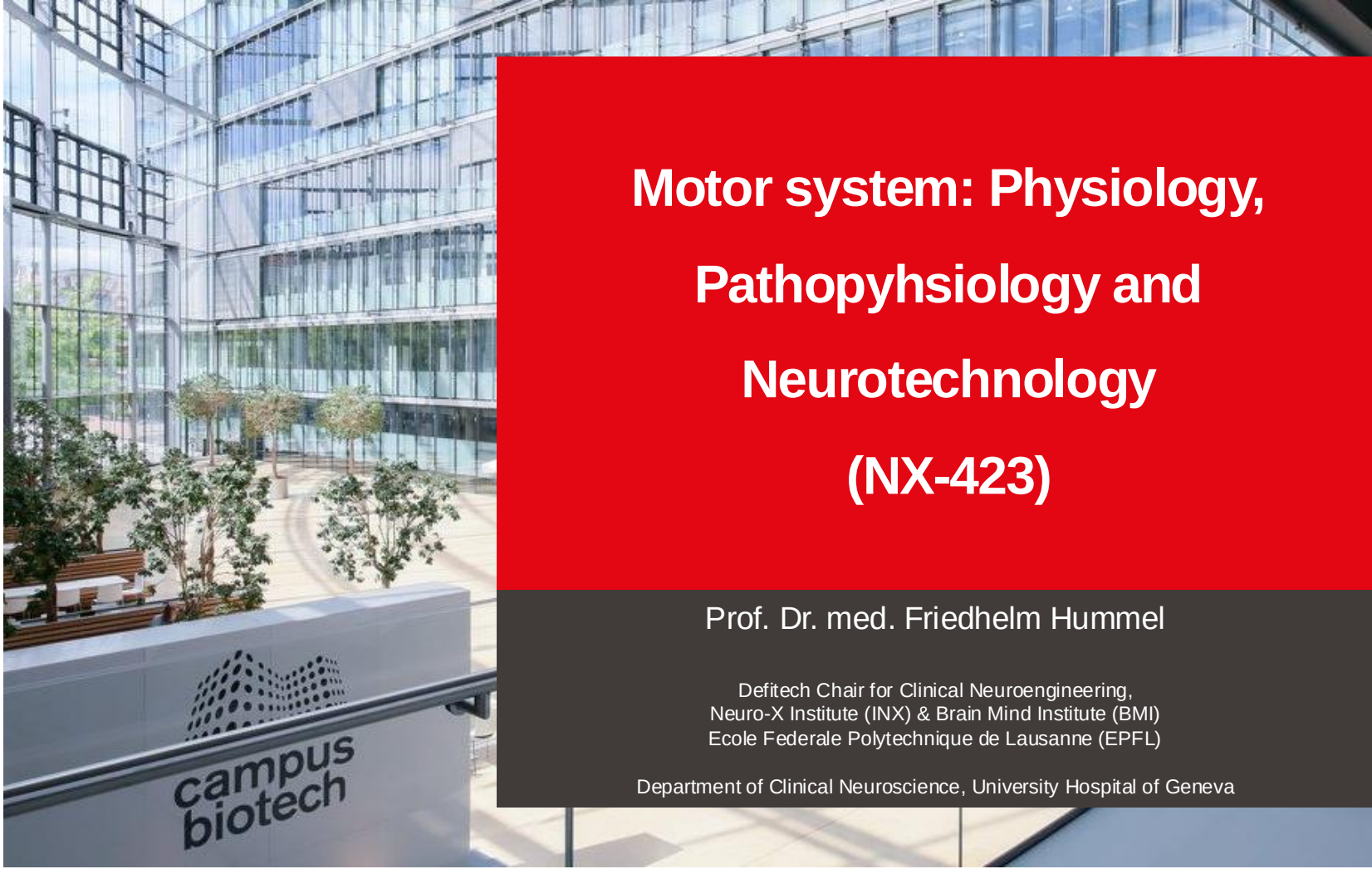
EPFL

Neuro X Institute

HUG Hôpitaux Universitaires Genève

Clinique romande de réadaptation



Motor system: Physiology, Pathopyhsiology and Neurotechnology (NX-423)

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Neuro-X Institute (INX) & Brain Mind Institute (BMI)
Ecole Federale Polytechnique de Lausanne (EPFL)

Department of Clinical Neuroscience, University Hospital of Geneva

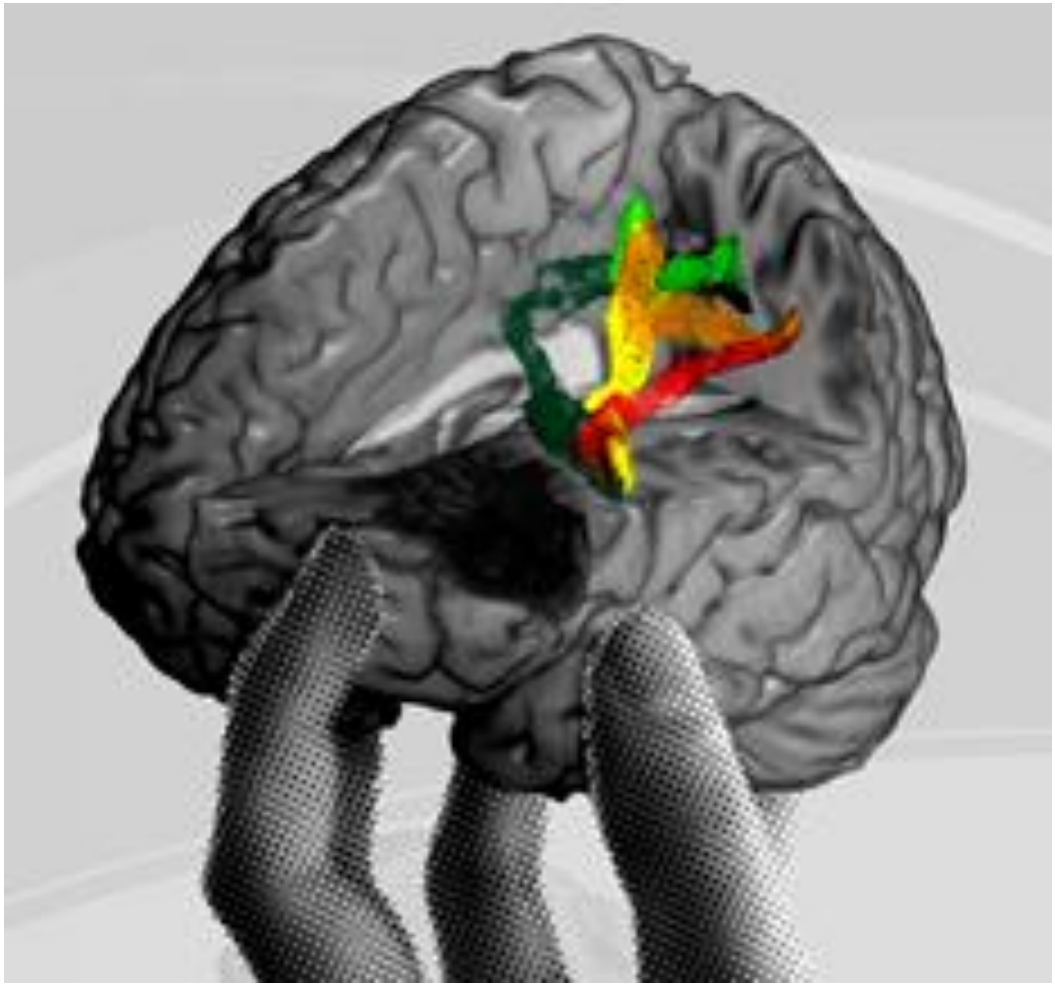
Neuro-X Master:

NX-423
Translational neuroengineering

To know and understand the motor system

To know different motor behavior (reflexes, motor performance, motor learning)

To know factors that impact on motor behavior, e.g., effort, reward



Why is the motor system important?

Special feature of the human motor system?

- Observable behavior is directly related to activity in the motor system.
- Without the motor system, one could experience sensation, thinking, reasoning, reading etc, but we would not be able to communicate the thoughts and abilities.
- Dexterity very unique human feature

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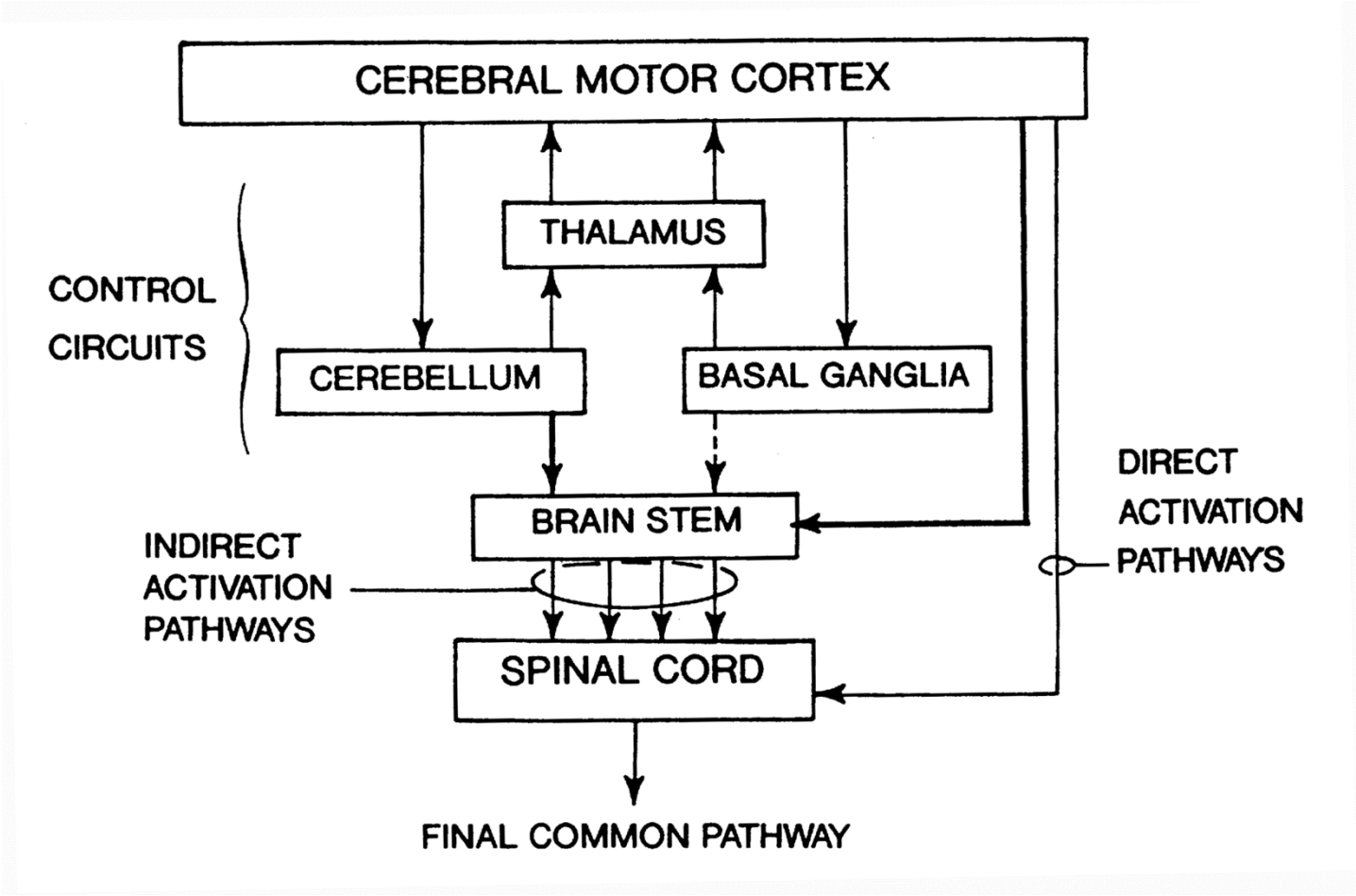
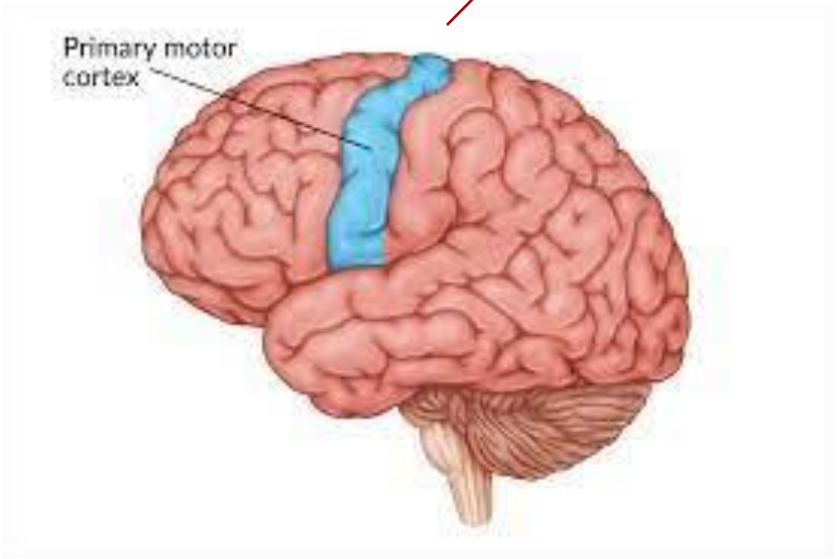
- Central Nervous system parts
  - Motor cortex, basal ganglia, cerebellum, brain stem, spinal cord
  - + prefrontal, parietal cortex

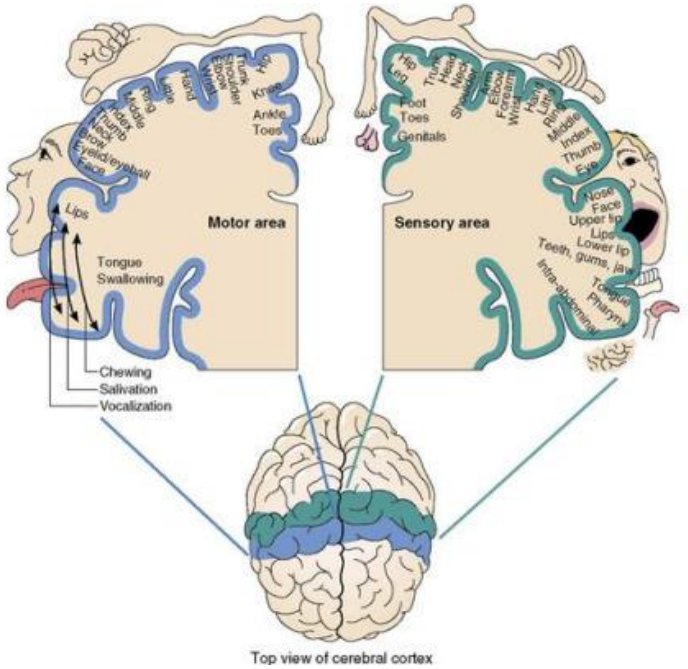
- Peripheral parts
  - Efferent
    - ✓ peripheral nerves (efferent)
    - ✓ muscles
  - Afferent
    - ✓ peripheral nerves (afferent)
    - ✓ muscle spindles etc

