

Decisional Capacity in Amyotrophic Lateral Sclerosis

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The cognitive and behavioral changes that can be observed in the neurodegenerative terminal disease amyotrophic lateral sclerosis (ALS), once characterized as purely a motor neuron disease, have become increasingly recognized over the past century. Detecting cognitive deficits earlier and identifying continued changes at regular intervals can lead to improved care, proactive treatments, and earlier discussions about end-of-life wishes. Although medical decisional capacity is required for every treatment decision made, its importance becomes paramount when making decisions on complex medical treatments that will invariably and significantly affect quality of life or life itself. In this review, we conducted a critical analysis of the evidence-based literature on the cognitive and behavioral impairments in ALS that can compromise medical decisional capacity. We review specific ALS-related clinical scenarios in which decisional capacity is of utmost importance and discuss a practical framework for cognitive and behavioral assessment that can be routinely and efficiently used, while being mindful of the confounding factors associated with ALS. Finally, we review models for preserving patient choices that can be used in patients with ALS to help safeguard autonomy and retain dignity toward the end of life.

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The impact of the neurodegenerative terminal disease amyotrophic lateral sclerosis (ALS) on the motor system has been well documented. Despite great variation in disease progression, patients with ALS eventually succumb to paralysis of the respiratory muscles. In North America and Europe, the prevalence of ALS ranges between 2.16 and 7.4 per 100,000 people.^{1,2} In the United States, about 5,600 patients are diagnosed with ALS every year, and approximately 18,000 Americans live with ALS at a given time.³ Within three

to five years after diagnosis of ALS, patients usually die of respiratory failure.⁴

Although physical deficits may be the most notable, cognitive deficits are equally important to recognize and address in patients with ALS. Cognitive abnormalities, affecting 35.6 to 50 percent of patients with ALS, can range from language deficits to frontotemporal dementia (FTD), leading to a wide spectrum of behavioral and functional impairments.⁵

Patient autonomy is a central principle in contemporary medicolegal doctrine. ALS-related cognitive and behavioral deficits can compromise this fundamental right of self-determination, as they can have a substantial impact on a patient's capacity to make medical decisions. Currently, there are no clear guidelines on determining decisional capacity in patients with ALS. With early assessment of cognitive changes among patients with ALS, barriers to treatment can be overcome, and further support can be tailored to individual patients' needs that may improve their overall quality of life and ensure their autonomy.

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Cognitive and Behavioral Impairments Associated with ALS

When first described by Charcot in 1874, ALS was characterized as a disease confined to the motor neuron system. In 1892, Marie noted emotional lability in patients with ALS. By early 1900s, case reports describing cognitive changes ranging from irritability to delusions and hallucinations began to emerge.⁶ Over the past 100 years, our understanding of ALS has notably evolved. Today, it is readily recognized as a multisystem disorder that can be associated with varying degrees of cognitive and behavioral dysfunctions. In 2007, an international research workshop held in Canada proposed a consensus on the classification system characterizing the cognitive and behavioral syndromes of ALS. There are five categories based on this conceptual framework: ALS-frontotemporal dementia (ASL-FTD), ALS-behavioral impairment (ALSbi), ALS-cognitive impairment (ALSci), FTD-motor neuron disease [MND]-like, and ALS-comorbid dementia.⁷

Amyotrophic Lateral Sclerosis-Frontotemporal Dementia

In this category, patients meet the criteria for the motor neuron disease of ALS and have frontotemporal lobar degeneration (FTLD), manifesting as frontotemporal dementia (FTD), as defined by the Neary criteria.⁸ There are three subtypes of FTD: a behavioral variant (bvFTD), progressive nonfluent aphasia (PNFA), and semantic dementia (SD). Of these subtypes, bvFTD is the most common presentation in ALS and is characterized by the insidious onset and gradual progression of altered social and personal conduct, emotional blunting, and loss of insight.^{7,9} Behavioral features seen in bvFTD can be further categorized into three subgroups: disinhibited type, apathetic type, and stereotypical type.^{6,9} bvFTD patients may have language deficits, with verbal fluency being the most common; however, the behavior component is the prominent feature of their decline from baseline.^{6,7}

