A few questions on the content of the previous lecture

slido

The mind-body problem summarizes ...

ⓘ Start presenting to display the poll results on this slide.

slido

If a method has high SPATIAL resolution, then it allows us to...

ⓘ Start presenting to display the poll results on this slide.

slido

If a method has high TEMPORAL resolution, then it allows us to...

ⓘ Start presenting to display the poll results on this slide.

Human lesion studies and brain stimulation methods

Dr. Lavinia Carmen Uscătescu

March 4th , 2024

Outline

1. Types of lesions and procedures
2. Inference and design in lesion studies
3. Stimulation methods: TMS and tES

Types of lesions and procedures

Science starts with observations

Eur Spine J. 2010 Nov; 19(11): 1815–1823.
Published online 2010 Aug 10. doi: 10.1007/s00586-010-1523-6

The Edwin Smith papyrus: a clinical reappraisal of the oldest known document on spinal injuries

Joost J. van Middendorp,[1] Gonzalo M. Sanchez,[2,3] and Alwyn L. Burridge[4]

Table 1 The diagnostic descriptions and therapeutic verdicts of the six spinal injury cases as reported in the Edwin Smith papyrus, based on the Sanchez and Burridge translation [9]

Case	Region	Injury type	Diagnosis of the spinal column	Significant symptoms	Injury of the spinal cord	Significant symptoms	Other documented signs and symptoms	Treatment verdict: "A medical condition…"
29	Cervical	Open	Fracture as a result of a penetrating injury	Stiffness of neck. Inability to rotate and bend the neck	No	–		"…I intend to fight with."
30	Cervical	Closed	Wrenching/sprain with disc injury[a]	Ability to rotate and bend the neck. Painful rotation and flexion of the neck	No	–		"…I can heal."
31	Cervical	Closed	Dislocation[a]	None reported	Yes	Motor and sensory loss of the upper and lower extremities, priapism, urinary incontinence, abdominal distention, priapism[b] and spermatorrhea[b]	Bloodshot eyes[c]	"…that cannot be healed."
32	Cervical	Closed	Compression fracture[a]	Inability to rotate and bend the neck ("face fixed")	No	–		"…I can heal."
33	Cervical	Closed	Burst fracture[a]	None reported	Yes	Motor and sensory loss of the upper and lower extremities	Stupor[c] and aphasia[c]	"…that cannot be healed."
48	Lumbar	Closed	Wrenching /sprain with disc injury	Immediate contraction of the leg after extending it because of vertebral pain	No	–		"…I can heal."

[a] This term is clarified in the case's additional subheading "Explanation", see Appendix
[b] This symptom was documented to be present in an injury located at "the middle vertebra of the back of neck"
[c] This symptoms is considered to be most likely the result of an inaccurately described closed head injury

Edwin Smith Surgical Papyrus ~ 1000 BC (based on an older treatise ~ 3000 BC)

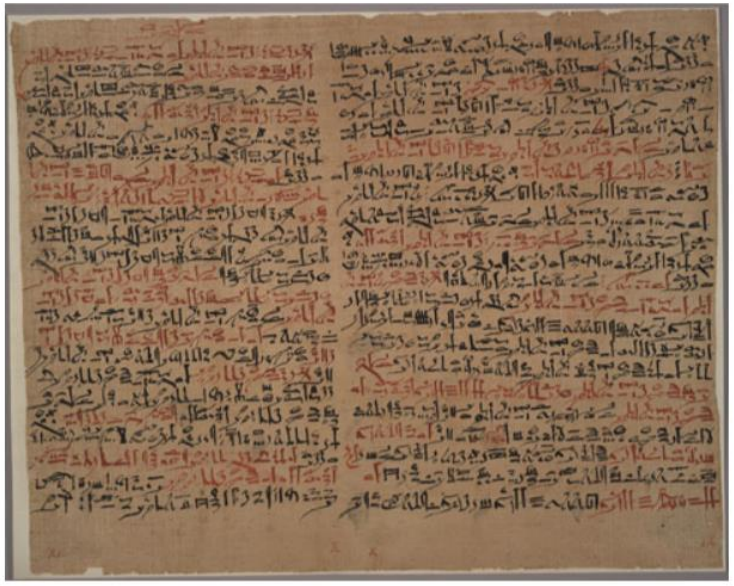


Fig. 1 Plate X and XI of the Edwin Smith papyrus including the five cervical spinal injury cases in hieratic script [7]

http://tinyurl.com/v98k9nh5

Phineas Gage

Executive functions

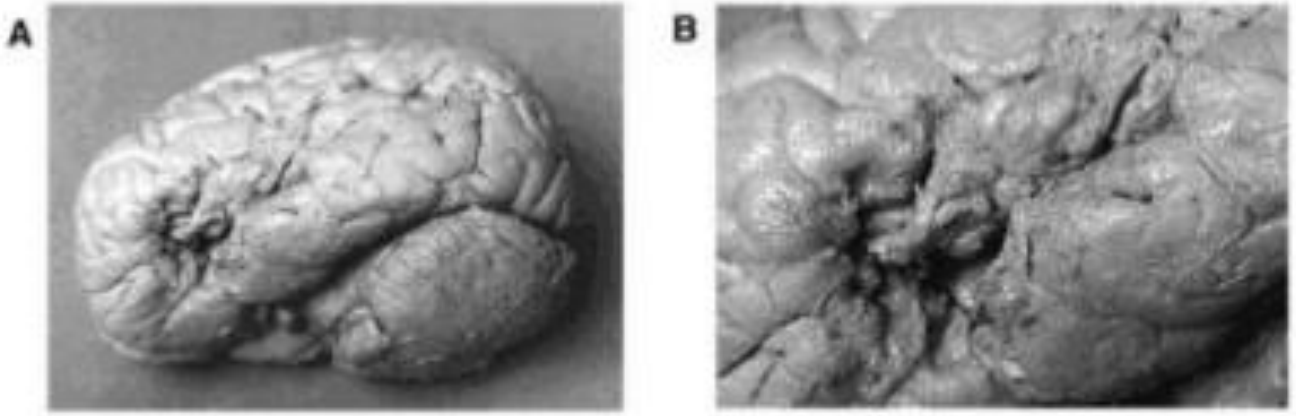
*“He is **fitful, irreverent**, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, **impatient** of restraint or advice when it conflicts with his desires, at times pertinaciously **obstinate**, yet **capricious** and vacillating, devising many plans of future operations, which are no sooner arranged than they are abandoned in turn for others appearing more feasible.”*

Harlow, (1868), pp. 13-14

Patient “Tan” (Louis Victor Leborgne)

Speech (Broca’s aphasia/ expressive aphasia)

Pierre Paul Broca
(1824 – 1880)



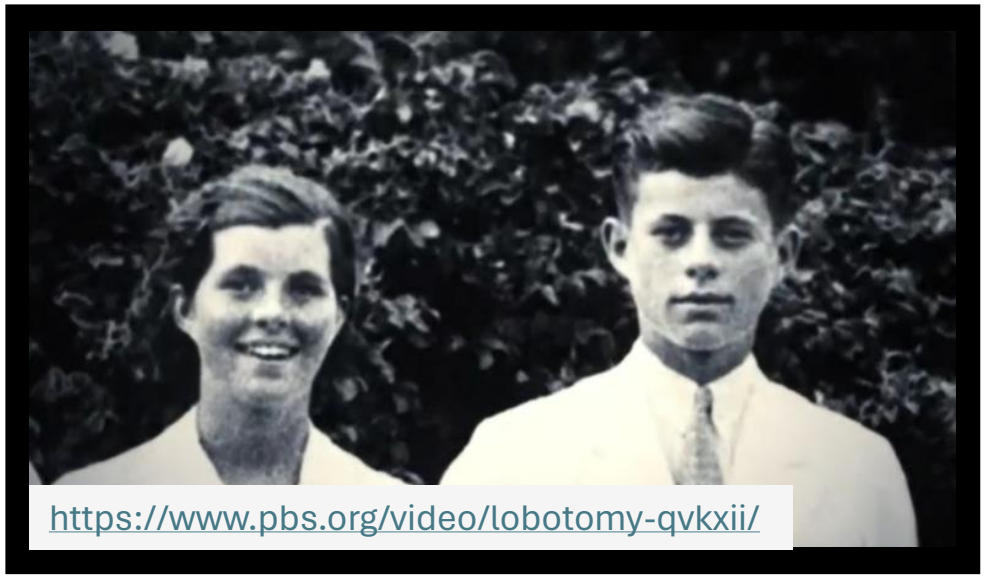
“In the mid 1800’s, a 30-year-old French citizen named Louis Victor Leborgne was admitted to a hospital after he ***lost the ability to speak****. He only spoke using* ***one syllable****. He would communicate entirely with the word “****tan,****” using it with* ***different voice inflections*** *and with* ***hand gestures*** *when appropriate. Because of his way of talking, he became known as “Patient Tan.””*

https://tinyurl.com/25nbhhnp

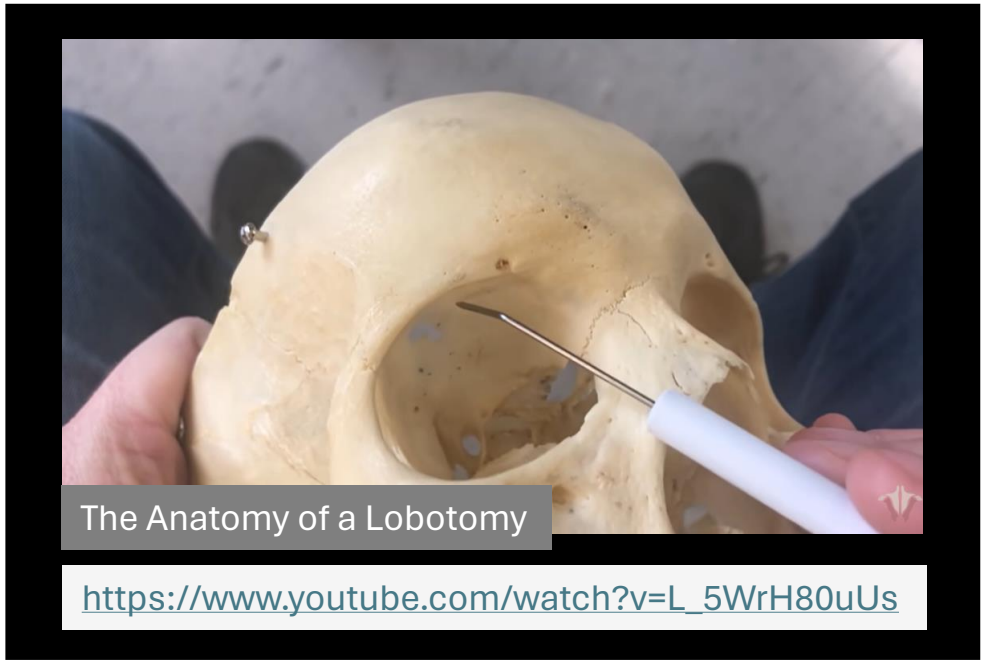
Lobotomy

Walter Freeman
(1895 – 1972)

Egas Moniz
(1874 – 1955)
Nobel Prize in Physiology or Medicine, 1949



https://www.pbs.org/video/lobotomy-qvkxii/

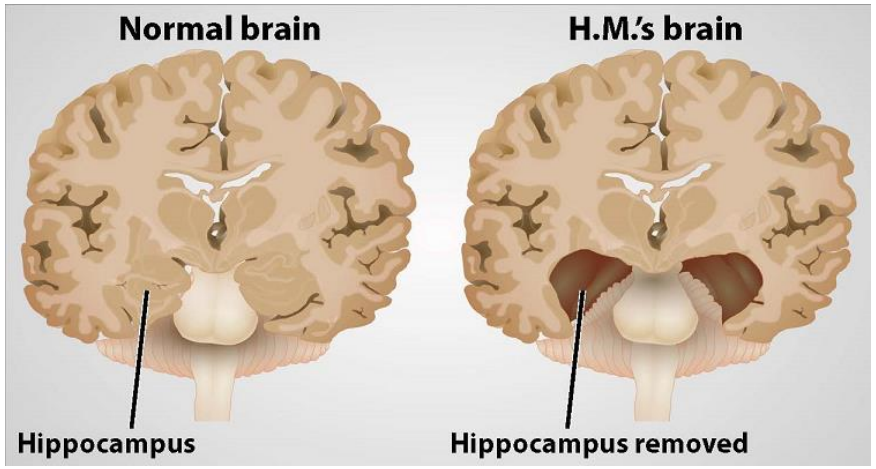


https://www.youtube.com/watch?v=L_5WrH80uUs

Patient H.M (Henry Molaison)

Memory (anterograde amnesia)

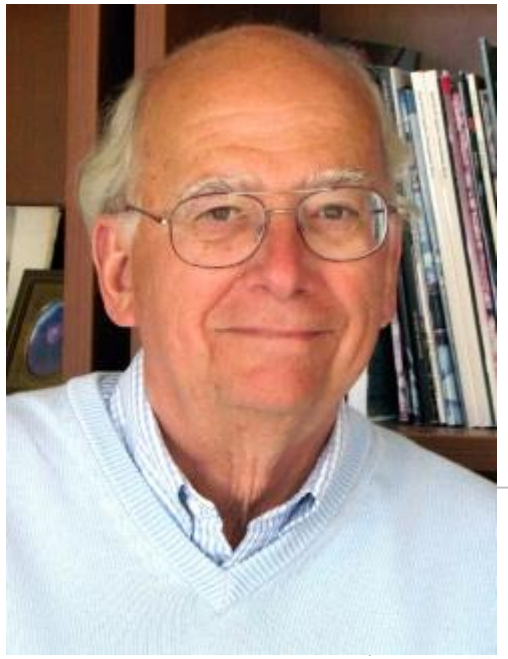
Brenda Milner



"When Milner first visited H.M., she saw that the epilepsy was now controlled but that his ***memory impairment*** *was [...]* ***severe*** *[...]. What she observed was someone who* ***forgot daily events*** *nearly as fast as they occurred, apparently* ***in the absence of any general intellectual loss or perceptual disorder****. He* ***underestimated his own age****, apologized for forgetting the names of persons to whom he had just been introduced, and described his state as* ***"like waking from a dream ... every day is alone in itself..."""*** (Milner et al., 1968, p. 217).

