

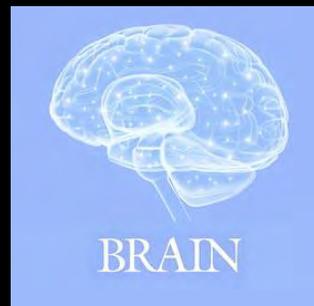


Gatsby Computational
Neuroscience Unit

Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

Anna Sadnicka PhD

Senior Clinical Research Fellow, Gatsby Computational Neuroscience Unit
Honorary Senior Lecturer, Department of Clinical and Movement Neurosciences, University College London
Honorary Neurology Consultant, National Hospital for Neurology and Neurosurgery



The National
Brain Appeal



Rosetrees
Supports the best medical research

Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

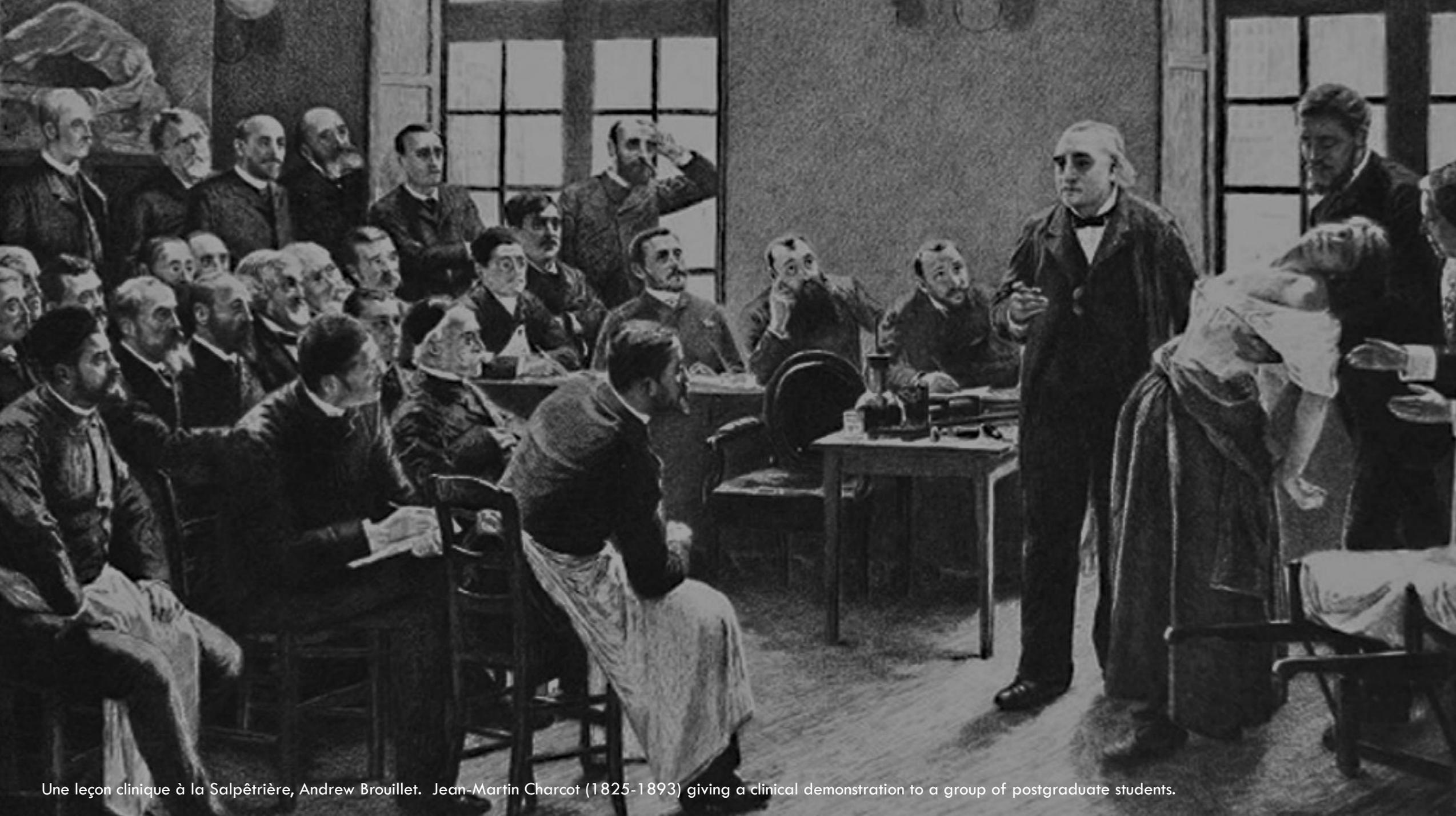
01 A Clinical Snapshot

02 Maladaptive **Plasticity** in Expert Motor Systems?

03 Disrupted Sensorimotor **Representations**?

04 A **Motor Control Framework** for Skill Failure

05 Translating Mechanism into **Motor Repair**



Une leçon clinique à la Salpêtrière, Andrew Brouillet. Jean-Martin Charcot (1825-1893) giving a clinical demonstration to a group of postgraduate students.

Definitions of movement disorders phenotypes

Bradykinesia	Slowness of initiation of voluntary movements with progressive reduction in speed and amplitude of repetitive actions.
Chorea	Irregular, purposeless, abrupt, rapid, brief, jerky, un-sustained movements that flow randomly from one part of the body to another.
Dystonia	Sustained muscle contractions which frequently cause twisting, repetitive, and patterned movements or abnormal postures.
Myoclonus	Sudden, brief, shock-like movements caused by muscle contractions.
Tics	Simple or co-ordinated, repetitive or sequential movements, gestures, and utterances that mimic fragments of normal behaviour.
Tremor	Involuntary, rhythmic, oscillatory movement of a body part.

Consistent movement statistic defines each phenotype

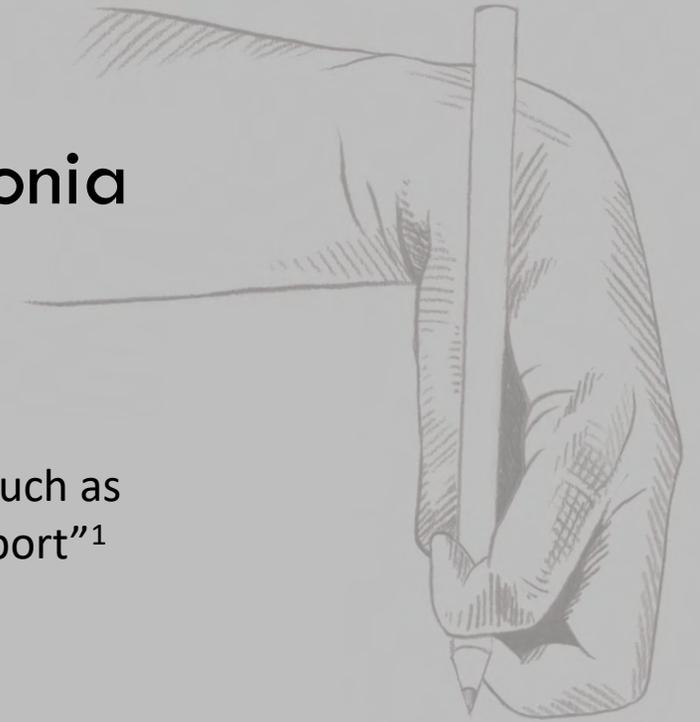


Bradykinesia	Slowness of initiation of voluntary movements with progressive reduction in speed and amplitude of repetitive actions.
Chorea	Irregular, purposeless, abrupt, rapid, brief, jerky, un-sustained movements that flow randomly from one part of the body to another.
Dystonia	Sustained muscle contractions which frequently cause twisting, repetitive, and patterned movements or abnormal postures.
Myoclonus	Sudden, brief, shock-like movements caused by muscle contractions.
Tics	Simple or co-ordinated, repetitive or sequential movements, gestures, and utterances that mimic fragments of normal behaviour.
Tremor	Involuntary, rhythmic, oscillatory movement of a body part.

Clinical definition of task-specific dystonia

“Task specific dystonia is a movement disorder that interferes with the performance of a **particular** task or skill such as writing, playing a musical instrument or participating in a sport”¹

¹NIH - US National Library of Medicine



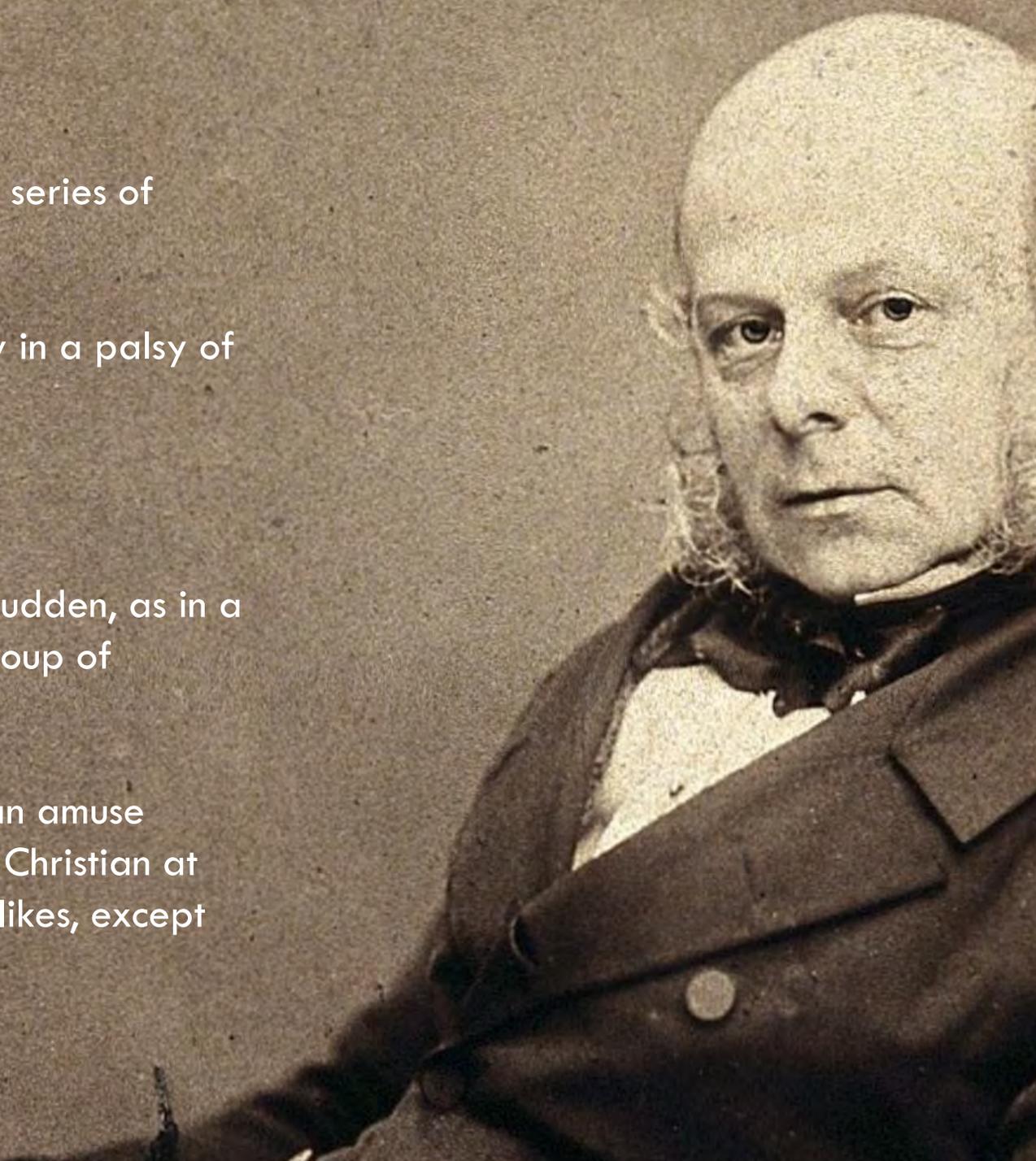
British surgeon Samuel Solly (1805–1871) presented a series of clinical lectures on “scrivener's palsy:

The disease, as the name implies, shows itself outwardly in a palsy of the writing powers.

The muscles cease to obey the mandates of the will.

It comes on very insidiously ... the loss of power is not sudden, as in a paralytic stroke nor is it a complete paralysis of any group of muscles.

The paralysed [sic] scrivener, though he cannot write, can amuse himself in his garden, can shoot, and cut his meat like a Christian at the dinner-table; indeed he can do almost anything he likes, except earn his daily bread as a scribbler ...





