

ferences in types of anticoagulants are unlikely to have influenced our findings. Despite proven efficacy of preventive treatment in younger as well as elderly patients,<sup>2</sup> AF remains largely undertreated for the prevention of stroke.<sup>3,4</sup> Of all patients diagnosed as having AF during follow-up in our study, 57.9% started anticoagulant treatment during the course of the study. We did not specifically assess for adverse effects. However, as we observed associations of exposure time both in users and in nonusers of anticoagulants, these do not appear explicable by bias due to treatment adverse effects.

Future studies will have to determine whether treatment of AF reduces the risk for dementia and whether optimal treatment consists of antithrombotic medication and/or optimizing cardiac output. Given the long lead time between subclinical cerebrovascular disease and manifest cognitive decline and dementia, determining the efficacy of treatment of AF for preventing dementia in trials will be time consuming and costly in the absence of reliable surrogate outcome markers. Until such markers become available, additional (observational) studies exploring the effect of different types of AF and treatments, as also suggested by Chen et al, may further increase insight in the association between AF and dementia. In any case, any potential benefit of treatment on cognition emphasizes the urge for compliance with current guidelines for treatment of AF.

Frank J. Wolters, MD

Renée F. A. G. de Bruijn, MD, PhD

M. Arfan Ikram, MD, PhD

**Author Affiliations:** Department of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlands (Wolters, de Bruijn, Ikram); Department of Neurology, Erasmus Medical Center, Rotterdam, the Netherlands (Wolters, de Bruijn); Department of Radiology, Erasmus Medical Center, Rotterdam, the Netherlands (Ikram).

**Corresponding Author:** M. Arfan Ikram, MD, PhD, Departments of Epidemiology and Radiology, Erasmus Medical Center, 's-Gravendijkwal 230, Na 2818, Rotterdam, Zuid-Holland 3015 CE, the Netherlands (m.a.ikram@erasmusmc.nl).

**Published Online:** March 21, 2016. doi:10.1001/jamaneurol.2015.5069.

**Conflict of Interest Disclosures:** None reported.

1. de Bruijn RF, Heeringa J, Wolters FJ, et al. Association between atrial fibrillation and dementia in the general population. *JAMA Neurol.* 2015;72(11):1288-1294.
2. Mant J, Hobbs FD, Fletcher K, et al; BAFTA investigators; Midland Research Practices Network (MidReC). Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet.* 2007;370(9586):493-503.
3. Fisher M, Moores L, Alsharif MN, Paganini-Hill A. Definition and implications of the preventable stroke. *JAMA Neurol.* 2016;73(2):186-189.
4. Yiin GS, Howard DP, Paul NL, et al; Oxford Vascular Study. Age-specific incidence, outcome, cost, and projected future burden of atrial fibrillation-related embolic vascular events: a population-based study. *Circulation.* 2014;130(15):1236-1244.

### Peripheral Causes of Cognitive Motor Dissociation in Patients With Vegetative or Minimally Conscious State

**To the Editor** Fernández-Espejo and colleagues<sup>1</sup> describe a patient with retained covert awareness who had a sharp reduction of behavioral command following.

With use of neuroimaging techniques that do not rely on the patient's ability to produce an external response, the authors<sup>1</sup> were able to demonstrate a dissociation between preserved voluntary motor imagery and absent skeletal muscle movements. Fiber tractography then showed selective structural damage to the white matter fibers connecting the thalamus and M1 bilaterally. The conclusion was that altered motor thalamocortical circuits were the cause of absent external responsiveness in this covertly aware patient. However, absent behavioral motor responses could have been caused by concurrent peripheral nervous system and muscle pathology. Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) are major causes of paralysis in critically ill patients,<sup>2</sup> including patients with neurologic issues.<sup>3</sup> In a recent series, CIP was described in 16 of 22 vegetative or minimally conscious patients (73%).<sup>4</sup>

In this study,<sup>1</sup> electrophysiological investigations of peripheral nerves and muscles were not performed, which leaves unsettled the possible contribution of CIP and CIM to the absence of motor behaviors.

In the accompanying editorial by Schiff,<sup>5</sup> the term *cognitive motor dissociation* is proposed to define patients with wide dissociation of motor and cognitive function. However, it seems intuitive that the evaluation of altered motor function should include the contribution of the peripheral nervous system and muscles. Diagnosis of CIP and CIM can be easily established at bedside and is worth considering in patients with suspected central cognitive motor dissociation.

Nicola Latronico, MD

**Author Affiliations:** Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy (Latronico); Department of Anesthesia, Critical Care, and Emergency, Spedali Civili University Hospital, Brescia, Italy (Latronico).

**Corresponding Author:** Nicola Latronico, MD, School of Specialty in Anesthesia and Critical Care Medicine, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Piazzale Ospedali Civili, 1 Brescia, BS 25123, Italy (nicola.latronico@unibs.it).