Split brain patients

Hemispheric specialization



Michael Gazzaniga

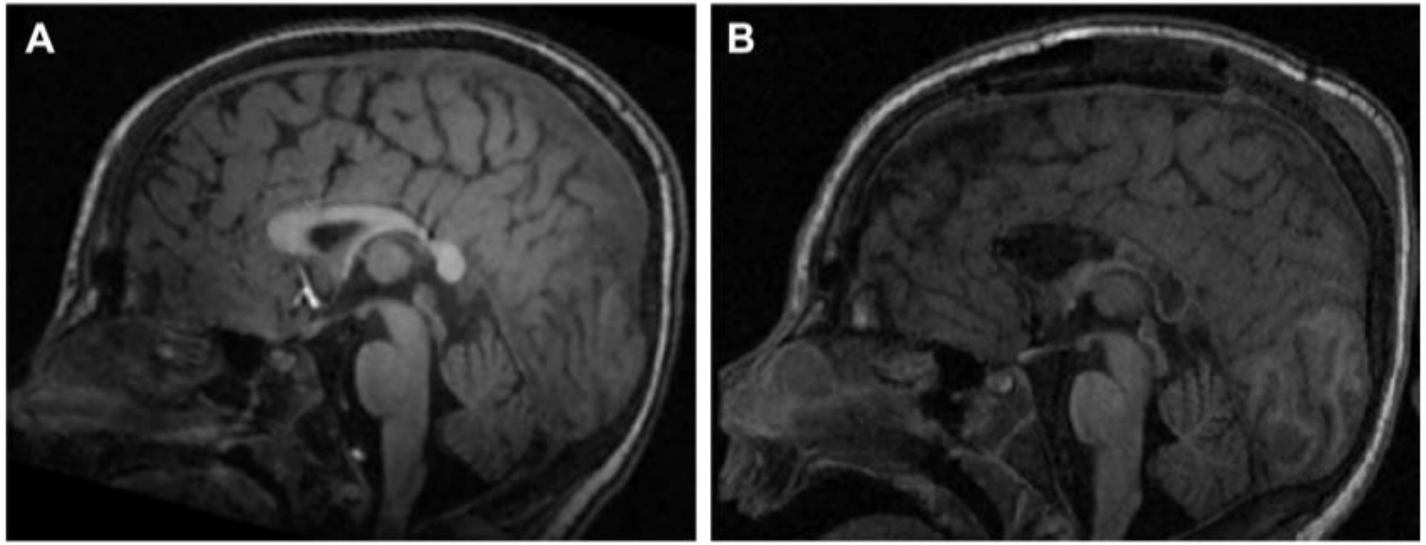


Figure 5 Complete corpus callosotomy.
Note: Magnetic resonance imaging (**A**) before and (**B**) after complete corpus callosotomy in an individual with Lennox-Gastaut syndrome.

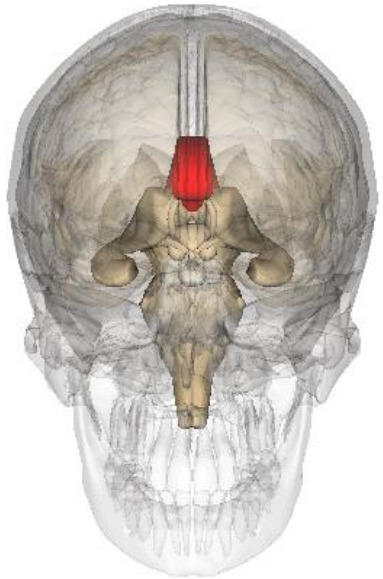
Ostendorf & Ng, (2017), https://pubmed.ncbi.nlm.nih.gov/28461749/

The Split Brain in Man

The human brain is actually two brains, each capable of advanced mental functions. When the cerebrum is divided surgically, it is as if the cranium contained two separate spheres of consciousness

by Michael S. Gazzaniga

https://www.jstor.org/stable/24926082?seq=1



Lesions can be permanent or reversible

Neuropsychologia. 2018 Jul 1; 115: 211–219.
doi: 10.1016/j.neuropsychologia.2017.09.019

Methods matter: A primer on permanent and reversible interference techniques in animals for investigators of human neuropsychology

Andrew H. Bell[a,b,*] and Janet H. Bultitude[c,d,e]

▸ Author information ▸ Article notes ▸ Copyright and License information PMC Disclaimer

Abstract Go to: ▸

The study of patients with brain lesions has contributed greatly to our understanding of the biological bases of human cognition, but this approach also has several unavoidable limitations. Research that uses animal models complements and extends human neuropsychology by addressing many of these limitations. In this review, we provide an overview of permanent and reversible animal lesion techniques for researchers of human neuropsychology, with the aim of highlighting how these methods provide a valuable adjunct to behavioural, neuroimaging, physiological, and clinical investigations in humans. Research in animals has provided important lessons about how the limitations of one or more techniques, or differences in their mechanism of action, has impacted upon the understanding of brain organisation and function. These cautionary tales highlight the importance of striving for a thorough understanding of how any intereference technique works (whether in animal or human), and for how to best use animal research to clarify the precise mechanisms underlying temporary lesion methods in humans.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6018620/

Table 1
Permanent and reversible lesion techniques in animal and human research.

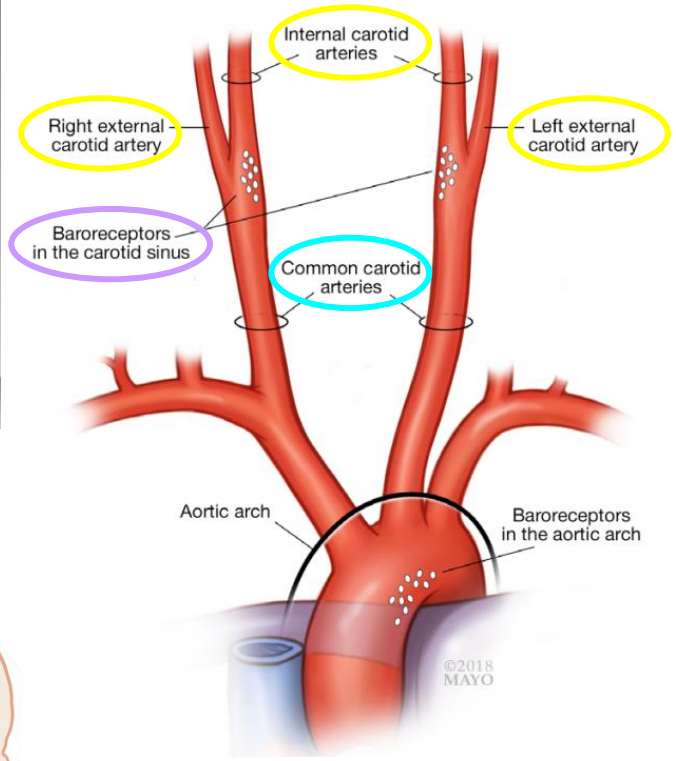
Technique	Durations	Tissue Specificity	Relative Size	Spare Fibres?
ANIMAL				
Permanent				
Aspiration	Permanent	Non-specific	Unlimited	No
Excitotoxic	Permanent	Specific	Small-Medium	Yes
Reversible				
Pharmacological Injections	Minutes to hours	Specific	Small	Yes
Cryogenic	Hours	Non-specific	Large	No
Genetic	Milliseconds to hours	Specific	Small	Yes
TMS	Millseconds to minutes	Non-specific	Small	No
FUS	Minutes	Non-specific	Small-Medium	No
HUMAN				
Permanent				
Lesion due to Stroke	Permanent	Non-specific	Variable	No
Lesion due to Trauma	Permanent	Non-specific	Variable	No
Temporary				
Wada test (Wada, 1949)	Minutes	Non-specific	Large (whole hemisphere)	No
TMS	Millseconds to minutes	Non-specific	Small	No
tDCS	Millseconds to minutes	Non-specific	Small to medium	No

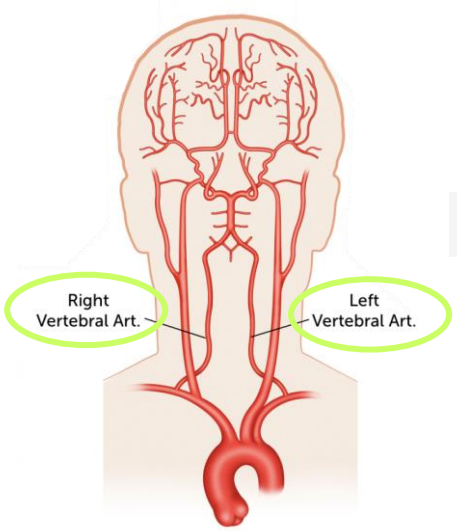
FUS = Focused Ultra-Sound; tDCS = Transcranial Direct Current Stimulation; TMS = Transcranial Magnetic Stimulation.

The Wada test
(intracarotid sodium amobarbital procedure)

Hemispheric specialization

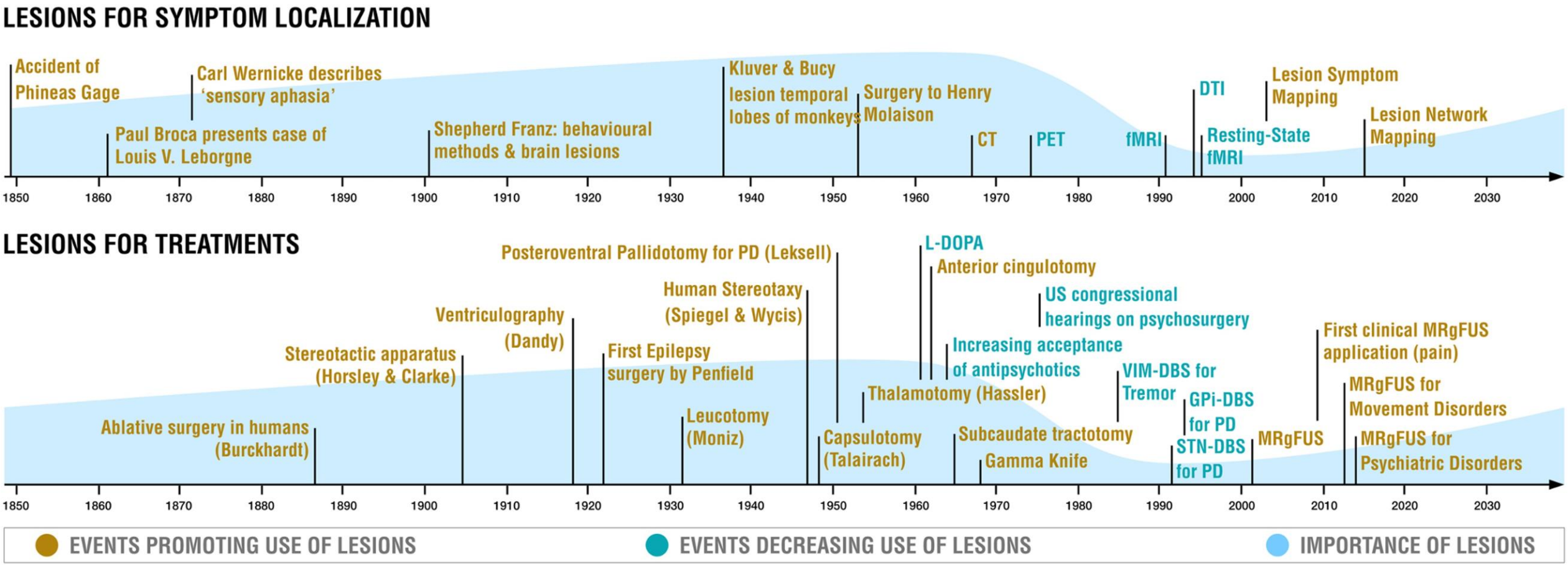
Juhn Wada
(1924 – 2023)





https://tinyurl.com/mmjs5uch

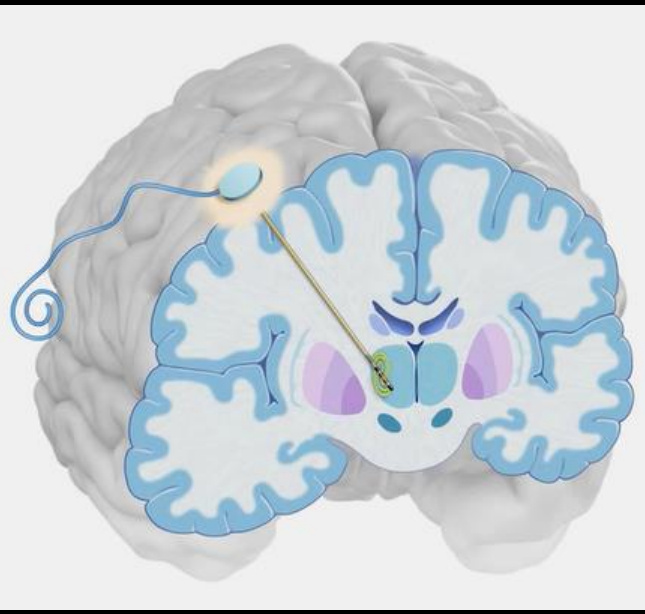
https://www.youtube.com/watch?v=SBKc_ncPzOo



Joutsa et al., (2023), *"The return of the lesion for localization and therapy"*, *Brain,* https://pubmed.ncbi.nlm.nih.gov/37040563/

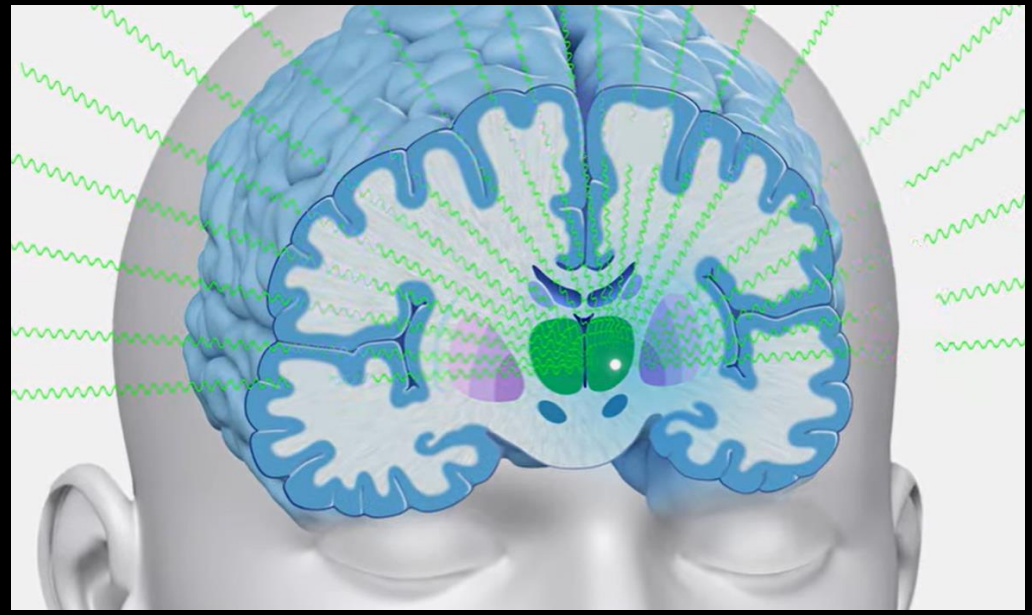
Treatment for Parkinson's Disease & Essential Tremor

Deep Brain Stimulation (DBS)



https://www.youtube.com/watch?v=xLgEcb447gA

MR-Guided Focused Ultrasound (MRgFUS)



https://www.youtube.com/watch?v=3Bwq2YxD9eU

Design and inference in lesion studies

single-case studies

in cognitive neuropsychology, the data from **different patients** are **not combined**; helpful for establishing how **cognitive processes** might be **subdivided**.

Brain Cogn. 1986 Jan;5(1):41-66. doi: 10.1016/0278-2626(86)90061-8.

On drawing inferences about the structure of normal cognitive systems from the analysis of patterns of impaired performance: the case for single-patient studies

A Caramazza

PMID: 3954906 DOI: 10.1016/0278-2626(86)90061-8

Abstract

An analysis of the logic of valid inferences about the structure of normal cognitive processes from the study of impaired cognitive performance in brain-damaged patients is presented. The logic of inferences from group studies and single-case studies is compared. It is shown that given certain assumptions, only the single-case method allows valid inferences about the structure of cognitive systems from the analysis of impaired performance. It is also argued that although the single-case approach is not entirely problem-free, the difficulties encountered are relatively minor.

https://pubmed.ncbi.nlm.nih.gov/3954906/

group studies

in neuropsychology, the performance of **different patients** is **combined** to yield a group average; helpful for establishing **lesion-deficit associations**.

