ALS, Cognitive Impairment & Dementia

ALS, Cognitive Impairment, and Dementia: A Professional’s Guide

Overview

Although cognitive and behavioral symptoms were documented in patients with ALS-type motor neuron disease in the late 1800’s, many of us were trained that ALS, and motor neuron diseases in general, do not impact thinking and behavior. Within the last 10 years, there has been a convergence of research on ALS clinical symptoms, neuro-radiographic patterns of pathology, and genetics that have shed important light on the association between motor neuron disease, cognition, and behavior. What was once considered a rare co-morbidity between two distinct diagnoses has now been identified as a common combination. Although prospective, population-based studies are few, the most recent studies suggest that up to 50% of ALS patients demonstrate mild to moderate cognitive and/or behavioral impairment that departs from longstanding levels of function, with up to 20% of ALS patients meeting criteria for full-blown dementia syndrome[1, 2]. Although dementia and cognitive impairment does not present in all cases of ALS, when dementia or cognitive impairment is present, it typically resembles the symptoms of Frontal Temporal Dementia (FTD) syndromes.

The most recent studies on cognitive and behavioral symptoms in ALS suggest a need to re-evaluate approaches to teaching about ALS, with a need to update medical providers. This allows us to better guide individual patients and their families through the illness. Knowing that a patient is dealing with cognitive function or behavioral challenges validates the patient, family, and patient care team experience. With this validation and added education, providers are in a better place to guide those affected by ALS through the illness. Further, there may be unique implications for treatment and disease management decision-making as a function of cognitive and/or behavioral impairment in the person with ALS. Research on the impact of cognitive and behavioral impairment in ALS is rapidly emerging.

What is Dementia?

Dementia is a term used to describe the condition for which a person has significant impairment of thinking or behavior, to the extent that it reflects a departure from the level at which a person has always functioned. The impairments in thinking and behavior have to be substantial enough to impair the person’s ability to conduct important life activities such as managing financial affairs, driving, and/or managing his/her medications. Different conditions, or disease, result in cognitive impairment and dementia. For example, Alzheimer’s disease results in Alzheimer’s dementia. FTD is a dementia that results from the progressive deterioration of the frontal and temporal lobe systems of the brain. In many cases, the disease process is due to a disturbance in TARDP protein, however; studies have demonstrated that FTD can occur from non-TARDP protein disturbances such as a disturbance in FUS protein. Whereas Alzheimer’s dementia typically presents with rapid forgetting as an initial symptoms, FTD typically presents with changes in language and/or behavior as initial symptoms. In ALS, some individuals develop dementia that most commonly presents as FTD, others develop cognitive and/or
behavioral impairment without dementia, and some patients never develop any cognitive or behavioral impairment.

**How many people with ALS develop impairments of cognition and behavior?**

There are several confounds in documenting the definitive epidemiology of cognitive and behavioral impairment in ALS. First, ALS patients can experience impairments of speaking or writing, making it difficult to identify tests that are valid in screening for such impairment. Second, the clinical presentation of ALS is so variable; it is difficult to identify the same set of tests that can be administered to all patients with ALS such that a conclusive characterization of impairment is obtained. Third, because ALS is a primary neurodegenerative disease, symptom progression over time makes it difficult to accurately assess the evolution of cognitive and/or behavioral impairments. Screening measures that were valid for assessment early in a patient’s course of illness and symptoms may not be valid to repeat in longitudinal assessment later in the patient’s course of illness and symptoms.

There have been many clinic-based studies of cognitive and behavioral impairment in ALS, using cross-sectional cohorts of patients. These studies show that up to 20% of ALS patients demonstrate dementia, roughly 30% of ALS patients develop impairment without dementia, and up to half of ALS patients are cognitively normal.

There have been at least 2 population-based studies of cognitive and behavioral impairment in ALS yielding quite similar results, despite differences in genetic backgrounds of the patients studied and methodological differences in the evaluation of cognition and behavior:

- **Phukan et al. 2012[5]** prospectively identified 160 incident Irish ALS patients and 110 matched control patients and administered neuropsychological tests to both groups. Dementia occurred in 14% of cases with a new diagnosis of ALS. Cognitive and/or behavioral impairment without dementia occurred in more than 40% of cases, and approximately 46% of cases demonstrated no cognitive or behavioral impairment.

