



Mixed Dementias: What an Alzheimer's Diagnosis Doesn't Explain

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Alzheimer's disease is widely regarded as the most common diagnosis in dementia. However, what the diagnosis does not explain is the varied individual courses people living with Alzheimer's experience. One reason for this may be that in fact, mixed dementia is very common. Mixed dementia describes the presence of more than one neuropathology causing dementia symptoms.

More than half of Alzheimer's cases are mixed

"Researchers don't know exactly how many older adults currently diagnosed with a specific type of dementia actually have mixed dementia," says the [Alzheimer's Association](#). One avenue of research into this question has been autopsy research funded by the National Institute on Aging. Research volunteers have each agreed to an autopsy analysis after death to investigate changes in the brain. So far, results of this research show that half of patients diagnosed with Alzheimer's "had pathological evidence of one or more coexisting dementias," says the Alzheimer's Association.

Most patients with dementia receive a single diagnosis, they add, and this diagnosis often forms the basis for a physician's prescribing decisions.

One of the neuropathologies that can occur in dementia is accumulation of a protein called TDP-43. Publishing in [Brain](#), James and colleagues concluded that this protein, traditionally associated with frontotemporal lobe dementia and Amyotrophic Lateral Sclerosis (ALS), is present in 52% of Alzheimer's patients.

They found that as the protein affects various parts of the brain through progressive stages, dementia symptoms increase. Other mixed pathologies they noted include cerebral infarcts in more than half of patients and Lewy bodies in 34%. In all, their analysis showed that "pure" Alzheimer's disease is by far the exception, not the norm.

Roderick Corriveau, PhD, program director for the National Institute of Neurological Disorders and Stroke, told listeners of the [Dementia Matters](#) podcast, "There's been a large shift in the way we think about dementia overall, including Alzheimer's disease." He says that clinical diagnosis does not always provide "an accurate picture of the brain pathologies or dementia disease pathways that are going on inside that person." He notes that the long-standing assumption or "hypothesis" that beta amyloid causes dementia is being put to the test through research today—along with research into numerous other pathways to dementia. He agrees that "the majority of all dementia cases of people who are 65 and older are mixed dementias," and says that a push to identify biomarkers to shed light on various pathologies is underway.

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Understanding the interrelationships among various pathways to dementia is also a topic of investigation, he adds. The synergy from one to another is not fully understood, and he says this gets to the question of “root cause.” For example, there is an understanding of how beta amyloid may cause vascular changes in the brain. The ApoE gene that is associated with a higher incidence of Alzheimer's disease can also impact vascular health, he says.

Clinically, says Corriveau, there are benefits to honing diagnoses. For example, he says, recognizing vascular issues could lead to a focus on controlling blood pressure that could be “life-changing”. Or not identifying Lewy bodies as a component of a patient's dementia could lead to use of medicines that “make things much, much worse”. (Learn more about these medication effects in [What is Lewy Body Dementia?](#))

Neurological evaluation and diagnosis

Recognition of the complexity of neuropathologies behind clinical dementia is important in understanding and managing the illness. Even specific pathologies “can be correlated with wildly different diagnoses and different people,” explains Corriveau.

This underscores the importance of neurological evaluation in patients with dementia. Pathological diversity is one reason GuideStar Eldercare [includes neurological evaluation within the first step of its Long-Term Care Antipsychotic Stewardship® program](#).

Neurology-forward approach: McKnights

“A neurological focus has helped us reduce our antipsychotic use, has reduced catastrophic behavioral expressions and helped avoid transitions to outside appointments or hospitalizations,” explained Janean Kinzie, vice president of social wellness and enrichment for American Senior Communities. She commented for a new ebook from McKnights, [A paradigm shift in treating behavioral and psychological symptoms of dementia](#).

Kinzie collaborated with members of the GuideStar team to pilot a neurology-forward assessment and treatment protocol, achieving an overall 68% reduction in antipsychotic use over six months (see [Reducing Antipsychotics in Nursing Homes: Results of a Peer-Reviewed Study](#) for details).



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The McKnights ebook explains that traditionally, psychiatrists have been called in to deal with Behavioral and Psychological Symptoms of Dementia (BPSD) because these symptoms were not being recognized “as a neurologic issue”. They add, “The fact is, though, when an individual has dementia, even if they are exhibiting psychiatric symptoms, the treatment should be in light of that neurological condition, not as if the individual is psychiatrically impaired...The key to unlocking effective treatment is by leading with neurology to treat this neurocognitive condition. From there, the psychiatric treatment becomes much more straightforward and effective.”

While urgent research on dementia and its multiple pathologies continues, the GuideStar clinical team is focused on advancing person-centered care for patients with dementia in real time. The evolving understanding of dementias as mixed is a call to lead with neurology as we assess and treat nursing home residents. Our goal: to reduce suffering while actively promoting the safety, functionality, and dignity of our shared patients.

888-837-5440
info@guidestareldercare.com

GUIDESTAR ELDERCARE
One Professional Center
2100 N Main Street,
Suite 304, Crown Point, IN 46307

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