Videos provided by Professor Steven Frucht



Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

01 A Clinical Snapshot

02 Maladaptive **Plasticity** in Expert Motor Systems?

03 Disrupted Sensorimotor **Representations**?

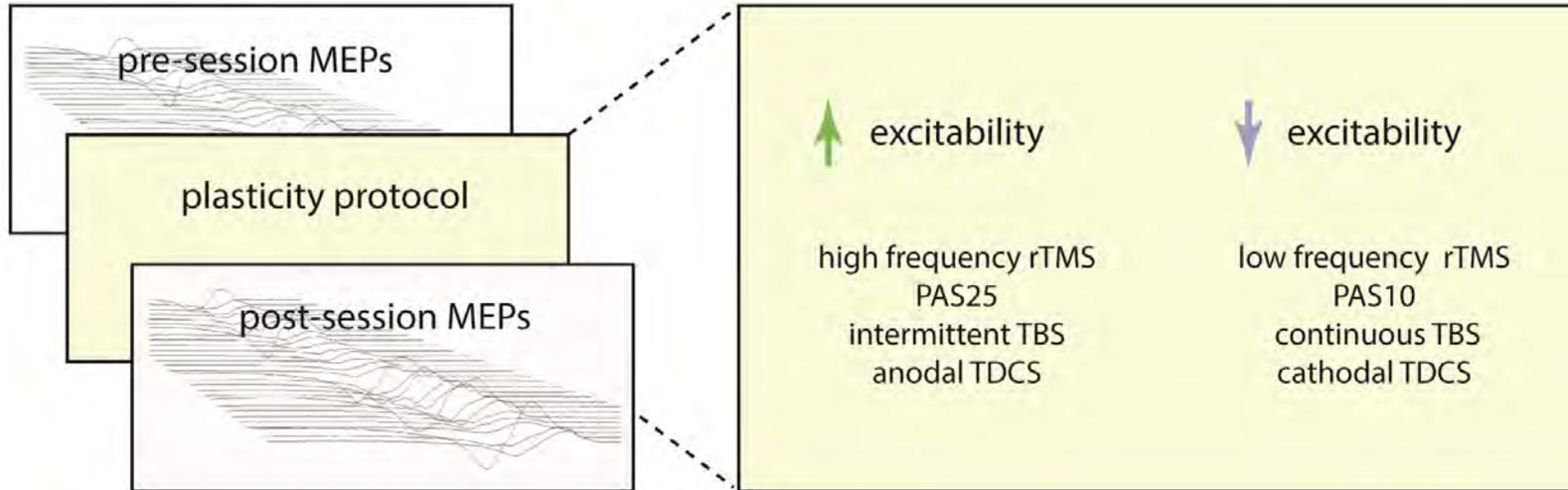
04 A **Motor Control Framework** for Skill Failure

05 Translating Mechanism into **Motor Repair**

Studying plasticity in humans

Non-invasive brain stimulation (NIBS)

Plasticity paradigms that ***predictably*** and ***consistently*** modify corticospinal excitability



Nomenclature:

MEP = motor evoked potential
rTMS = repetitive transcranial magnetic stimulation
PAS = paired associative stimulation
PAS25 or PAS10 = interstimulus interval separated by 25ms or 10ms
TBS = theta burst stimulation
TDCS = transcranial direct current stimulation

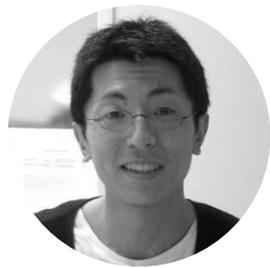
RAPID REPORT

Cerebellar modulation of human associative plasticity

Masashi Hamada¹, Gionata Strigaro¹, Nagako Murase^{1,2}, Anna Sadnicka¹, Joseph M. Galea¹, Mark J. Edwards¹ and John C. Rothwell¹

¹*Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, Queen Square, London WC1N 3BG, UK*

²*Neurology Department, National Kyoto Hospital, 1-1 Mukoubata-cho, Fukakusa, Fushimi-ku, Kyoto city, Kyoto, 612-8555, Japan*



Masashi
Hamada

Key point

- Increases in the strength of synaptic connections in the motor cortex (long term potentiation) can be induced in humans by repetitively pairing peripheral nerve stimuli and motor cortex transcranial magnetic stimuli given 21–25 ms apart – paired associative stimulation (PAS).
- This ‘associative plasticity’ effect has been assumed to relate to synchronicity between sensory input and motor output, with a similar mechanism proposed to underlie effects at all inter-stimulus intervals.
- Here we show that modulation of cerebellar activity using transcranial direct current stimulation can abolish associative plasticity in the motor cortex, but only for sensory/motor stimuli paired at 25 ms, not at 21.5 ms.
- The results indicate that human associative plasticity can be affected by cerebellar activity and that at least two different mechanisms are involved in the effects previously reported in studies using PAS at different inter-stimulus intervals.

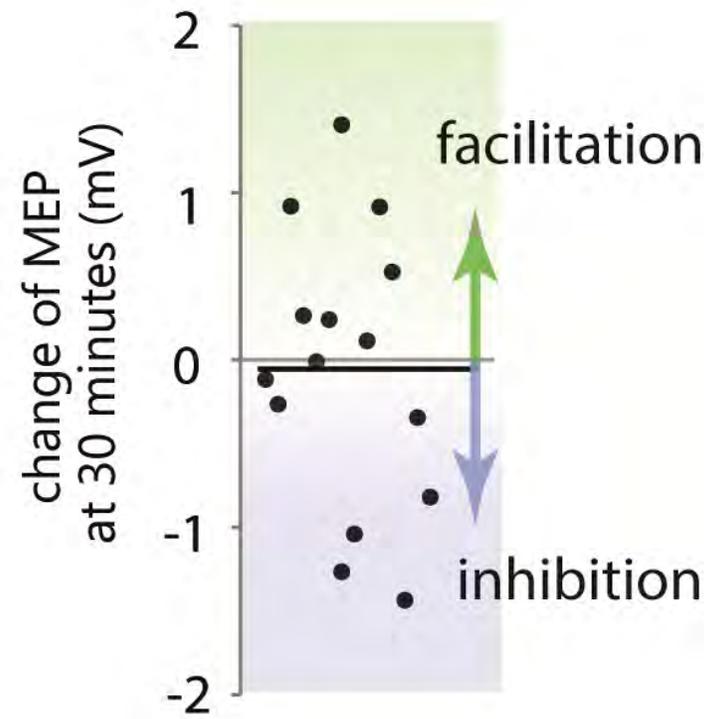


Masashi Hamada

APB

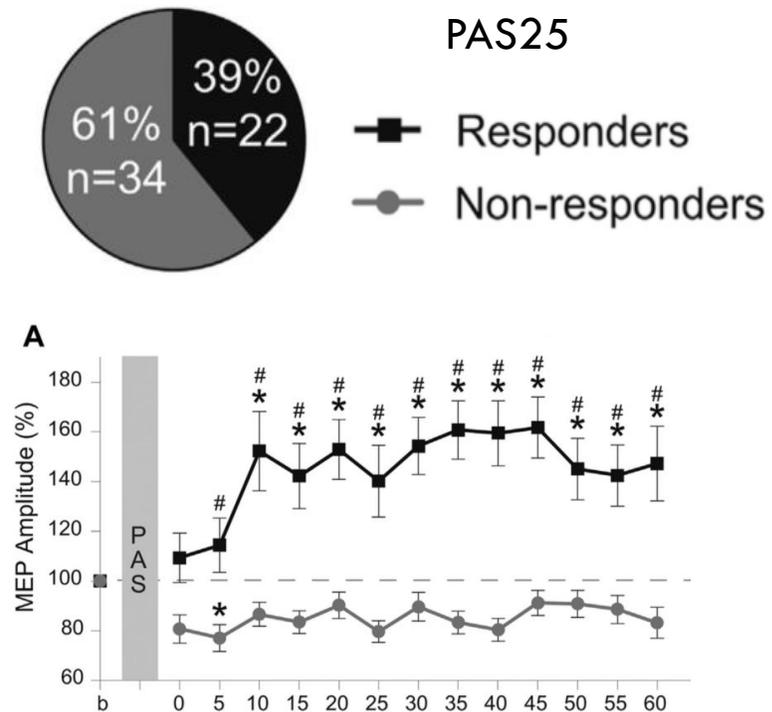


Target muscle

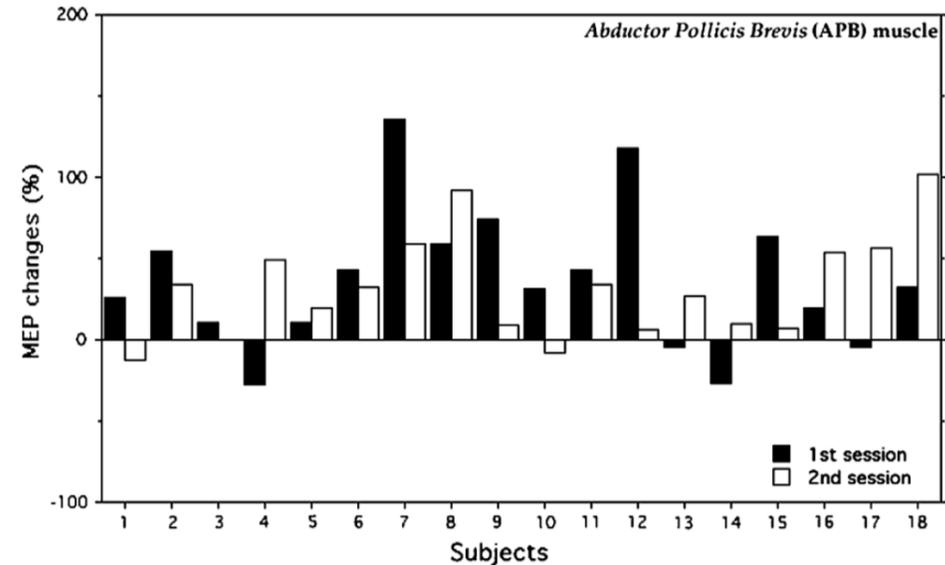


Sources of variability

Inter-individual



Intra-individual variability



López-Alonso V, Cheeran B, Río-Rodríguez D, Fernández-Del-Olmo M. Inter-individual variability in response to non-invasive brain stimulation paradigms. *Brain Stimul.* 2014 May-Jun;7(3):372-80. doi: 10.1016/j.brs.2014.02.004. Epub 2014 Feb 15. PMID: 24630849.

Modulation of corticospinal excitability by paired associative stimulation: Reproducibility of effects and intraindividual reliability . Fratello, 2006

Is plasticity *causally* related to dystonia?

Dystonia is a hyperkinetic movement disorder in which there is too much movement.

The motor cortex as the common final output that controls movement is therefore likely to be comparatively hyperexcitable as too much movement for given context is being produced.

Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

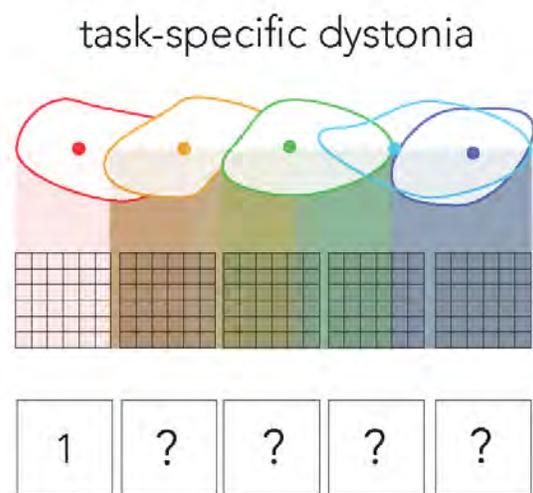
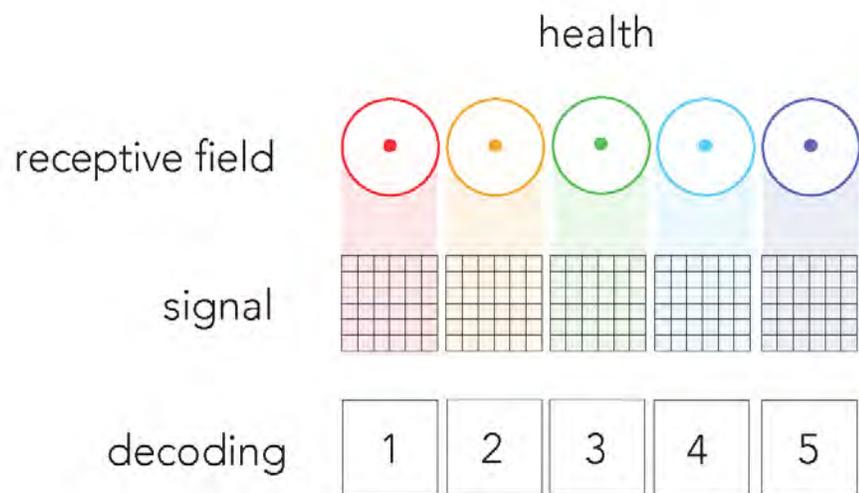
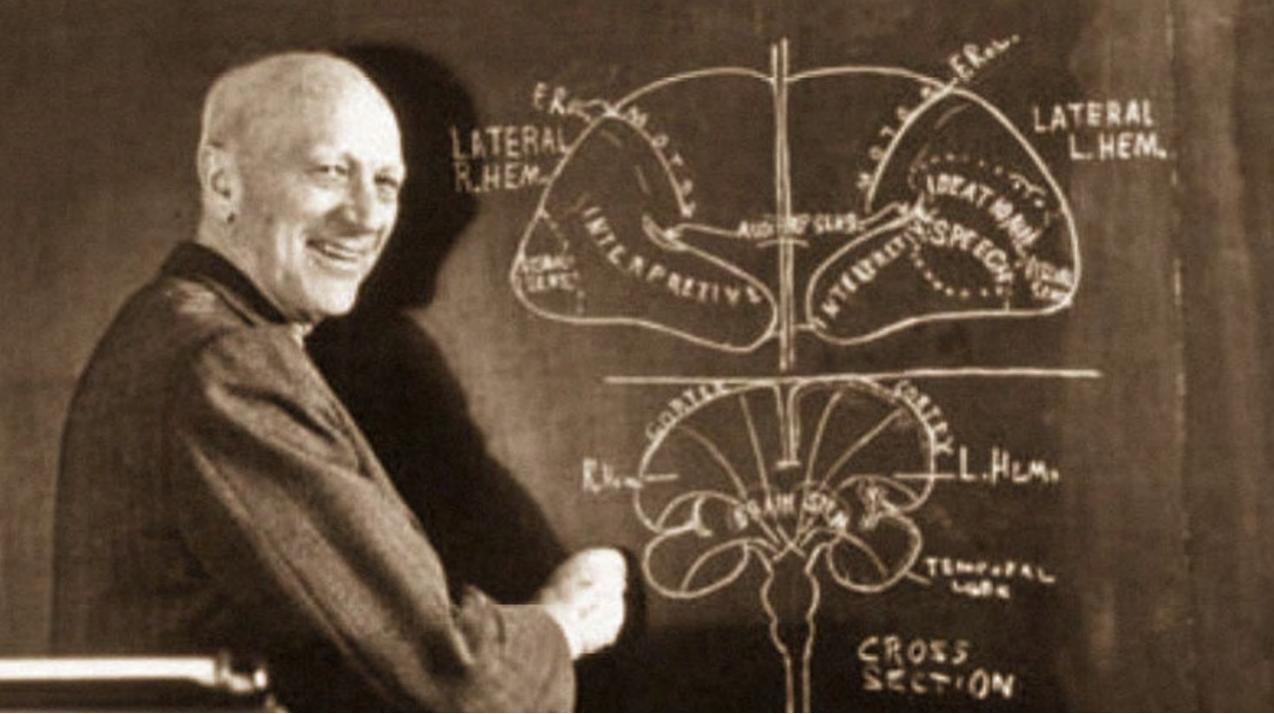
01 A Clinical Snapshot

