The neural circuits for motor control

Dancing scene from mastaba of mereruka

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SWC Room 284
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
Simple motor control is based on rhythmic movements

Extensor

Flexor
The locomotor step cycle

Four phases of the step cycle:

- Swing
- Stance

Joint angle (degrees):

- Hip
- Knee
- Ankle

Time (0.1 s)
The locomotor step cycle

How many muscles are there in one mouse hindlimb?
Muscles and motor units
Motor neurons are organised in “pools”

Romanes, 1951

Surmeli et al., 2011
Motor neurons drive muscle contraction

Alynick et al., 2015
Monitoring limb position via proprioception
Muscle activation and proprioception
Sensory pathways could drive rhythmic firing in the spinal cord
The spinal cord can generate rhythmic firing of motor neurons

Machado et al., 2015
Locomotion is based on rhythmic movements generated in the spinal cord

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 neurones, 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 "centro"; 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
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
Reciprocal inhibition
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
The unit burst generator as an alternative to the half-centre model
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

Sainsbury Wellcome Centre
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
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....

<table>
<thead>
<tr>
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<th>“classical”</th>
<th>“modulatory”</th>
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Adaptive motor control

a snapshot of 27 descending tracts....

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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.
Postural control is an active process that requires descending commands.

Macpherson and Fung, 1999
Postural control is an active process that requires descending commands.
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
Reticulospinal pathways

Origin in the PRN and MRN, and project in the medial longitudinal fasciculus
Reticulospinal pathways

excite both extensors and flexor motor neurons

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

<table>
<thead>
<tr>
<th>Monosynaptic EPSP</th>
<th>Extensors</th>
<th>Flexors</th>
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<tbody>
<tr>
<td></td>
<td>GS</td>
<td>FDL-PL</td>
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<tr>
<td>Deiters' only</td>
<td>14/38</td>
<td>1/25</td>
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<tr>
<td>MLF-RF only</td>
<td>10/38</td>
<td>16/25</td>
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Reticulospinal pathways have diffuse projections into the spinal cord

Liang et al., 2015
Reticulospinal pathways

A subset of reticulospinal neurons respond to postural perturbation
Vestibulospinal tracts

Maintain balance and posture using rotation and acceleration of the head
The lateral vestibular nucleus projects to all spinal levels
Assaying balance in the mouse
Assaying balance in the mouse
Mice can efficiently compensate for balance perturbations
Responses to a balance perturbation have two phases

Extensors
Flexors
Selective ablation of LVN\textsubscript{lumbar} neurons

1. AAV-DTR -GFP
2. DT
3. Fluorogold + 10 days

Fluorogold (lumbar SC)
LVN
Ipsilateral

LVN
Contralateral

Retrogradely labeled LVN neurons

Control
Ablation
Vestibulospinal neurons are not required for treadmill locomotion.

Control

Ablation

GS

TA

VL

ST

0.2 sec

Duration (sec)

Step duration
Swing duration
Stance duration

Control
Ablation
LVN_{lumbar} ablation causes poor reflexive balance control
LVN\textsubscript{lumbar} ablation causes poor reflexive balance control.
LVN_{lumbar} ablation abolishes both early and late phase responses
Possible circuits originating in the LVN

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**Early phase**
Extensor activation
15-30 ms

- LVN_E
  - Extensor MN
  - Flexor MN
  - Ia IN

**Late phase**
Co-activation
40+ ms

- LVN_L
  - Reticulo-spinal
  - Or
  - V2a IN

Sainsbury Wellcome Centre
Defining LVN cell-types

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

LVN_{E} = LVN neurons innervating MNs
LVN inputs are restricted to extensor motor neurons

ChAT-Cre; RGT

RV-ΔG-GFP(GS) Nissl

LVN neurons/animal

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<th>BF</th>
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Ankle Knee
Positional analysis of LVN_E neurons shows restricted cell body position and terminal projections.

LVN_E neuron – in LVN

Distance from bregma (mm)

LVN_E terminals in the spinal cord

LVN_E terminals ChAT
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

AAV-GFP
Photostimulation of LVN-PRN neurons activates hindlimb muscles.
Reticulospinal neurons are also required for postural reflexes

Control

PRN-spinal ablation
Reticulospinal neurons generate a different phase of postural responses to vestibulospinal

Early

Late

Extensor

Flexor

Control

Ablation

Late

Latency (ms)

0 20 40 60 80

GS TA VL ST
A postural response involves different brain areas, inputs and descending pathways.

**Acceleration?**

- Beam: GS, TA, VL, ST

**Computation?**

- Lumbar SC: MN, LVN, LVE, RABV-ChR2

- Lumbar SC: MN, LVN, RABV-ChR2, PRN

Time (ms): 0 - 100