Case Reports > Cogn Neuropsychol. 2015 Oct-Dec;32(7-8):385-411.
doi: 10.1080/02643294.2015.1131677.

Cognitive neuropsychology and its vicissitudes: The fate of Caramazza's axioms

Tim Shallice [1] [2]

Affiliations + expand

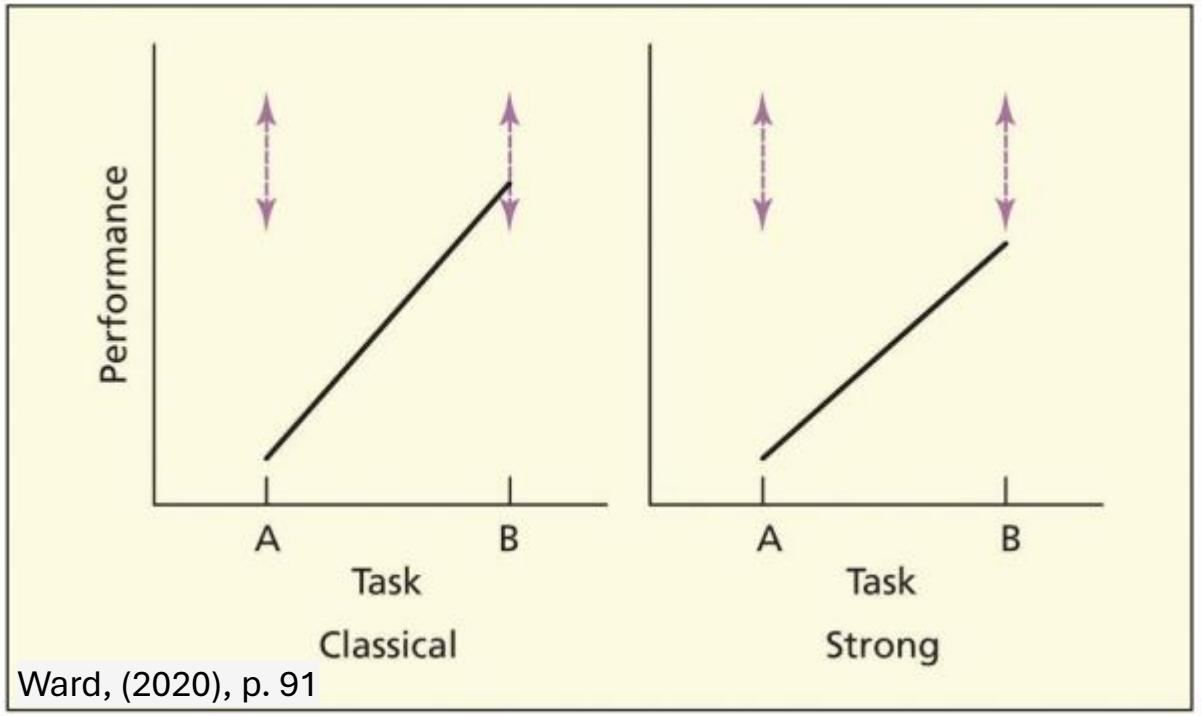
PMID: 27355606 DOI: 10.1080/02643294.2015.1131677

Abstract

Cognitive neuropsychology is characterized as the discipline in which one draws conclusions about the organization of the normal cognitive systems from the behaviour of brain-damaged individuals. In a series of papers, Caramazza, later in collaboration with McCloskey, put forward four assumptions as the bridge principles for making such inferences. Four potential pitfalls, one for each axiom, are discussed with respect to the use of single-case methods. Two of the pitfalls also apply to case series and group study procedures, and the other two are held to be indirectly testable or avoidable. Moreover, four other pitfalls are held to apply to case series or group study methods. It is held that inferences from single-case procedures may profitably be supported or rejected using case series/group study methods, but also that analogous support needs to be given in the other direction for functionally based case series or group studies. It is argued that at least six types of neuropsychological method are valuable for extrapolation to theories of the normal cognitive system but that the single- or multiple-case study remains a critical part of cognitive neuropsychology's methods.

https://pubmed.ncbi.nlm.nih.gov/27355606/

Single dissociation



Ward, (2020), p. 91

classical dissociation

performance on one task lies within the control range (shown by dotted lines)

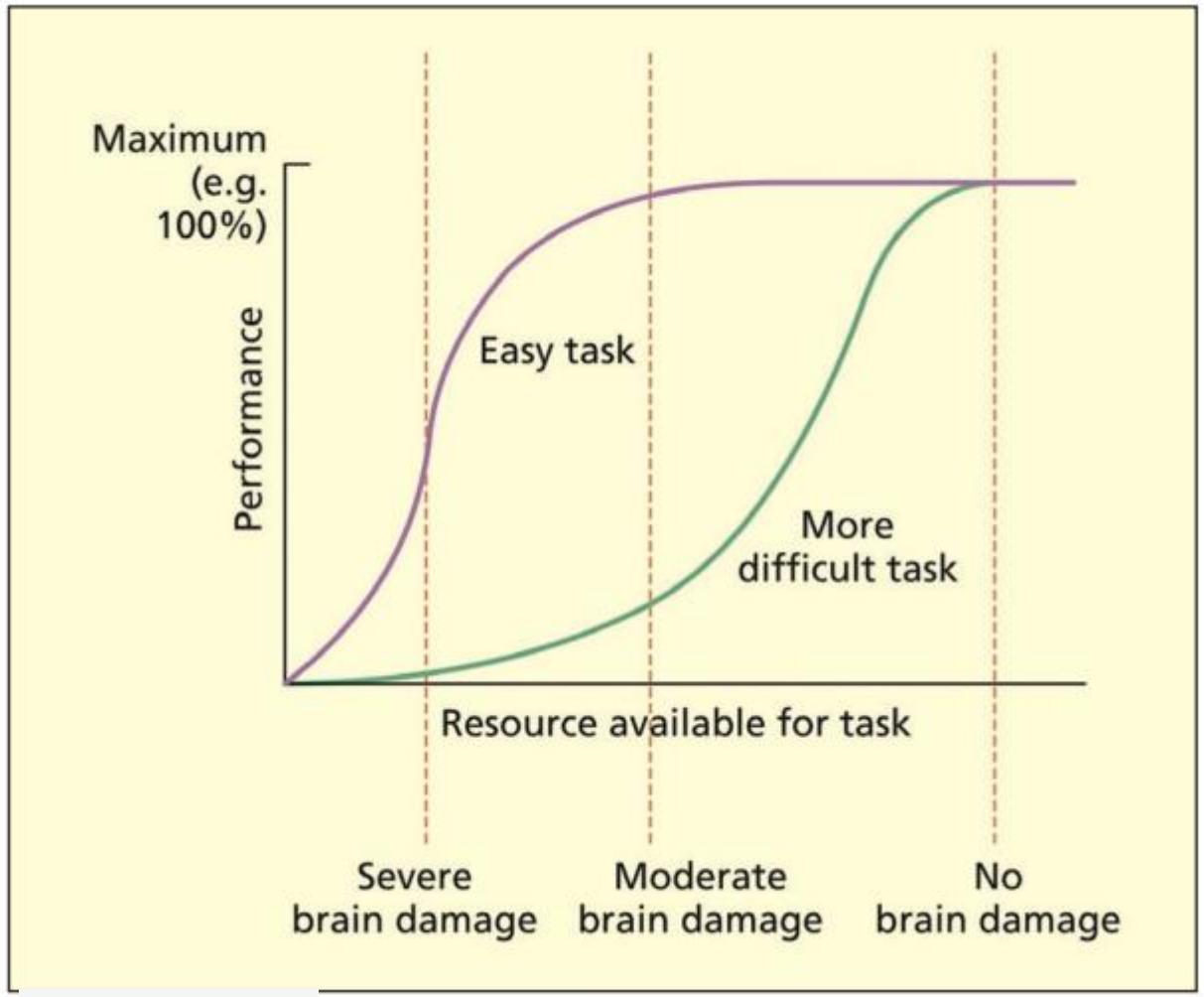
strong dissociation

both tasks fall outside the control range, but one task is significantly more impaired than the other

In both **classical** and **strong** dissociation, one inference that we can make is that **task A and task B** utilize **different cognitive processes** with **different neural resources**.

Another inference may be that the patient simply performs one of the tasks suboptimally. For example, the patient may have misunderstood the instructions or have adopted an unusual strategy for performing the task.

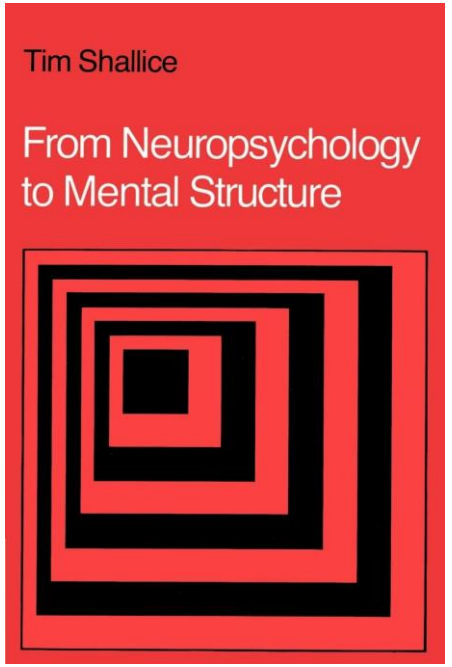
Tim Shallice, in his 1988 book, *"From Neuropsychology to Mental Structure"*, termed this the "Task-demand artifact".



Ward, (2020), p. 92

Another inference may be that the two tasks share the **same neural/cognitive resource**, but **one task uses it more**, so the damage to this resource will affect one task more than the other.

Tim Shallice, in his 1988 book, *"From Neuropsychology to Mental Structure"*, termed this the "Task-resource artifact".

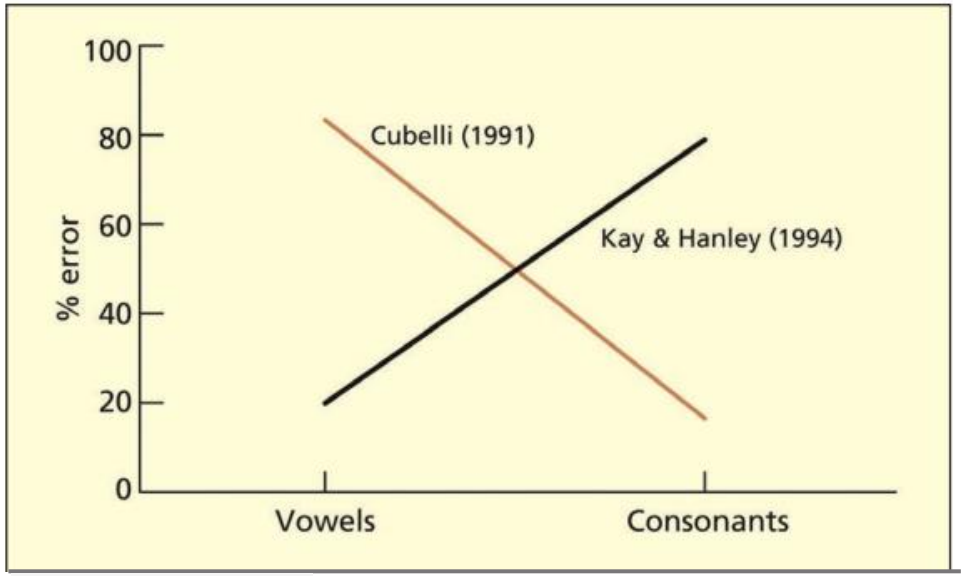


Double dissociation

double dissociation

two single dissociations

that have a **complementary profile of abilities**



Ward, (2020), p. 90

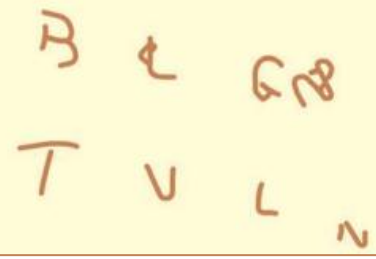
Kay and Hanley's patient made spelling errors selectively on consonants

(e.g., "record" → recorg)

Kay and Hanley's patient could write vowels better than Cubelli's patient.

Cubelli's patient (CF) could write consonants better than Kay and Hanley's.

CF's writing of BOLOGNA and TAVOLINO



Stimulation methods

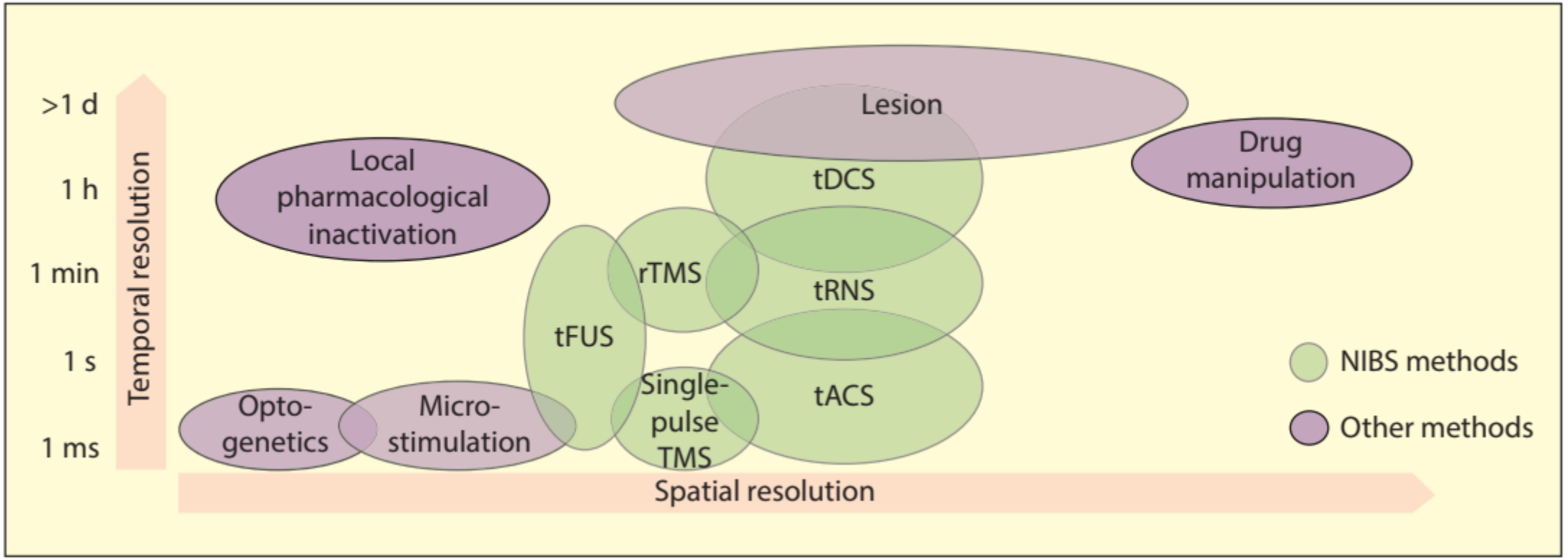
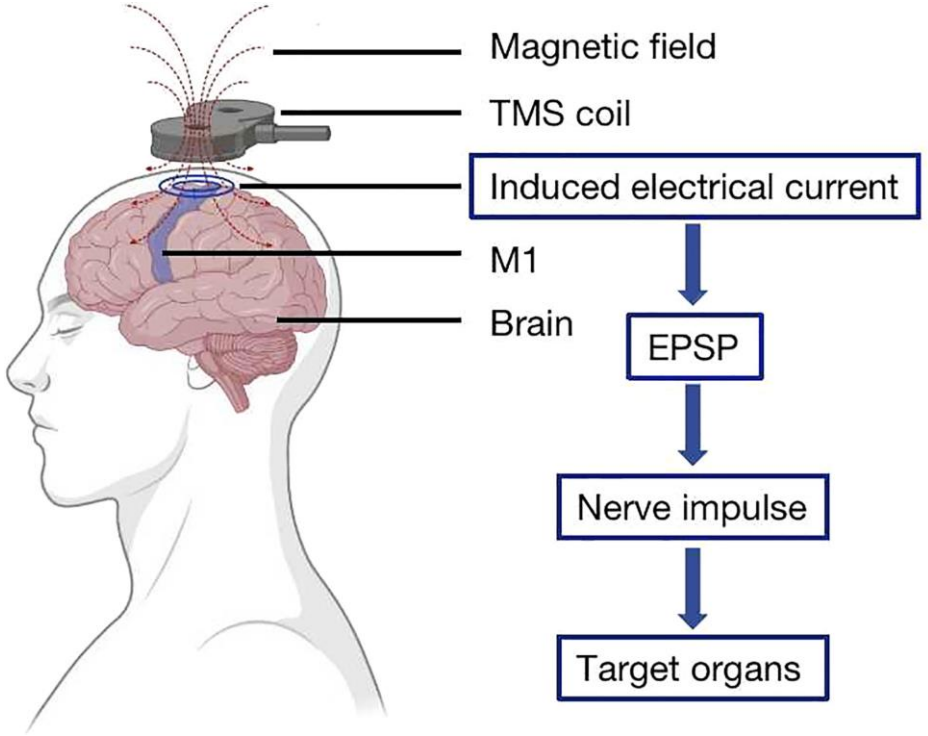