- *Reflexes*
  - Mono-
  - Polysynaptic
- *Motor behavior*
  - Simple
  - Complex
- *Motor learning*
  - Short-/longterm
  - Motivation, Effort, Reward
- *Interactions with other systems (motor-language)*


CEREBRAL MOTOR CORTEX
THALAMUS
CONTROL
CIRCUITS
CEREBELLUM
BASAL GANGLIA
BRAIN STEM
DIRECT
ACTIVATION
PATHWAYS
INDIRECT
ACTIVATION
PATHWAYS
SPINAL CORD
FINAL COMMON PATHWAY

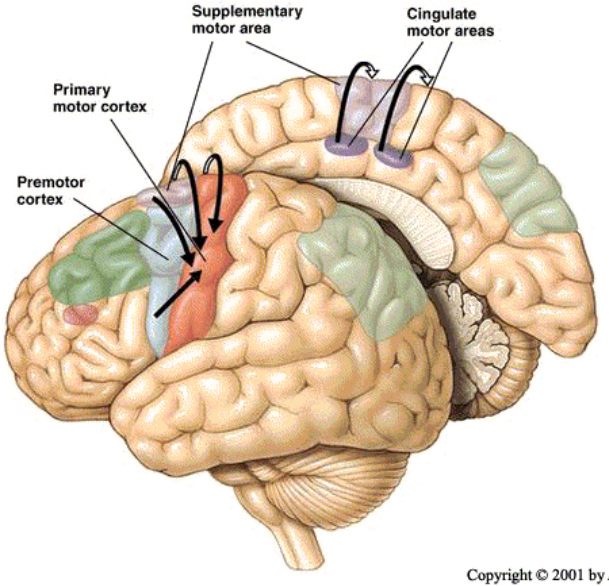


Homuncular organization

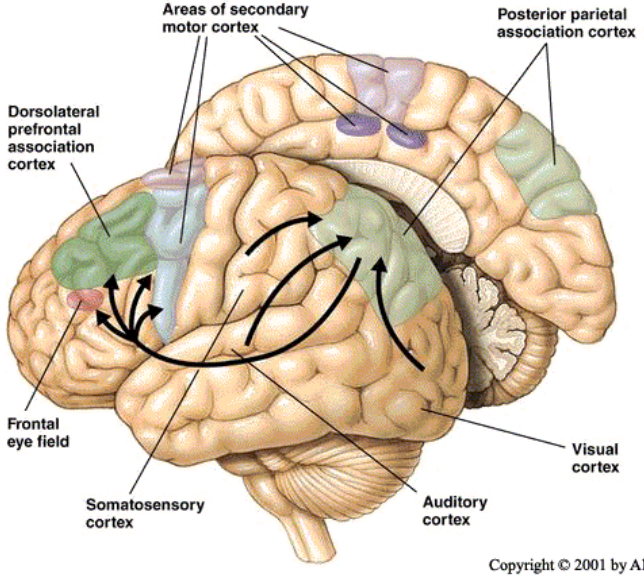


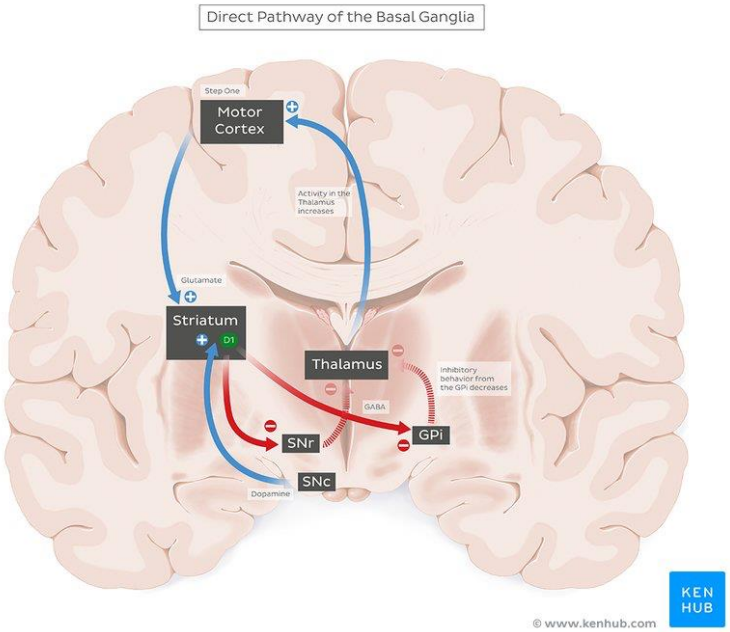
Secondary motor cortex organization

► Four Areas of the Secondary Motor Cortex



► Cortical Input and Output Pathways




Direct Pathway of the Basal Ganglia
Step One
Motor Cortex
Activity in the Thalamus increases
Glutamate
Striatum
D1
Thalamus
GABA
Inhibitory behavior from the GPi decreases
SNr
GPi
SNc
Dopamine
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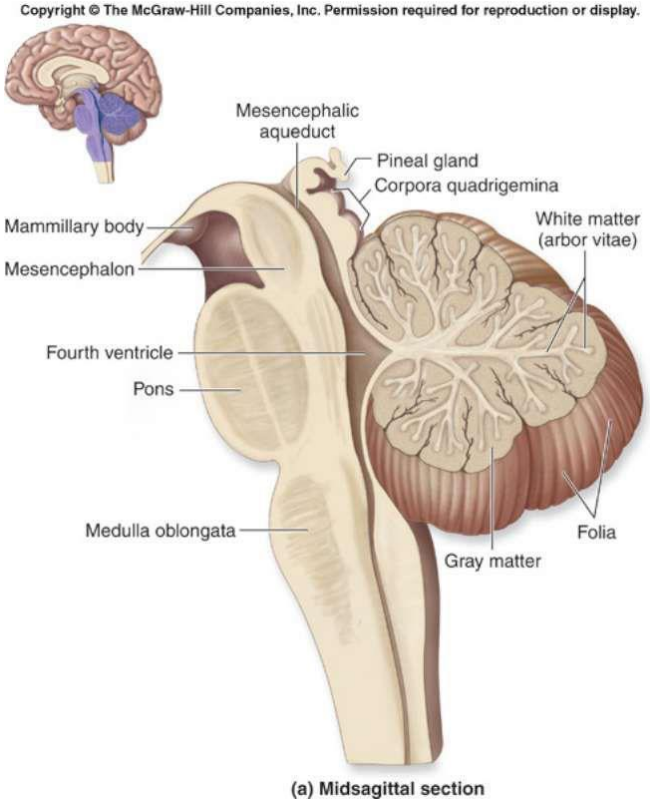
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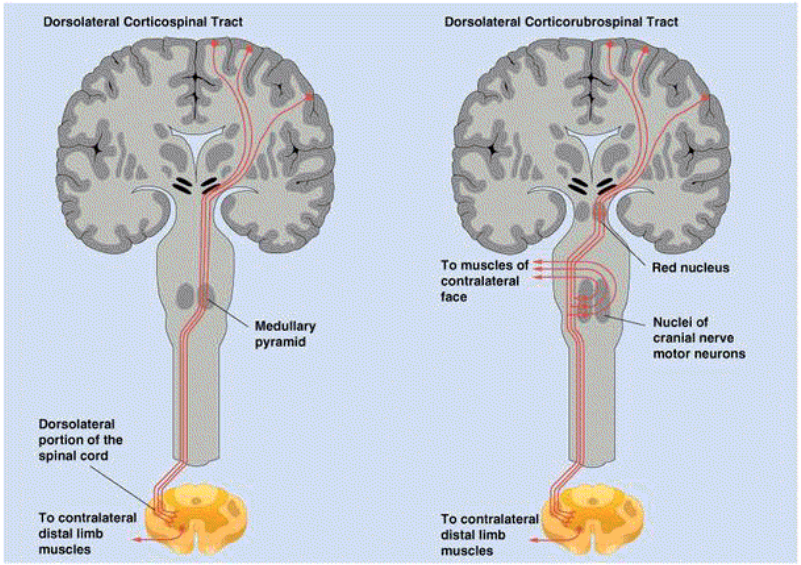
Mesencephalic aqueduct
Pineal gland
Corpora quadrigemina
Mammillary body
Mesencephalon
White matter (arbor vitae)
Fourth ventricle
Pons
Medulla oblongata
Folia
Gray matter
(a) Midsagittal section

► The Two Divisions of the Dorsolateral Motor Pathway



Cortico-spinal tract:

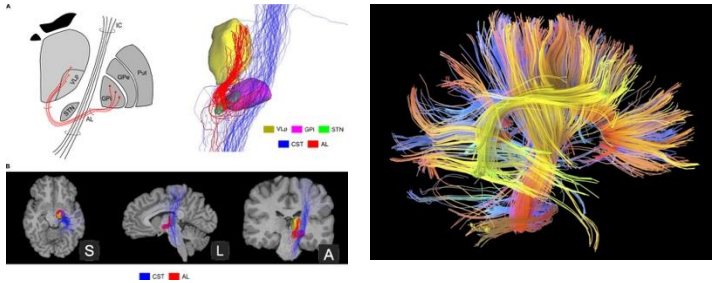
- **Origins**: primary motor cortex (MI), premotor cortex, supplemental motor cortex, anterior paracentral gyrus, parietal lobe and cingulate gyrus
- Termination in spinal cord
- Control of peripheral muscles

Cortico-bulbar tract:

- control over facial muscles;
- control over muscles of mastication
- control over external eye muscles:
- control of tongue
- control over swallowing reflexes

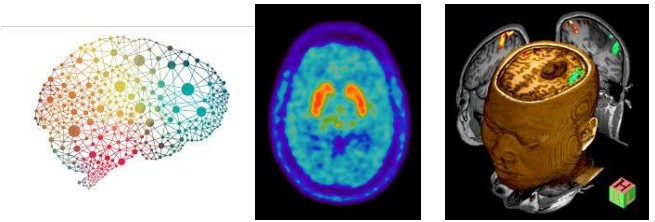
Structural assessment:

- CT, MRI, tUS based
  - Volume, e.g., Cortical thickness
  - Fractional anisotropy
  - Lesions/degeneration vs. structural growth
- Section
- Structural connectomics/dysconnectomics



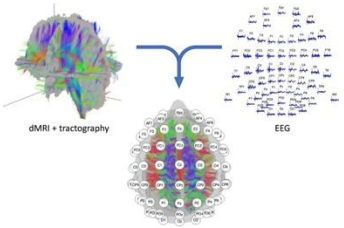
Functional assessment:

- CT, MRI, M/EEG, TMS, tUS, NIRS, PET, SPECT based
  - Focal activation, deactivation
  - Network activation/deactivation
  - Network interactions
  - Transmitter-related activity (Dopa PET, MRS, paired-pulse TMS)
- Resting state activity vs. Task-related activity

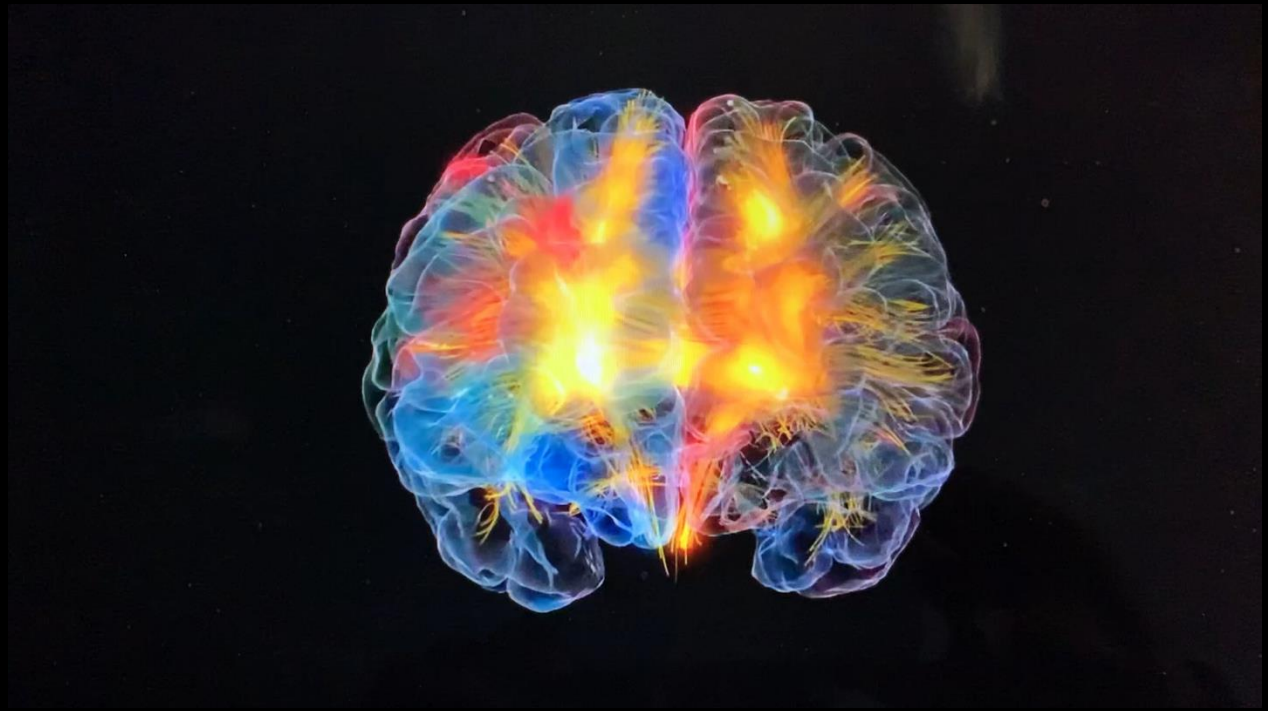


Functional-structural assessment:

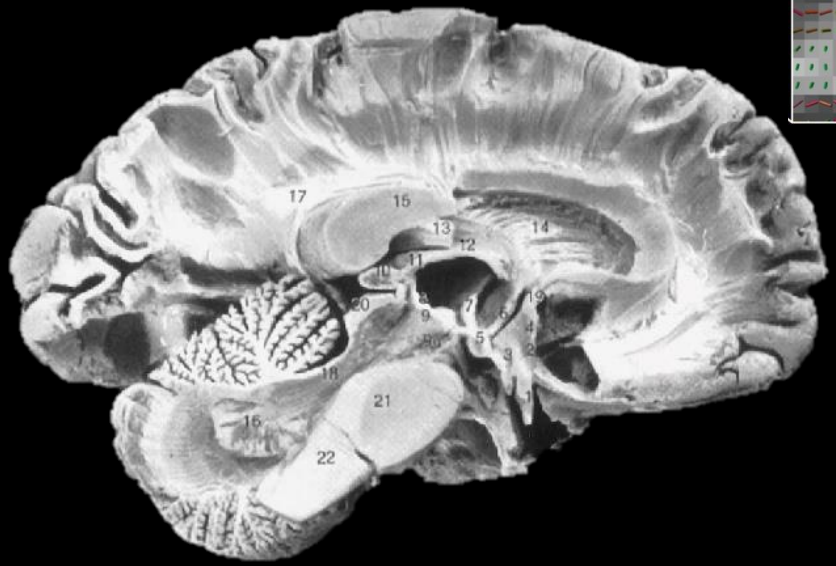
- Interaction between structural ‘architecture’ and functional use of the architecture



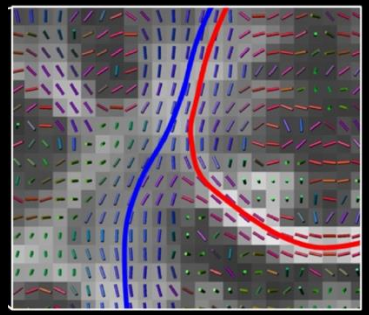
Motor network – functional connectome



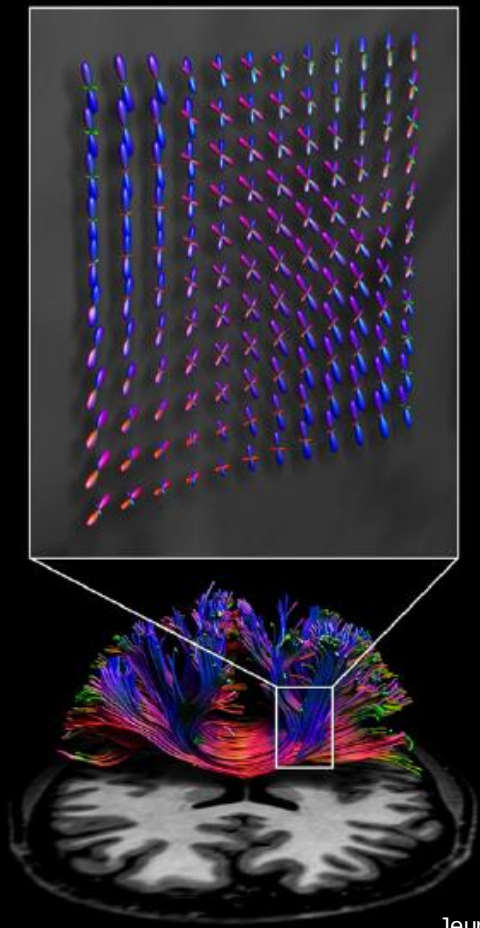
1. Tractography



Huber 1971

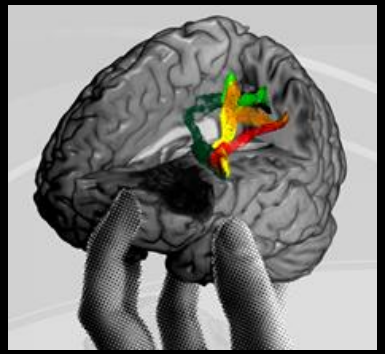


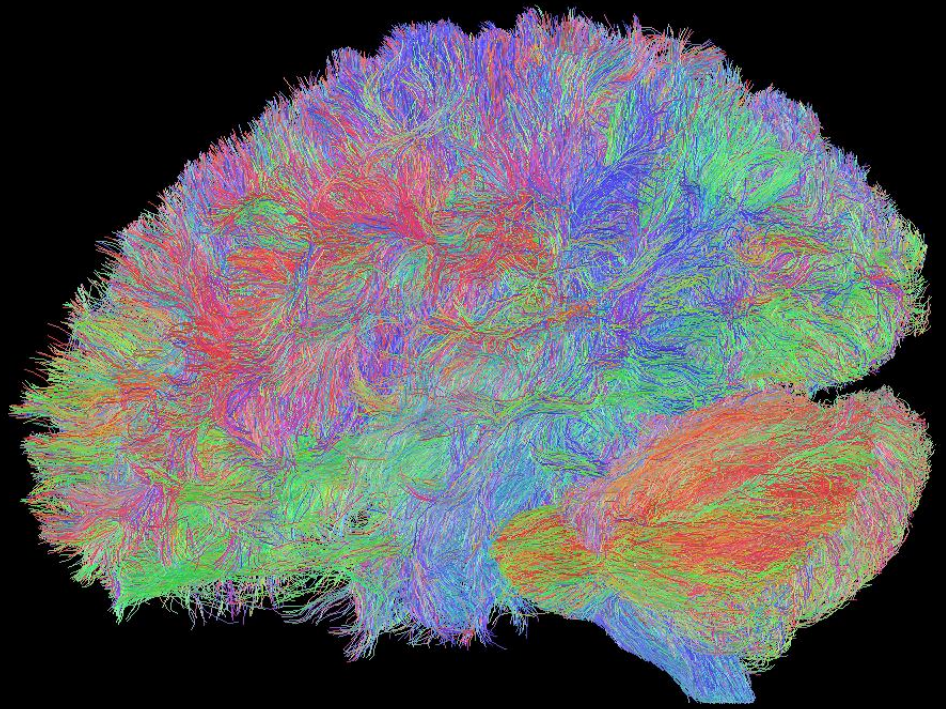
Non invasive



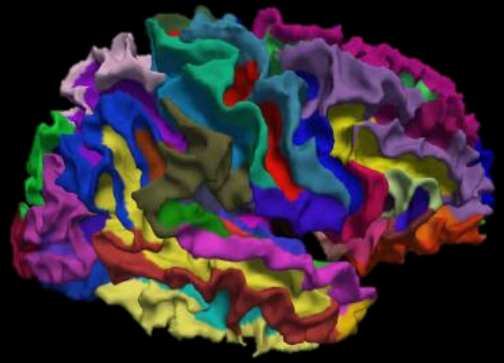
Jeurissen et al. 2019

Motor network – structural connectome

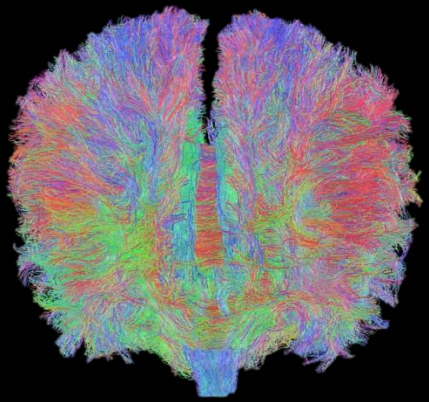




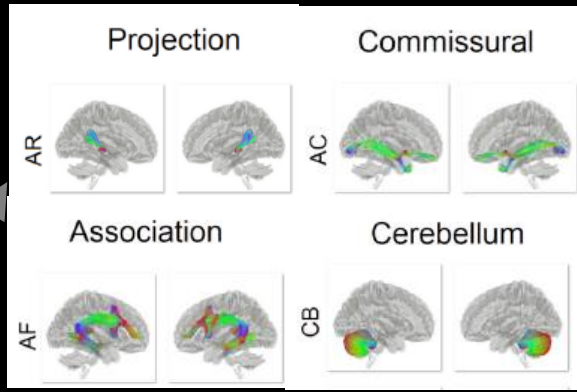
Motor network – structural connectome



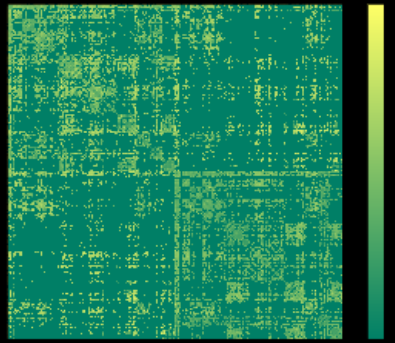
Brain parcellation



Tractography



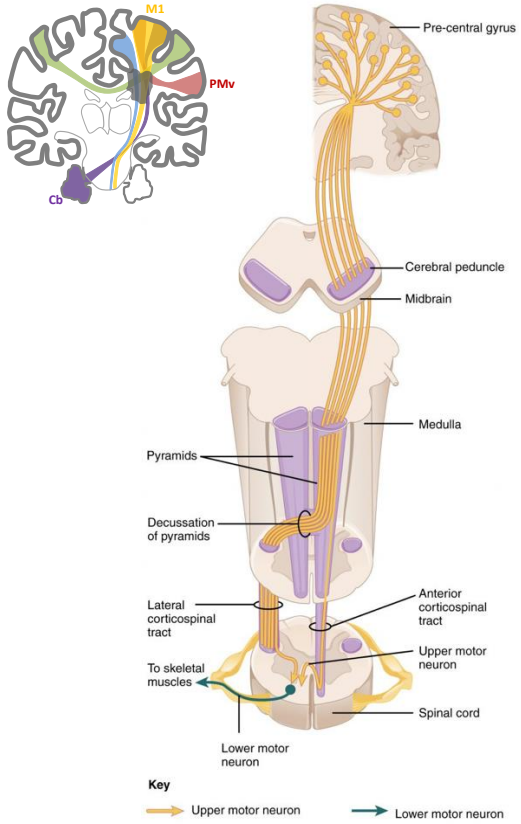
WM Fascicles

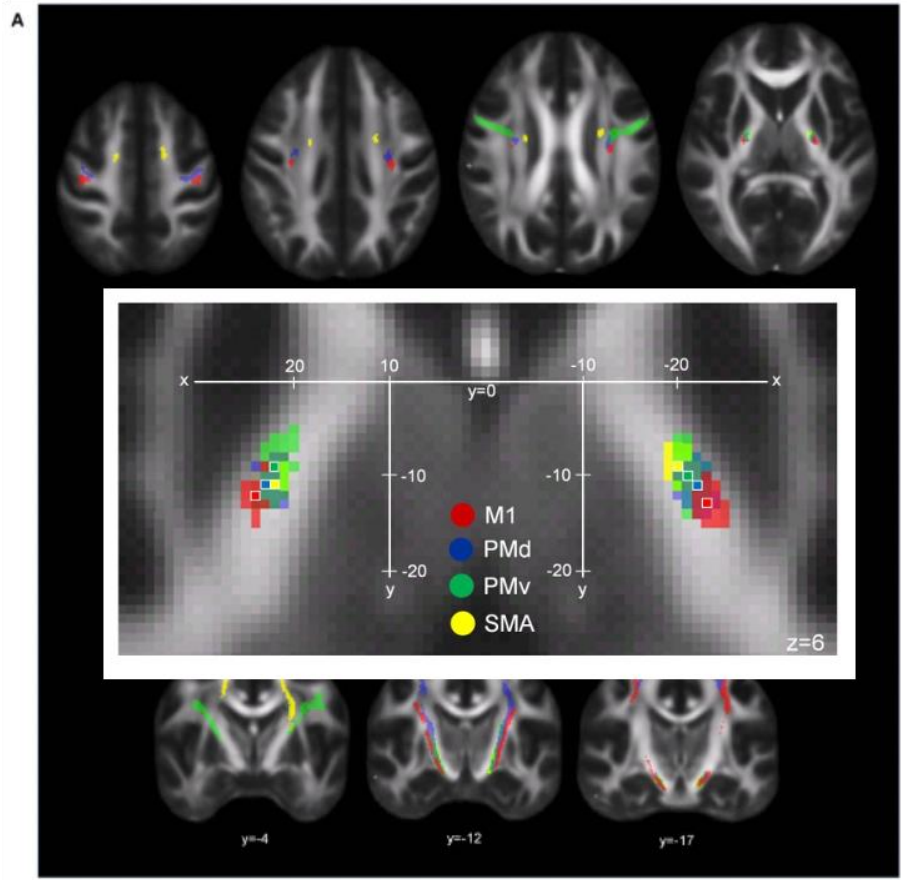


Connectome

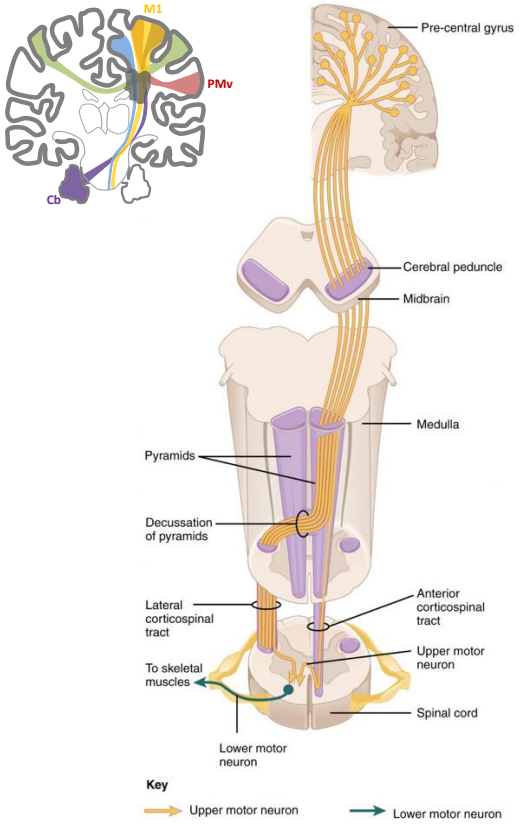
Jeurissen et al. 2019

Motor network – structural connectome



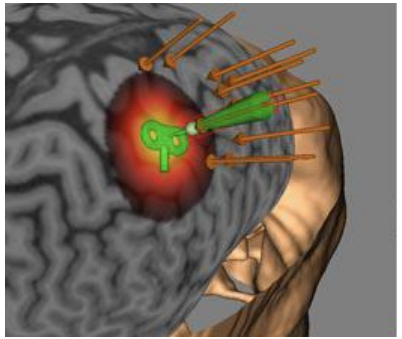


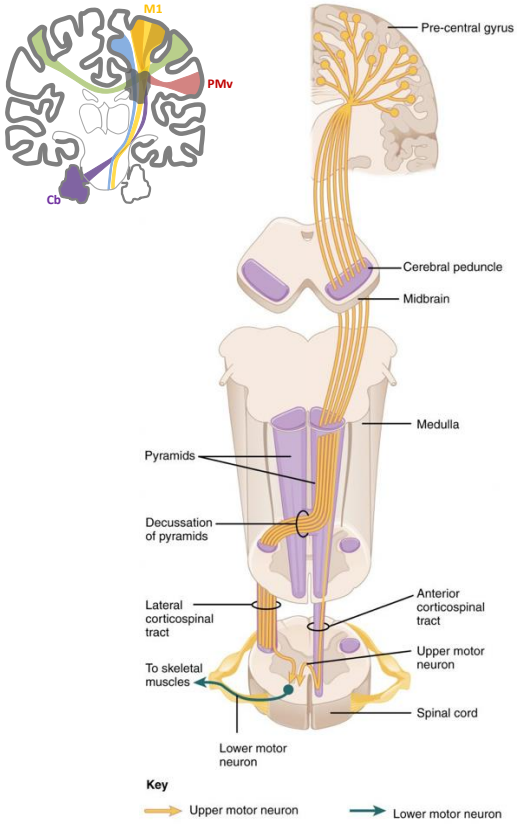
Schulz et al., *Stroke* (2012)



