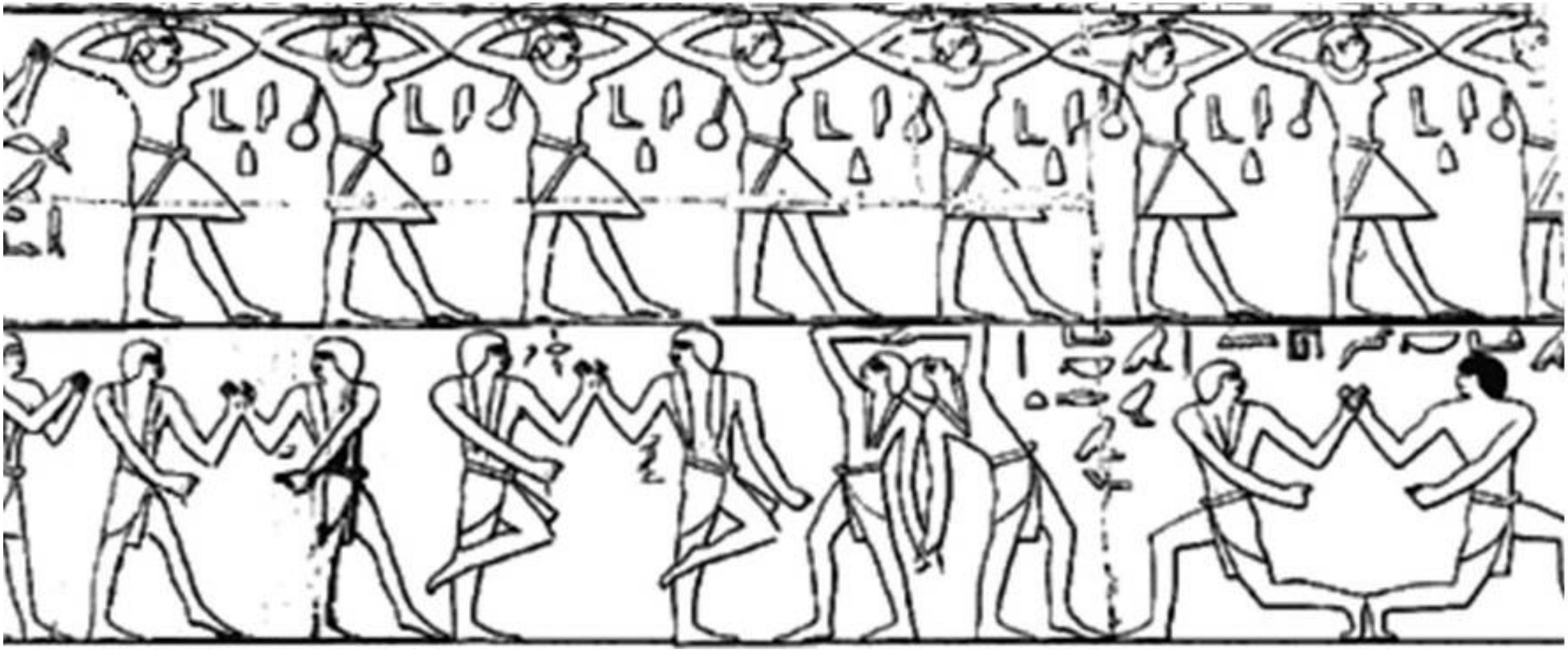
The neural circuits for motor control



Dancing scene from mastaba of mereruka

Andy Murray
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SWC Room 284

Sainsbury Wellcome Centre

Outline

- **Today**
  - Why motor control is the most important topic in neuroscience
  - Types of motor circuits
  - The spinal cord, locomotion and central pattern generators
  - Subconscious motor pathways

- **Friday 11th Nov**
  - Conscious motor pathways
  - Feedback and feedforward control
  - Error signalling and motor learning

Why is motor control important?

1. It’s the only reason we have a brain

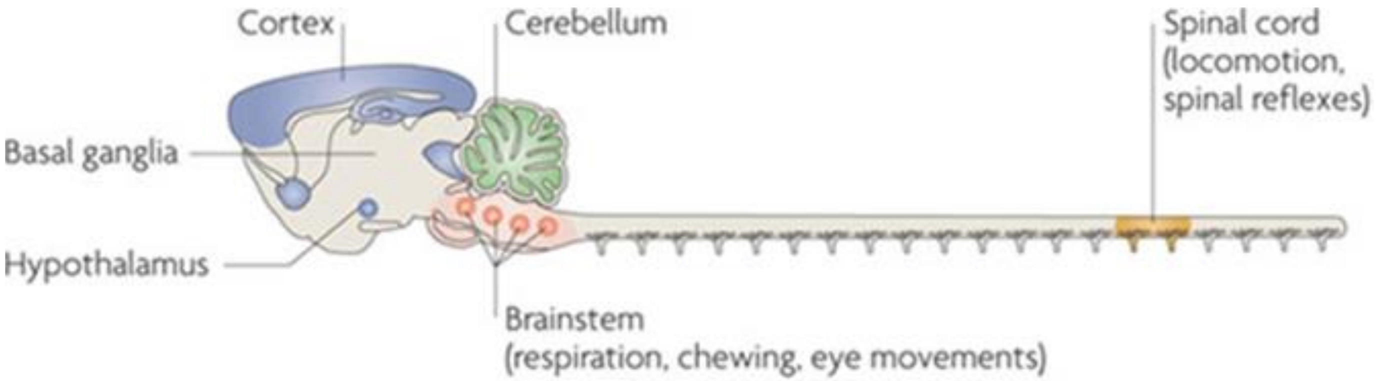
Why is motor control important?

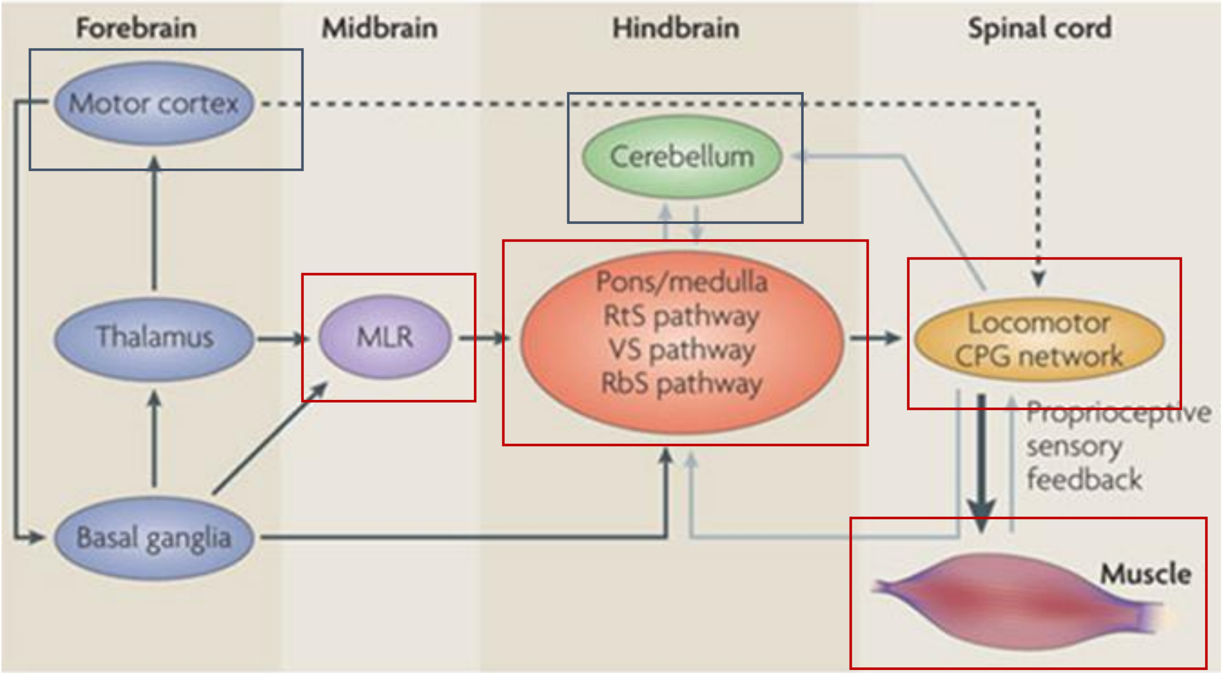
2. We have a reasonable chance of understanding the neural circuitry and computation

- *We understand the problem*
- *We understand how the problem can be solved (number of muscles that are controlled, how muscles are activated etc.)*

- *As motor control is all the brain does, if we understand the (tractable) then (to some extent) we understand the brain*

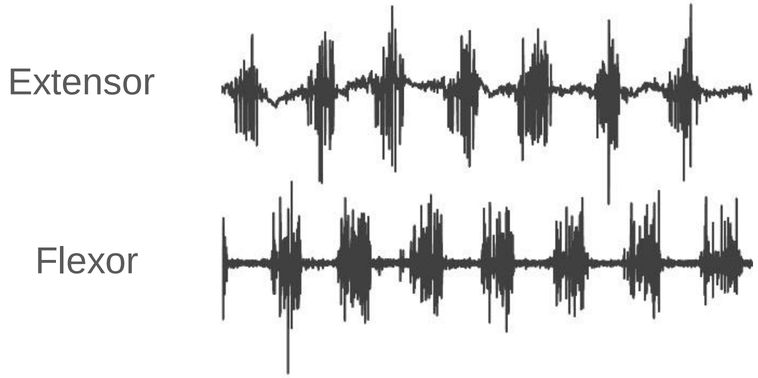
Levels of motor circuit





Goulding, 2009

Simple motor control is based on rhythmic movements



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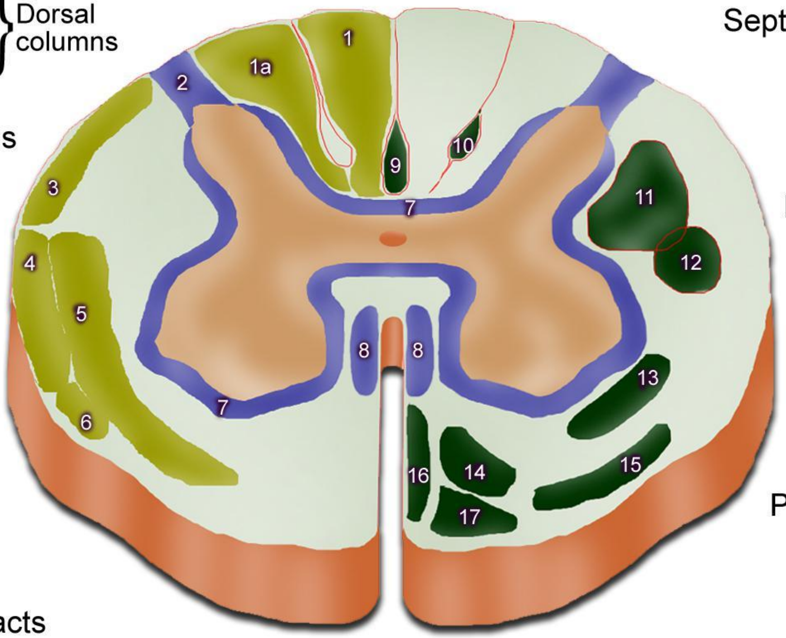
The spinal cord

1. Fasciculus gracilis
1a. Fasciculus cuneatus

} Dorsal columns

2. Dorsolateral fasciculus or tract of Lissauer
3. Posterior or dorsal spinocerebellar tract
4. Anterior or ventral spinocerebellar tract
5. Spinothalamic, spinoreticular, spinomesencephalic (spinotectal), and spinohypothalamic tracts
6. Spinoolivary tract
7. Fasciculi proprii
8. Medial longtudinal or sulcomarginal fasciculi



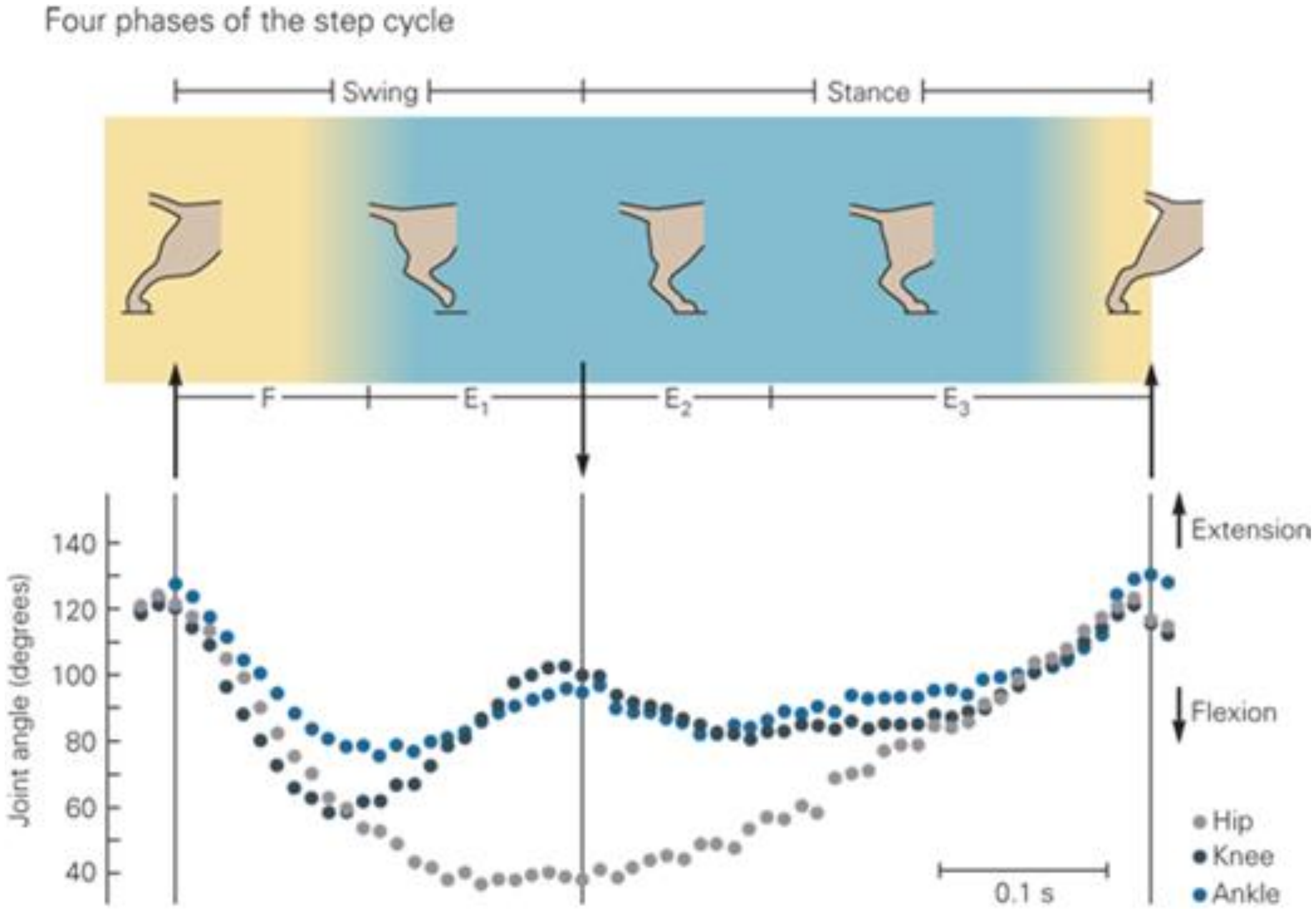
Ascending tracts

Decending tracts

Bidirectional tracts

9. Septomarginal fasciculus
10. Interfascicular or semilunar fasciculus
11. Lateral corticospinal or pyramidal
12. Rubrospinal tract
13. Medullary or lateral reticulospinal tract
14. Pontoreticulospinal or medial reticulospinal tract
15. Vestibulospinal tract
16. Anterior or ventral corticospinal tract
17. Tectospinal tract

The locomotor step cycle



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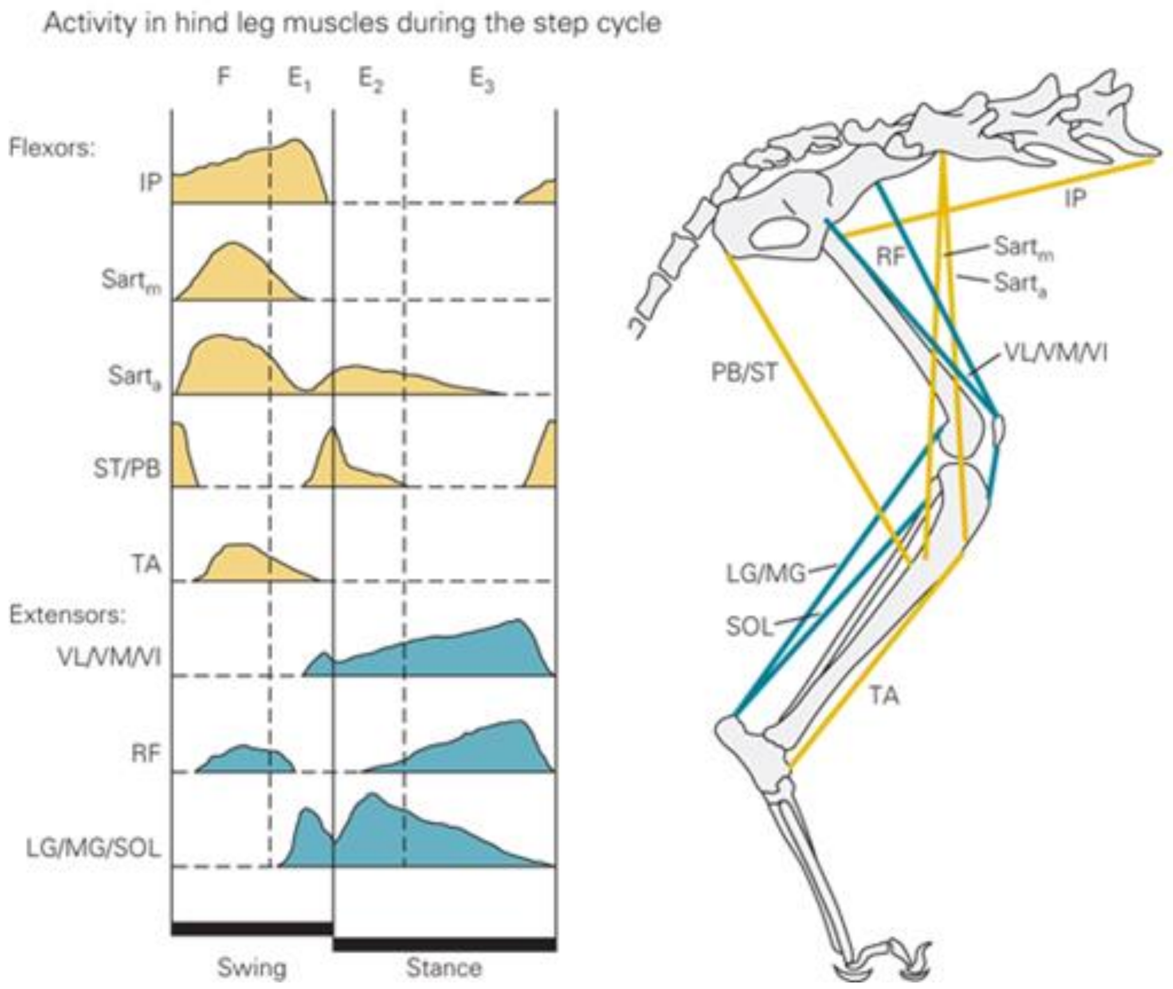
The locomotor step cycle



How many muscles are there in one mouse hindlimb?

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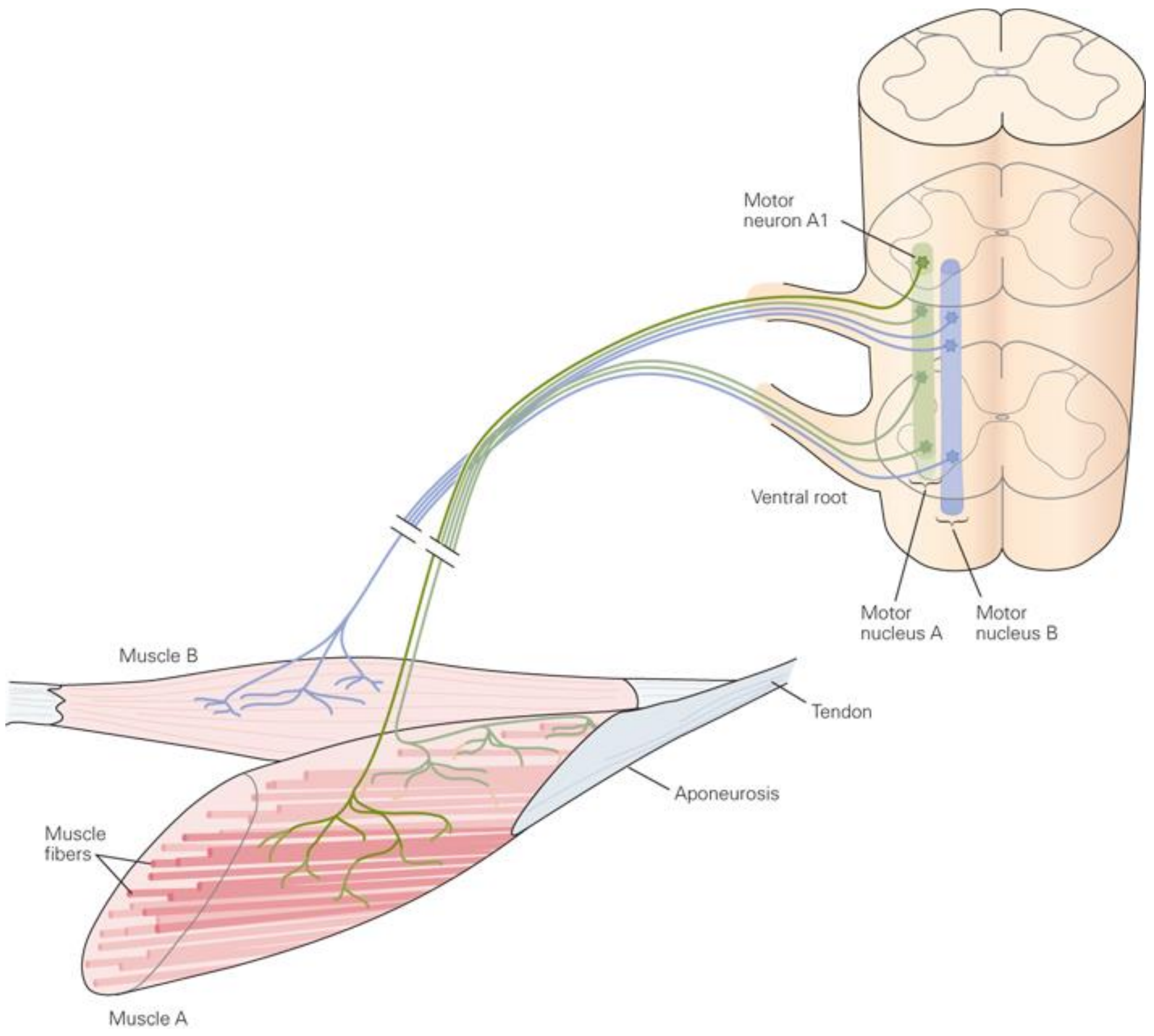
Muscles and motor units



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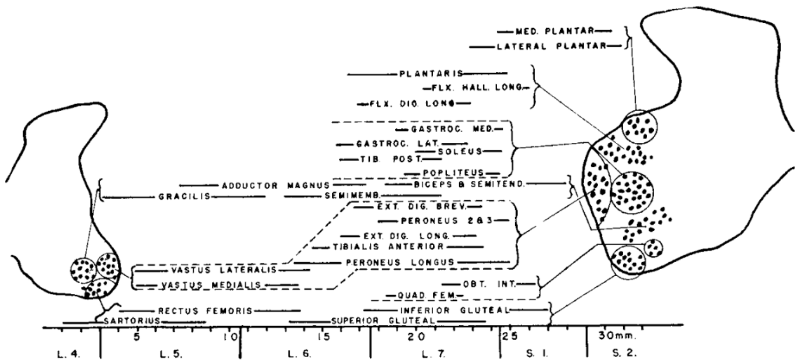
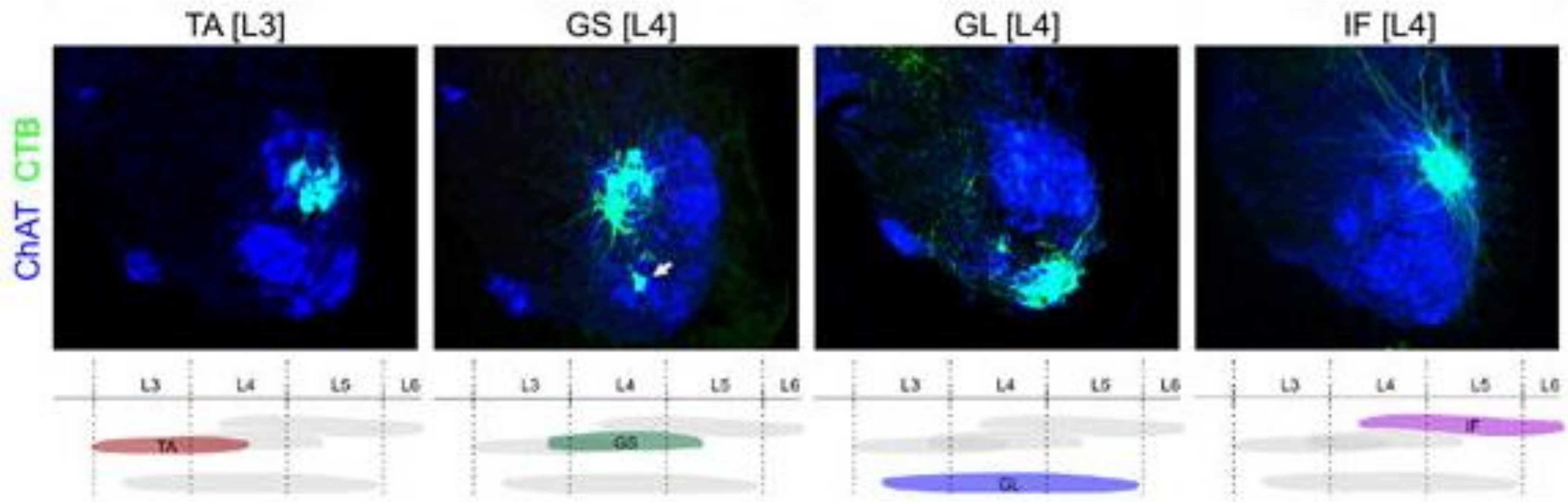
Motor neurons are organised in “pools”