Patients with PNFA have problems with language expression, but their ability to comprehend is intact. Symptoms usually include anomia, grammatical errors, paraphasia, stuttering, oral apraxia, alexia, and agraphia.^{6,7} Patients with ALS rarely present with the SD subtype of FTD, which is characterized by fluent speech with anomia and poor comprehension of word meanings and object

Table 1 Consensus Diagnostic Criteria for Frontotemporal Dementia (Ref. 8, p 1548)

Main diagnostic criteria
Insidious onset and gradual progression
Early decline in social interpersonal conduct
Early impairment in regulation of personal conduct
Early emotional blunting
Early loss of insight
Other criteria supporting diagnosis
Behavioral changes (such as mental rigidity, distractibility, stereotypy)
Speech and language changes (such as mutism or pressure, echolalia, perseveration)
Physical signs (such as primitive reflexes, muscle rigidity and tremor, low blood pressure)

identity, resulting in impairment of conceptual knowledge.^{6,7,9}

It is important to note that the presentation of FTD in ALS can occur before, simultaneously, or after motor neuron symptoms manifest. The most common scenario is that the FTD symptoms precede the motor symptoms of ALS.^{6,10} Patients with FTD also have early onset of executive dysfunction, including problems with planning, organizing, prioritizing, and verbal fluency.⁶

ALS-Behavioral Impairment

Not all patients with ALS and behavioral impairments meet the criteria for FTD. In these cases, the patients are categorized as having ALSbi.^{6,7,11} They have at least two diagnostic features from the Neary criteria (Table 1),^{8,12} the Hodges criteria (Table 2),¹³ or both, supported by two sources: caregiver report and patient interview/observation or structured interview.⁷ Common behavioral changes seen with ALSbi are apathy, distractibility, mental rigidity, lack of volition and mental effort, and perseverative and stereotyped behavior.^{6,7,9,11}

Psychiatric disorders, personality disorders, psychological response to the illness, and pseudobulbar

Table 2 Consensus on Diagnostic Criteria of Behavioral Variant of Frontotemporal Dementia (Adapted from Ref. 13, Table 3, p 2460)

Diagnostic features
Disinhibition
Apathy/inertia
Loss of sympathy or empathy
Perseverative, stereotyped, or ritualistic behavior
Hyperorality and dietary change
Executive dysfunction

affect should be ruled out as potential causes of the behavioral changes before giving a diagnosis of ALSbi.⁷ Because apathy is the most common behavioral change, other factors such as fatigue, weakness, and respiratory dysfunction should be considered as potential confounders as well.¹¹

ALS-Cognitive Impairment

Patients with ALS and mild cognitive dysfunction that does not meet the full Neary criteria fall into the ALSci category. According to the current diagnostic criteria, patients must score below the fifth percentile on at least two executive-functioning tests.⁷ These patients have a range of impairments, including problems with verbal fluency, attention, and working memory, which are further characterized as frontal dysexecutive syndrome.^{6,7,9-11} Verbal fluency deficits include letter and category fluency problems.⁹ Memory and other language deficits are not as common as problems with verbal fluency.¹⁰ Memory problems present as poor immediate recall, and language deficits present as mutism, echolalia, and perseverations.^{9,10}

As noted with ALSbi, patients with ALSci should also undergo a full workup to rule out confounding causes of poor performance on cognitive tests, such as premorbid intellectual level, pseudobulbar affect, delirium, poor sleep, pain, fatigue, and medications.¹⁰

FTD-Motor Neuron-Like Disease

In this category, FTLD is the primary diagnosis with neuropathological evidence of motor neuron degeneration that is insufficient to be classified as ALS.⁷

ALS Comorbid Dementia

This category includes patients who meet the criteria for ALS and non-FTD dementias, such as Alzheimer's, vascular, or mixed dementia.^{6,7}

