Educational course: TMS

Single pulse TMS, paired TMS and repetitive TMS: Mechanisms of action

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COI: Nothing to declare

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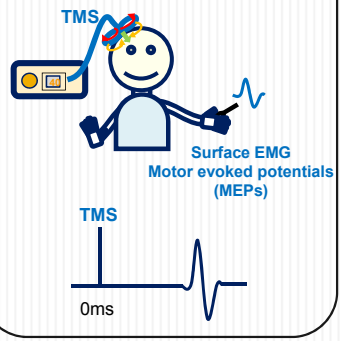
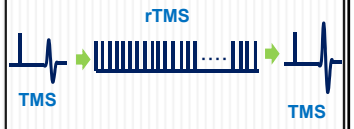
Transcranial magnetic stimulation

1.Single pulse TMS



2.repetitive TMS: rTMS

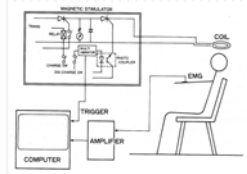


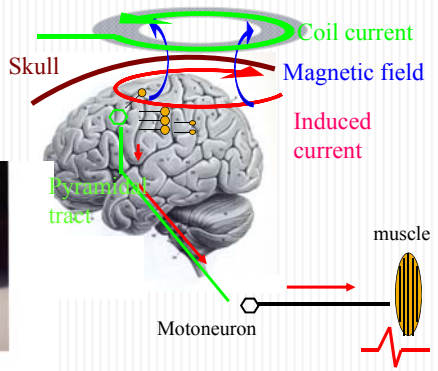
After rTMS, long lasting MEP changes occurs, reflecting with cortical excitability changes.

What's TMS?

- Induced currents activates neurons.
- Human brain can be activated non-invasively.

TMS





Currents induced in the brain by the magnetic field changes produced by huge currents in the coil electrically activate neurons (electric stimulation)

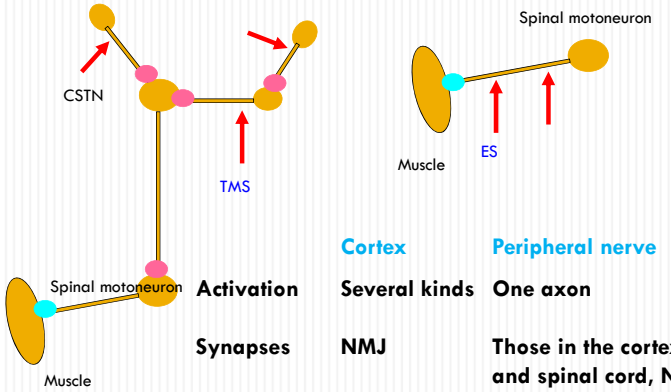
Today's Talk

1.What are stimulated by single pulse TMS?

2.To study modulation effects on M1. cerebellum, sensory inputs and others

3.What happens after repetitive TMS?

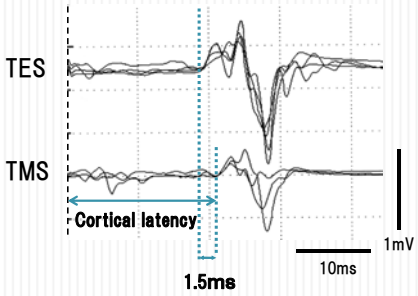
MEP and CMAP



	Cortex	Peripheral nerve
Activation	Several kinds	One axon
Synapses	NMJ	Those in the cortex and spinal cord, NMJ

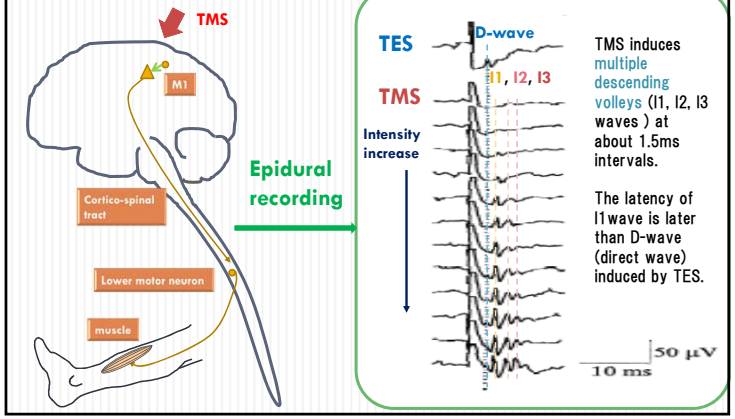
Difference of cortical latency by TMS and TES

Muscle evoked potentials (MEP) of the first dorsalis interosseous muscle (FDI)



The cortical latency of MEP to TMS is about 1.5ms longer than that to TES.