Transcranial Magnetic Stimulation

(for details Lecture NIBS)





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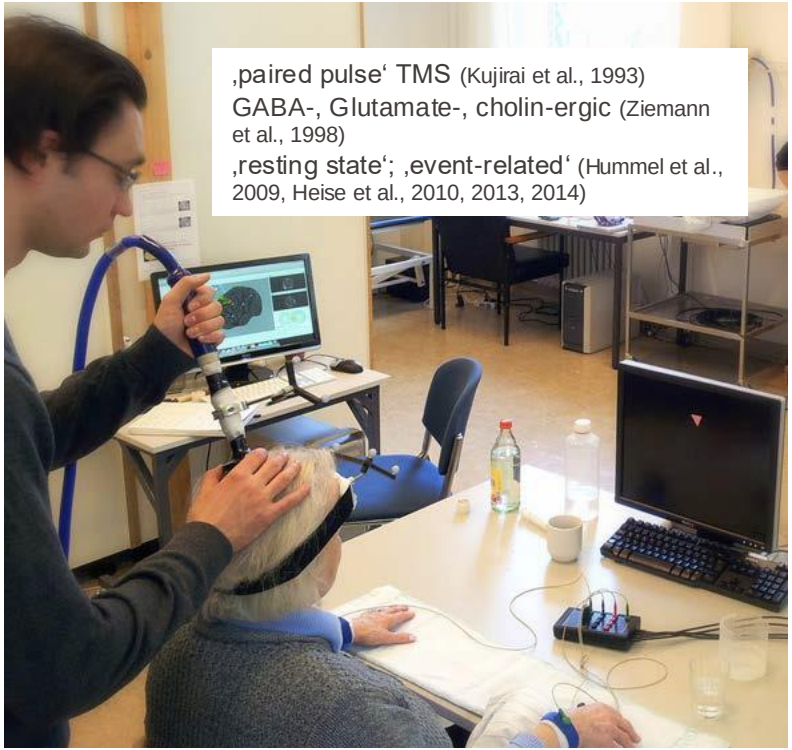
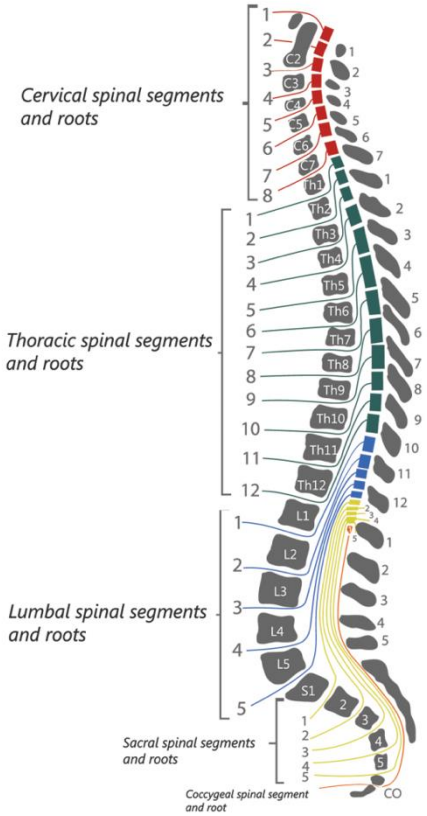
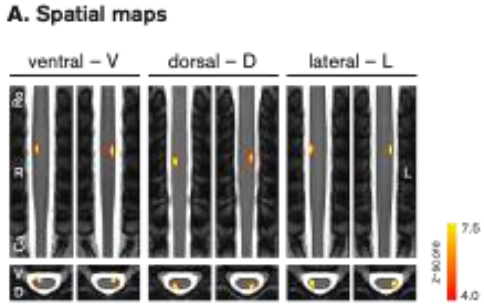
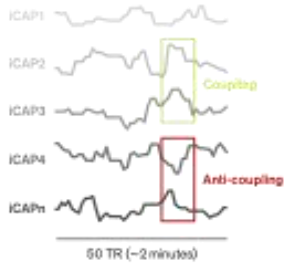


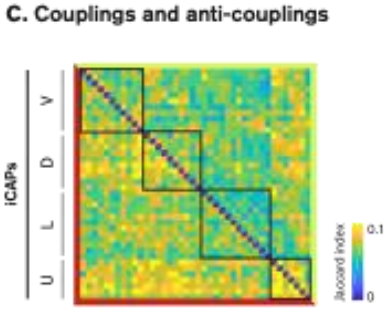
‚paired pulse' TMS (Kujirai et al., 1993)
GABA-, Glutamate-, cholin-ergic (Ziemann et al., 1998)
‚resting state'; ‚event-related' (Hummel et al., 2009, Heise et al., 2010, 2013, 2014)

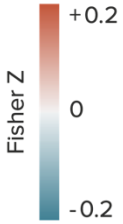
Motor network – spinal connections

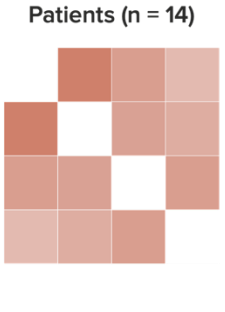




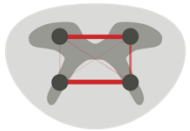


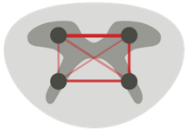






For comparison: same acquisitions, other dataset

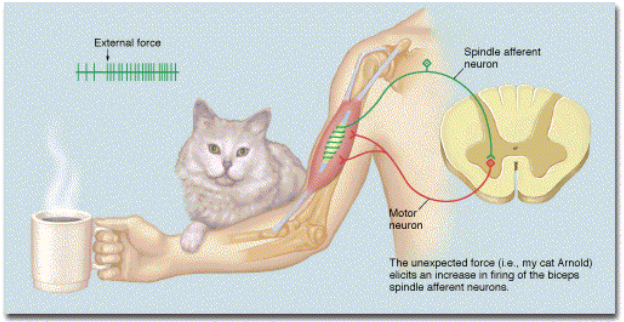




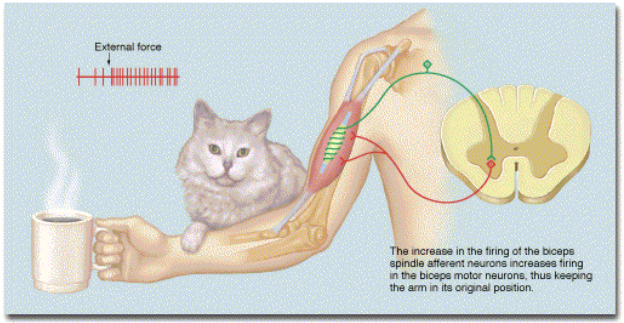
Kinany et al., *Neuron* (2019

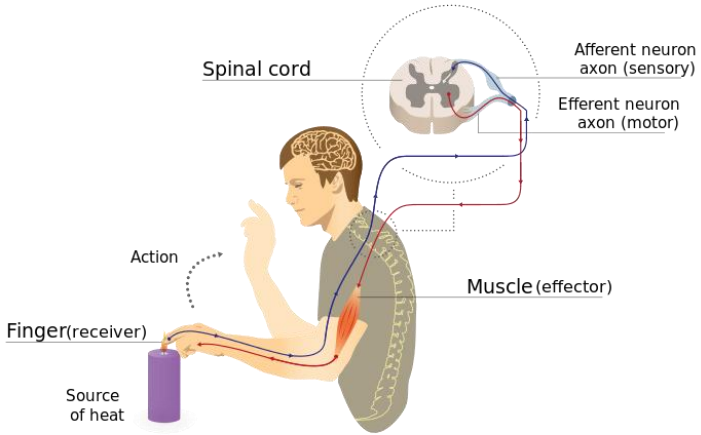
Motor behavior

Automatic Maintenance of Limb Position (Continued)

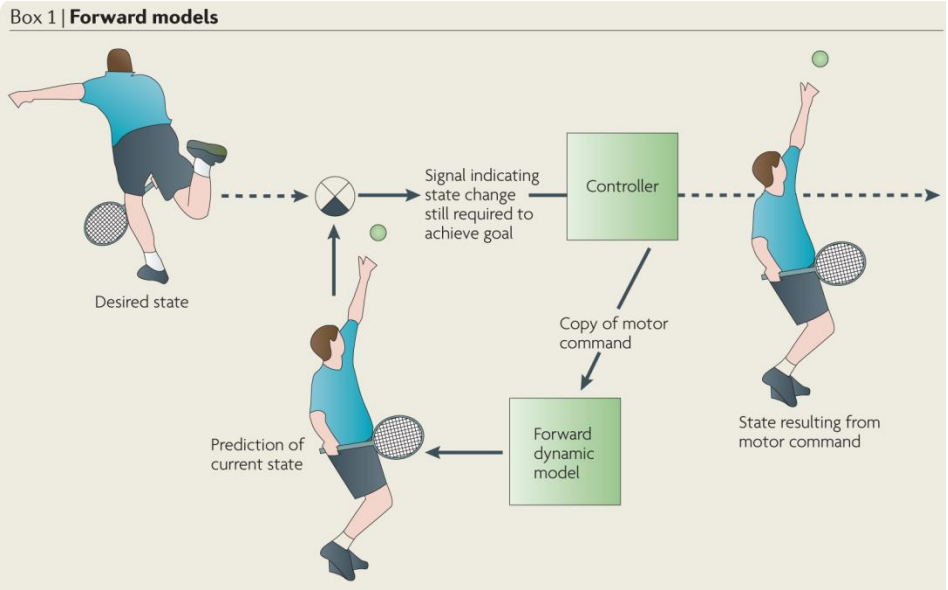


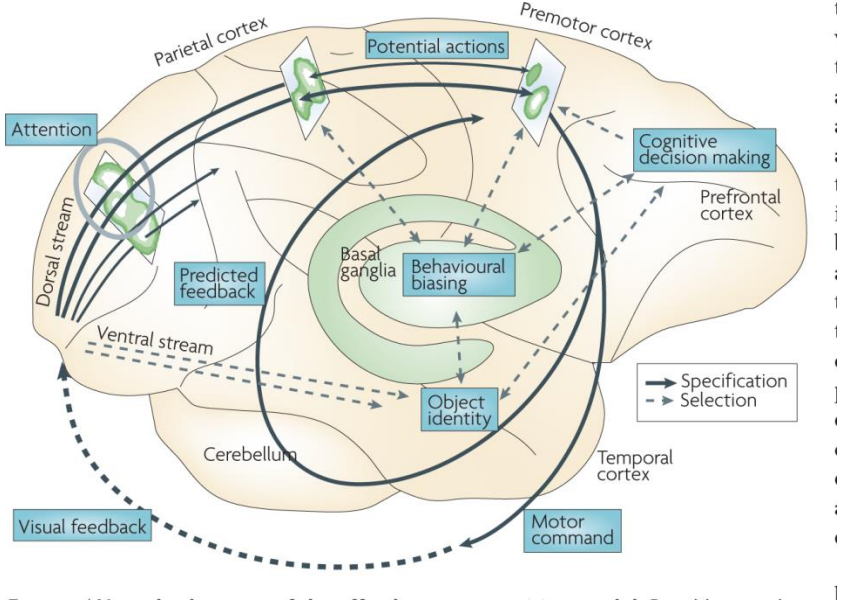
Automatic Maintenance of Limb Position



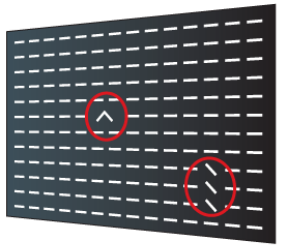


Complex movements



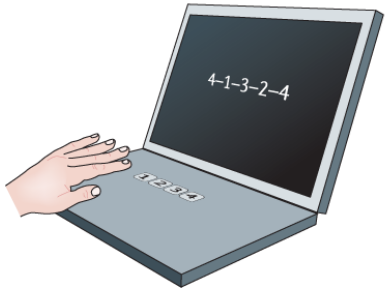


Yarrow et al., *Nat Nsc Rev 2009*



Passage of time and/or sleep

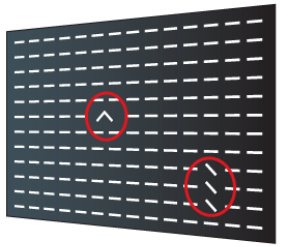
Training → Memory formation and within-session fast learning → Consolidation (stabilization and offline learning) → Memory reactivation and modification → Long-term memory retention



Susceptibility to interference and/or performance deterioration

During additional practice, re-testing and/or sleep

Censor et al., *Nat Rev Nsc* 2012



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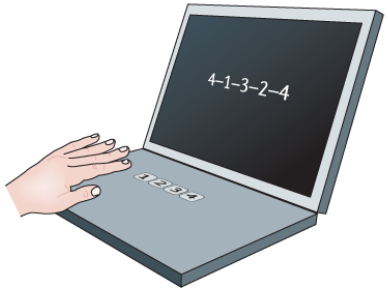