- **Montuschi et al. 2014[6]** prospectively identified and evaluated 201 incident Italian ALS patients with neuropsychological tests. Despite vastly different genetic backgrounds than the previously published Irish population-based study, rates of impairment were quite similar between studies with 13% of the Italian patients meeting criteria for dementia, 37% of the Italian patients demonstrating cognitive impairment without dementia, and approximately 50% of Italian patients demonstrating no cognitive or behavioral impairment. Interestingly, there was one case of co-morbid Alzheimer’s dementia noted in the Italian study.

**Signs, Symptoms and Risk Factors of Dementia**
Cognitive and behavioral impairment in ALS can vary widely from individual to individual. Studies of impairment in ALS to-date likely have not fully characterized the full-range of cognitive and behavioral involvement possible.

The most commonly documented sign of cognitive and/or behavioral impairment in ALS is in the domain of executive function. Executive function impairment can reflect disturbances in reasoning, judgment, sequencing, ordering, inferring, regulating emotions, planning, retrieval inefficiency, and a person’s ability to be self-aware. When executive function is impaired, individuals can demonstrate behaviors that are in excess of what is normal such as pacing, repeating actions or phrases, getting stuck on certain ideas or thoughts, increased anxiety, increased emotional reactivity, and/or agitation. Alternatively, when executive function is impaired, individuals can also demonstrate behaviors reflecting absence of what is normal such as social withdrawal, indifference, lack of motivation, lack of follow through with instruction or direction, lack of interest, and/or lack of empathy or understanding for others.

Cognitive impairment in ALS can also disturb language, including written and oral expression, but also receptive aspects of language such as comprehension. Individuals can demonstrate slowed word-finding, even in the absence of bulbar symptoms of dysphagia and dysarthria. Spelling can be disturbed, although studies of spelling impairment in ALS have been confounded by the influence of educational quality and quantity. Individuals can “lose” meaning of words, no longer recognizing what words mean or using words correctly in sentences.

Although much less commonly documented and studied, memory impairment has been observed in patients with ALS[7]. Further, the impairment of memory does not seem to be exclusively due to co-morbid executive dysfunction.

Studies have documented that individuals who are older, less educated, and with bulbar symptoms of ALS, are more likely to have cognitive and/or behavioral impairment[6, 8]. Such factors remain poorly understood, however, and are an important focus of ongoing research.

Individuals with cognitive and/or behavioral impairment in ALS have been shown to have shorter survival times[9]. It is unclear whether this relates to older age in the cognitively and/or behaviorally impaired, or a more diffuse disease process resulting in faster longitudinal progression of illness.

**Diagnosis of Cognitive and Behavioral Impairment in ALS**

The gold standard for diagnosing cognitive and behavioral impairment in ALS is a comprehensive neuropsychological evaluation. The evaluation should include standardized measures that allow for appropriate control of writing and speech impairments the patient with ALS may have. The evaluation findings should be interpreted using normative data for measures that have been validated for use in ALS and for use in individuals with dementia. When comprehensive neuropsychological evaluation is not possible, due to geographical restriction, or limitations in the patient’s mobility and transportation, screening measures for cognitive and behavioral function can be useful.
In 2009, Strong and colleagues introduced consensus criteria[2] for the diagnosis of cognitive and behavioral impairment in ALS. This paper, and studies considered in the formulation of the consensus criteria relied heavily on the Neary criteria for Frontal Temporal Dementia (FTD)[10] which includes 3 variants of FTD (Frontal Temporal Dementia, Progressive Non- Fluent Aphasia, and Semantic Dementia. Studies suggest that Frontal Temporal Dementia is the most common variant in ALS, although the other two variants of FTD occur in ALS albeit likely less frequently. 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. There are two other known sets of clinical criteria for FTD (Hodges Criteria[11], Gorno-Tempini[12]); however the relationship between the cognitive and behavioral impairment and ALS are not as well-studied to date.

Since the publication of this initial consensus criteria paper, research has exploded in the area of cognitive and behavioral impairment in ALS, with many new insights. Cognitive and behavioral symptoms may proceed or follow the onset of traditional ALS symptoms such as muscle atrophy, spasticity, changes in speech, changes in breathing, and/or changes in swallowing. Whereas the Strong and colleagues consensus criteria stress the presence of executive function impairment, several studies have documented non-executive cognitive impairment in ALS.

