Distortions in the synaptic organization of motor commands to proximal and distal muscles following hemiparetic stroke

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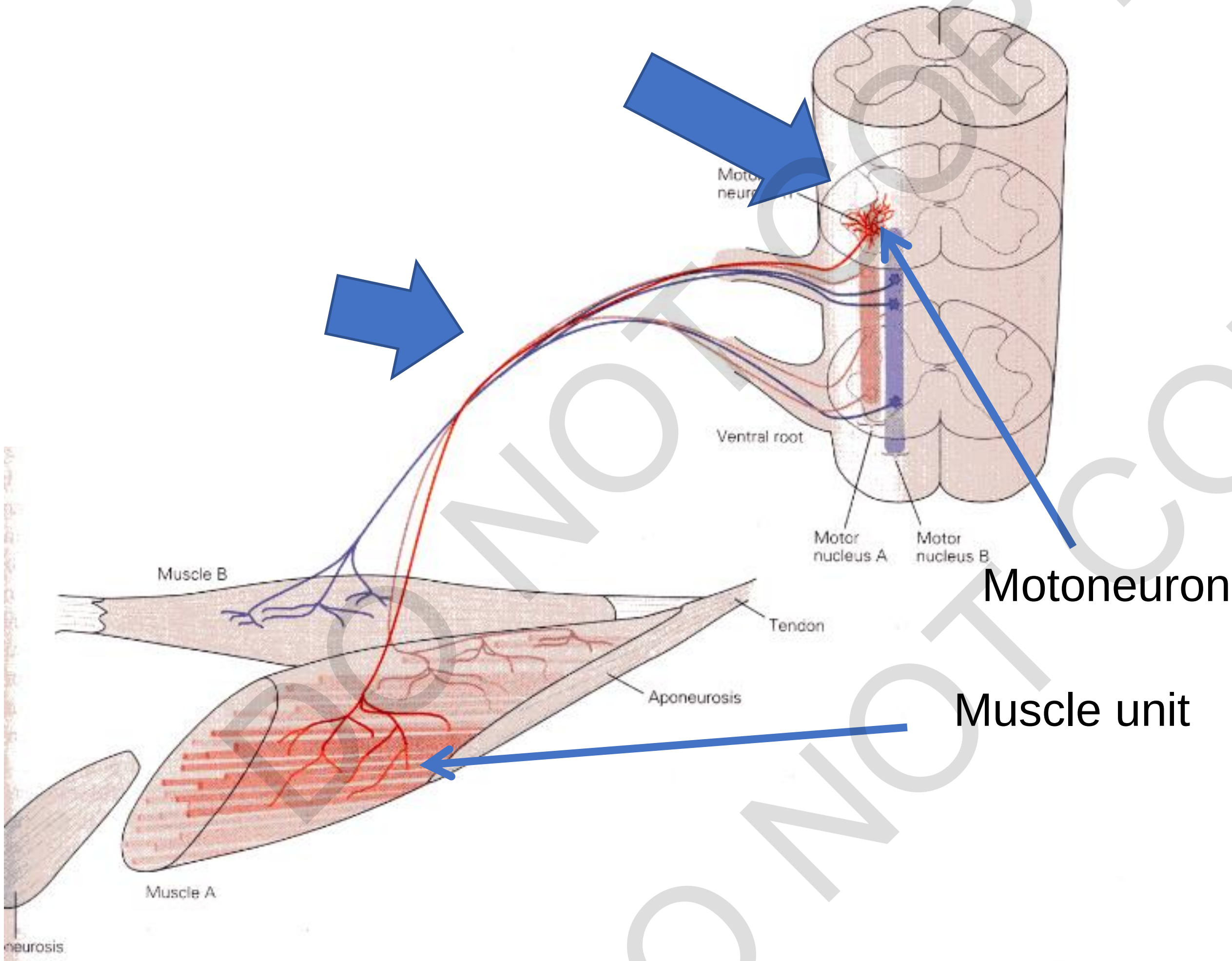

Ventral root
Motor nucleus A
Motor nucleus B
Motoneuron
Muscle B
Tendon
Aponeurosis
Muscle unit
Muscle A

Hemiparetic stroke, paradoxical effects on motor unit recruitment and rate modulation

- Compressed range of recruitment, implied motoneuron thresholds are reduced and that they are more excitable.
- Impaired rate modulation, implying motoneurons are less excitable.

- Gemperline, Allen, Walk, Rymer. Characteristics of motor unit discharge in subjects with hemiparesis. Muscle Nerve. 1995.
- Mottram, Suresh, Heckman, Gorassini, Rymer. Origins of Abnormal Excitability in Biceps Brachii Motoneurons of Spastic-Paretic Stroke Survivors. J Neurophysiol. 2009.
- Mottram, Heckman, Powers, Rymer, Suresh. Disturbances of motor unit rate modulation are prevalent in muscles of spastic-paretic stroke survivors. J Neurophysiol. 2014.

