

Welcome

Fort Lauderdale, Florida 09/2019

Intro & Overview

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I “Why, sometimes I've believed as many as six impossible things before breakfast.”

“Begin at the beginning,” *the King said, very gravely*, “and go on till you come to the end: then stop.”

“Would you tell me, please, which way I ought to go from here?” the

“That depends a good deal on where you want to get to.”

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DISCLAIMER

Here to help

Not original =shoulders of Giants

Not the position of our sponsors or the
NFL

I am not telling you what to do

DISCLAIMER #2

Kaizen is **the practice of continuous improvement.**

- 1 Better process brings better results
- 2 big results come when many small changes accumulate over time.
- 3 everyone is invited to help make improvements.
- 4 While the majority of changes may be small, the direction of change is positive

改善

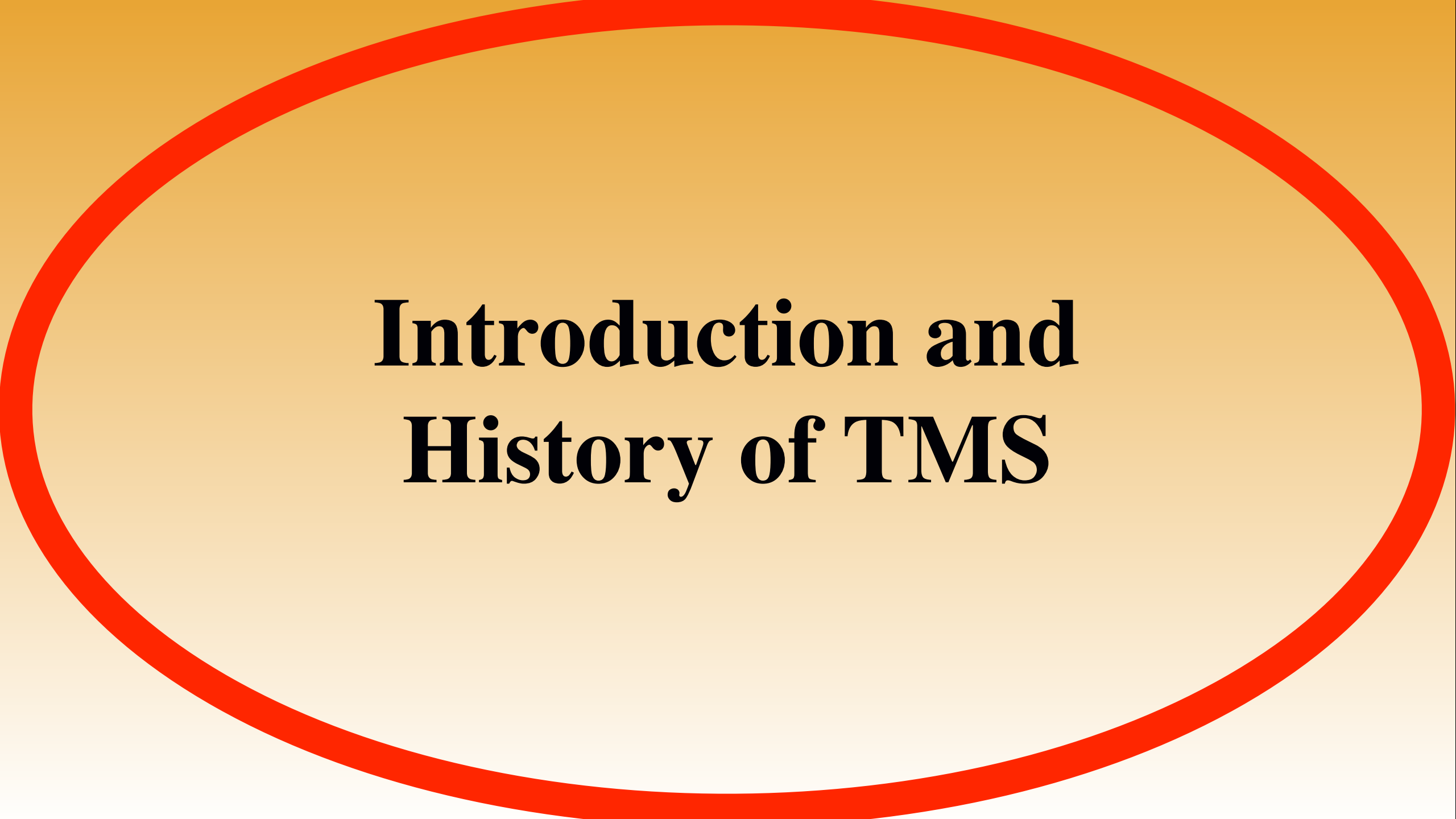
Overview

HELP PEOPLE
FIND NEW WAYS TO HELP PEOPLE
SHARE NEW WAYS TO HELP PEOPLE

Several thin, white, parallel lines of varying lengths and orientations are positioned in the bottom right corner of the slide, creating a modern, abstract graphic element.

Saturday
09/28/2019

- Introduction and History of TMS
- Mechanism of Action & Effects
- Contraindications & Risks
- Indications & Off Label Use