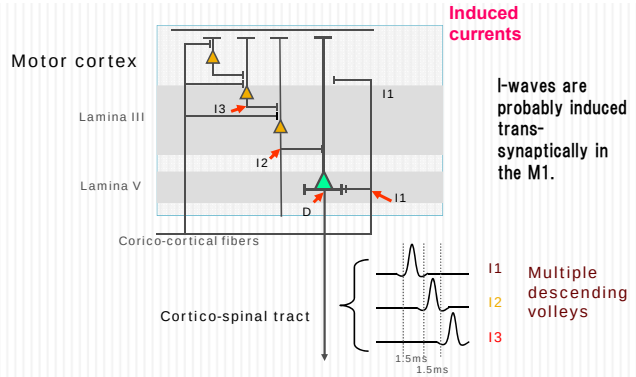
Multiple descending volleys



TMS induces multiple descending volleys (I1, I2, I3 waves) at about 1.5ms intervals.

The latency of I1wave is later than D-wave (direct wave) induced by TES.

Hypothesis for generator of I-waves

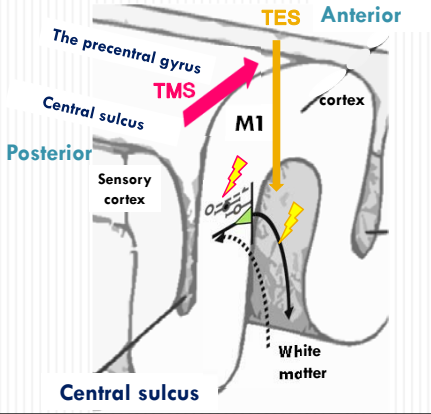


I-waves are probably induced trans-synaptically in the M1.

Multiple descending volleys

modified figure in Amassian et al1999

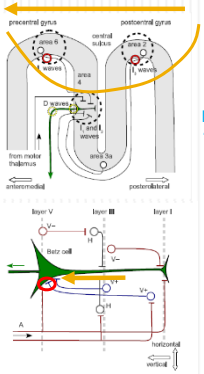
The primary motor cortex (M1)



However, the pyramidal neurons are not positioned in the bank of the precentral gyrus, but in anterior wall of the central sulcus (area 4) .

Simple model of TMS

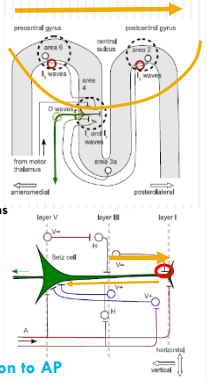
PA stimulation



Anteriorly directed currents in brain
Activates anteriorly directed interneurons
Synaptic delay (1.5ms)
Depolarization
Utility time
Action potential generation
I1 wave activation
Burst (repetitive discharge at around 1.5ms intervals (I2,I3)

From stimulation to action potential
1.5ms+1ms = 2.5ms−3ms

AP stimulation



Posteriorly directed currents in brain
Activates posteriorly directed interneurons
Synaptic delay (1.5ms)
Conduction in the dendrites
05m/sec
Depolarization
Action potential generation
I1 wave activation
Burst (repetitive discharge at around 1.5ms intervals (I2,I3)