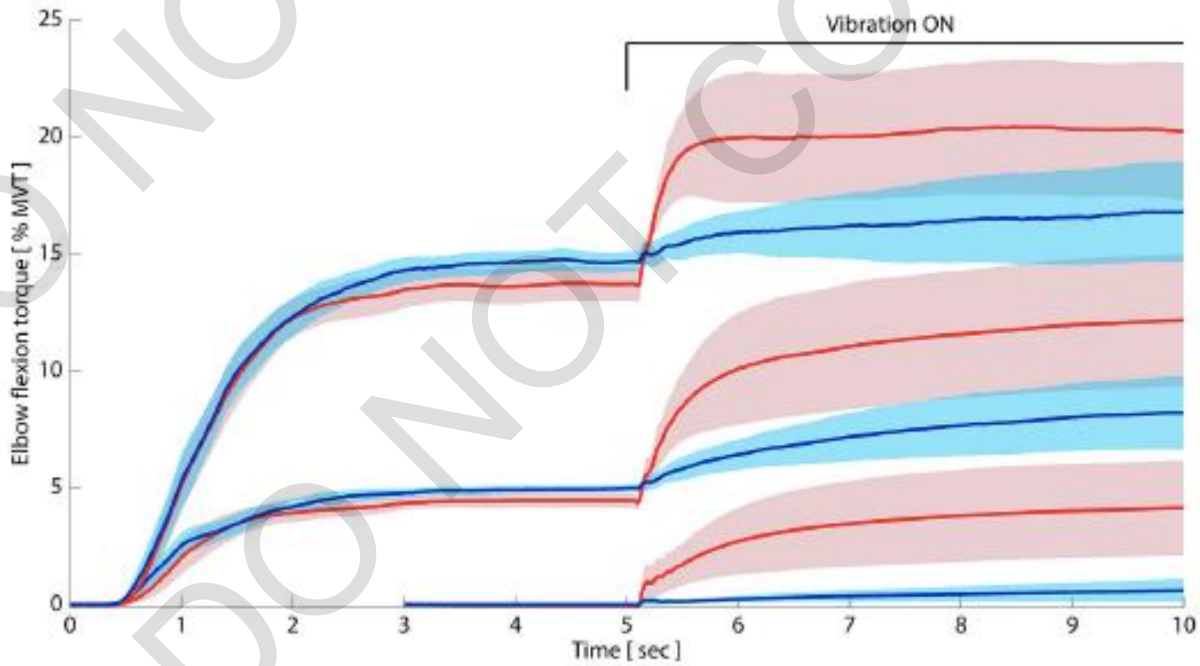
Increased drive from the brainstem as the mechanism of both + and -?

Vestibulospinal

Miller DM, Rymer WZ. Front Hum Neurosci. 2017.
Miller DM, Baker JF, Rymer WZ. Clin Neurophysiol. 2016.
Miller DM, Klein CS, Suresh NL, Rymer WZ. Clin Neurophysiol. 2014.

Reticulospinal, monoaminergic component

McPherson JG, McPherson LM, Thompson CK, Ellis MD, Heckman CJ, Dewald JPA. Front Hum Neurosci. 2018.



