



ALS, Cognitive Impairment (CI) and Frontotemporal Lobar Dementia (FTLD): A Professional's Guide

Overview

A link between ALS and cognitive dysfunction was first noted in the late 1800's, but only in the last few years has additional research shed important light on the association. What was once considered a rare link between two distinct diagnoses has now been identified as a more common combination. Some recent studies suggest that 20-25% of ALS patients may have FTLN, and as many as half may have mild-to-moderate cognitive or behavioral abnormalities.

Because the general thinking among healthcare professionals has long been that ALS did not affect cognitive function, the recent studies on CI and FTLN suggest a need to re-evaluate some commonly-held approaches to teaching, treating and guiding patients and caregivers. Knowing that a patient is dealing with cognitive function or behavioral challenges will help direct professionals and caregivers to specific approaches geared to the problems the person and family will be likely to experience.

What is FTLN?

FTLN is a progressive condition that involves selected degeneration of the frontal and anterior temporal lobes of the brain, producing personality changes, language difficulty or behavioral disturbances in the patient. FTLN is different from Alzheimer's disease and presents with different signs and symptoms. For example, people with FTLN typically develop *behavior* symptoms and personality changes first, while people with Alzheimer's disease usually develop *memory* problems first. Most of those with FTLN may not experience memory problems at all.

The terminology cognitive impairment (CI) is more commonly used to describe the milder conditions of thought and behavior dysfunction.

A Summary of the Research

There is some new and interesting research with which professionals should be familiar:

- A study published in *Neurology*, in October 2002, by C. Lomen-Hoerth, Thomas Anderson and Bruce Miller, looked at 36 patients with sporadic FTLN and no known motor neuron disease, found that 14% had definite ALS, and 36% had possible ALS.





- A study published in *Neurology*, in April 2003, by C. Lomen-Hoerth, J. Murphy, J.H. Kramer, R.K. Olney and B. Miller, found that frontal executive deficits are present in half of ALS patients, and of those, many met strict research criteria for FTLD. More specifically, of 44 ALS subjects, 52% met recently developed research criteria for possible or probable FTLD.
- A study published in *Neurology*, in December 2003, by Yang W. Sopper MM, Leystra-Lantz C, and Strong MJ. Found that the presence of cognitive impairment in ALS patients was associated with microtubule-associated tau protein positive neuronal and glial. This suggests that the basis for the cognitive impairment is a disturbance in tau protein metabolism.
- At the 2004 American Academy of Neurology meetings, Strong and colleagues presented evidence that an alteration in tau protein phosphorylation is associated with the presence of tau aggregates in ALS, further confirming the suggestion that the basis of this process in ALS is a disturbance in tau protein metabolism.
- A study by EK Zimmerman, PJ Eslinger, Z. Simmons and AM Barrett (presented at the 2004 annual meeting of the International Neuropsychological Society) found that over 90% of patients with bulbar ALS had deficits in their ability to properly recognize the emotions of others (emotional perceptual deficits).
- In a study presented at the 2004 American Academy of Neurology meeting by C. Flaherty-Craig and Z. Simmons, social judgment was found to be poorer in individuals with ALS than in normal controls.
- A prospective longitudinal study (now underway) by M. Strong, G. Grace, T. Lee and J. Orange of newly-diagnosed ALS patients is assessing cognition, speech and language measures, indices of clinical progression and measures of cerebral perfusion from contrast-enhanced CT scans. The study is designed to provide a detailed longitudinal analysis of the natural history of cognitive impairment in people with ALS and whether such cognitive impairment will progress to a more definitive frontotemporal dementia.





Signs, Symptoms and Risk Factors of FTLD

Because people with ALS typically experience a steady disintegration in their ability to speak, swallow, move and perform activities of daily living, it is easy to overlook the presence of some common signs of cognitive or behavioral dysfunction such as poor insight, deficits in planning, agitation or euphoria. Executive function, a skill particularly affected in ALS patients with cognitive problems, refers to the ability to effectively handle a variety of visual, aural and other sensory data at the same time, as when one drive a car through busy streets at rush hour. This ability to integrate and organize information is also required when patients are asked to make complex decisions about life-style changes when given detailed information about changes in swallowing, breathing ability, and limb control.