FIGURE 5.1: A taxonomy of current approaches that directly manipulate brain function either as a result of brain damage (lesions) or via short- or long-term brain stimulation. The latter can occur either invasively (shown in purple) or noninvasively (shown in green). Noninvasive brain stimulation methods (NIBS) include TMS (repetitive, rTMS or single-pulse), electrical stimulation methods (tDCS, transcranial direct current stimulation; tACS, transcranial alternating current stimulation; tRNS, transcranial random noise stimulation) or even using ultrasound (tFUS, transcranial focal ultrasound stimulation).

From Polania, Nitsche, & Ruff (2018).

Ward, (2020), p. 88

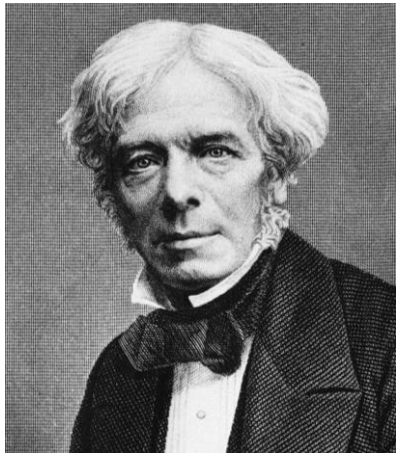
Transcranial magnetic stimulation (TMS)



Zhou et al., (2022)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9483183/

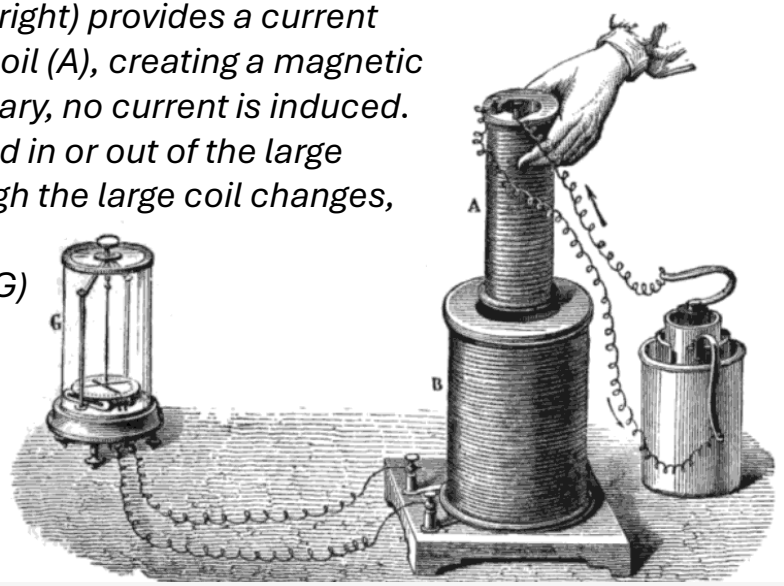
Faraday's law of induction

in physics: a quantitative relationship expressing that a **changing magnetic field induces a voltage** in a circuit



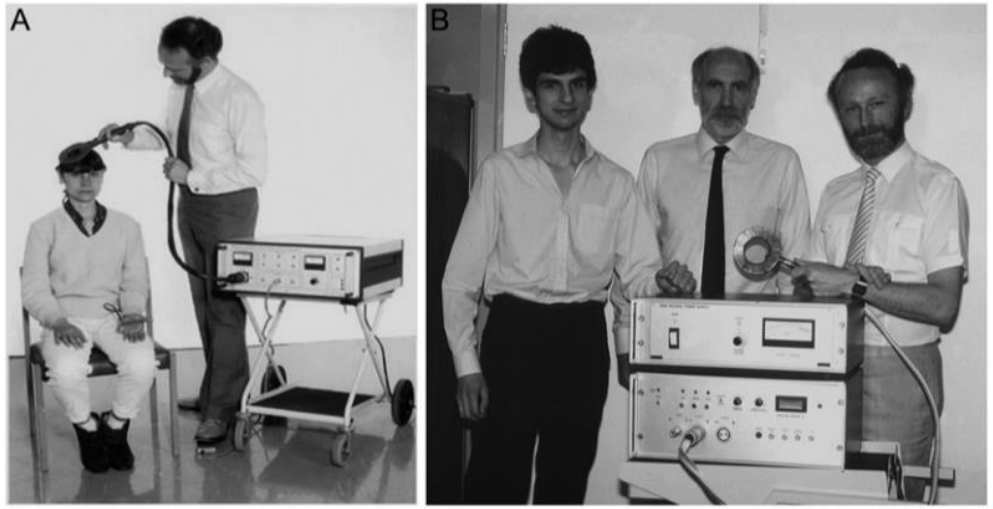
Michael Faraday
(1791 – 1867)

Faraday's experiment showing induction between coils of wire: The liquid battery (right) provides a current which flows through the small coil (A), creating a magnetic field. When the coils are stationary, no current is induced. But when the small coil is moved in or out of the large coil (B), the magnetic flux through the large coil changes, inducing a current which is detected by the galvanometer (G)



https://en.wikipedia.org/wiki/Faraday%27s_law_of_induction

Figure 7.
(A) Anthony T. Barker *during demonstration of transcranial magnetic stimulation (TMS) in London,* ***1985****.*



(B) *Anthony T. Barker (right), Ian L. Freeston (middle), and Reza Jalinous (left) presenting a TMS device in 1985.*

John Rothwell and Anthony Barker

Reminiscing about the invention of Transcranial Magnetic Stimulation

https://www.youtube.com/watch?v=1DI3EC2pQ44

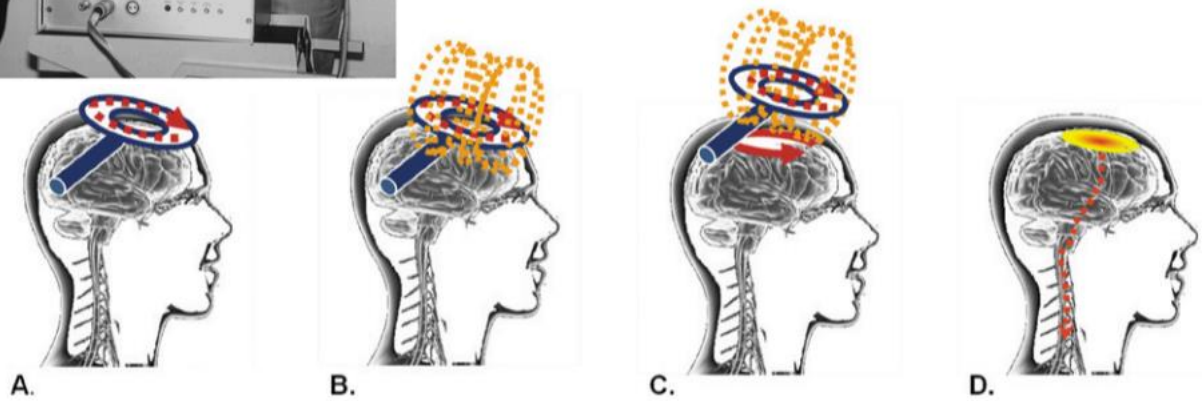
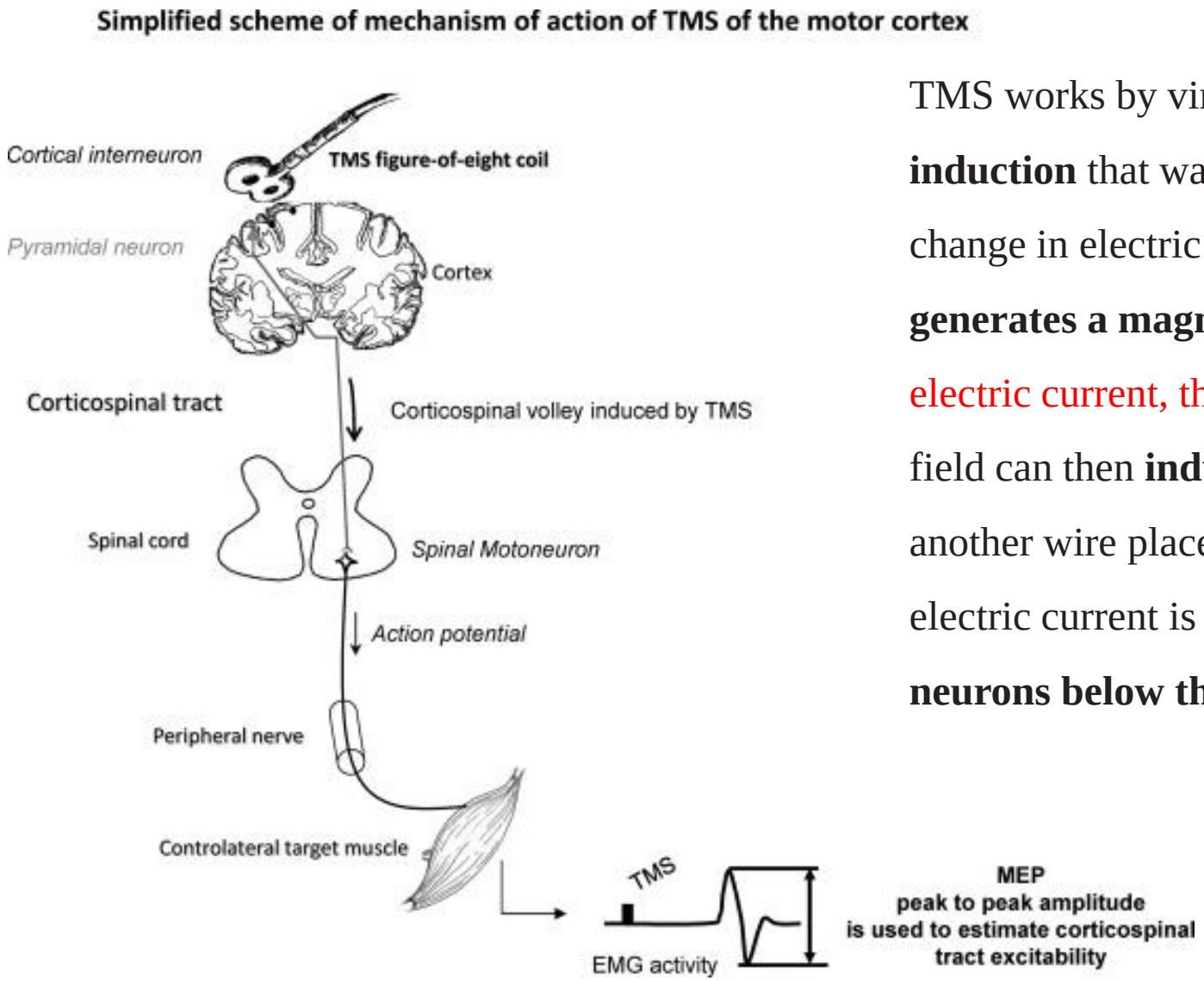


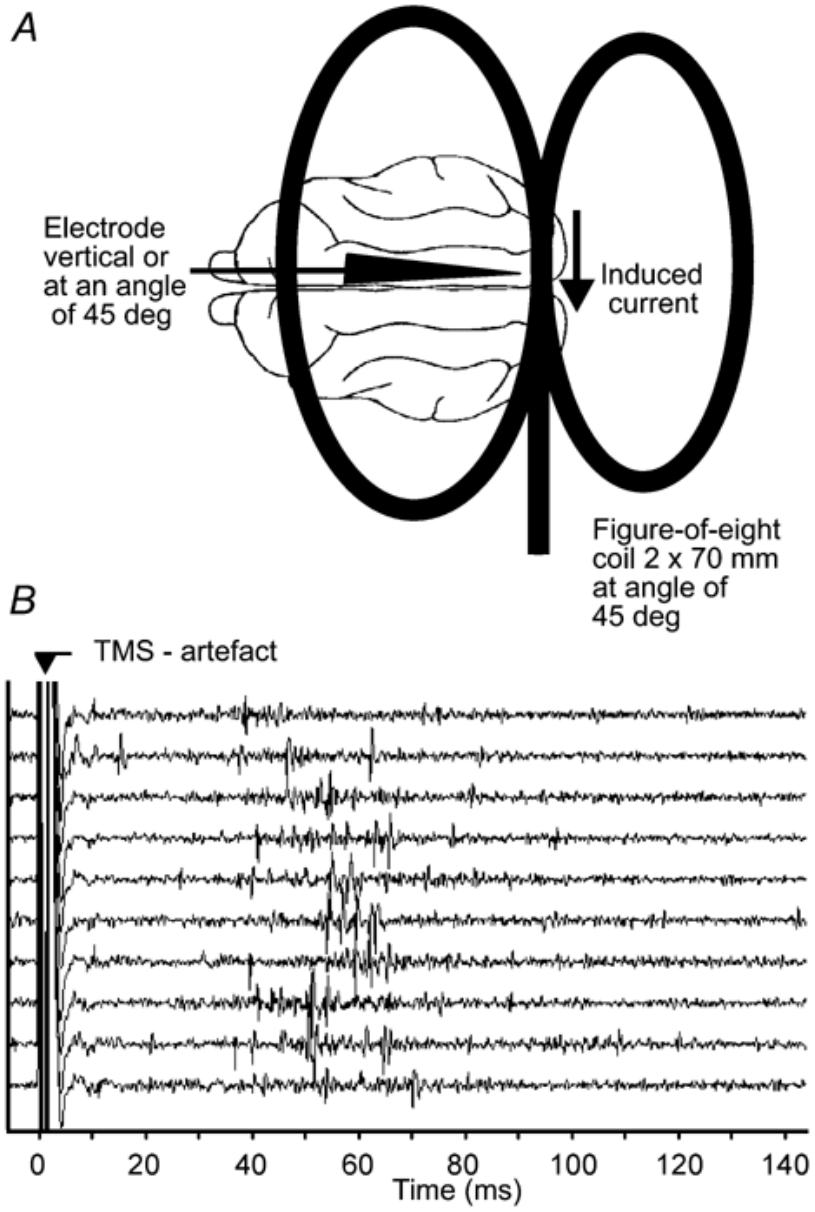
Figure 8.
(A) *Time-varying electric current flowing in the coil.*
(B) *Time-varying magnetic field generated by electric current of the coil.*
(C) *Electric current in cortical layers* ***induced*** *by magnetic field is* ***opposite*** *to the electric current flow produced by coil, "Lenz's law."*
(D) *Depolarization of cortical neurons activating the corticospinal tract during transcranial magnetic stimulation.*

Vidal-Dourado et al., (2014)
https://pubmed.ncbi.nlm.nih.gov/23787954/



TMS works by virtue of the principle of **electromagnetic induction** that was first discovered by **Michael Faraday**. A change in electric current in a **wire (the stimulating coil) generates a magnetic field**. The greater the *rate of change* in electric current, the greater the magnetic field. The magnetic field can then **induce a secondary electric current** to flow in another wire placed nearby. In the case of TMS, the secondary electric current is induced, not in a metal wire, but in the **neurons below the stimulation** site. (Ward, 2020)

Klomjai et al., (2015), https://pubmed.ncbi.nlm.nih.gov/26319963/



Moliadze et al., (2003), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2343567/

TMS causes **neurons underneath the stimulation site** to be **activated**. If these neurons are involved in performing a critical cognitive function, then **stimulating them** artificially **will disrupt** that function.