Holstege and Kuypers, *Neurosci*. 23: 809-21, 1987

Note bilateral effects

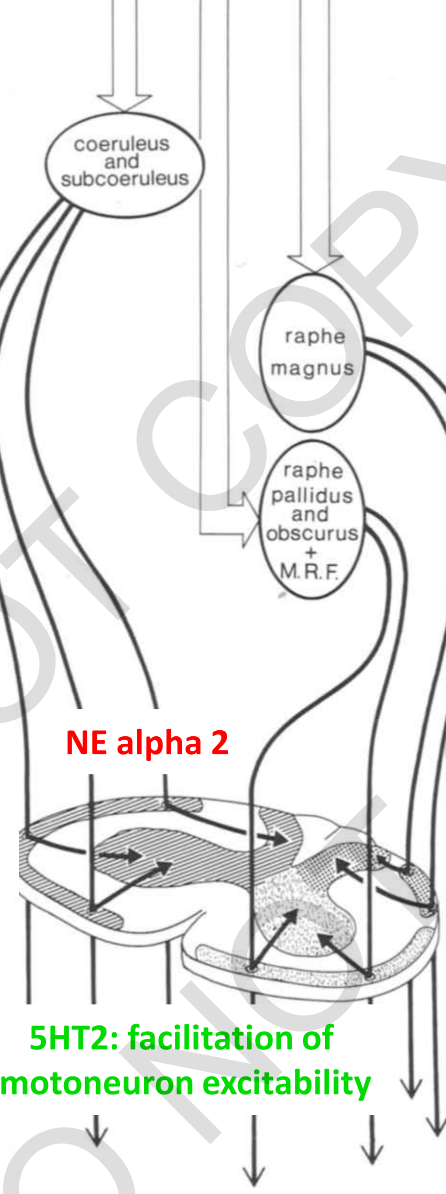
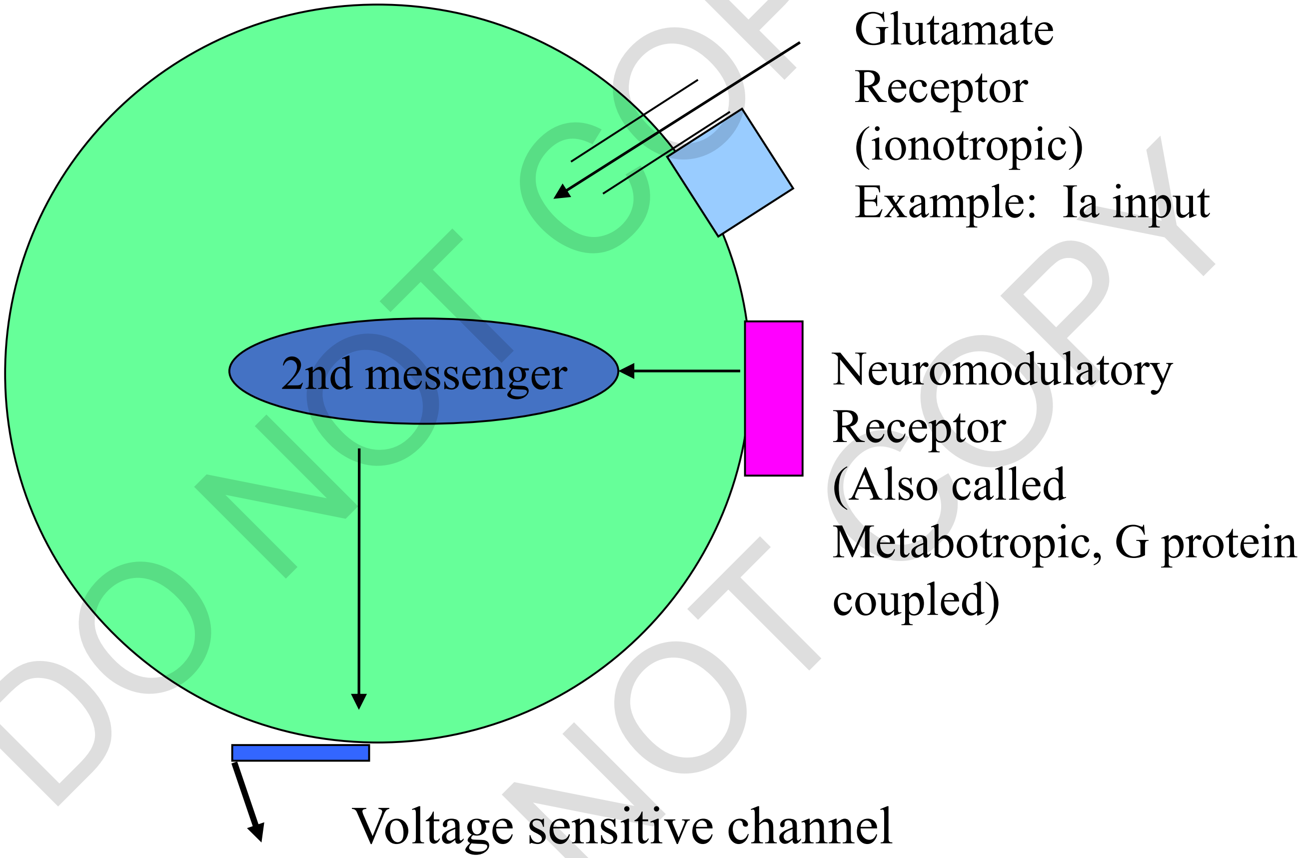
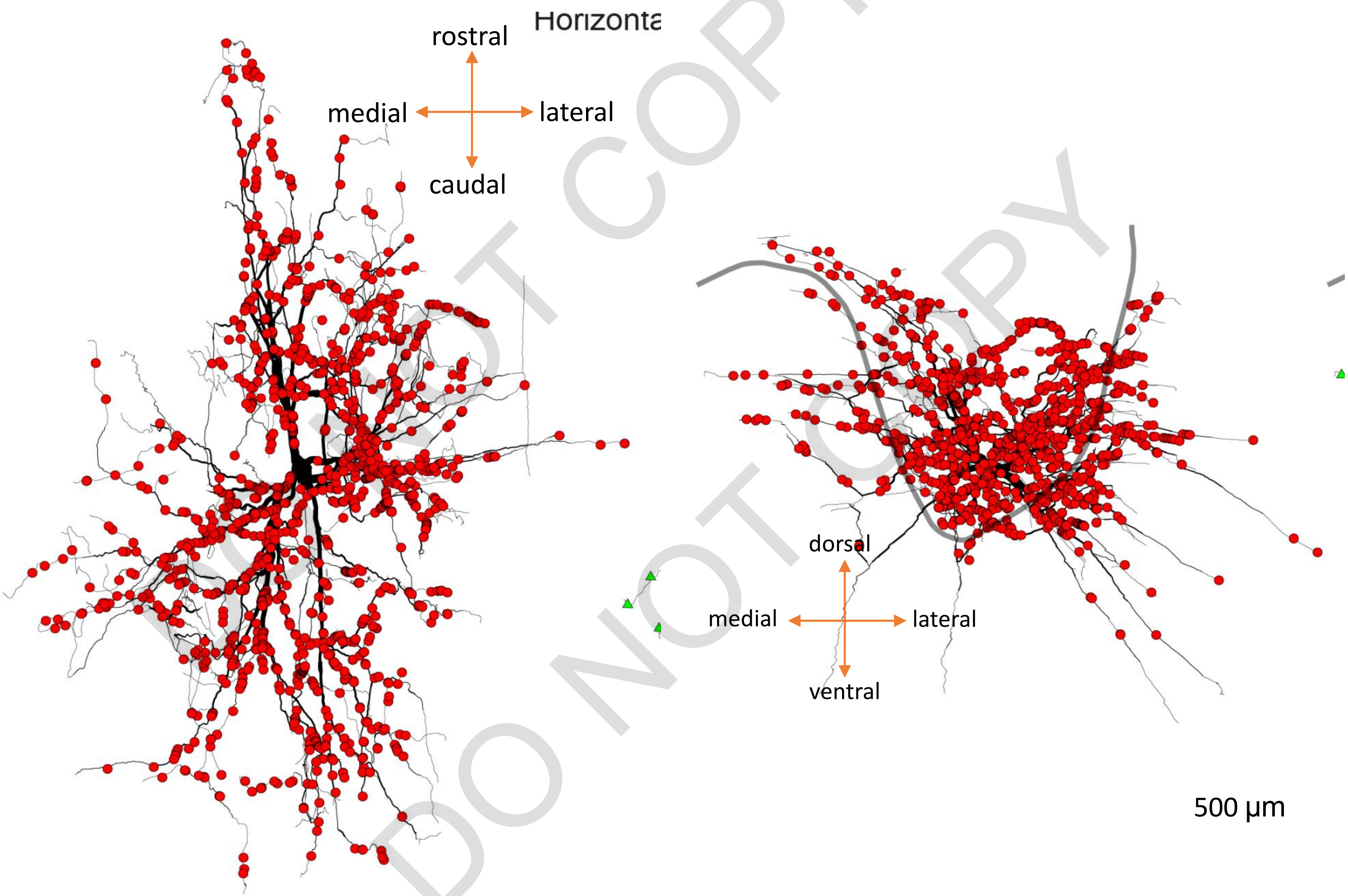


