Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Section Editor

Editors' note: ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS

In "ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS," Crockford et al. presented data that show that patients with ALS have impaired cognition and behavior and that these deficits worsen with increasing severity of disease. Raaphorst et al. question whether these changes are the result of frontotemporal dementia or nocturnal hypoventilation due to ALS-associated respiratory muscle weakness. They suggest that it would be helpful to have data on the number of stage 4 patients (patients with respiratory or nutritional insufficiency requiring intervention) who required noninvasive ventilation (NIV) and the extent of each subject's respiratory dysfunction. Abrahams and Crockford reply that 27.78% of stage 4 patients required NIV, but that there was no significant difference in cognition or behavior and requirement for NIV or lack thereof. However, they agree with Raaphorst et al. that given that respiratory dysfunction is a feature of late-stage ALS and memory impairment is associated with advanced-stage ALS, ventilatory support could potentially improve memory deficits in this population. They emphasize that further research on the relationship between respiratory dysfunction and cognition/behavior in ALS is required, as the current data on this topic come from a single small study.

Ariane Lewis, MD, and Steven Galetta, MD
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Reader response: ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS

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We read the article by Crockford et al.[1] with great interest. Approximately 35% of patients with amyotrophic lateral sclerosis (ALS) have cognitive and behavioral changes, and 15% have frontotemporal dementia (FTD). The authors found increasing cognitive and behavioral impairment in patients with ALS, in relation to disease severity. We question the extent that these symptoms are ALS specific and reflect spread of the degenerative process in the prefrontal cortex, thus corroborating the link between ALS and FTD.

In ALS, respiratory muscle weakness (e.g., a vital capacity [VC] of 60%–80% of predicted) is associated with cognitive deficits (letter fluency and verbal memory), which improve by noninvasive ventilation (NIV).[2,3] Behavioral impairment (apathy and hallucinations) may also be due to nocturnal hypoventilation.[4] Patients in King's clinical stages 1–3 may already have some degree of respiratory involvement (e.g., a VC between 60%–80% without complaints of hypoventilation) associated with cognitive and behavioral impairment.

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To appreciate more fully the important findings, it would be helpful if the authors present relevant data on respiratory assessments for each subgroup and their relation to cognitive and behavioral data. In addition, the proportion of King's stage 4 patients on NIV, if any, may be of interest.[5]

1. Crockford C, Newton J, Lonergan K, et al. ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS. Neurology 2018;91:e1370–e1380.
2. Newsom-Davis IC, Lyall RA, Leigh PN, Moxham J, Goldstein LH. The effect of non-invasive positive pressure ventilation (NIPPV) on cognitive function in amyotrophic lateral sclerosis (ALS): a prospective study. J Neurol Neurosurg Psychiatry 2001;71:482–487.
3. Kim SM, Lee KM, Hong YH, et al. Relation between cognitive dysfunction and reduced vital capacity in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2007;78:1387–1389.
4. NICE guideline. Motor neurone disease: assessment and management. In: NICE (National Institute for Health and Care Excellence) [online]. Available at: nice.org.uk/guidance/ng42. Accessed October 1, 2018.
5. Lakerveld J, Kotchoubey B, Kubler A. Cognitive function in patients with late stage amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2008;79:25–29.

Author response: ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS

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We thank Raaphorst et al. for the comment on our article.[1] We acknowledged the possible role of respiratory functioning in both the discussion and analysis of data without stage 4 patients; however, 27.78% (n = 15) of stage 4 patients in this study were on noninvasive ventilation (NIV) at the time of testing for at least 2 weeks. No substantial differences were found in any cognitive or behavioral domain between NIV and non-NIV stage 4 patients.

Few studies examine, in depth, the effect of respiratory dysfunction on cognition/behavior in amyotrophic lateral sclerosis (ALS). Moreover, the evidence that NIV ameliorates neuropsychological dysfunction is based on a single small study (n = 9), which found improved functioning in 2 of 6 memory measures, and not on verbal fluency.[2] The effect of respiratory dysfunction on cognition/behavior is not properly understood, and there is little evidence that this potential effect is transient.

Although we acknowledge the possible moderating role that respiratory insufficiency may play in cognitive dysfunction in ALS, this is not the sole driver of our results.[1] However, this highlights an important avenue for further research.