Other Categories

Research into ALS and cognitive impairments is ongoing. Of note, it is increasingly recognized that ALSbi and ALSci are not mutually exclusive states.^{10,11} Often, patients meet the criteria for both categories, with those with ALSci being more susceptible to behavioral changes. A suggested new category for these patients would be ALSci/bi.¹¹

Considerations for Cognitive and Behavioral Assessment in ALS

Estimates of cognitive impairment in ALS range from 35.6 to 50 percent.⁵ A range of comprehensive neuropsychological tests can provide nuanced and specific data on cognitive ability. However, the time- and resource-intensive nature of neuropsychological batteries hinders their practical and widespread use in ALS clinics.^{6,14} A more plausible approach would be to detect possible cognitive and behavioral impairment at an early stage *via* brief screening tests and then to refer patients with positive results for more extensive testing.^{7,10} One practical framework proposed by Strong and colleagues⁷ involved a hierarchical approach outlining the following testing paradigms: a brief screening of 2 to 5 minutes, a more extensive assessment of 5 to 20 minutes, and formal neuropsychiatric testing. As they noted, screening tests cannot be used in formal diagnosis of cognitive ALS-FTD, ALSbi, or ALSci.

As of 2009, the practice parameter update from the American Academy of Neurology acknowledged the lack of consensus on the best screening tests for cognitive impairment in ALS.¹⁵ However, the domains that are most commonly investigated in screening instruments for cognitive impairment in ALS are executive functions, including verbal fluency, memory, attention and concentration, language, visual-spatial skills, and emotional functioning.^{6,7,9,10} An effective screening test would also take into account input from the caregivers and family members who may be better able to observe subtle changes in cognitive and behavioral functioning compared with baseline.⁹

A good screening examination should include a test that measures verbal fluency, whether written or oral, since studies have indicated that fluency deficits may be the earliest sign of cognitive dysfunction in ALS.^{7,16} Many investigators have recommended word-generation tests for screening, some of which can be completed in less than two minutes.¹⁷ Gordon *et al.*¹⁸ also found good results when using a word-generation task as a brief screening measure in patients with ALS.¹⁸ A word generation test is also a good screening tool for identifying dysfunction of the frontal lobes, which has been well characterized in ALS.⁹

The Mini Mental Status Examination (MMSE), one of the most commonly used cognitive screening

instruments in all clinical settings, may be of limited utility in patients with ALS, because it provides a poor assessment of the executive and behavioral dysfunction common in ALS. Another widely used cognitive screening instrument is the Montreal Cognitive Assessment (MOCA). Some practitioners have favored its use in this setting because it measures the aspects of cognition that are most likely to be altered in ALS, including verbal fluency.⁷

Other intermediate-length tests (5–20 minutes) that have been shown to be effective in various studies include the Frontal Assessment Battery (FAB), ALS Cognitive Behavioral Scale (ALS-CBS), Penn State Rapid Screening Battery (PSRSB), Frontal Behavioral Inventory (FBI), Neuropsychiatric Inventory (NPI), and Frontal Systems Behavior Scale (FrSBe).⁷ Floris *et al.*¹⁹ showed that the Frontal Assessment Battery (FAB) has excellent sensitivity (92–100%) and good specificity (75–100%) in detecting cognitive impairment in ALS. However, it cannot assess for ALS-related behavioral disturbances, such as apathy and disinhibition. Other brief neuropsychological instruments such as the ALS Cognitive Behavioral Scale (ALS-CBS) can assess both cognitive and behavioral features. However, the ALS-CBS assessment is limited to predominantly frontal domains and can therefore miss the general cognitive deficits associated with ALS.¹⁹

These observations provide an explanation as to why there is no universally accepted best screening test for cognitive and behavioral impairments in ALS. However, being knowledgeable about the test options and their associated limitations can enable clinicians to choose based on clinical information, time constraints, and comfort with the use of each test.

