

## Mixed dementia

A topic in the Alzheimer's Association® series on understanding dementia.

### About dementia

Dementia is a general term for a decline in mental ability severe enough to interfere with daily life. Dementia is not a single disease; it's the umbrella term for an individual's changes in memory, thinking or reasoning. There are many possible causes of dementia, including Alzheimer's. Disorders grouped under the general term "dementia" are caused by abnormal brain changes. These changes trigger a decline in thinking skills, also known as cognitive abilities, severe enough to impair daily life and independent function. They also affect behavior, feelings and relationships. Brain changes that cause dementia may be temporary, but they are most often permanent and worsen, leading to increasing disability and a shortened life span. Survival can vary widely, depending on such factors as the cause of the dementia, age at diagnosis and coexisting health conditions.

### Mixed dementia

Mixed dementia is a condition in which abnormalities characteristic of more than one type of dementia occur at the same time in the brain. Physicians may also call this condition "dementia-multifactorial." In the most common form of mixed dementia, the abnormal protein deposits associated with Alzheimer's disease coexist with blood vessel problems linked to vascular dementia. Alzheimer's brain changes also often coexist with Lewy bodies: the abnormal protein deposits characteristic of dementia with Lewy bodies (DLB) and Parkinson's disease dementia. In some cases, a person may have brain changes linked to Alzheimer's disease, vascular dementia and dementia with Lewy bodies.

### Prevalence

Studies suggest that mixed dementia is more common than previously recognized. More than 50% of people with dementia who were studied at Alzheimer's Disease Research Centers had evidence of more than one cause of dementia. In other community-based studies, the percentage of mixed dementia cases is considerably higher. The likelihood of having mixed dementia increases with age and is highest in people age 85 or older.

Autopsy studies play a key role in shedding light on mixed dementia because scientists can't yet measure most dementia-related brain changes in living individuals.

In the most informative studies, researchers correlate each participant's cognitive health and any diagnosed problems during life with a highly detailed analysis of the brain after death.

One such study is the Rush Memory and Aging Project, conducted by the Rush Alzheimer's Disease Center and the Rush Institute for Healthy Aging in Chicago and funded by the National Institute on Aging (NIA). Data from the 1,000 volunteers in this study showed that more than 94% of the participants had at least one known neuropathology — i.e., characteristics in the brain that are known hallmarks of cognitive decline and dementia including plaques and tangles. Of those participants who had at least one neuropathology, 78% had two or more, 58% had three or more, and 35% had four or more. The researchers were surprised to find nearly 250 unique combinations of neuropathologies. Recent studies also show that the likelihood of having mixed dementia increases with age and is highest in the oldest individuals (people age 85 or older).

### **Symptoms**

Mixed dementia symptoms may vary, depending on the types of brain changes involved and the brain regions affected. In many cases, symptoms may be similar to — or even indistinguishable from — those of Alzheimer's or another specific type of dementia. In other cases, a person's symptoms may suggest that more than one type of dementia is present. Researchers expect to gain a greater understanding of mixed dementia symptoms as long-term studies continue to shed light on the relationship between cognitive function and underlying brain abnormalities.

### **Diagnosis**

Most individuals whose autopsies show they had mixed dementia were diagnosed with one specific type of dementia during life, most commonly Alzheimer's disease. For example, in the NIA study involving long-term cognitive assessments followed by brain autopsy, 94% of participants who were diagnosed with dementia were diagnosed with Alzheimer's. Yet, the autopsies of those diagnosed with Alzheimer's showed that 54% had coexisting pathology in addition to hallmark Alzheimer's brain changes. The most common coexisting abnormality was previously undetected blood clots or other evidence of vascular disease. Lewy bodies were the second most common coexisting brain change.

### **Causes and risk factors**

Although mixed dementia is infrequently diagnosed during life, many researchers believe it deserves more attention because the combination of two or more types of

dementia-related brain changes may have a greater impact on the brain than one type. Evidence suggests that the presence of more than one type of dementia-related change may increase the chances that a person will develop symptoms. In the NIA study, having more than one type of dementia pathology more than tripled the odds of being diagnosed with dementia compared with a having a single pathology.

### **Outcomes**

Many researchers are convinced that a more in-depth understanding of mixed dementia, coupled with recognition that vascular changes are the most common coexisting brain change, may create an opportunity to reduce the number of people who develop dementia. Controlling overall risk factors for diseases of the heart and blood vessels — such as blood pressure, cholesterol levels, body weight and diabetes — may also protect the brain from vascular changes. This protection may help avoid the double impact from vascular changes and other dementia-related abnormalities that seems to increase the risk of being diagnosed with dementia.

### **Treatment**

Because most people with mixed dementia are diagnosed with a single type of dementia, physicians often base their treatment decisions on the single type of dementia that's been diagnosed. No drugs are specifically approved by the U.S. Food and Drug Administration (FDA) to treat mixed dementia. Physicians who think that Alzheimer's disease is among the conditions contributing to a person's dementia may consider prescribing the drugs that are FDA-approved for Alzheimer's. Since most of the drugs approved to treat Alzheimer's disease symptoms have shown a similar benefit in treating vascular dementia, there is reason to believe they may also be of help in mixed dementia. Two of the drugs — galantamine (Razadyne) and rivastigmine (Exelon) — have been shown to offer modest benefit in mixed dementia.

The ability to detect the presence of multiple underlying brain abnormalities will gain importance if researchers succeed in developing next-generation drugs targeting specific dementia-related protein abnormalities, such as those associated with Alzheimer's and dementia with Lewy bodies.

TS-0094 | Updated November 2021