Fig. 6.

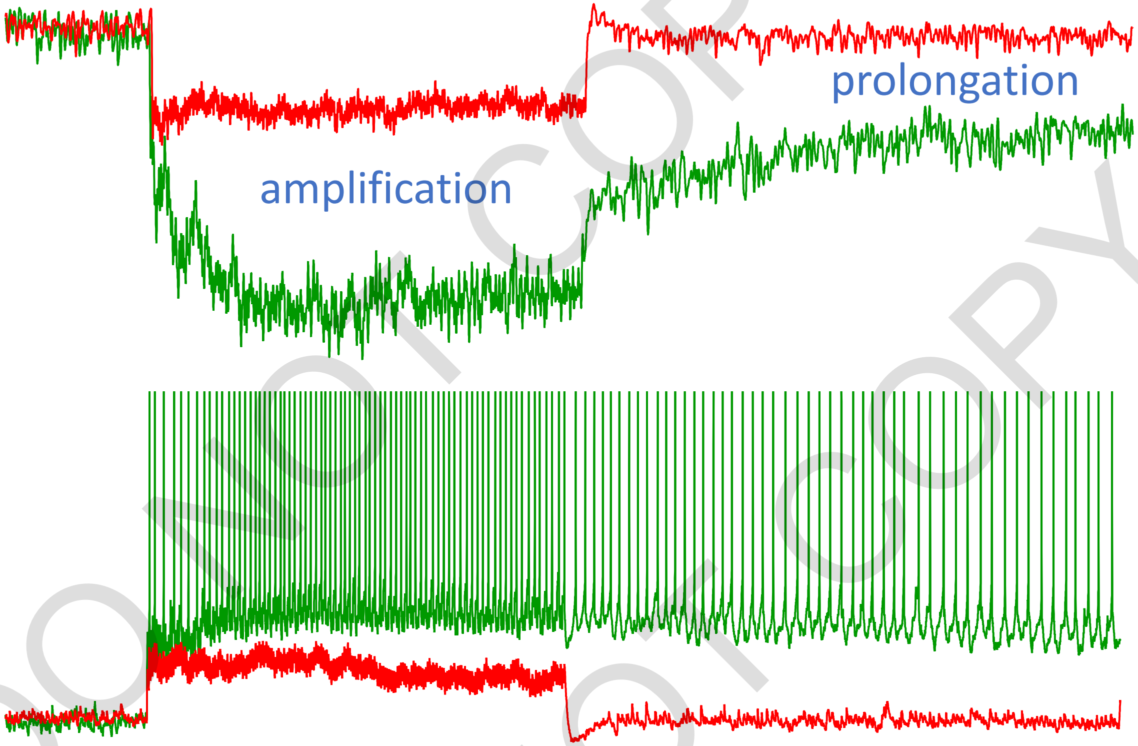
Neuromodulatory synaptic input
vs
Ionotropic synaptic input