When assessing for cognitive and behavioral deficits in this setting, an important consideration is to adapt the existing tests to patients who may have limited verbal or motor ability due to the motor symptoms of ALS, such as dysarthria and marked weakness. For example, the Frontal Assessment Battery (FAB) is particularly suitable for patients with motor and speech impairments given the nature of the test.¹⁴ An ALS patient with significant motor dysfunction who is cognitively intact may score artificially low on a screening test that relies heavily on normal verbal and motor ability.⁶ This possibility is a considerable concern, as such a patient may wish to make medical decisions that are critically important

to both quality of life and dying with dignity. It would be a great loss to a patient if he were mistakenly deemed to lack the capacity to make such decisions due to an invalid or inappropriate screening test. The clinician conducting the screening examination should be meticulous in taking into account all complicating factors that could be responsible for the patient's altered mental status.

As in all medically ill patients who undergo screening for cognitive impairment, it is important to ensure that an underlying psychiatric condition is not contributing to the apparent deficit. Therefore, it is prudent to complete screening for anxiety and depression as part of a comprehensive cognitive workup in patients with ALS.⁹

ALS-Associated Clinical Scenarios and Decisional Capacity

Since ALS is a progressive neuromuscular disease that is inevitably fatal, the mainstay of ALS management is palliation with symptom control.¹⁵ In this context, the primary role of the treatment providers becomes the optimization of quality of life.²⁰

Although medical decisional capacity is essential for every treatment decision made, its importance becomes paramount when making decisions on complex medical treatments that will invariably and significantly affect quality of life or life itself. There are several treatment interventions commonly encountered in ALS management, where decisional capacity is critical, given the complexity surrounding their risk-benefit profile, cost, and logistic plausibility.

Respiratory

In most cases, the cause of death in patients with ALS is progressive respiratory failure. Assisted ventilation can be noninvasive or invasive, depending on the stage of the disease. Life cannot be sustained indefinitely in patients with ALS with noninvasive positive pressure ventilation (NIPPV). Ultimately, patients may need invasive ventilation such as tracheostomy/long-term mechanical ventilation (TMV).²⁰ The question of decisional capacity can arise surrounding the initiation, withholding, and withdrawal of assisted ventilation.

Nutrition

Bulbar dysfunction is seen in 20 to 30 percent of patients with ALS, which can eventually place the patients at risk for malnutrition, dehydration, and

aspiration. When conservative management of dysphagia fails, placing a feeding gastrostomy tube becomes a treatment option.^{20,21} The most commonly used approach is the percutaneous endoscopic gastrostomy (PEG). There has not been a consensus on the indication and timing of PEG placement, which can make the decision process more challenging for the patients.²⁰

End-of-Life Care

Given the progressive nature of ALS and its devastating impact on patients, earlier referral to hospice and more aggressive use of palliative treatments have been called for to ensure a more peaceful terminal phase.²⁰

In addition to withholding and withdrawal of interventions, physician-assisted dying and euthanasia are two other possibilities to be mindful of in end-of-life care for patients with ALS. The distinguishing feature between physician-assisted dying and euthanasia is who administers the lethal dose of medication. In physician-assisted dying, the physician's role is limited to providing a patient with a prescription of lethal medication that is self-administered by the patient. In euthanasia, the physician both provides and administers the medication.²¹ According to one survey in The Netherlands, where both practices are legal, 20 percent of patients with ALS resorted to euthanasia or physician-assisted dying.²⁰ A 2015 groundbreaking ruling by the Ottawa Supreme Court would make physician-assisted dying available to consenting adults who have a "grievous and irremediable" condition, causing "endless suffering," physical or psychological. The Court has given the Parliament one year to craft a legislative response reflecting this decision. One of the plaintiffs in this case was Gloria Taylor, a patient with ALS.²² In the United States, the federal government, all 50 states, and the District of Columbia prohibit euthanasia under general homicide laws. The federal government does not have laws for physician-assisted dying; such legislation is generally initiated at the state level. There are four states where physician-assisted dying has been legalized: Oregon, Washington, and Vermont *via* legislation and Montana *via* court ruling.²³ In 2014, New Mexico had a similar court ruling; however, the decision is currently under appeal by the New Mexico Attorney General.²⁴