02 Maladaptive Plasticity in Expert Motor Systems?

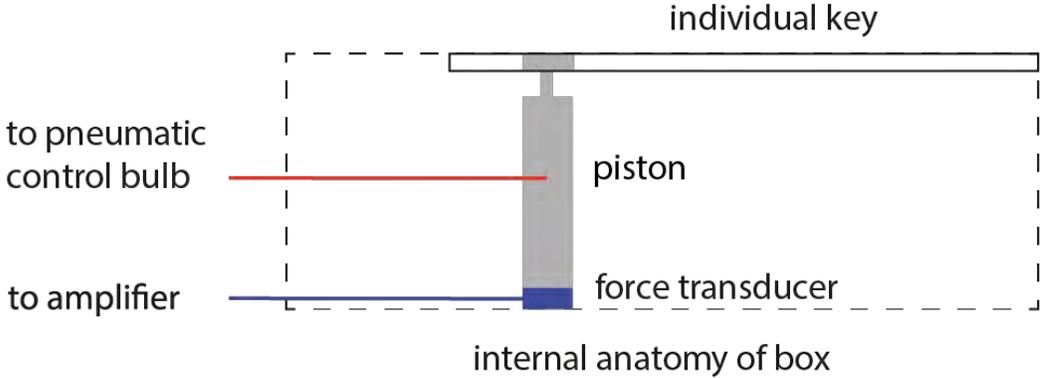
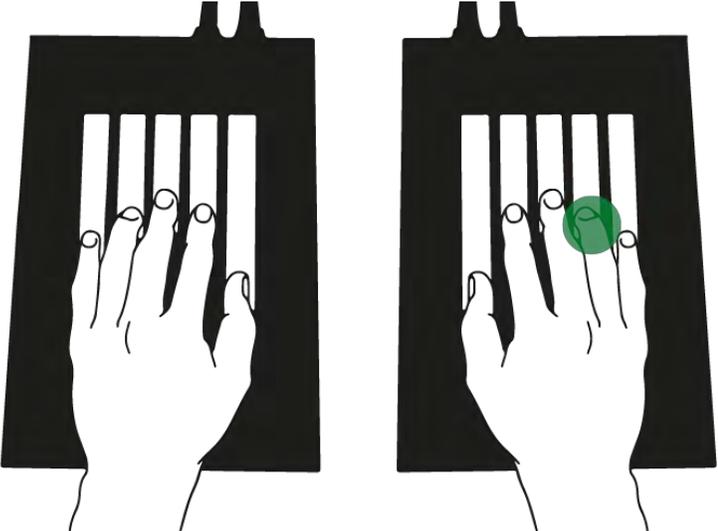
03 Disrupted Sensorimotor **Representations?**

04 A **Motor Control Framework** for Skill Failure

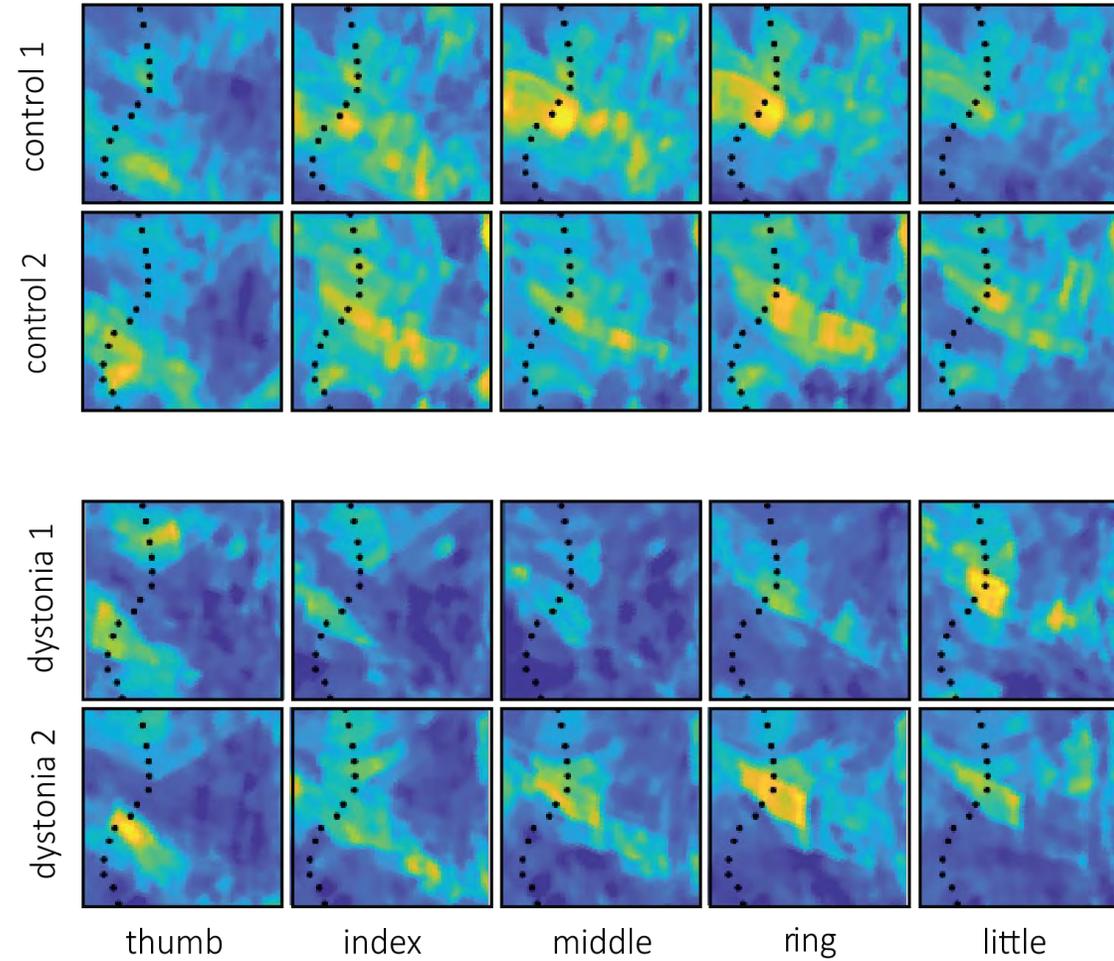
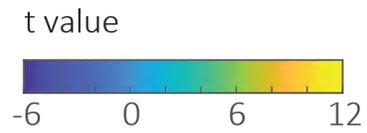
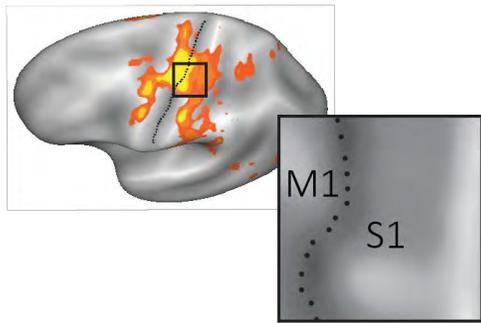
05 Translating Mechanism into **Motor Repair**



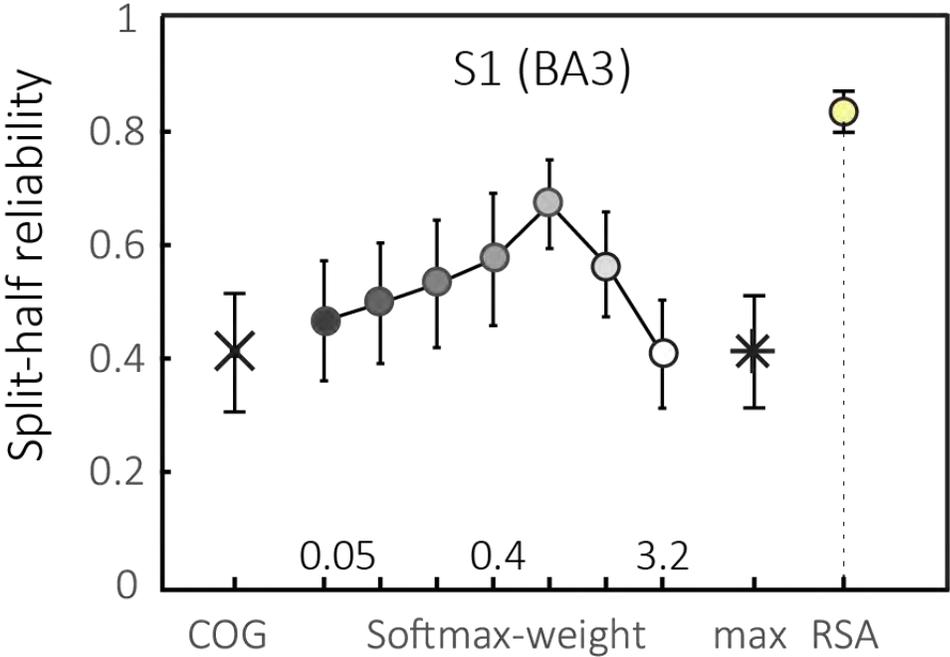
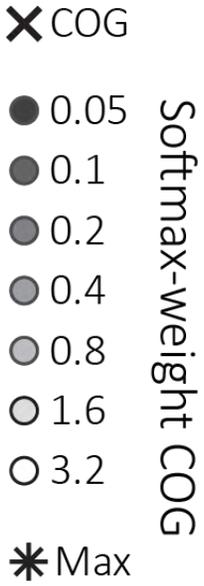
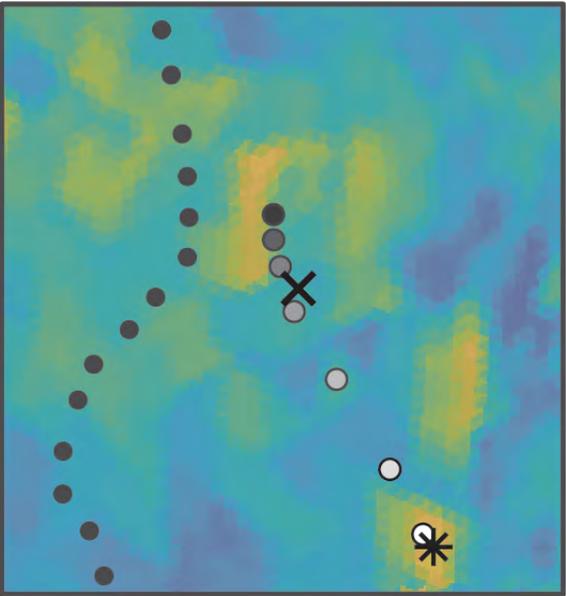
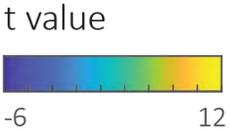
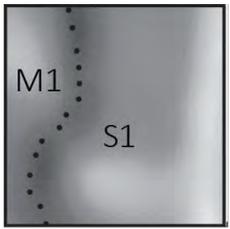
Re-examining the 'homunculus' ...



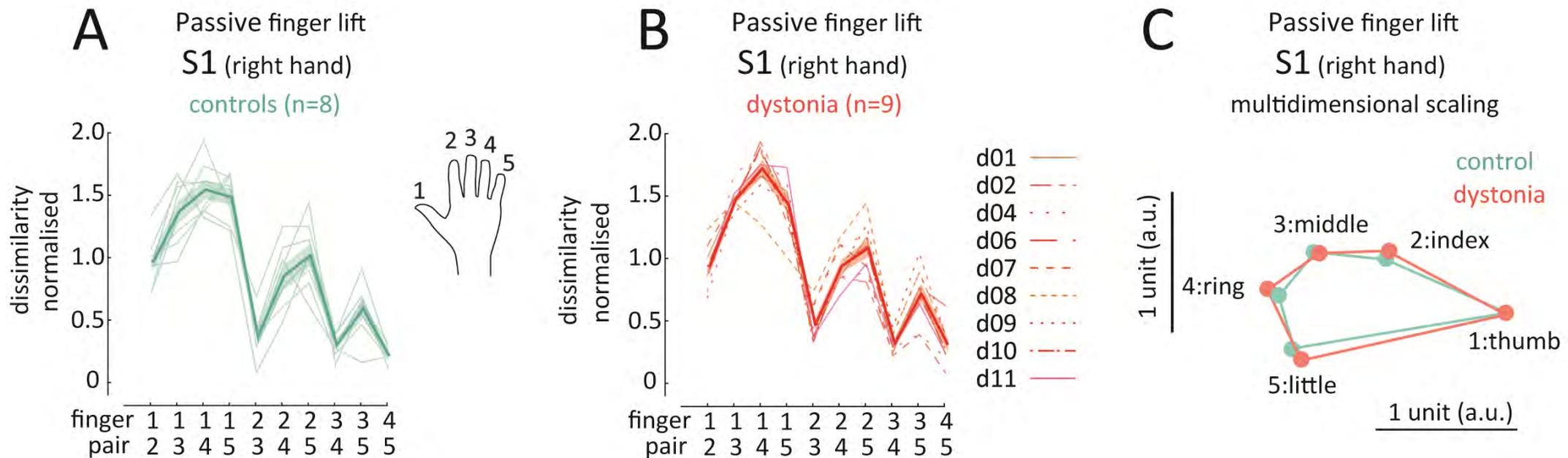
Re-examining the 'homunculus' ...



Re-examining the 'homunculus' ...



Re-examining the 'homunculus' ...



Sadnicka A, Wiestler T, Butler K, Altenmüller E, Edwards MJ, Ejaz N, Diedrichsen J. Intact finger representation within primary sensorimotor cortex of musician's dystonia. *Brain*. 2023 Apr 19;146(4):1511-1522.

Makin T, Krakauer J. Against cortical reorganization (2023) *eLife* 12:e84716.

Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

01 A Clinical Snapshot

02 Maladaptive **Plasticity** in Expert Motor Systems?

03 Disrupted Sensorimotor **Representations**?

04 A **Motor Control Framework** for Skill Failure

05 Translating Mechanism into **Motor Repair**

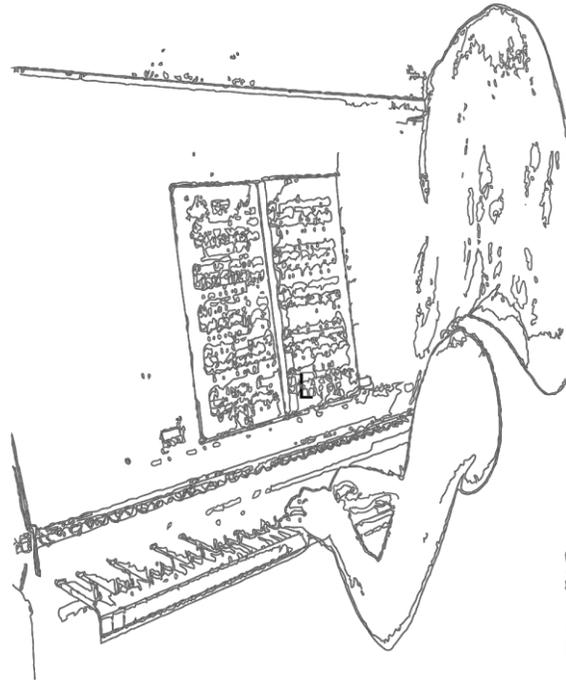
Motor skill learning between selection and execution

Jörn Diedrichsen¹ and Katja Kornysheva^{1,2}

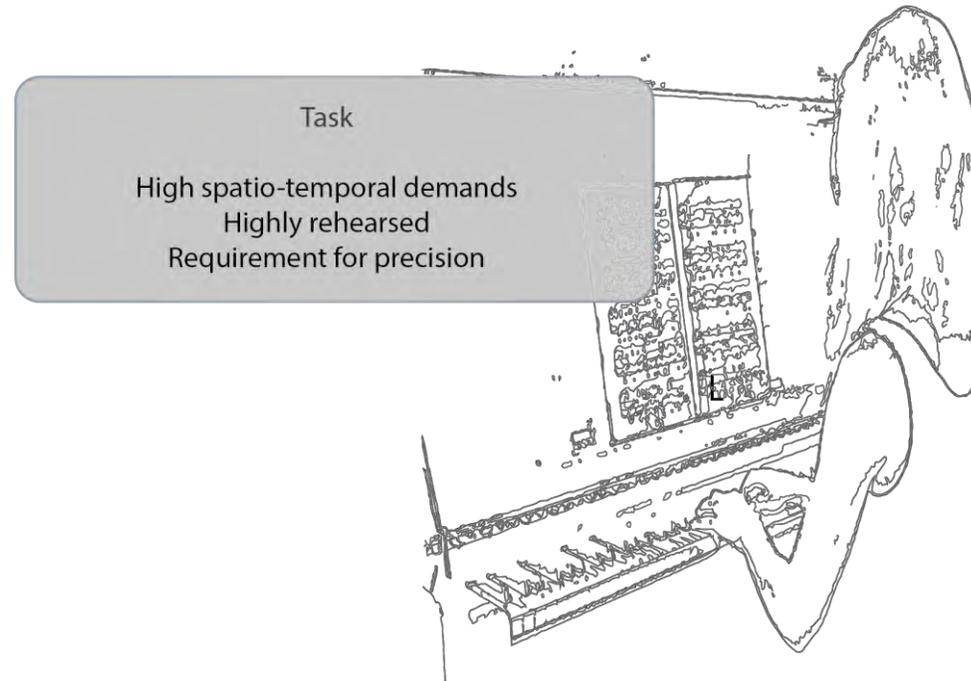
¹Institute of Cognitive Neuroscience, University College London, London, UK