Romanes, 1951



Surmeli et al., 2011

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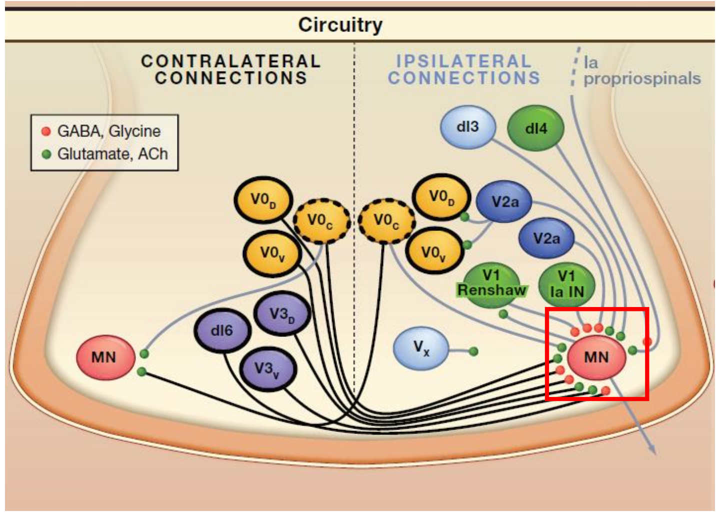
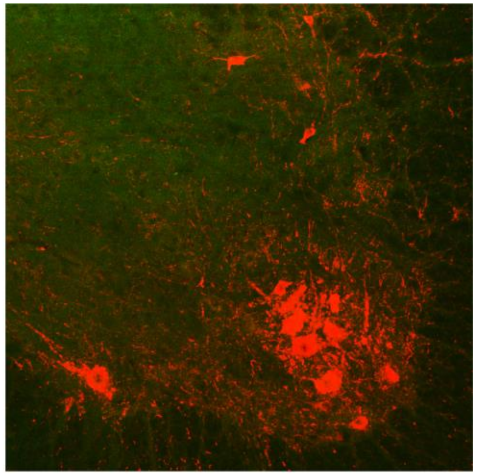
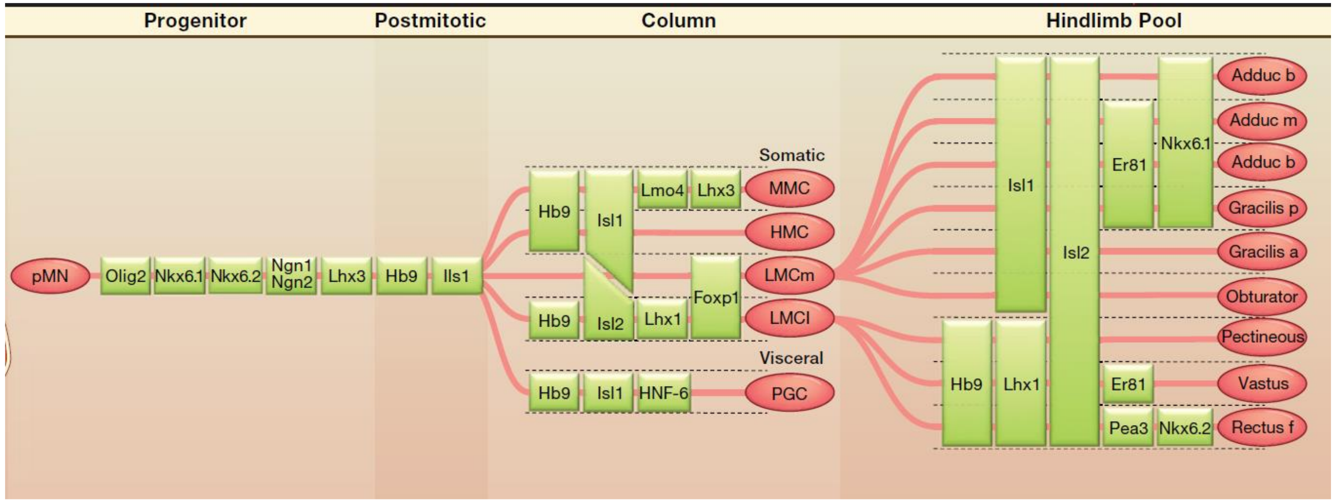
Motor neurons drive muscle contraction



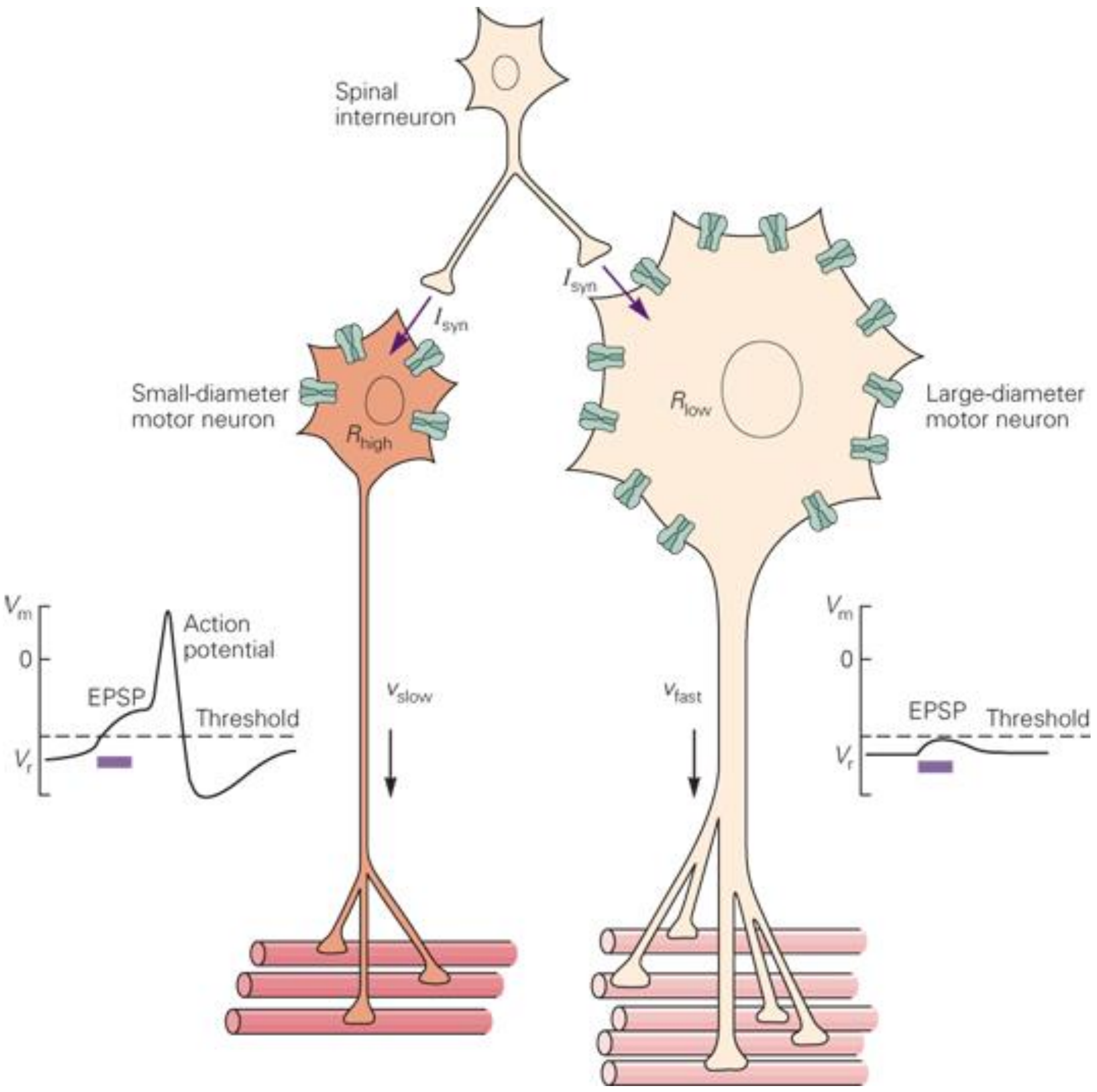
ChAT





Alynick et al., 2015

Title



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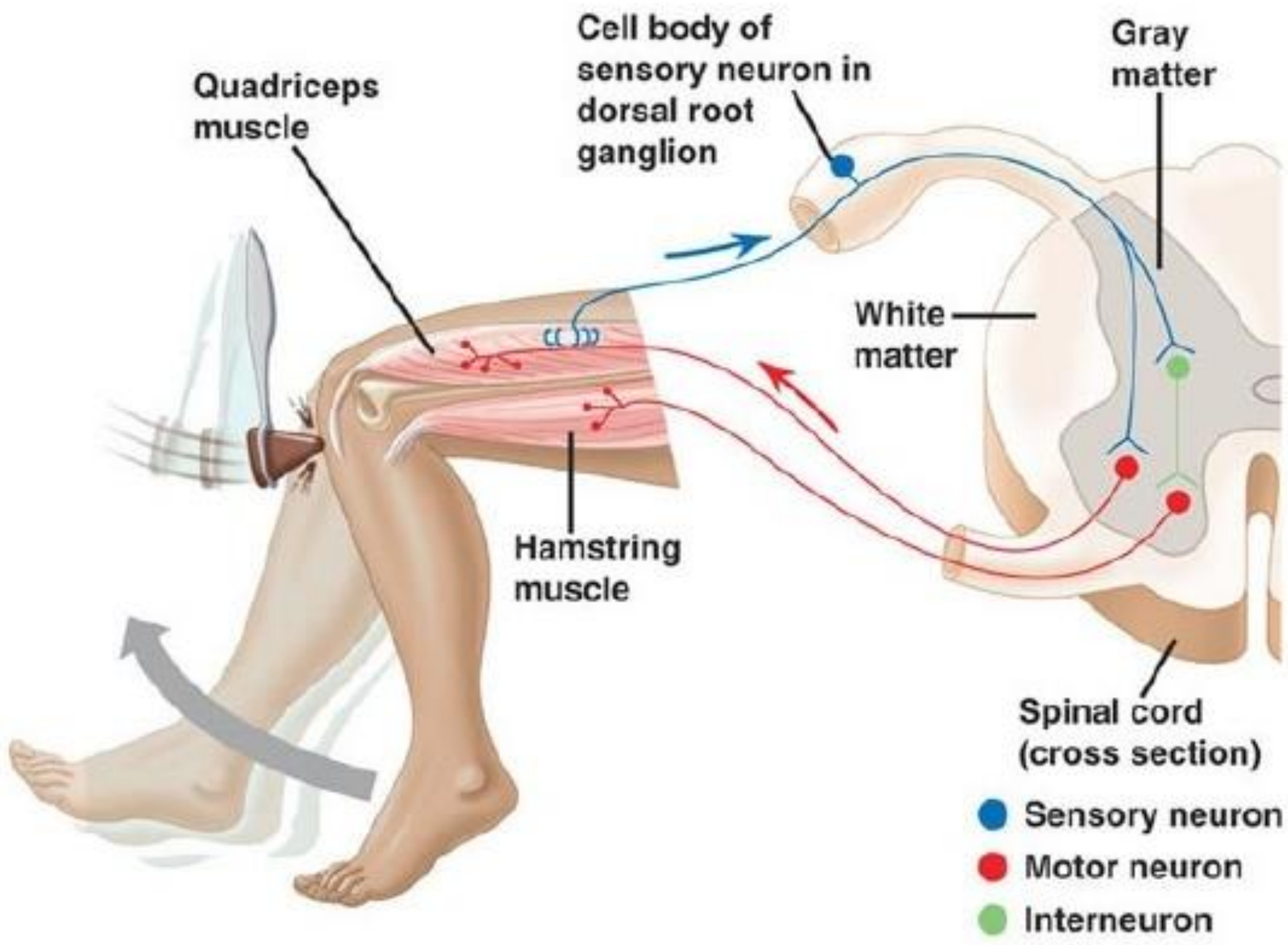
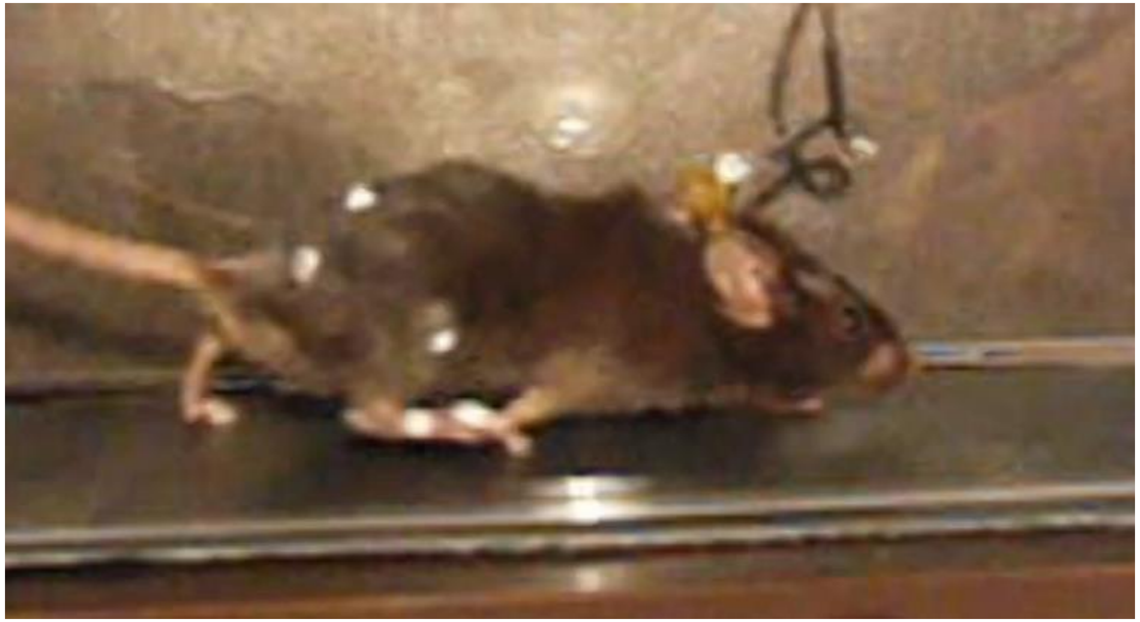
Monitoring limb position via proprioception



Muscle activation and proprioception



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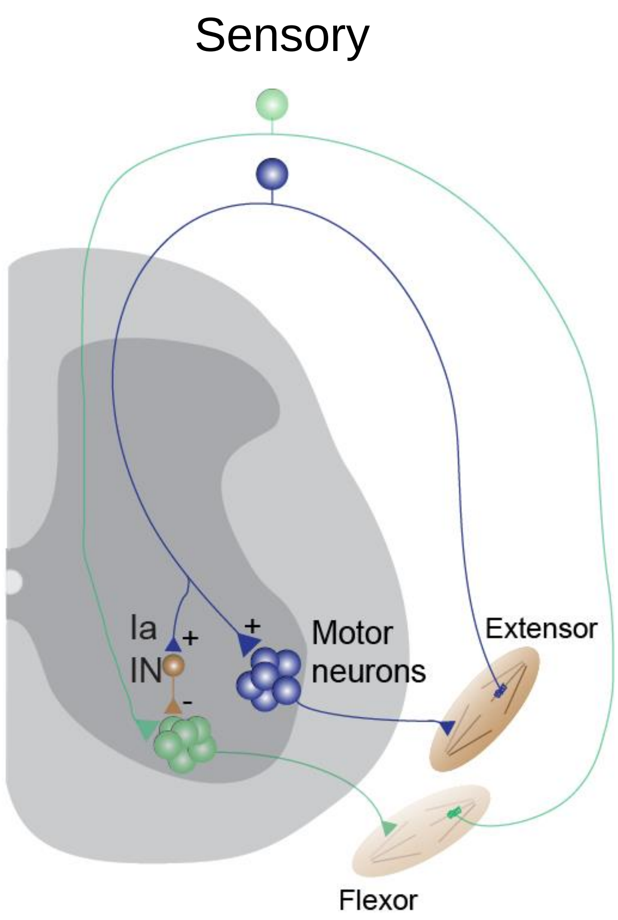
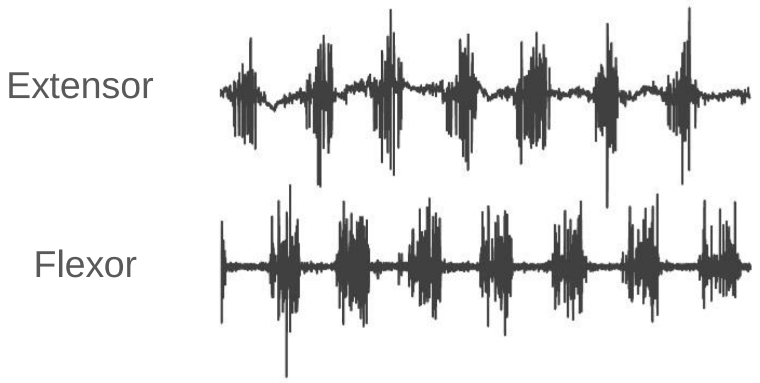
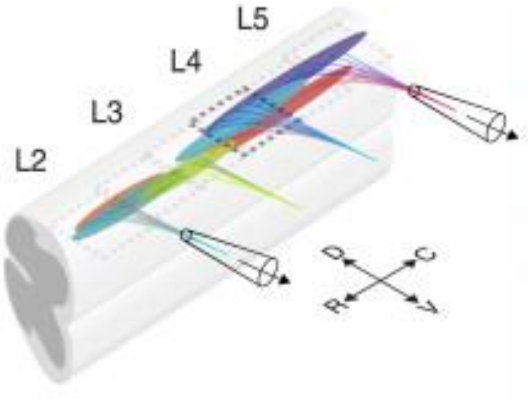
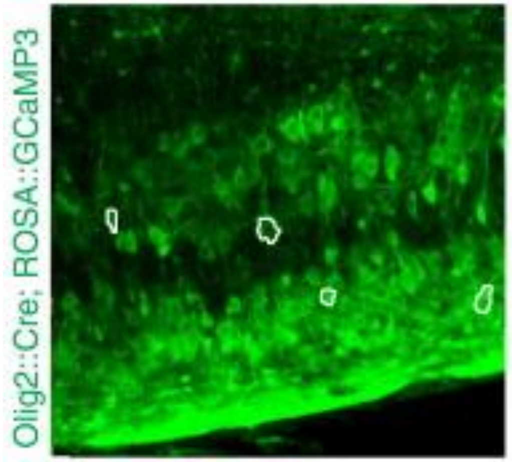
Sensory pathways could drive rhythmic firing in the spinal cord

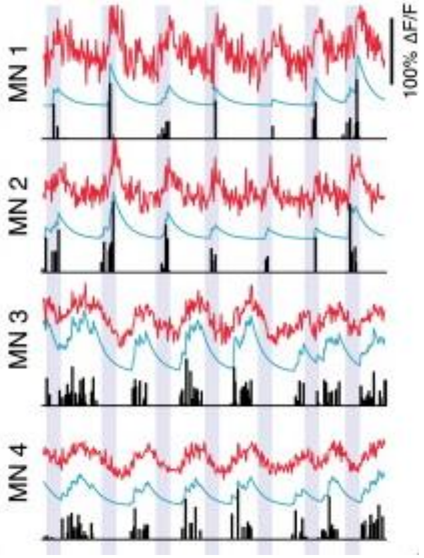


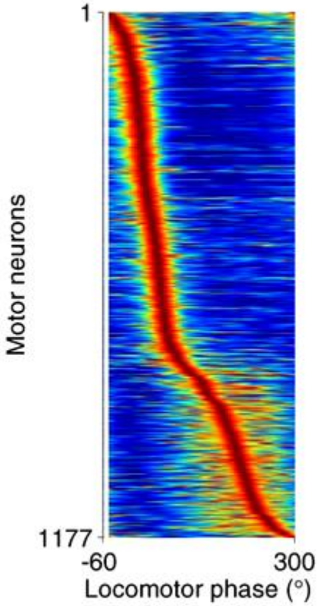


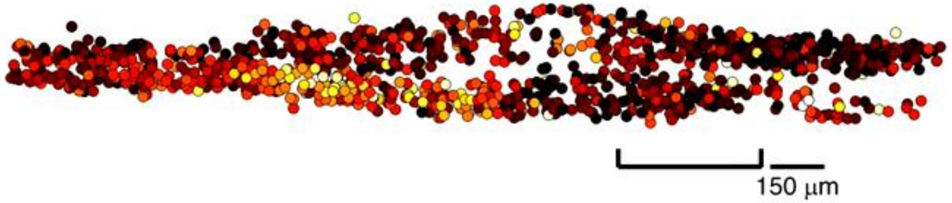
The spinal cord can generate rhythmic firing of motor neurons

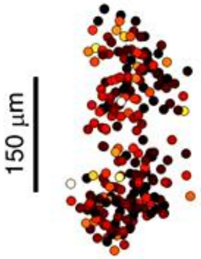












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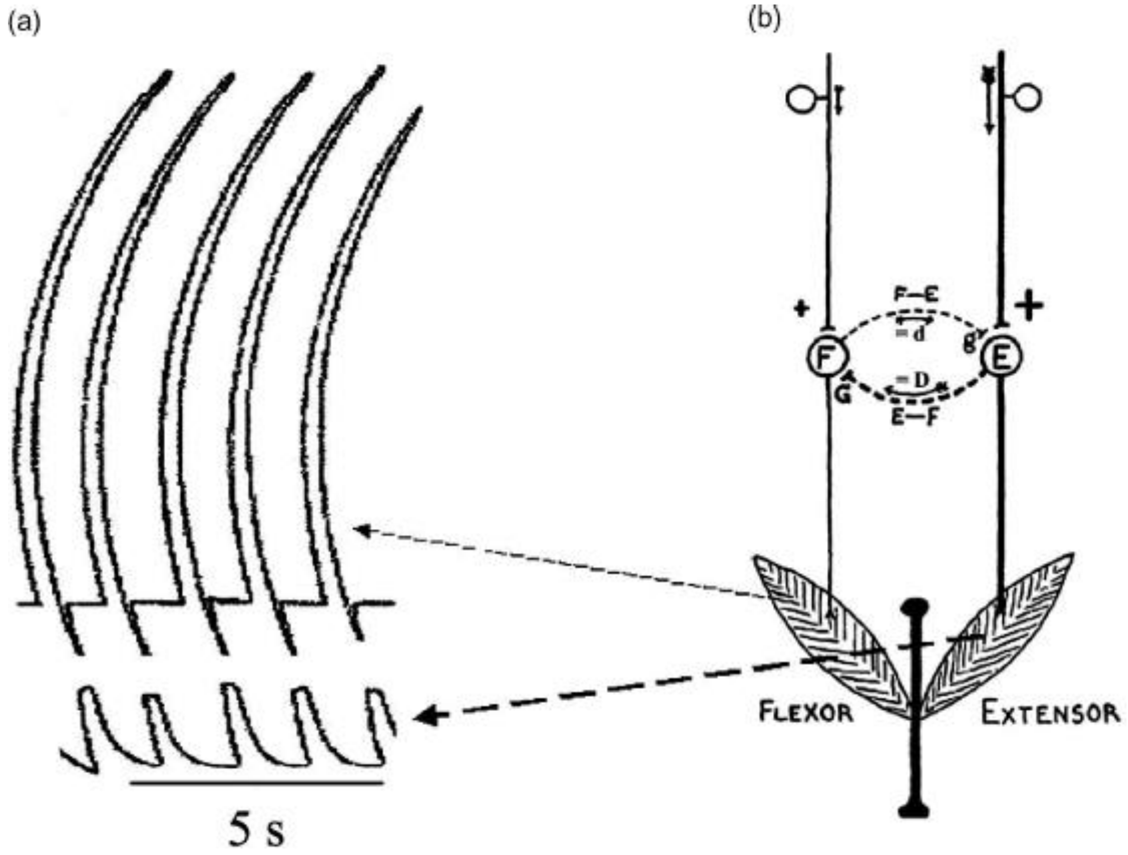
Machado et al., 2015