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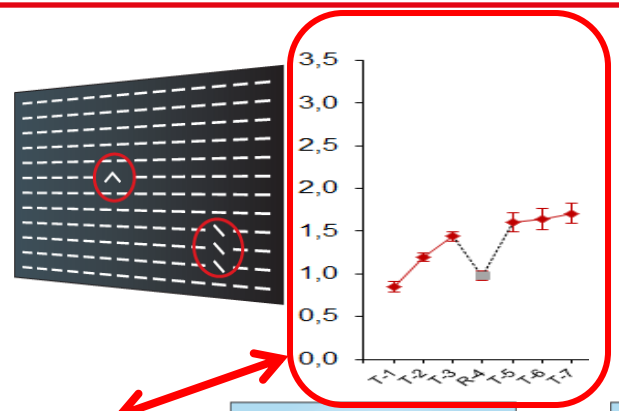

Passage of time and/or sleep

Training → Memory formation and within-session fast learning → Consolidation (stabilization and offline learning) → Memory reactivation and modification → Long-term memory retention

Susceptibility to interference and/or performance deterioration

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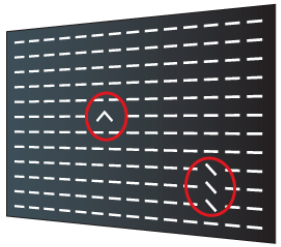
Censor et al., *Nat Rev Nsc* 2012



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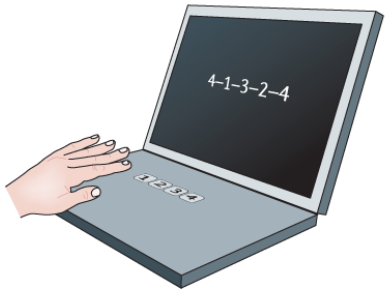

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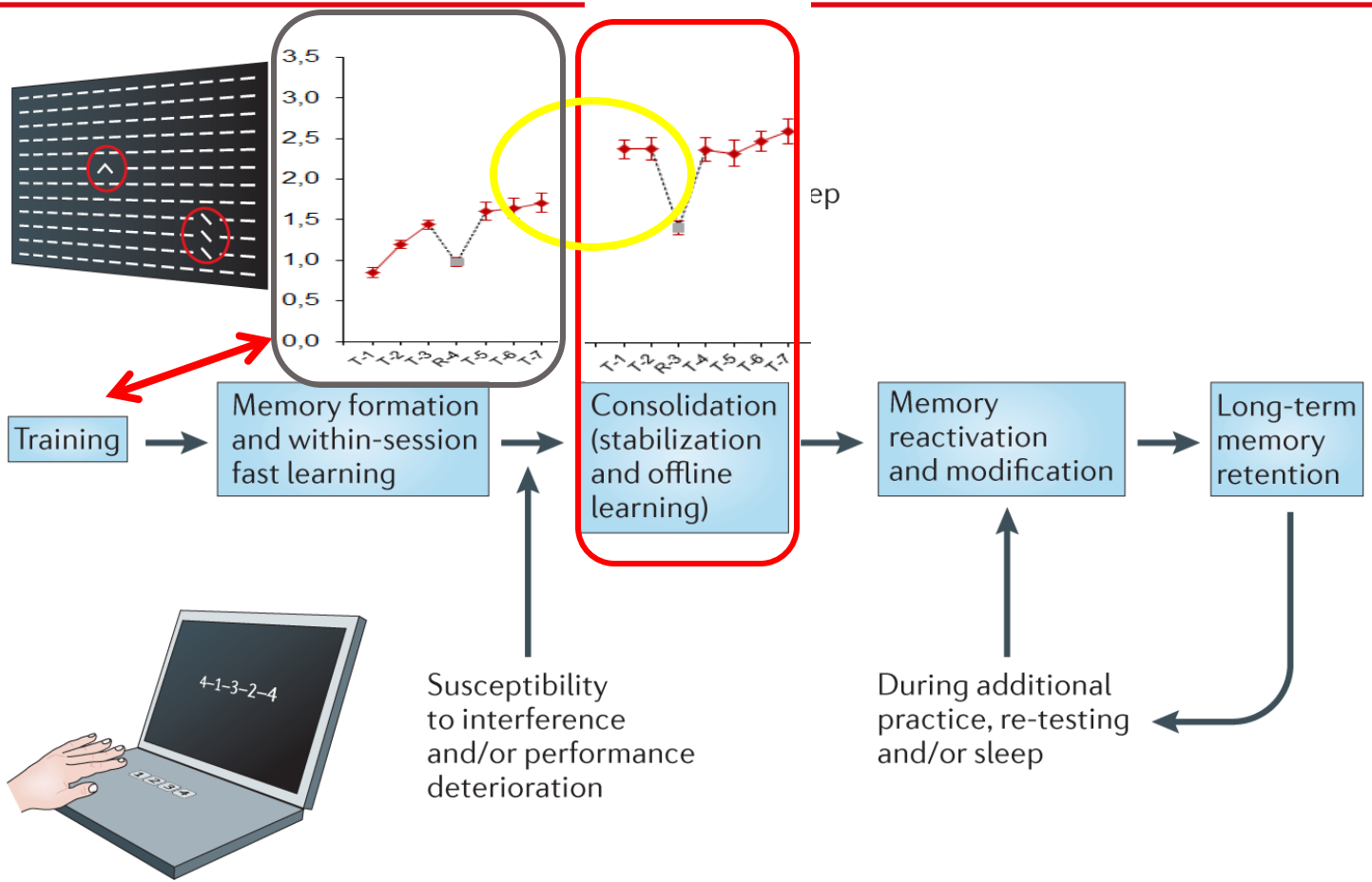
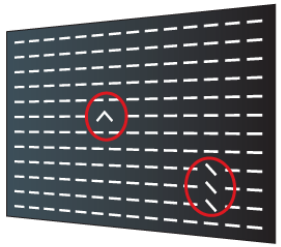
Censor et al., *Nat Rev Nsc* 2012

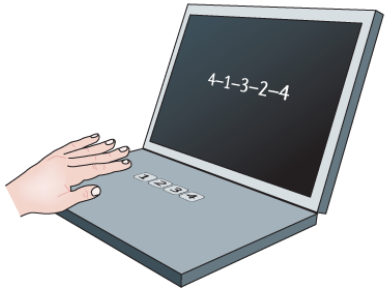


Censor et al., *Nat Rev Nsc* 2012



Passage of time and/or sleep

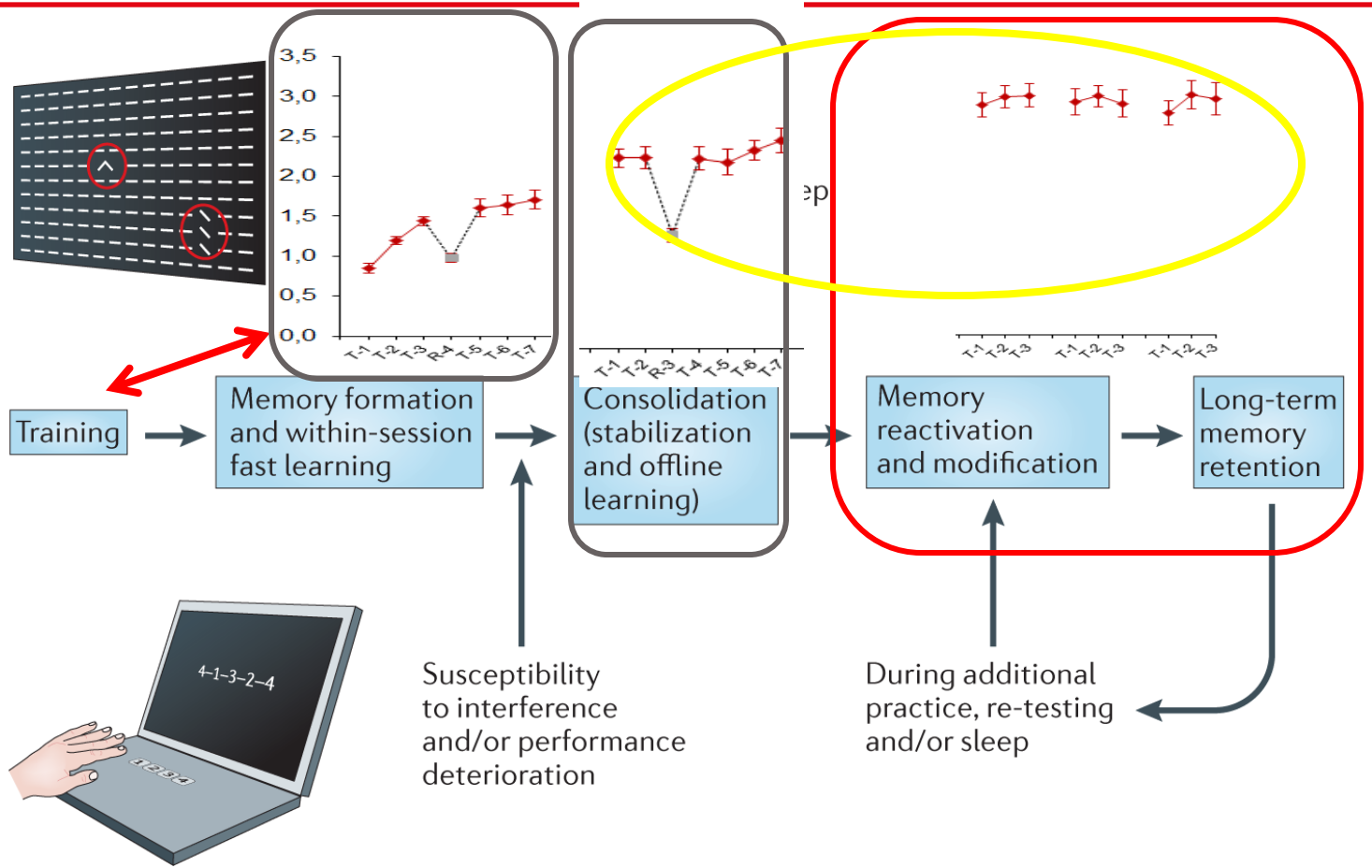
Training → Memory formation and within-session fast learning → Consolidation (stabilization and offline learning) → Memory reactivation and modification → Long-term memory retention



Susceptibility to interference and/or performance deterioration

During additional practice, re-testing and/or sleep

Censor et al., *Nat Rev Nsc* 2012



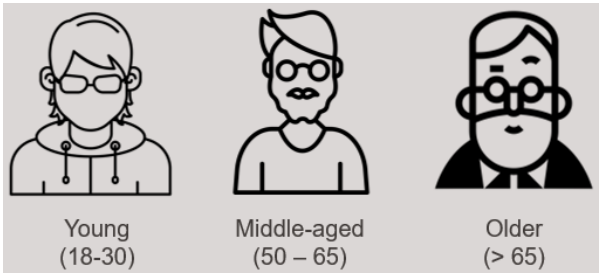
Censor et al., *Nat Rev Nsc* 2012

- Well-established paradigm

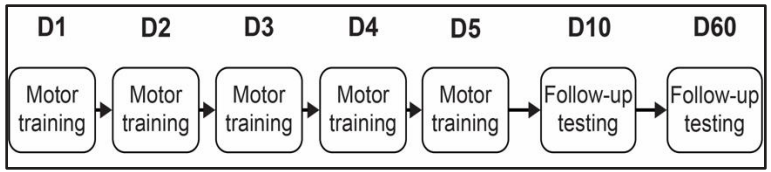
(Draaisma et al., 2022; Maceira-Elvira et al., 2022; Walker et al., 2003; Wessel et al., 2021; Zimerman et al., 2013)