²Department of Neuroscience, Erasmus Medical Center, Rotterdam, The Netherlands

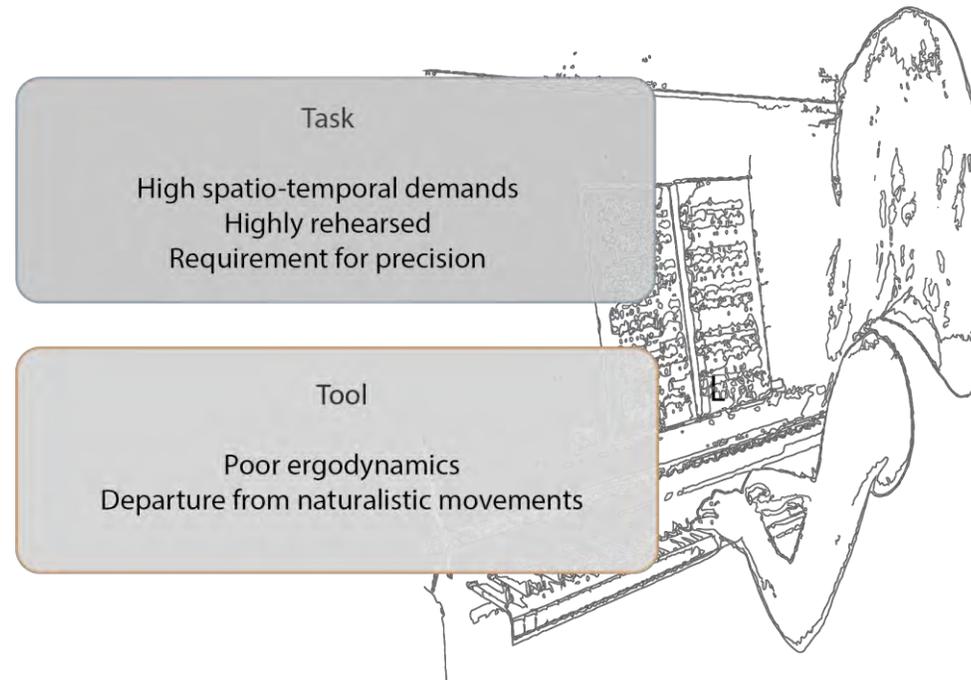
Environment risk factor profile



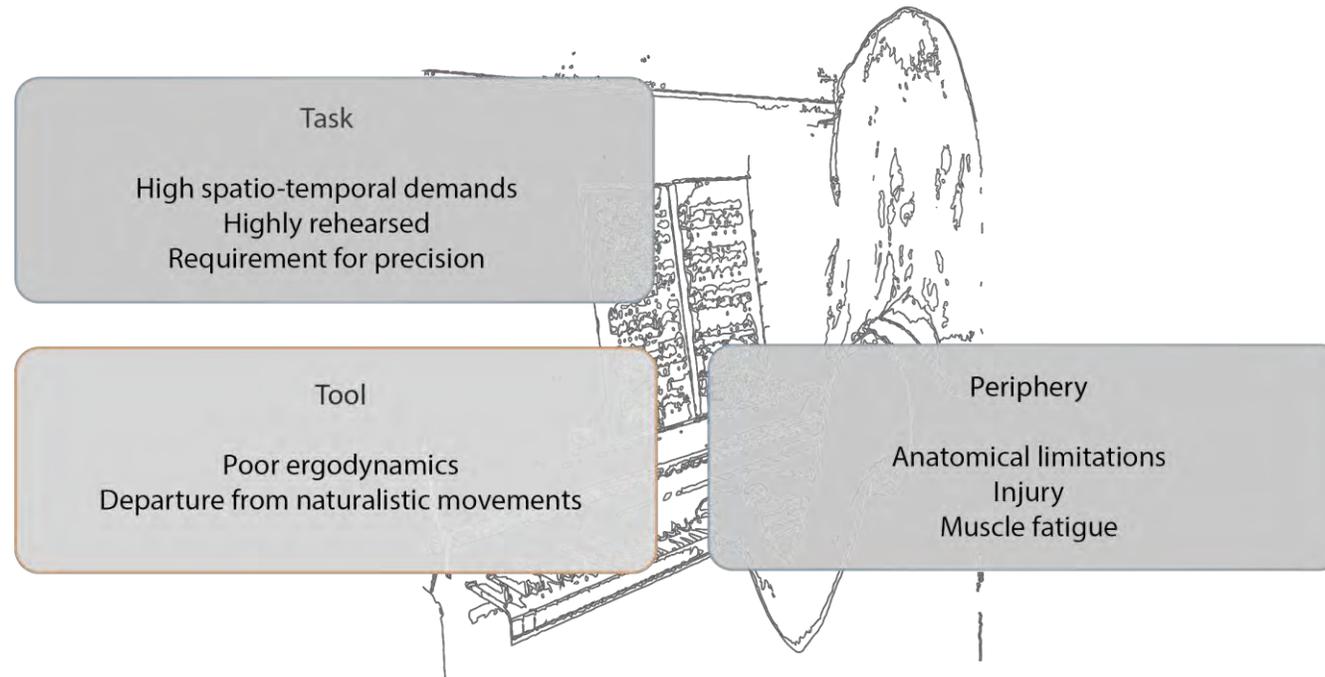
Environment risk factor profile



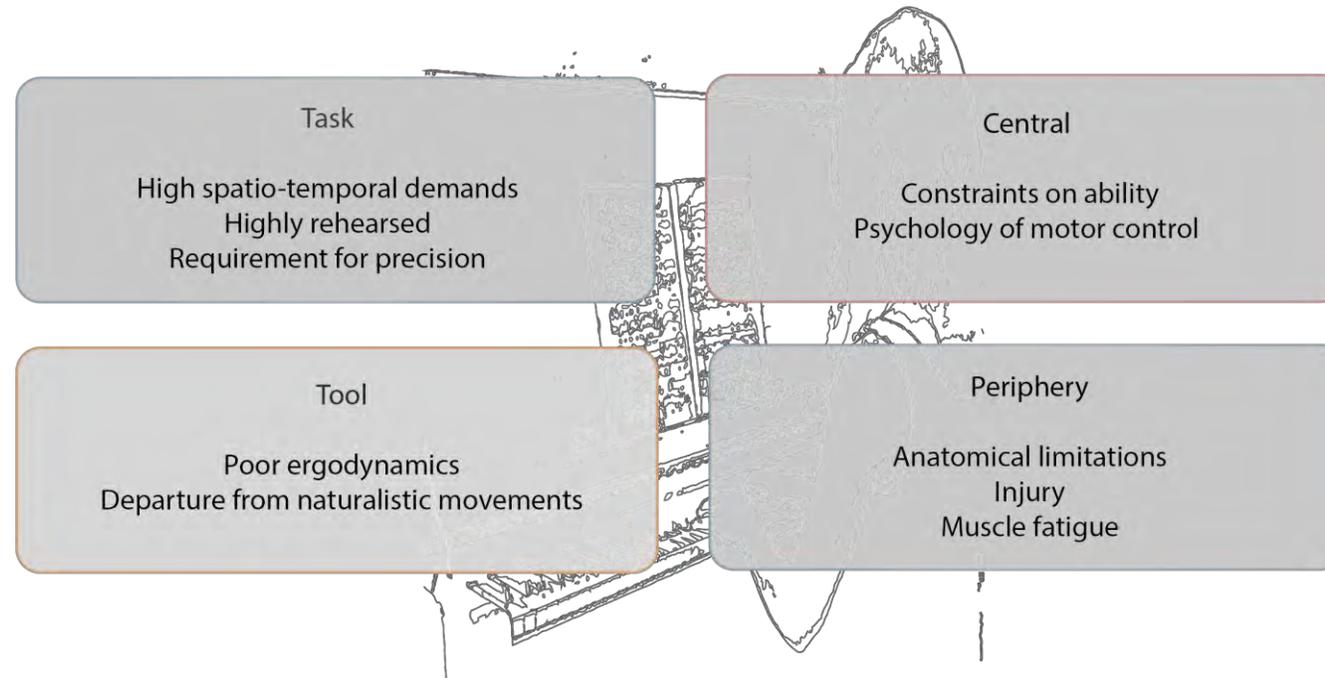
Environment risk factor profile



Environment risk factor profile

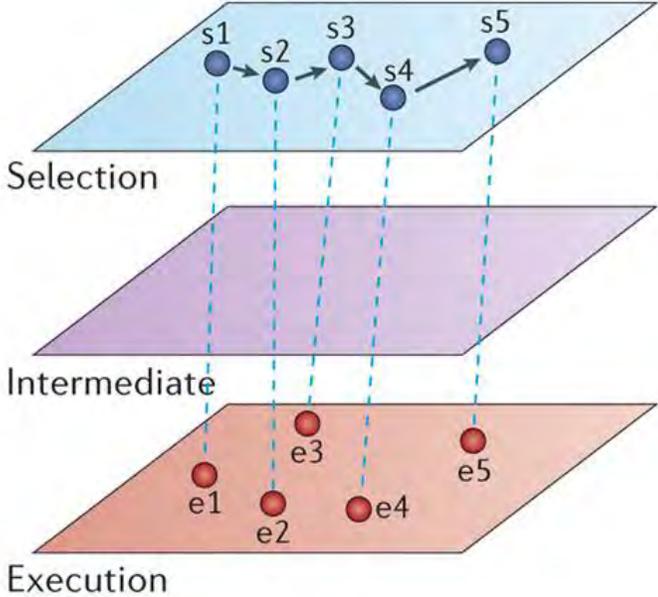


Environment risk factor profile



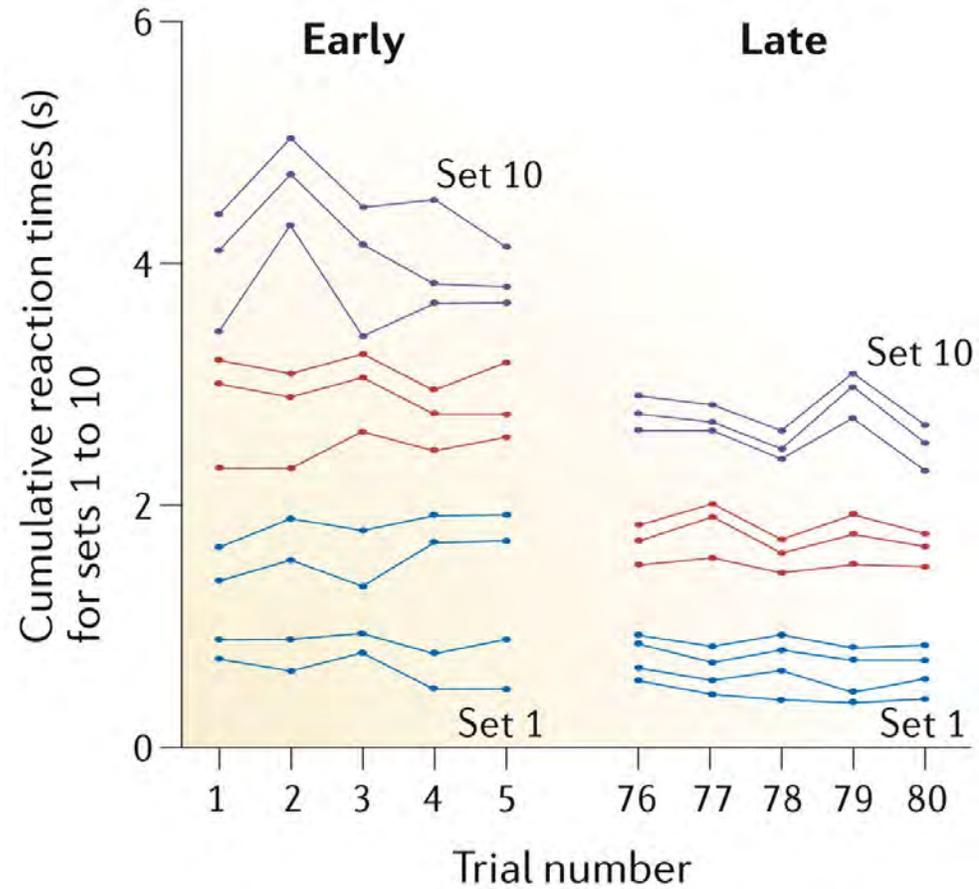
Skill learning in health

Early learning

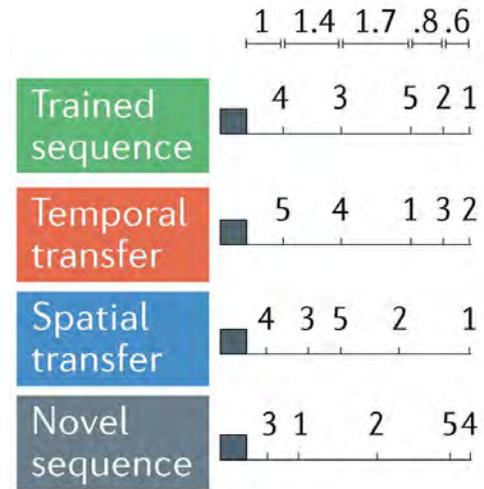


Adapted from Diedrichsen, J. Kornysheva K. Motor skill learning between selection and execution. *Trends Cogn. Sci.* 19, 227-233 (2015).

Skill learning in health



Skill learning in health



(1.) Each hand should first practise its part alone, in slow tempo and with a uniform degree of loudness. Then, by way of a test, try to play in faster tempo and an even *mezzo-piano* instead of the previous *forte*. If the slightest indistinctness should be detected, resume the first method of practice. Both hands must not play together until the mechanical difficulties are overcome. The study of execution with *crescendos* and *diminuendos*, etc., must then be worked out along the same lines, i. e., better the hands play together, each must have learned to perform its part alone with strict observance of the dynamic marks of expression. These rules apply, of course, to the study of all these Etudes.

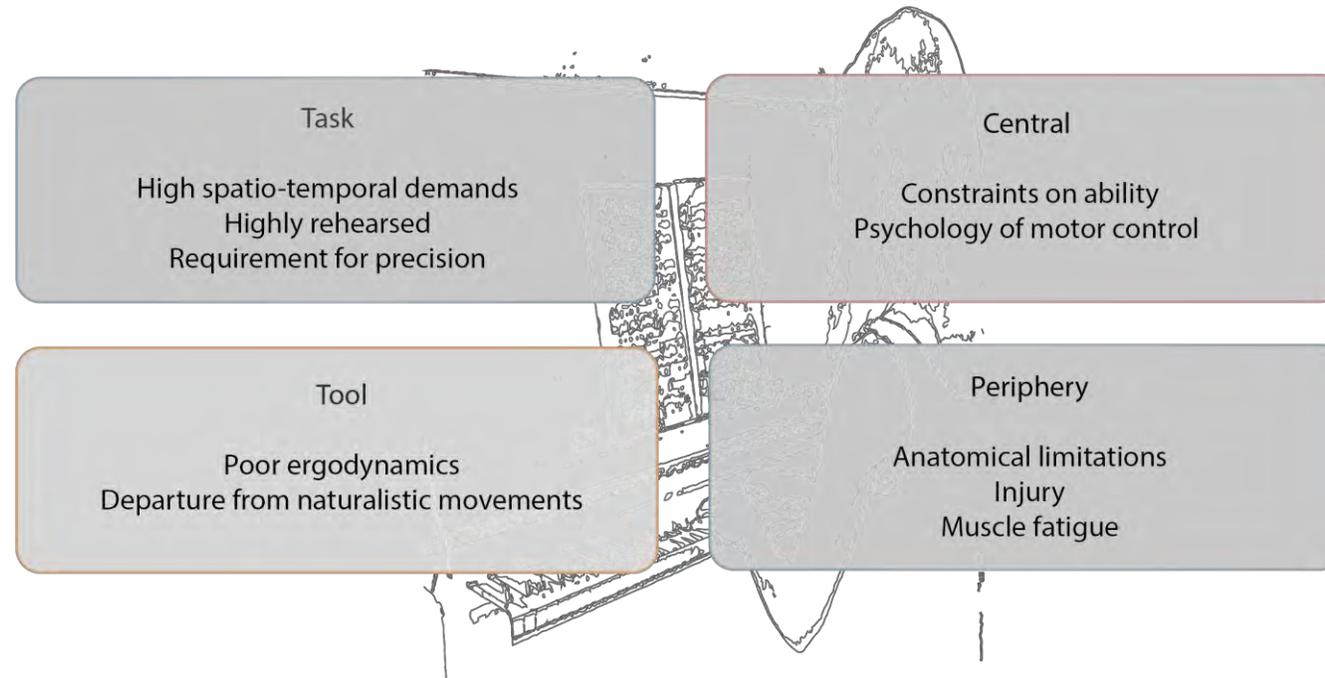
(2.) The teacher must insist upon a *systematic* arpeggiation, wherever this figure occurs; and discourage with equal strictness, the habit of breaking the chords where no arpeggio is explicitly marked. The slightest latitude allowed in this matter, at the beginning of instruction, will work irrepa-

rable injury.

Execute the first arpeggiated chord as follows:

The difference in the execution of these two arpeggiated chords depends, in part, on their different time-value, and in part on the different manner in which the chord-tones combine. The necessity for the *successive* arpeggiation in measure 1, is evident from the lack of fullness which would result from a mode of execution similar to that in measure 10; because, in the former case, the right-hand part would merely double the left-hand part at an interval of 3 octaves.

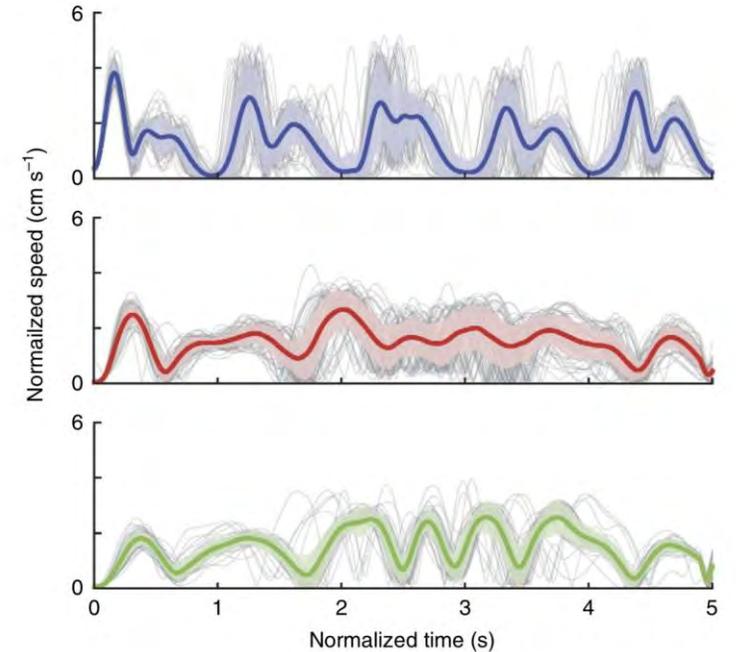
Environment risk factor profile



Repetitive practice

Limitations of neural network supporting skill likely to be contributory factor

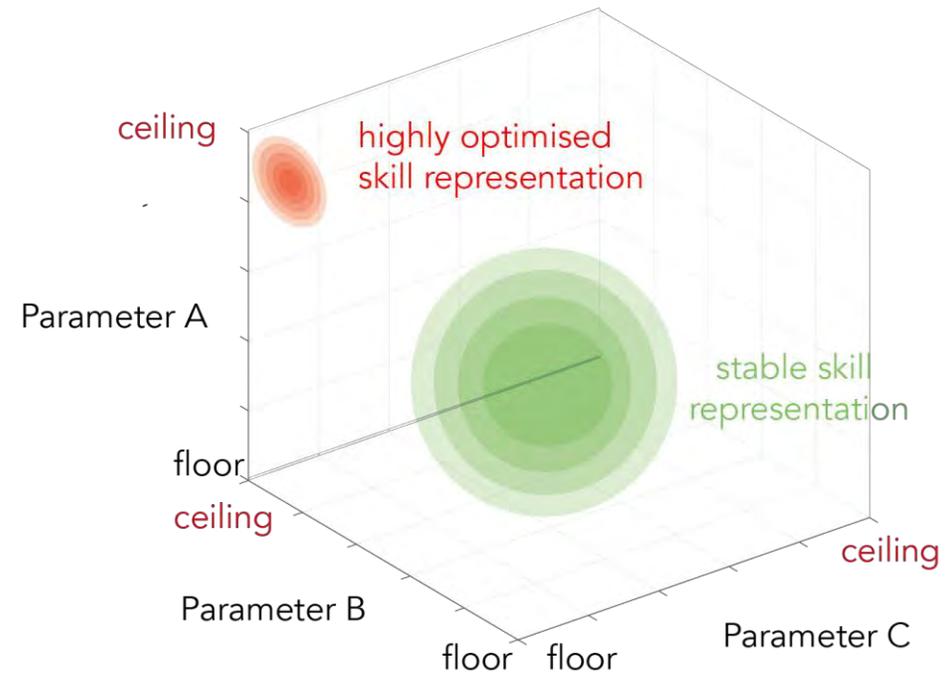
- Repetitive practice leads to progressively longer motor chunks
- Performance gains become increasingly contextual and tied to individual task with poor transfer to other tasks noted

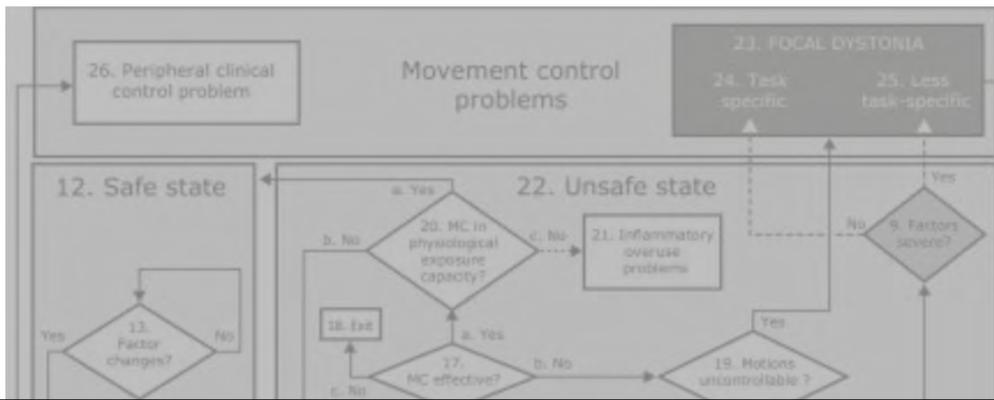


Ramkuma, P et al., Chunking as the result of an efficiency computational trade-off. *Nat Commun.* 7, 12176 (2016)

Wu et al., Learning to combine high variability with high precision: lack of transfer to a different task. *J. Mot. Behav.* 47. 153-165 (2015)

Overtrained skills

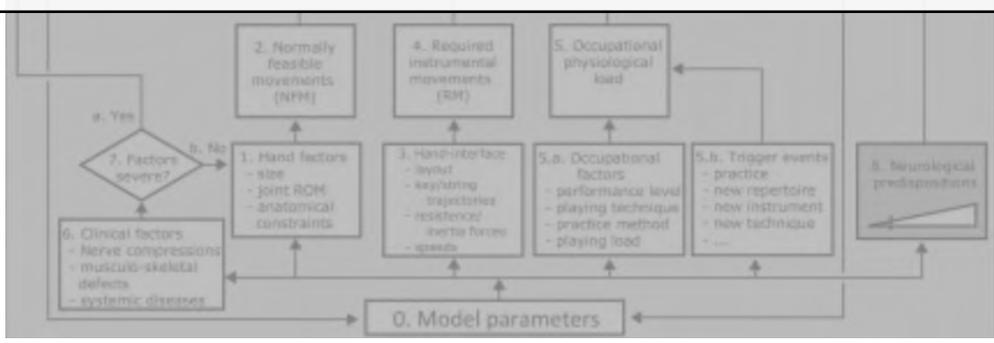




Onset often marked by unresolved mismatch between capacity of motor system and task requirements