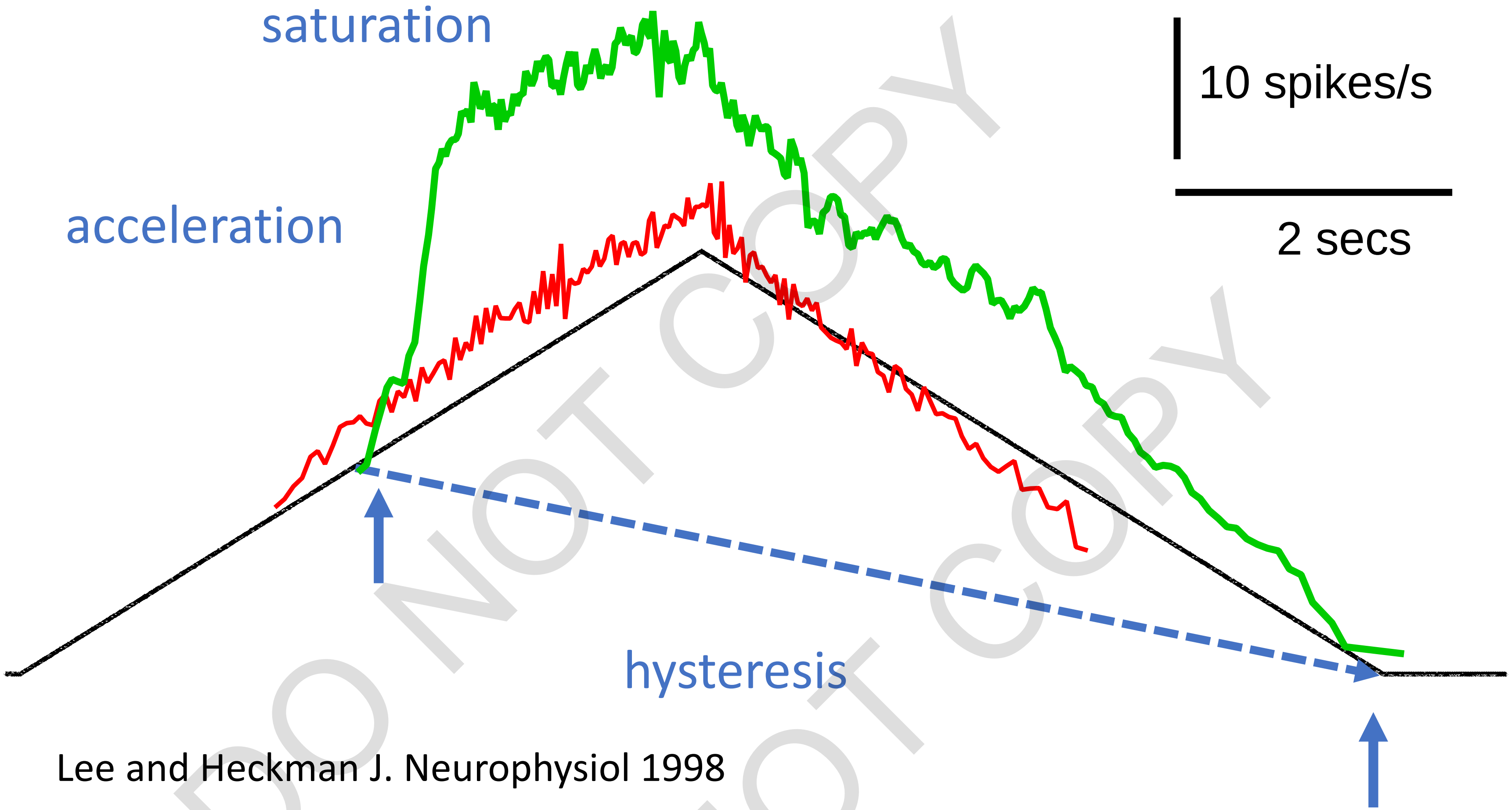
Noradrenergic synapses on a neck motoneuron, Ken Rose lab, Queens University



Effects of 5HT to facilitate motoneuron excitability: PICs



Schwindt, Crill, early 80's
Hounsgaard, Kiehn, Hultborn et al, mid to late 80's



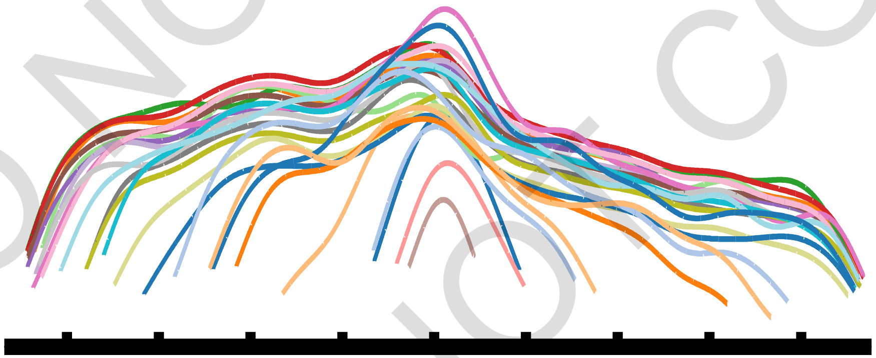
Lee and Heckman J. Neurophysiol 1998

Motor unit firing patterns consistent with strong PICs are a hallmark of normal motor output

