認知神經科學研究所

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TMS basics and Applications

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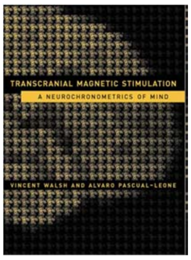
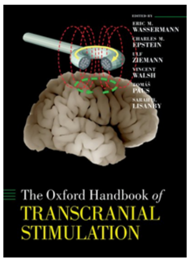
References



Transcranial Magnetic Stimulation
A Neurochronometrics of Mind

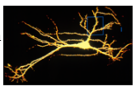


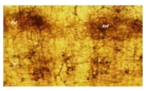
The Oxford Handbook of
Transcranial Magnetic Stimulation

The goal of *cognitive neuroscience* is to understand how mental processes (like comprehending what I am saying) come from events in the brain.

Molecules in nerve cell membranes don't comprehend.

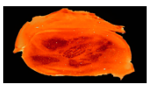
No single neuron comprehends. Neither do ten neurons.





Do a thousand (= 10^3) ?

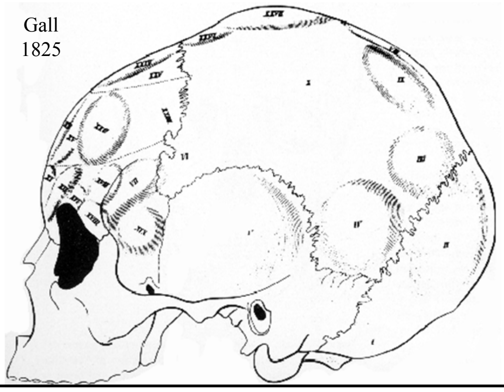
A million (= 10^6) ?

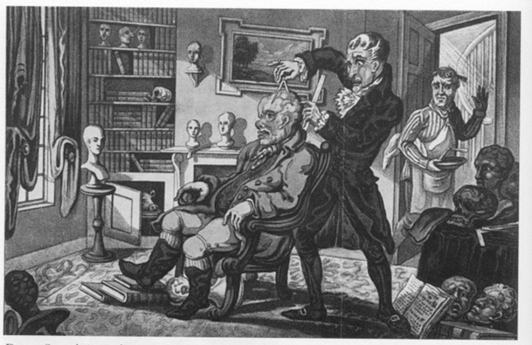


10^{12} must because that is how many neurons are in your brain!

Gall's Phrenology

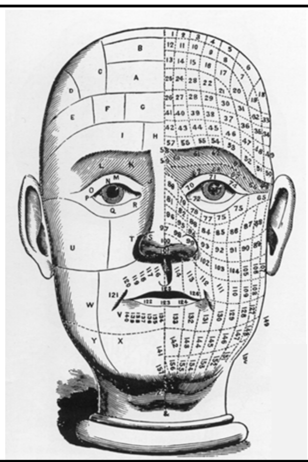
Gall
1825



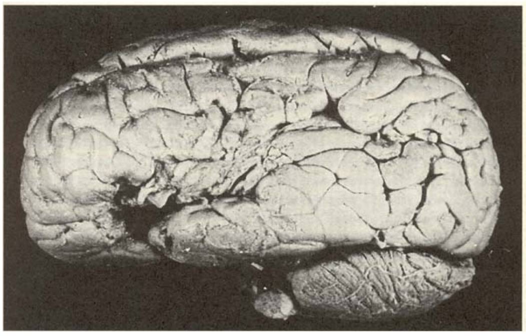


Doctor Spurzheim in his consulting room measuring the head of a rather peculiar looking patient. A bemused barber looks on. Coloured aquatint by J. Kennerly, 1816, after R. Cocking.

