Sensory regulation of quadrupedal locomotion: a top-down or bottom-up control system?

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Thibaudier Y, Hurteau MF. Sensory regulation of quadrupedal locomotion: a top-down or bottom-up control system? J Neurophysiol 108: 709–711, 2012. First published April 18, 2012; doi:10.1152/jn.00302.2012.—Propriospinal pathways are thought to be critical for quadrupedal coordination by coupling cervical and lumbar central pattern generators (CPGs). However, the mechanisms involved in relaying information between girdles remain largely unexplored. Using an in vitro spinal cord preparation in neonatal rats, Juvin and colleagues (Juvin et al. 2012) have recently shown sensory inputs from the hindlimbs have greater influence on forelimb CPGs than forelimb sensory inputs on hindlimb CPGs, in other words, a bottom-up control system. However, results from decerebrate cats suggest a top-down control system. It may be that both bottom-up and top-down control systems exist and that the dominance of one over the other is task or context dependent. As such, the role of sensory inputs in controlling quadrupedal coordination before and after injury requires further investigation.

HINDLIMB LOCOMOTION IS GENERATED and regulated by interactions between spinal networks, supraspinal inputs, and sensory feedback from the periphery (Rossignol et al. 2006). At the core of the locomotor control system are spinal neuronal networks, so-called central pattern generators (CPGs), which can produce rhythmic-patterned outputs without supraspinal inputs or sensory feedback. The CPGs responsible for forelimb and hindlimb locomotion are localized in the cervical and lumbar spinal cord, respectively (Kiehn 2006). It is thought that each limb is controlled by a separate CPG but that functional and anatomical connections exist to coordinate their activities. Neuronal pathways contained within the spinal cord (i.e., propriospinal) are thought to be critical for quadrupedal coordination by coupling cervical and lumbar CPGs (Juvin et al. 2005). However, the mechanisms involved in relaying information between girdles remain largely unexplored.

In a recent article, Juvin and colleagues (2012) used an in vitro spinal cord preparation in neonatal rats (0–3 days old) to study the sensory regulation of quadrupedal coordination. Spinal cords were placed in a recording chamber containing artificial cerebro-spinal fluid. Motor activity from fore- and hindlimb CPGs were recorded from ventral roots at cervical (C8) and lumbar (L2) levels, respectively. Trains of electrical stimulation were applied to the C8 and L2 dorsal roots to simulate sensory feedback from the fore- and hindlimbs, respectively. In some experiments, the recording chamber was partitioned into two compartments (rostral and caudal) with a Vaseline barrier. The Ca$^{2+}$ concentration could be reduced in a given compartment to block all chemical synaptic transmissions within it.

The results show that stimulating the L2 or C8 dorsal roots induced coordinated locomotor-like activity at cervical and lumbar levels, indicating that sensory inputs from the hindlimbs and forelimbs can activate the spinal locomotor CPGs located at the other girdle. Interestingly, stimulating the L2 dorsal root while synaptic transmission at the L2 spinal segment was blocked (low Ca$^{2+}$ solution) could still activate the cervical CPGs. In contrast, stimulating the C8 dorsal root while synaptic transmission at the C8 spinal segment was blocked did not evoke hindlimb locomotor-like activity. Therefore, the authors concluded that sensory inputs from the hindlimb can activate cervical CPGs by bypassing lumbar CPGs, whereas sensory inputs from the forelimb need to activate cervical CPGs to activate lumbar CPGs. As a result, Juvin et al. (2012) proposed that ascending propriospinal pathways have a more important role in regulating quadrupedal coordination than descending propriospinal pathways, in other words a “bottom-up” control system.

In contrast, studies in decerebrate cats appear to show a “top-down” control system (Akay et al. 2006; Miller et al. 1977). For instance, Miller et al. (1977) showed that cutaneous stimulation of the metacarpals (forepaw stimulation) or metatarsals (hindpaw stimulation) during quadrupedal locomotion increased the activity of homolateral hindlimb and forelimb muscles, respectively. However, evoked responses were of greater amplitude in the hindlimbs compared with the forelimbs, suggesting an asymmetry in reflex projections between cervical and lumbar levels. However, Miller et al. (1977) reported the phasic modulation of reflex responses from a single session in only one cat. A more thorough investigation from several animals with proper statistical tests are required to demonstrate a preferential top-down control system. In another study, Akay et al. (2006) used a transverse split-belt treadmill that enabled the fore- and hindlimbs to walk at different speeds. Decreasing the speed of locomotion of the forelimbs from 0.6 m/s to 0.3 m/s reduced the hindlimb locomotor cycle so that a 1:1 stepping ratio was maintained between the fore and hindlimbs. In contrast, modulating hindlimb speed from 0.6 m/s to 0.3 m/s did not alter forelimb cycle duration, thus altering the fore-hindlimb stepping ratio. Thus, studies in adult decerebrate cats suggest that forelimb-related activity has a greater impact on the regulation of quadrupedal locomotion than hindlimb-related activity.