Maceira-Elvira et al., *Science Advances* 2022

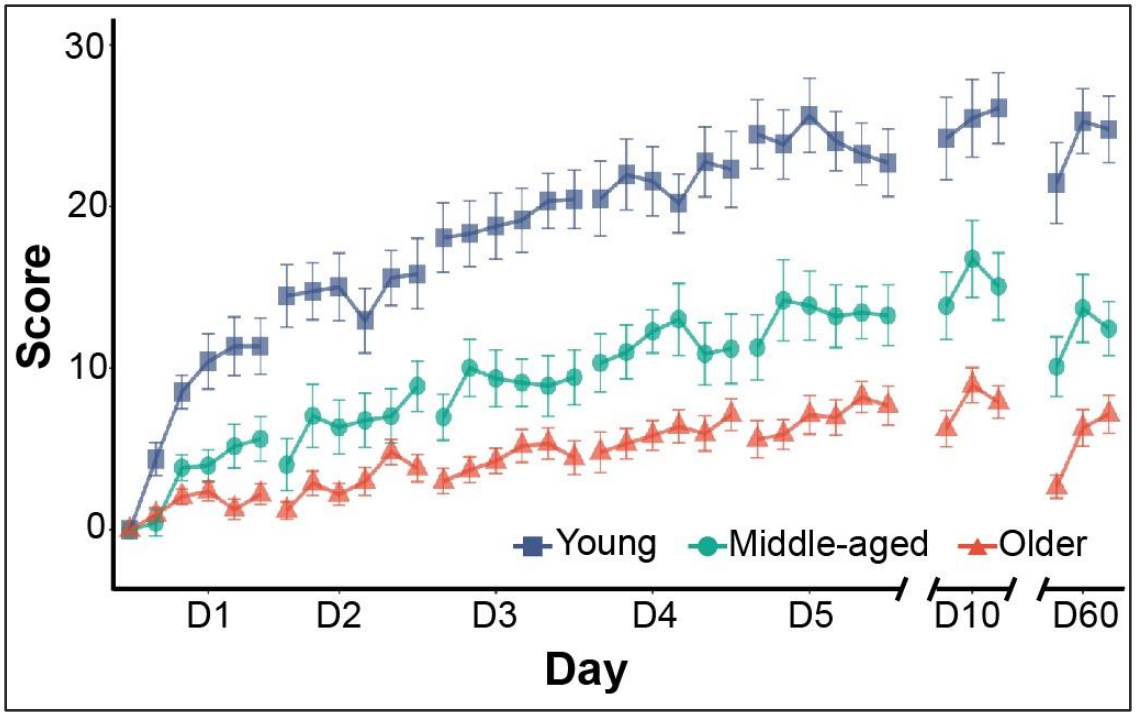
20 min. training



Participants	22	15	15	Σ = 52



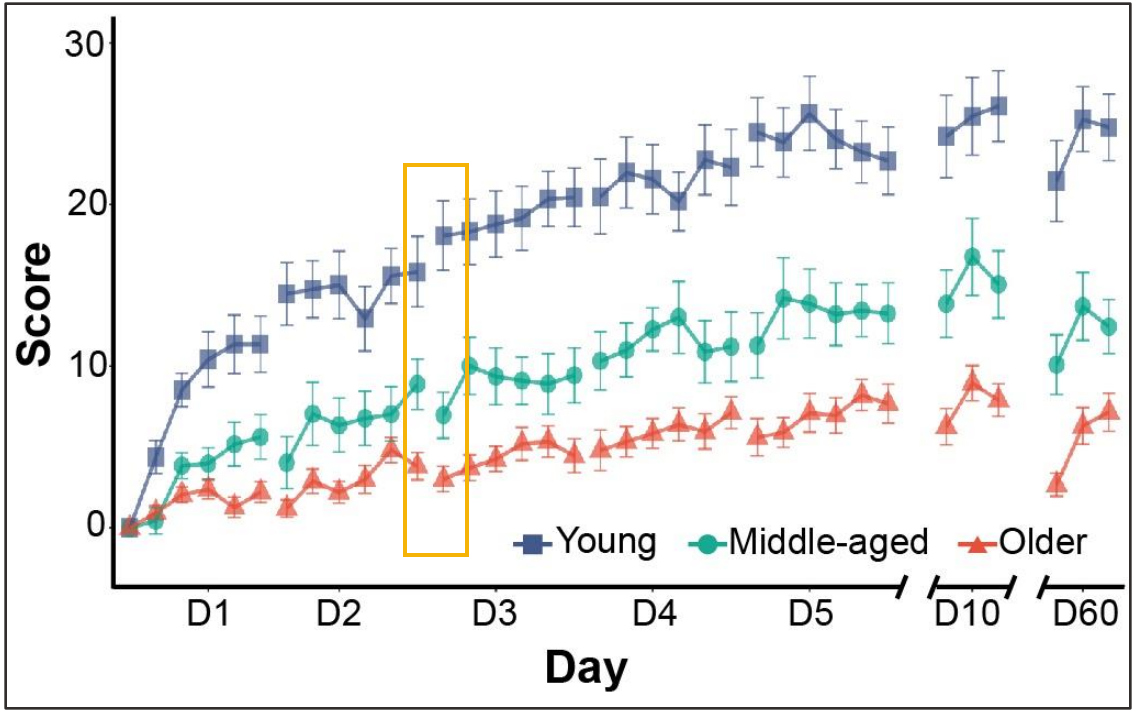
Maceira-Elvira et al., *Science Advances* 2022



a) Overnight improvements

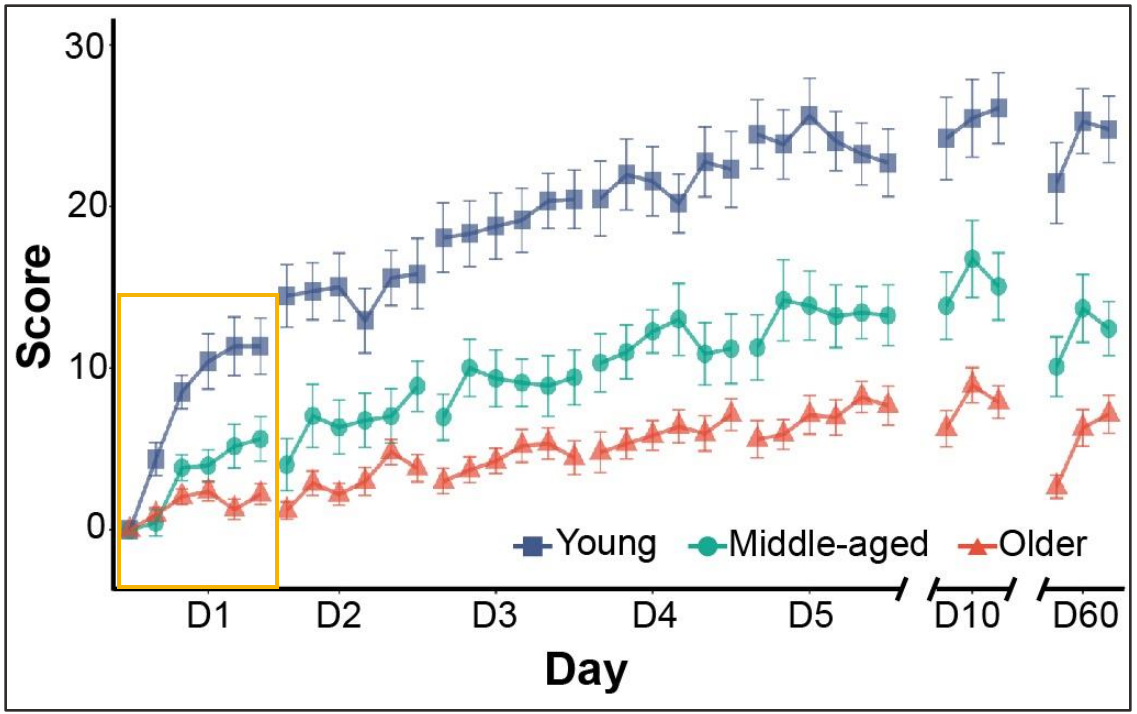
b) Improvement on 1st training day

Maceira-Elvira et al., *Science Advances* 2022



a) Overnight improvements

Maceira-Elvira et al., *Science Advances* 2022

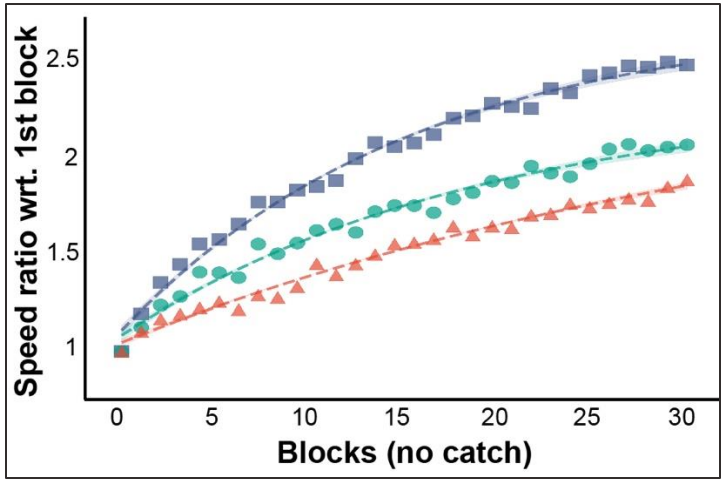


a) Overnight improvements

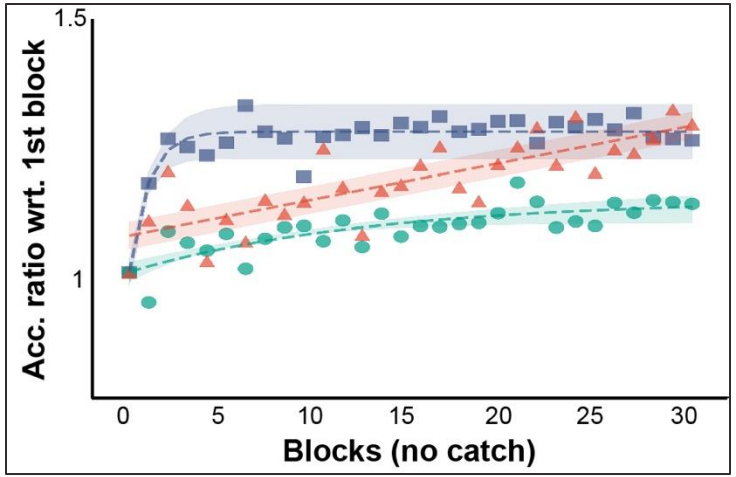
b) Improvement on 1st training day

Maceira-Elvira et al., *Science Advances* 2022

Speed dynamics



Accuracy dynamics

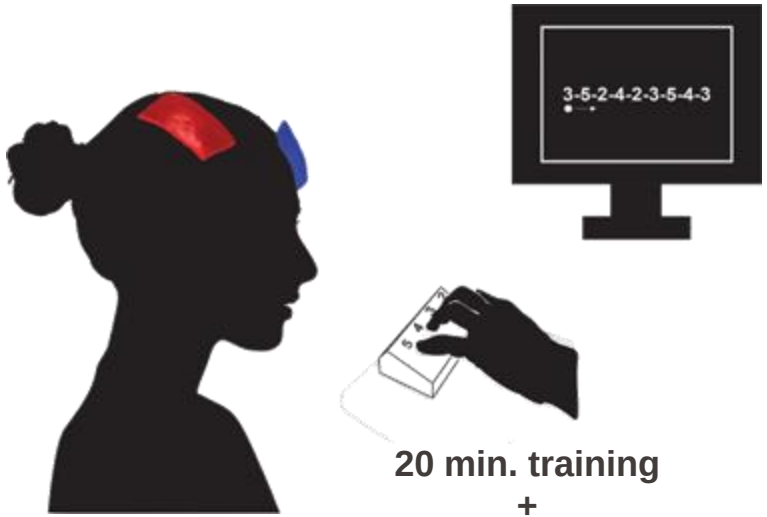


Young

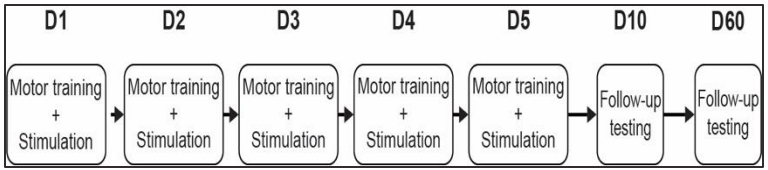
Middle

Older

Maceira-Elvira et al., *Science Advances* 2022



20 min. training
+
stimulation

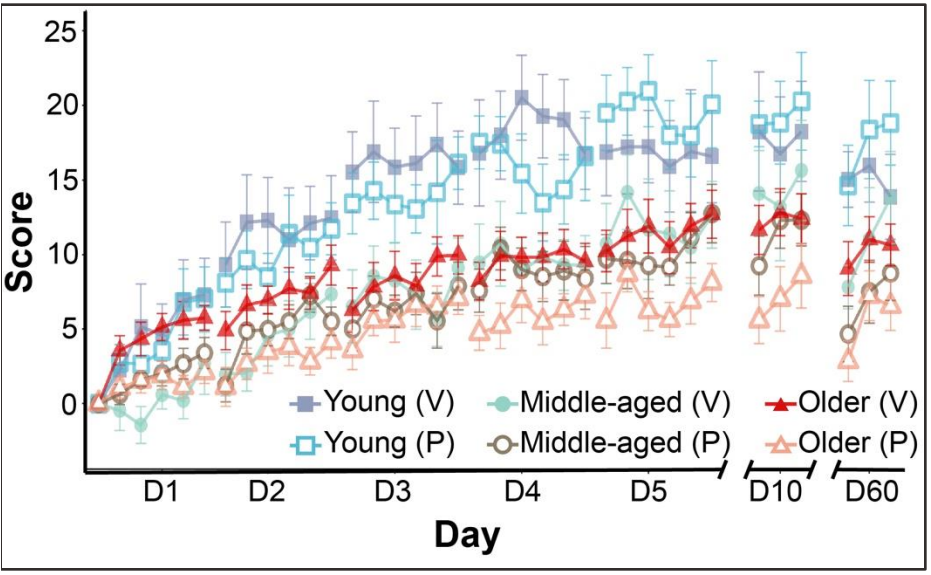


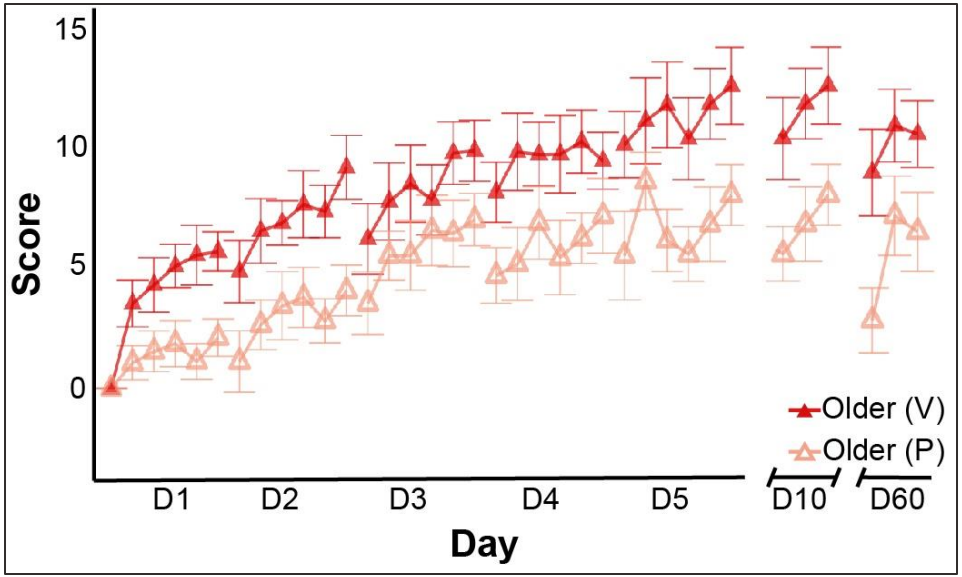
Participants	19	19	23	Σ = 61

Stimulation

- Right M1, region controlling left hand
- Double-blind, placebo-controlled

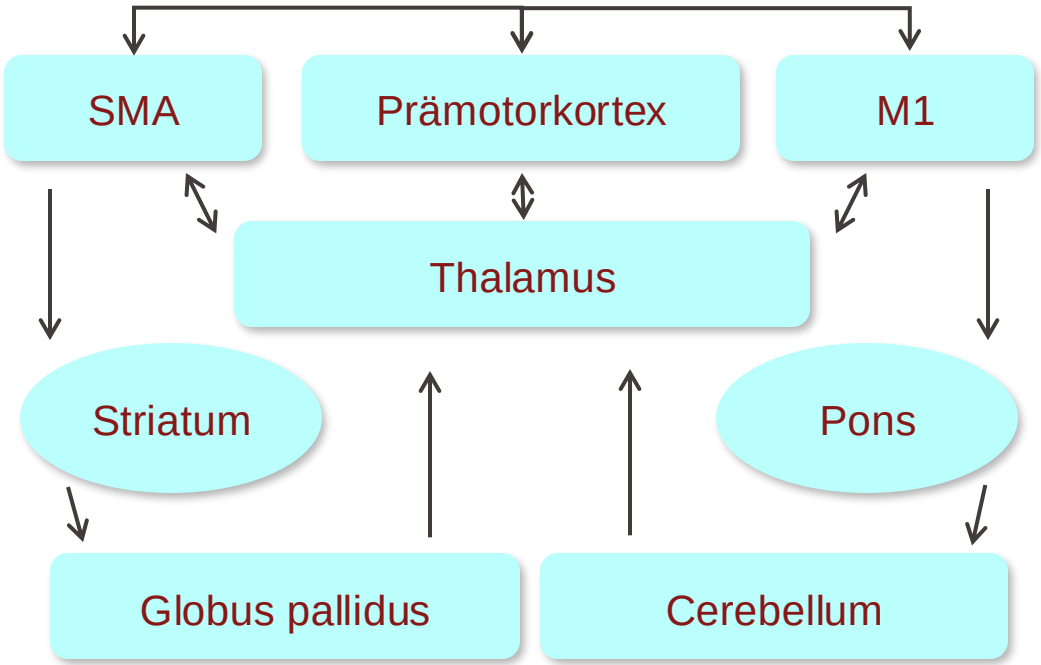
Maceira-Elvira et al., *Science Advances* 2022





