Locked in, but not out?

Leigh R. Hochberg, MD, PhD
Merit E. Cudkowicz, MD, MSc

Correspondence to Dr. Hochberg: lhochberg@partners.org

Neurology® 2014;82:1852–1853

The most devastating aspect of amyotrophic lateral sclerosis (ALS) may not be the loss of mobility or spontaneous respiration but the inability to communicate. For people with ALS who elect mechanical ventilation, the inexorable disease progression can lead to an incomplete locked-in syndrome (LIS)[1,2] and then to a total LIS where neither eye movements nor any other efferent capacity remains. The moment that occurs, consciousness undoubtedly persists, but for an unknown period of time. In some cases, years later, family members maintain that their loved one is communicating by changing pupil size or pulse rate, or just a look in the eye. The dispassionate physician remains uncertain, perhaps believing that consciousness requires not just an internal dialogue but also observing the results of thoughts or actions. Others may quietly hope that consciousness cannot survive extended periods of immobility, unannounced and unmitigated discomfort, and complete disconnection.

The emerging and ambitious field of brain–computer interfaces (BCIs), although in its infancy, aims to provide improved communication methods for people with LIS. By recording from the scalp or intracranially and converting evoked or volitional electrical neural activity to command signals for a computer, there has been some early success in providing spelling systems, cursor control, or even robotic arm control for people with tetraplegia and anarthria.[3–7] Though both scalp-based EEG and corticography signals have been recorded in people with ALS with total LIS, we are aware of no reports of restoring communication using a neural signal-based BCI in this most severely affected population.[8] Recent fMRI studies of people with traumatic brain injury have identified blood oxygenation level–dependent (BOLD) responses consistent with consciousness when none was thought present.[9,10] These studies drive further research, though more portable methods of communication would be required (and desirable) for people with LIS.

In this issue of *Neurology*®, a respected BCI research group reports on the use of near infrared spectroscopy (NIRS) in a 67-year-old woman with ALS who had been completely locked in for more than 2 years.[11] Her evoked potential EEG based on auditory mismatch and oddball presentations supported the presence of cortical processing, but an EEG-based BCI system was not successful. Similar to BOLD fMRI, NIRS uses scalp-based detectors to identify slow changes in cortical deoxyhemoglobin concentration, which reflect changes in underlying metabolic activity. Sentences that were known to be true or false were read aloud, and the subject was asked to think "yes" or "no." Twenty-five seconds later, the NIRS response was measured, and a common machine learning approach (a support vector machine) was used to classify "yes" or "no" responses, which were then reported by the computer back to the subject. Classification accuracy was tested in multiple sessions administered in three 1- to 2-week periods over the course of a year. Pooling the 3 sessions together, the positive predictive value of "yes" responses was 80.9%, and the negative predictive value of "no" responses was 72.9%, statistically significant indicators (above the 50% chance level) of a change in hemodynamic response reflecting the subject's apparent recognition of the veracity of the recited statements. While on some days classification performance was the same as chance, 11 of 74 sessions yielded 100% accuracy to questions whose answers were either of broad knowledge or of autobiographical relevance (see the report's supplemental material), and for each 1- to 2-week period an accuracy of at least 70% was achieved. The 70% threshold may be important, since simple BCIs that enable toggling of a virtual switch can be paired with serially presented alphabets or other augmentative and assistive communication technologies. When enhanced with a backspace key, letter groupings, or word prediction, 70% accuracy may be adequate for a BCI-based communication system.

It is worth noting some limitations. First, an inconsistent ability to confirm a true or false sentence, as presented in this report, may or may not be sufficient to infer that the subject communicated. With only slightly more than half of the sessions yielding

See page 1930

From the Neurotechnology Trials Unit and the Neurological Clinical Trial Institute (L.R.H., M.E.C.), Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston; and the Center for Neurorestoration and Neurotechnology (L.R.H.), Rehabilitation Research and Development Service, Office of Research and Development, Department of Veterans Affairs, and Brown University School of Engineering and Institute for Brain Science, Providence, RI.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the editorial.

an average accuracy greater than 70%, confidence in the accuracy of any single classification is limited. Similarly, there is not yet sufficient evidence (nor does the report claim) that NIRS is ready to be deployed as a tool to assess consciousness in this population. One cannot know whether the technology itself was at times unable to detect cortical processing or whether the technology (perhaps even perfectly) accurately demonstrated day-to-day fluctuations in the subject's level of alertness, motivation, participation, or cognitive capacity.[12] A prior report of NIRS in 17 people with total LIS had insufficient data to confirm the neurologic state of that cohort.[13]

Nevertheless, this report should resonate with both BCI research and ALS clinical care. Particularly in light of those sessions where 100% accuracy was achieved, Gallegos-Ayala et al. provide new evidence that consciousness and cognition may indeed survive extended periods of total LIS. Whether this finding evokes hope, fear, introspection, or some combination of these, for the neurologist guiding people with ALS and their families, this report underscores the critical importance of discussions regarding preferences for life-sustaining care through the progression of neuromuscular disease.