From stimulation to AP
1.5ms+7ms 8ms

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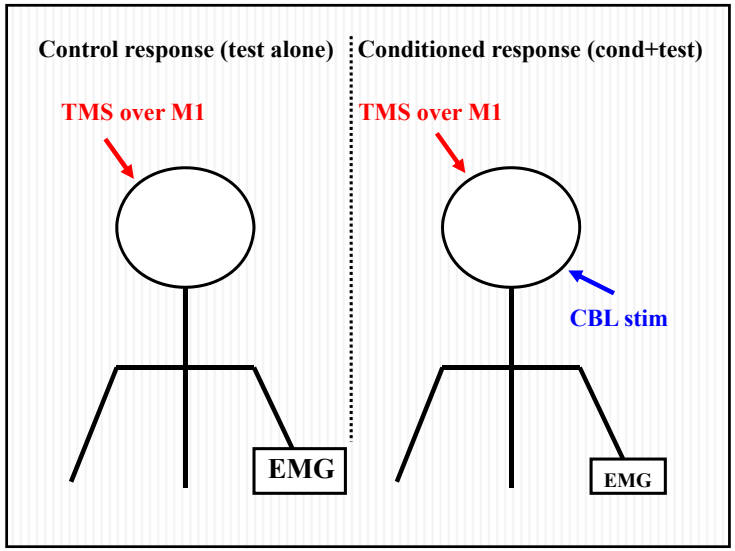
cerebellum, sensory inputs and others

3.What happens after repetitive TMS?



Randomized conditioning-test paradigm

Stimulation

conditioning stimulus — **cerebellar stimulation (ES or TMS)**

test stimulus — **TMS over M1**

EMG recording

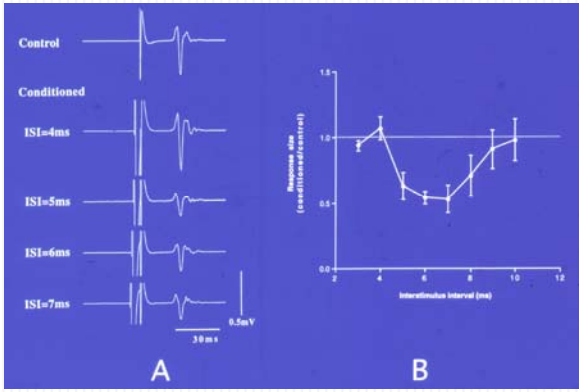
surface EMG from the FDI

Interstimulus intervals

3 – 10 ms

Analysis

comparison between control and conditioned tirals



Characteristics of the suppression

Conditioning stimulus suppresses EMG responses to TMS over the motor cortex, whereas it does not affect those to electrical stimulation over M1.

effects should occur at the cortex

Position and polarity of effective conditioning stimulus suggests that conditioning stimulus should be over the cerebellum contralateral to the motor cortex.

Cerebellar effect ?

Motor cortical suppression by cerebellar stimulation in patients

Reduced suppression (abnormal)

cerebellar hemispheric lesion
(CCA, paraneoplastic synd
CVD, DPH intoxication)

cerebellar efferent system
(sup cbl peduncle lesion,
dentate, motor thalamus)

degenerative ataxia

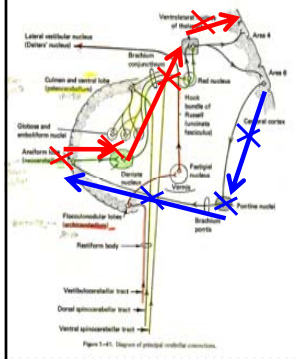
Normal suppression with ataxia

cerebellar afferent system
(pontine nucl, middle cerebellar peduncle)

sensory ataxia
(neuropathy, tabes dorsalis
sensory thalamic lesion)

Fisher's syndrome
hypothyroidism

Summary of the results

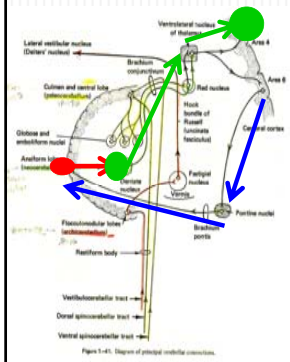


Normal cerebellar inhibition
Non-cerebellar ataxia
- sensory ataxia
- Fisher's syndrome
- hypothyroidism

Cerebellar ataxia
- Cerebellar afferent pathway ✕
- frontal ataxia, pontine nucleus
- middle cerebellar peduncle