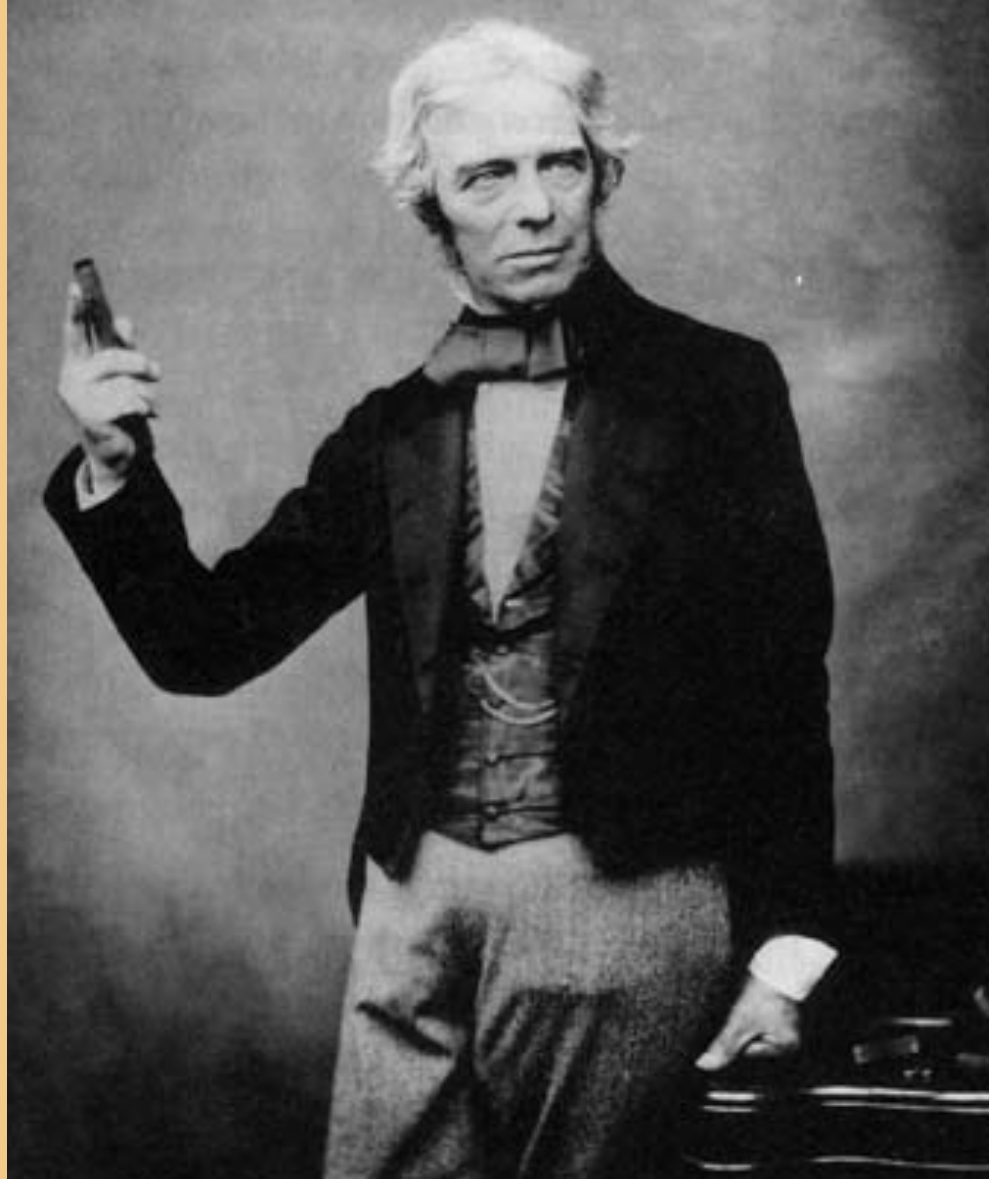


Introduction and History of TMS

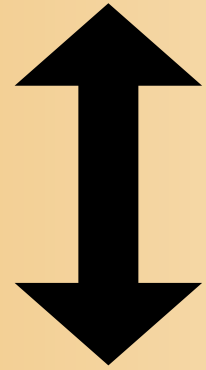
History of TMS

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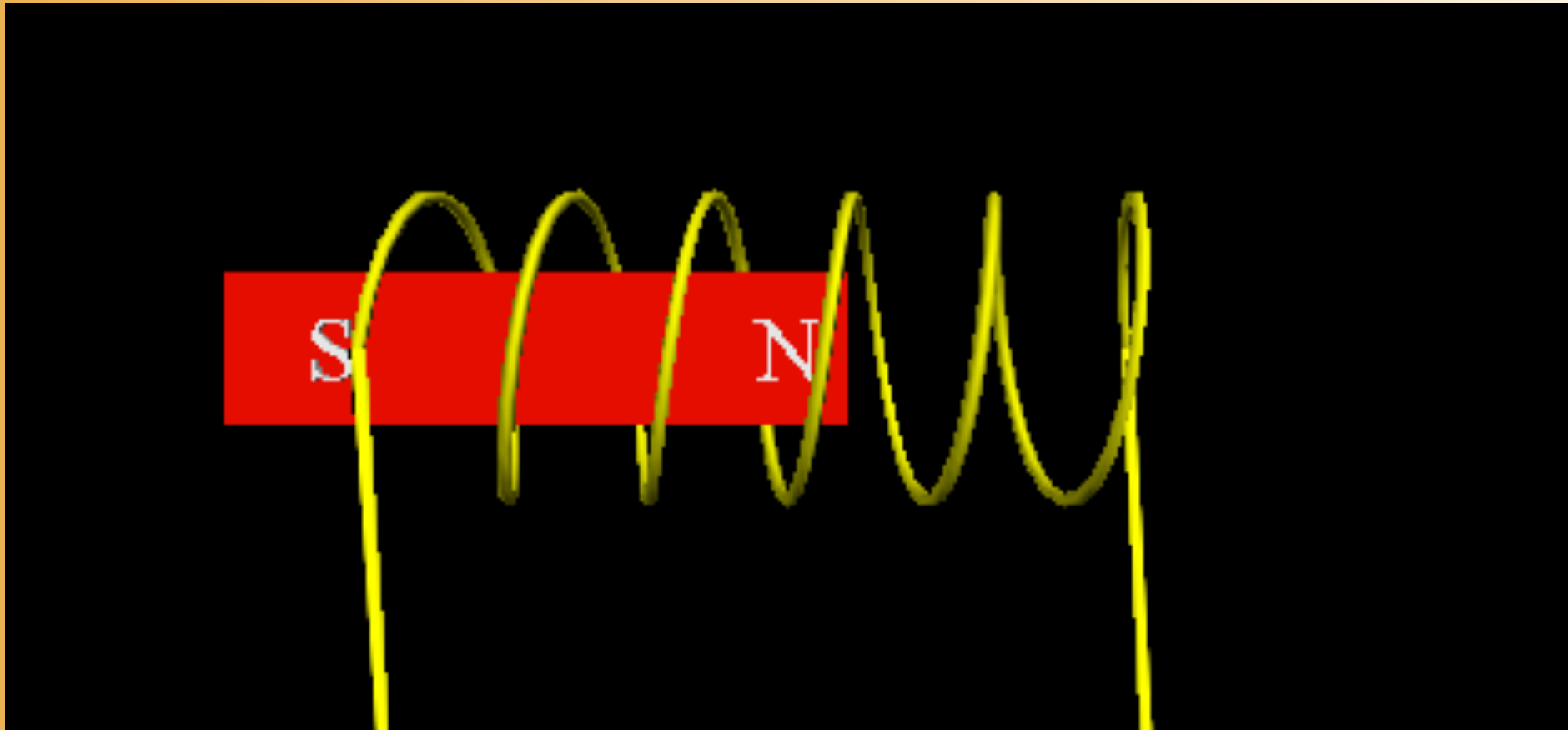
Michael
Faraday
1831
Magnetism
and
electricity
are inter-
convertible



Electricity

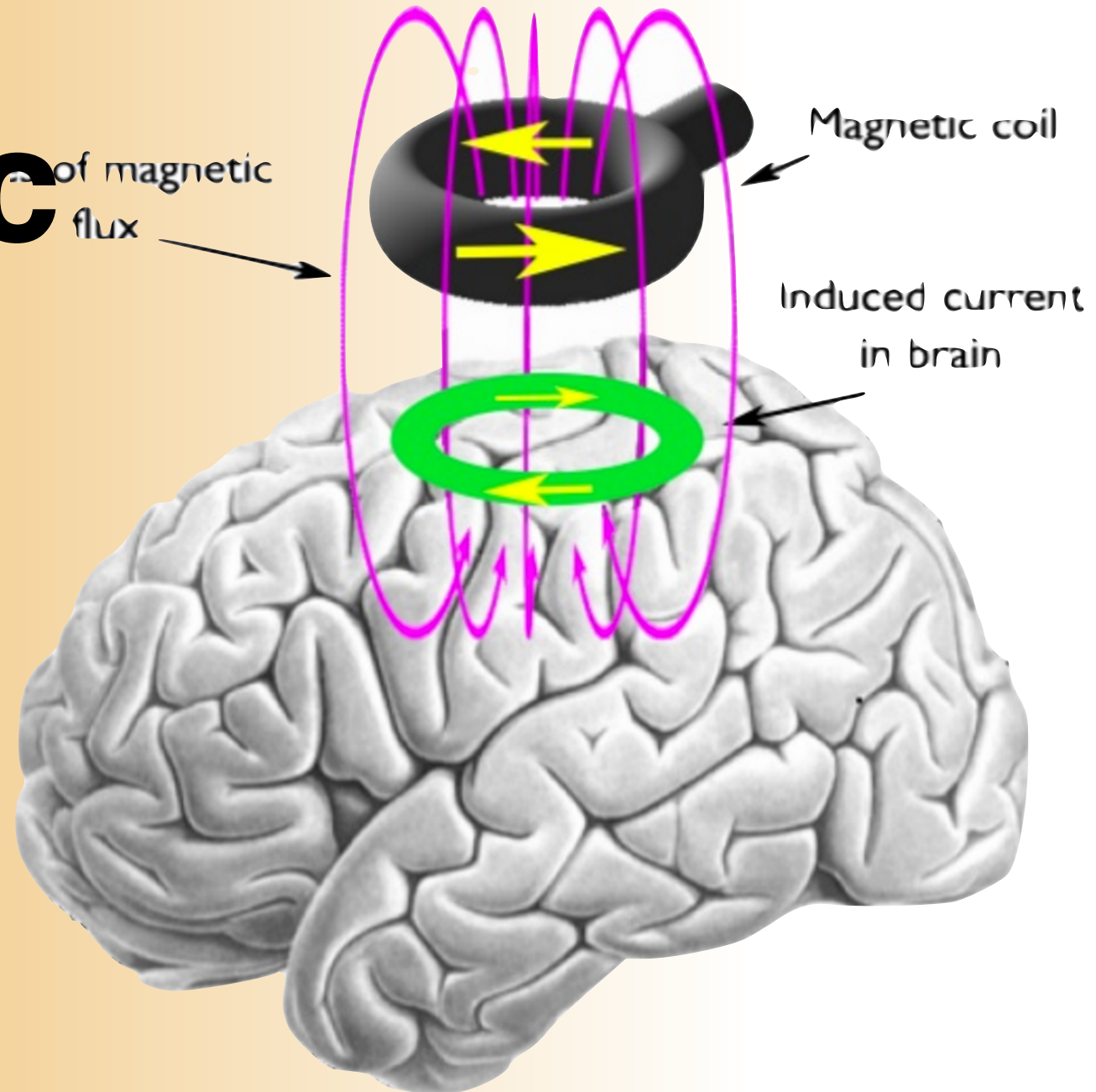


Magnetism

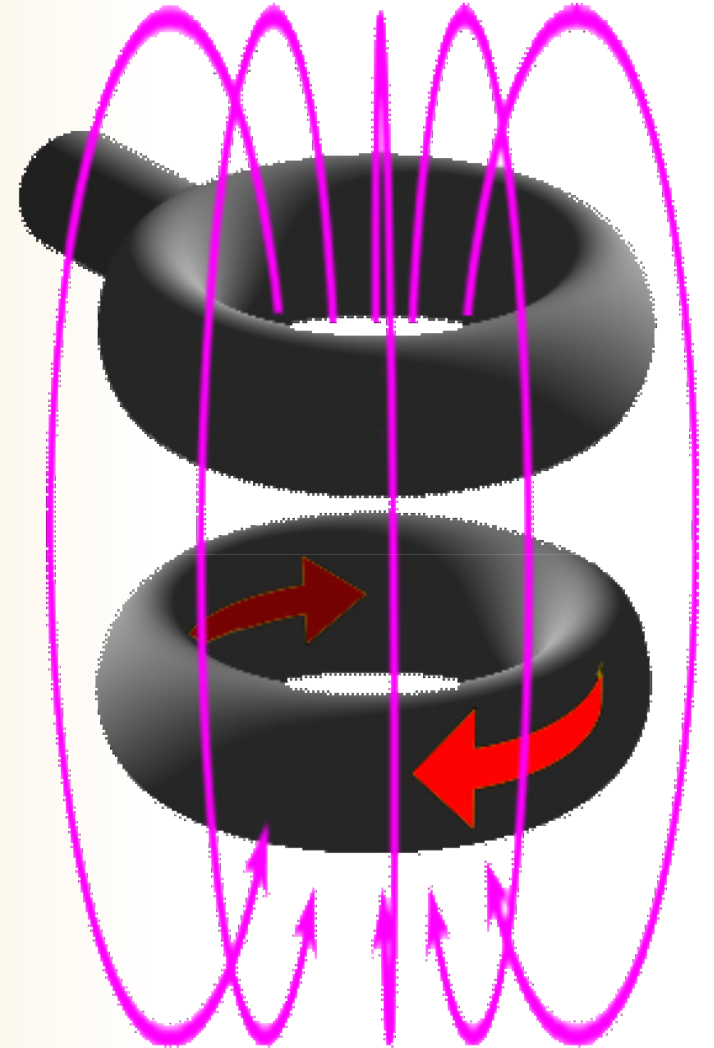
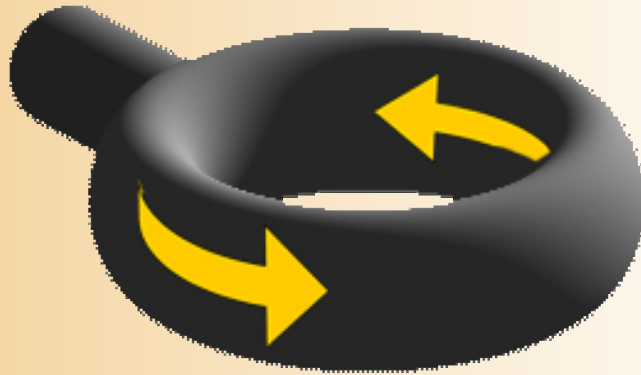