Locomotion is based on rhythmic movements generated in the spinal cord

T. Graham Brown

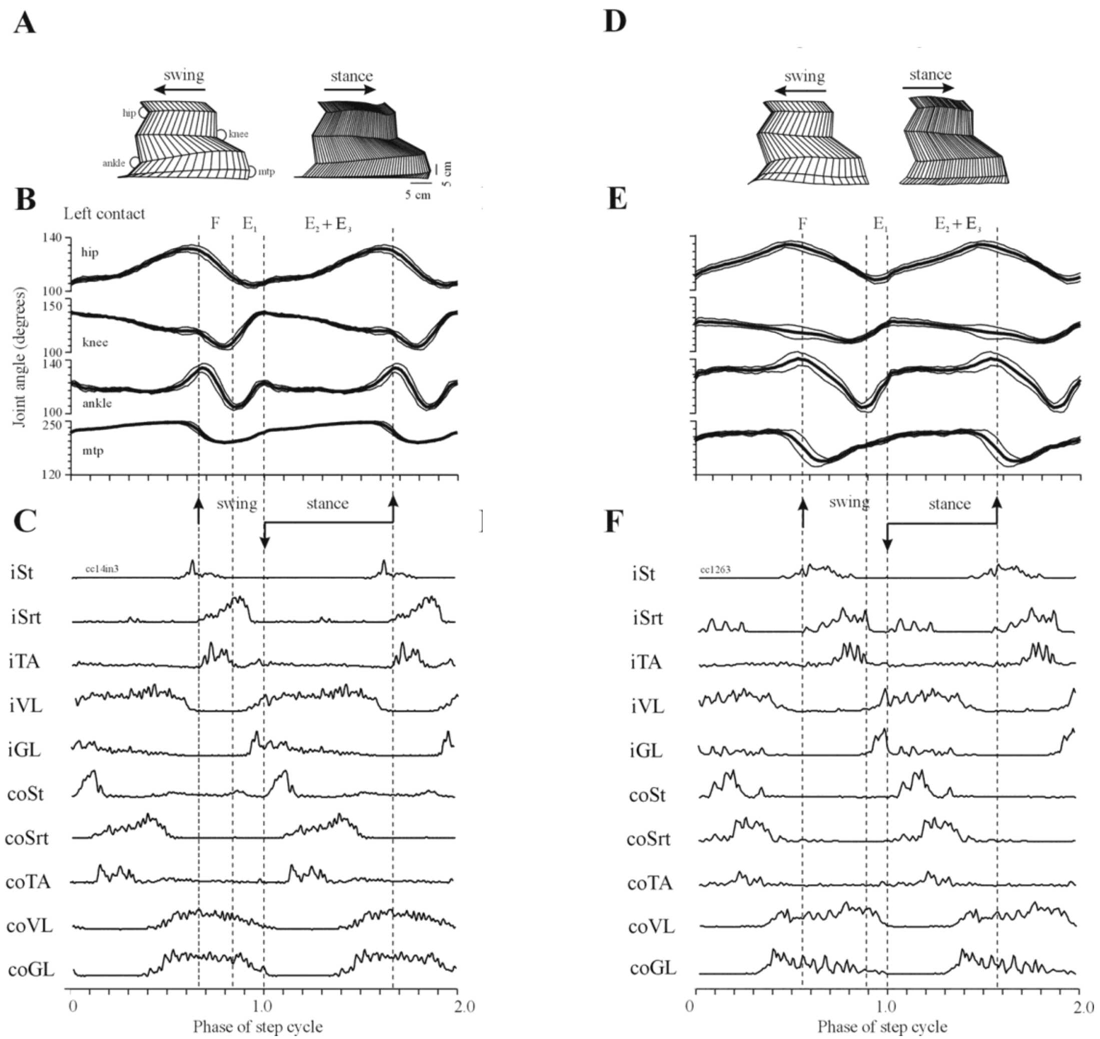
8. The experiments seem to show that the fundamental unit of activity in the nervous system is not that which we term the spinal reflex. They show the independence of the efferent neurone, and suggest that the functional unit is the activity of the independent efferent neurone; or rather, that it is the mutually conditioned activity of the linked antagonistic efferent neurones ("half-centres") which together form the "centre": and they also suggest that the primitive activity of the nervous system is seen in such rhythmic acts as progression and respiration.

Brown, 1914



The spinal cord can generate rhythmic locomotion

Intact | Spinalised (T13; 38 days)



Rossignol and Bouyer, 2004

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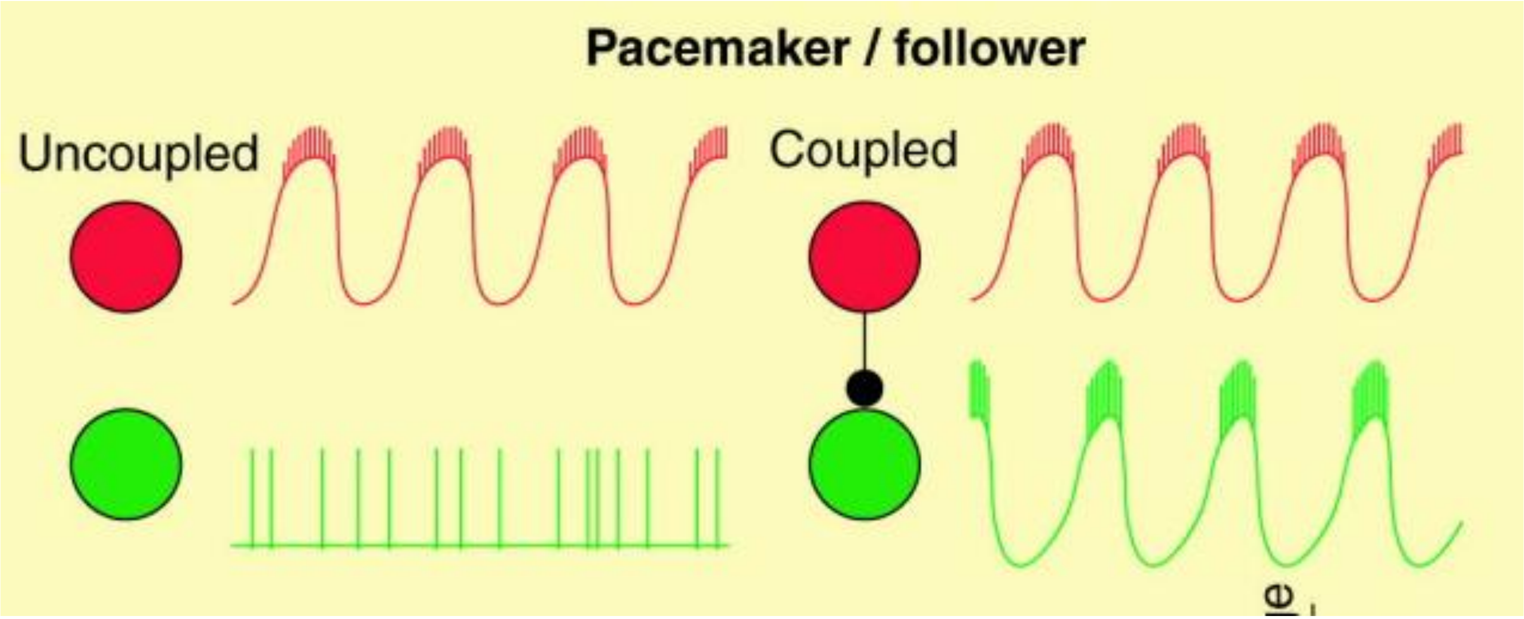
The central pattern generator

How do neural circuits generate rhythmic firing?

1. Reflex pathways
2. Pacemaker neurons
3. Reciprocal inhibition

Pacemaker neurons



Crustacean stomatogastric ganglion

Respiratory centres

Current Biology

Volume 11, Issue 23, 27 November 2001, Pages R986–R996

Review Article

Central pattern generators and the control of rhythmic movements

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Eve Marder, Dirk Bucher

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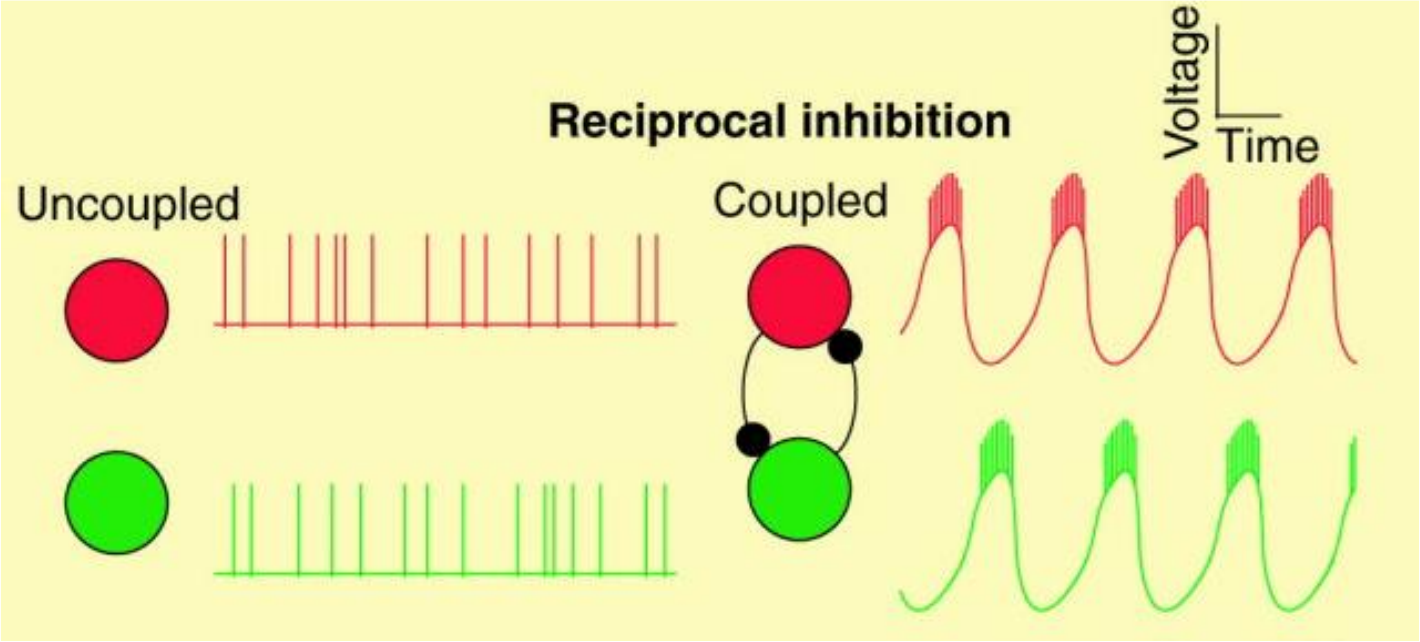
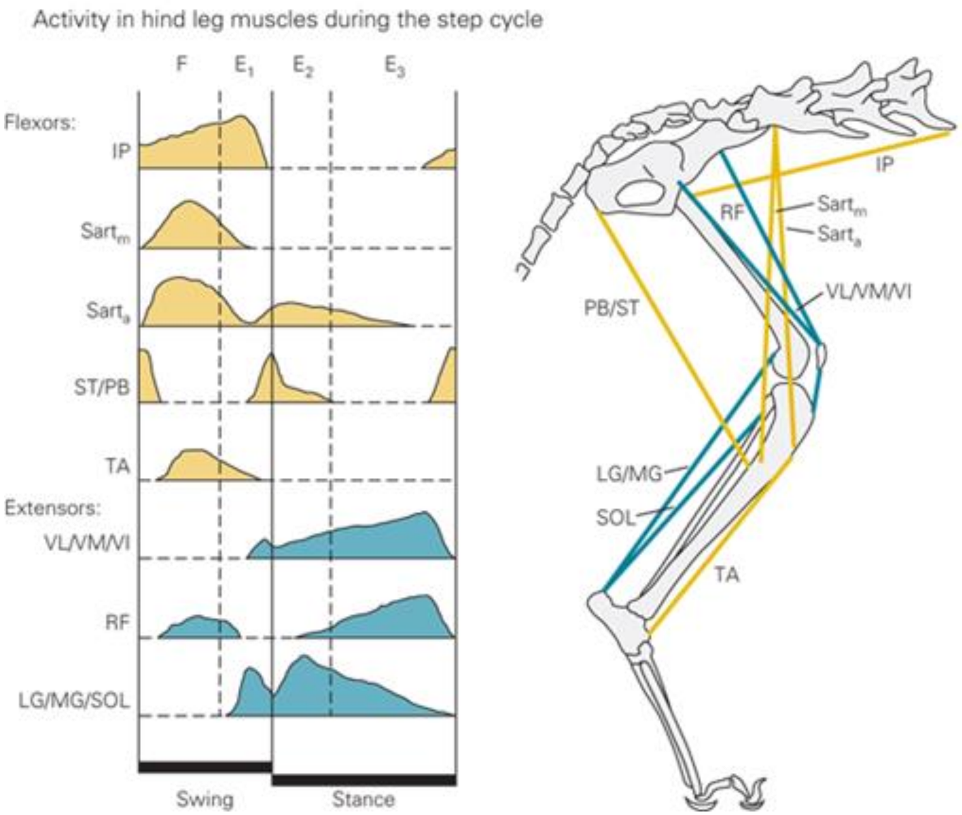
http://dx.doi.org/10.1016/S0960-9822(01)00581-4

Reciprocal inhibition

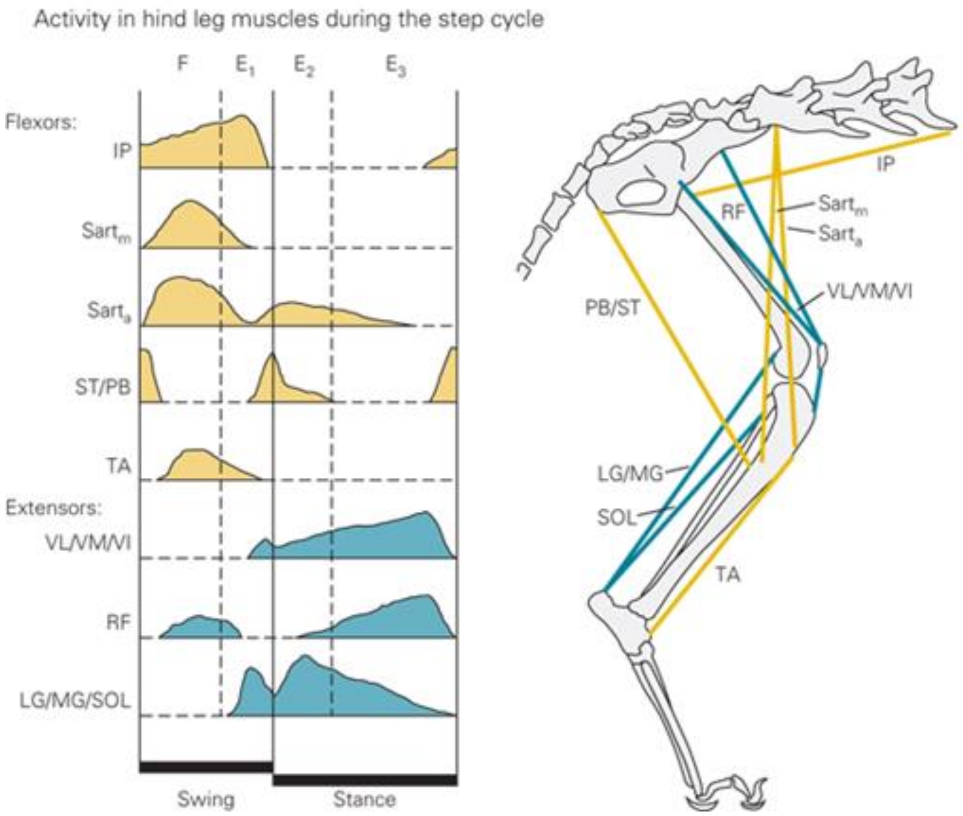


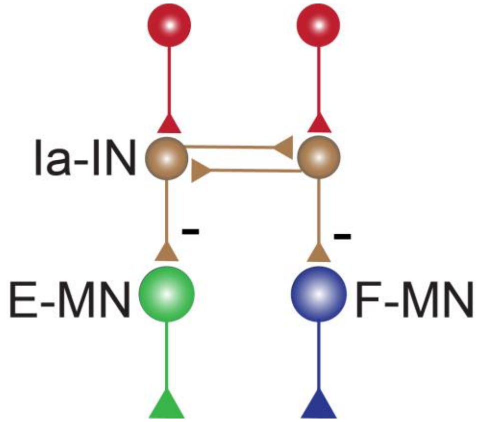
Swimming

The unit burst generator as an alternative to the half-centre model

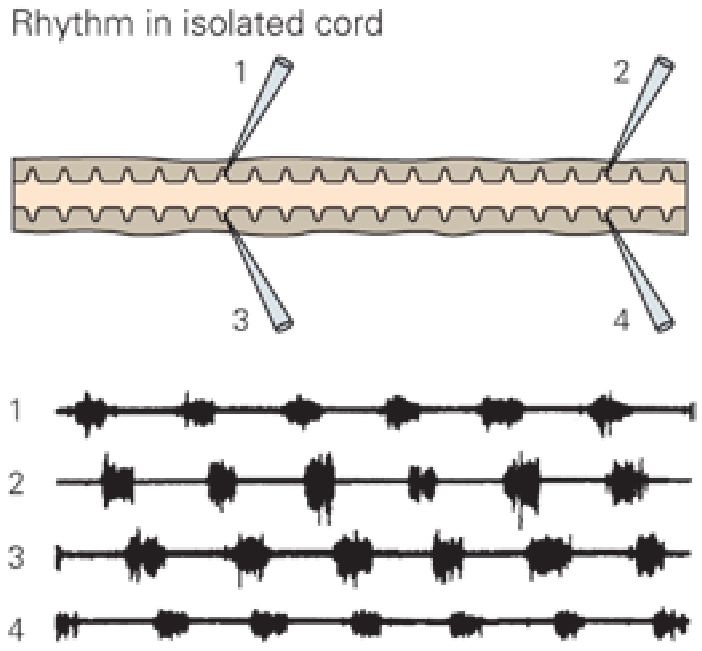


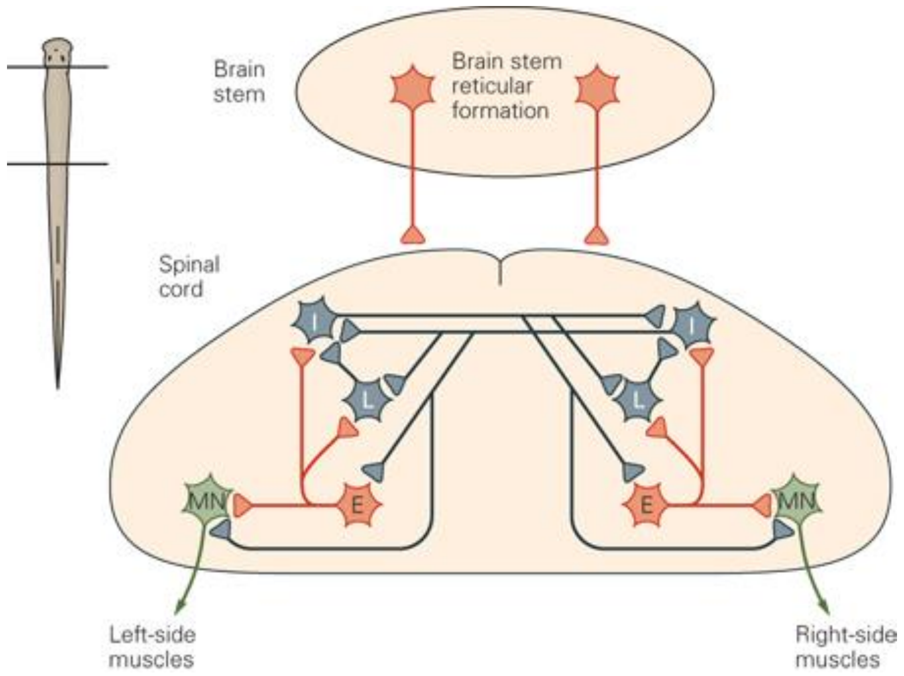
The unit burst generator as an alternative to the half-centre model





The unit burst generator as an alternative to the half-centre model





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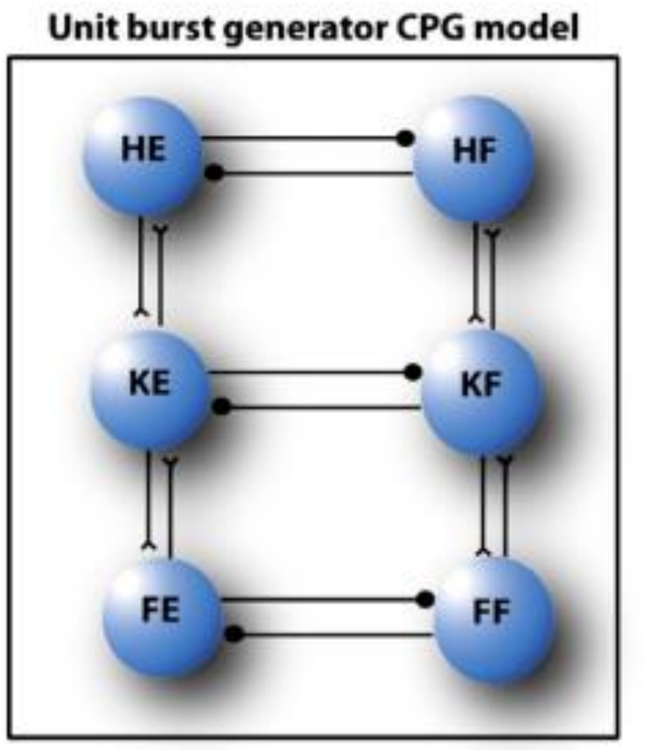
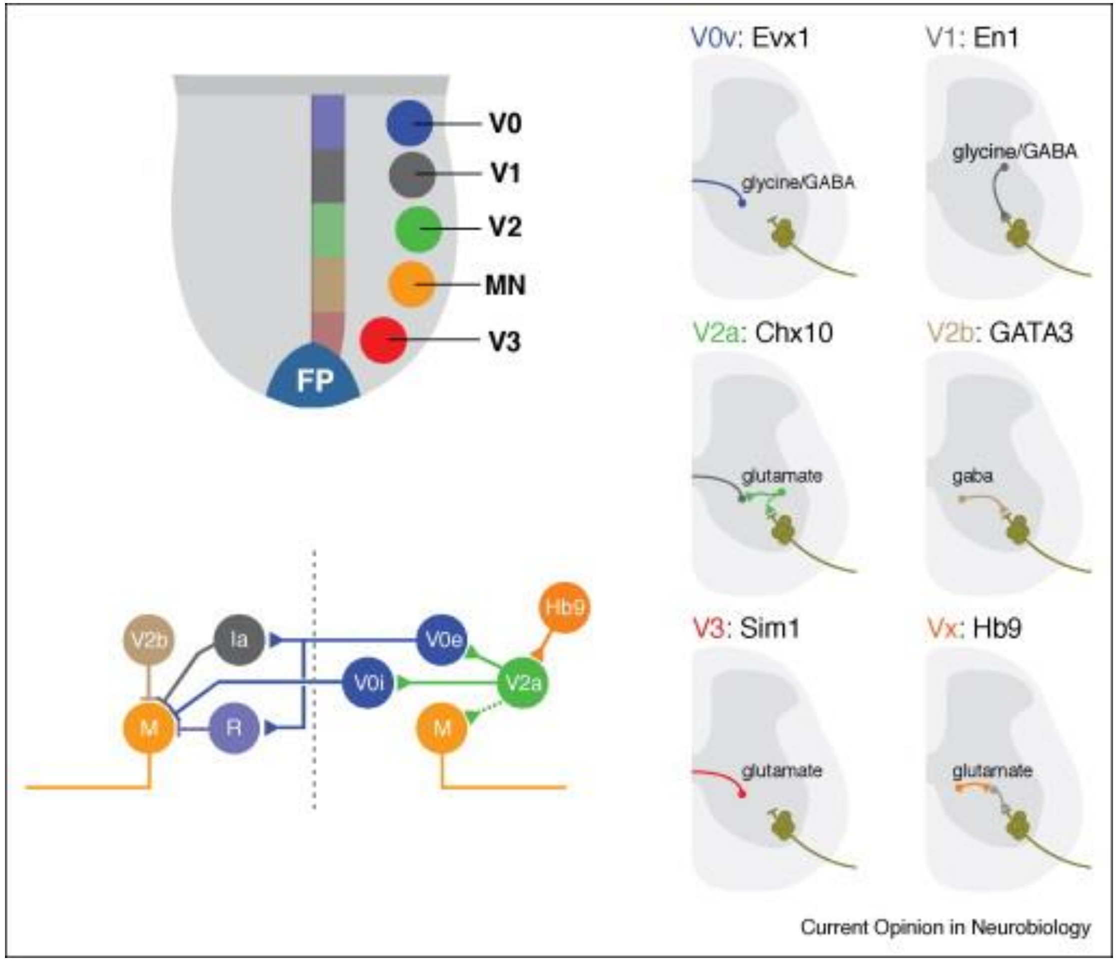
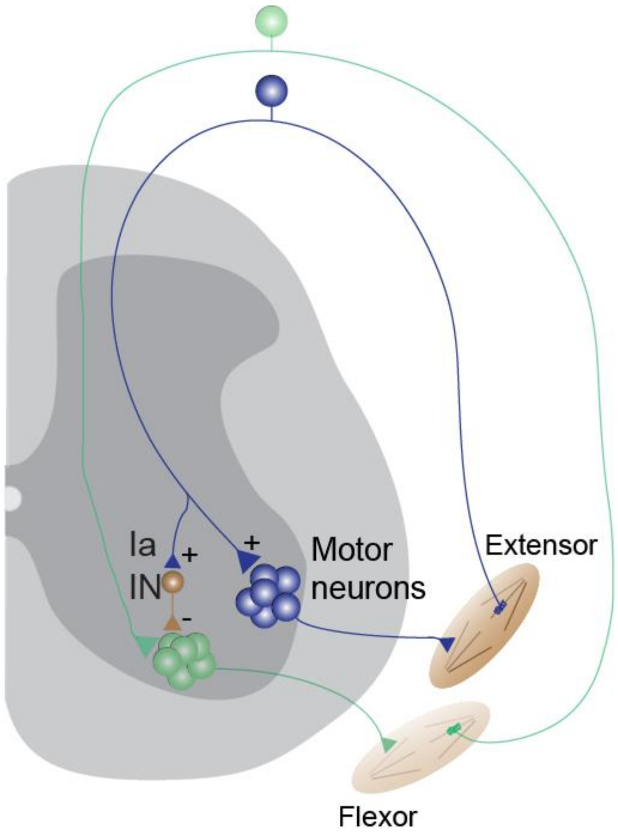


