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Emulation of the origin and persistence of overflow in focal task-specific dystonia

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Question

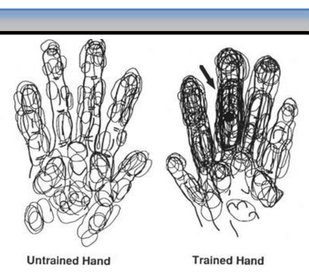
How does overflow in focal task-specific dystonia develop and why does it persist?

What did we find?

Repetitive & correlated use of two distinct sensory regions is sufficient to cause development of motor overflow

Introduction

• **Focal task-specific dystonia** is characterized by excessive muscle contraction producing abnormal postures during selective motor activity that often involve highly skilled, repetitive movements.



Sensory confusion (Byl & Merzenich)

Commonly known for:

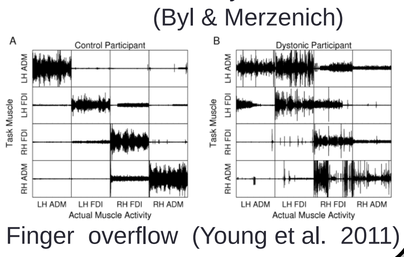
- Writer's cramp
- Musician's cramp
- Occupational dystonia

Characteristic features

- overflow
- Prolonged abnormal postures
- Prolonged or permanent motor deficit
- Loss of fine motor control

Physiological evidence

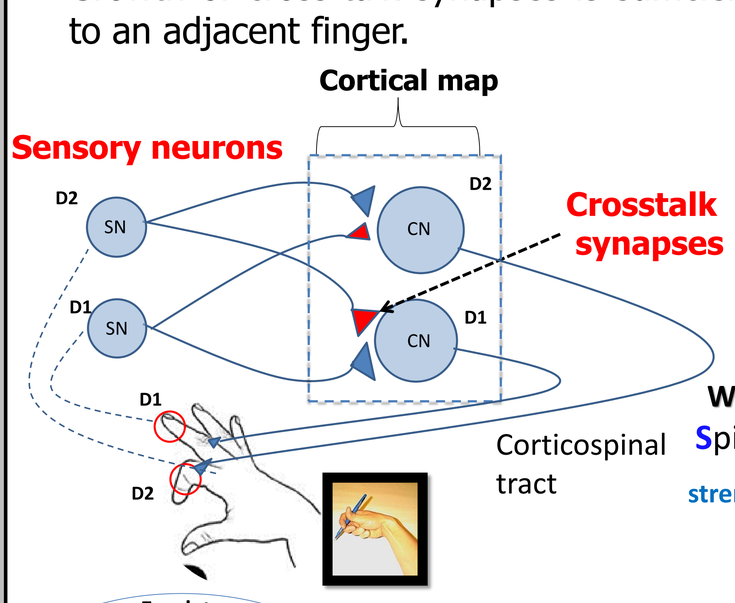
- De-differentiation in cortical representation (Bly et al. 1997)
- Abnormal tactile form perception and spatial and sensory processing (Bara-Jimenex et al. 2000)
- Loss of muscle selectivity in fingers(Young et al. 2011[1])



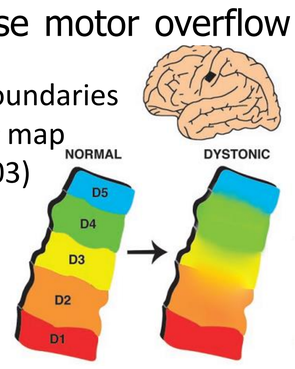
Finger overflow (Young et al. 2011)

Overflow idea

- Growth of cross-talk synapses is sufficient to cause motor overflow to an adjacent finger.

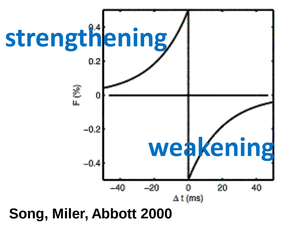


Blurred boundaries in sensory map (Nudo 2003)



What is the plasticity mechanism ?

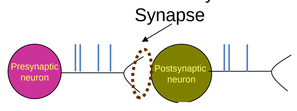
Spike-Timing-Dependent Plasticity



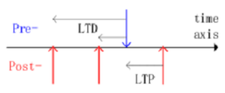
Song, Miler, Abbott 2000

- Neurons that fire together wire together.
- Correlated pre-post synaptic activity strengthens connection

Excitatory Synapse



$\Delta t = t_{post} - t_{pre}$



Emulate above 4 spiking neurons 4 synapse circuit here!