Although this process is described as a *"virtual lesion"* or a *"reversible lesion,"* a more accurate description would be in terms of interference. The **neurons are being activated** both from an **internal source** (the task demands themselves) **and an external source** (the TMS), with the latter disrupting the former.

Of course, if the region is not involved in the task, then interference would not occur in this way. (Ward, 2020)

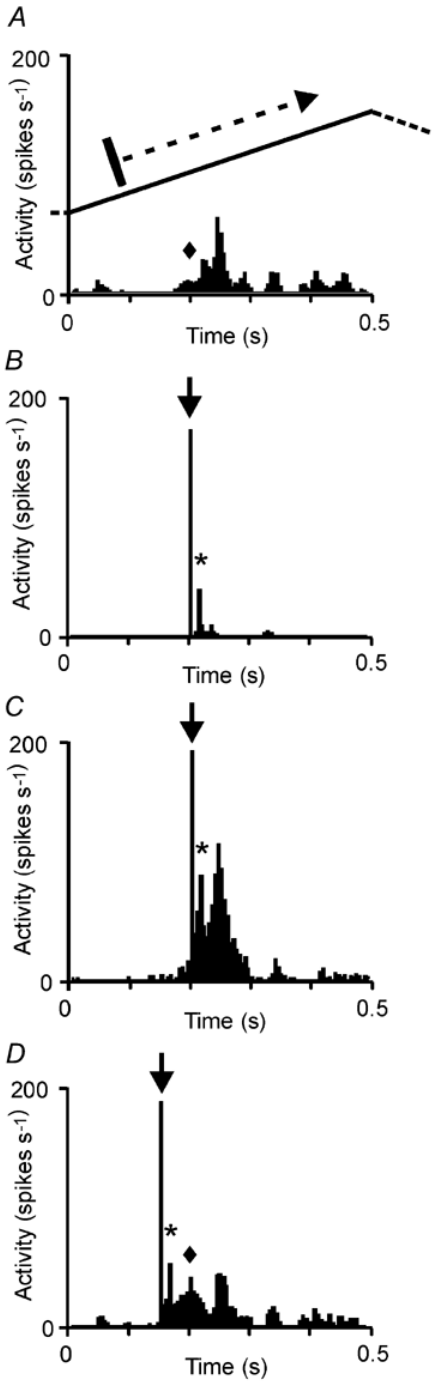


Figure 4
Effect of TMS on visual responses to moving bars.

Visual response of a ***cortical neuron (simple cell)***
to a ***bar moving across its receptive field****.*
For simplicity, only the response to one direction
of bar motion is shown here (see inset of motion trajectory).

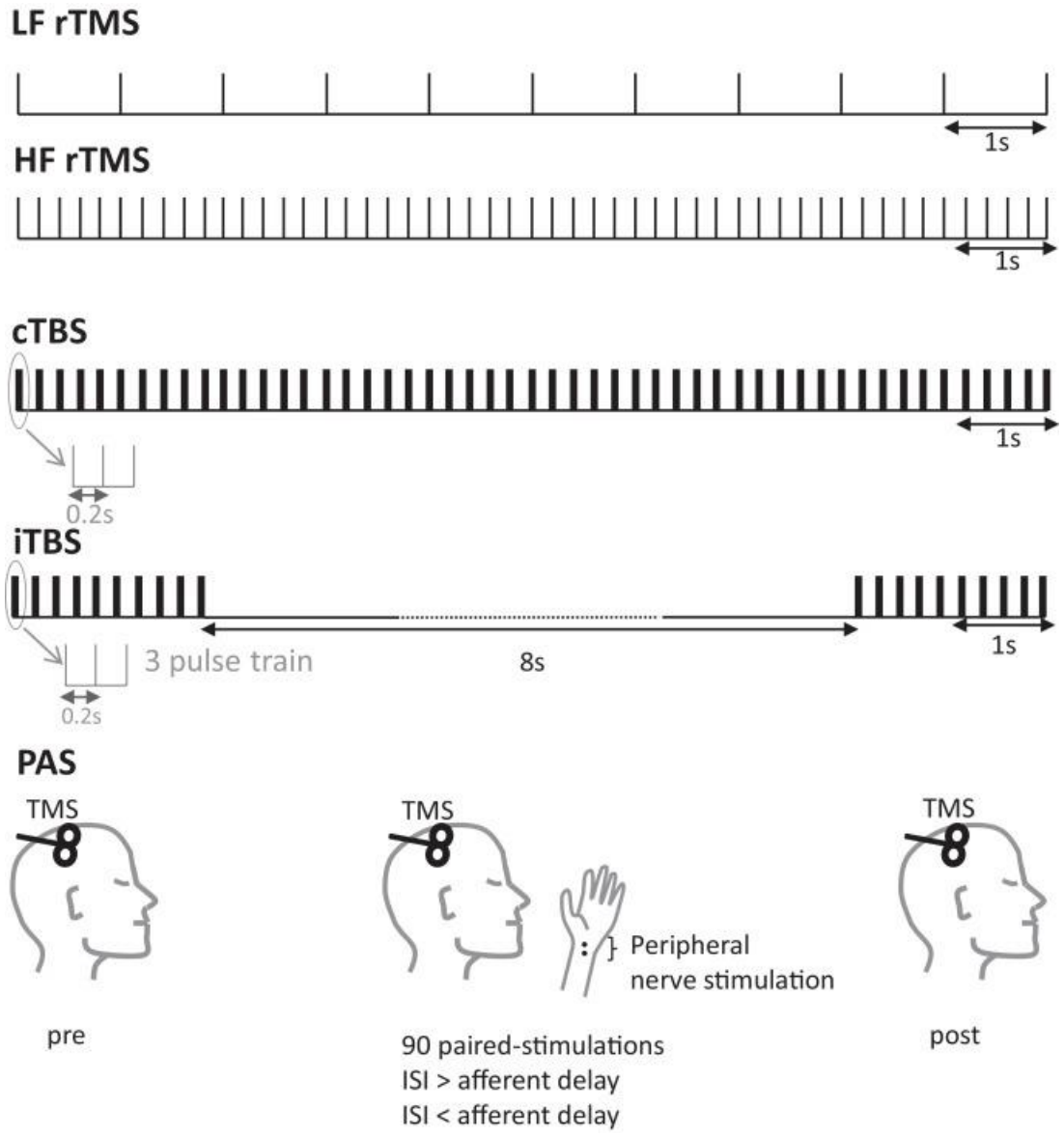
A, visual stimulation alone*.*

B, TMS alone*.*

C and D, TMS combined with visual stimulation*,*
with TMS given at two different times.

Note that the activity ***evoked by TMS alone (asterisks)*** *is*
less than *the increase of visual activity during* ***combined***
TMS and moving bar *(see response components labelled*
with asterisks and diamonds). Arrows indicate the TMS artefact.

Moliadze et al., (2003)



single-pulse TMS (including paired-pulse TMS => explore brain functioning

repetitive TMS (rTMS) => induce long term changes in brain

Fig. 2.

Simple repetitive TMS (rTMS) *protocols consist of identical stimuli spaced by an identical* ***inter-stimulus interval (ISI).***

Effects *depend on* ***stimulation frequency****: at* ***low frequency*** *(LF rTMS < 1 Hz), rTMS* ***depresses excitability in the motor cortex****, whereas at* ***high frequency*** *(HF rTMS > 5 Hz),* ***cortical excitability is increased****.*

Theta burst stimulation (TBS) *involves bursts of* ***high-frequency*** *stimulation (3 pulses at 50 Hz)* ***repeated*** *with an ISI of 200 ms (5 Hz).*

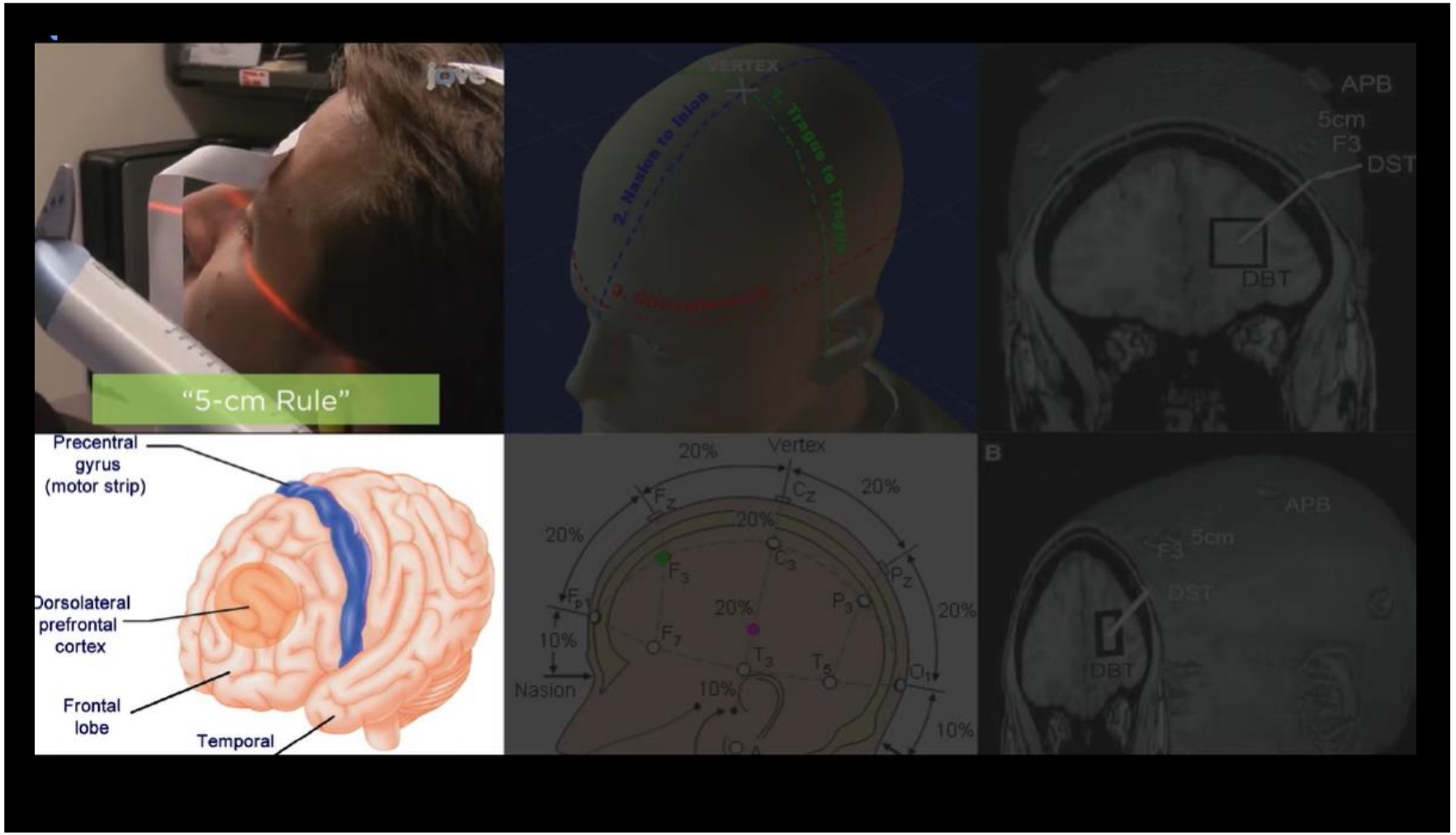
In an ***intermittent TBS (iTBS)*** *protocol, bursts are delivered for 2 s, then repeated every 10 s (2 s of TBS followed by a pause of 8 s).*

However, in a ***continuous TBS protocol (cTBS)****, bursts are repeated for 40 s without any pause.*

Paired associative stimulation (PAS) *protocols combine a repetitive stimulation of peripheral nerve afferents of the target muscle with TMS over its motor area. Intervention consists of 90 to 100 PAS.*

Klomjai et al., (2015)

An in-depth presentation on TMS by Dr. Zhi-De Deng, staff scientist at the National Institute of Mental Health Non-invasive Neuromodulation Unit



https://www.nimh.nih.gov/news/media/2020/zhi-de-deng-transcranial-magnetic-stimulation-physics-devices-and-modeling

Experimental applications

Yale SCHOOL OF MEDICINE ≡ MENU

Steele, Assaf to Study Brain Mechanisms in Adults with Autism Spectrum Disorder

August 14, 2023

Steele, Assaf to Study Brain Mechanisms in Adults with Autism Spectrum Disorder

medicine.yale.edu • 1 min read

Vaughn R. Steele, PhD, assistant professor of psychiatry, and Michal Assaf, MD, director of research at the Mary W. Parker Autism Center and adjunct associate professor of psychiatry, are the principal investigators on a project funded by the National Institute of Mental Health that will study brain mechanisms in adults with autism spectrum disorder (ASD).