We still don't know the neuronal basis for rhythm generation in the spinal cord

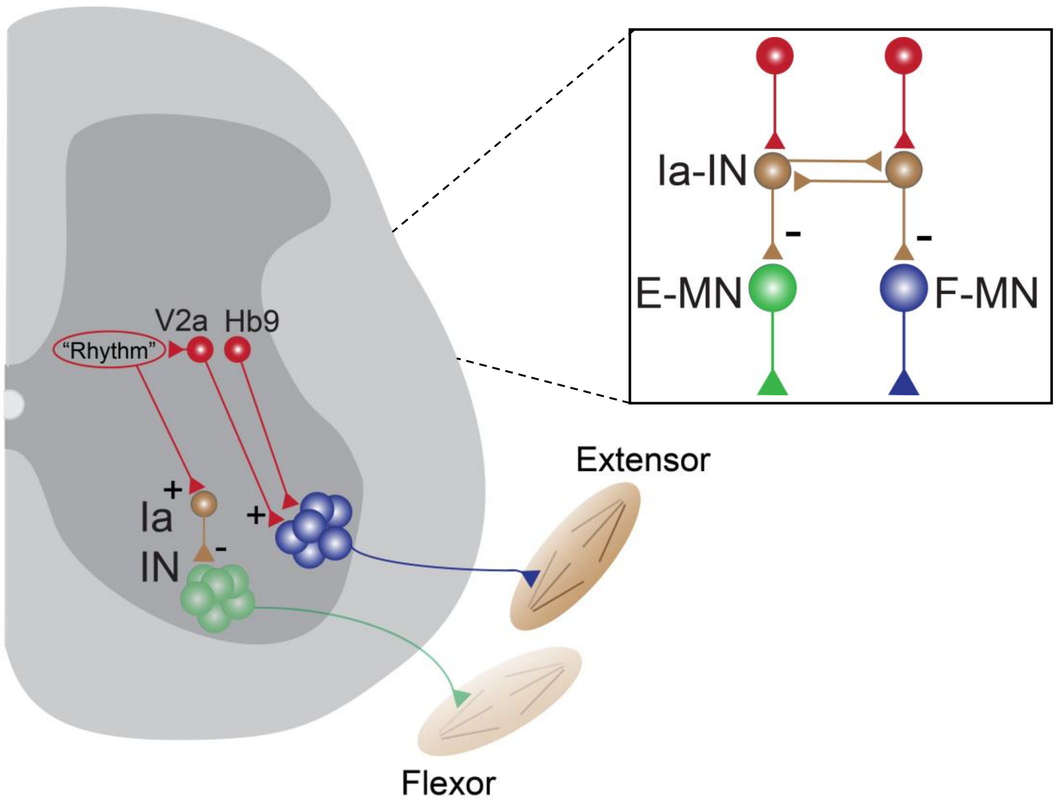


Spinal cord is (probably) a network oscillator modulated by sensory feedback

Sensory feedback



Network oscillator



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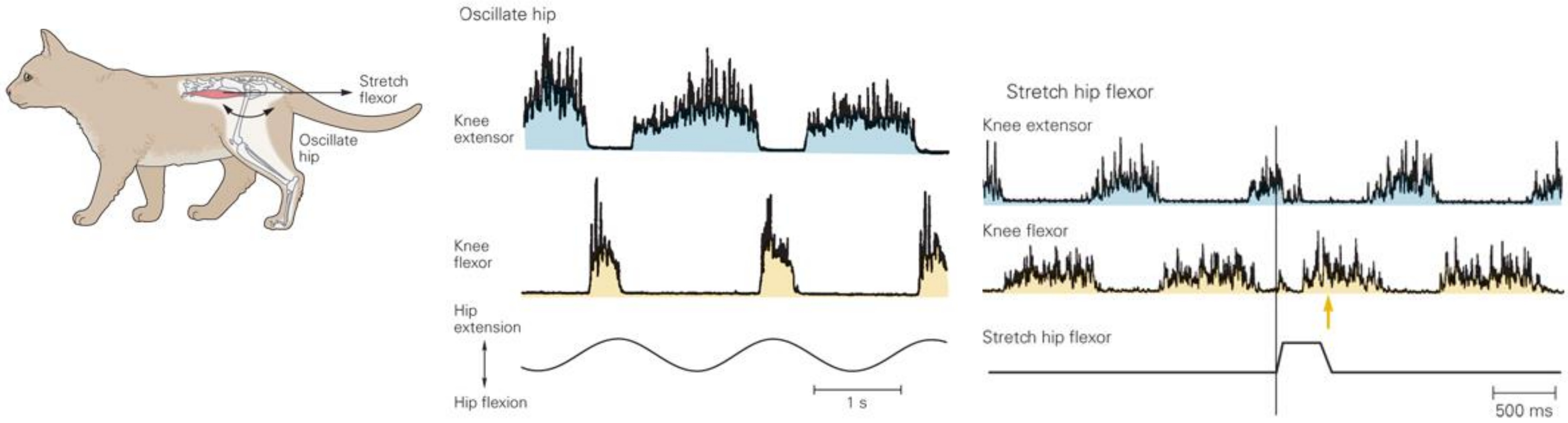
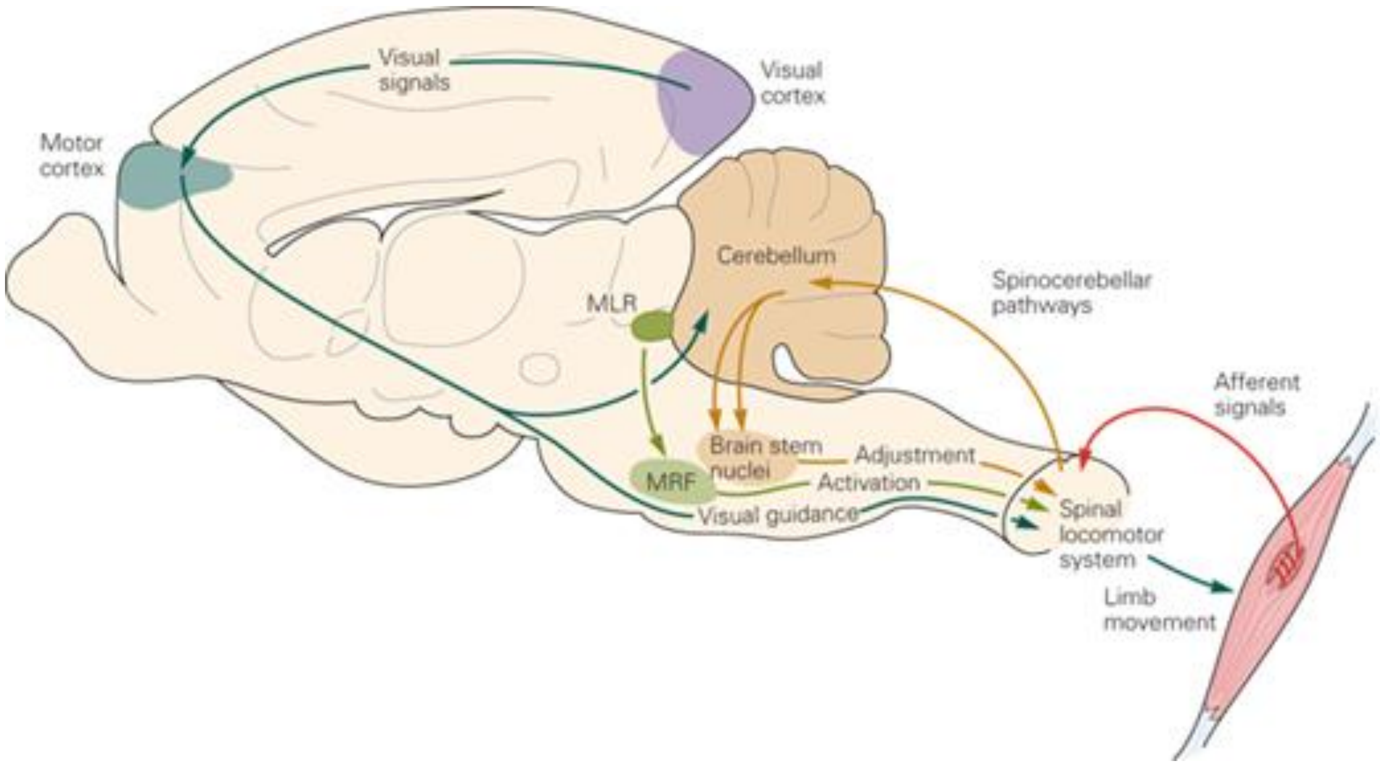
Proprioception **modulates** the step cycle



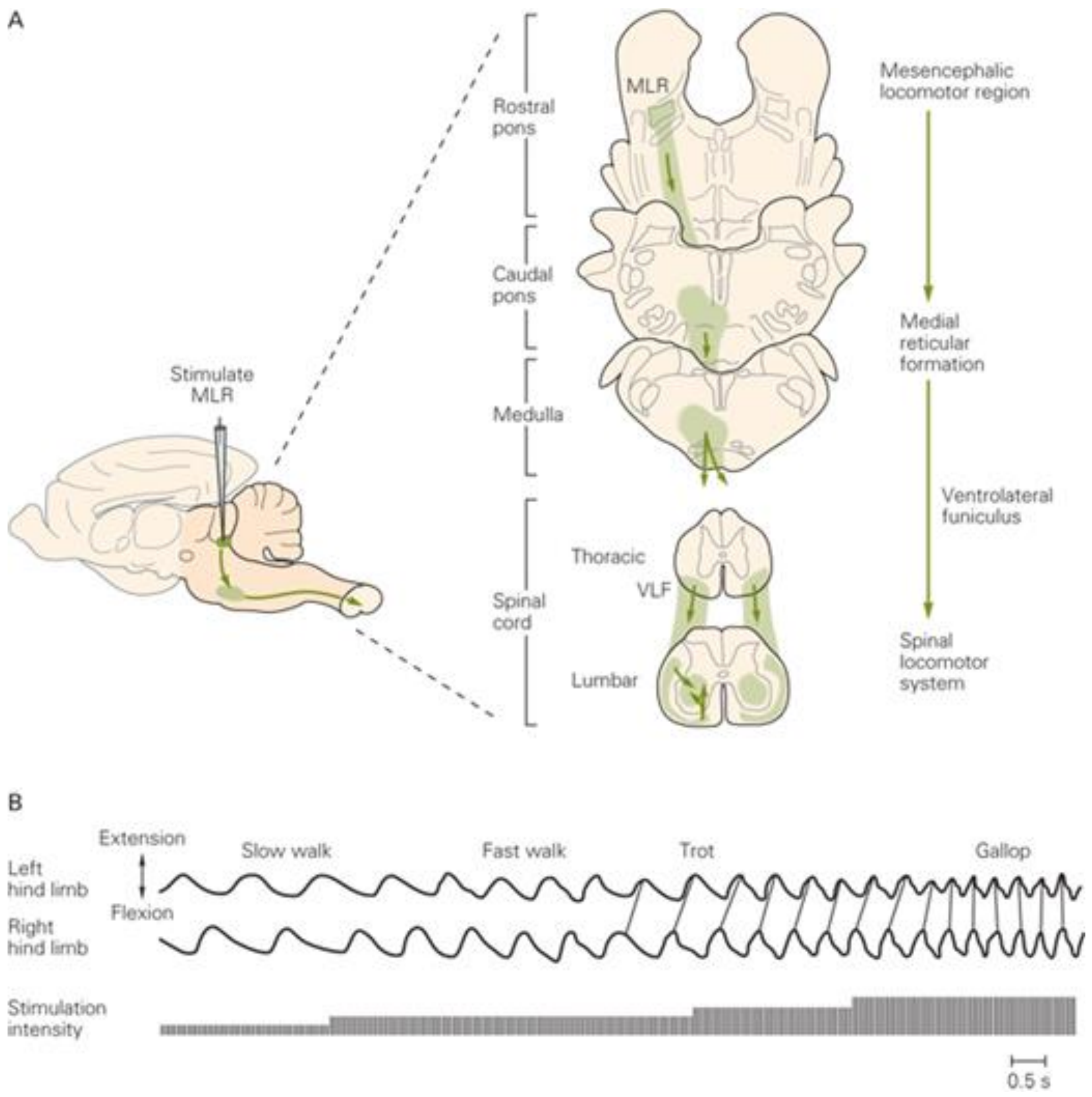
When do we need the brain?

1. When something unexpected happens

2. When we want conscious control over our movements



Activation of spinal CPGs – the mesencephalic locomotor region



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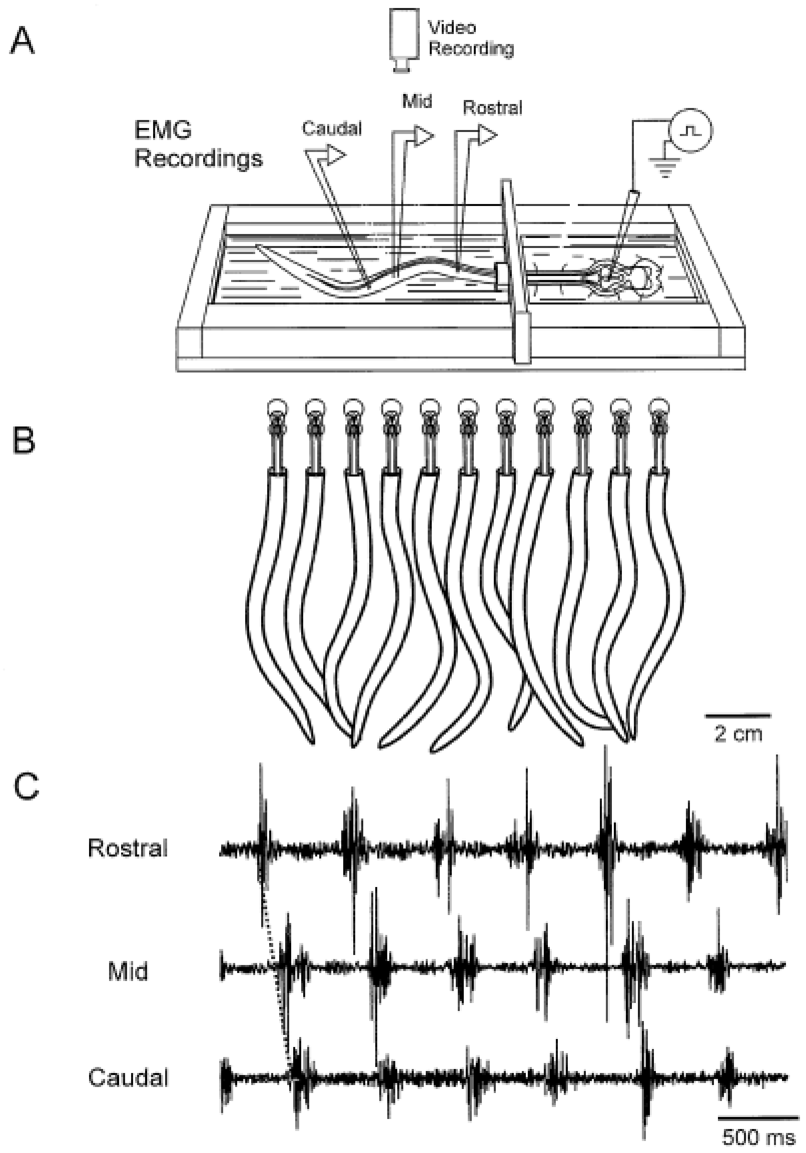
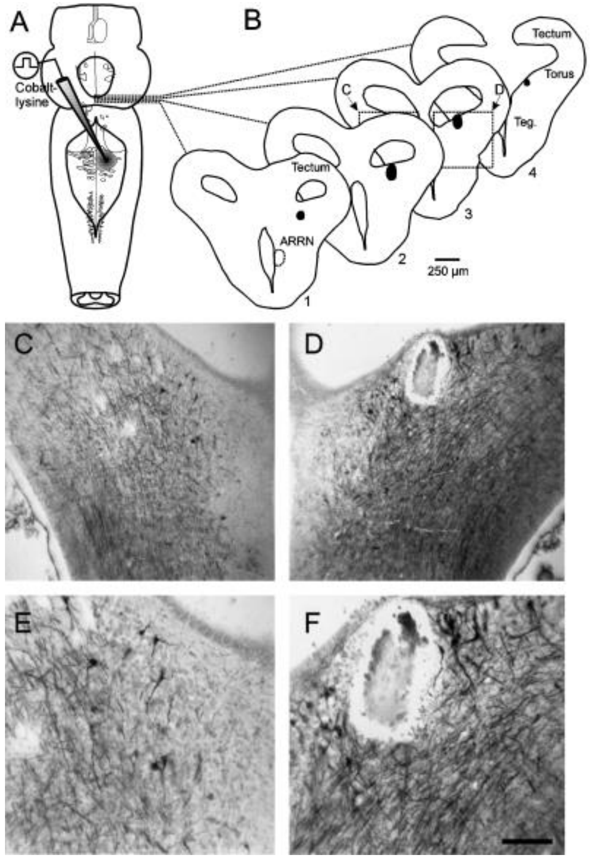
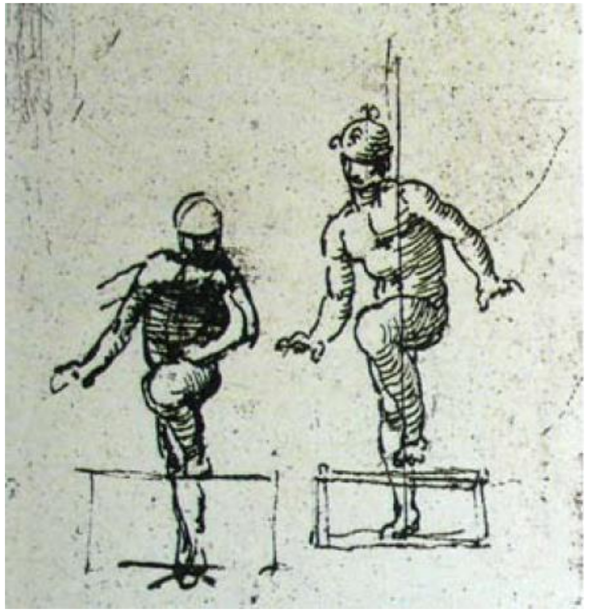
The MLR is conserved across species





Sirota et al., 2000

Animal movement must be continuously flexible



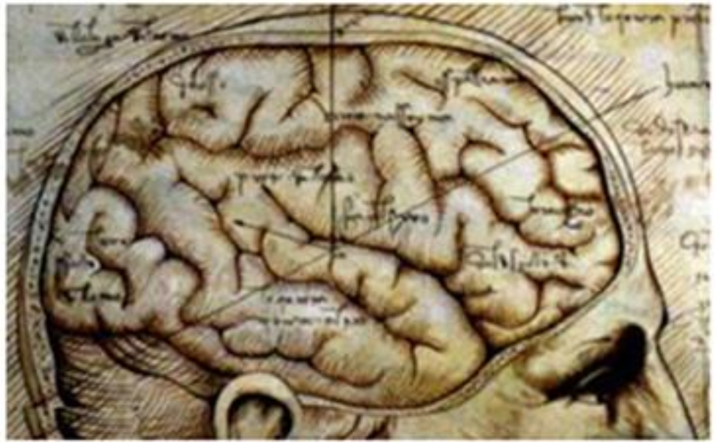
Da Vinci, ~1500

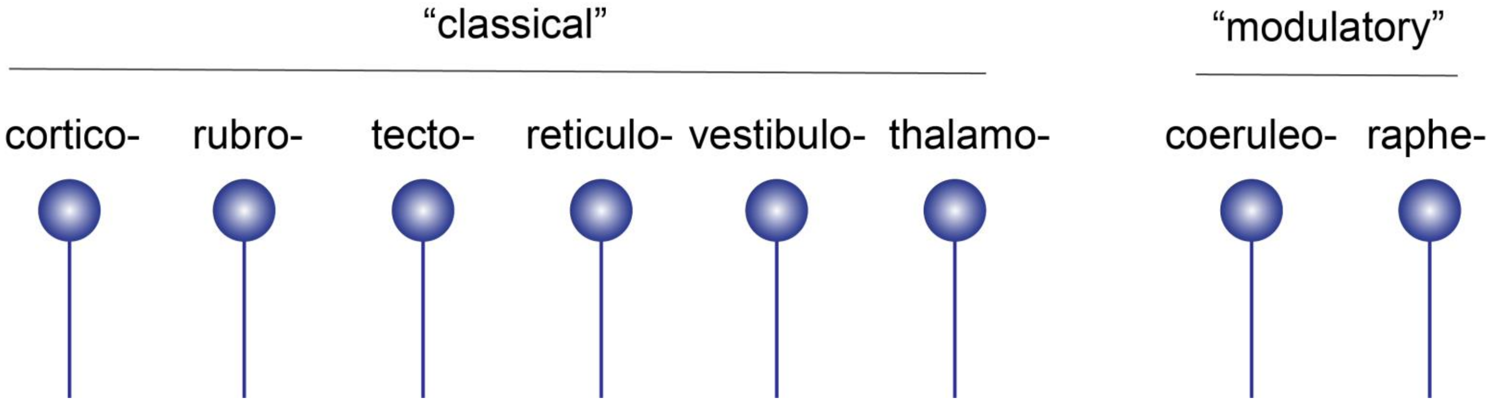
Borelli, 1681

Marey, 1873

Adaptive motor control

a snapshot of 27 descending tracts….