Each patient with these changes will display a unique presentation of deficits – with behavioral changes alone, cognitive problems alone, or both problems simultaneously. Many patients, due to their cognitive dysfunction, lose insight into their illness and thus rarely report these deficits. Family members often misinterpret changes as symptoms of frustration with the illness itself or with the caregiver.

Risk factors for developing cognitive problems, behavior changes or a full-fledged dementia syndrome may include: older age, bulbar onset ALS, a reduction in FVC and a family history of dementia.

Diagnosis of FTLD

Frontotemporal Lobar Dementia diagnoses are based upon the Neary criteria¹ and include three subtypes of frontotemporal abnormality: the frontal variant (FTD), Progressive Non-fluent Aphasia (PNFA) and Semantic dementia (SD). Recent research suggests that the frontal variant subtype is the most common subtype among ALS patients. Core Neary criteria for FTD include early decline in social and personal conduct, emotional blunting, and loss of insight. Supportive criteria include executive dysfunction as measured by neuropsychological tests.

Neary Criteria for Frontotemporal Dementia (Supportive Features not Included)

- I. Core Diagnostic Features (all must be met)
 - A. Insidious onset and gradual progression
 - B. Early decline (within 2 years after onset) in social interpersonal conduct
 - C. Early impairment (within 2 years after onset) in regulation of personal conduct
 - D. Early (within 2 years after onset) emotional blunting
 - E. Early (within 2 years after onset) loss of insight





To diagnose the presence of dementia, a full neuropsychological examination and neurobehavioral evaluation are required. The following simple screening tools can be useful to identify those who should be referred for evaluation:

- Word Generation Tests

With **word generation tests**, patients are asked to generate words in categories, as rapidly as possible. This verbal fluency test taps into a part of the frontal lobe that is commonly atrophied in ALS patients, and this test appears to be the most sensitive in identifying ALS patients with even subtle cognitive abnormalities.

- Neurobehavioral Questionnaires

Behavior changes are equally common in ALS patients, even among those patients who have normal cognitive function. Caregivers, rather than the patient, may be asked a series of questions about behavior, since lack of insight is commonly associated with FTLD. Effective instruments for assessment of behavior change include the **short form of the Neuropsychiatric Inventory (NPI-Q)** and the **Frontal Behavioral Inventory (FBI)**. These short questionnaires can be administered to the caregiver by a team member in the clinic.

Each FTLD subtype involves unique symptoms, depending on the affected lobes. For example:

- Frontotemporal Dementia, (FTD) or “frontal”, is associated with apathy, disinhibition, decreased speech output, disorganization and poor insight
- Semantic Dementia, (SD) or “temporal”, is seen with loss of semantic knowledge, poor word comprehension, word finding problems, and loss of good insight
- Progressive Non-Fluent Aphasia (PA), or “left perisylvian”, is associated with non-fluent, difficult to execute speech, poor use of learned grammar, and good comprehension.

Research is underway to develop or select different evaluation tools for assessing CI and FTLD in people with ALS. These tools may help people with speaking difficulties and offer a different perspective to the cognitive assessment process.

Research suggests a high correlation between the results of neuro-imaging tests and those of neuro-psychological tests. MRIs identify changes in the brain and can predict CI.





It can be helpful to ask caregivers something like, “Has Mr. Smith’s behavior changed? Have you noticed he is withdrawn or gets agitated?” Such discussion may stimulate a conversation about signs and symptoms the caregiver has noticed in daily life.

The diagnosis of CI or FTLD may come either before or after the diagnosis of ALS. With those for whom the CI or FTLD diagnosis is made first, before the diagnosis of ALS, common issues include longstanding marital problems and affairs, financial problems, isolation, poor insight into ALS symptoms, and a lack of what would be considered normal despair. For those for whom the ALS diagnosis is made first, before the diagnosis of CI or FTLD, common problems include over-reaction to illness, as compared to others, increasing difficulty using communication devices, and difficulty making decisions or understanding the need for supportive equipment.