However, several factors require further investigation before determining if quadrupedal coordination during locomotion relies more heavily on a top-down or bottom-up control sys-
tem. For example, studies in cats were performed following a precollicular decerebration (i.e., the cortex and all neural tissue rostral to the colliculi was removed). In this preparation, all mechanisms of coordination pertaining to cortical interactions are abolished. Moreover, following decerebration, descending serotonergic drive is increased (Crone et al. 1988), which could perhaps favor a descending control system for quadrupedal locomotion. Studies in intact animals are required to test the hypothesis of a preferential top-down control system in the cat. Age is another factor that could explain the apparent conflicting results between species. Indeed, in neonates, the locomotor pattern is constantly evolving, as is its sensory regulation. For instance, low-intensity stimulation of the quadriceps nerve during the flexor phase prolonged the ongoing flexor burst in rats aged 1–3 days, whereas in rats aged 4–6 days, the same stimulation terminated the flexor burst and reset the cycle to extension (Izuka et al. 1997). As such, it is important to determine if the results of Juvin et al. (2012) extend to the adult rat that has acquired a more stable locomotor pattern.

The choice of dorsal roots stimulated in Juvin et al. (2012) also raises some questions. The motor output from the L2 ventral root is thought to be more flexor related, whereas C8 output is more extensor related (Juvin et al. 2005). It is possible that sensory regulation of spinal segments whose output is more related to flexion or extension is also different. Inasmuch, the differences observed in the ascending and descending modulation of propriospinal pathways by sensory feedback could be due to different types of signals entering the spinal cord at the L2 and C8 segments. For example, just for the hindlimbs, it was shown that stimulating the L5 dorsal root had a more potent effect on locomotor-like activity than stimulating the L2 dorsal root (Hinchley et al. 2010). As stated, motor output from the L2 ventral root is more flexor related. On the other hand, output from the L5 segment is more extensor related. If sensory inputs entering L2 and L5 also reflect their flexor or extensor nature, then it is likely that they differently regulate quadrupedal coordination. In a walking animal, a disturbance occurring during the swing phase (i.e., more related to flexor activities) requires more drastic postural corrections compared with a perturbation during stance (i.e., more related to extensor activities) where the animal is in a more stable position. Thus, it is important to determine what sensory inputs enter the spinal cord at C8 and L2 because they could have strikingly different influences on their respective CPGs and in their regulation of descending or ascending propriospinal pathways.

Moreover, a better identification of the ascending propriospinal pathways described by Juvin et al. seems to be necessary. Indeed, it remains to be determined if these projections are direct or if they synapse on spinal interneurons before contacting cervical CPGs. A similar experimental approach with synaptic blockades at additional spinal segments could shed some light on this issue. Another question is whether the ascending propriospinal pathways project ipsilaterally and/or contralaterally. Results from the stick insect indicate a primarily ipsilateral connection (Dean 1989). Evidently, the coupling within the mammalian spinal cord could be strikingly different from that of the stick insect, an invertebrate with a double nerve chain and six limbs. An experiment using midsagittal sections of the spinal cord could provide answers to this question.

Juvin et al.’s article provides rare insights into the intraspinal pathways regulating quadrupedal coordination by showing that sensory feedback can modulate spinal CPGs located at the other girdle. However, determining how these pathways are modulated in a more intact system is imperative. It will also be important to determine the types of sensory feedback that are essential for fore-hindlimb coordination. Stimulating dorsal roots does not permit identifying the sources and modalities of sensory feedback. For hindlimb locomotion, studies in cats and humans have shown that sensory signals related to hip position and loading of ankle extensors are important in regulating the stance-to-swing transition (Rossignol et al. 2006). Cutaneous feedback from the foot in cats and humans can also produce coordinated reflex responses that are important for maintaining stability during locomotion (Rossignol et al. 2006). Therefore, several types of sensory signals could activate propriospinal pathways involved in regulating quadrupedal locomotion, but their relative importance could vary in a state- and phase-dependent manner.

In summary, sensory feedback is important in regulating pathways that coordinate the activity of cervical and lumbar locomotor networks. Although Juvin et al. (2012) suggest that sensory feedback from the hindlimbs plays a relatively more important role in regulating quadrupedal locomotion, it may be that both bottom-up and top-down control systems exist and that dominance of one over the other reflects the specifics of the task. A better understanding of the pathways coordinating movement of the four limbs could have important implications for locomotor rehabilitation after neurological injury, which disrupts quadrupedal coordination. For instance, after partial or complete spinal cord injury, coordination of the four limbs in humans (Dietz 2011) and animals (Barriere et al. 2010) is disrupted. Altered interactions between descending commands, spinal networks, and sensory feedback must also change the regulation of pathways regulating cervical and lumbar CPGs. As such, the role of sensory inputs in controlling quadrupedal coordination before and after injury requires further investigation. This new knowledge could lead to novel therapeutic strategies that focus on stimulating specific sensory inputs to improve coordination of the four limbs after neurological injury.

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AUTHOR CONTRIBUTIONS

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