Assessing Decisional Capacity in ALS

A central principle in contemporary medicolegal doctrine of the United States is the concept of patient autonomy. The tenet of informed consent is derived from this fundamental right of self-determination. The right to refuse treatment is supported by both common law and constitutional rights in the United States.²⁵ To disregard a patient's refusal and proceed with a medical intervention may constitute assault and battery. Conversely, to mistakenly honor the treatment refusal of a patient who lacks medical decision-making capacity may have dire consequences for the patient.²⁶

Medical decision-making capacity encompasses a few essential elements. A patient must be able to understand his condition and the diagnostic and available therapeutic options. In the discussion of treatment options, the patient must understand the associated benefits, risks, and reasonable alternatives. In addition, the patient must be able to engage in a rational process of manipulating the relevant information and choose an option in alignment with his value system. Finally, the patient must be able to communicate a clear and consistent choice to a medical provider.²⁶⁻²⁸

There are a few noteworthy clinical features of ALS that can impair medical decision-making capacity. As discussed above, in the behavioral variant type of frontotemporal dementia (bvFTD), which is the most frequently encountered type of ALS-FTD, loss of insight is a common presentation. This clinical feature can interfere with the patient's ability to understand his condition and the need for treatment.^{7,10} In cases of ALS-behavioral impairment (ALSbi), mental rigidity can hinder a patient's ability to grasp the relevant information adequately and arrive at a rational decision.^{6,7,9,11} In cases of ALS-cognitive impairment (ALSci), problems with verbal fluency, attention, and working memory can obstruct various aspects of the capacity process, including the patient's ability to understand and retain information and communicate a clear, consistent choice.^{6,7,9-11}

As with any adult patient, those with ALS are presumed to have capacity until determined otherwise.²⁹ It is important to remember that capacity is task and time specific, highlighting that there is no such thing as global incapacity. Incapacity is not a status-based judgment; being elderly or having ALS

or even dementia does not automatically equate to incapacity.^{27,29} In addition, capacity is fluid, in that it is more than an all-or-nothing status. Providers can work with the patient to help preserve capacity through a supported decision-making process by educating the patient about treatment choices and assisting the patient to make and communicate preferences and decisions.³⁰

Preservation of Patient Decision-Making Rights

Presently, the consensus is lacking on any particular preservation-of-competence method that has been shown to work well in patients with ALS. In its absence, advance directives and surrogate decision-making can be used to preserve patients' choices so that they can give directions for future medical care and have their wishes honored in the event of incapacity.³¹

Advance Directives

An advance directive is a written statement executed by a competent adult and designed to provide information on the individual's wishes regarding the nature and the extent of future medical care if the patient no longer has decisional capacity.²⁵ The individual has the right to make, change, or revoke an advance directive at any time, highlighting the importance of patient autonomy.³² There are two types of advance directive.

A living will is an instructional advance directive that allows the patient to lay out, with various degrees of specificity, the clinical circumstances under which the patient would not want to receive life supporting or sustaining treatment and the types of treatment to be provided, withheld, or withdrawn.^{25,32}

A durable power of attorney for health care is a proxy form of an advance directive that identifies and designates a person or persons to make decisions about the patient's medical care if the patient lacks capacity.^{25,32} It is important to note that this is also a form of surrogate decision-making.²⁹ Therefore, the role of the proxy will be further discussed in the next section along with that of the surrogate.