Redfield
1866

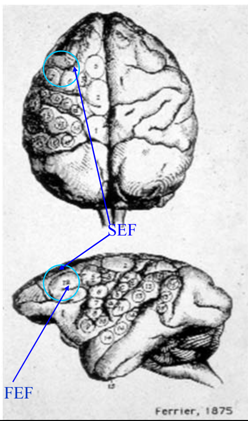


Paul Broca, 1861 : Tan’s brain



Early electrical stimulation and units recording experiments

(Fritsch and Hitzig; Ferrier; Adrian)



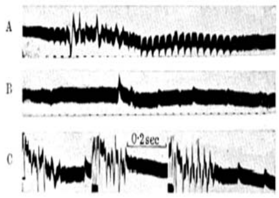
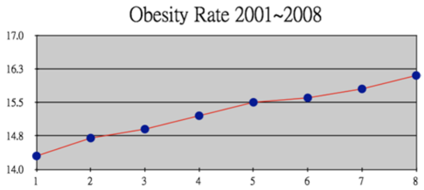
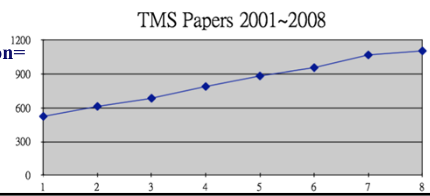


Fig. 9. Cat under deep dial anaesthesia.
A. Spontaneous group of waves at 6 per sec.
B. Deeper anaesthesia. Activity reduced to occasional waves.
C. Same state as B. Wave groups set up by short periods of stimulation. Stimuli marked at the foot of the record.

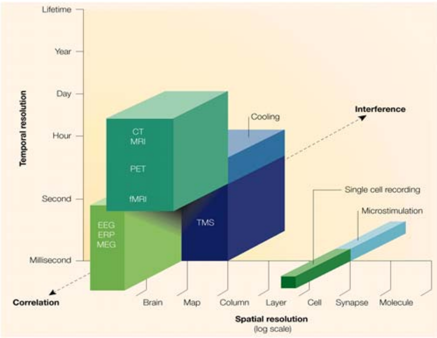
Why causality is important?



Pearson Correlation= 0.991; p<0.0001

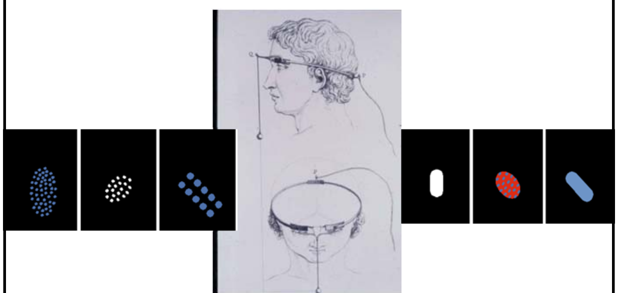


The role of TMS in Cognitive Neuroscience

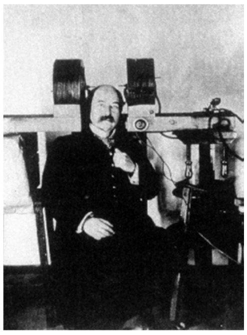


Source: Walsh & Cowey, 2000 Nature Review Neuroscience

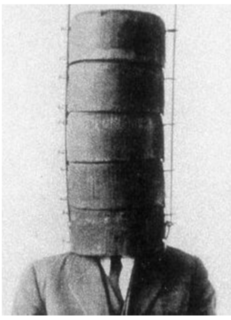
The development of TMS,
the search for phosphenes and
current progress of TMS



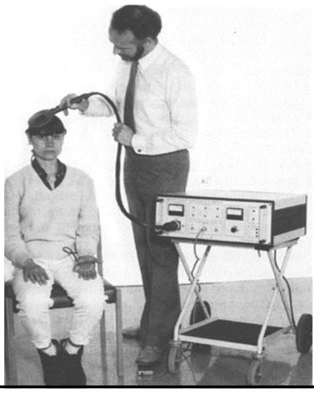
Thompson’s demonstration: magnetically induced phosphenes (1910)



Size matters: Magnusson and stevens (1911) arrangement of coils to provide a magnetic field of sufficient strength to induce phosphenes

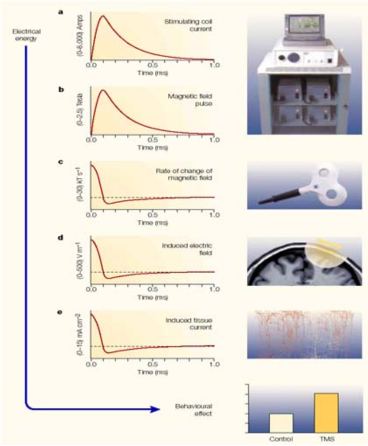


First demonstration of modern TMS over the primary motor cortex by Tony Barker in Sheffield in 1985



The current incarnation of TMS machines was developed by Tony Barker in Sheffield in 1985

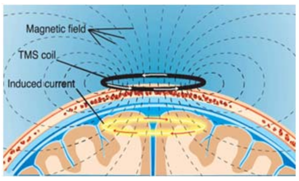
How does TMS work?