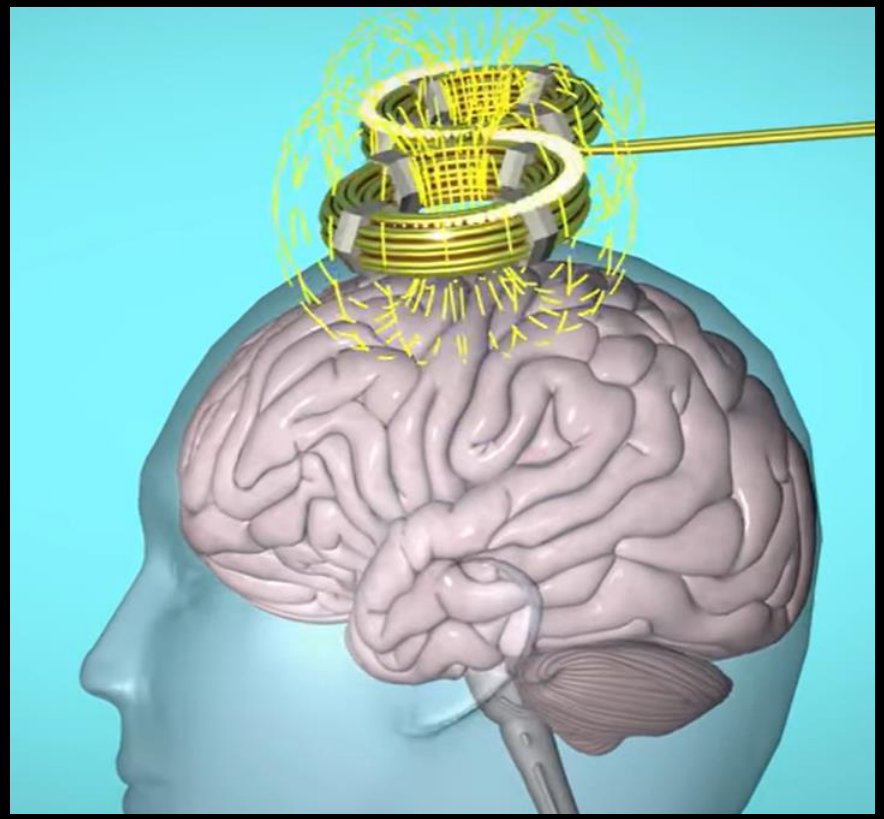
The $3.78 million grant seeks to better understand deficits in "mentalizing," a high-order social cognitive process that allows people to build representations of other people's state of mind and adjust their own behaviors accordingly. These deficits are hypothesized to result in difficulties in social communication ASD.

Steele, Assaf, and their research team at the Olin Neuropsychiatry Research Center in Hartford will use functional magnetic resonance imaging scans and transcranial magnetic stimulation (TMS) to better understand mentalizing in autistic individuals.

This research study aims to validate the neural mechanism of mentalizing in ASD, offering a crucial first step toward assessing the potential effectiveness of TMS in enhancing social behaviors in future clinical studies.

Potential clinical applications

Physical rehabilitation after stroke



https://www.youtube.com/watch?v=i0GKbmbES08

Treatment-resistant depression

Cureus. 2019 May; 11(5): e4736.
Published online 2019 May 23. doi: 10.7759/cureus.4736

Use of Transcranial Magnetic Stimulation for Depression

Monitoring Editor: Alexander Muacevic and John R Adler

Sukaina Rizvi[1] and Ali M Khan[2]

▸ Author information ▸ Article notes ▸ Copyright and License information PMC Disclaimer

Abstract Go to: ▸

Transcranial magnetic stimulation (TMS), a research tool with various effects on brain cells, can depolarize cerebral neurons noninvasively. This method offers temporal and spatial resolution and can be combined with other neurocognitive and neuro-experimental techniques. Prefrontal TMS therapy repeated daily for four to six weeks is a neuromodulation technique approved by the US Food and Drug Administration for the treatment of major depressive disorder (MDD) in patients resistant to medications. This technique utilizes electromagnetic induction to excite neuronal cells. Several recent studies have enhanced our understanding of this novel treatment intervention. This report reviews recent studies on the mechanism of action, patient eligibility, effectiveness, and safety of TMS in treating depression.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6649915/

Curr Neuropharmacol. 2019 Aug; 17(8): 787–807.
Published online 2019 Aug. doi: 10.2174/1570159X17666190409142555

Brain Stimulation in Obsessive-Compulsive Disorder (OCD): A Systematic Review

Chiara Rapinesi,[1,*] Georgios D. Kotzalidis,[1] Stefano Ferracuti,[2] Gabriele Sani,[1,3] Paolo Girardi,[1,3] and Antonio Del Casale[1]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7059162/

Review › Front Neurol. 2020 Feb 18:11:114. doi: 10.3389/fneur.2020.00114. eCollection 2020.

Effect of Repetitive Transcranial Magnetic Stimulation on Pain Management: A Systematic Narrative Review

Seoyon Yang [1], Min Cheol Chang [2]

https://pubmed.ncbi.nlm.nih.gov/32132973/

› Neurosci Biobehav Rev. 2019 Sep:104:118-140. doi: 10.1016/j.neubiorev.2019.06.007.
Epub 2019 Jul 2.

Transcranial electrical and magnetic stimulation (tES and TMS) for addiction medicine: A consensus paper on the present state of the science and the road ahead

Hamed Ekhtiari [1], Hosna Tavakoli [2], Giovanni Addolorato [3], Chris Baeken [4], Antonello Bonci [5], Salvatore Campanella [6], Luis Castelo-Branco [7], Gaëlle Challet-Bouju [8], Vincent P Clark [9], Eric Claus [10], Pinhas N Dannon [11], Alessandra Del Felice [12], Tess den Uyl [13], Marco Diana [14], Massimo di Giannantonio [15], John R Fedota [16], Paul Fitzgerald [17], Luigi Gallimberti [18], Marie Grall-Bronnec [8], Sarah C Herremans [4], Martin J Herrmann [19], Asif Jamil [20], Eman Khedr [21], Christos Kouimtsidis [22], Karolina Kozak [23], Evgeny Krupitsky [24], Claus Lamm [25], William V Lechner [26], Graziella Madeo [27], Nastaran Malmir [28], Giovanni Martinotti [15], William M McDonald [29], Chiara Montemitro [30], Ester M Nakamura-Palacios [31], Mohammad Nasehi [32], Xavier Noël [6], Masoud Nosratabadi [33], Martin Paulus [34], Mauro Pettorruso [15], Basant Pradhan [35], Samir K Praharaj [36], Haley Rafferty [7], Gregory Sahlem [37], Betty Jo Salmeron [27], Anne Sauvaget [38], Renée S Schluter [39], Carmen Sergiou [40], Alireza Shahbabaie [20], Christine Sheffer [41], Primavera A Spagnolo [42], Vaughn R Steele [16], Ti-Fei Yuan [43], Josanne D M van Dongen [40], Vincent Van Waes [44], Ganesan Venkatasubramanian [45], Antonio Verdejo-García [46], Ilse Verveer [40], Justine W Welsh [29], Michael J Wesley [47], Katie Witkiewitz [10], Fatemeh Yavari [20], Mohammad-Reza Zarrindast [48], Laurie Zawertailo [23], Xiaochu Zhang [49], Yoon-Hee Cha [34], Tony P George [23], Flavio Frohlich [50], Anna E Goudriaan [51], Shirley Fecteau [52], Stacey B Daughters [50], Elliot A Stein [16], Felipe Fregni [7], Michael A Nitsche [53], Abraham Zangen [54], Marom Bikson [55], Colleen A Hanlon [37]

https://pubmed.ncbi.nlm.nih.gov/31271802/

Transcranial electric stimulation (tES)

Electroconvulsive therapy (ECT)

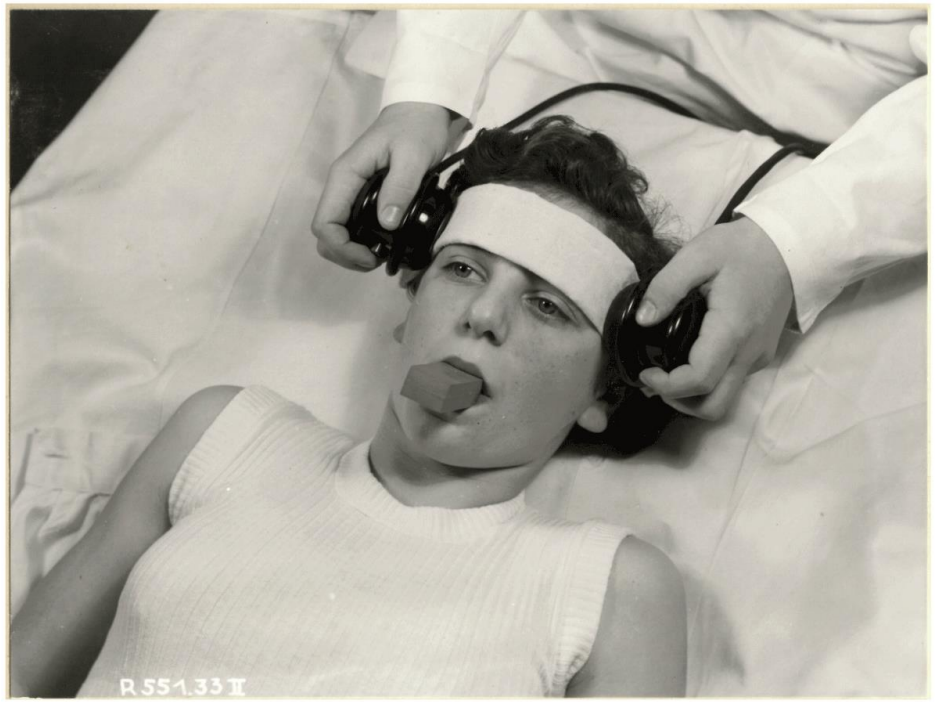


Illustration: Siemens' new electrodes relaying on Braunmühl's recommendations. Source: picture dated 1 955, used in an advertising brochure in 1957, Siemens MedArchives, Erlangen, Germany.

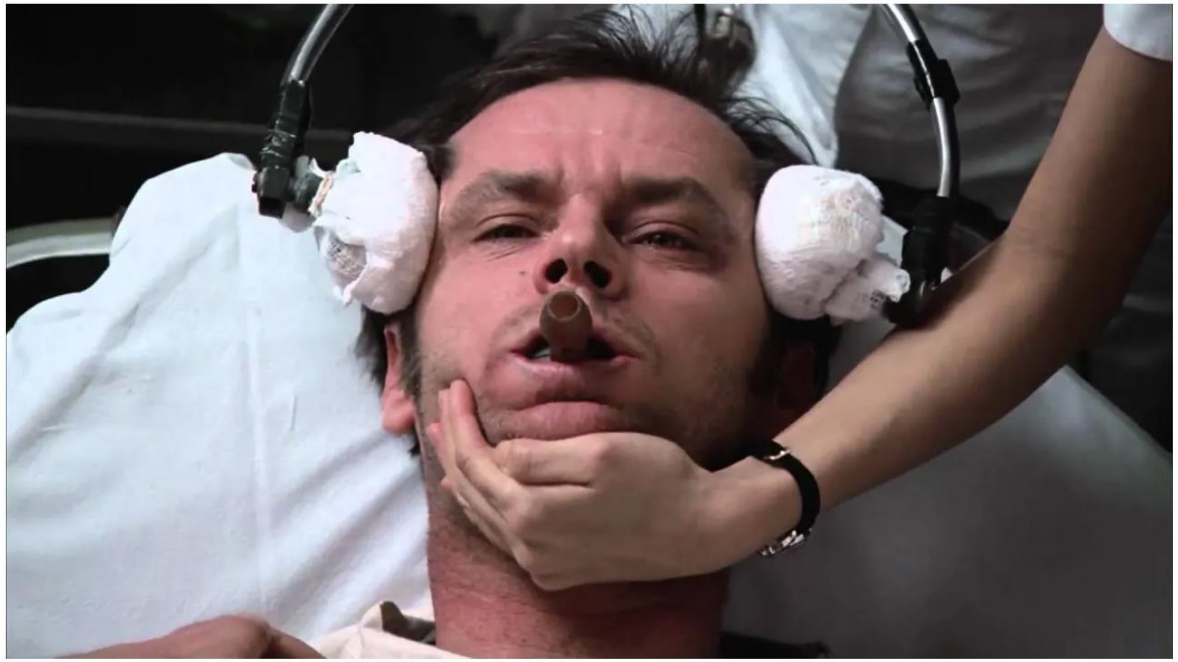
https://tinyurl.com/56u99uf4

See also https://www.youtube.com/watch?v=LPBTEHYlZK4

CHANGING THE IMAGE PROBLEM OF ELECTROCONVULSIVE THERAPY

Many people still think of electroconvulsive therapy as a barbaric treatment, often dramatised in movies, but modern ECT that includes patient's families can help dispel the stigma

By Cheryl Critchley, University of Melbourne



Thanks to movies like One Who Flew Over the Cuckoo's Nest, ECT has an image problem. Picture: Fantasy Films

https://tinyurl.com/m6a88up

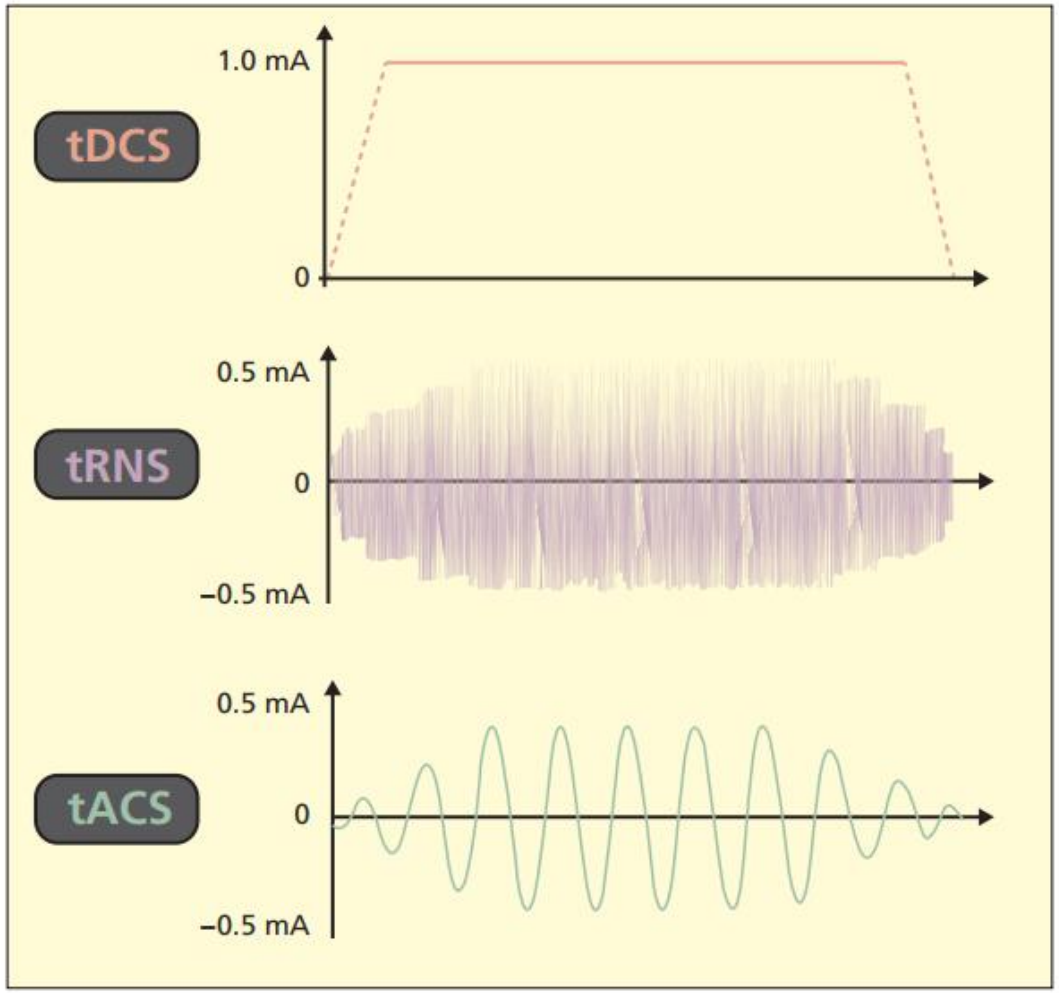


FIGURE 5.16: In transcranial electrical stimulation (tES) methods, electrical current is passed between two stimulating pads. The direction of the current can be constant (tDCS), or can vary randomly (tRNS), or can alternate rhythmically (tACS).

