EJN EUROPEAN JOURNAL OF NEUROSCIENCE

European Journal of Neuroscience, Vol. 32, pp. 1030–1031, 2010 doi:10.1111/j.1460-9568.2010.07441.x

COGNITIVE NEUROSCIENCE

COMMENTARY
The importance of recognizing paradoxes (Commentary on Madhavan *et al.*)

EJN FEATURED ARTICLE

Alvaro Pascual-Leone[1,2]

[1]Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

[2]Institut Universitari de Neurorehabilitació Guttmann, Universidad Autónoma de Barcelona, Badalona, Spain

The word paradox is derived from the Greek prefix *para-*, meaning 'contrary or opposed', and the word *doxos*, meaning 'opinion'. As defined by the Oxford English Dictionary, paradox is 'a statement or tenet contrary to received opinion or belief, especially one that is difficult to believe'. Paradoxes represent instances where the present knowledge is lacking and expectations are inconsistent with actual events or findings. Paradoxes surprise us and should evoke a desire to gain deeper understanding. Therefore, realizing and highlighting paradoxes is important as unique opportunities to acquire new knowledge and question assumed truths. A recent book, *The Paradoxical Brain* (Kapur *et al.*, 2010), provides a comprehensive overview and discussion of the importance of paradoxes in brain sciences.

In this issue of EJN, Madhavan *et al.* (2010) provide evidence that following a stroke, activity in the non-lesioned motor cortex may be maladaptive for some aspects of lower limb motor control. The notion that activity in the non-lesioned motor cortex may limit functional recovery after a stroke is supported by findings in human and animal studies (Ward & Cohen, 2004; Fregni & Pascual-Leone, 2006; Allred *et al.*, 2010), and fits with the longstanding realization that functional consequences of a brain lesion are not simply the manifestation of the injury (Allred & Jones, 2008). Initially following an injury, rapid changes may occur to minimize the damage and prevent excitotoxic and neurotoxic cascades. These may be followed by complex processes to cope with behavioral consequences of the insult that may in the long run prove adaptive (beneficial) or maladaptive (deleterious) for the affected individual. Ultimately, behavior after a lesion reflects the capacity of the brain to adapt to the injury, and is thus a manifestation of the plastic adaptation of dynamic neural networks, constrained by pre-existing connections and influences (Pascual-Leone *et al.*, 2005; Pascual-Leone, 2009). The final behavioral consequence of a brain injury may be degraded (worse-than-normal) performance, but also paradoxically superior (better-than-normal) performance, or there might be improvement of function or recovery of the deleterious consequences of a pre-existing insult or disease (Kapur, 1996).

Madhavan *et al.* (2010) find that strong ipsilateral conductivity from the non-lesioned cortex results in greater degradation of lower limb motor performance, specifically in patients with relatively preserved cortico-spinal projections from the lesioned hemisphere. It might have been sensible to assume that more damage would have worse functional consequences and that some preserved connections would be better than none. However, paradoxically, for a task where patients had to simultaneously dorsiflex their ankle in one limb and plantarflex the ankle in the other limb, strong ipsilateral drive from the non-lesioned cortex to paretic ankle motoneurons appears to worsen the functional outcome in patients with some persevered contralateral projections. The results are consistent with ideas of 'motor conflict' generated by partly degraded signals and fit well with approaches that call for differential interventions for treatment of the lesioned and non-lesioned hemispheres to optimize functional outcomes following a stroke (Schallert *et al.*, 2003).

Integrating diffusion tensor imaging and transcranial magnetic stimulation results, Madhavan *et al.* (2010) present an algorithm to divide patients into two groups depending on measures of cortico-spinal integrity and excitability. The algorithm predicts that some patients will benefit from a reduction in ipsilateral drive from the non-lesioned hemisphere, for example by non-invasive brain stimulation, while others will benefit from having their non-lesioned cortex facilitated. Such approaches offer the promise of individualized optimization of neurorehabilitation approaches.

It will be important to investigate the mechanisms governing shifting cortico-spinal and interhemispheric connectivity and function, neural network dynamics, and the mapping relations between brain activity and behavior following injury or stroke. Such information could be employed to foster the recovery of desirable functions and to suppress changes that may lead to undesirable behaviors. Attention to paradoxical phenomena, such as described in Madhavan *et al.* (2010), holds the promise of enabling a paradigmatic shift in our understanding of brain function and dysfunction, and of generating valuable insights that may lead to novel treatment strategies designed to alleviate impairment and disability resulting from disease and injury.

References

Allred, R.P. & Jones, T.A. (2008) Experience – a double edged sword for restorative neural plasticity after brain damage. *Future Neurol.*, **3**, 189–198.

Allred, R.P., Cappellini, C.H. & Jones, T.A. (2010) The "good" limb makes the "bad" limb worse: experience-dependent interhemispheric disruption of functional outcome after cortical infarcts in rats. *Behav. Neurosci.*, **124**, 124–132.

Fregni, F. & Pascual-Leone, A. (2006) Hand motor recovery after stroke: tuning the orchestra to improve hand motor function. *Cogn. Behav. Neurol.*, **19**, 21–33.

Kapur, N. (1996) Paradoxical functional facilitation in brain-behaviour research. A critical review. *Brain*, **119**, 1775–1790.

Kapur, N., Pascual-Leone, A., Ramachandran, V.S., Cole, J., Della Sala, S., Manly, T. (eds.) (2010) *The Paradoxical Brain*. Cambridge University Press, Cambridge.

Madhavan, S., Stinear, J. & Rogers, L. (2010) A paradox: after stroke the non-lesioned lower limb motor cortex may be maladaptive. *Eur. J. Neurosci.*, **32**, 1032–1039.

Pascual-Leone, A. (2009) Characterizing and modulating neuroplasticity of the adult human brain. In Gazzaniga, M.S. (Ed), *The Cognitive Neurosciences IV*, 4th edn. Bradford Books, Cambridge, 437 pp.

Pascual-Leone, A., Amedi, A., Fregni, F. & Merabet, L.B. (2005) The plastic human brain cortex. *Annu. Rev. Neurosci.*, **28**, 377–401.

Schallert, T., Fleming, S.M. & Woodlee, M.T. (2003) Should the injured and intact hemispheres be treated differently during the early phases of physical restorative therapy in experimental stroke or parkinsonism? *Phys. Med. Rehabil. Clin. N. Am.*, **14**(1 Suppl), S27–S46.

Ward, N.S. & Cohen, L.G. (2004) Mechanisms underlying recovery of motor function after stroke. *Arch. Neurol.*, **61**, 1844–1848.