Adaptive motor control

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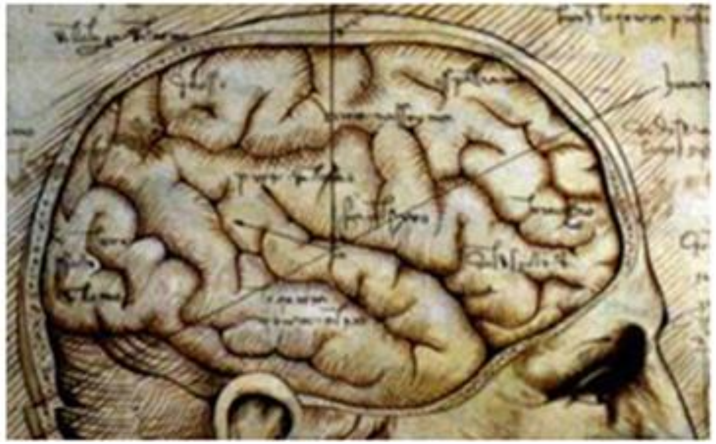
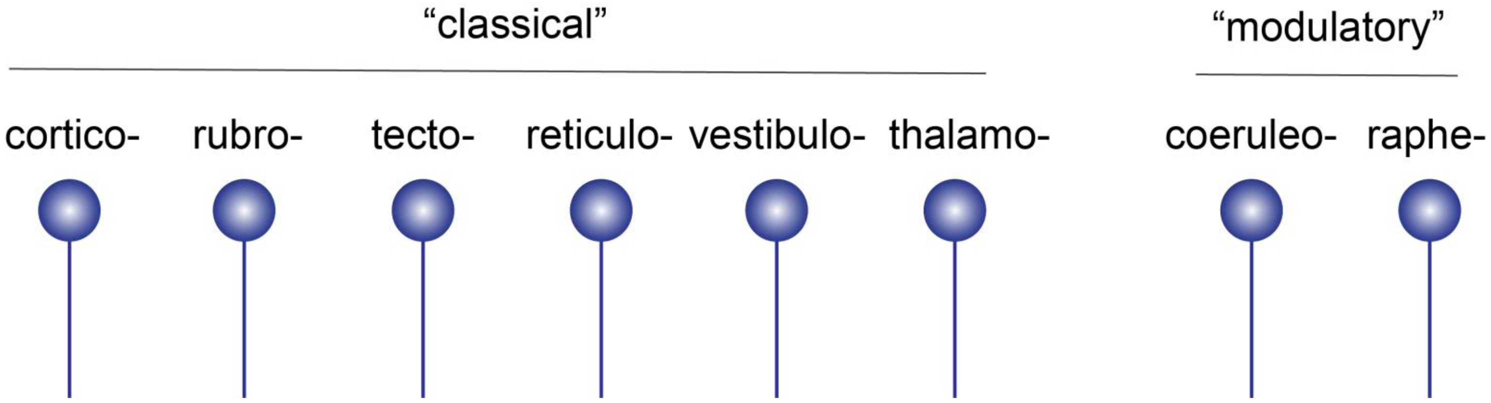




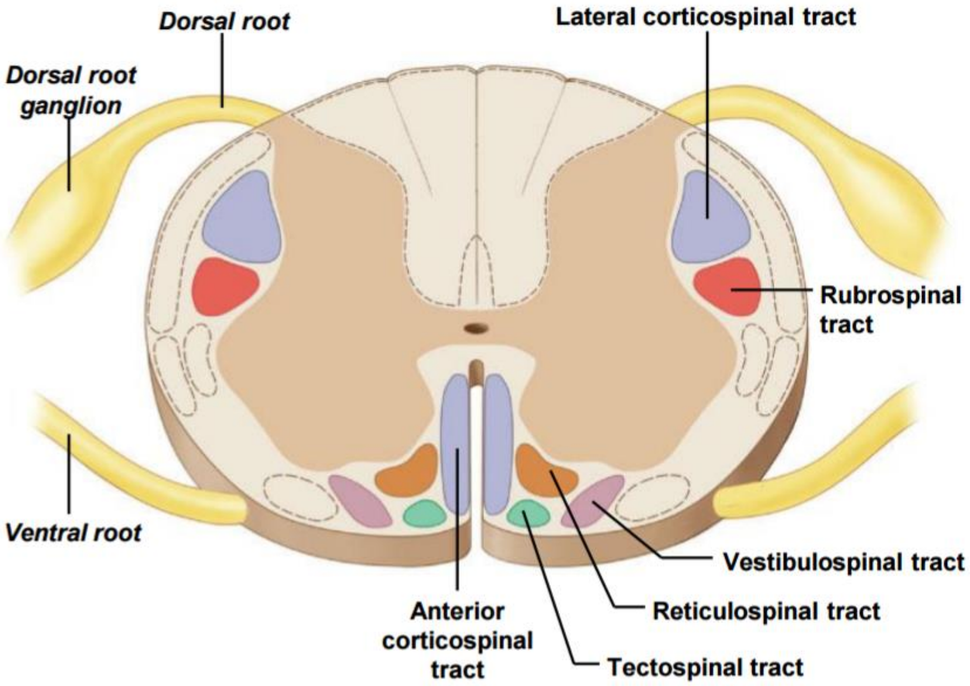
Descending tracts are anatomically organised

Subconscious motor tracts (extrapyramidal) - regulation of balance, muscle tone, eye, hand and upper limb position

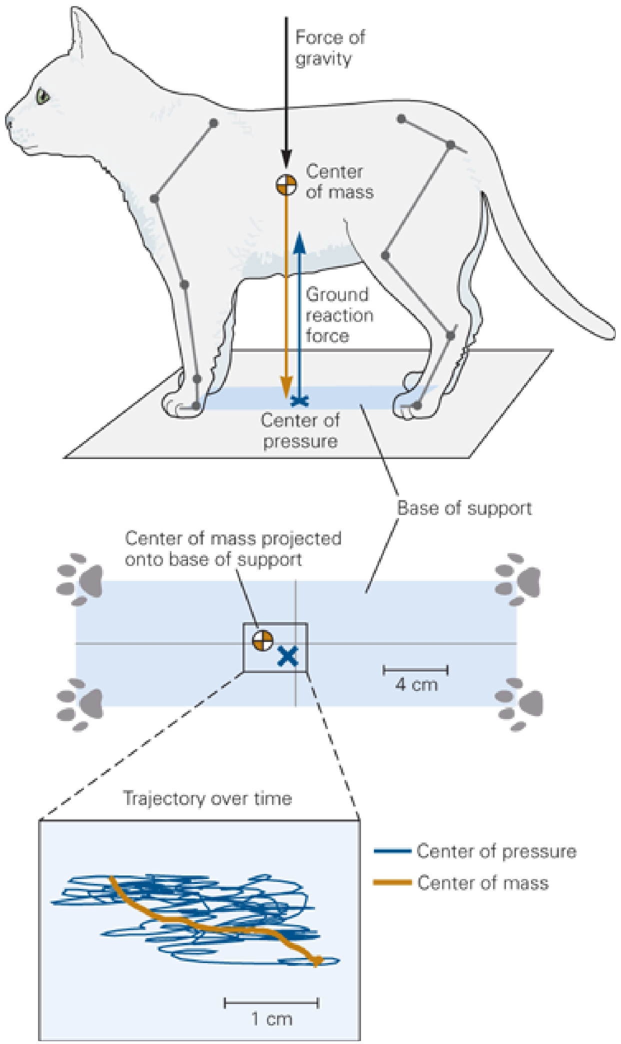
- Vestibulospinal
- Tectospinal
- Reticulospinal

Conscious motor tracts (pyramidal)

- Corticospinal



Postural control is an active process that requires descending commands



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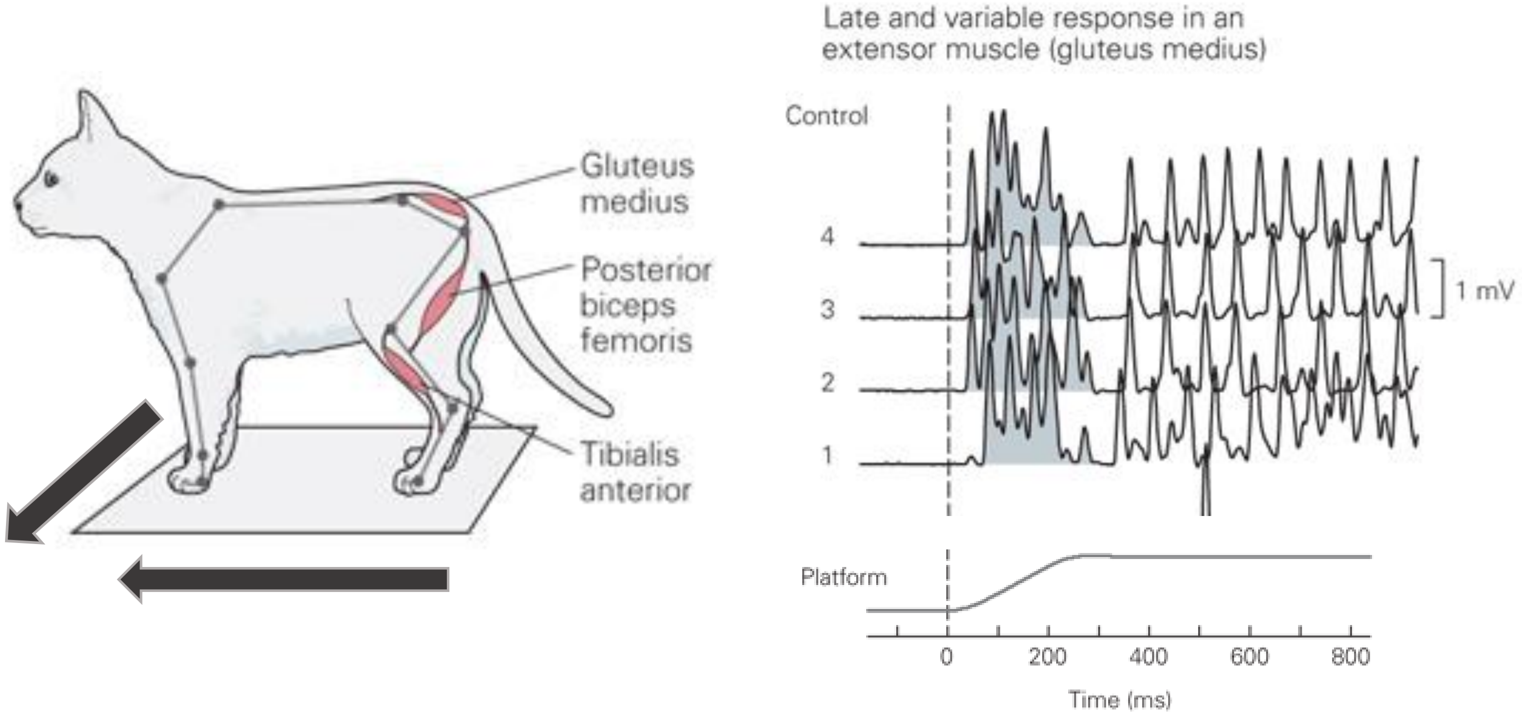
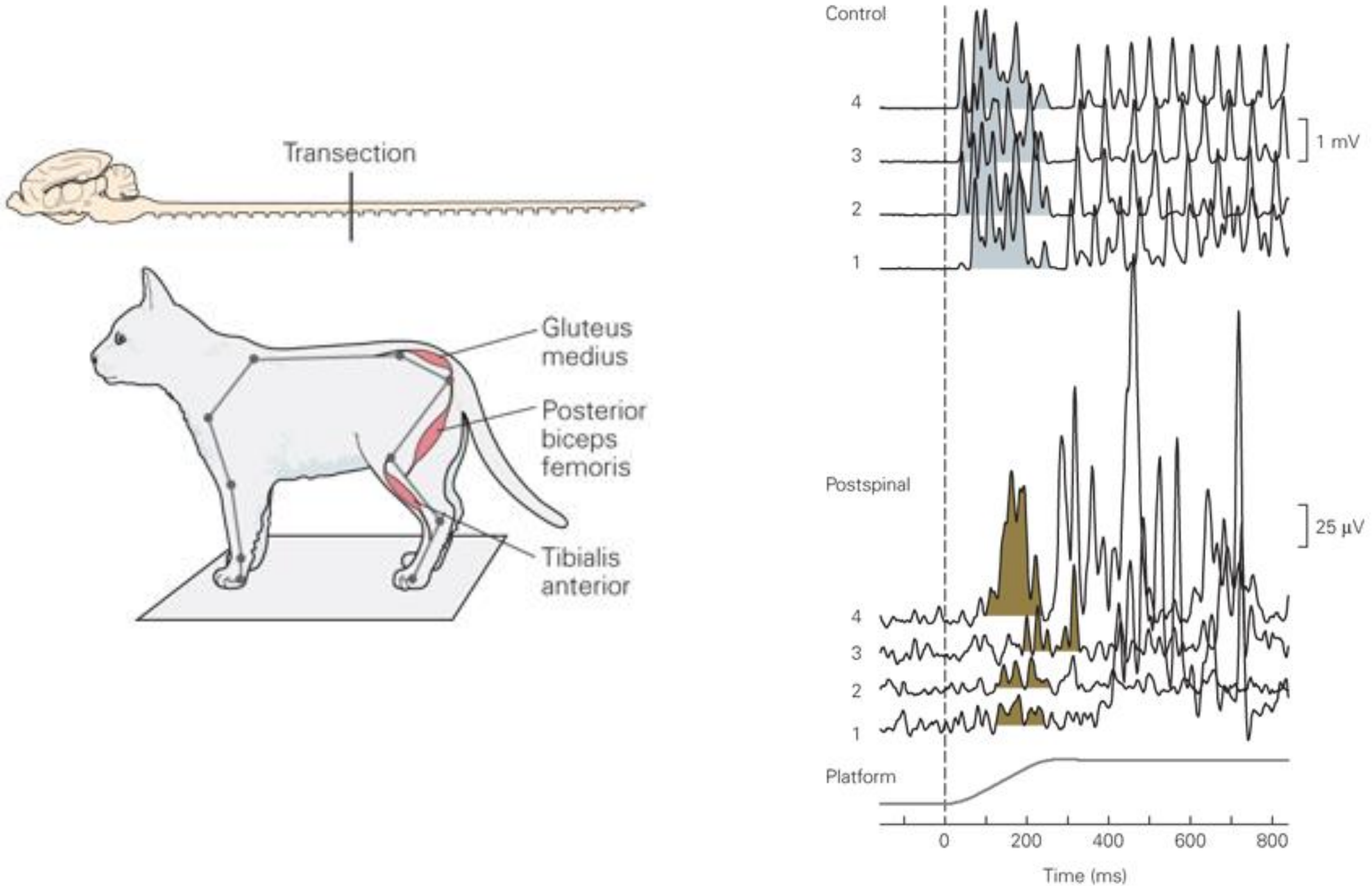
Postural control is an active process that requires descending commands



Macpherson and Fung, 1999

Postural control is an active process that requires descending commands



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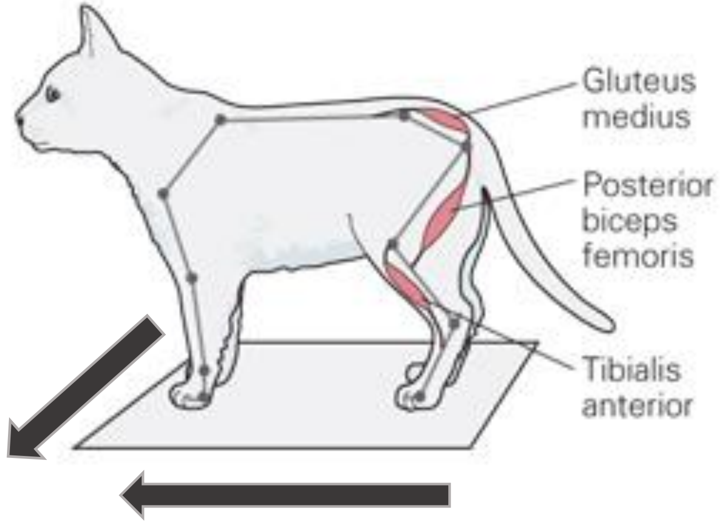
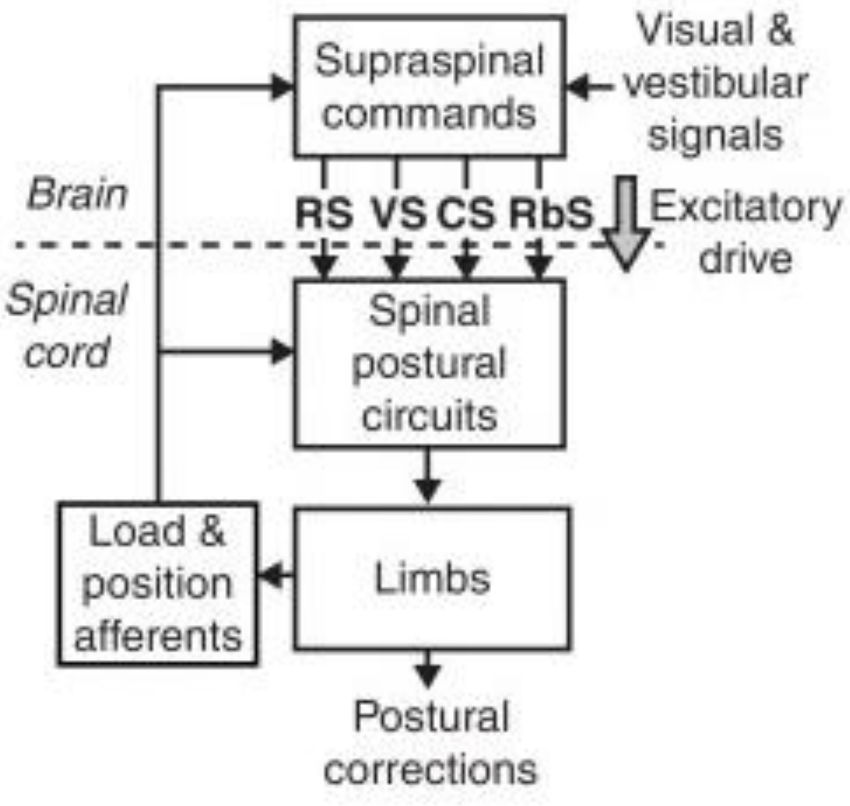
Postural control requires sensory motor integration

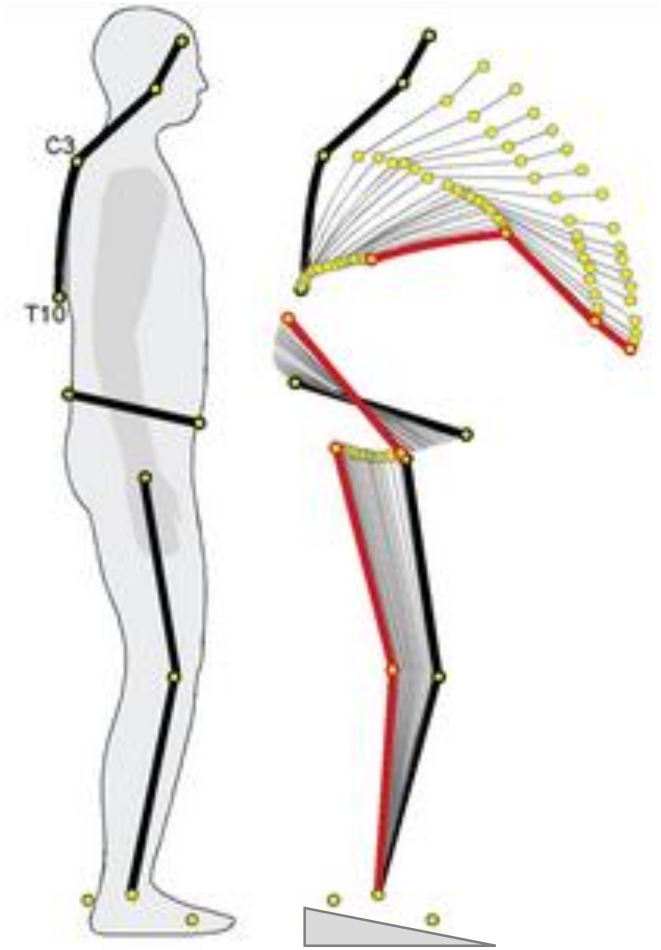




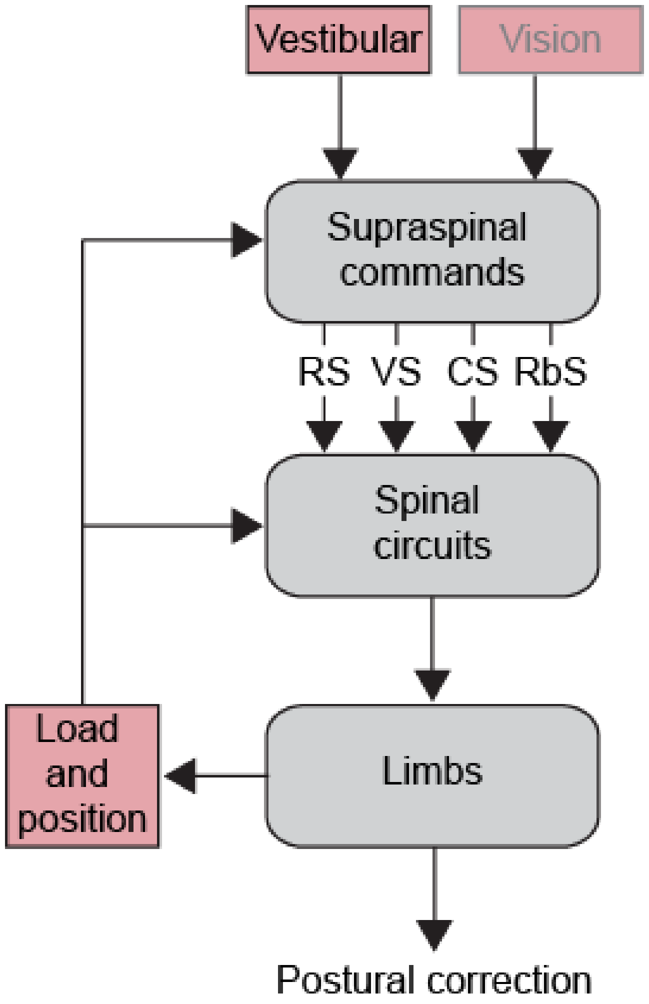
Deliagina et al., 2012

Postural control and balance – you only notice when it's not there

Courtesy of Prof. Fay Horak, OHSU



Postural pathways

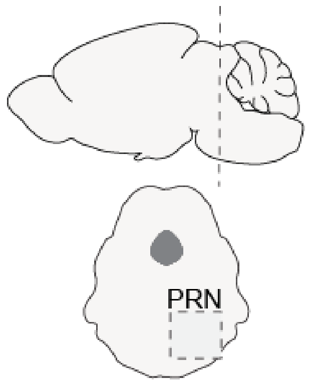


Deliagina et al., 2014

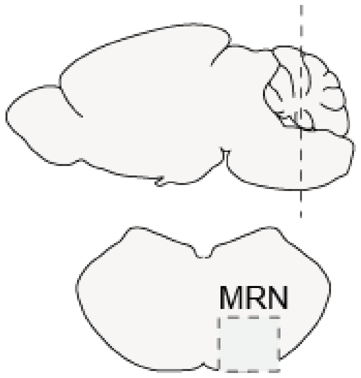
Reticulospinal pathways

Originate in the PRN and MRN, and project in the medial longitudinal fasciculus

Pontine reticular nucleus



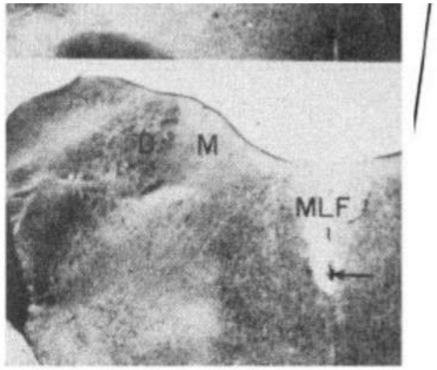
Medullary reticular nucleus

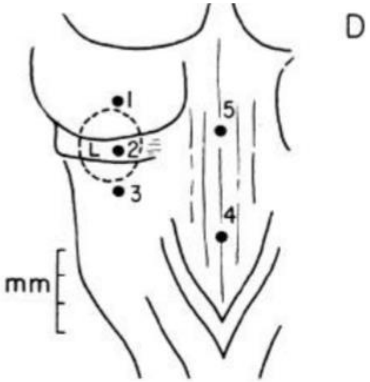


Reticulospinal pathways

excite both extensors and flexor motor neurons

4





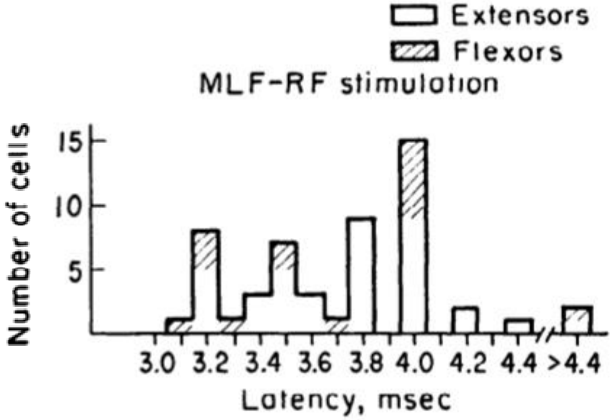


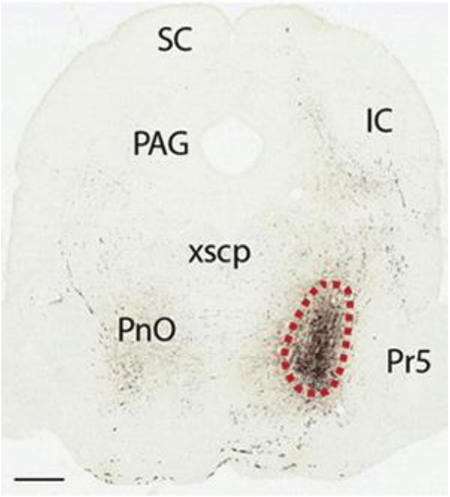
TABLE 1. *Effect of stimulation of Deiters' nucleus and medial longitudinal fasciculus (MLF-RF) on hindlimb motoneurons*