*A magnetic field,
when encountering a coil,
induces a current*

Magnetic
outside:
Induces
Current
Inside



Magnetic
outside:
Induces
Current
Inside



Magnetic outside:

Makes

Brain create

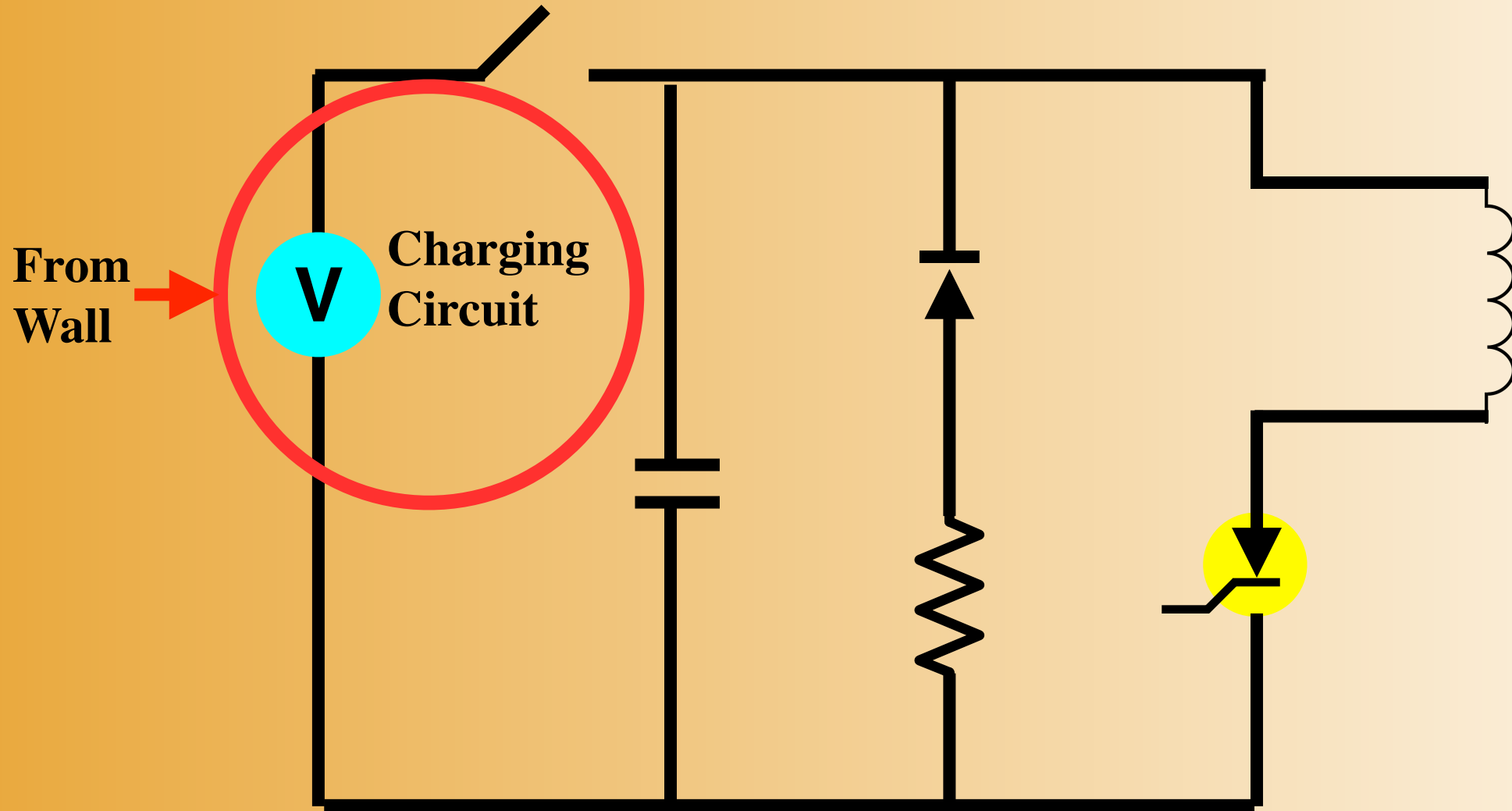
Electric Inside

The Transcranial Magnetic Stimulation (TMS) Circuit.