Screening tools that are useful for evaluating the presence/absence of cognitive and behavioral impairment in ALS include:

- **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 executive cognitive functions of the frontal lobe that is commonly impacted in ALS, and this test appears to be sensitive in identifying ALS patients with even subtle cognitive abnormalities[13].

- **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 or self-awareness is a behavioral symptom unto itself in ALS. Effective instruments for assessment of behavior change include the short form of the Neuropsychiatric Inventory (NPI-Q) [14]and the Frontal Behavioral Inventory (FBI). These short questionnaires can be administered to the caregiver by a team member in the clinic.

  It can be helpful to ask caregivers or family members if there are any changes in the patient’s behavior. Such discussion may stimulate a conversation about signs and symptoms the caregiver has noticed in daily life. In many cases, caregivers or family members may not notice changes but members of your health care team do see changes such as the patient not following directions during assessment or evaluation of breathing, the patient not following advice of the physical therapist or occupational therapist, continued choking in a dysphagic
patient that has been educated by the speech language pathologist about swallowing precautions. If you suspect that cognitive or behavioral impairment may be present, it is important to clarify with family members and/or caregivers of the patient.

**Communicating the Diagnosis of Cognitive and/or Behavioral Impairment**

Many health care providers can consider the risk of sharing a diagnosis of cognitive and/or behavioral impairment with the ALS patient and/or his family. The goal of communicating the diagnosis is practical and this is something to keep in mind. Often times, family members and caregivers need to know and want to know so that they can set appropriate expectations for the patient, knowing when to encourage the patient to do more for him/herself, and knowing when others need to step in and act on the patient’s behalf. Team members caring for the patient need to know to whom and how to communicate advice, directions, and symptom management information. If a patient is cognitively impaired or lacks self-awareness of behavior, it is not a good use of time to inform the patient of disease/symptom management instructions, but rather to spend time with family members and caregivers who will have to make decisions on the patient’s behalf. Establishing formal power-of-attorney, conservatorship, health care surrogacy, and sometimes even guardianship are very important to address to make sure that the patient is kept safe and that liability for the patient and family is reduced.

Using terms such as “dementia” are not always helpful. It can be very helpful to reassure patients, family members, and caregivers that there are cognitive and/or behavioral symptoms the patient is having as a part of having ALS. In clinical trials, if cognitive and/or behavioral impairment is present in a patient, an appropriate representative must give informed consent with verbal assent from the patient.

**Potential Implications for Survival and Adherence**

For reasons that are not yet completely understood, survival is shorter in ALS patients with cognitive and/or behavioral impairment relative to ALS patients without cognitive and/or behavioral impairment. Impaired ALS patients may be less likely to opt for life-prolong symptom management procedures such as noninvasive positive pressure ventilation (NIPPV) or percutaneous endoscopic gastrostomy (PEG) than are people with ALS without impairment[15]. 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.

**Recommendations for Routine Management and Care**

Here are some suggestions for working with the ALS patient who has cognitive and/or behavioral impairment:

- Use 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 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 caregiver, 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 and transfers. Patients with cognitive and/or behavioral impairment 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.

Advice for Providers who Manage ALS Symptoms

It is increasingly important to recognize that cognitive and/or behavioral symptoms may be part of the heterogeneous and dynamic presentation of ALS. More importantly, it is crucial to keep in mind that studies continue to emerge suggesting that cognitive and behavioral impairments can be manifest in Primary Lateral Sclerosis[16, 17] and Progressive Muscular Atrophy[18, 19]. Therefore, as we continue to work with people and families affected by motor neuron disease, clinical and scientific understanding can grow as a function of our inquiry and documentation of all symptoms observed throughout the course of a patient’s journey.

References


Revised October 2014 by Beth K. Rush, Ph.D., ABPP.

The ALS Association thanks and acknowledges Beth K. Rush, Ph.D., ABPP from the Mayo Clinic for sharing her time and expertise on revising this factsheet. In addition, The Association thanks J. Murphy and M. Lyon for their contributions to this FYI.

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.