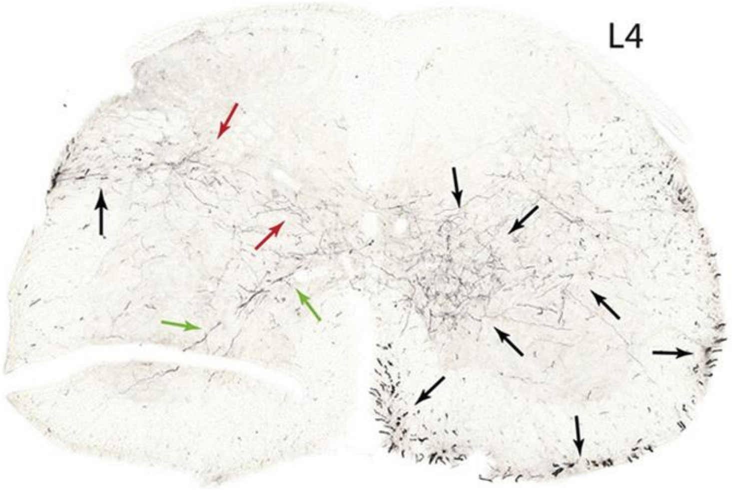
	Extensors				Flexors	
	GS	FDL-PL	BASM	PLANT	BST	PER
Monosynaptic EPSP						
Deiters' only	14/38	1/25	0/10	1/5	0/13	0/10
MLF-RF only	10/38	16/25	10/10	2/5	10/13	9/10

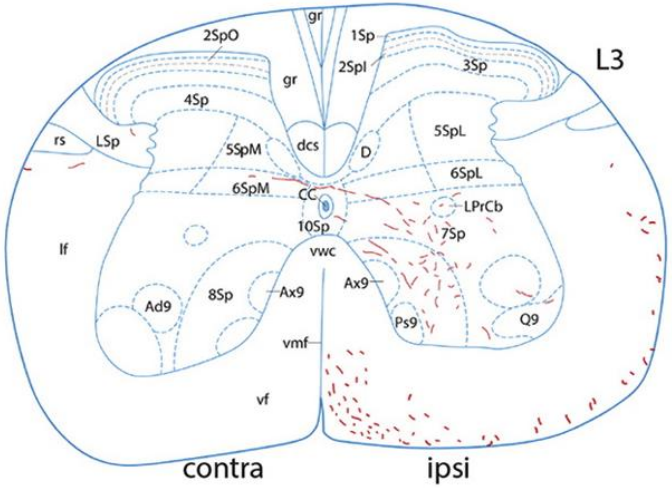
Wilson and Yoshida, 1969

Reticulospinal pathways

have diffuse projections into the spinal cord



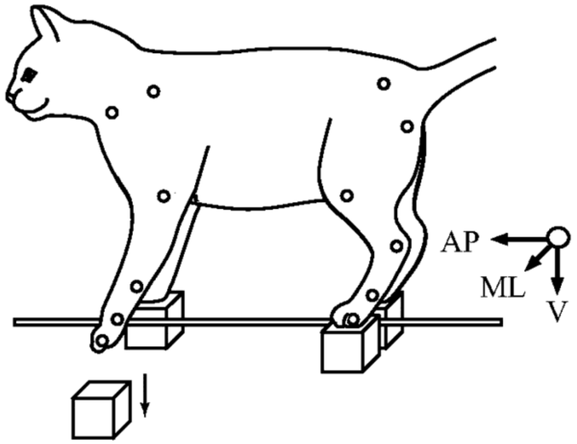


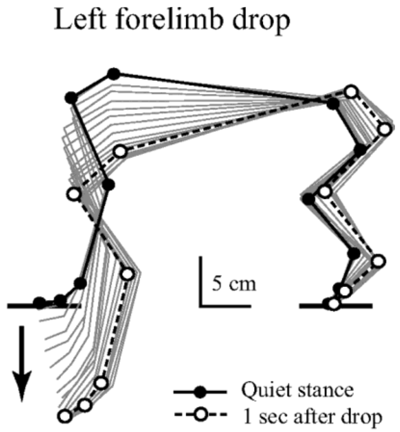


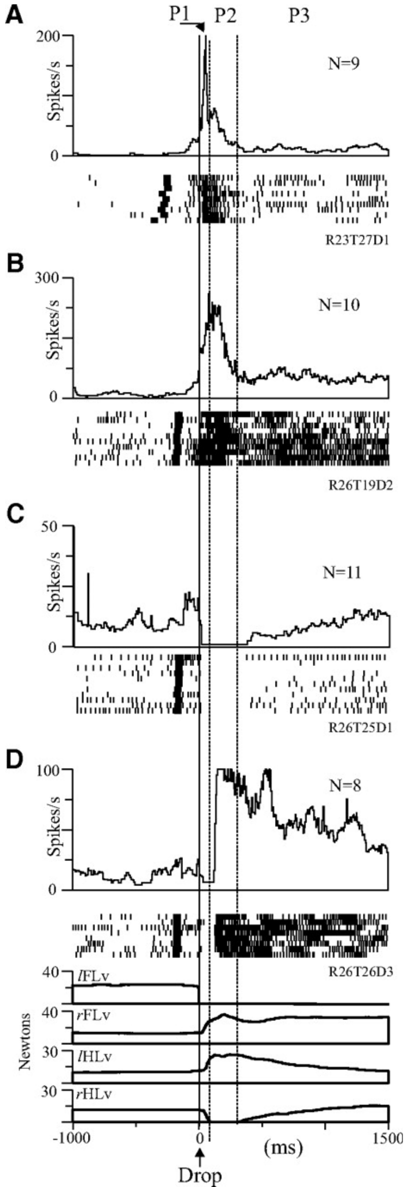
Liang et al., 2015

Reticulospinal pathways

A subset of reticulospinal neurons respond to postural perturbation







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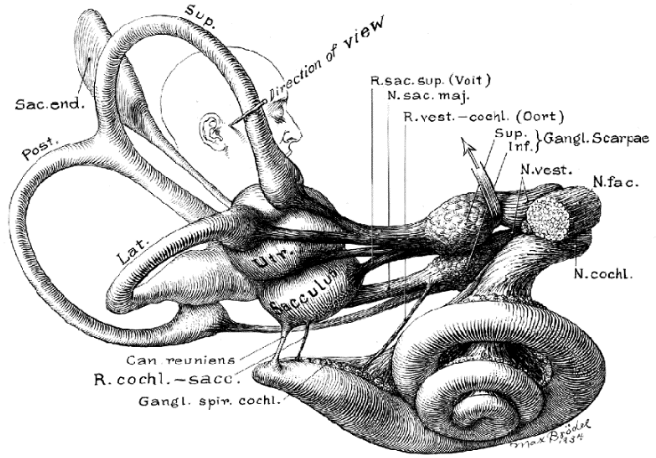
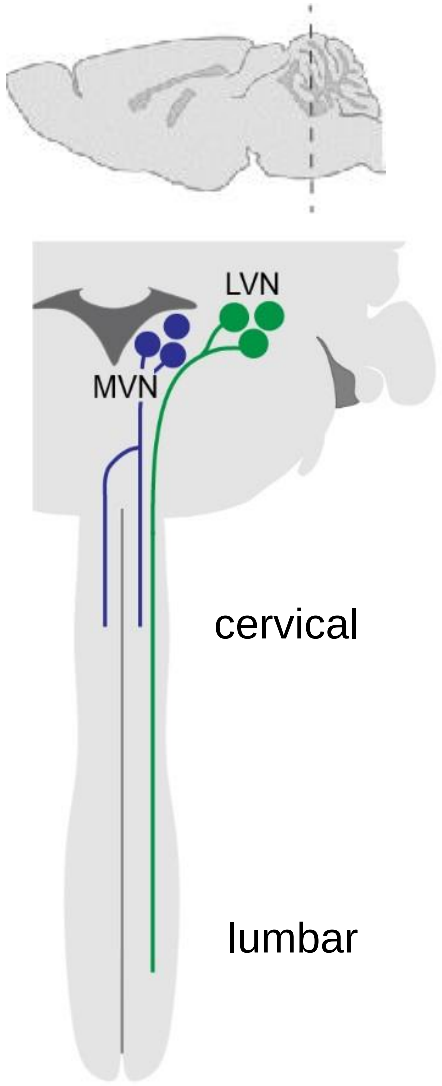
Stapley and Drew, 2009

Vestibulospinal tracts

Maintain balance and posture using rotation and acceleration of the head





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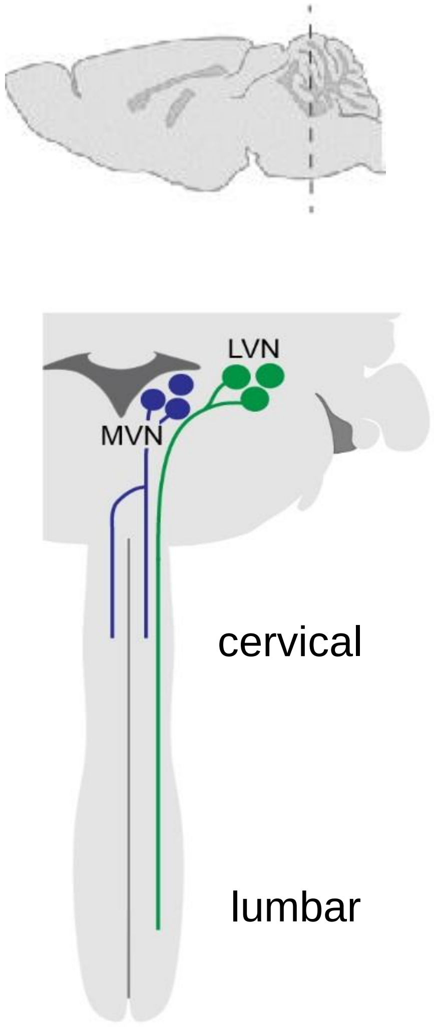
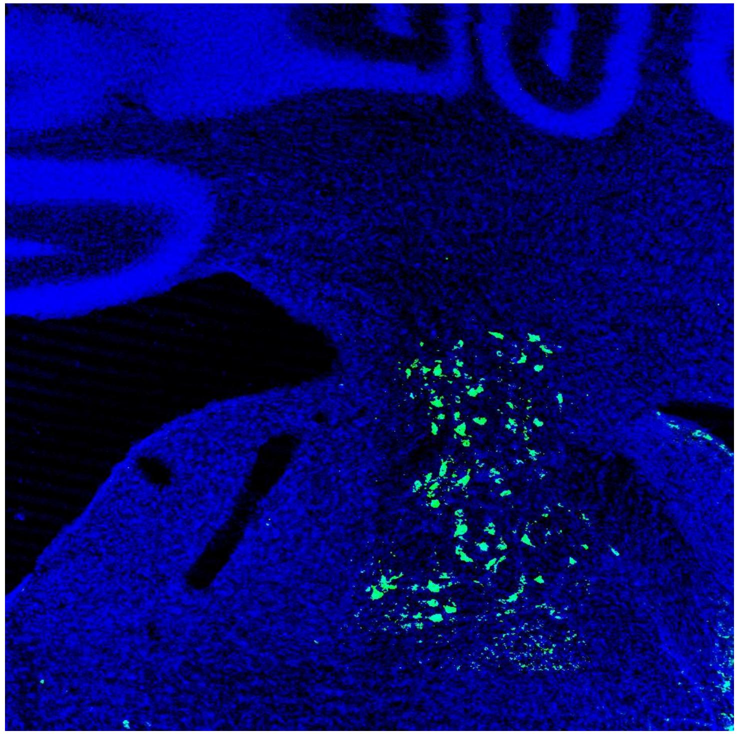
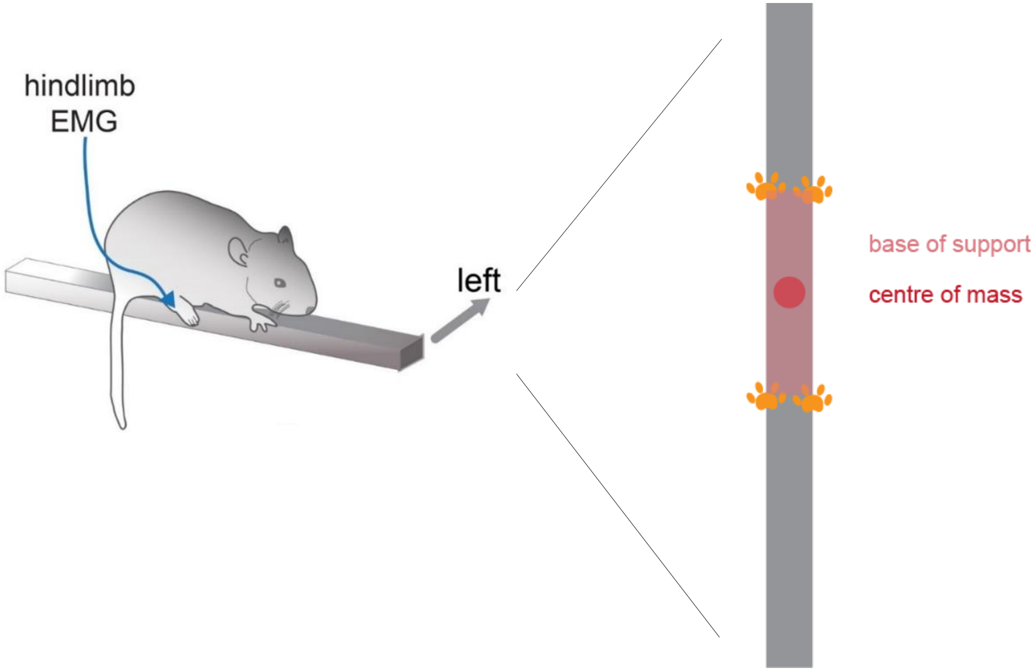
The lateral vestibular nucleus projects to all spinal levels



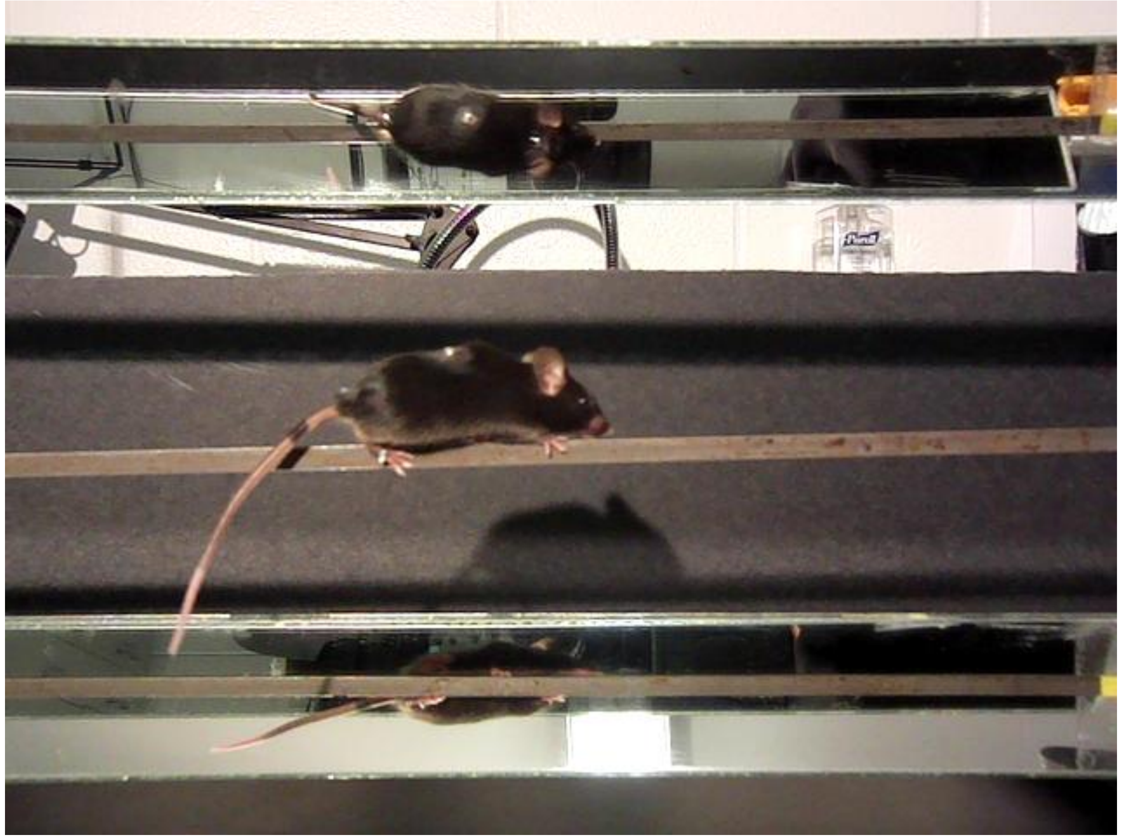
Fluorogold (lumbar SC) Nissl



Assaying balance in the mouse



Assaying balance in the mouse



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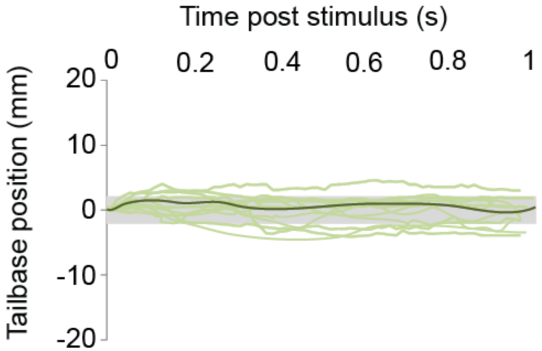
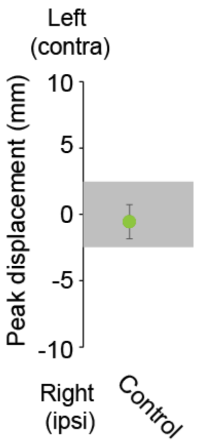
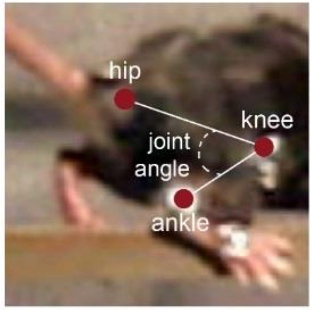
Mice can efficiently compensate for balance perturbations