Communicating the Diagnosis of FTLD

If caregivers or patients report that behavior is sometimes getting in the way of daily life, some clinicians will begin to talk about the possibility of cognitive or behavioral changes seen in ALS, include the possibility of CI or FTLD. Some clinicians have found it helpful to focus on “personality changes” or “behavior changes”. A sizable group of ALS patients with these changes do not in fact meet criteria for dementia, so it is not helpful to use the word “dementia” until a thorough exam has confirmed this diagnosis. Cognitive changes or impairment can be used, based on the individual patient and family.

If assessment suggests FTLD is present, the diagnosis is sometimes actually a relief to caregivers and family because it often explains behavior that was previously misunderstood.

Potential Implications for Survival and Adherence

For reasons that are not yet completely understood, survival is shorter in patients who have both ALS and CI or FTLD combined than for patients with ALS alone. Some suspect that survival may be shortened partly because ALS patients with CI or FTLD are less likely to opt for noninvasive positive pressure ventilation (NIPPV) or percutaneous endoscopic gastrostomy (PEG) than are people with ALS who do not have CI or FTLD.

Clinical observations suggest that patients with ALS and cognitive deficits are also more likely to refuse a variety of treatment recommendations than do those with ALS alone. Perhaps due to poor insight into their ever-changing clinical needs, ALS patients with cognitive deficits appear to be less adherent with NIPPV, more likely to refuse to use walkers and wheelchairs, and less likely to make necessary changes in eating safety. Regardless of whether the patient has been diagnosed with a full-blown dementia syndrome, the clinician should be aware if the patient has cognitive and behavioral issues that are interfering with treatment decisions. The clinician may





effectively use techniques other than logic to inform the patient of the importance of these of these intervention options. Caregiver participation in these discussions may be helpful, particularly when the patient is having difficulty making appropriate decisions about complex end-of-life issues such as feeding tubes, ventilatory support and hospice.

Recommendations for Routine Management and Care

People with cognitive dysfunction benefit from the following approaches:

- Use more simple tools for communication than you would use with patients who have ALS alone.
- Use more simple and straightforward language and communicate clearly and directly.
- Supervise eating more closely. ALS patients with frontal lobe abnormalities and poor swallowing ability may have difficulty following medical advice to limit solid foods, or they may place too much food in their mouth.
- Assess the patient's ability to make decisions by talking with them and the caretaker, as ALS patients are faced with complicated medical, financial and sometimes legal issues. Even those patients with sub-threshold cognitive deficits that do not meet criteria for dementia may lack the ability to make sound judgments about their care. Poor insight is very common, so caregiver involvement may be appropriate.
- Supervise walking. Patients with FTLD often have a loss of impulse control and may make poor decisions about where to walk, how far to walk, or when to use equipment such as a walker.
- Remind caregivers and the family to try to avoid taking the person's behavior personally. Help them understand there is a physiological cause for the behavior.
- Encourage the caregiver and the family to try to build an atmosphere of comfort and love, with a calm and orderly environment.

Implications for Professionals

For years, professionals have taken some level of comfort from the thought that although ALS poses unique and serious challenges, the one issue patients and families were not likely to have to face was a decrease in cognitive function. Unfortunately, research now suggests that this may not be true for all ALS patients.

The diagnosis and treatment for FTLD with ALS is still evolving. However, on a positive note, some researchers are optimistic that the discovery of the association of ALS with FTLD among some patients may speed the understanding of the etiology of ALS and provide important clues to the puzzle ALS still presents.





“While one might think that the picture has become more complex,” said Michael Strong, MD, of the Department of Clinical Neurological Sciences in London, Ontario, Canada, “knowing that there is another group of cells in the nervous system – apart from the motor neurons – that are involved in the disease will allow us to expand the search for the basic mechanism underlying the damage to these cells.”