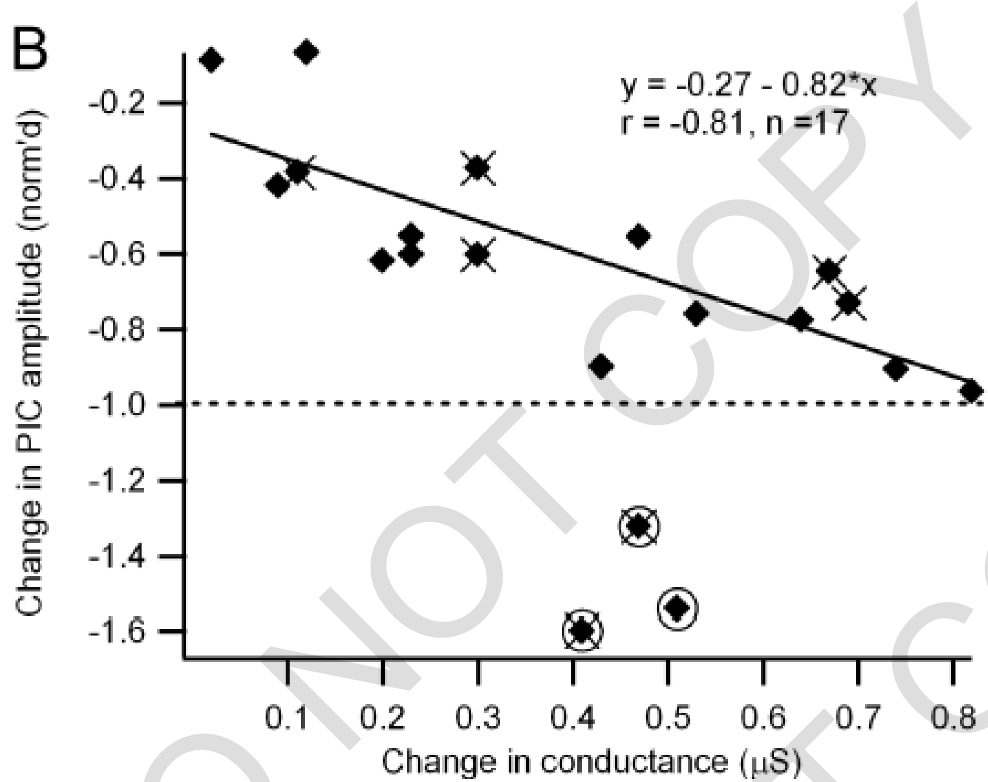
e.g. Monster and Chan 1977

DeLuca and Contessa 2012

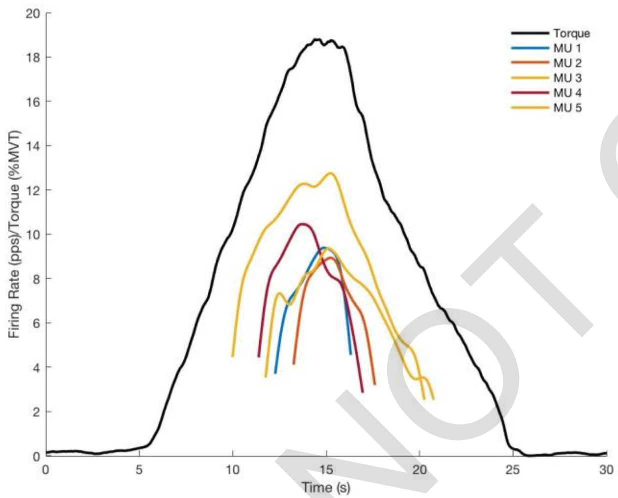
Fuglevand et al 2015

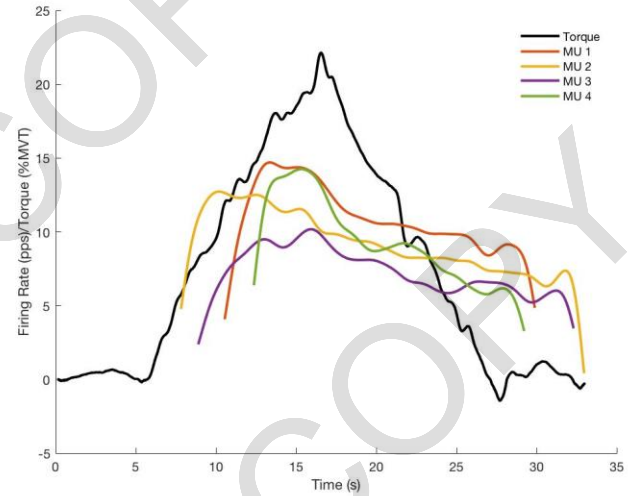


Thompson et al unpublished



Kuo, Lee, Johnson, Heckman, Heckman, J. Neurophys 2003

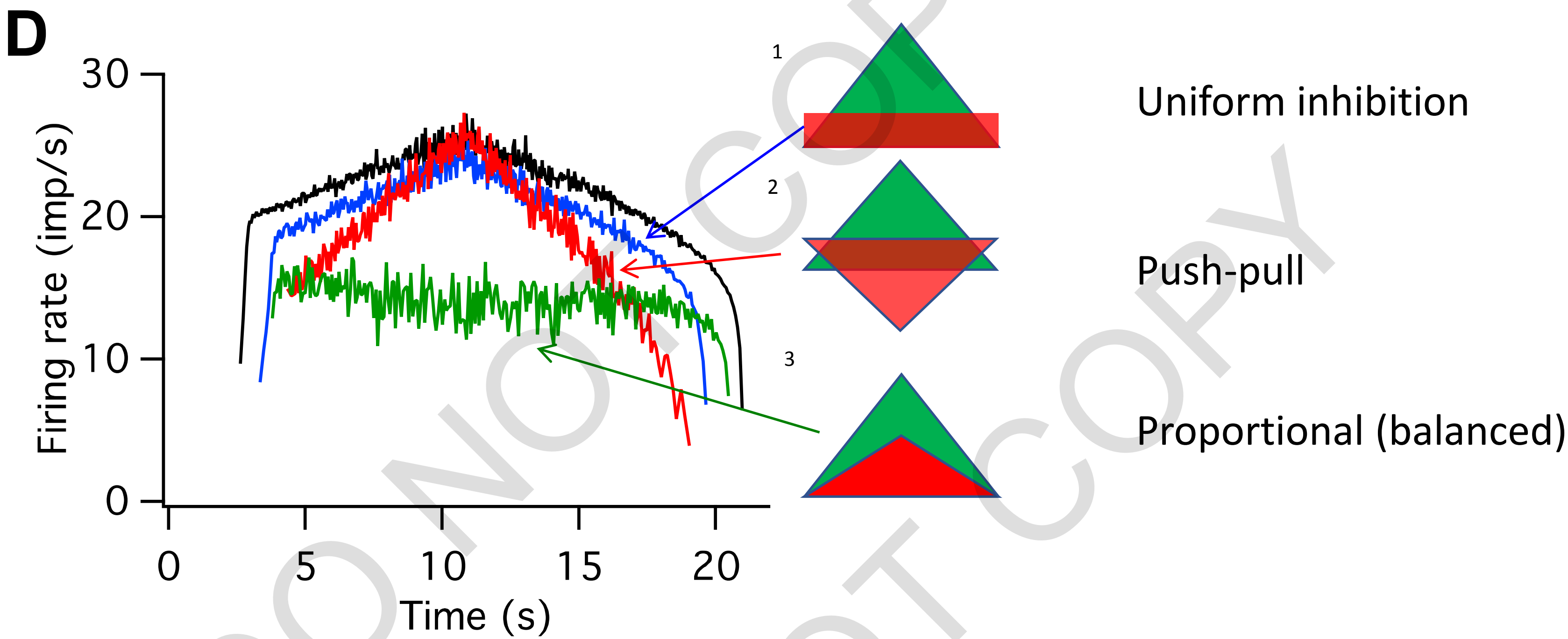


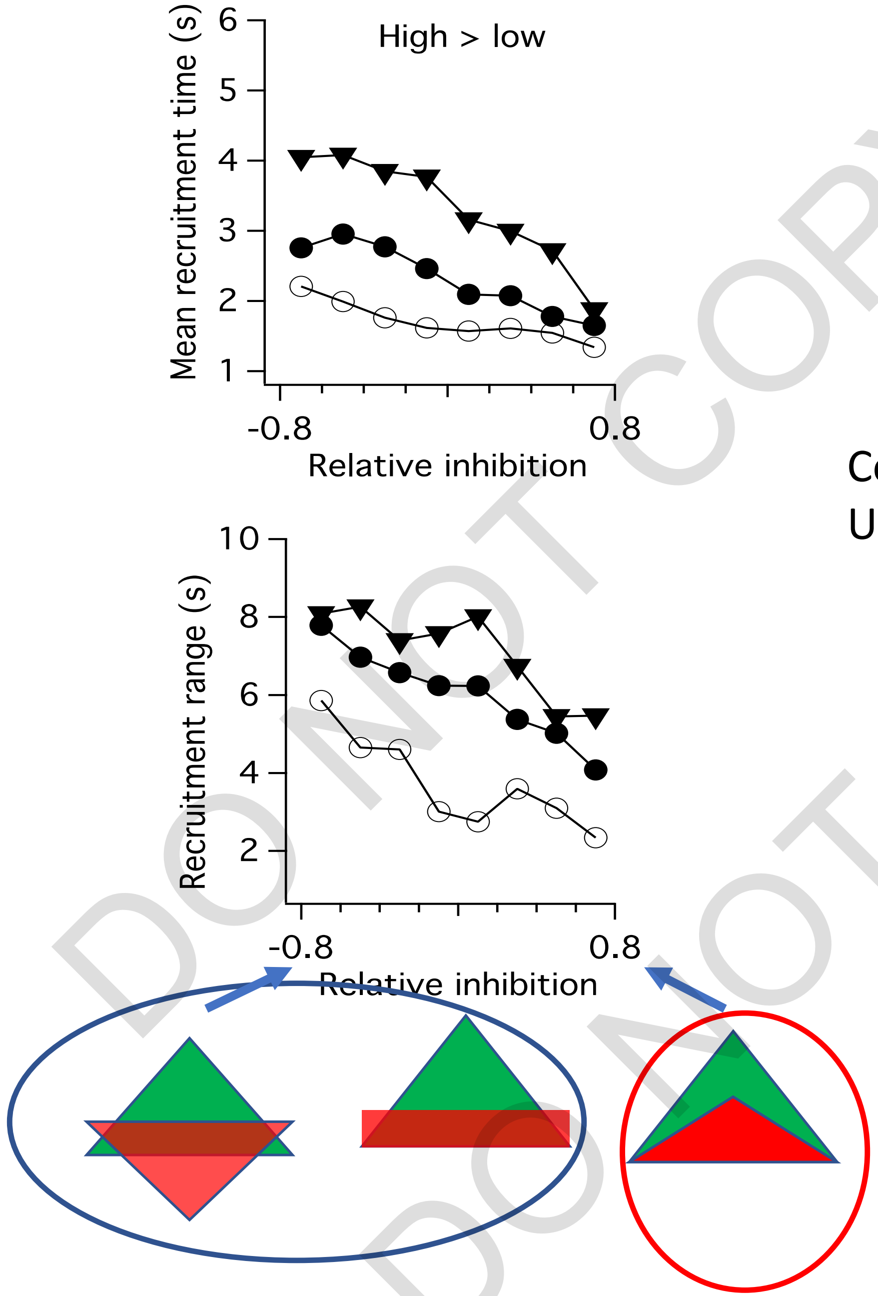


Data from Al Hasan in Jules Dewald's lab

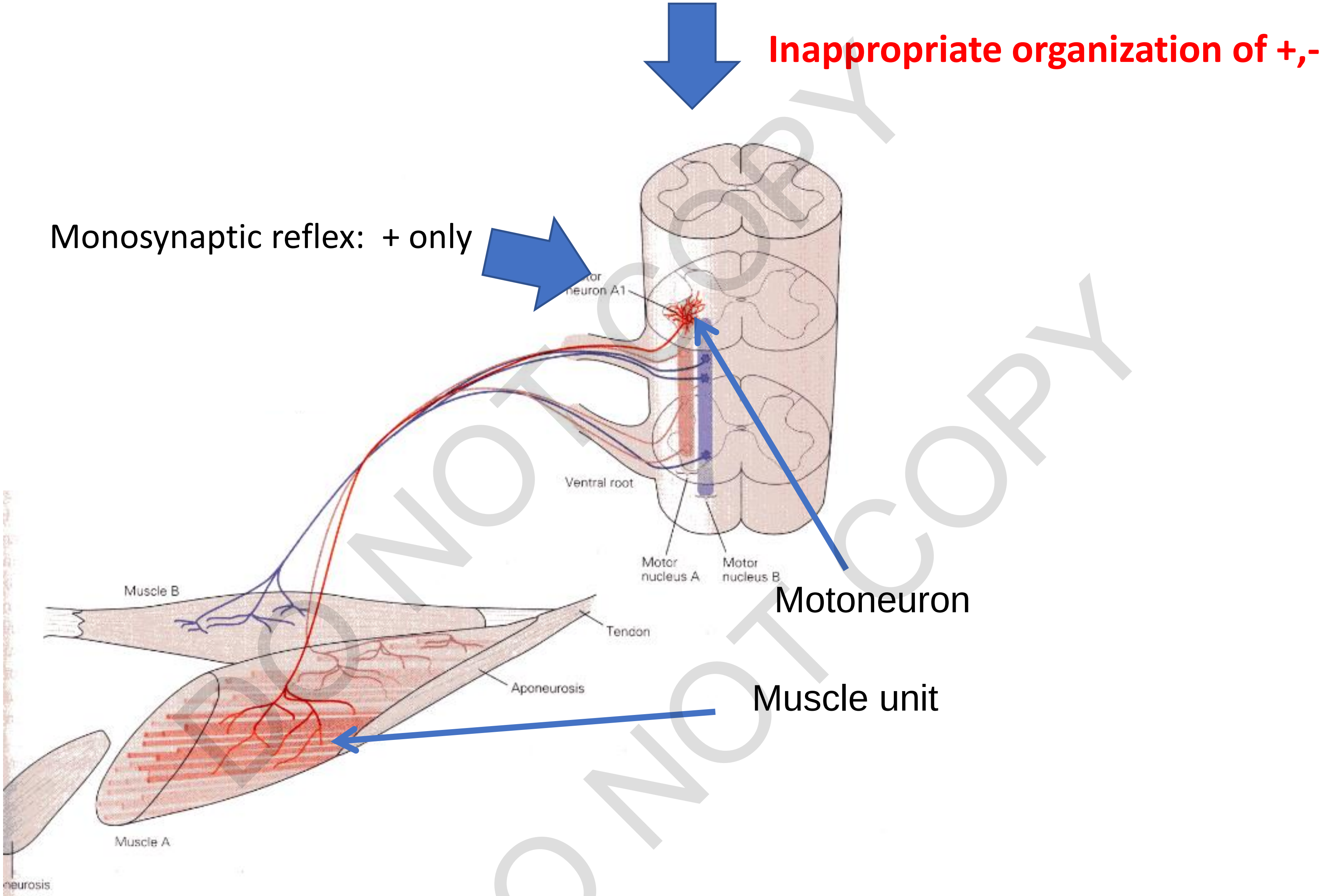