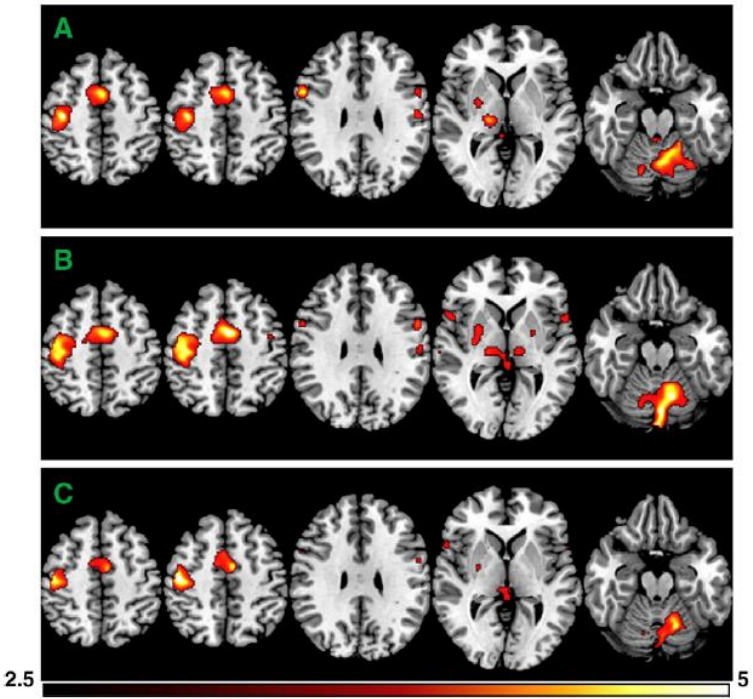
Maceira-Elvira et al., *Science Advances* 2022

Motor Learning: Interregional interactions in the motor system

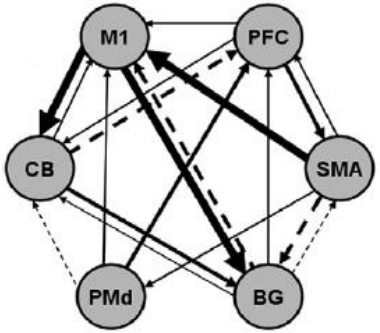


nach Doyon et al, 2003. Neuropsychologia, 41(3); 252–262

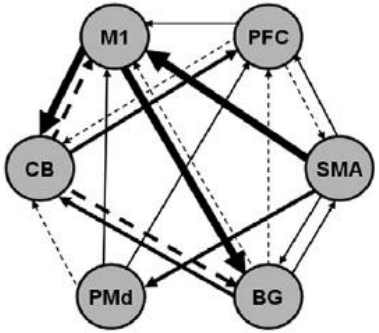
Motor Learning: Interregional interactions in the motor system

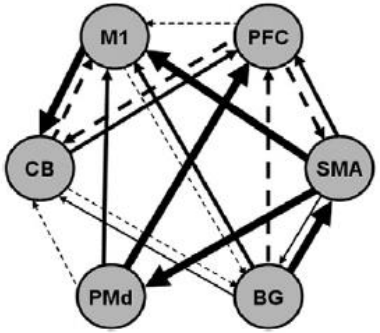


Pre-Training

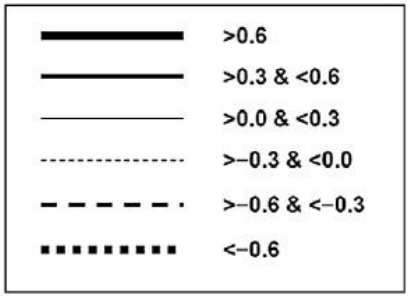


2 weeks post-training

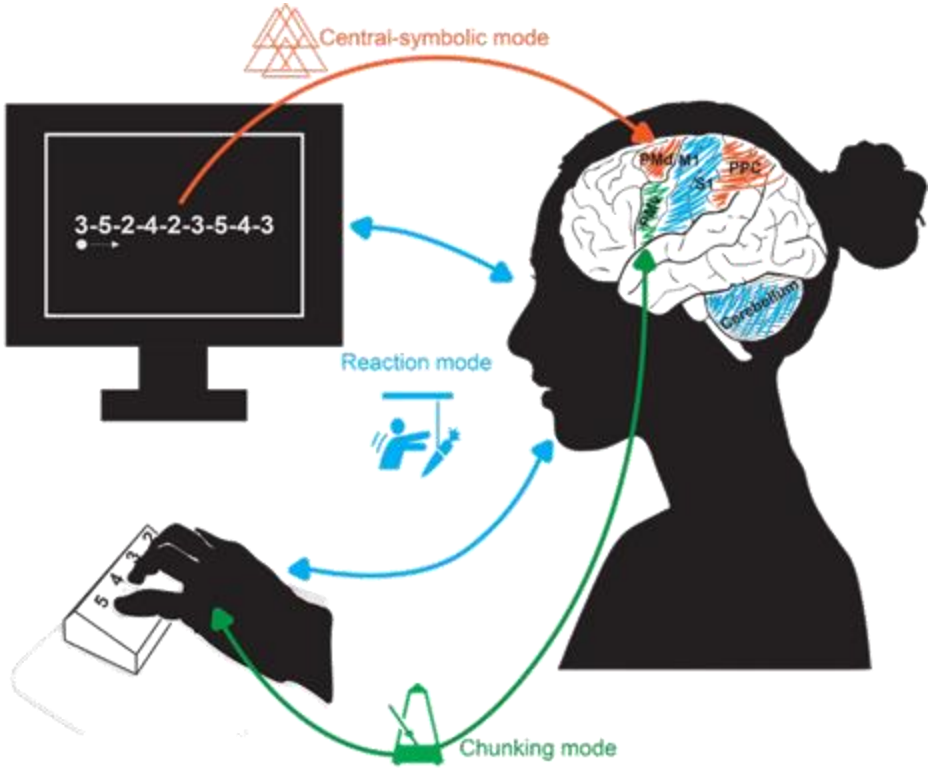




4 weeks post-training



Ma et al, 2010. Brain Research, 1318; 64-76



*C-SMB: Cognitive framework for Sequential Motor Behavior (Verwey et al., 2014)

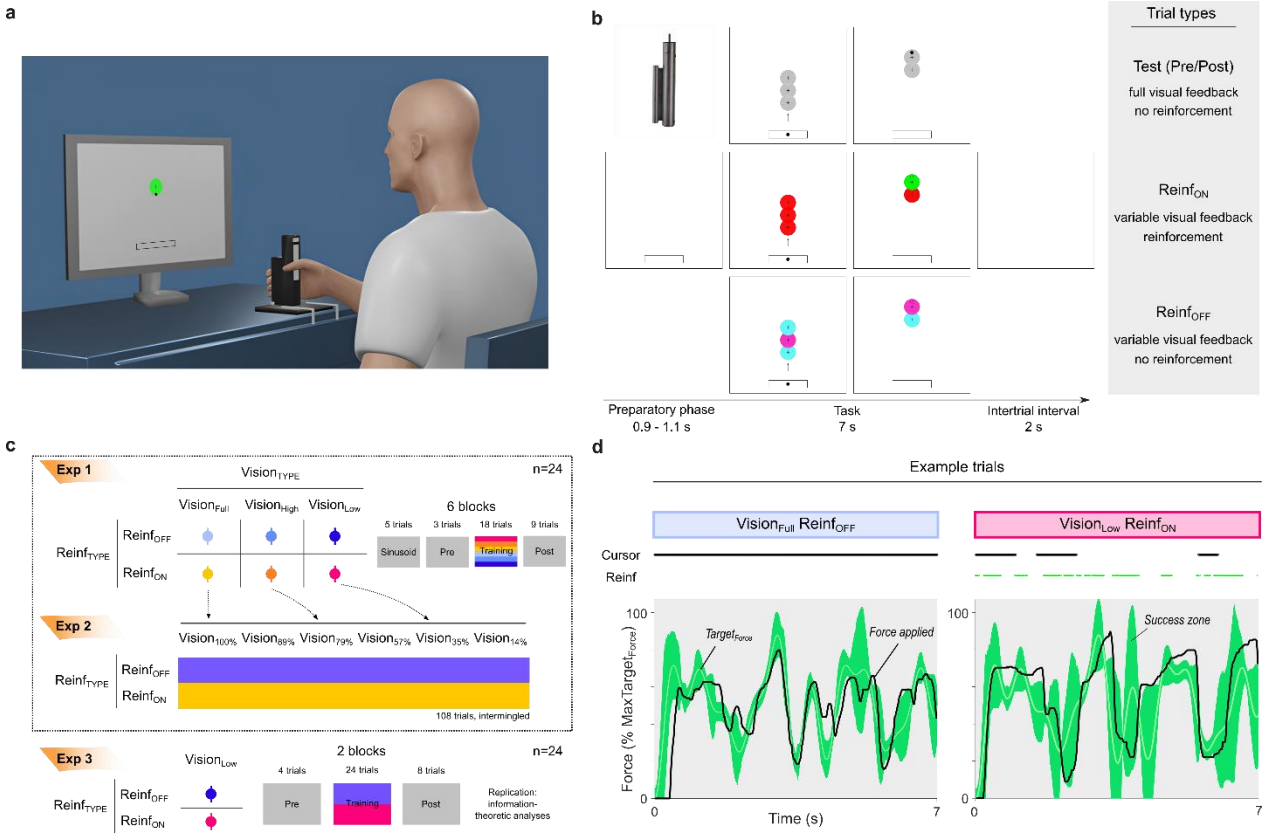
- M1-S1-Cerebellum network (Laird et al., 2011)
- Spatial coordinates in premotor and parietal (Yokioi & Diedrichsen, 2019)
- Temporal coordinates in premotor (Kornysheva & Diedrichsen, 2014)
- Spatial coordinates precede temporal coordinates (Hikosaka et al., 1999)

Maceira-Elvira et al., *Science Advances* 2022

Motor learning –

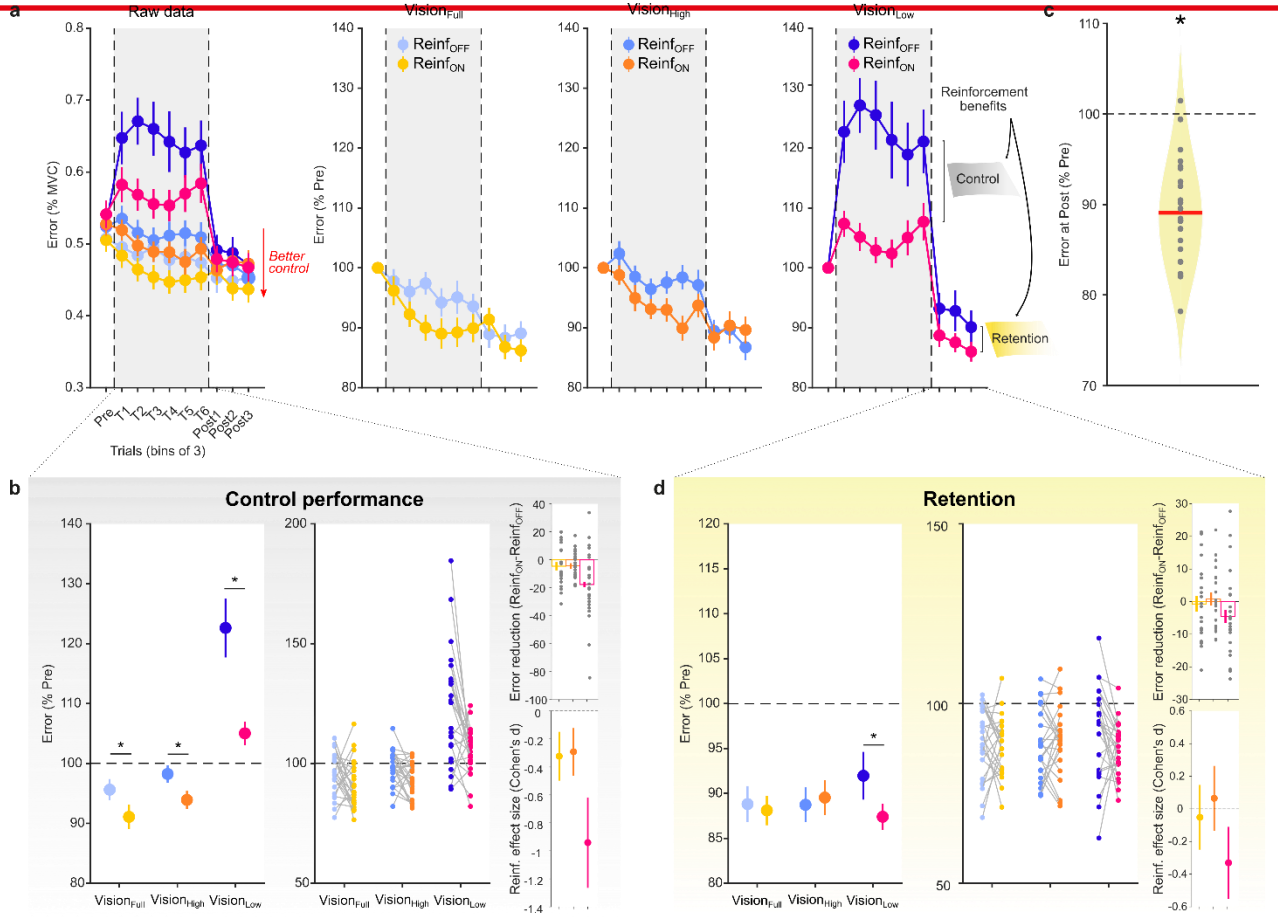
modulated by behavioral aspects like effort, reward, reinforcement