1. Crockford C, Newton J, Lonergan K, et al. ALS-specific cognitive and behavior changes associated with advancing disease stage in ALS. Neurology 2018;91:e1370–e1380.
2. Newsom-Davis IC, Lyall RA, Leigh PN, Moxham J, Goldstein LH. The effect of non-invasive positive pressure ventilation (NIPPV) on cognitive function in amyotrophic lateral sclerosis (ALS): a prospective study. J Neurol Neurosurg Psychiatry 2001;71:482–487.

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Editors' note: To harvest?: A reality-based ethical dilemma and fictional dialogue

In the humanities section article "To harvest?: A reality-based ethical dilemma and fictional dialogue," Drs. Smith and Riggs debate the ethics of harvesting a patient's organs if their surrogate wants the organs donated but reports that the patient did not want to be an organ donor and then later revokes the comment about the patient not wanting to be a donor. They question whether the surrogate's willingness to consent should override the possibility that the patient previously dissented and whether a statement made in passing that an individual does not want to be an organ donor represents informed dissent. Dr. Sethi notes that it is challenging to distinguish between uninformed and informed dissent when one cannot speak directly to the individual involved to ascertain whether they were competent and knowledgeable at the time of the dissent. However, he proposes that it may be helpful to interview the patient's other family members about the issue of dissent. Drs. Smith and Riggs voice appreciation for Dr. Sethi's thoughtful response and comment that it is helpful to contemplate ethical controversies in a hypothetical context to be better prepared to address them in real life.

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Reader response: To harvest?: A reality-based ethical dilemma and fictional dialogue

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I read with rapt attention the reality-based ethical dilemma and fictional dialogue on organ harvesting after cardiac death by Drs. Smith and Riggs.[1] For informed consent to be truly informed, the information provided to the patient is a necessary and obligatory premise.[2] One may argue that it also depends on the competence and knowledge of the physician or the person providing the information to the patient. Informed dissent too has to meet the above prerequisites. In the authors' fictional case,[1] it is impossible to determine the quality of the consent or dissent. The mother and close family members should be interviewed in depth in an attempt to ascertain this information. So, will I let the organs be harvested or not? To that question, I would answer, "No."

1. Smith MS, Riggs JE. To harvest?: a reality-based ethical dilemma and fictional dialogue. Neurology 2018;91:666–667.
2. Conti AA. From informed consent to informed dissent in health care: historical evolution in the twentieth century. Acta Biomed 2017;88:201–203.

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Author response: To harvest?: A reality-based ethical dilemma and fictional dialogue

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We appreciate the rapt attention that our piece[1] evoked in Dr. Sethi. That is exactly the response we were hoping for in readers. When faced with these kinds of ethical dilemmas, one always wishes for more information. Ultimately, however, in these difficult situations, some decision and course of action (right or wrong) will occur. It is far better to have at least contemplated these issues beforehand, rather than only after one finds him/herself immersed in such issues.

1. Smith MS, Riggs JE. To harvest?: a reality-based ethical dilemma and fictional dialogue. Neurology 2018;91:666–667.

CORRECTIONS

TDP43 pathology in the brain, spinal cord, and dorsal root ganglia of a patient with FOSMN

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In the article "TDP43 pathology in the brain, spinal cord, and dorsal root ganglia of a patient with FOSMN" by Rossor et al.,[1] first published online January 30, 2019, the headings for table 2 should read "MCV, m/s" and "DML, ms." The authors regret the errors.

Reference

1. Rossor AM, Jaunmuktane Z, Rossor MN, Hoti G, Reilly MM. TDP43 pathology in the brain, spinal cord, and dorsal root ganglia of a patient with FOSMN. Neurology 2019;92:e951–e956.

Journal Club: Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages

Neurology® 2019;93:88. doi:10.1212/WNL.0000000000007523

In the article "Journal Club: Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages" by Charidimou et al.,[1] the following reference should have been included, detailing a study by Dr. Nicolas Raposo et al.:

Raposo N, Planton M, Péran P, et al. Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages. Neurology 2017;89:697–704.

The authors regret the error.

Reference

1. Charidimou A, Giese AK, Pasi M, et al. Journal Club: Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages. Neurology 2018;91:574–577.

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TDP43 pathology in the brain, spinal cord, and dorsal root ganglia of a patient with FOSMN

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