health.harvard.edu/health.

There’s little question that dementia, a permanent impairment of intellectual functioning, makes people more vulnerable to delirium: Two-thirds of those who develop delirium were suffering from dementia

beforehand.

The trickier question is delirium's relationship to dementia. In a review article published in 2006 in the *New England Journal of Medicine,* Dr. Inouye, noting cases of "persistent delirium," argued that the boundary between delirium and dementia is blurred. She says that in her two decades of delirium research, she has encountered many instances when patients became delirious and "have never been the same since." In patients with dementia, she says, the slope of their cognitive decline often takes a sharp downward turn after a delirious episode.

Changes in the brain

How delirium, or its underlying pathology, might cause — or, at the very least, accelerate — dementia is an open question. There are some theories. Delirium may be the brain's response to systemic inflammation, which can disrupt the blood-brain barrier that shields the brain from harmful substances circulating in the blood. Once the barrier is breached, delirium may occur first, followed by permanent brain damage.

Brain cells "talk" to one another with chemicals called neurotransmitters. A shortfall in one of those neurotransmitters, acetylcholine, might bring on delirium. A long-term or severe disturbance of the "circuits" that depend on acetylcholine may have permanent effects.

Other researchers are looking for a connection between delirium and the clumps of beta-amyloid protein in the brain that are believed to cause Alzheimer's disease. It's well known that general anesthesia can lead to delirium. Researchers at Massachusetts General Hospital say it may also cause permanent damage by stimulating the production of beta-amyloid. Their test-tube experiments have shown that isoflurane, a drug used in general anesthesia, kills brain cells and increases generation of the Alzheimer's protein. More research needs to be done to prove their hypothesis.

Calendars and clocks

These theories and others may lead to diagnostic tests and effective treatments for delirium. For example, donezepil (Aricept), a drug that's used to maintain acetylcholine levels in Alzheimer's patients, may help with delirium, although early study results haven't been very impressive.

Meanwhile, the best approach is minimizing the disorientation and other aspects of delirium. Dr. Inouye has devised a program for hospital patients that reduces the risk of developing delirium. Parts of it have been adopted at hospitals throughout the country. The program stresses keeping people oriented by having clocks and calendars in their rooms and making sure they have glasses and hearing aids. Regular sleeping patterns are encouraged by exposing patients to daylight and setting schedules so they're not woken up at night. Families can help simply by spending time with patients, especially when they are hallucinating.

A description of the program is available on a Web site created by Dr. Inouye. Just type “hospital elder life program” into a search engine like Google and you’ll find it.