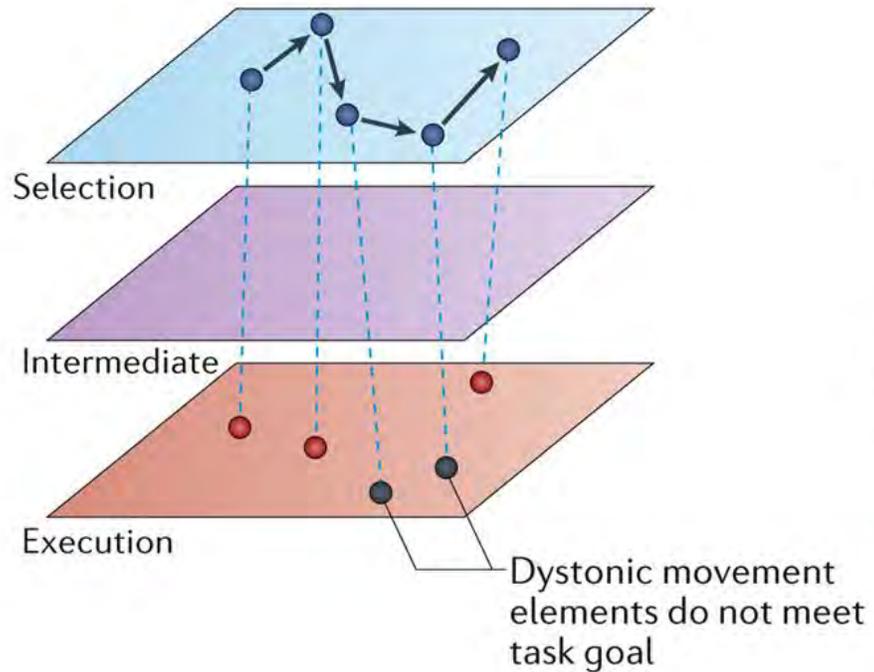
Capacity : limits of the neural control network and the periphery

Requirement : exact movement required of the body to achieve desired movement goals

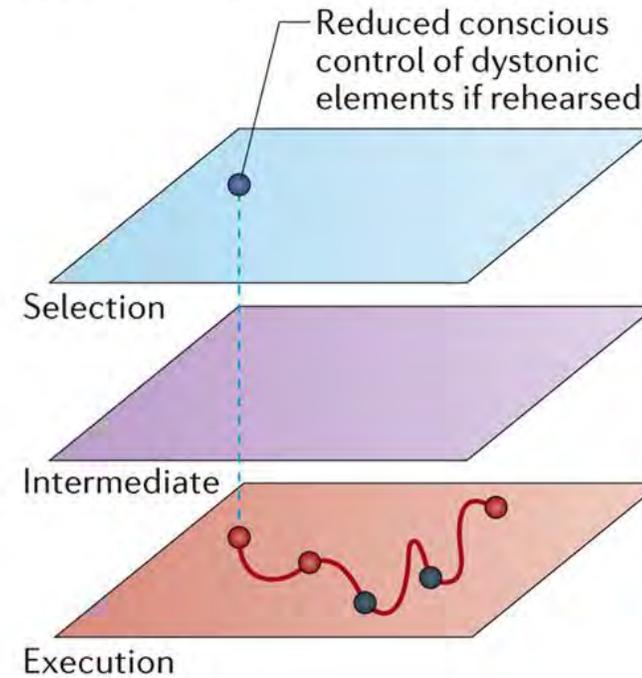


Ill-equipped corrective mechanisms

Remapping *de novo*

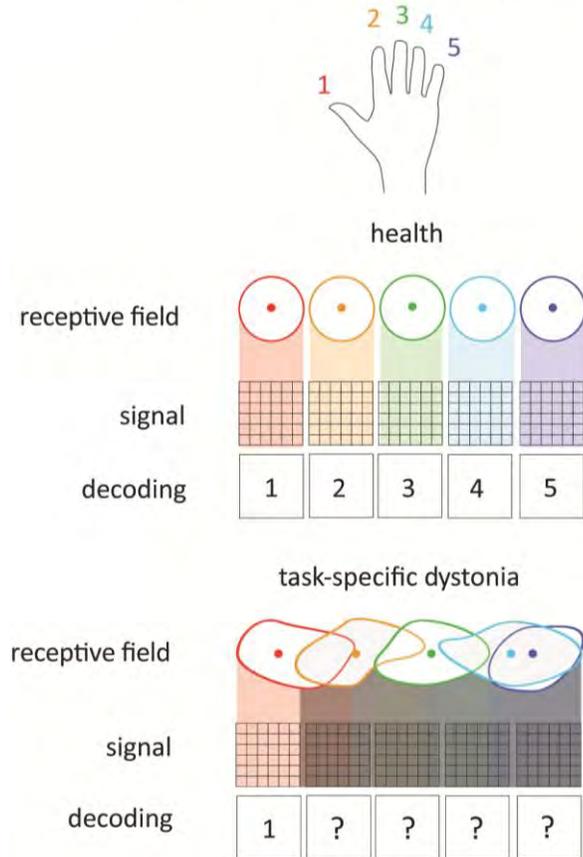


After repetition



‘Where’ is the neural representation then?

traditional distorted somatotopy model

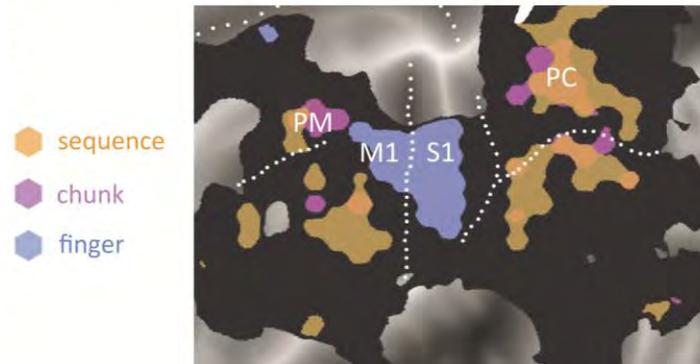
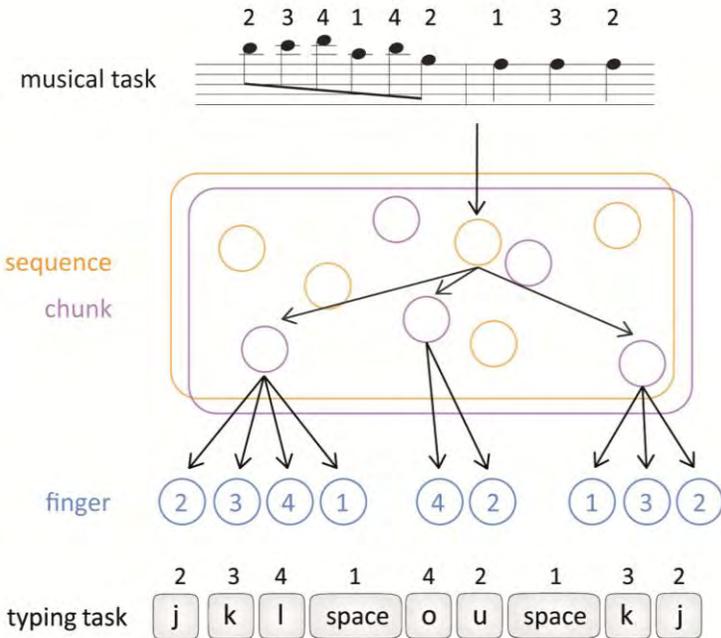
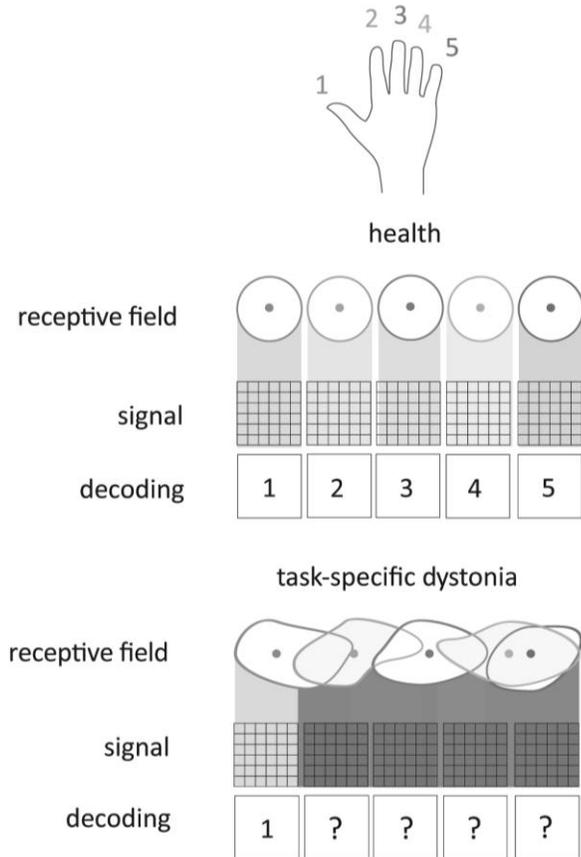


Sadnicka A, Wiestler T, Butler K, Altenmüller E, Edwards MJ, Ejaz N, Diedrichsen J. Intact finger representation within primary sensorimotor cortex of musician's dystonia. *Brain*. 2023 Apr 19;146(4):1511-1522.

Makin T, Krakauer J. Against cortical reorganization (2023) *eLife* 12:e84716.

'Where' is the neural representation then?

traditional distorted somatotopy model

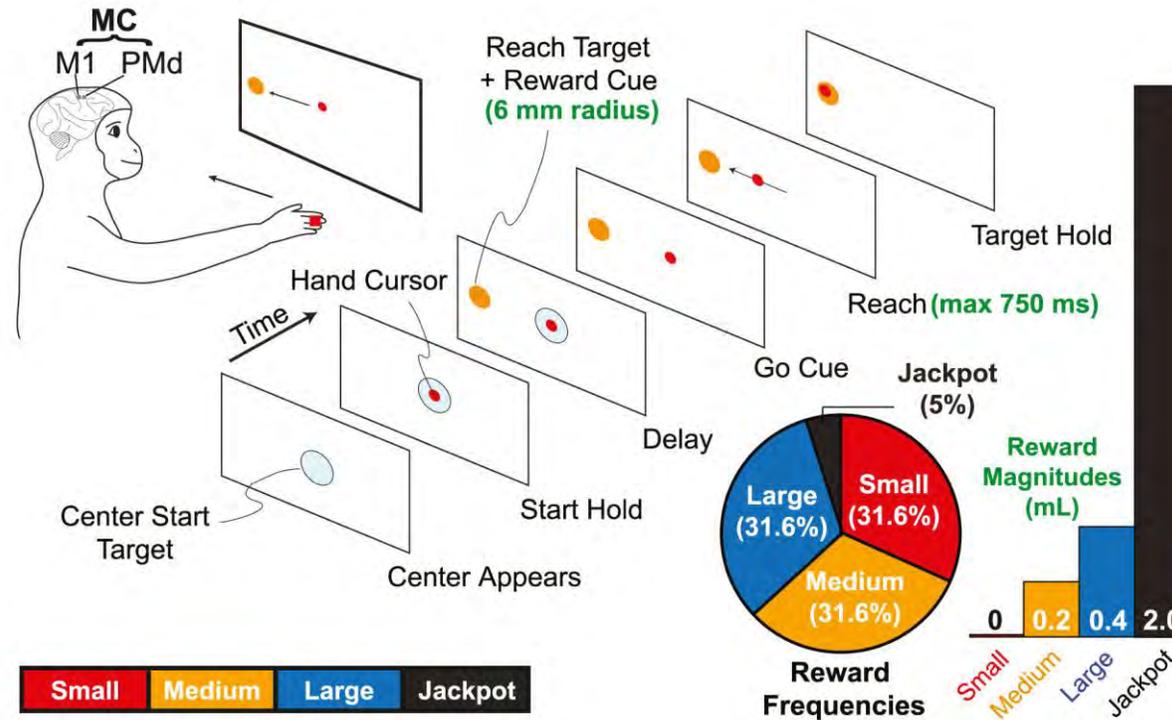


Extreme Task-Specificity in Writer's Cramp

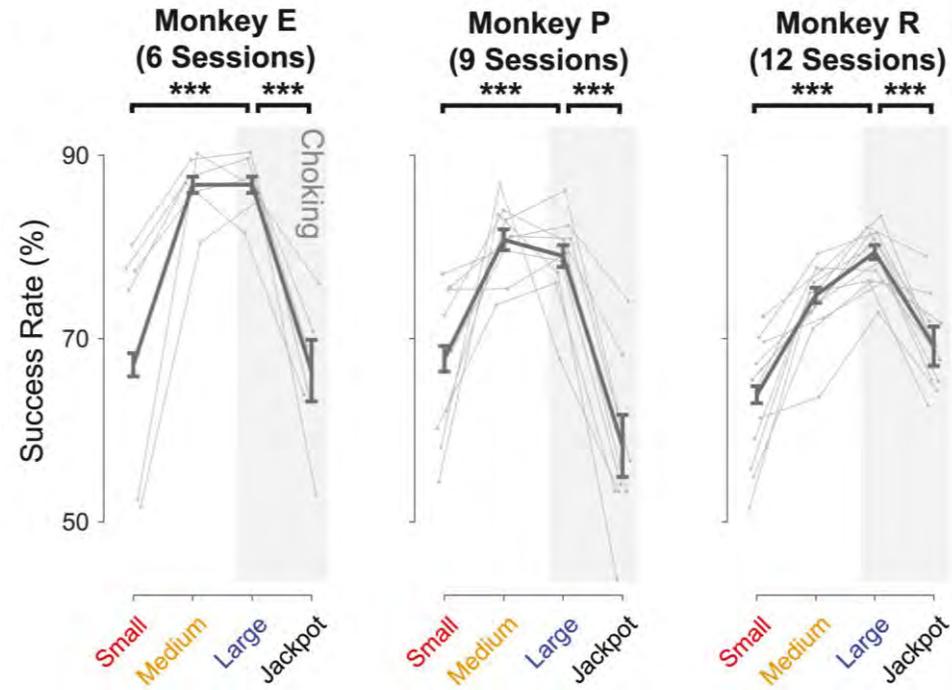
[Ejaz A Shamim](#)^{1,2}, [Jason Chu](#)^{1,3}, [Linda H Scheider](#)^{1,4}, [Joseph Savitt](#)⁵, [H A Jinnah](#)⁶, [Mark Hallett](#)¹

A 52-year-old right-handed Caucasian man presented with an eight year history of trouble writing. He was an accountant and cartographer for the National Guard. He participated in daily drills where he had to make a dot on a map and circle the dot and then write a couple of words where bombing practice was to occur. Although these were just practice drills, they were very tense situations. He started having difficulty making the dot. He would try to make a dot but could not place the pen on the map. His superiors told him the problem was stress-related. He soon developed difficulty writing words. He then sought the help of physicians, psychiatrists, and orthopedic surgeons without any answers. He was also a banjo player and subsequently noticed that his fingers would curl while playing. He was diagnosed with FHD about 11 years after onset.