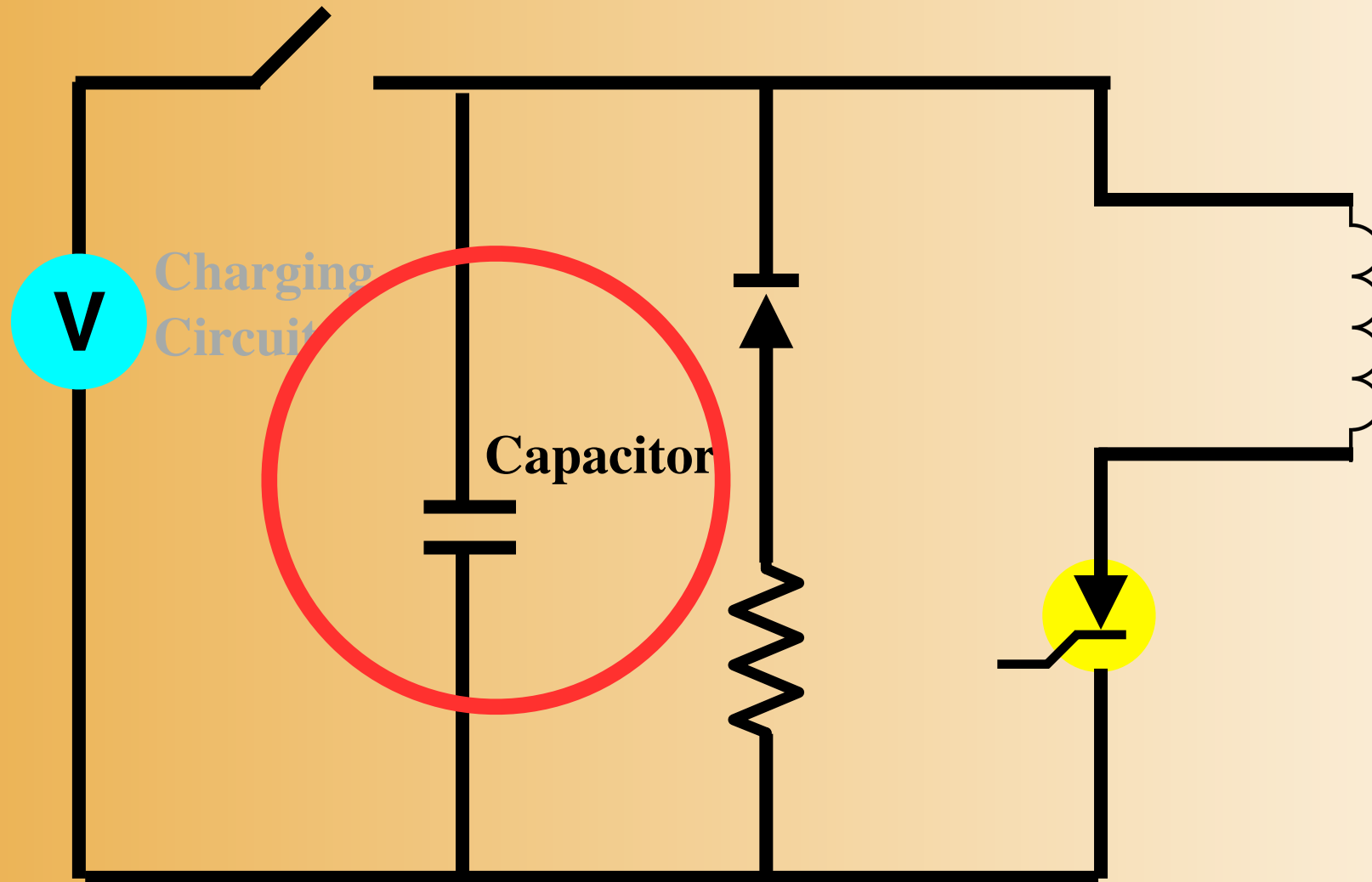
Capacitor (with Capacitance C), a

**Thyristor switch (T),
a Stimulating Coil (with Inductance L) and a
Resistance R (in the coil, cables).**

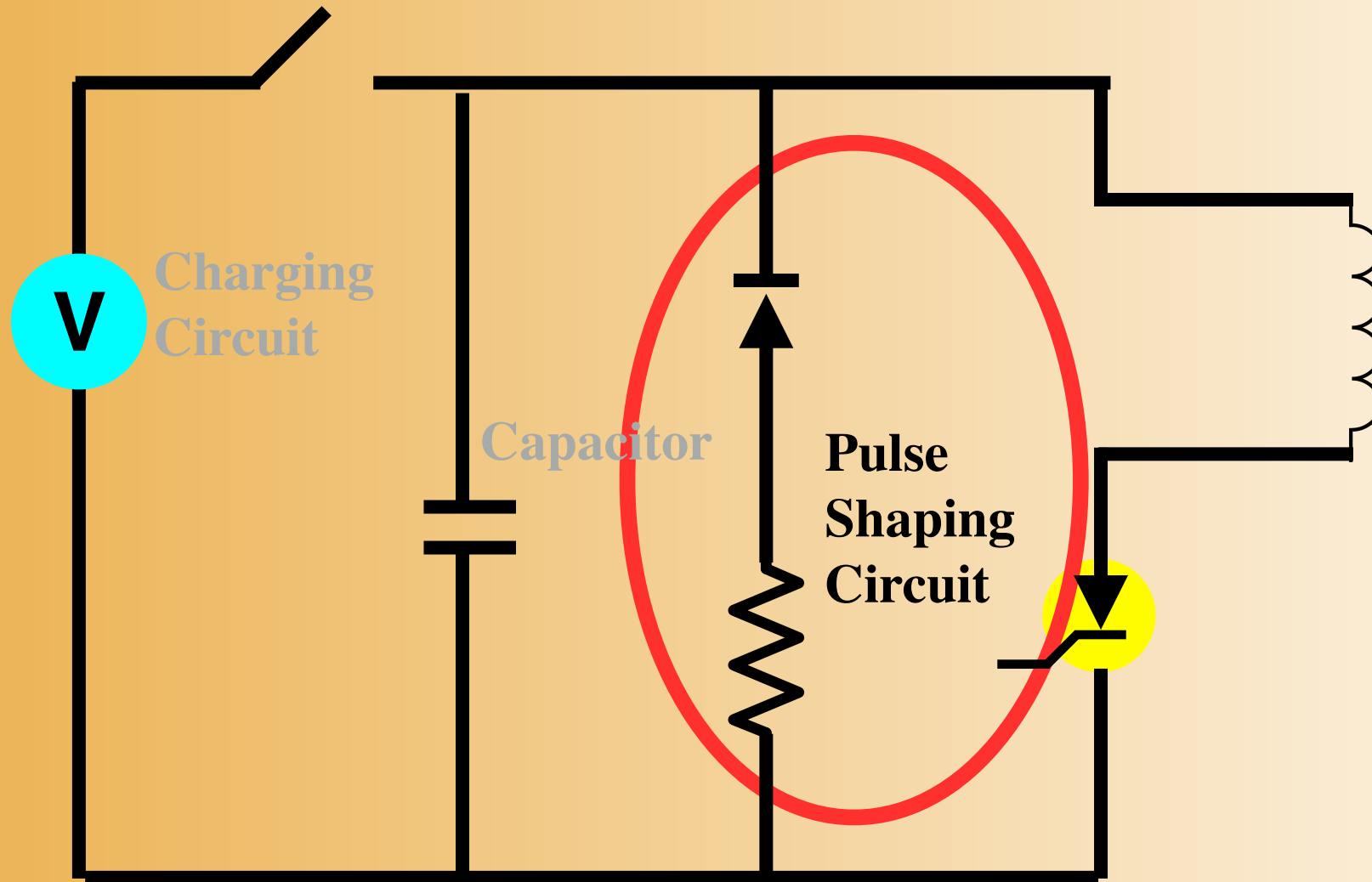
The Capacitor is first charged and then discharged through the Coil, by gating the Thyristor into a conducting state.