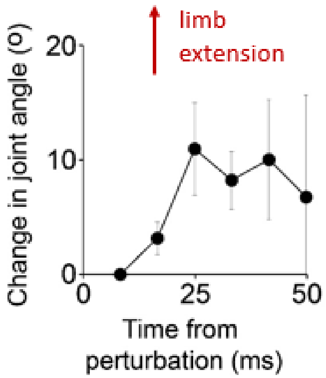
Top view

Tail base marker

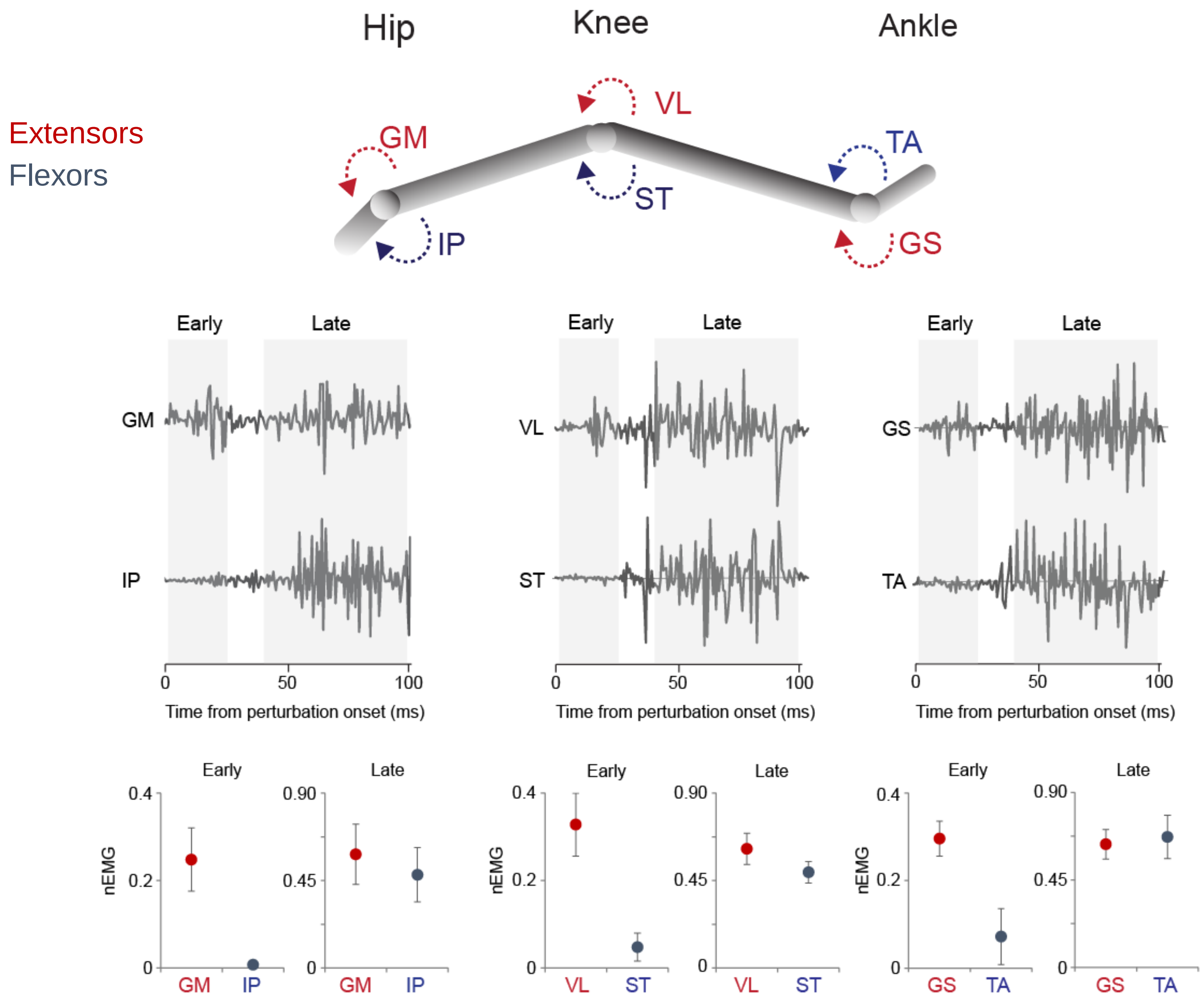








Responses to a balance perturbation have two phases



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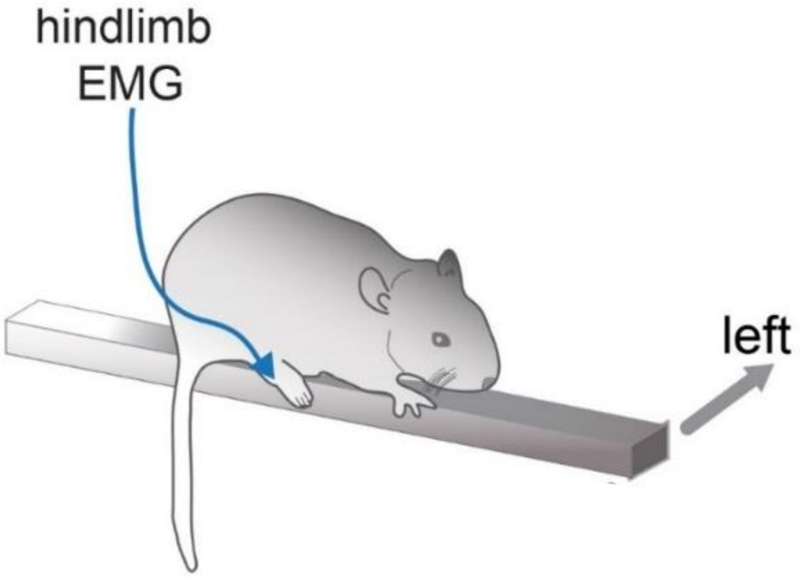
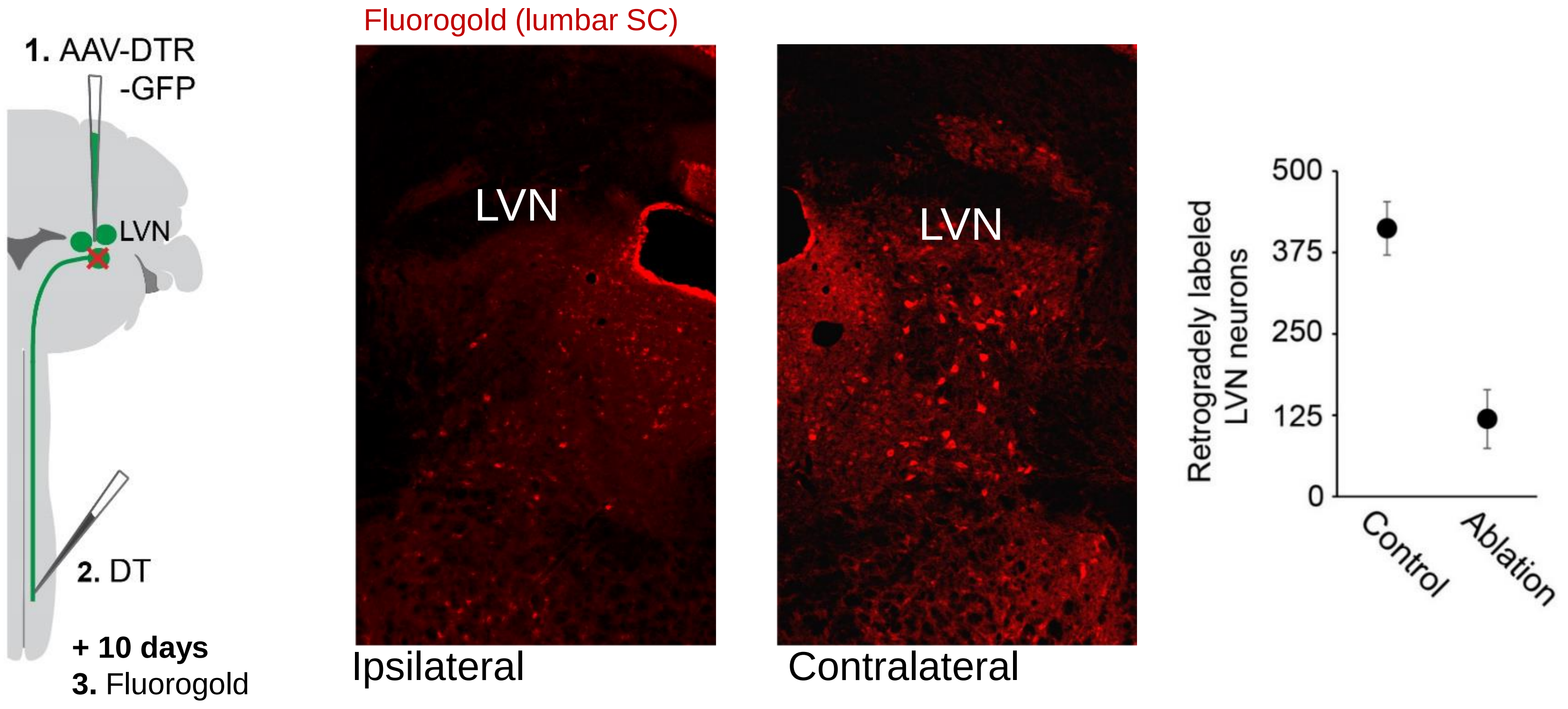
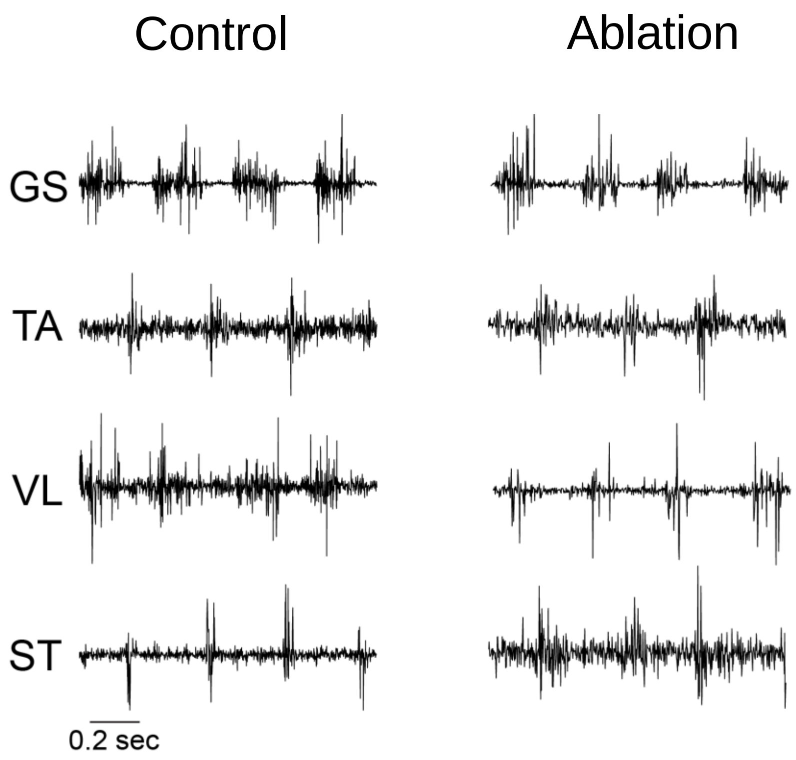
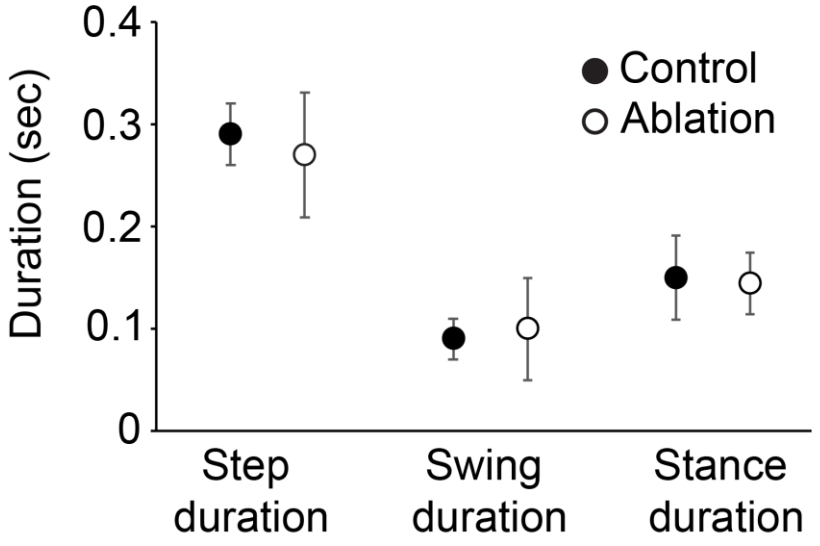

hindlimb
EMG
left

Selective ablation of LVN_{lumbar} neurons



Vestibulospinal neurons are not required for treadmill locomotion





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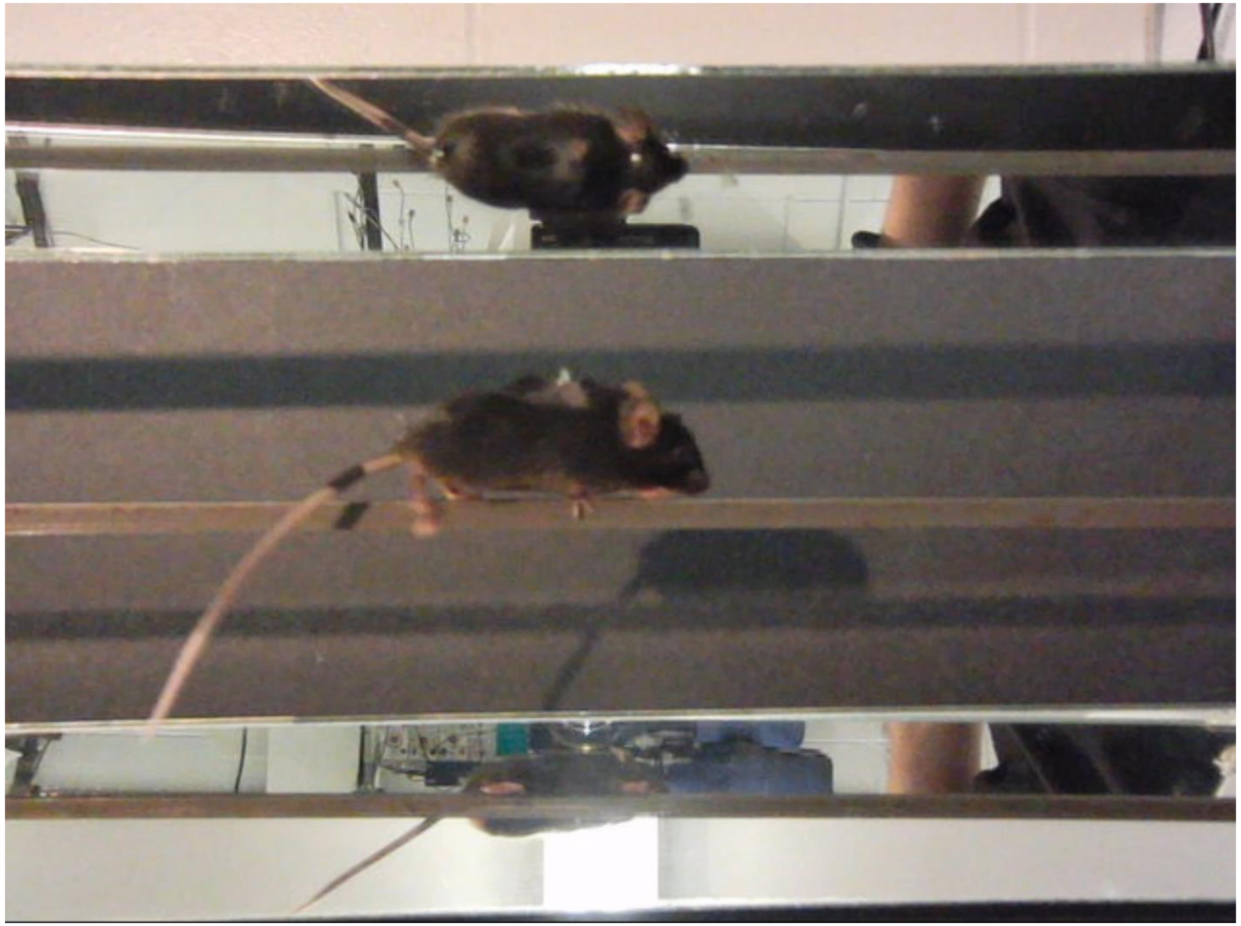
LVN_{lumbar} ablation causes poor reflexive balance control



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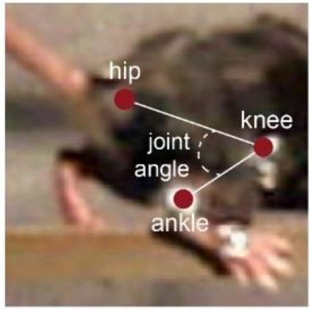
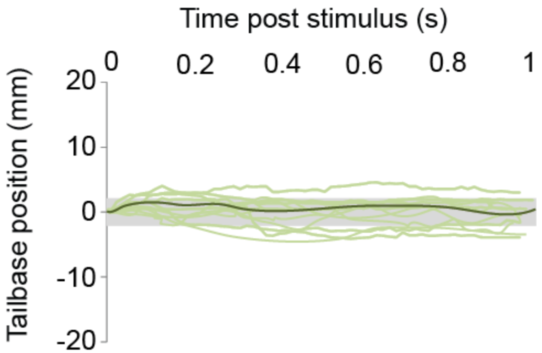
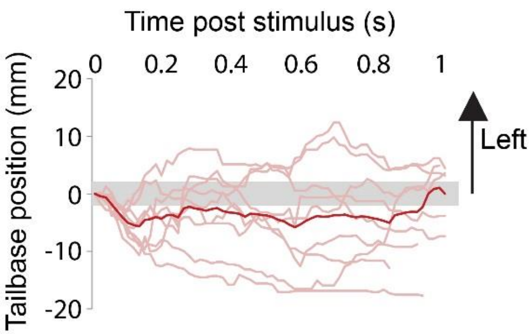
LVN$_{lumbar}$ ablation causes poor reflexive balance control

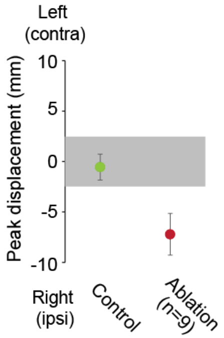
Top view

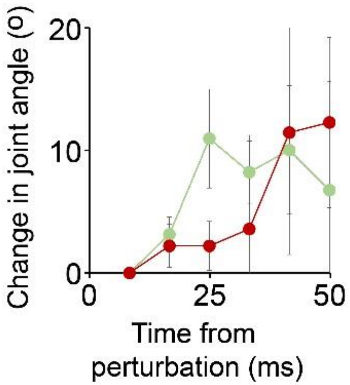


LVN^{lumbar} ablation (right)









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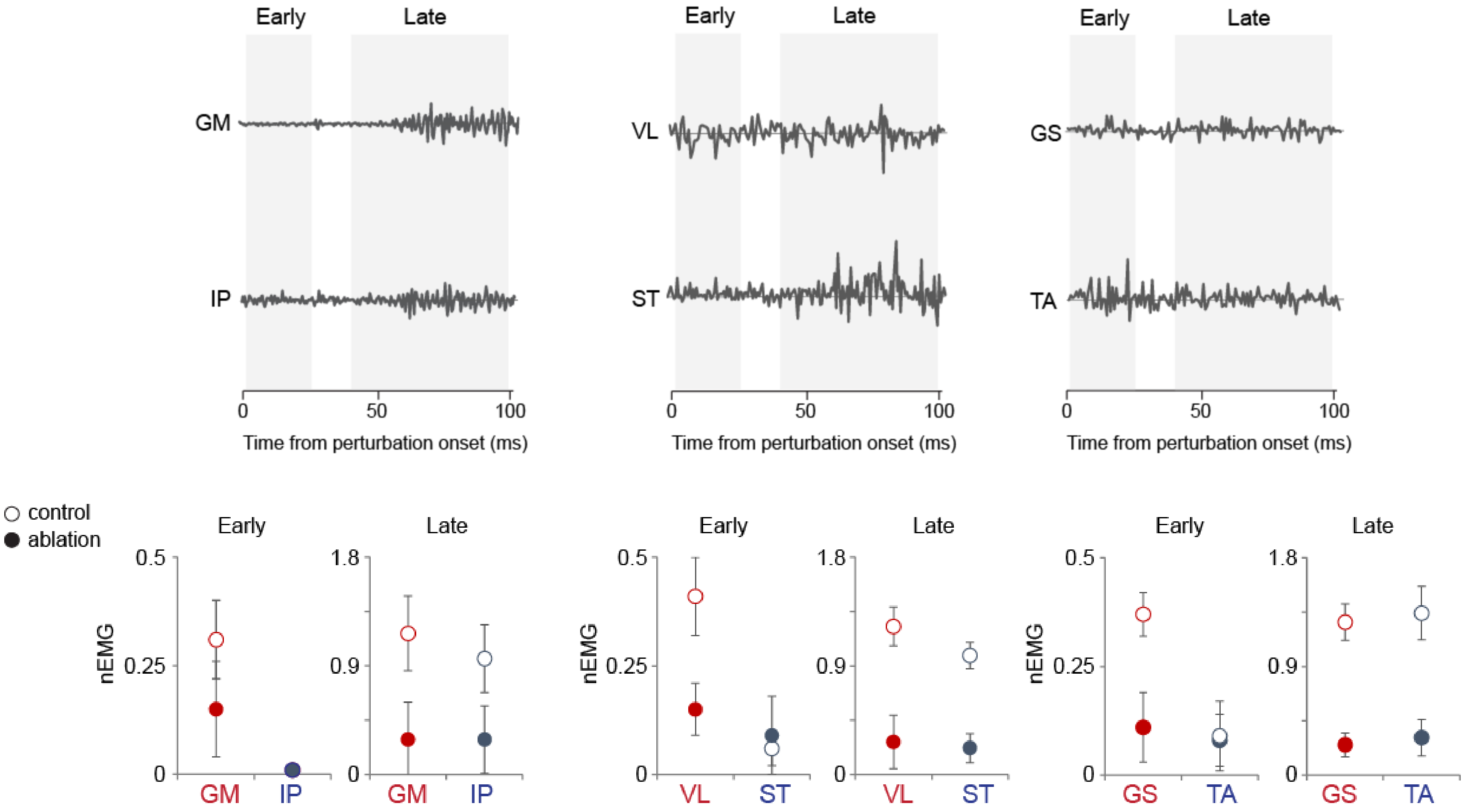
LVN_{lumbar} ablation abolishes both early and late phase responses



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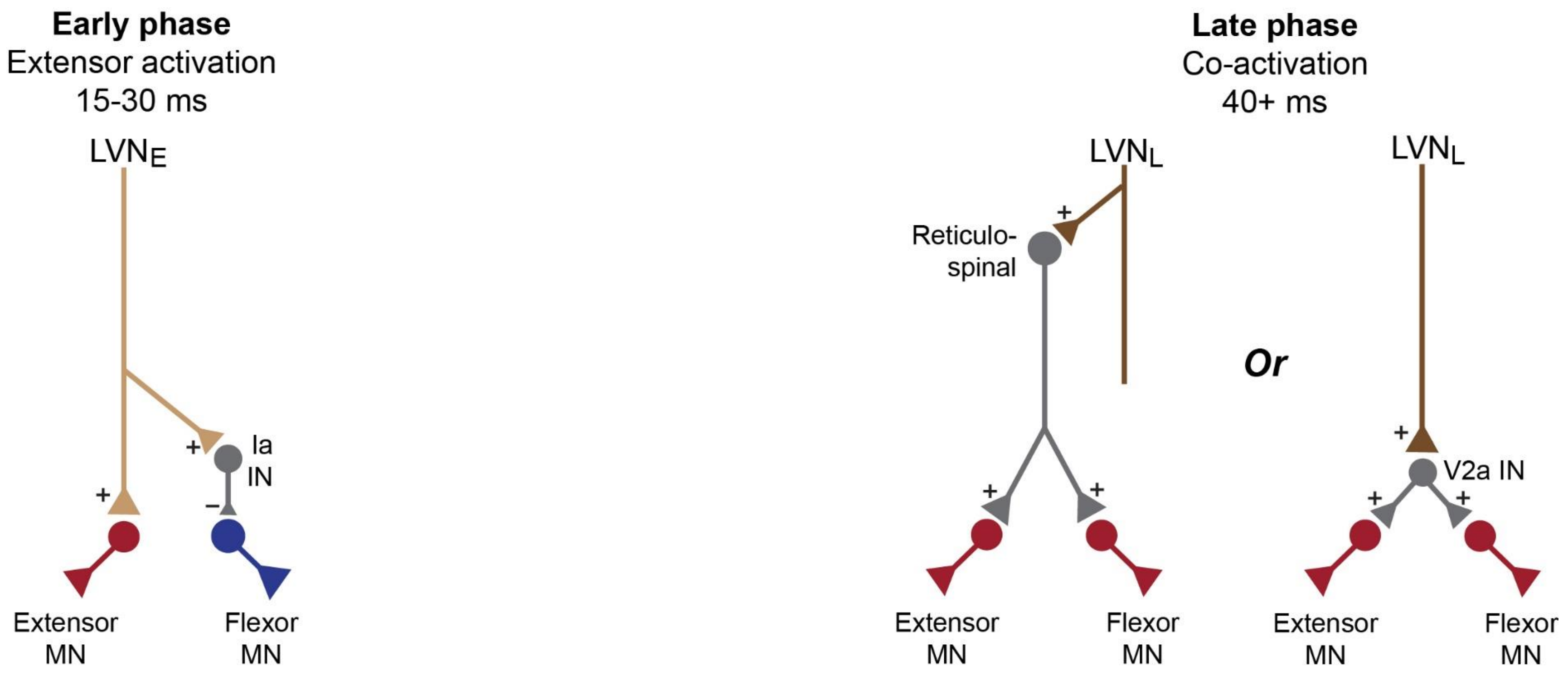
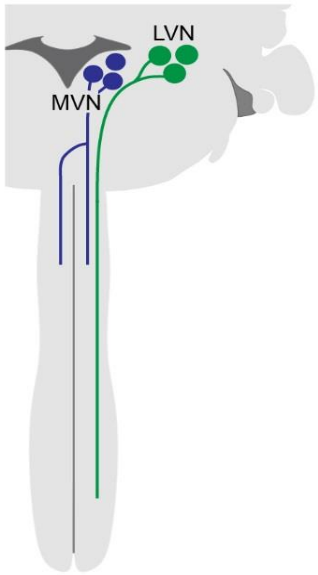
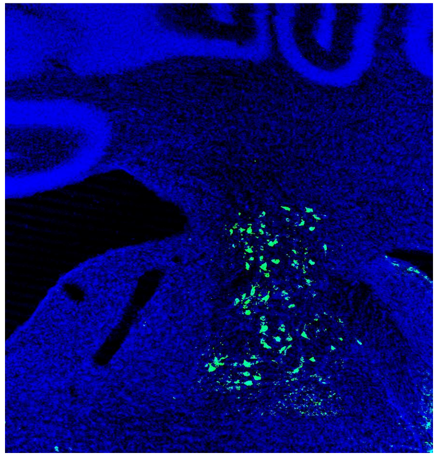
Possible circuits originating in the LVN



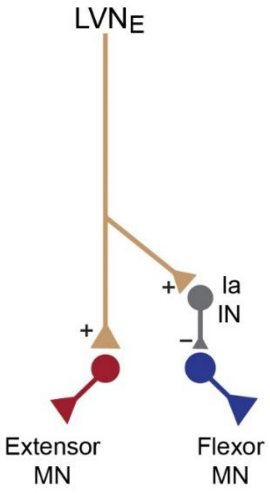
Defining LVN cell-types

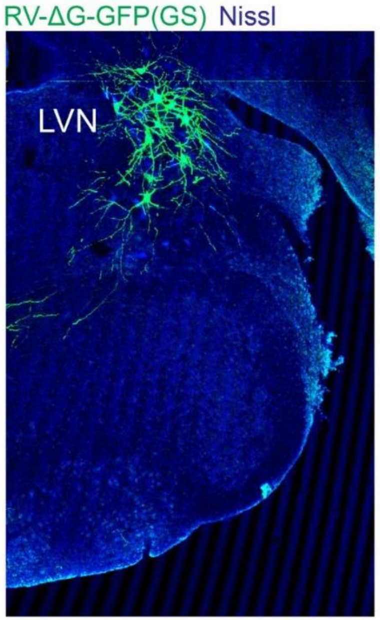
LVN_{lumbar} = all LVN neurons projecting to lumbar spinal cord



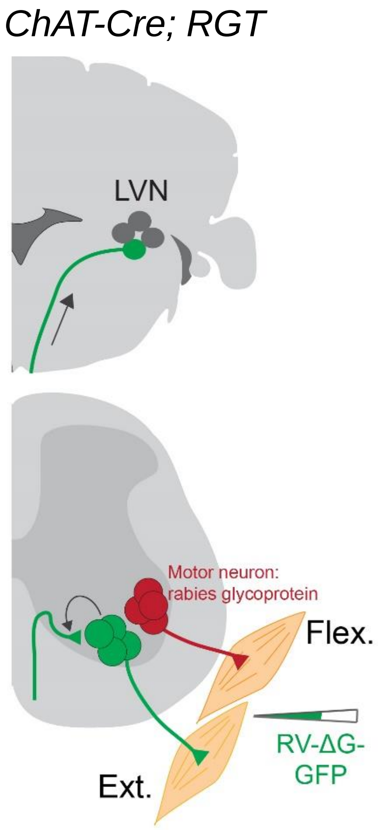


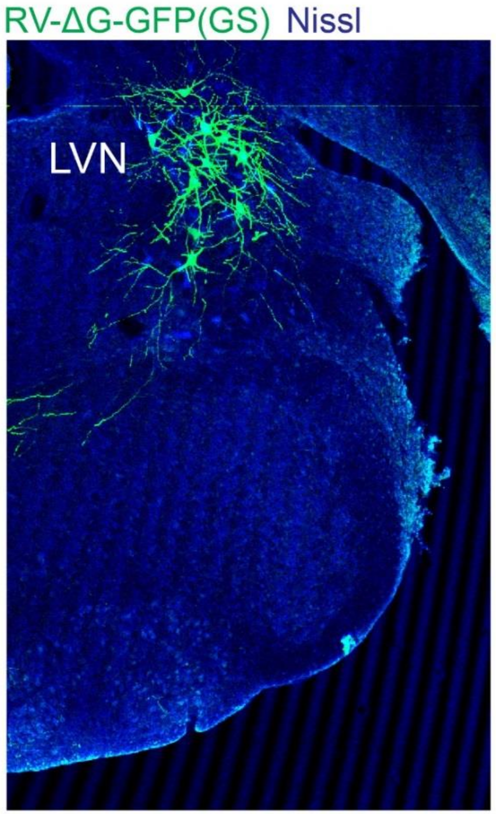
LVN_E = LVN neurons innervating MNs

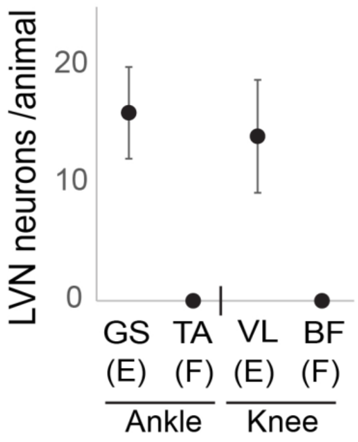




LVN inputs are restricted to extensor motor neurons

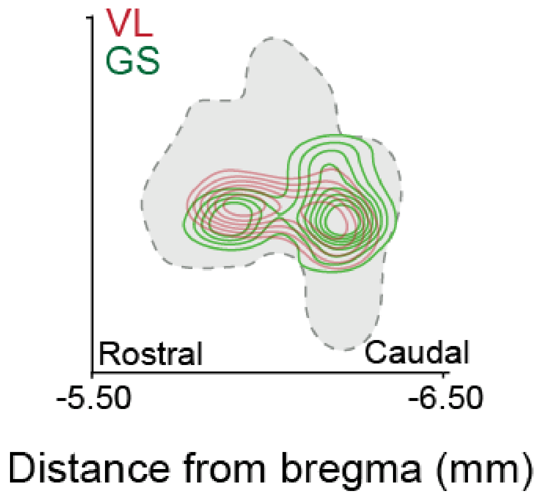




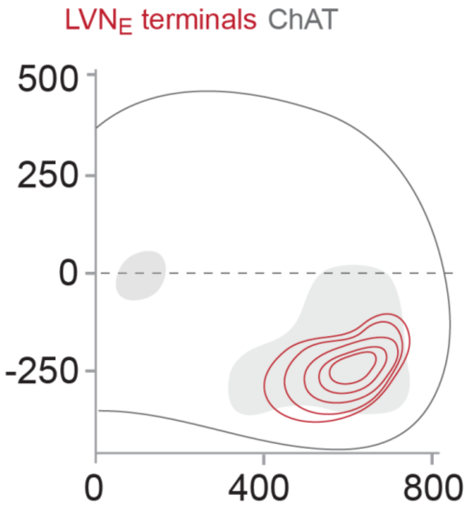


Positional analysis of LVN_E neurons shows restricted cell body position and terminal projections