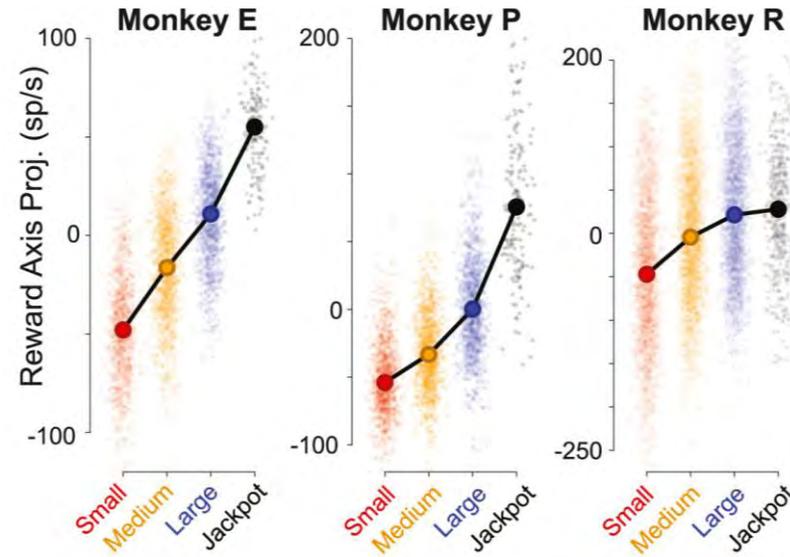
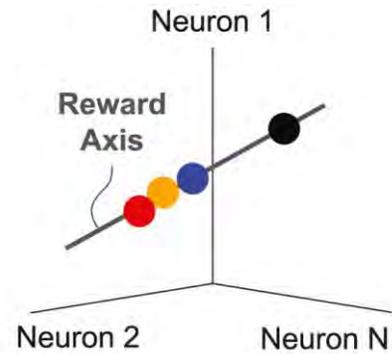
Choking under pressure



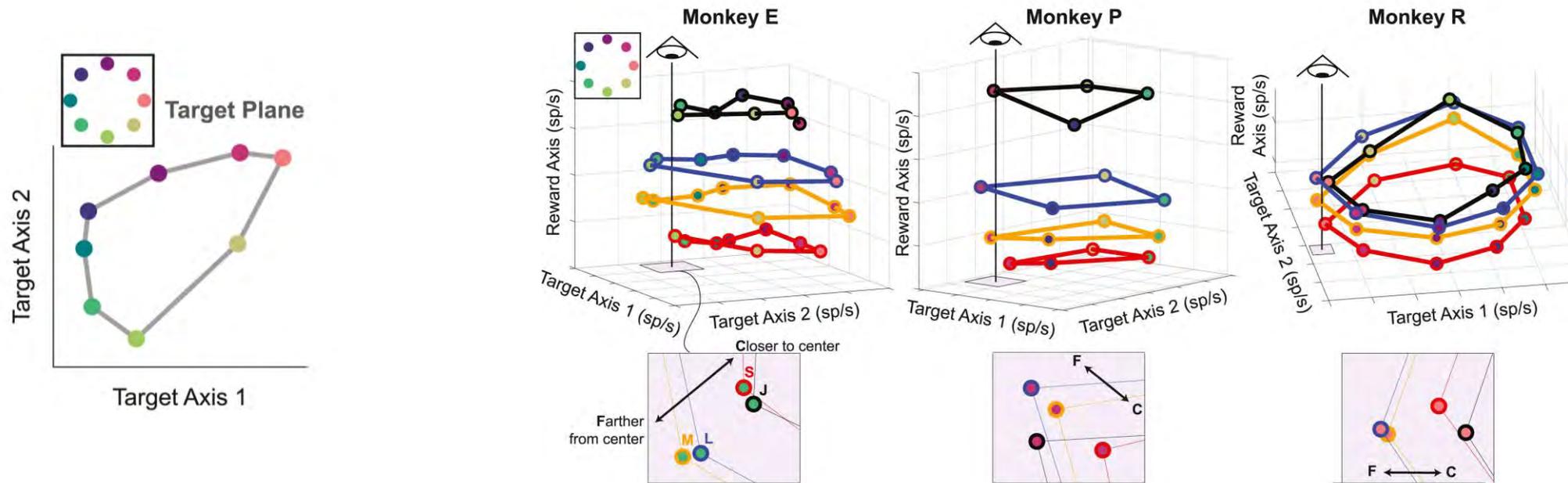
Choking under pressure



Choking under pressure



Choking under pressure



Precision Disrupted: Rethinking the Neural Basis of Task-Specific Dystonia

01 **A Clinical Snapshot**

02 Maladaptive **Plasticity** in Expert Motor Systems?

03 Disrupted Sensorimotor **Representations?**

04 A **Motor Control Framework** for Skill Failure

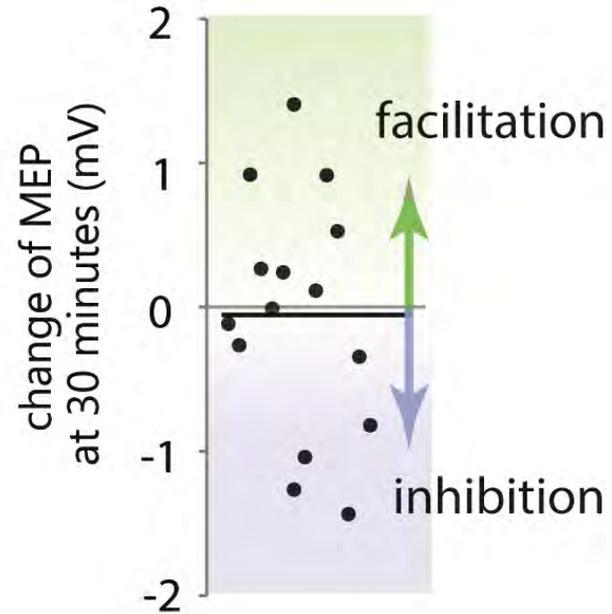
05 Translating Mechanism into **Motor Repair**

Reset plasticity?

APB



Target muscle

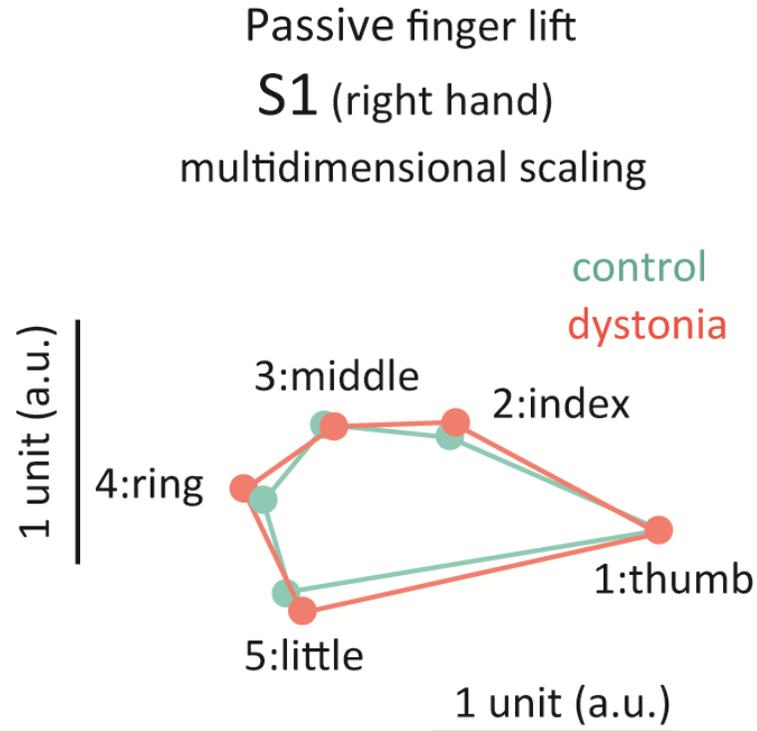


Cerebellar Stimulation Fails to Modulate Motor Cortex Plasticity in Writing Dystonia

Anna Sadnicka, MD,^{1,2} Masashi Hamada, MD, PhD,^{1,2,3}
Kailash P. Bhatia, MD, FRCP,² John C. Rothwell, PhD²
and Mark J. Edwards, MD, PhD^{2*}

¹Shared first authorship; ²Sobell Department of Motor Neuroscience and Movement Disorders, University College London, London, United Kingdom; ³Department of Neurology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Re-train digit representations?



Botulinum toxin injections



David
Simpson



Steven
Frucht



Before



After

A motor control model of task-specific dystonia and its rehabilitation

21

Anna Sadnicka^{a,b,*}, Jaume Rosset-Llobet^c

^a*Motor Control and Movement Disorder Group, Institute of Molecular and Clinical Sciences,
St George's University of London, London, United Kingdom*

^b*Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology,
London, United Kingdom*

^c*Institut de l'Art. Medicina & Fisiologia, Terrassa, (Barcelona) Spain*

**Corresponding author: e-mail address: asadnick@sgul.ac.uk*

Differential learning



Schöllhorn

Skill improves not by repeating an “ideal” pattern but by adding structured variability

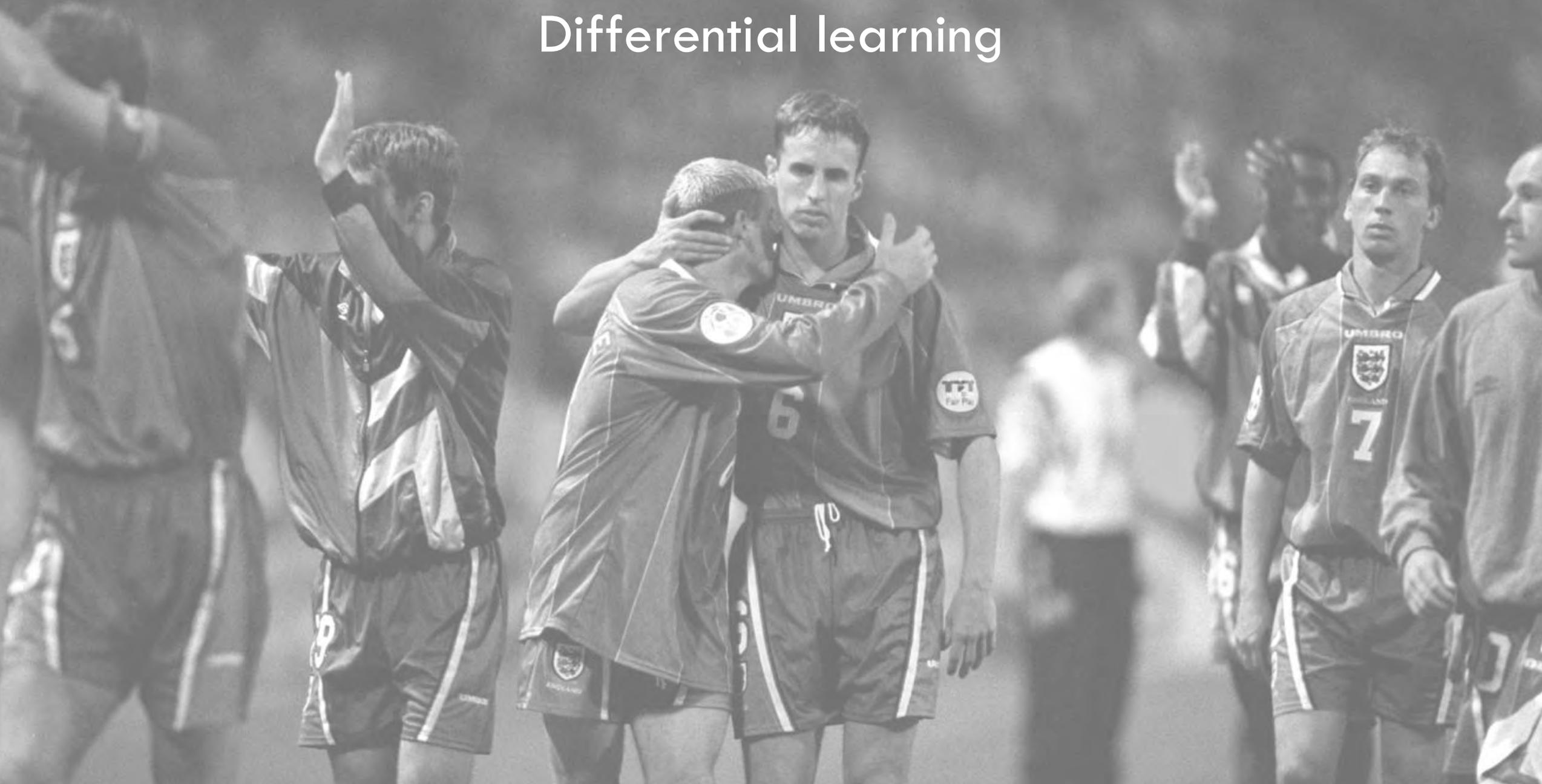
Learners explore many sensorimotor states rather than converging on one solution

Noise and fluctuations become informational, guiding self-organisation of stable, adaptable control