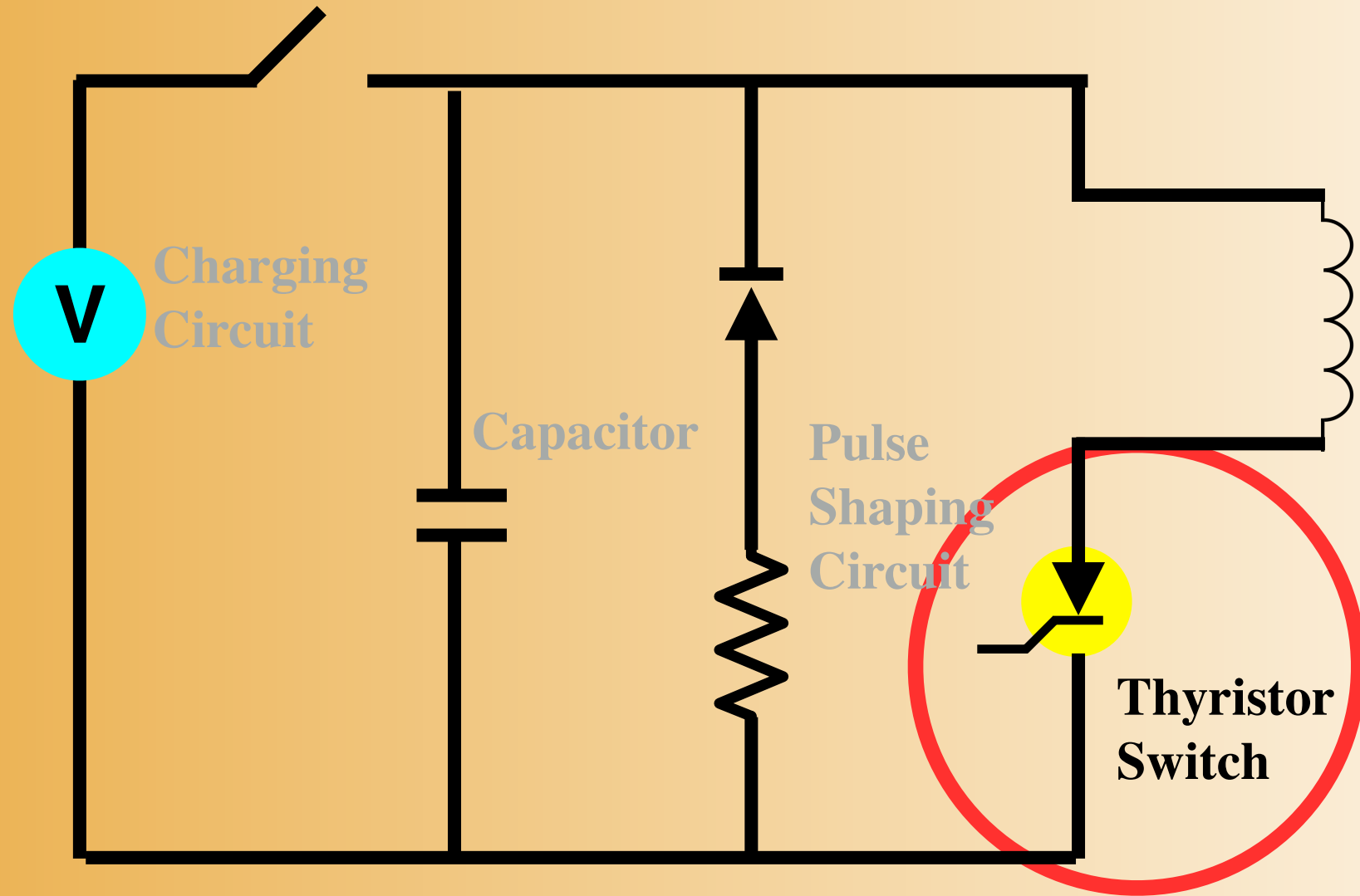
1. Energy Acquisition *from wall plug*



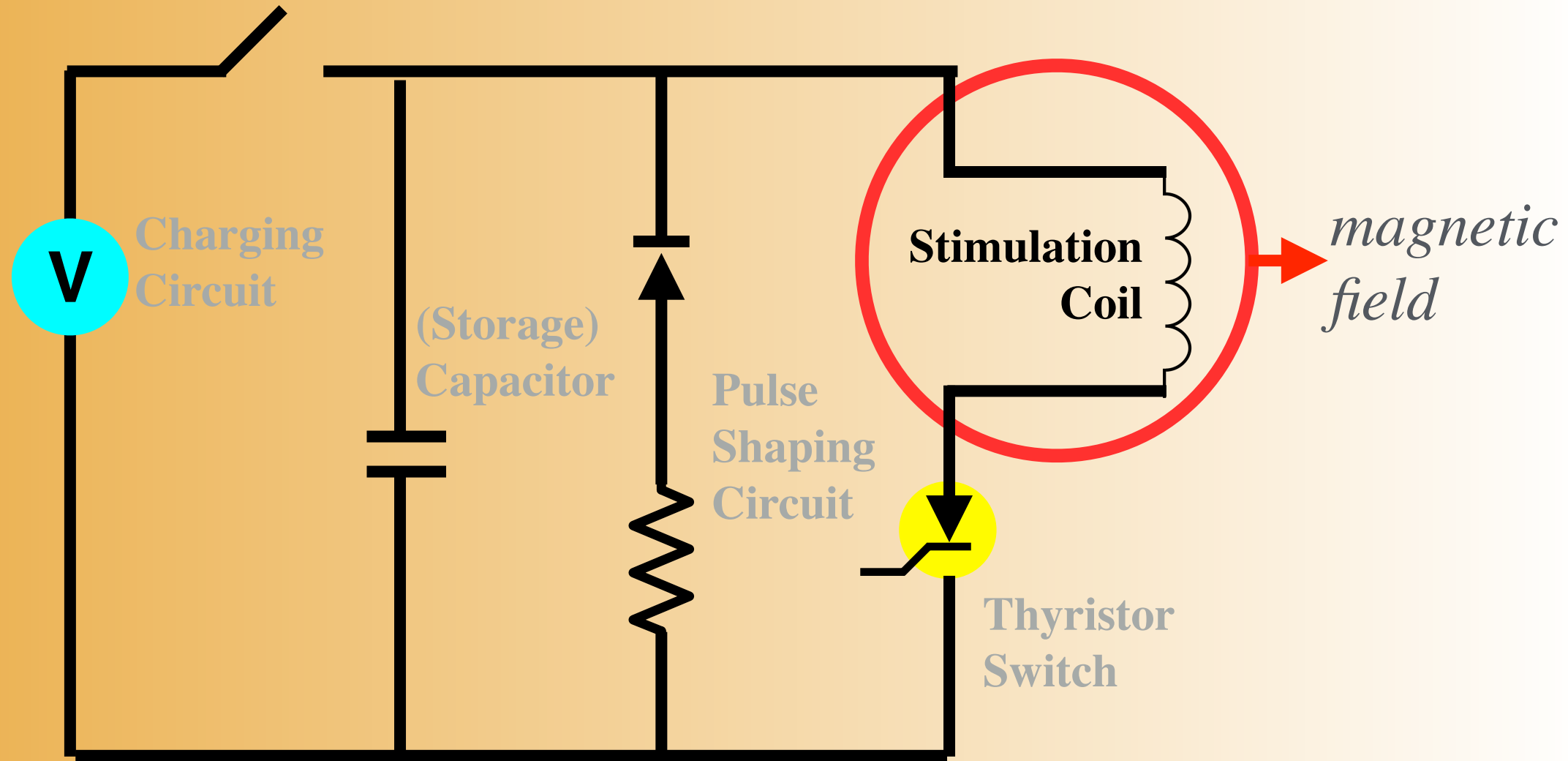
2. Energy Storage, *in capacitor(s)*



3. Shaping Circuitry - *Faster pulses -> more magnetic energy*



4. Turned On, *to conductive state*



5. Electricity through the coil, ... induces a magnetic field

TMS- GIANTS (HISTORY)

Mark Hallett

Pascual-Leone 1994 High-frequency rTMS
increases motor excitability as a function of
frequency and intensity

Mark George

Ulf Ziemann

Kujirai (TMS to probe motor cortical excitability)

Fadiga TMS to probe cognitive processes

Chen Repetitive TMS to induce long-term
change of excitability

Huang 2005 Theta-burst stimulation

Ziemann 1996 Pharmacology-TMS

Pascual-Leone 1995 Focal TMS to map practice-
dependent plasticity unimanual practice of a piece on the piano led
to rapid enlargement of the hand representations in the trained motor cortex, as
tested by focal TMS mapping

TMS- GIANTS (HISTORY)

TMS **to treat brain disorders**

Pascual-Leone (1996 662) significant decrease in depression scores in patients with drug-resistant major depression

TMS- GIANTS (HISTORY)

REFERENCES

Barker AT, **Jalinous** R, Freeston IL (1985) Non-invasive magnetic stimulation of human motor cortex [letter]. *Lancet* 1: 1106–1107

Chen R, Classen J, Gerloff C, Celnik P, **Wassermann** EM, **Hallett** M, Cohen LG (1997) Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. *Neurology* 48:1398–1403

Fadiga L, Fogassi L, Pavesi G, **Rizzolatti** G (1995) Motor facilitation during action observation: a magnetic stimulation study. *J Neurophysiol* 73:2608–2611

George MS, Lisanby SH, Avery D, McDonald WM, Durkalski V, Pavlicova M, Anderson B, Nahas Z, Bulow P, Zarkowski P, Holtzheimer PE 3rd, Schwartz T, Sackeim HA (2010) Daily left prefrontal transcranial magnetic stimulation therapy for major depressive disorder: a sham-controlled randomized trial. *Arch Gen Psychiatry* 67:507–516

rTMS Time Line



rTMS Time Line

Barker, 1984

1984

**Anthony
Barker,
Invents
Single Pulse
TMS
for Diagnosis**



**Barker
2016**

rTMS Time Line

**Cadwell
repetitive
TMS
1987**



1984

**Anthony
Barker,
Invents
Single Pulse
TMS
for Diagnosis**



NeuroReport 6, 1853–1856 (1995)

Daily repetitive transcranial magnetic stimulation (rTMS) improves mood in depression

Mark S. George,^{1,2}

1984

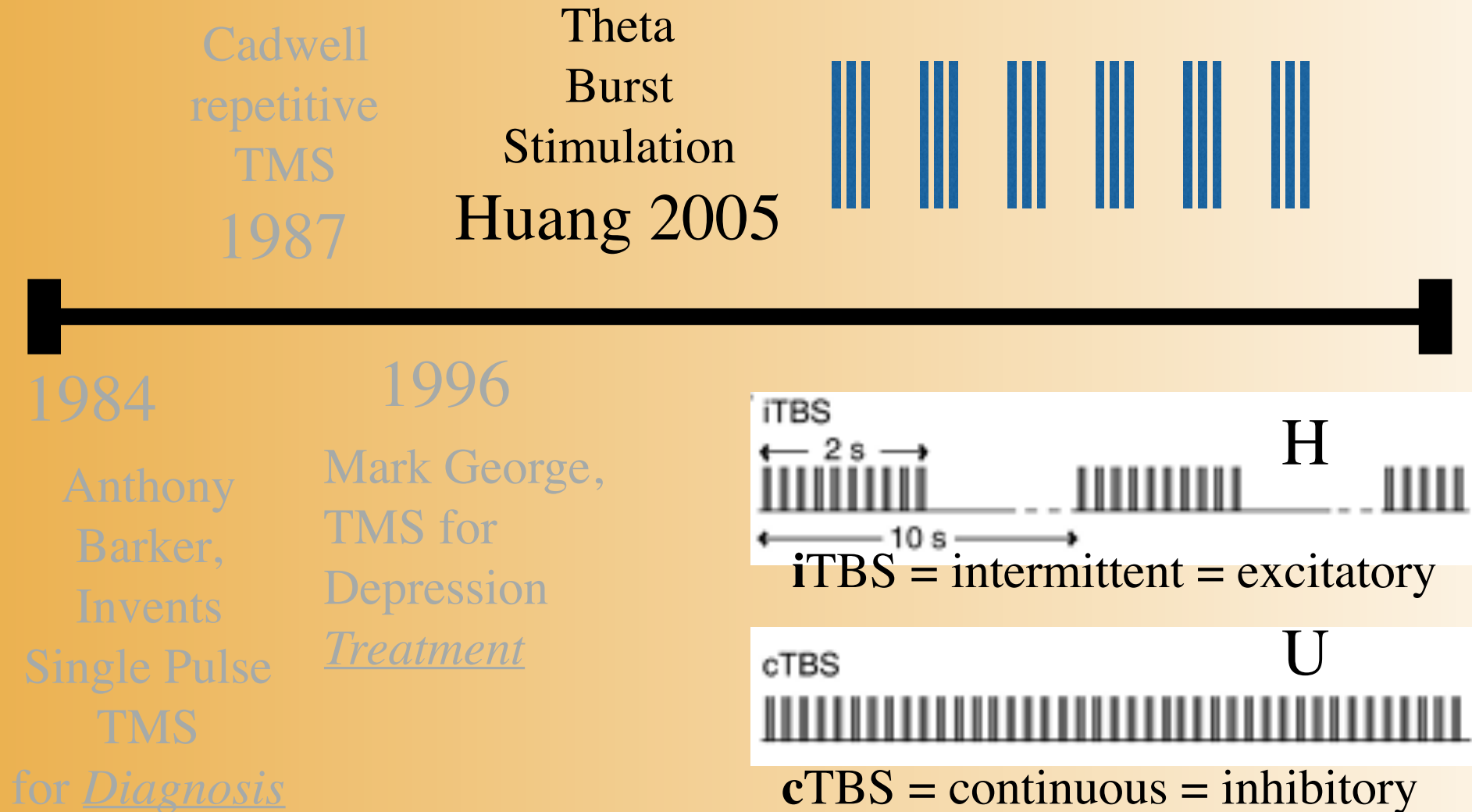
Anthony
Barker,
Invents
Single Pulse
TMS
for *Diagnosis*

