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Peripheral causes of cognitive motor dissociation in patients with vegetative or minimally conscious state – Reply

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We thank Latronico and colleagues for their comments regarding our article[1]. They proposed that peripheral nervous system and muscle pathology [2] may have contributed to the lack of behavioural responses exhibited by our patient. As mentioned in our Discussion section, Shea and Bayne [3] had previously argued a similar peripheral explanation for the absence of overt motor behaviour in patients with preserved covert motor behaviour[4]. In vegetative and minimally conscious patients, peripheral damage is most commonly related to motor axonal neuropathy [5], which, as Latronico and colleagues point out, is a major cause of *paralysis* [2]. 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 upper limbs), head, and torso, as well as very consistent withdrawal to painful stimulation (see information about clinical assessments in the original supplementary information). 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 [6]. Based on this, we disagree with Latronico and colleagues' 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, our patient exhibited other symptoms in addition to the lack of command following (e.g. 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 understanding of the full clinical profile exhibited by each individual patient.

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