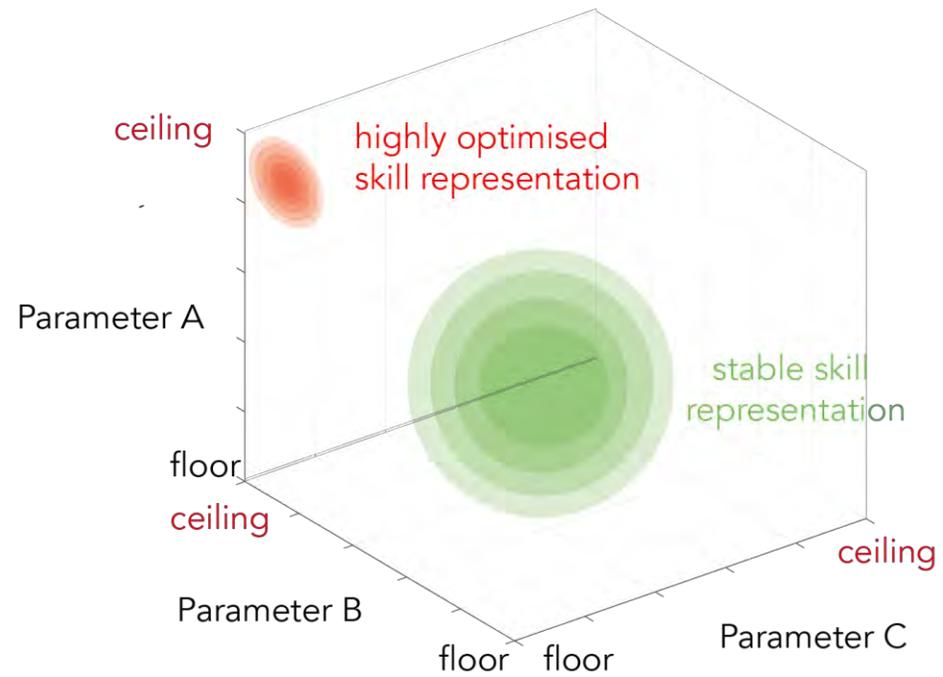
No explicit corrections, minimal repetition; practice uses continuous perturbations to expand the motor repertoire

Produces robust, flexible, context-resilient skill through exploration rather than prescription

Differential learning



Differential learning



Differential learning

Examples of parameters to vary:

Joint combinations, positions, directions

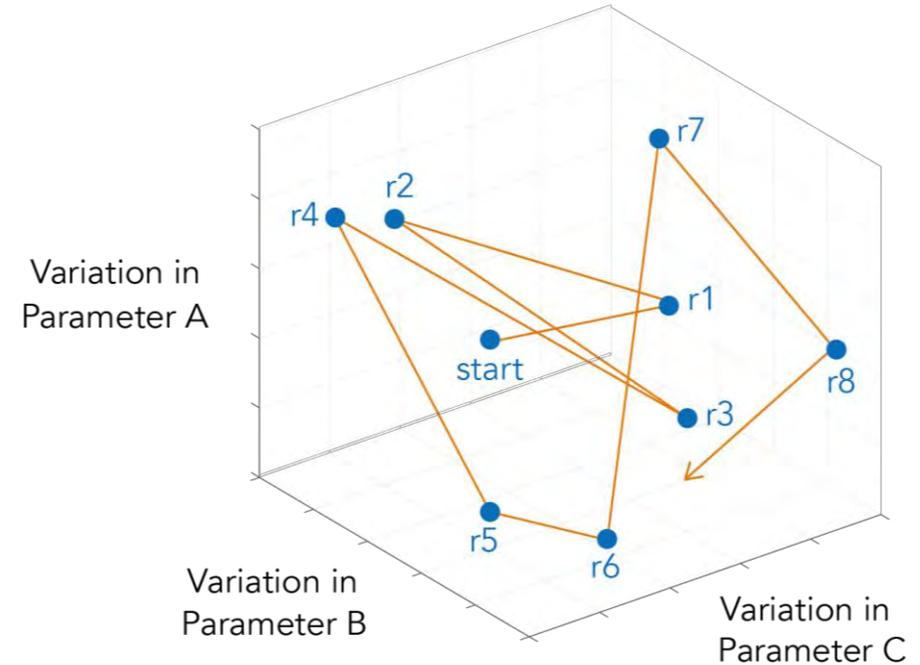
Size of movements

Speed of movements

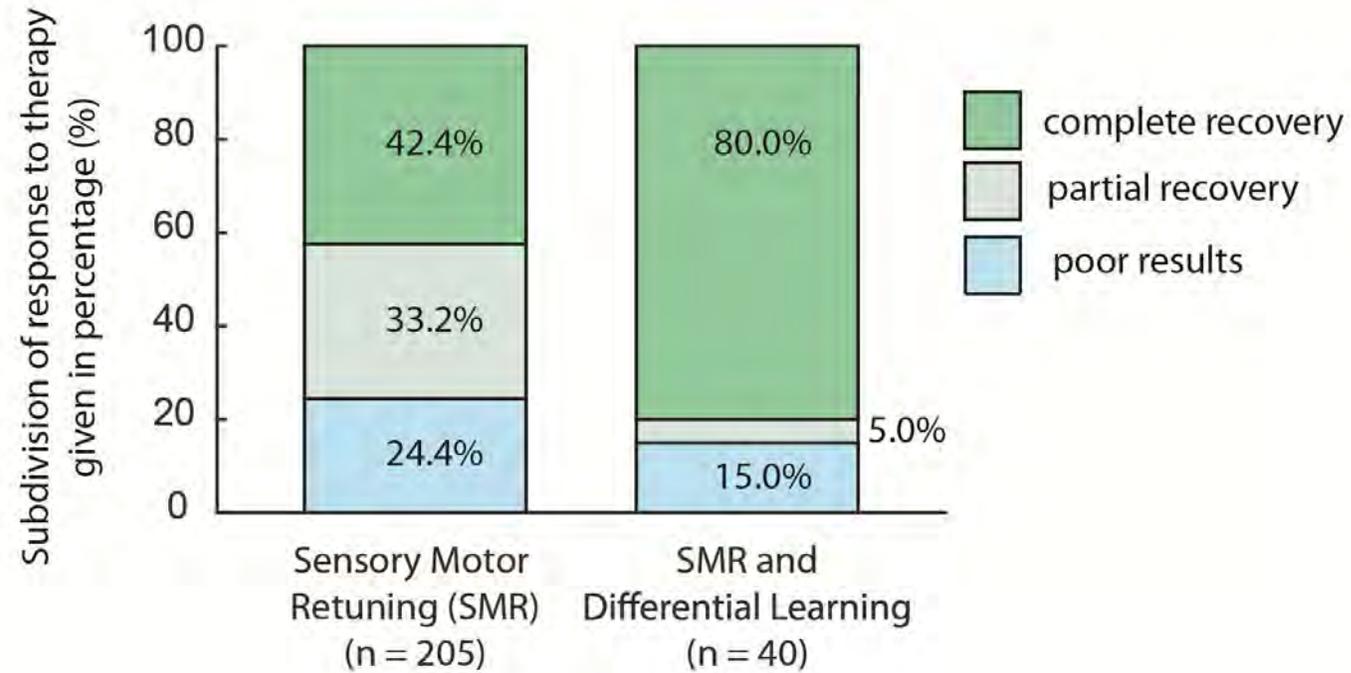
Place of contact of finger with instrument

Amount of pressure applied by fingers

Accentuations of notes



differential learning





Glenn
Nielsen

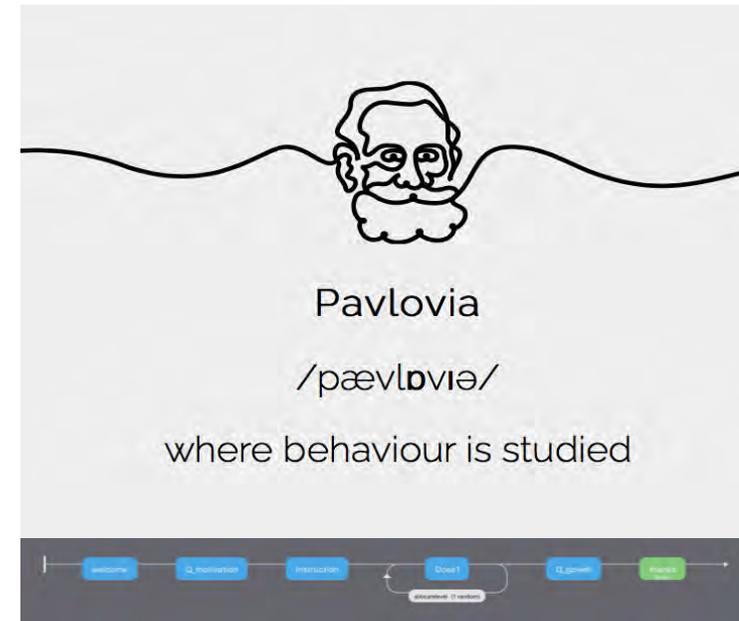
Creating Clinical Tools



Kate
Holt



Cameron Moss, gait retraining



Collaborative Clinical Academic Networks



Prevention



Maria Herrojo Ruiz ✓ • 3rd+

Reader at Goldsmiths, University of London. Joint director ...

2yr • Edited •

[+ Follow](#) ...

What an exciting day we had at the [Royal College of Music](#) delving into the neuroscience of expert performance with Anna Sadnicka, [Katja Kornysheva](#), [Aaron Williamon](#), [George Waddell](#), Beatriz Calvo Merino and Mark Edwards. Immensely grateful for the insightful questions and spirited post-symposium discussion. A huge thank you to all speakers and attendees!



Summary 1

Skilled movement is a pinnacle of human development, but the demands of mastery come with vulnerability.

By integrating risk factors with the neuroscience of skill learning, we can build a motor-control framework that explains how precision fails.

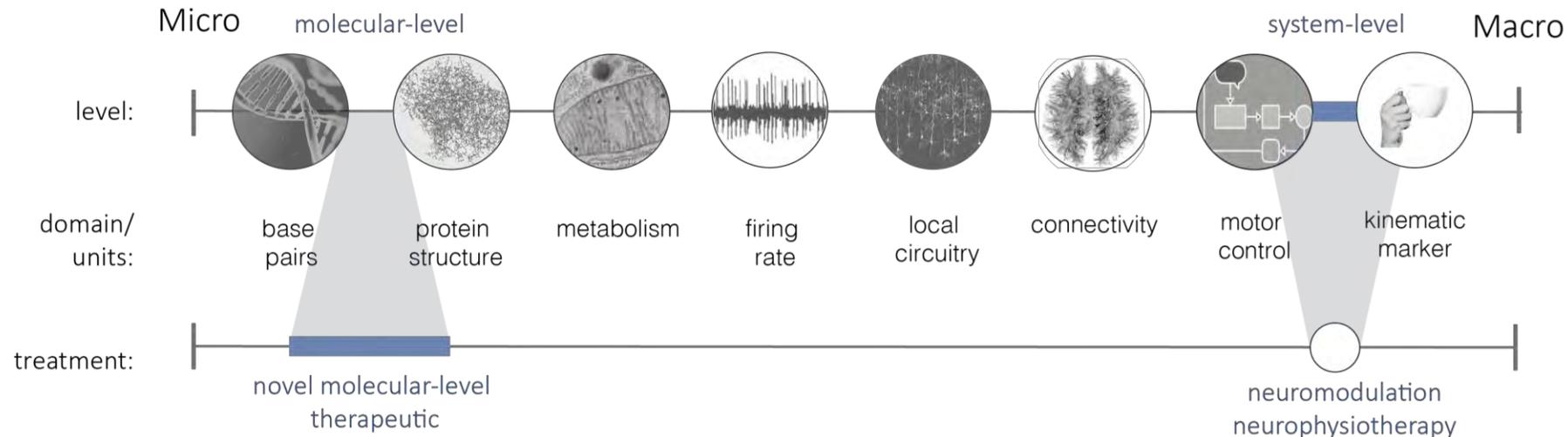
Reintroducing variability through Differential Learning can restore flexibility, stability, and performance.

Summary 2

Rethinking mechanism: Different neurological disorders demand different notions of “mechanism.” Systems-level motor control models align naturally with modern neuromodulatory interventions.

Measuring real change: Emerging technologies enable naturalistic movement capture, opening the door to quantifying and understanding with contemporary analytical methods

Axes and units of mechanism in neurorehabilitation: We can finally quantify and unpack complex interventions such as neurophysiotherapy.



Thank you

Computational Movement Disorders Lab

Iván Varela, Kate Sampson, Mireia Coll,
Isobel Platt, Marta Sartori

Gatsby Computational Neuroscience Unit, UCL
Maneesh Sahani, I-Chun Lin, Mike Sainsbury

Sainsbury Wellcome Centre, UCL

Niko Sirmpilatze, Sofia Miñano,

NeuroGEARS

Gonçalo Lopes, Andre Almeida, Joao Frazao

SENSE Research Unit, UCL

Ulises Serratos Hernandez, Diego Kaski

Department of Clinical Movement Neurosciences, UCL

Anthony Schapira, Sonia Gandi, Imran Sayed

City St George's University of London

Glenn Nielsen, Ann-Marie Strudwick, Cameron Moss,
Kate Holt, Tom Hart, Francesca Morgante

Centre of Human Brain Health, University of Birmingham

Katja Kornysheva, Joseph Galea

Computational Neurology, University of Oxford

Sanjay Manohar, John Grogan

Phenomenology of Movement Disorders

Steven Frucht, Pichet Termsarasab

Mentors

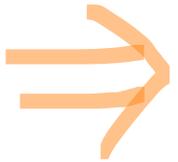
Tom Warner, **Mark Edwards**, John Rothwell,
Kailash Bhatia, Francesca Morgante, James Rowe

Come and see lab posters!



P19: Decoding Movement Disorder Scales: From Item Features to Shared Principles of Motor Assessment

M. Coll*¹ and I.S. Platt*¹, I. Varela¹, M. Sartori², K. Sampson¹, A. Sadnicka¹, *Contributed equally
¹University College London



P21: From Tacit Expertise to Quantitative Insight: A Bonsai-Based Multimodal Platform for Motor Assessment in Movement Disorders

M. Sartori*¹, I. Varela*¹, M. Coll¹, I.S. Platt¹, A. Almeida², J. Frazão², G. Lopes², A. Sadnicka¹ *Contributed equally
¹University College London, ²NeuroGears