1996

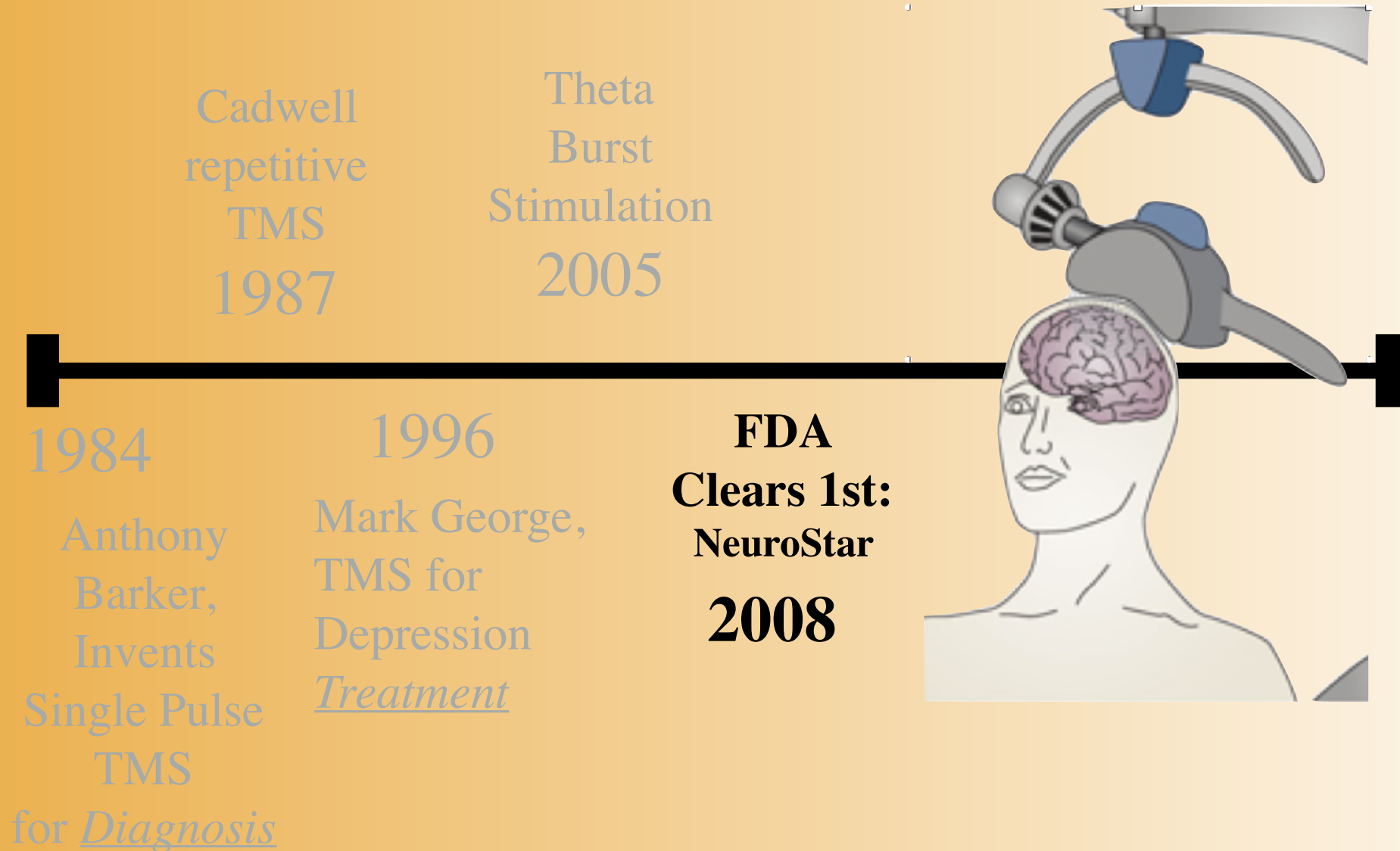
Mark George,
TMS for
Depression
Treatment