**Published Online:** March 28, 2016. doi:10.1001/jamaneurol.2016.0140.

**Conflict of Interest Disclosures:** None reported.

1. Fernández-Espejo D, Rossit S, Owen AM. A thalamocortical mechanism for the absence of overt motor behavior in covertly aware patients. *JAMA Neurol.* 2015;72(12):1442-1450.
2. Latronico N, Bolton CF. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. *Lancet Neurol.* 2011;10(10):931-941.
3. Latronico N, Fenzi F, Recupero D, et al. Critical illness myopathy and neuropathy. *Lancet.* 1996;347(9015):1579-1582.
4. Bagnato S, Boccagni C, Sant'angelo A, Prestandrea C, Romano MC, Galardi G. Neuromuscular involvement in vegetative and minimally conscious states following acute brain injury. *J Peripher Nerv Syst.* 2011;16(4):315-321.
5. Schiff ND. Cognitive motor dissociation following severe brain injuries. *JAMA Neurol.* 2015;72(12):1413-1415.

**In Reply** We thank Latronico for the comments regarding our article.<sup>1</sup> Latronico proposed that peripheral nervous system and muscle pathology<sup>2</sup> may have contributed to the lack of behavioral responses exhibited by our patient. As mentioned in our Discussion section, Shea and Bayne<sup>3</sup> had previously argued a similar peripheral explanation for the absence of overt motor

behavior in patients with preserved covert motor behavior.<sup>4</sup> In vegetative and minimally conscious patients, peripheral damage is most commonly related to motor axonal neuropathy,<sup>5</sup> which, as Latronico points out, is a major cause of paralysis.<sup>2</sup>

While we did not specifically test for electrophysiological signs of peripheral pathology, our patient showed no evidence of paralysis. In fact, he exhibited frequent spontaneous movements of the limbs (more frequently in the upper limbs), head, and torso, as well as very consistent withdrawal to painful stimulation (see information about clinical assessments in the Supplement of our article<sup>1</sup>). In contrast, he was incapable of producing voluntarily motor responses to command. Therefore, the main deficit he exhibited, which our study aimed to explain, was not an absence of skeletal movement, but a lack of voluntary control of his motor responses, and thus the underlying mechanism is necessarily central.<sup>6</sup>

Based on this, we disagree with Latronico's suggestion for a role of peripheral pathology in explaining our patient's lack of overt command-following capabilities. Nevertheless, as we mentioned in our Discussion section,<sup>1</sup> our patient exhibited other symptoms in addition to the lack of command following (eg, lack of visual pursuit or vocalizations) for which our results may not offer a complete explanation. In this context, we agree that the evaluation of the peripheral nervous system and muscles, in combination with neuroimaging and clinical assessments, may contribute to a more comprehensive un-

derstanding of the full clinical profile exhibited by each individual patient.

**Davinia Fernández-Espejo, PhD**

**Adrian M. Owen, PhD**

**Author Affiliations:** School of Psychology, University of Birmingham, Birmingham, England (Fernández-Espejo); The Brain and Mind Institute, The University of Western Ontario, London, Ontario, Canada (Owen).

**Corresponding Author:** Davinia Fernández-Espejo, PhD, School of Psychology, University of Birmingham, 2.32 Hills Bldg, Birmingham, West Midlands B15 2TT, England ([d.fernandez-espejo@bham.ac.uk](mailto:d.fernandez-espejo@bham.ac.uk)).

**Published Online:** March 28, 2016. doi:10.1001/jamaneurol.2016.0143.

**Conflict of Interest Disclosures:** None reported.

1. Fernández-Espejo D, Rossit S, Owen AM. A thalamocortical mechanism for the absence of overt motor behavior in covertly aware patients. *JAMA Neurol.* 2015;72(12):1442-1450.
2. Latronico N, Bolton CF. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. *Lancet Neurol.* 2011;10(10):931-941.
3. Shea N, Bayne T. The vegetative state and the science of consciousness. *Br J Philos Sci.* 2010;61(3):459-484.
4. Fernández-Espejo D, Owen AM. Detecting awareness after severe brain injury. *Nat Rev Neurosci.* 2013;14(11):801-809.
5. Bagnato S, Boccagni C, Sant'angelo A, Prestandrea C, Romano MC, Galardi G. Neuromuscular involvement in vegetative and minimally conscious states following acute brain injury. *J Peripher Nerv Syst.* 2011;16(4):315-321.
6. Bracht T, Schnell S, Federspiel A, et al. Altered cortico-basal ganglia motor pathways reflect reduced volitional motor activity in schizophrenia. *Schizophr Res.* 2013;143(2-3):269-276.