BCI research is on track to create vital new opportunities for people with LIS. The current report suggests that NIRS might provide the basis for a home-based communication system, permitting serial selection of letters or choices every 25 seconds. It may also be possible that early exposure to BCIs (of any type) would permit the user to learn better strategies for faster and more accurate neural control of external devices, even as motor power declines. It is reasonable to imagine a day—not too far in the future—where we will advise people with ALS and others with LIS that robust communication, particularly in these days of ubiquitous text messaging and e-mails, can be maintained or restored with BCIs. For our patients with ALS and their families, we wonder how this might affect decisions to pursue or maintain chronic mechanical ventilation and nutrition. The ability for our patients to continue to participate in that decision-making, by proclamation rather than proxy, will be revolutionary.[14]

STUDY FUNDING

VA B6453R and NIDCD R01DC009899 (L.R.H.).

DISCLOSURE

L. Hochberg participated in a workshop sponsored by GE Healthymagination and received meals and a portable sound brick. Dr. Hochberg is the Sponsor-Investigator of the Investigational Device Exemption for the BrainGate pilot clinical trials. Dr. Hochberg is on the Board of Trustees (without compensation) of The Boston Home and the Board of Directors (without compensation) of SpeakYourMind Foundation. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs. Dr. Cudkowicz served on the data and safety monitoring board for Synapse and Trophos and was a consultant for Teva, GlaxoSmithKline, Neuraltis, and Cytokinetics, Inc. Dr. Cudkowicz is also the primary investigator of the NeuroNEXT Clinical Coordination Center. Go to Neurology.org for full disclosures.

REFERENCES

1. Laureys S, Pellas F, Van Eeckhout P, et al. The locked-in syndrome: what is it like to be conscious but paralyzed and voiceless? Prog Brain Res 2005;150:495–511.
2. Bauer G, Gerstenbrand F, Rumpl E. Varieties of the locked-in syndrome. J Neurol 1979;221:77–91.
3. Vaughan TM, Wolpaw JR. Special issue containing contributions from the fourth international brain-computer interface meeting. J Neural Eng 2011;8:020201.
4. Sellers EW. New horizons in brain-computer interface research, Clin Neurophysiol 2013;124:2–4.
5. Hochberg LR, Serruya MD, Friehs GM, et al. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 2006;442:164–171.
6. Hochberg LR, Bacher D, Jarosiewicz B, et al. Reach and grasp by people with tetraplegia using a neurally controlled robotic arm. Nature 2012;485:372–375.
7. Collinger JL, Wodlinger B, Downey JE, et al. High-performance neuroprosthetic control by an individual with tetraplegia. Lancet 2013;381:557–564.
8. Birbaumer N, Murguialday AR, Cohen L. Brain computer interface in paralysis. Curr Opin Neurol 2008;21:634–638.
9. Rodriguez Moreno D, Schiff ND, Giacino J, Kalmar K, Hirsch J. A network approach to assessing cognition in disorders of consciousness. Neurology 2010;75:1871–1878.
10. Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med 2010;362:579–589.
11. Gallegos-Ayala G, Furdea A, Takano K, Ruf CA, Flor H, Birbaumer N. Brain communication in a completely locked-in patient using bedside near-infrared spectroscopy. Neurology 2014;82:1930–1932.
12. Nijboer F, Birbaumer N, Kübler A. The influence of psychological state and motivation on brain-computer interface performance in patients with amyotrophic lateral sclerosis: a longitudinal study. Front Neurosci 2010;4.
13. Naito M, Michioka Y, Ozawa K, et al. A communication means for totally locked-in ALS patients based on changes in cerebral blood volume measured with near-infrared light. IEICE Trans Inf Syst 2007;E90-D:1028–1037.
14. Giacino JT, Fins JJ, Laureys S, Schiff ND. Disorders of consciousness after acquired brain injury: the state of the science. Nat Rev Neurol 2014;10:99–114.