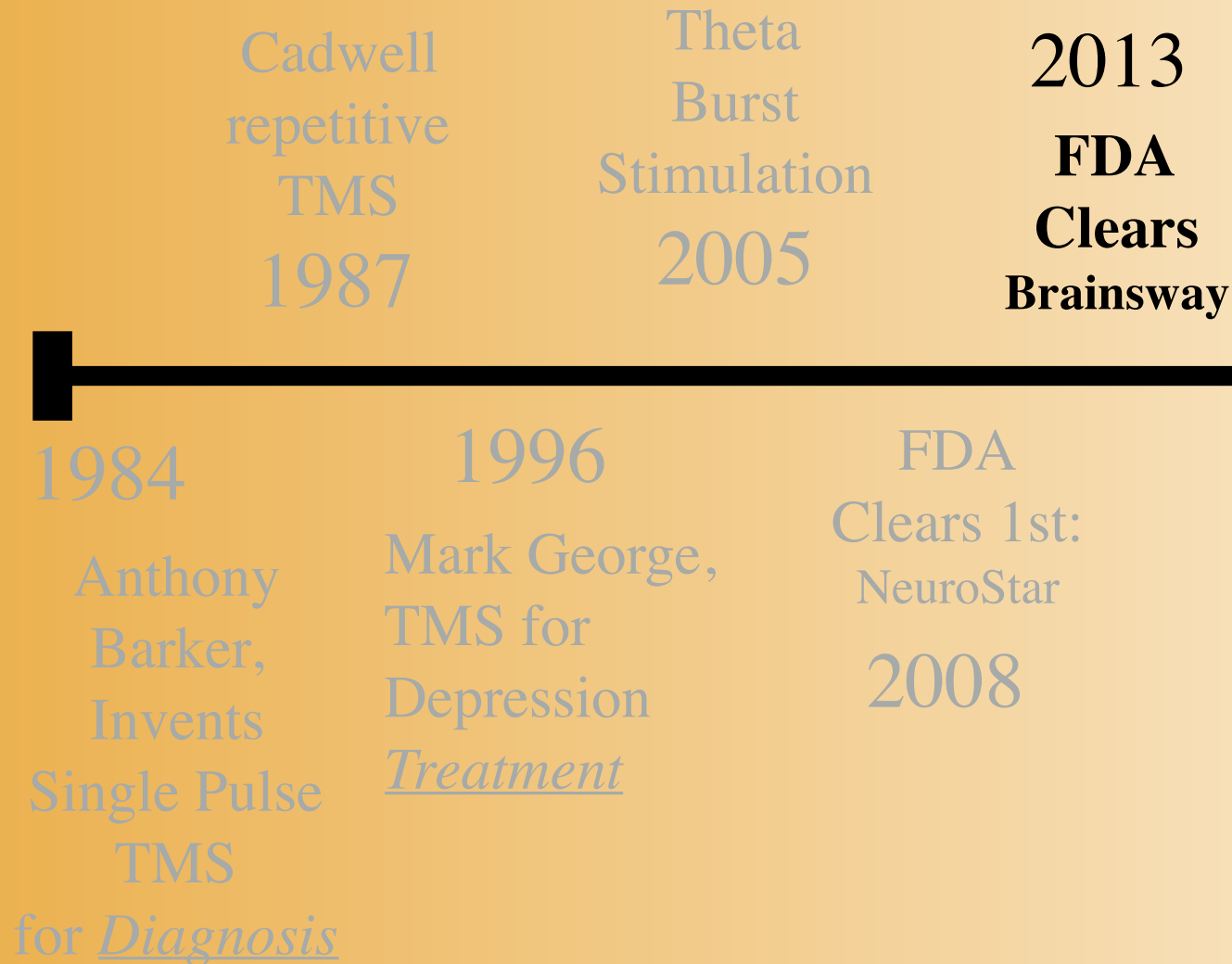
rTMS Time Line



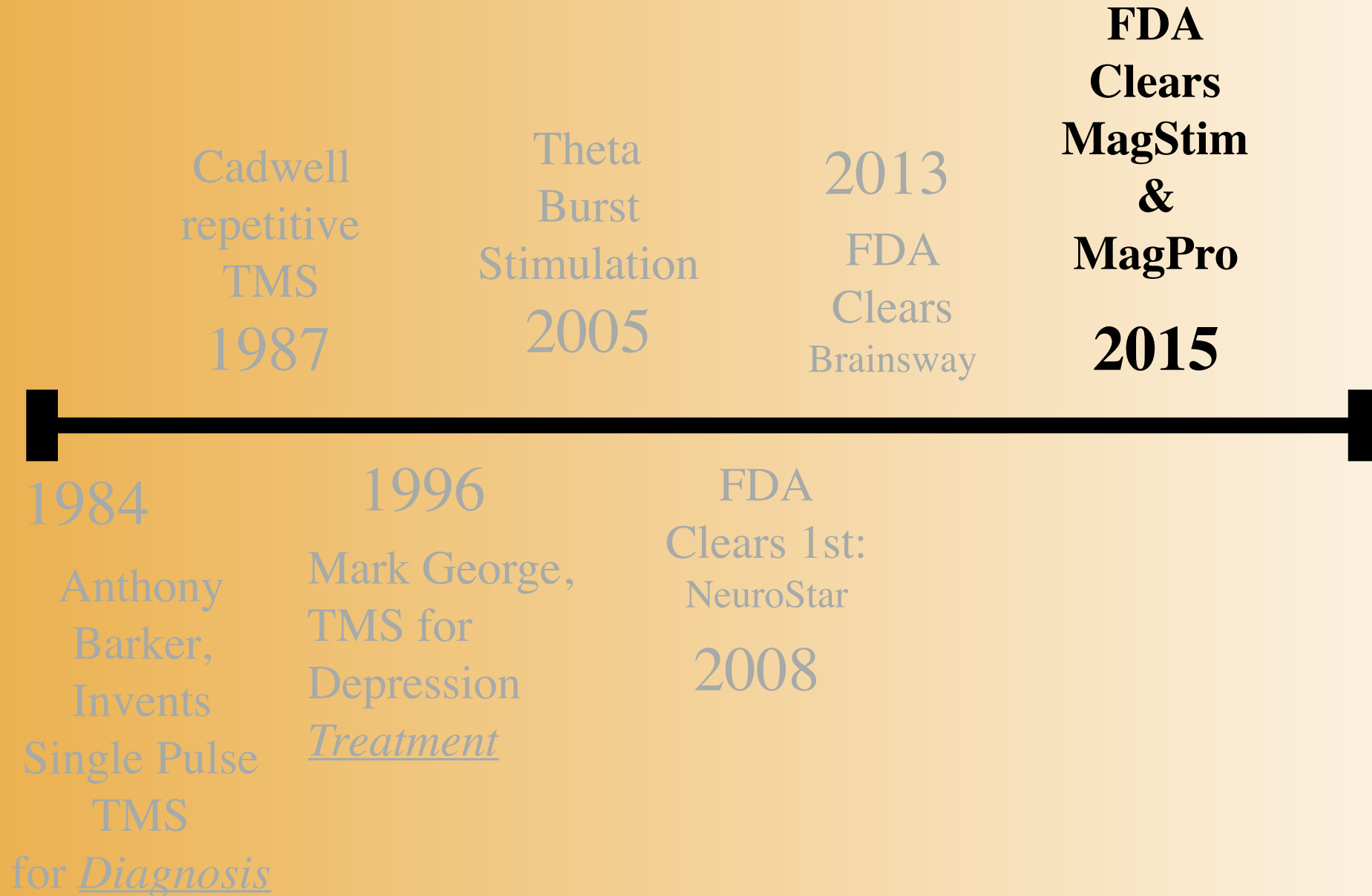
rTMS Time Line



rTMS Time Line



rTMS Time Line



rTMS Time Line

FDA
Clears
MagStim
&
MagPro
2015



rTMS Time Line



FDA
Clears
MagStim
&
MagPro
2015

2013

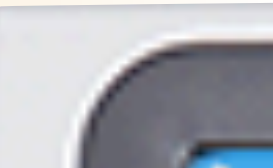
FDA
Clears
Brainsway

**FDA
Clears
CloudTMS
2016**

Anthony
Barker,
Invents
Single Pulse
TMS
for *Diagnosis*

Mark George,
TMS for
Depression
Treatment

Cone
Coil
Deep-
TMS



TMS DEVICES & SYSTEMS

6

TMS

Companies

NeuroStar (US)

BrainsWay (Israel)

MagStim (UK)

MagPro (Denmark)

CloudTMS (Russia)

Apollo (Germany)

NeuroStar (US)
1st FDA Cleared
TMS System
2008



most widely used system in the US (~650)



BrainsWay

uses MagPro
Power and
Stimulator

Stimulates the Whole Brain



MagStim invented TMS



MagPro

CloudSoft
Low Cost
Easy To Use



Mechanism of Action

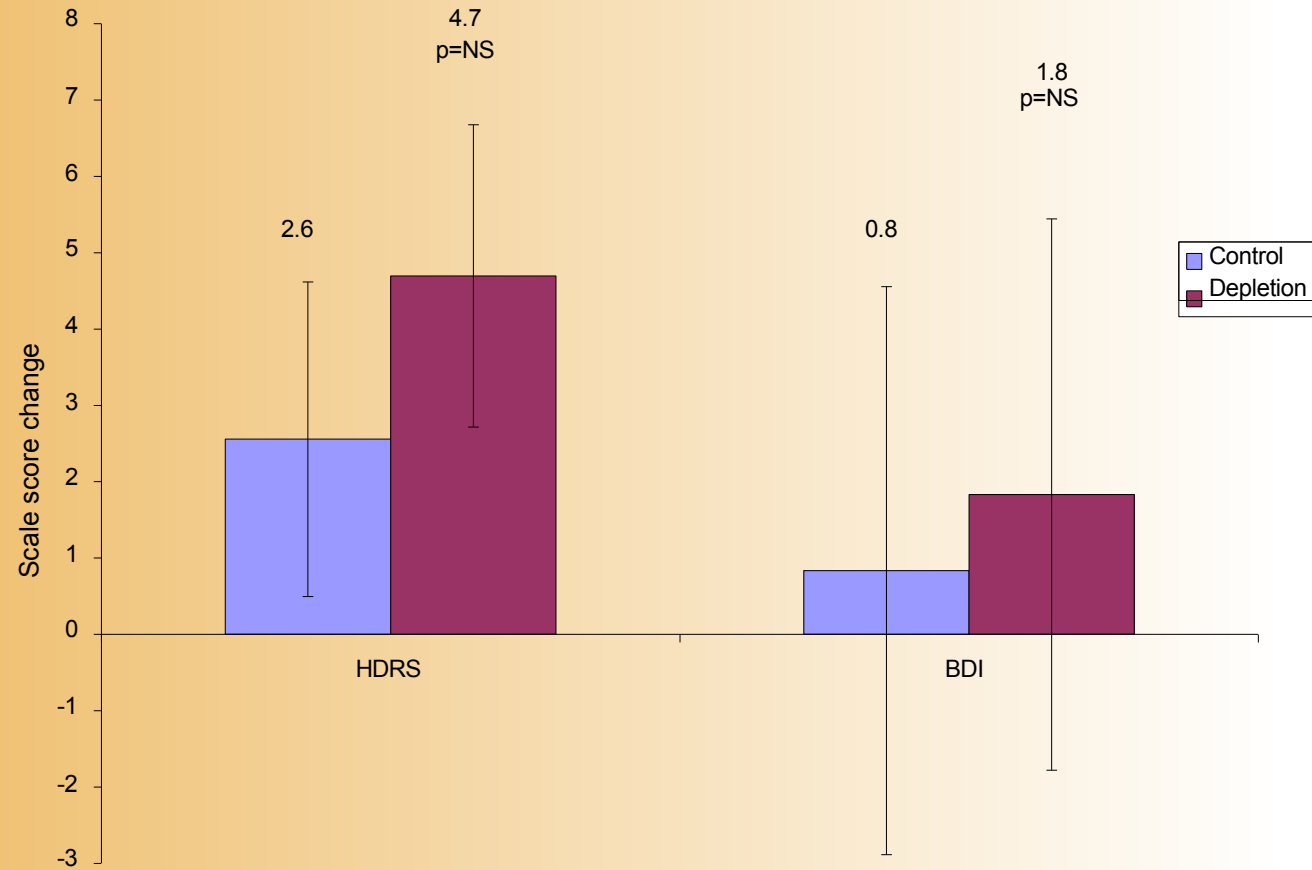
How it Works

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EFFECTS & MECHANISM

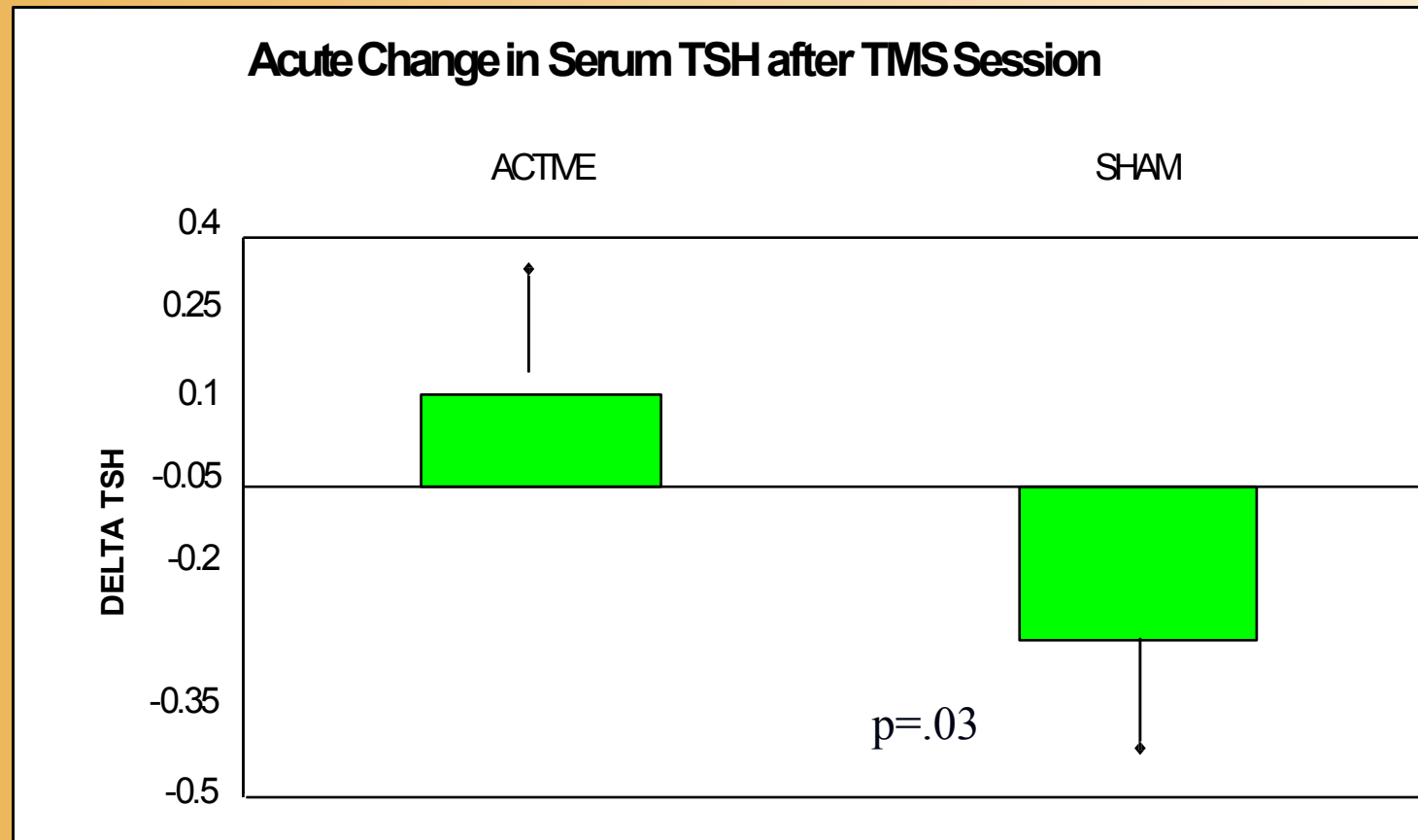
- Based on the hypofrontality found in neuroimaging studies it was rational to use a focal stimulation technique to activate neural circuitry in the DLPFC