Abnormal cerebellar inhibition ✕
Cerebellar hemispheric dysfunction
Cerebellar efferent pathway
- superior cerebellar peduncle
- motor thalamus
- thalamo-M1 fibers

Simple interpretation of mechanism for cerebellar suppression



TMS activates Purkinje cells (near to coil)

Purkinje cells inhibit dentate nucleus which tonically activates M1 through dentate-thalamo-cortical pathway

M1 background activity is suppressed by disfacilitation

Cerebellar afferent pathways have no contribution to cerebellar suppression

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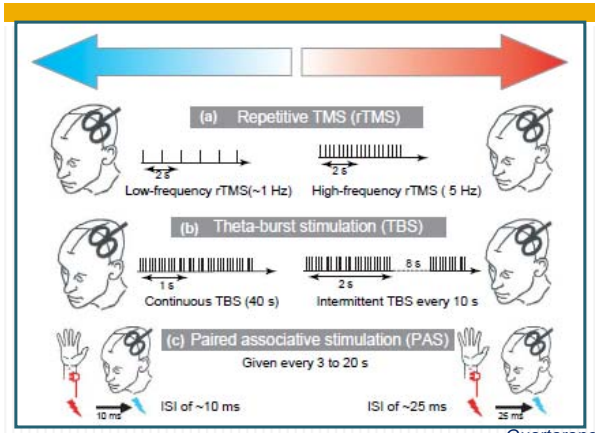
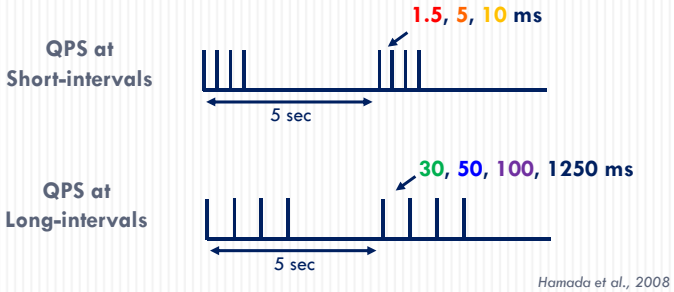
repetitive TMS



Quartarone et al 2006

Quadri-pulse stimulation: QPS

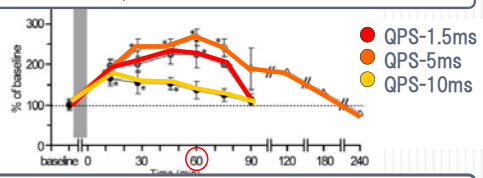
Four pulses of monophasic TMS are applied every 5 sec for 30 minutes (360 burst) over M1



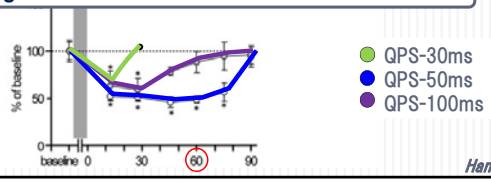
Hamada et al., 2008

Aftereffects of QPS depends on inter-stimulus intervals of 4 pulses

Short-interval QPS induce LTP like effects



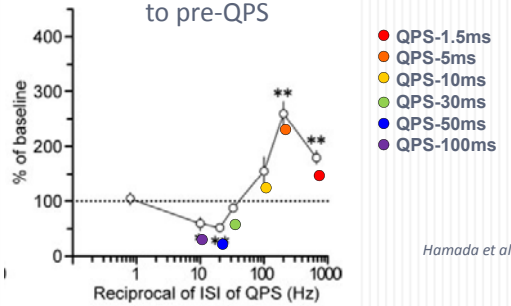
Long-interval QPS induce LTD like effects



Hamada et al., 2008

QPS and BCM curve

MEP ratio at 30min after QPS to pre-QPS



Hamada et al., 2008

LTP/LTD like effects after QPS seems to follow BCM theory.

Conclusion

- NIBS activates inter-neurons and inputs fibers in M1.
- Preferentially activated components by NIBS depends on stimulus intensity or current directions.
- MEPs to NBS reflects the combination of all synaptic changes in M1.
  Each NIBS may have its specific combination of several synapses.