Motor learning – re-enforcement

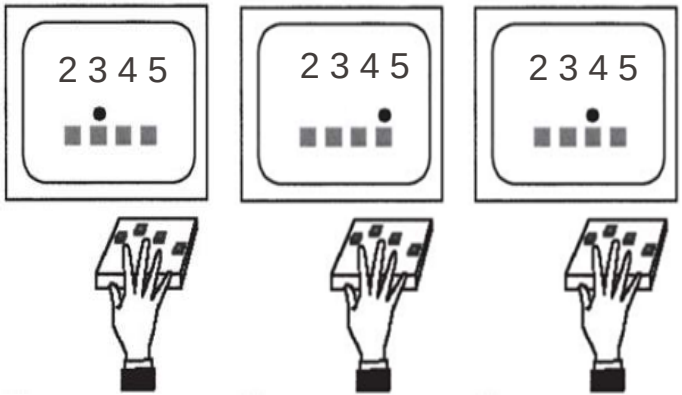


Vassiliadis *et al., 2024* Nature Human Behavior; Vassiliadis *et al.*, under review

Motor learning – re-enforcement



Vassiliadis *et al., 2024* Nature Human Behavior; Vassiliadis *et al.*, under review



3 groups of subjects :

(A) Start: 0$, the better the performance the more money

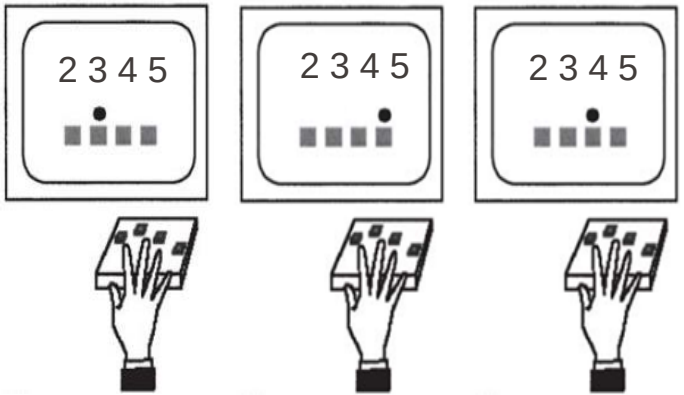
➔ Reward: total 60$

(B) Start: 120$, the more errors the less money

➔ punishment: total 60$

(C) Fixed amount: 60$

Abe et al., *Curr Biol* 2011



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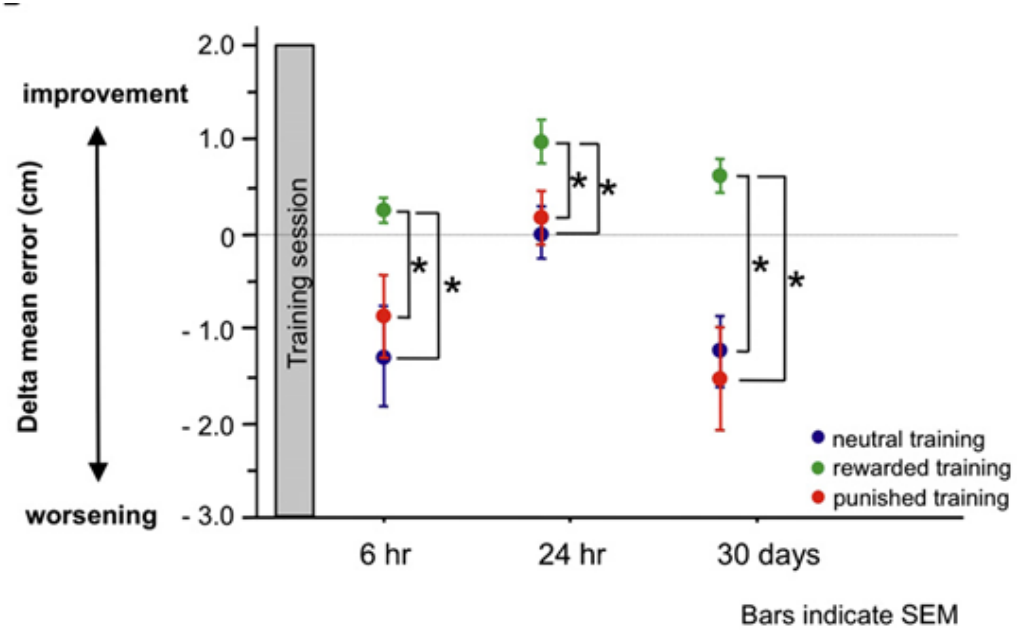
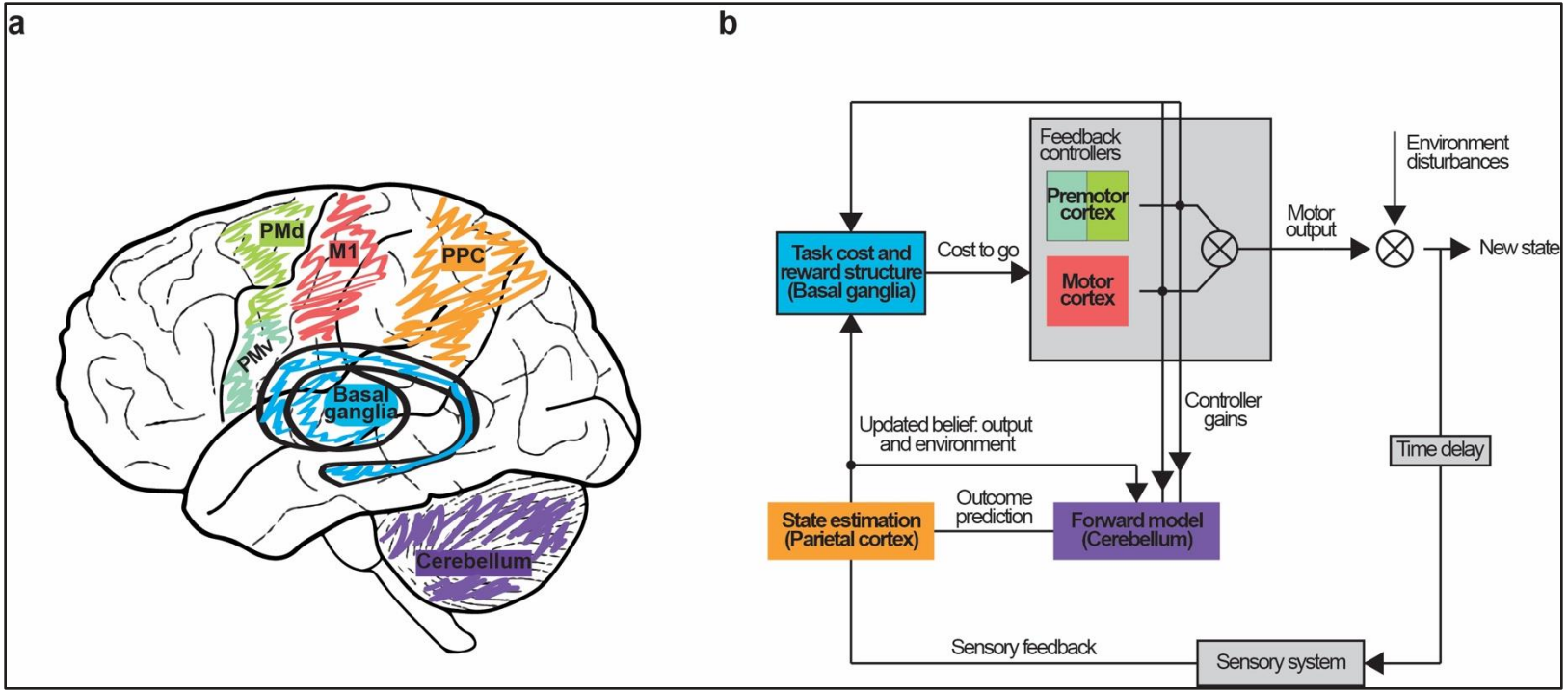


Reward modulates the success of learning

Abe et al., *Curr Biol* 2011



*Based on the model proposed by Shadmehr & Krakauer in 2008

Is the motor cortex involved in language processing?

- Representation of action related language
- Acquisition by Hebbian learning

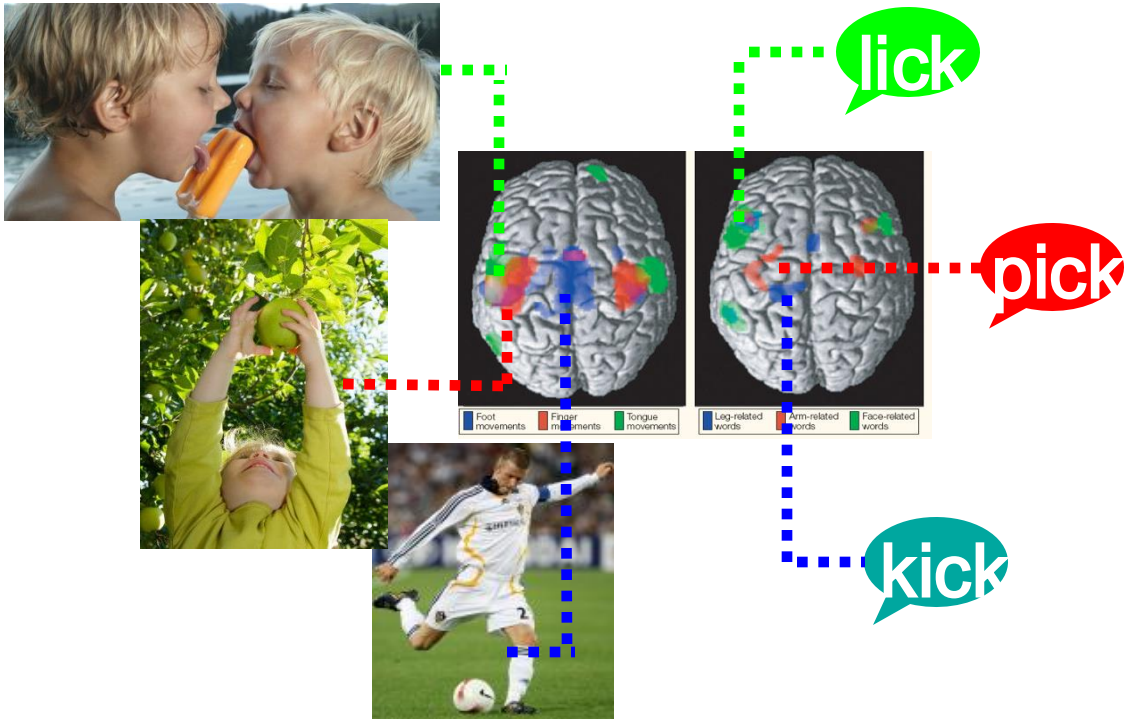


Fig. 1: adapted and modified from Pulvermüller, Nature Rev Neuroscience, 2005.

Pulvermüller, Hauk, Hummel, 2000, 2001, Hauk et al. 2008

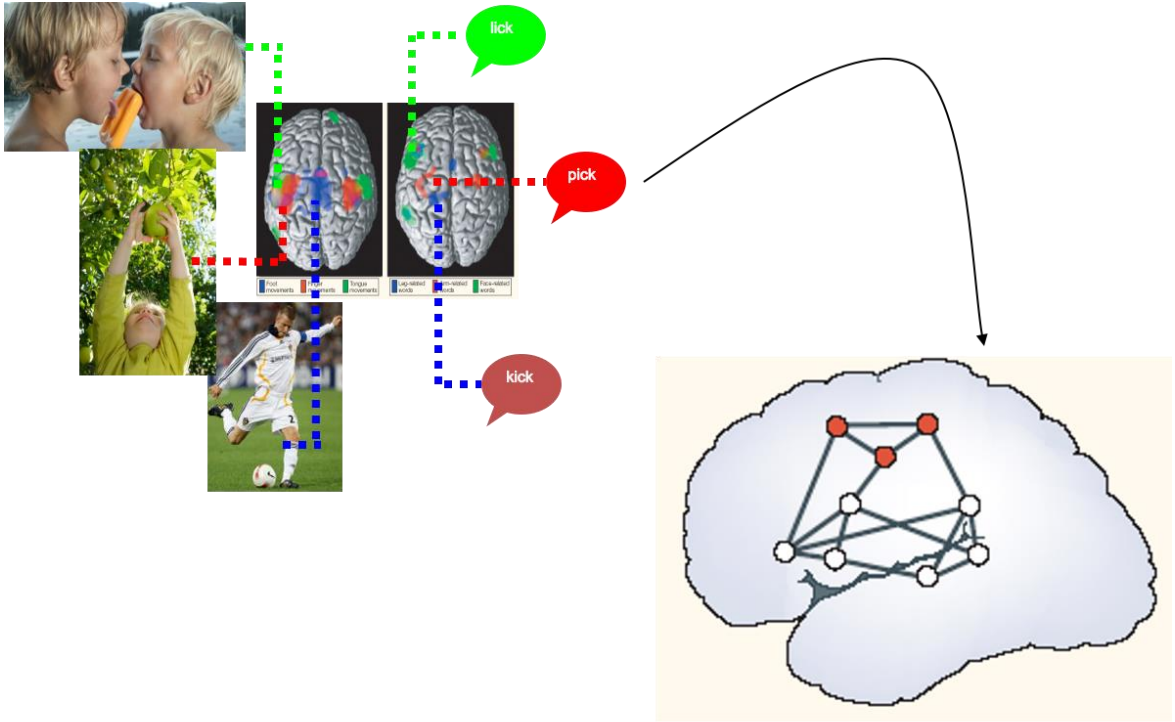


Fig. 1: adapted and modified from Pulvermüller, Nature Rev Neuroscience, 2005.

Liuzzi et al. Current Biology 2010

Motor systems consists of

- Cortical
- Subcortical
- Spinal
- Peripheral parts
- Can be evaluated non-invasively by neuroimaging and electrophysiological measures

Motor behavior

- Simple (reflexes) to Complex (learning), modulated by reward, effort etc.
- Implemented by network interactions
- Can be modulated by behavioral or neuromodulation interventions

Pathological conditions affecting the motor system

- Stroke (see next course)
- Spinal cord injury (see course G. Courtine)
- Parkinson (see course O. Blanke)
- Tourette Sd
- Dystonia
- Amyotrophic lateral sclerosis (ALS)
- Muscle dystrophies
- Spino-cerebellar degeneration

Questions?