WriteClick: Editor's Choice

Editors' Note: In this week's WriteClick, ethics expert Bernat furthers the discussion about what it means to be conscious and outlines the difference between the Yu et al. diagnosis of "unresponsive wakefulness syndrome" vs "minimally conscious state" and the roles that EEG fMRI and neurologic examination play in these assessments. Burke et al. comment on Benarroch's article and highlight that further HCN channel investigation may shed some light on the mechanisms behind benign familial neonatal epilepsy. Richard Tenser extends the finding by Tan et al. that acyclovir-resistant herpes simplex virus may have contributed to the pathophysiology of encephalitis in the authors' patients.

Megan Alcauskas, MD, and Robert C. Griggs, MD

PATIENTS WITH UNRESPONSIVE WAKEFULNESS SYNDROME RESPOND TO THE PAIN CRIES OF OTHER PEOPLE

James L. Bernat, Lebanon, NH: Yu et al.[1] reported additional cases of patients diagnosed in a vegetative state (unresponsive wakefulness syndrome) by clinical criteria. However, they showed fMRI or processed EEG responses indicating awareness, and therefore these patients should be diagnosed correctly as in a minimally conscious state. These cases and similar previous cases show that the neurologic examination alone may, in some cases, be insensitive to detect the presence of awareness. The medical and ethical importance of this finding has been emphasized in numerous publications over the past 6 years.[2–4]

The impact of functional neuroimaging in showing the limitations of the neurologic examination to detect awareness is reminiscent of the earlier impact of DNA genetic studies in showing the limitation of the clinical phenotypic classification of neurogenetic syndromes.

The investigators should collect all the cases in which the neurologic examination has been found inadequate to assess awareness and contrast those with the majority of cases in which the clinical examination was accurate. Perhaps there are common features of the clinically misdiagnosed cases that could inform our understanding of awareness with and without responsiveness.

1. Yu T, Lang S, Vogel D, et al. Patients with unresponsive wakefulness syndrome respond to the pain cries of other people. Neurology 2013;80:345–352.
2. Coleman MR, Davis MH, Rodd JM, et al. Toward the routine use of brain imaging to aid the clinical diagnosis of disorders of consciousness. Brain 2009;132:2541–2552.
3. Wilkinson DJ, Kahane G, Horne M, Savulescu J. Functional neuroimaging and withdrawal of life-sustaining therapy from vegetative patients. J Med Ethics 2009;35:508–511.
4. Bernat JL. Current controversies in states of chronic unconsciousness. Neurology 2010;75(suppl 1):S33–S38.

HCN CHANNELS: FUNCTION AND CLINICAL IMPLICATIONS

David Burke, James Howells, Susan E. Tomlinson, Sydney, Australia: Dr. Benarroch[1] highlighted the function of HCN channels. Studies of axonal excitability using threshold tracking techniques allow HCN function to be quantified indirectly in human peripheral nerve in vivo.[2] These physiologic studies may clarify the activity of different voltage-dependent channels expressed on the studied axons, even in CNS disease. For example, abnormalities have been shown in benign familial neonatal epilepsy, a condition due to mutation of the *KCNQ2* gene encoding $K_v7.2$. The abnormalities in axonal excitability were those appropriate for loss of slow K^+ channel function.[3] Current protocols for studying the accommodation to hyperpolarization produced by HCN currents now use strong long hyperpolarizing currents as conditioning stimuli to alter membrane potential.[4] This has allowed further insight into the nature of HCN current in human myelinated axons; specifically, that HCN1 is probably expressed on large myelinated axons, but that isoform expression may differ for myelinated afferent and efferent axons.[5] In defined patient groups with epilepsy, these techniques could help clarify whether there is abnormal HCN function. In neuropathic pain, the situation is less certain because the action potentials of small nociceptive afferents can only be characterized with microneurography.

1. Benarroch EE. HCN channels: function and clinical implications. Neurology 2013;80:304–310.
2. Bostock H, Cikurel K, Burke D. Threshold tracking techniques in the study of human peripheral nerve. Muscle Nerve 1998;21:137–158.

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