Continued study of the link between ALS and FTLN is needed, particularly in regard to understanding clinical implications, the value of imaging in diagnosis, and the genetic underpinnings of the combined diseases. The vulnerability of frontal and motor neurons suggests there may be a significant overlap between ALS and FTLN, and even a shared etiology.

Research

Flaherty-Craig C, Simmons Z. Deficient social judgment in non-bulbar amyotrophic lateral sclerosis. *Neurology* 2004(suppl 5);62:A323-A324

J.R. Hodges, et al; “Survival in frontotemporal dementia,” *Neurology*, August, 2003, pp. 349-354.

Lomen-Hoerth, Catherine, MD, PhD; Anderson, Thomas, MD; Miller, Bruce, MD, “The overlap of amyotrophic lateral sclerosis and frontotemporal dementia,” *Neurology*, October, 2002, pp. 1077-1078.

Lomen-Hoerth, Catherine, MD, PhD; et al. “Are amyotrophic lateral sclerosis patients cognitively normal?” *Neurology*, April 2003, pp 58-61.

Olney, RK, Murphy J, Forshew DA, et al. “The effects of executive and behavioral dysfunction on the course of ALS/MND.” *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, 2003; 4(suppl 1): 14.

Strong MJ, Grace GM, Orange JB, Leeper HA, Menon R, Aere C. “A prospective study of cognition in ALS.” *Neurology* 1999;53:1665-1670.

Strong MJ, Yang W, Strong WL, Pant H. “Insoluble tau protein isoforms in amyotrophic lateral sclerosis with cognitive impairment (ALSci),” *Neurology*, 2004, supplement.

Wilson CM, Grace GM, He BP, Strong MJ, “Cognitive impairment in sporadic amyotrophic lateral sclerosis (ALS): a pathological continuum underlying a multisystems disorder,” *Neurology*, 2001;57:651-657.

Yang W, Sopper MM, Leystra-Lantz C, Strong MJ. “Microtubule-associated tau protein positive neuronal and glial inclusions in amyotrophic lateral sclerosis,” *Neurology* 2003; 61(12):1766-73.





Zimmerman EK, Eslinger PJ, Simmons Z, Barrett AM. Emotional perceptual deficit in persons with amyotrophic lateral sclerosis. J Int Neuropsych Soc 2004 (in press).

Resources

The ALS Association
Patient Services Department
27001 Agoura Road, Suite 250
Calabasas Hills, CA 91301
Telephone: 818.880.9007
Fax: 818.880.9006
Toll-free Patient Hotline: 800.782.4747 or 818.880.9007
E-mail: alsainfo@national.org

Family Caregiver Alliance
690 Market Street, Suite 600
San Francisco, CA 94104
Telephone: 415.434.3388 or 800.445.8106
www.caregiver.org
E-mail: info@caregiver.org

The Family Caregiver Alliance offers a range of resources, including a “Fact Sheet on Behavior Management Strategies” for dementia.

The ALS Association thanks J. Murphy and M. Lyon for their contributions to this FYI.

Created 2005

Disclaimer: The material contained herein is provided for informational purposes only, and should not be construed as medical or legal advice on any subject matter.

No recipients of content from The ALS Association should act or refrain from acting on the basis of any content provided without seeking the appropriate medical or legal professional advice on the particular facts and circumstances at issue from a physician, attorney, or other licensed professional in the recipient’s state.

The information contained on this web site is protected by copyright and may not be published, broadcast or otherwise distributed without the prior written authorization of The ALS Association.

© 2005 by The ALS Association



The ALS Association, 27001 Agoura Road, Suite 250, Calabasas Hills, CA 91301-5104,
Phone: (800) 782-4747 / alsinfo@alsa-national.org / www.alsa.org

fyi...
for your information



The ALS Association, 27001 Agoura Road, Suite 250, Calabasas Hills, CA 91301-5104,
Phone: (800) 782-4747 / alsinfo@alsa-national.org / www.alsa.org