Ward, (2020), p. 110

Unlike **ECT**, where the voltage used is higher (70 to 120 volts, for a duration of 100 milliseconds to 6 seconds), **tES** uses a **very weak electric current** passed between two stimulating pads.

Review > Neuropsychol Rehabil. 2011 Oct;21(5):602-17. doi: 10.1080/09602011.2011.557292. Epub 2011 Aug 5.

Transcranial electrical stimulation (tES – tDCS; tRNS, tACS) methods

Walter Paulus [1]

Affiliations + expand

PMID: 21819181 DOI: 10.1080/09602011.2011.557292

Abstract

Weak transcranial direct current stimulation (tDCS) with a homogenous DC field at intensities of around 1 mA induces long-lasting changes in the brain. tDCS can be used to manipulate brain excitability via membrane polarisation: cathodal stimulation hyperpolarises, while anodal stimulation depolarises the resting membrane potential, whereby the induced after-effects depend on polarity, duration and intensity of the stimulation. A variety of other parameters influence tDCS effects; co-application of neuropharmacologically active drugs may most impressively prolong or even reverse stimulation effects. Transcranial alternating stimulation (tACS) and random noise stimulation (tRNS) are used to interfere with ongoing neuronal oscillations and also finally produce neuroplastic effects if applied with appropriate parameters.

https://pubmed.ncbi.nlm.nih.gov/21819181/

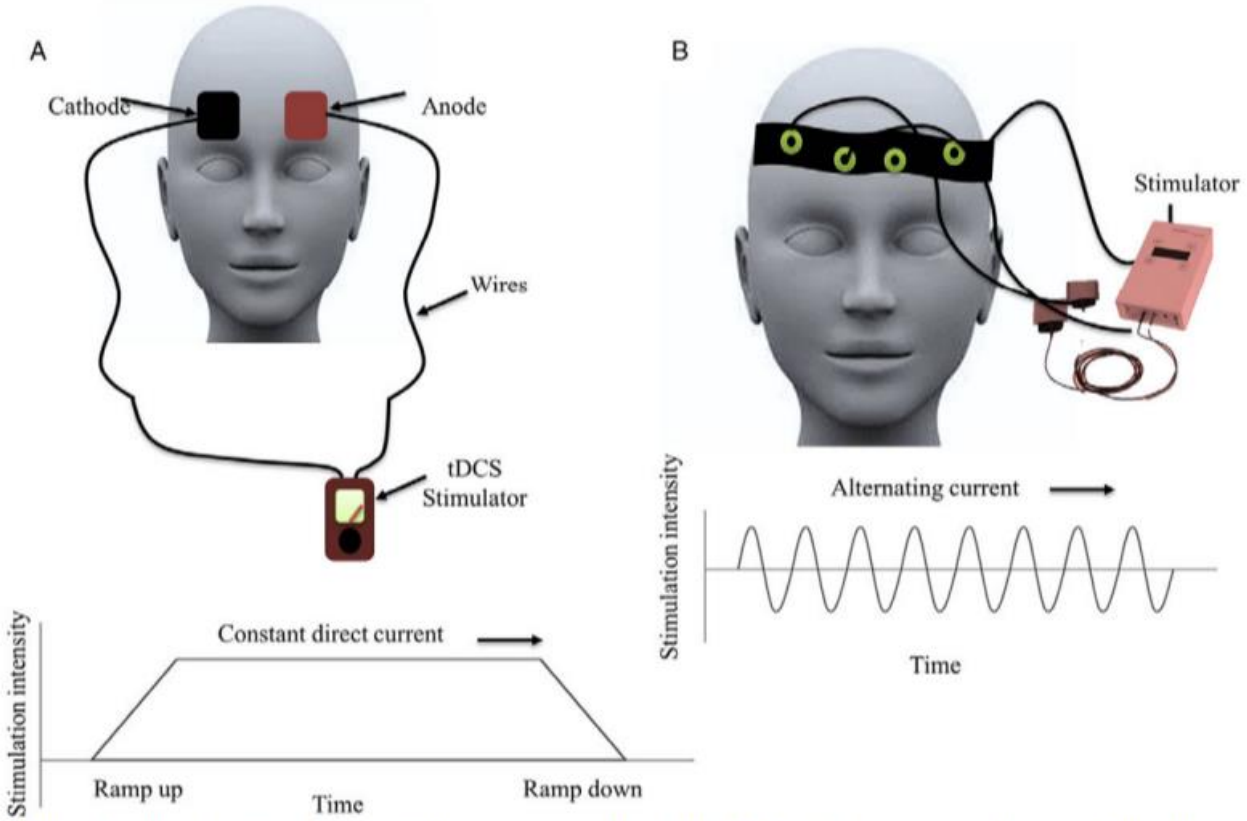
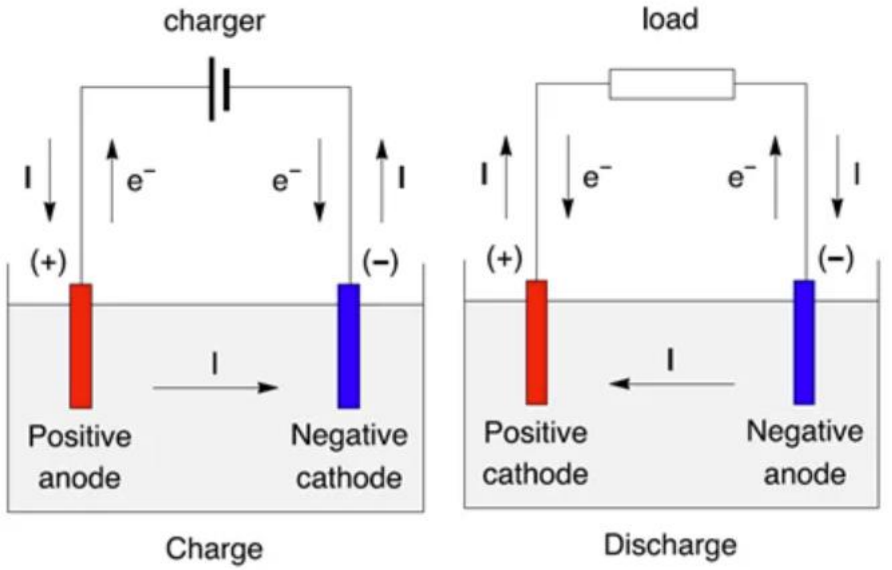


Figure 3: *Schematic representation of the transcranial direct (tDCS) and alternating (tACS) current stimulation: (A) tDCS: transcranial direct current stimulation showing anodal and cathodal electrodes placed over bifrontal regions and the graph below plots stimulation intensity overtime demonstrating that the intensity ramps up and down, and the intensity provided over the stipulated time. (B) tACS: transcranial alternating current stimulation showing headband containing electrodes and the graph below shows that the stimulation intensities vary in a sinusoidal manner overtime with the alternating polarity of current applied.*

Bhattacharya et al., (2021), https://pubmed.ncbi.nlm.nih.gov/34238393/

Don't **PANIC** - **P**ositive is **A**node, **N**egative **I**s **C**athode.



https://tinyurl.com/mw6t2cjz

After a period of stimulation (e.g., 10 min) a cognitive task is performed and this can be compared with sham stimulation, or **anodal** and **cathodal** stimulation can be directly contrasted.

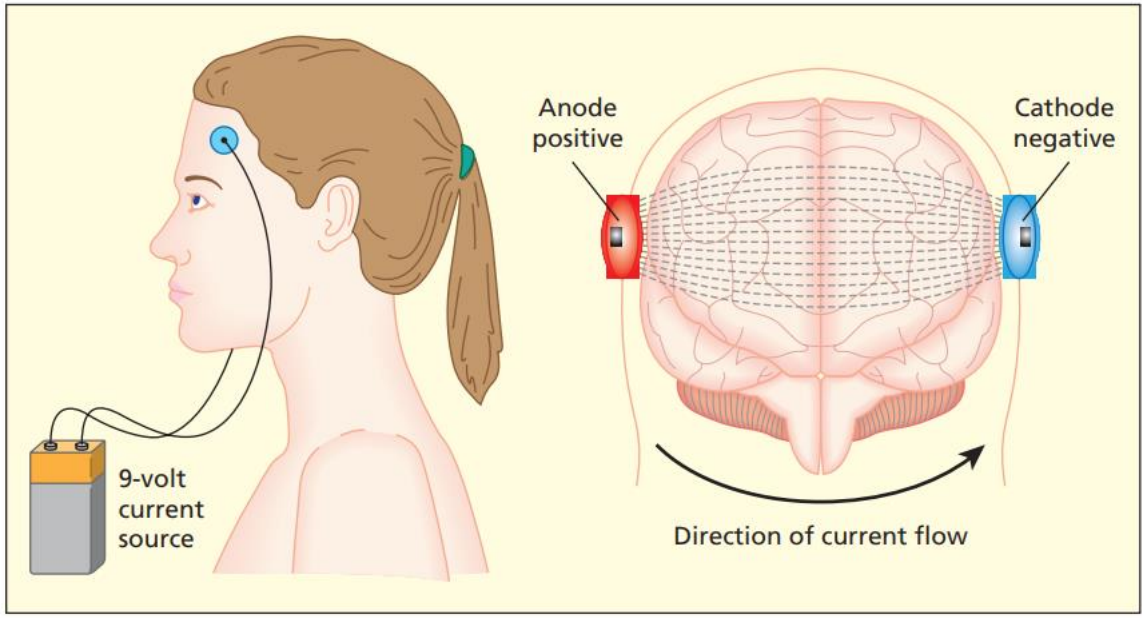
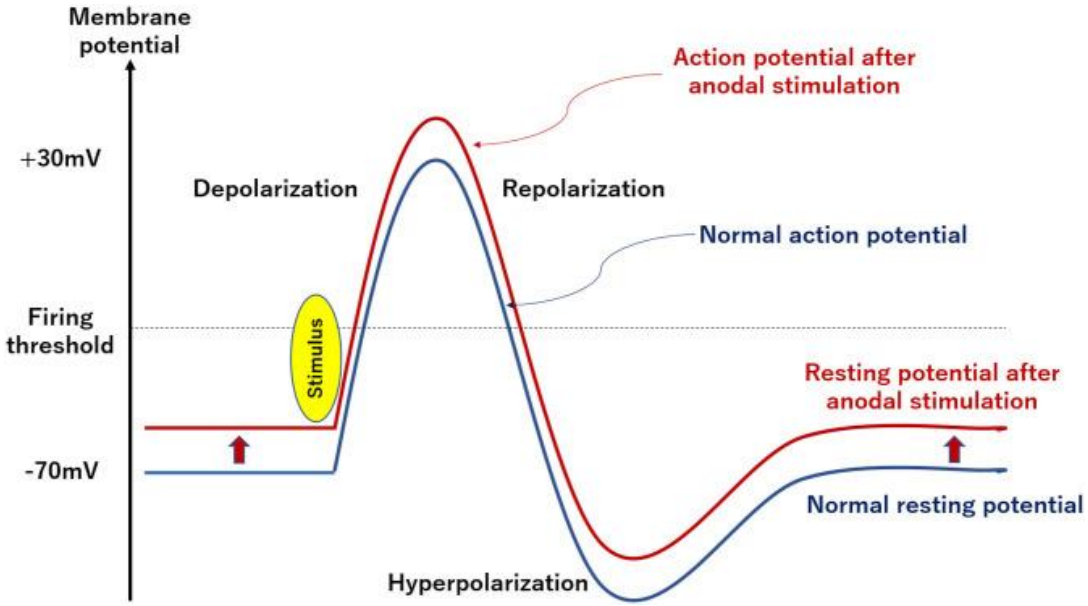


FIGURE 5.17: The method of tDCS uses a very weak electric current applied using stimulating pads attached to the scalp. Direct current involves the flow of electric charge from a positive site (an anode) to a negative site (a cathode).

Ward, (2020), p. 111

Cathodal tDCS stimulation tends to **disrupt** performance (i.e., it is conceptually equivalent to a virtual lesion approach).

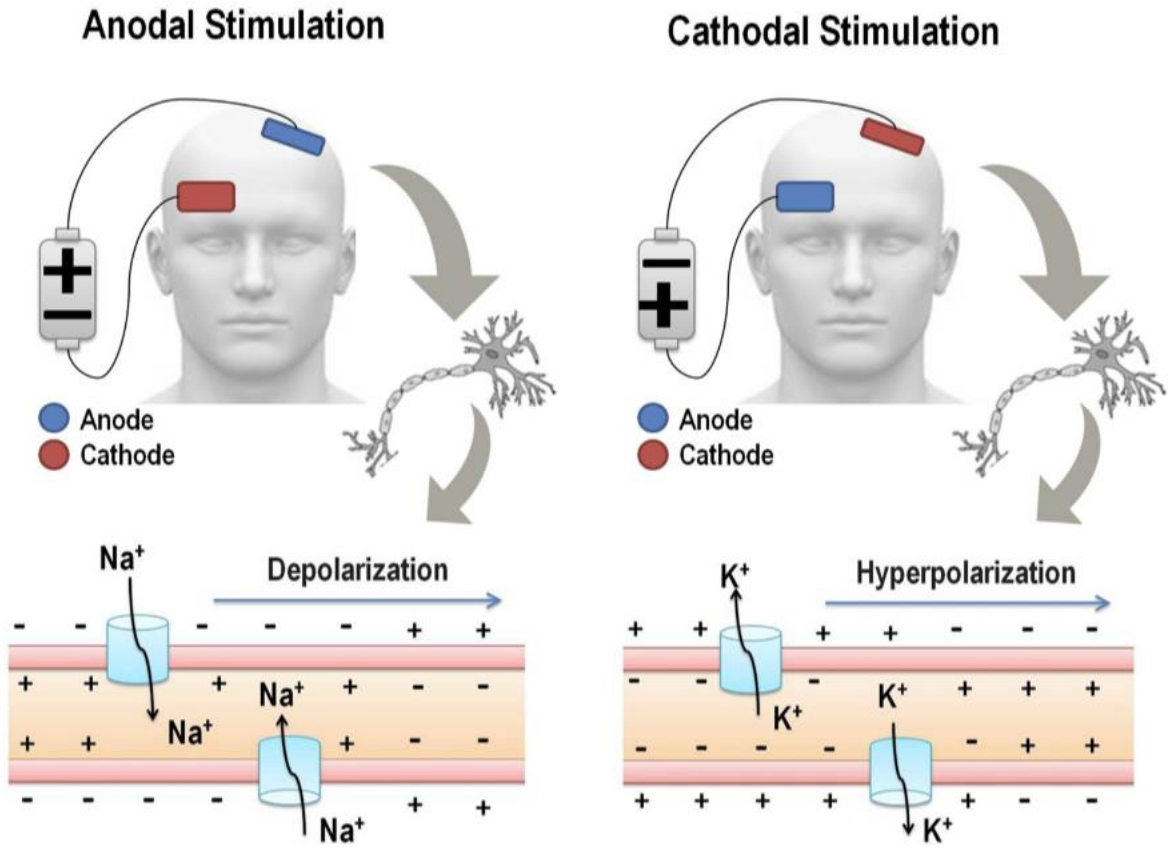
Anodal tDCS stimulation tends to **enhance** performance.