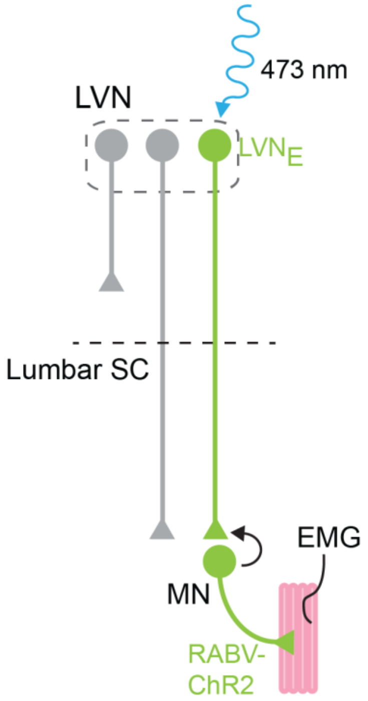
LVN_E neuron – in LVN

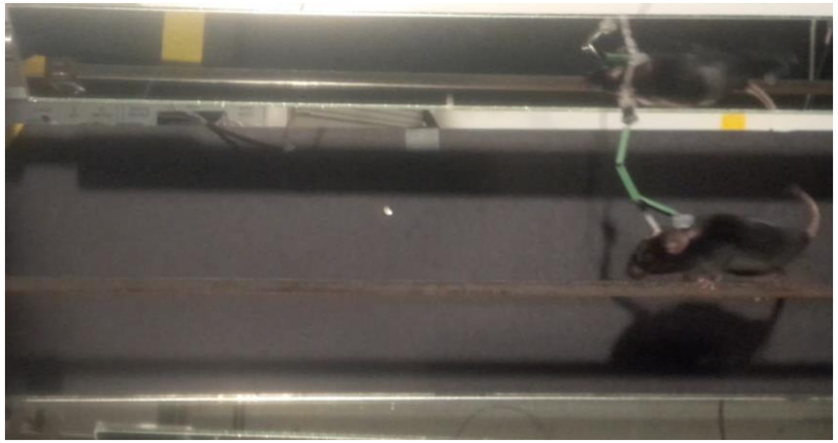


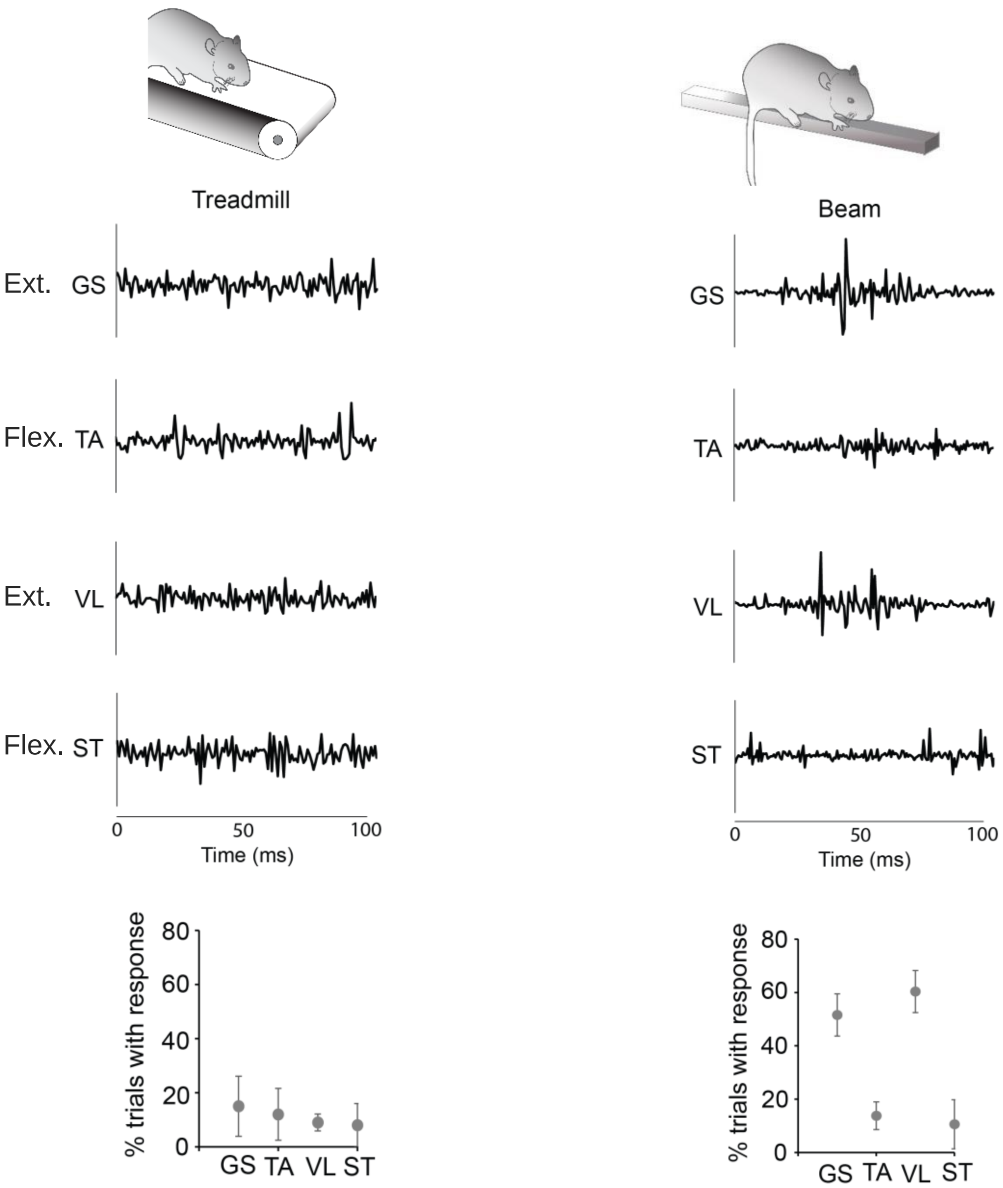
LVN_E terminals in the spinal cord



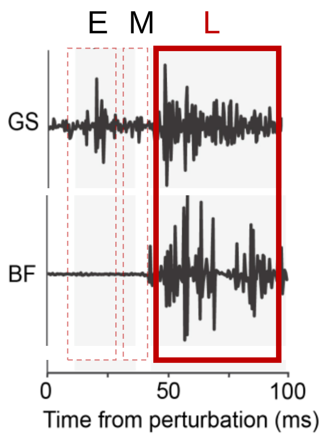
Activation of postural responses is context dependent

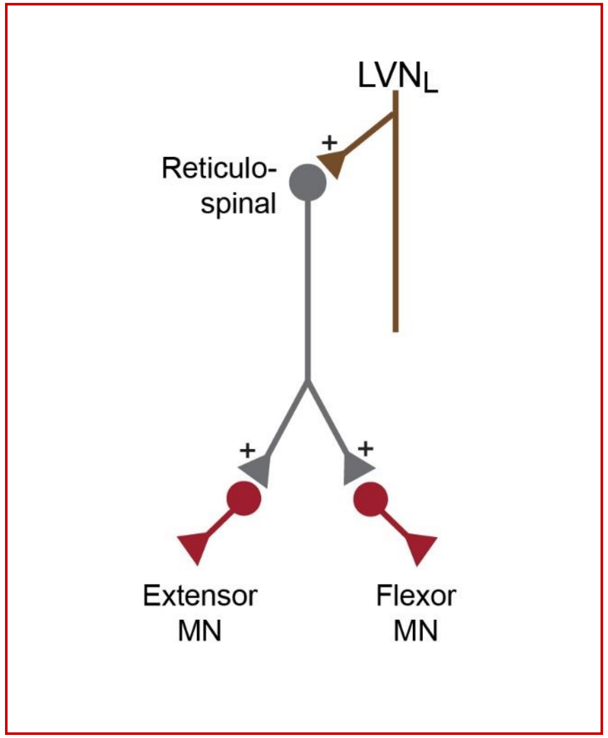




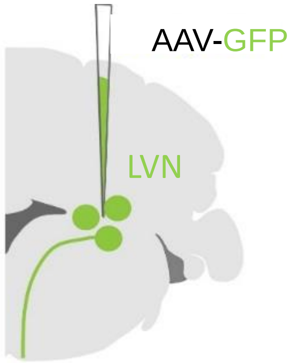


A vestibulospinal-reticulospinal circuit for long-latency postural responses

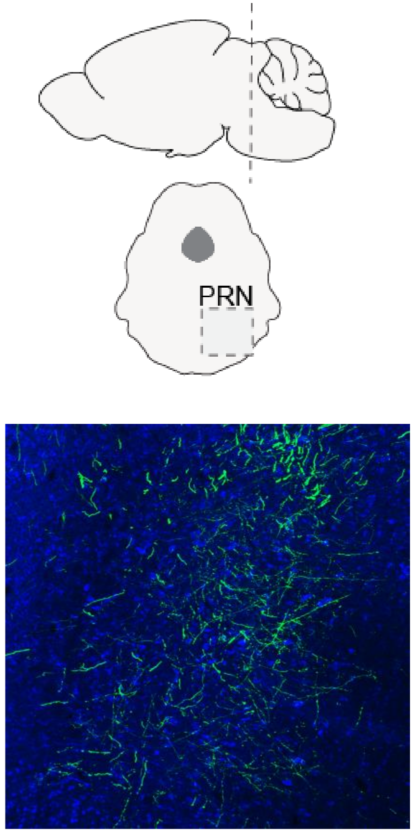




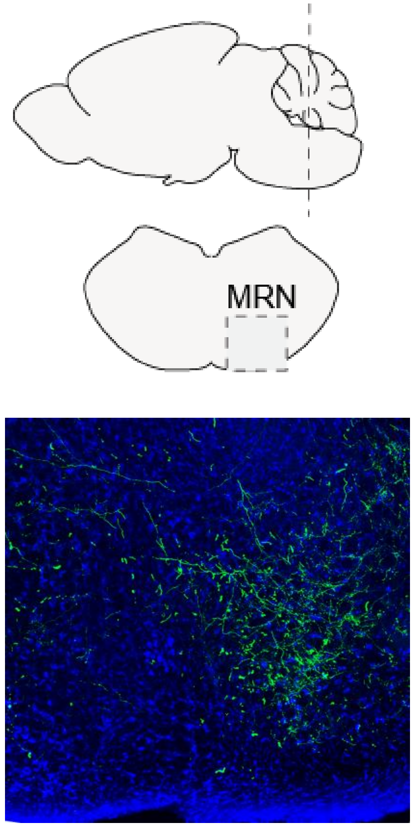
The LVN innervates both the MRN and PRN



Pontine reticular nucleus



Medullary reticular nucleus



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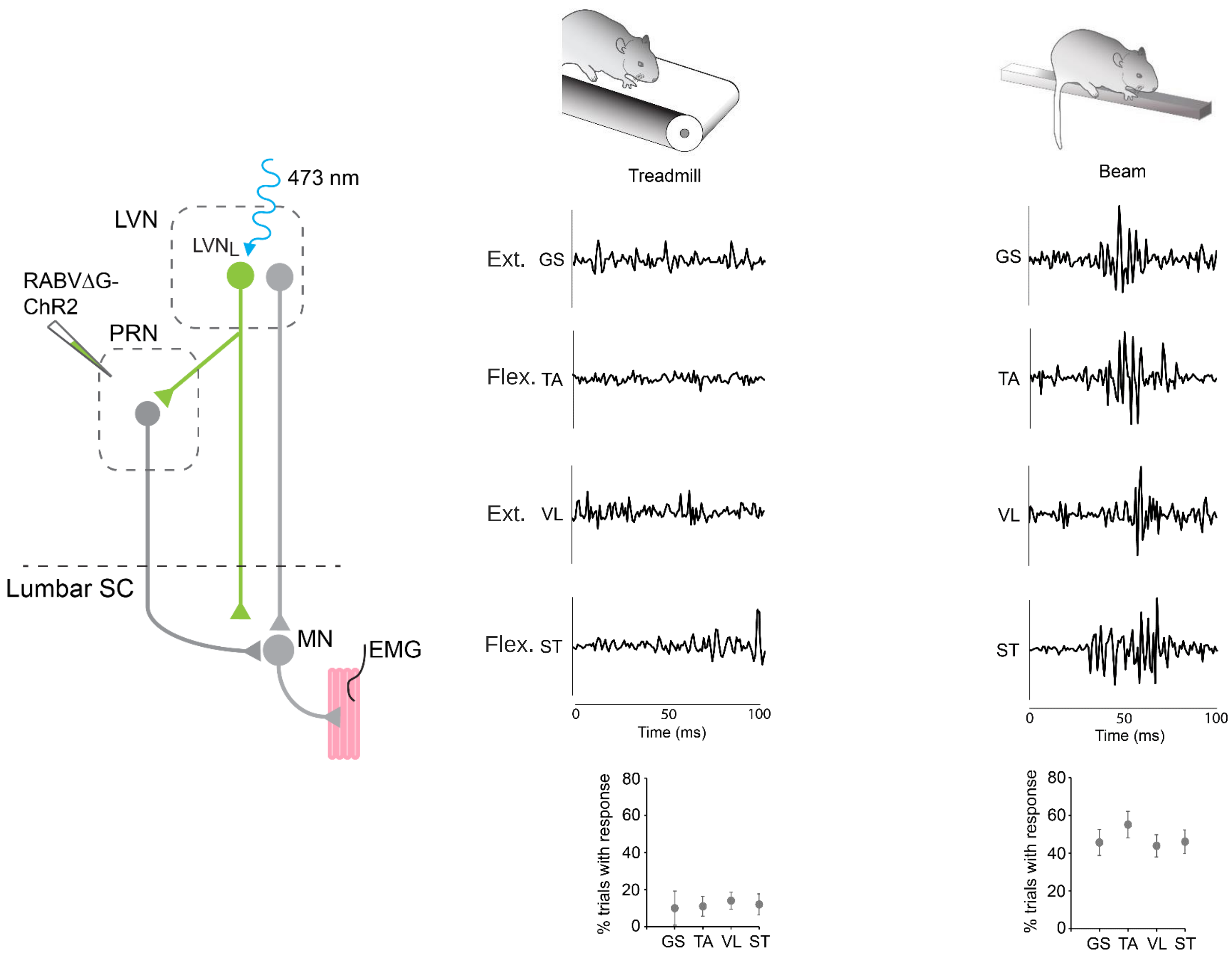
Photostimulation of LVN-PRN neurons activates hindlimb muscles



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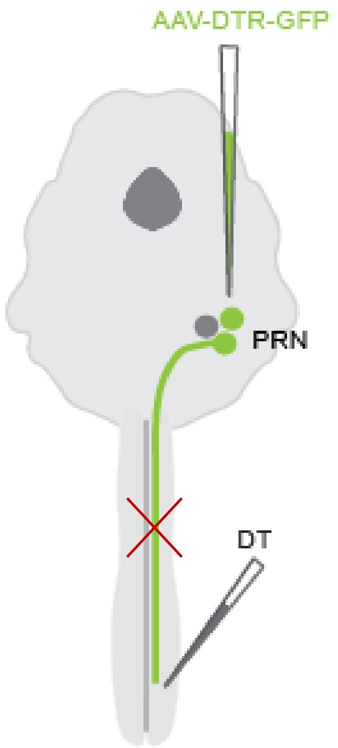
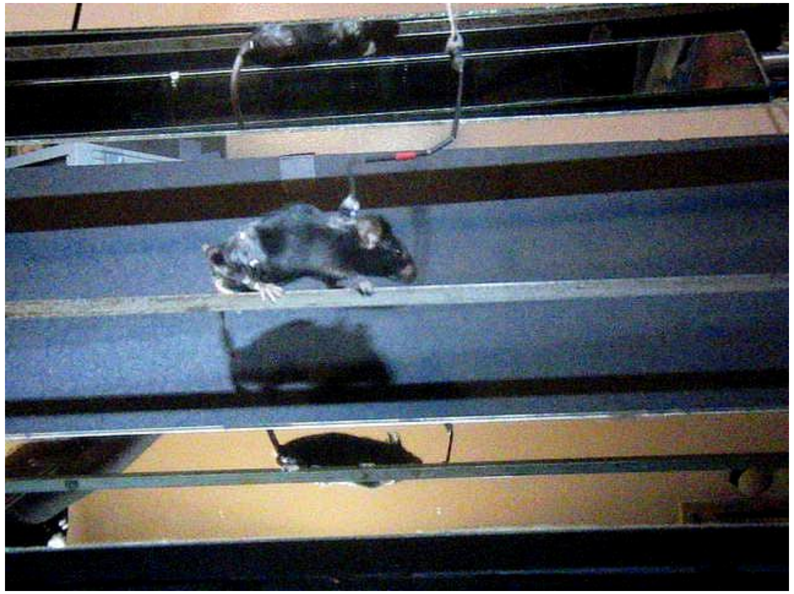
Reticulospinal neurons are also required for postural reflexes

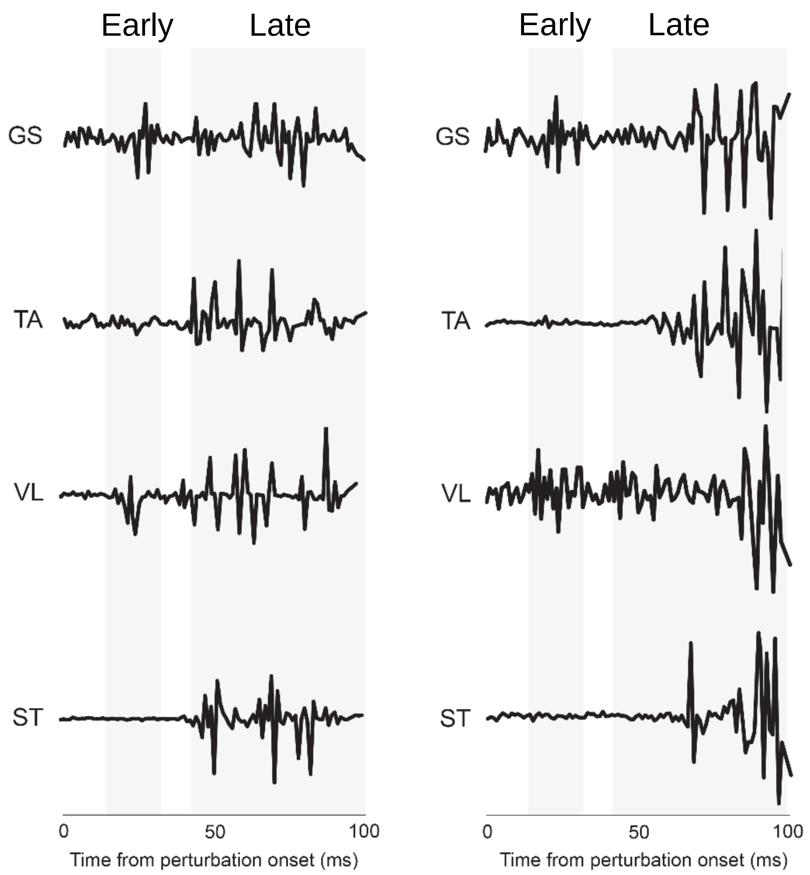


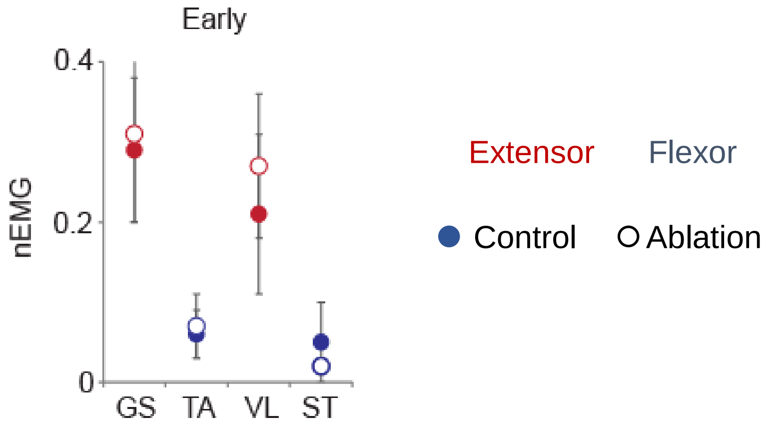


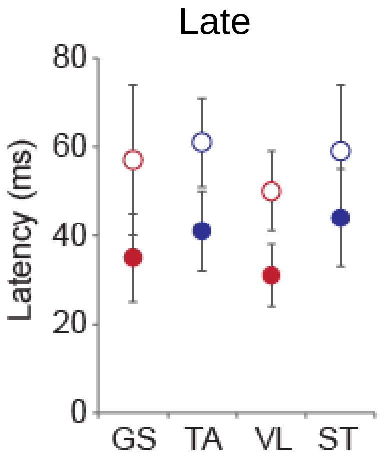
Control

PRN-spinal ablation

Reticulospinal neurons generate a different phase of postural responses to vestibulospinal







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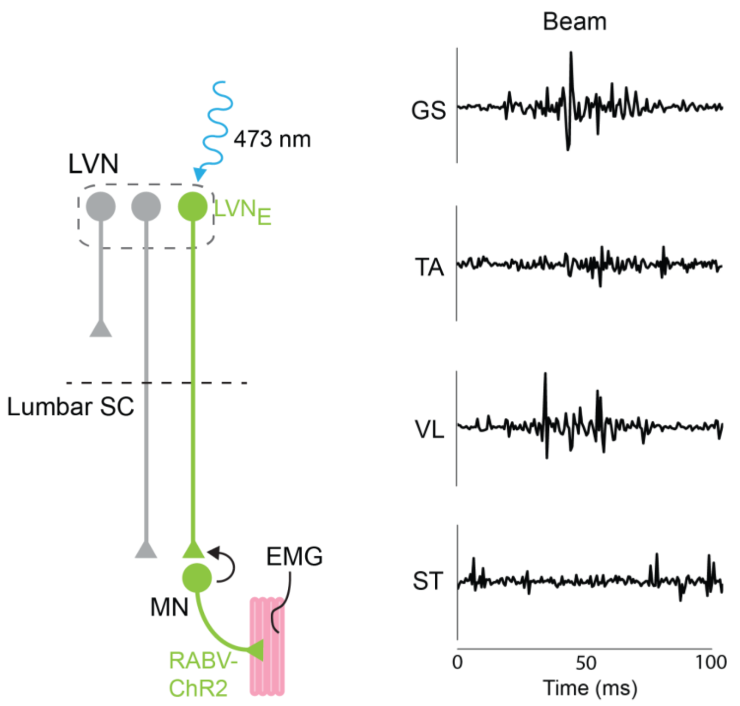
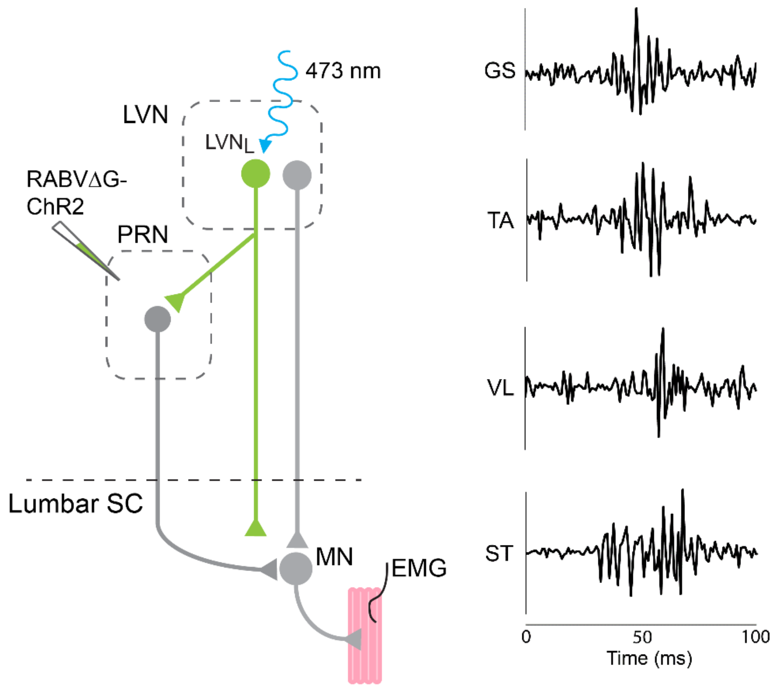
A postural response involves different brain areas, inputs and descending pathways

Acceleration?



Computation?



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