“ALS is not just a disease of the motor system,” said Catherine Lomen-Hoerth, M.D., Ph.D., Professor of Neurology at the University of California, San Francisco. She spoke in a recent ALS Association webinar, in which she outlined the growing recognition that pure motor forms of ALS may be only one of a spectrum, at the other end of which is frontotemporal lobar degeneration, a disease formerly considered entirely separate. Researchers increasingly appreciate there is a large overlap between the two, a change in viewpoint that has been underscored by the recent discovery of the C9orf72 gene, which causes both disorders, even within the same family. The webinar is available at: https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=64622647&rKey=0f6c5f24d7ac43e1

“The discovery of the C9orf72 gene is important for many reasons,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., who hosted the webinar. “Among the most important clinically is that it highlights that ALS is a disease that may affect patients in multiple ways.”

Non-motor symptoms have been recognized in ALS for over 100 years, Dr. Lomen-Hoerth said. Among the most significant non-motor symptoms of the disease are cognitive and behavioral changes, which may affect up to half of all people with ALS. In its milder forms, cognitive (i.e., thinking) changes may manifest as slight problems finding the right word or difficulty thinking through complex tasks. Mild behavioral changes may include slight increase in frustration or mild depression. These may be difficult to distinguish from the normal range of the person’s behavior and may not have a significant impact on the person’s function or relationships with the family or caregivers.

But, said Dr. Lomen-Hoerth, in about half of all people with ALS, these changes become pronounced enough to have an impact, and in almost a quarter, they qualify for the diagnosis of dementia.

The specific form of dementia most commonly found in ALS is called frontotemporal lobar dementia (FTLD), or just frontotemporal dementia (FTD). FTLD is a distinct form of dementia, not the same as Alzheimer’s disease, she said. It causes progressive personality changes, language difficulty, and/or behavioral disturbance. It is caused by degeneration of the frontal and temporal lobes of the brain, which are involved in cognition and behavior. Dementia can occur in ALS patients without mutations in the C9orf72 gene, but it is believed that mutations in the gene are the major genetic cause of ALS/FTLD. The C9orf72 gene can cause just motor forms of ALS, or just FTLD, or symptoms of both ALS and FTLD in the same person.

Not every cognitive or behavioral change in ALS is a sign of dementia or FTLD, she cautioned. For instance, depression is a common reaction to any serious diagnosis, including ALS, but is
also a symptom caused by FTLD. Non-FTLD depression is expected to respond to antidepressants better than FTLD depression. If a patient is not breathing strongly, they may build up carbon dioxide in the bloodstream, especially at night, which may cause the same type of clouded thinking and loss for words seen with FLTD. Nighttime ventilation may clear this up. Language problems due to motor impairment of the throat muscles may mimic the loss of verbal ability caused by brain atrophy.

The presence of FTLD has important clinical consequences. Survival in patients with both ALS and FTLD is shorter than in patients with ALS alone, by one year on average. This may be due to less compliance with non-invasive ventilation or gastrostomy tube, both of which extend survival, but depend on cognitive skills for the best results.

“There is also significant distress from FTLD for caregivers and family,” Dr. Lomen-Hoerth said. “The patients are often cold and hard to reason with, there is poor safety awareness, and it can be difficult for them to manage important decisions.” Keeping choices for the patient simple, and avoiding surprises, is a key part of behavioral management. A safety assessment by a social worker can make the home safer.

It is valuable for the family to have a formal diagnosis of FTLD or other dementing disorder, she said. “The knowledge that it is not something the caregiver is doing wrong, but is part of the disease process,” can be very important.

A commercial test for the C9orf72 gene may be available this spring. It would be most appropriate for patients with some history of ALS or dementia in the family, Dr. Lomen-Hoerth said. “I don't generally advise sporadic patients to be tested for chromosome 9.”

The ALS Association has a group of publications to educate people with ALS, their families, and physicians about cognitive changes and FTLD in ALS. For more information about ALS and FTD, visit http://www.alsa.org/als-care/resources/publications-videos/factsheets/fyi-cognitive-impairment.html and http://www.alsa.org/assets/pdfs/fyi/cognitive_changes_family.pdf