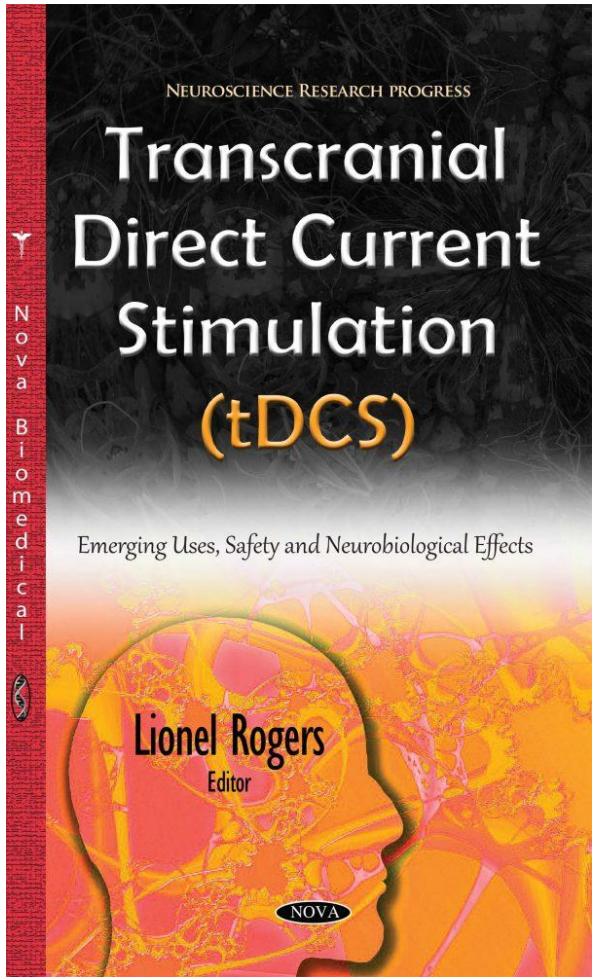
Yamada & Sumiyoshi, (2021)
https://pubmed.ncbi.nlm.nih.gov/33613218/

Anodal tDCS stimulation tends to **enhance** performance.

Cathodal tDCS stimulation tends to **disrupt** performance.



Rozisky et al., in Rogers (2015), p. 65



Review > Front Neurol. 2021 Feb 15:12:587771. doi: 10.3389/fneur.2021.587771.
eCollection 2021.

Neurobiological After-Effects of Low Intensity Transcranial Electric Stimulation of the Human Nervous System: From Basic Mechanisms to Metaplasticity

Sohaib Ali Korai [1], Federico Ranieri [2], Vincenzo Di Lazzaro [3], Michele Papa [1 4], Giovanni Cirillo [1 2]

Affiliations + expand

PMID: 33658972 PMCID: PMC7917202 DOI: 10.3389/fneur.2021.587771

Free PMC article

Abstract

Non-invasive low-intensity transcranial electrical stimulation (tES) of the brain is an evolving field that has brought remarkable attention in the past few decades for its ability to directly modulate specific brain functions. Neurobiological after-effects of tES seems to be related to changes in neuronal and synaptic excitability and plasticity, however mechanisms are still far from being elucidated. We aim to review recent results from *in vitro* and *in vivo* studies that highlight molecular and cellular mechanisms of transcranial direct (tDCS) and alternating (tACS) current stimulation. Changes in membrane potential and neural synchronization explain the ongoing and short-lasting effects of tES, while changes induced in existing proteins and new protein synthesis is required for long-lasting plastic changes (LTP/LTD). Glial cells, for decades supporting elements, are now considered constitutive part of the synapse and might contribute to the mechanisms of synaptic plasticity. This review brings into focus the neurobiological mechanisms and after-effects of tDCS and tACS from *in vitro* and *in vivo* studies, in both animals and humans, highlighting possible pathways for the development of targeted therapeutic applications.

https://pubmed.ncbi.nlm.nih.gov/33658972/

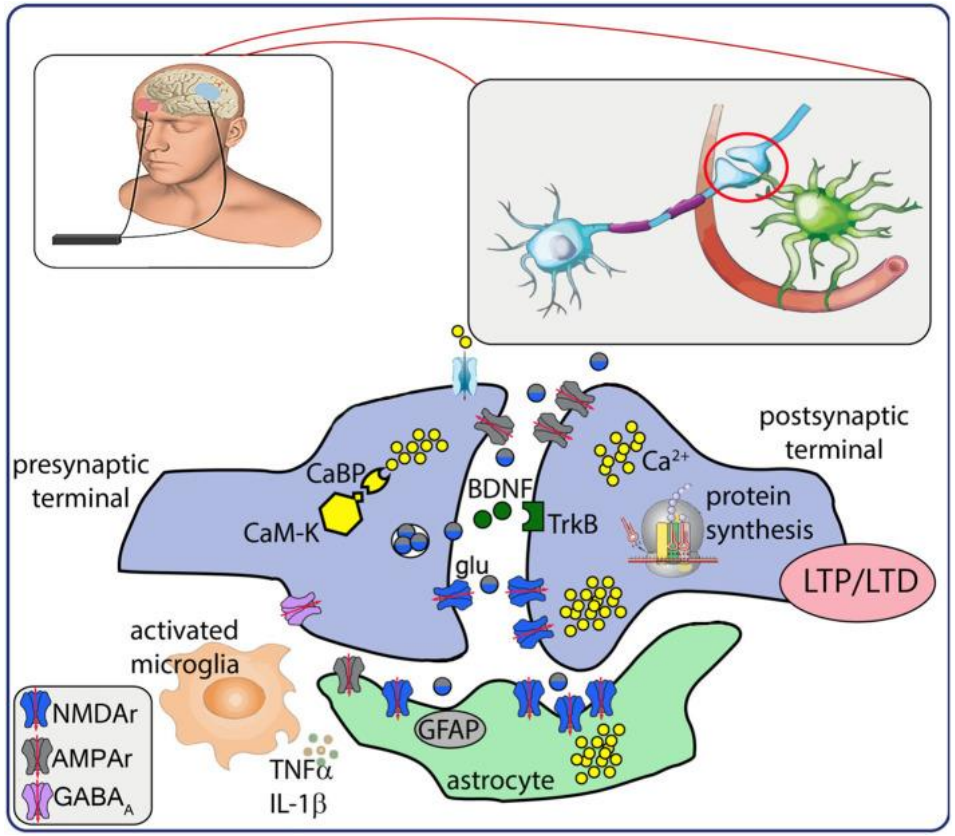


Figure 1 *Presynaptic mechanisms result in* ***glutamate*** *release that* ***activates AMPA/NMDA receptors, modulates BDNF release*** *and* ***interaction with tyrosine kinase (TrkB) receptor,*** *responsible for a cascade of intracellular events that lead to de novo protein synthesis.*
Electrical stimulation also modulates activation of ***astrocytes*** *and neuroinflammatory response.*
Altogether, these mechanisms may underlie the establishment of ***LTP/LTD****.*

Table 1: Key features of different modes of NIBS

Type of NIBS	Major features	Type of stimulation	Possible utility or clinical indications
TMS	Noninvasive magnetic stimulation	Magnetic	TMS has the largest number of studies for clinical applications. It is the only NIBS with approved clinical indication (treatment-resistant depression) and recommendation for clinical use
tDCS	Noninvasive and direct current	Electrical	tDCS is potentially a valuable tool to treat neuropsychiatric disorders such as depression and anxiety
tACS	Noninvasive and alternating current	Electrical	Can modulate altered oscillatory patterns such as in Parkinson's disease (PD) leading to reduced tremor amplitude
tRNS	Noise based on stochastic resonance	Electrical	This stimulation can temporarily increase cortical excitability and can lead to increased perception or improved cognition. Low frequency-tRNS may reduce tinnitus loudness and tRNS may improve neuropathic pain.
taVNS	Noninvasive and auricular	Electrical	As alternative to the invasive VNS procedure. taVNS applied to patients with drug-resistant epilepsy may decrease seizure frequency
TUS	Transcranial ultrasound	Ultrasound	Modulate the human cortical and subcortical functions with high degree of spatial specificity
GVS	Galvanic vestibular stimulation	Electrical	GVS has been found to improve stability during balance tasks in healthy individuals and may have application in PD and related disorders

GVS: galvanic vestibular stimulation; NIBS: noninvasive brain stimulation; TMS: transcranial magnetic stimulation; tACS: transcranial alternating current stimulation; tRNS: transcranial random noise stimulation; tDCS: transcranial direct current stimulation; taVNS: transcutaneous auricular vagal nerve stimulation.

Bhattacharya et al., (2021), https://pubmed.ncbi.nlm.nih.gov/34238393/

Computational approaches

Neuroimage. 2015 Aug 15:117:202-21. doi: 10.1016/j.neuroimage.2015.05.041. Epub 2015 May 22.

Dynamic causal modelling of brain-behaviour relationships

L Rigoux [1], J Daunizeau [2]

Affiliations + expand

PMID: 26008885 DOI: 10.1016/j.neuroimage.2015.05.041

Abstract

In this work, we expose a mathematical treatment of brain-behaviour relationships, which we coin behavioural Dynamic Causal Modelling or bDCM. This approach aims at decomposing the brain's transformation of stimuli into behavioural outcomes, in terms of the relative contribution of brain regions and their connections. In brief, bDCM places the brain at the interplay between stimulus and behaviour: behavioural outcomes arise from coordinated activity in (hidden) neural networks, whose dynamics are driven by experimental inputs. Estimating neural parameters that control network connectivity and plasticity effectively performs a neurobiologically-constrained approximation to the brain's input-outcome transform. In other words, neuroimaging data essentially serves to enforce the realism of bDCM's decomposition of input-output relationships. In addition, post-hoc artificial lesions analyses allow us to predict induced behavioural deficits and quantify the importance of network features for funnelling input-output relationships. This is important, because this enables one to bridge the gap with neuropsychological studies of brain-damaged patients. We demonstrate the face validity of the approach using Monte-Carlo simulations, and its predictive validity using empirical fMRI/behavioural data from an inhibitory control task. Lastly, we discuss promising applications of this work, including the assessment of functional degeneracy (in the healthy brain) and the prediction of functional recovery after lesions (in neurological patients).

https://pubmed.ncbi.nlm.nih.gov/26008885/

Cortex. 2020 May:126:49-62. doi: 10.1016/j.cortex.2020.01.004. Epub 2020 Jan 24.

Rethinking causality and data complexity in brain lesion-behaviour inference and its implications for lesion-behaviour modelling

Christoph Sperber [1]

Affiliations + expand

PMID: 32062142 DOI: 10.1016/j.cortex.2020.01.004

Abstract

Modelling behavioural deficits based on structural lesion imaging is a popular approach to map functions in the human brain, and efforts to translationally apply lesion-behaviour modelling to predict post-stroke outcomes are on the rise. The high-dimensional complexity of lesion data, however, evokes challenges in both lesion behaviour mapping and post stroke outcome prediction. This paper aims to deepen the understanding of this complexity by reframing it from the perspective of causal and non-causal dependencies in the data, and by discussing what this complexity implies for different data modelling approaches. By means of theoretical discussion and empirical examination, several common strategies and views are challenged, and future research perspectives are outlined. A main conclusion is that lesion-behaviour inference is subject to a lesion-anatomical bias that cannot be overcome by using multivariate models or any other algorithm that is blind to causality behind relations in the data. This affects the validity of lesion behaviour mapping and might even wrongfully identify paradoxical effects of lesion-induced functional facilitation - but, as this paper argues, only to a minor degree. Thus, multivariate lesion-brain inference appears to be a valuable tool to deepen our understanding of the human brain, but only because it takes into account the functional relation between brain areas. The perspective of causality and inter-variable dependence is further used to point out challenges in improving lesion behaviour models. Firstly, the dependencies in the data open up different possible strategies of data reduction, and considering those might improve post-stroke outcome prediction. Secondly, the role of non-topographical causal predictors of post stroke behaviour is discussed. The present article argues that, given these predictors, different strategies are required in the evaluation of model quality in lesion behaviour mapping and post stroke outcome prediction.

https://pubmed.ncbi.nlm.nih.gov/32062142/

Let's visualize some stroke lesions

Cortex. 2020 May:126:49-62. doi: 10.1016/j.cortex.2020.01.004. Epub 2020 Jan 24.

Rethinking causality and data complexity in brain lesion–behaviour inference and its implications for lesion–behaviour modelling

Christoph Sperber [1]

Affiliations + expand

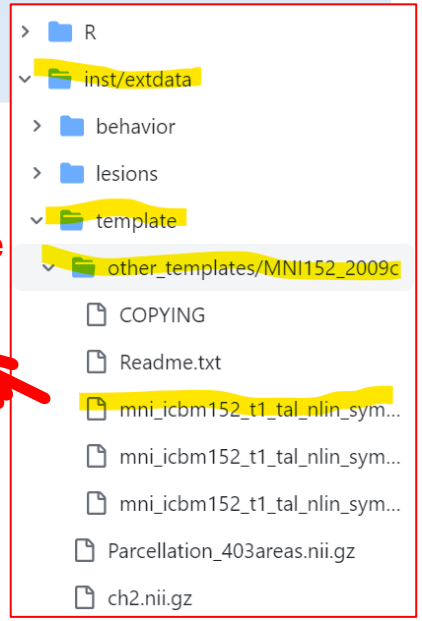
PMID: 32062142 DOI: 10.1016/j.cortex.2020.01.004

Their code and data are freely available at:

https://github.com/dorianps/LESYMAP

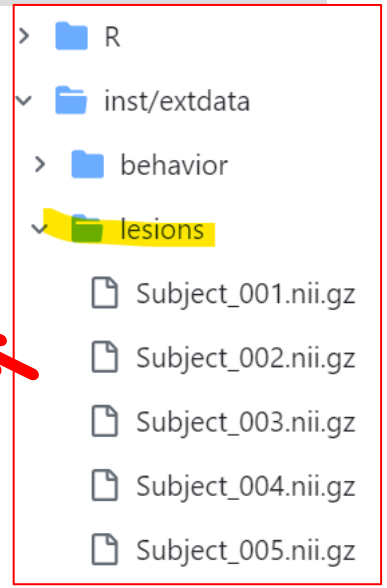
(isn't open science wonderful?!)

First download the structural file (the **template** on which we can visualize the lesions)



Use this open-source software to load neuroimaging files for visualization

Then download the lesion files (you can choose any of the 131 files/patients available)



Come to my talk ☺

It will be in Romanian

(but I am happy to explain everything in English as well, if necessary, just let me know).

Zoom link available here:
https://stiinta-cercetare.ro/event/lavinia-uscatescu/