Worldwide, as with the legality of physician-assisted dying and euthanasia, the legality of medical treatment directives varies by jurisdiction. Treatment directives are legally binding in countries such as Australia, Belgium, Canada, Denmark, England and Wales, New Zealand, Spain, and The Nether-

lands. Austria, Germany, Norway, Sweden, and Switzerland have also taken official steps to recognize treatment directives with some proposals and bills in recent years. However, in countries such as France, Italy, and Japan, treatment directives have no legal status at all.³³

In the United States, the Patient Self-determination Act, codified by the Omnibus Budget Reconciliation Act of 1990, became law in 1991.^{25,32} Under this Act, patients' rights under state laws concerning advance directives include the right to participate in and direct their own health care decisions, the right to accept or refuse medical or surgical treatment, and the right to prepare an advanced directive.²⁵

All 50 states and the District of Columbia have passed legislation to legalize some form of advance directive. However, the laws governing advance directives vary from state to state, and an advance directive in one state may not have legal recognition in another. In addition, there are statutes allowing physicians to decline to follow the advance directives, if they are inconsistent with ethical, sound medical practice, and sometimes to override the patient's decision altogether.³⁴

Surrogate Decision-Making

In the absence of advance directives, decision-making authority falls onto surrogates. The surrogate selection process can take various paths.

Even without having a formal advance directive, the patient can informally designate a surrogate by informing the health care provider. This process usually requires the presence of a witness.²⁹

When there is a conflict among potential surrogates or no potential surrogate can be secured, the court can appoint a surrogate, known as a guardian or a conservator. The petition is usually filed by a relative or by the administrator of an institution/facility. This process can be time consuming and expensive.

Without a formal patient-appointed proxy, an informal patient-designated surrogate, or a court-appointed guardian, the health care provider can select the surrogate pursuant to the existing legal guidelines.²⁹ Most state legal codes identify a hierarchical list of potential surrogates²⁷; 43 states have default surrogate laws.³⁰ Default surrogates are the most common type. It is noteworthy that many states impose limitations on default surrogates that vary based on jurisdictions. The limitations range from

not allowing them to consent to extraordinary interventions to restricting their authority to withhold or withdraw life-sustaining treatment under certain situations only.²⁹

For those patients without any family or friends, referred to as “unbefriended patients,” the decision-making authority may fall on the court-appointed guardian, the provider, or the ethics committee of the institution.^{29,30}

In terms of the role of surrogate, a three-step hierarchy has been proposed: the patient’s expressed wishes; the surrogate’s substituted judgment, where the surrogate infers the patient’s wishes from prior statements and conduct; and the patient’s best interest where the focus is on his welfare in the absence of evidence of his wishes.^{25,29} This sequential order reflects and ensures the unrelenting respect for patient autonomy.

Conclusion

The following guidelines are offered for patients with ALS in clinical settings. By conducting brief cognitive and behavioral screening of patients at regular intervals, those who start to show deficits in these areas can be identified and monitored closely. These patients can then undergo more extensive testing and, if deemed necessary, complete full neuropsychological testing and subsequent competence assessment. When assessing cognition, evaluators should be mindful of conditions that mimic cognitive decline such as depression, anxiety, pseudobulbar affect, medication side effects, delirium, and hypoxia.

These cognitive and behavioral screening tests for ALS can be incorporated in the inpatient and outpatient settings with reproducibility and validity, which can help recognize deficits that affect decision-making. Detecting cognitive deficits earlier and identifying continued changes at regular intervals can lead to improved care, proactive treatments, and earlier discussions about end-of-life wishes. Screening tests that assess executive and emotional functioning should take into account the caregivers’ input. In addition to being a part of the screening tests, family members and caregivers should strive to be knowledgeable about the patient’s goals of care *via* direct communication, advance directives, or assignment of surrogate decision makers.

Since decisional capacity is task and time specific, reassessing a patient’s goals of care periodically is

equally as important, as the patient’s wishes may change as the illness advances. The progression of ALS is not predictable and is quite variable. Being proactive about a patient’s cognitive and behavioral deficits as well as knowing his preferences and decisions regarding complex medical decisions can help safeguard autonomy and ensure that dignity will be retained toward the end of life.

This review highlights the need for a well-established infrastructure to assess medical decision making capacity in patients with ALS. The question of how to correlate clinical deficits in cognitive and behavioral function to the patient’s capacity to make medical decisions remains a challenge.

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