Example of computer simulation insights

Powers et al J. Neurophysiol, 2012

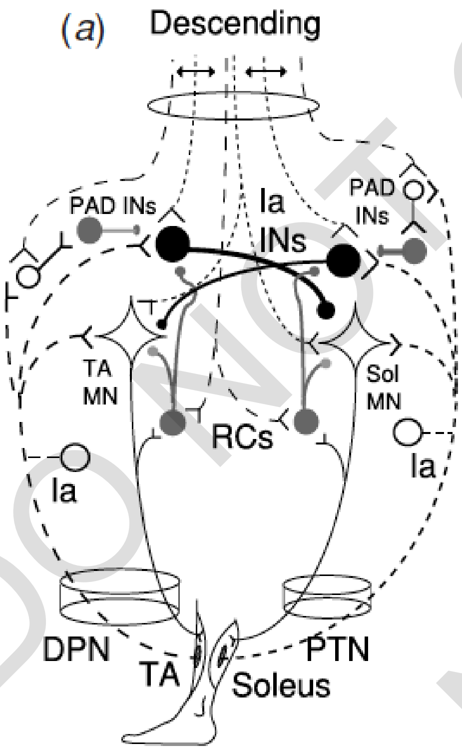




Computer simulations,
Unpublished, Powers and Heckman


Inappropriate organization of +,-
Monosynaptic reflex: + only
Ventral root
Motor nucleus A
Motor nucleus B
Motoneuron
Muscle B
Tendon
Aponeurosis
Muscle unit
Muscle A

Why does proportional inhibition emerge post-stroke? Perhaps loss of voluntary control of reciprocal inhibition.



Peirrot-Deseilligny, Burke 2005

So overall, the (highly preliminary) conclusion is:

- Motoneurons are hyperexcitable with larger PICs due to increased monoaminergic component of reticulospinal
- This excitability is evident from reflexes (especially Ia monosynaptic)
- Volitional drive is impaired and may activate non-reciprocal (balanced, proportional)

Further tests of this hypothesis based on:

- Differences between muscles
- Drugs
- Computer simulations