MDD Responders to TMS are resistant to Tryptophan Depletion induced depressed mood



O'Reardon JP, Cristancho P et al., Dep & Anx 2007

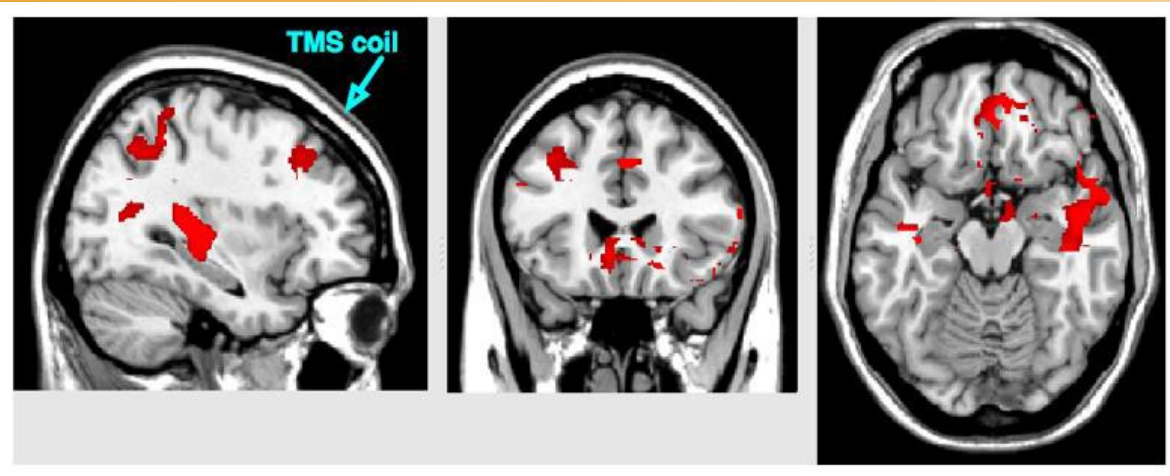
TSH rises with active TMS



TMS MECHANISM

Acute Effects

- Induces electric current
- Depolarizes neurons in superficial cortex
- Leads to local and trans-synaptic changes in brain activity



Example

Left prefrontal TMS

22 depressed individuals

Activation demonstrated at site of stimulation and also at synaptically connected cortical and subcortical regions

TMS

MECHANISM

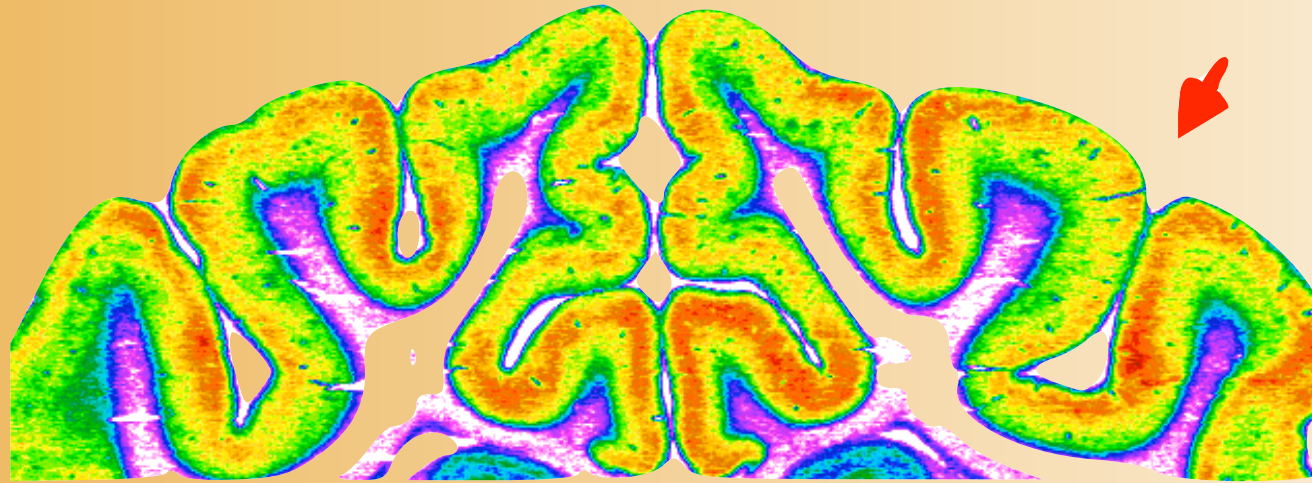
How does
it work?

(Mechanism
of action)

**Brain re-growth happens
by “axonal sprouting” -
(axons grow new nerve endings &
reconnect neurons).**

**These new connections
between nerve cells,
increase brain connectivity
to improve function.**

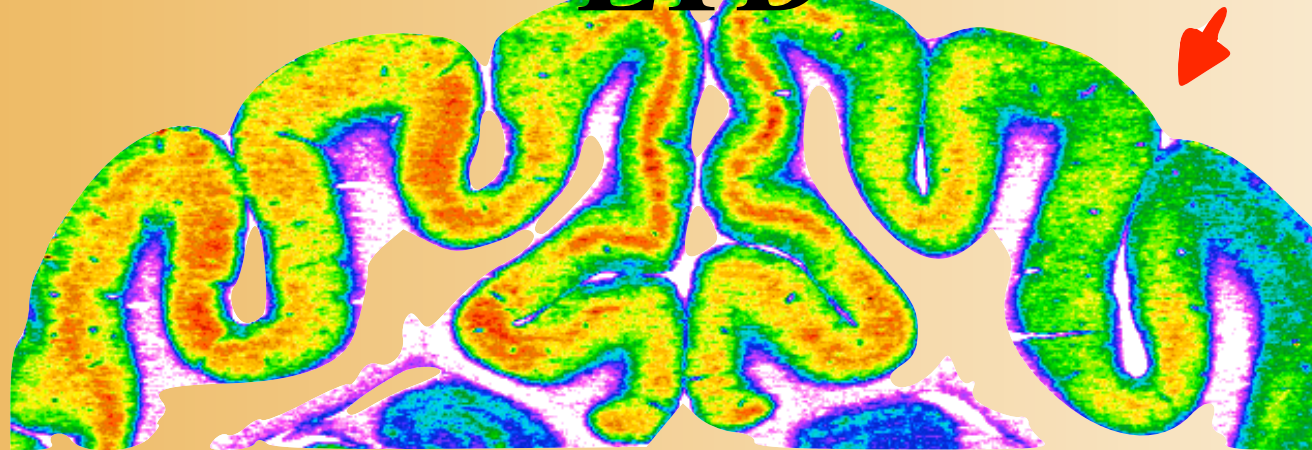
None



control

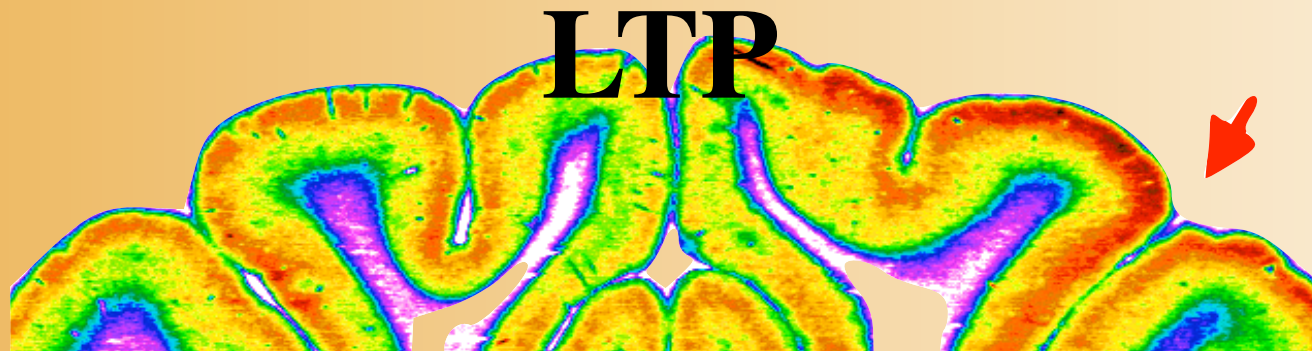
LTD

1 Hz



decreased
activity

10 Hz



LTP

increased
activity

How does
it work?
(Mechanism
of action)

Depolarization of DLPFC Cortical Neurons

Increases Activity of DLPFC Cortical Neurons

Upregulates BDNF

Increases Dopamine in Prefrontal Cortex

Increased Frontal Lobe Activity

Increased Neurogenesis in Hippocampus

**Increased TSH in association with acute mood change
in depression**

Normalization of the DST with rTMS

TMS

How does
it work?

(Mechanism
of action)

MECHANISM

Brain re-growth happens
by “axonal sprouting” -
(axons grow new nerve endings &
reconnect neurons).

These new connections
between nerve cells,
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to improve function.