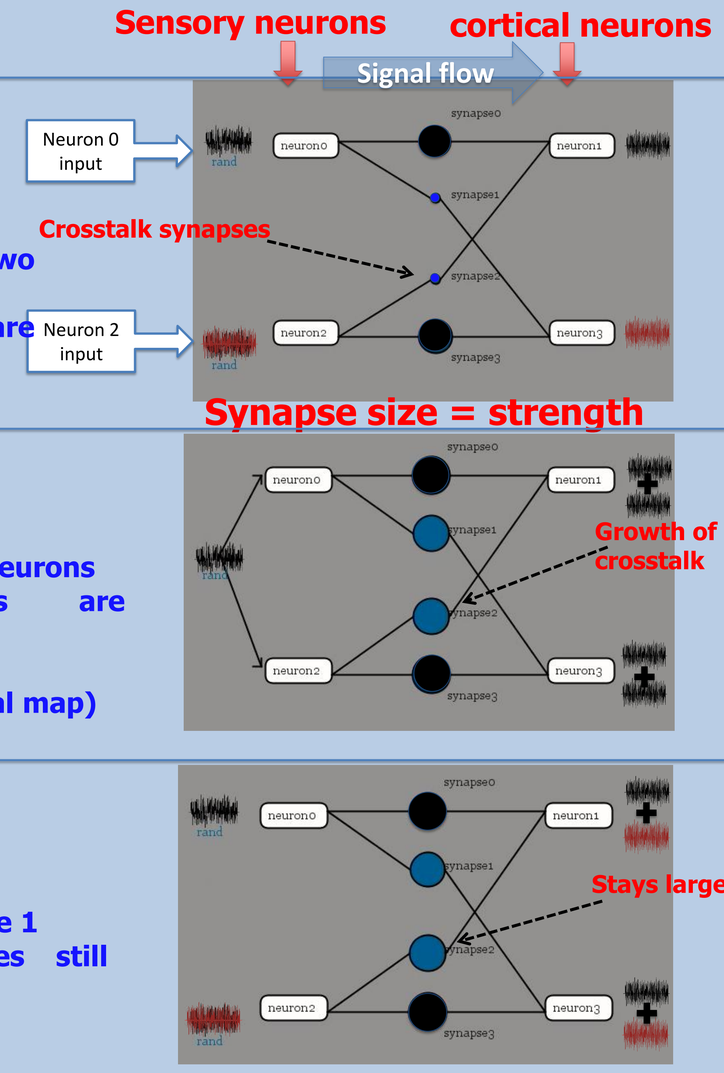
FPGA (Field Programmable Gate Arrays)

- Fast
- Rapid prototyping
- Scalable
- For High speed emulation

Development of overflow in dystonia

Questions: Will **repetitive** & **correlated** movement lead to the growth of cross-talk?

Will the disease perpetuate after the correlated movement has ended?



Phase 1:

Uncorrelated inputs

- Two different stimuli to two input sensory neurons
- Pre-post synaptic activities are uncorrelated.
- Cross-talk is suppressed.

Phase 2:

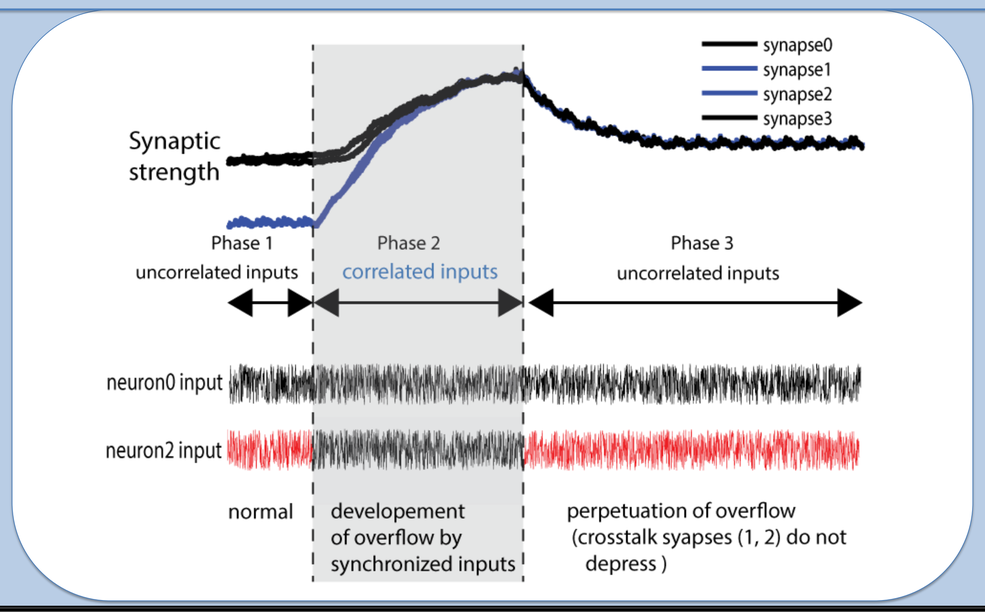
Correlated inputs

- Coupled stimuli to two input neurons
- Pre-post synaptic activities are correlated.
- Growth of cross-talk (=De-differentiation in cortical map)
- Overflow develops

Phase 3:

Uncorrelated inputs

- Inputs are the same as phase 1
- Pre-post synaptic activities still correlated.
- Overflow persists.



How does the result relate to dystonia?

- This is a model of development of overflow in focal task-specific dystonia.
- Blurred boundaries in cortical representation is found in dystonia and we showed how it could develop and eventually leads to motor overflow.

Terminology:

De-differentiation
= blurred boundary
= enlargement
in cortical
representation

Implication of the result

- Once dystonia occurs, it sticks. (Hysteresis phenomenon).
- Temporal sensory abnormalities could lead to motor permanent abnormalities.
- De-differentiation in sensory cortex, increased receptive field size could increase sensorimotor loop gain. (Sanger & Merzenich 2000[2])
- Treatment should target suppressing the cross-talk.
- Amblyopia can also be simulated with the same mechanism shown here.

Limitation

- This is a reduced representation of neural structures

Conclusion

- Repetitive and correlated movement is sufficient to produce the development of overflow in focal task-specific dystonia
- Spiking neurons with mere STDP rule are sufficient to produce this
- High speed emulation with physiologically realistic learning rate over years.

[1] Young SJ, van Doornik J, and Sanger TD. Finger muscle control in children with dystonia. *Movement disorders : official journal of the Movement Disorder Society 26: 1290-1296, 2011.*

[2] Sanger TD, and Merzenich MM. Computational model of the role of sensory disorganization in focal task-specific dystonia. *Journal of neurophysiology 84: 2458-2464, 2000.*

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