PERSPECTIVES

Descending interactions with spinal cord networks: a time to build?

David Parker

Department of Physiology, Development and Neuroscience, University of Cambridge, Downing Site, Cambridge CB2 3DY, UK

Email: Djp27@cam.ac.uk

Descending inputs from the brainstem influence spinal cord locomotor networks, but the nature of the interaction is not well understood. Soffe *et al.* (2009) have examined this interaction in detail by taking advantage of their elegant experimental approach in a model system, the tadpole, and suggest a need to revisit classical assumptions of the role of descending inputs to spinal locomotor networks.

Classical approaches to understanding nervous systems are largely reductionist: we take systems apart and examine their components in isolation. This approach assumes that function can be determined from a knowledge of isolated components that exist in external relationships to each other and interact through deterministic chains of cause and effect (i.e. the interactions do not alter the properties of the components). While the reductionist approach is debated in the philosophy of science, in practice it is often simply accepted. In the physical sciences it has been known for many years that multi-component systems can exhibit emergent behaviour that cannot be understood from knowledge of the isolated parts (Anderson, 1972). The main problem of reducing a system to its components (avoiding philosophical arguments) is that it does not follow that you can build up to understand actual function (i.e. that components examined individually will function in the same way in interaction). While this is probably appreciated, analytical problems surrounding even relatively simple aspects mean that we are often limited to this approach.

Locomotion reflects the integrated activity in a distributed system of components (sensory inputs, spinal cord locomotor networks, and various descending inputs from the brain; see Orlovsky *et al.* 1999). These have largely been studied independently, the complexity of even simple systems dictating that integrative analyses typically examine how one component feeds into another rather than their mutual interactions. Spinal cord locomotor networks have been studied extensively in this way. These networks can generate rhythmic outputs in isolation when activated by bath applied excitatory amino acid agonists (see references in Soffe *et al.* 2009): the resulting activity and the effects of imposed descending and sensory inputs have been studied extensively. This approach is nevertheless artificial, and at least to some extent rests on (or leads to) the assumption that bath applied excitants mimic an unpatterned descending excitatory drive that spinal cord networks convert into a rhythmic output. Descending inputs are considered to have multiple roles, including the initiation, regulation, and termination of locomotor activity, and postural control (see Orlovsky *et al.* 1999). Although ascending inputs are known to modulate descending activity in time with locomotor rhythms in several systems (see references in Soffe *et al.* 2009), the details of this interaction are not well understood.

As with other systems, the tadpole spinal cord generates swimming-like activity in NMDA, but lesion experiments have shown that reliable sustained activity requires the presence of at least some of the caudal hindbrain (Li *et al.* 2006). While it is not generally highlighted, the activity in completely isolated spinal cord preparations is variable (as an exercise, compare the 'typical' clockwork rhythms when only ventral root activity is shown with the often less regular activity when ventral root recordings are paired with intracellular recordings; the activity is usually less regular in the latter case, presumably because the smaller sample sizes offers less probability of showing a preparation that generated a regular rhythm). This is not to revisit arguments of whether spinal networks exist or not, simply to highlight the point raised by Soffe *et al.* 2009, that analyses of independent components, whether of locomotion or other functions, have limits.

In this issue of *The Journal of Physiology*, Soffe *et al.* 2009 suggest a need to reconsider the view that descending inputs provide unpatterned excitatory inputs to spinal cord rhythmic generating networks. In a large number of recordings they failed to find evidence for tonic or unpatterned activity in reticulospinal neurons. In this paper they instead demonstrate a mutual interaction that alters the properties of the individual components. During swimming reticulospinal neurons are rhythmically activated (by postinhibitory rebound) as a result of ascending cycle-to-cycle reciprocal inhibitory inputs from the spinal locomotor network, and they in turn provide cycle-to-cycle rhythmic descending excitation that activates locomotor network neurons. This mutual interaction places hindbrain reticulospinal neurons as integral parts of the rhythm generating network, and raises the question of whether actual function could be understood from knowledge of either component individually. Bath applied excitatory amino acids would not mimic the temporal and spatial aspects of the descending signals, which may give rise to the often forgotten anomalies of activity in isolated spinal cords (see Ayers *et al.* 1984). The authors suggest that the routine use of excitatory amino acids in activating spinal networks has been misleading, and ignores a potentially important rhythmic aspect of descending reticulospinal commands.

Of course caveats apply. The analysis is in an early developmental stage in a lower vertebrate, and the situation may change during development or evolution. In discussing developmental aspects of the descending excitatory input Soffe *et al.* 2009 say that the rhythmic component of the descending drive will not become less important during development, but this is not known. Nevertheless, their study illustrates the utility of detailed analyses in simpler model systems. Analyses of isolated spinal networks have dominated for at least the last two decades. This study highlights a need to build (where possible) on this traditional reductionist approach.

References

Anderson P (1972). *Science* **177**, 393–396.

Ayers J, Carpenter G, Currie S & Kinch J (1983). *Science* **221**, 1312–1314.

Li W-C, Soffe SR, Wolf E & Roberts A (2006). *J Neurosci* **26**, 4026–4035.

Orlovsky GN, Deliagina TG & Grillner S (1999). *Neuronal Control of Locomotion*. Oxford University Press, Oxford.

Soffe SR, Roberts A & Li W-C (2009). *J Physiol* **587**, 4829–4844.

The Journal of Physiology