What does TMS do to

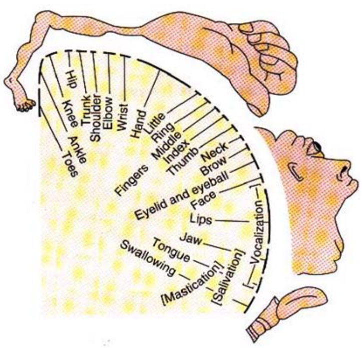
Magnetic field passes unimpeded through skull.

Rapid rise and fall in magnetic field induces electrical currents in brain
→ depolarises neurons



Ruohonen J.
Background physics for magnetic stimulation.
Suppl Clin Neurophysiol. 2003;56:3-12

Functional spatial resolution of TMS
(In theory : 5mm~15mm)



- Interfering motor programming
- Motor mapping

Temporal resolution of TMS and different stimulation methods

High Frequency but subthreshold rTMS (theta-burst) mimics long term potentiation (LTP).

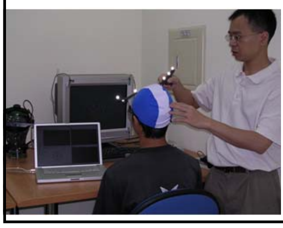
Repetitive TMS: exploring the possible brain areas involved in a task.

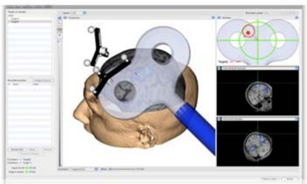
Single pulse: probing the exact timing of the neural process in a task.

Double pulse: prolonging the TMS effect or probing functional connectivity.

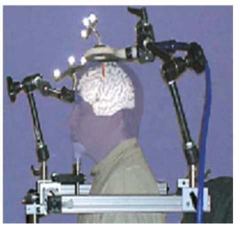
Low Frequency rTMS (1Hz; 10 mins): decrease the activities of the stimulated site for a short period of time.

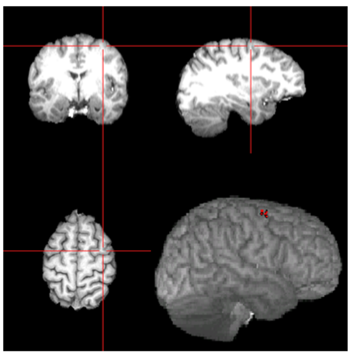
Frameless stereotaxy System





Improved spatial resolution: Brainsight frameless stereotaxy system and Talairach coordinates





TMS, lesion patients studies and other neuroimaging techniques

Creating an ideal patient.
Reversibility.
Local but not diffused lesion.
No Reorganization and Plasticity.
Precise time window.
Necessity of an area for one specific function

Inability for ventral brain area.
The underlying mechanism is still not very clear.
The spatial resolution is not perfect.

Safety and ethical issues

For details see Wassermann, 1998

- Noise: The audible noise (a sharp crack) from the coil can reach over 80 dB and be uncomfortable.
- Single pulse: It is widely agreed that, with simple precautions, single pulse TMS has no deleterious effects either in the short or long term.
- Multiple pulses: Repetitive pulse stimulation (rTMS) carries a small risk of inducing a seizure (esp. stimulating motor cortex).

TMS and Intervention of Depression and Migraines

In vitro studies with rats showed long-term treatment (11 wks) with rTMS increased the overall viability of mouse monoclonal hippocampal HT22 cells and had a **neuroprotective effect against oxidative stressors**, e.g. amyloid beta and glutamate

No cognitive impairments or structural alternations in the rats brain.

Application of TMS in Cognitive Neuroscience

The application of TMS in cognitive neuroscience: some examples

Muscle movement: Barker et al. (1985)

Visual suppression: Amassian et al. (1989); Corthout et al. (1999)

TMS & PET (connectivity): Paus (1997)

Visual search and Eye movements: Ashbridge et al. (1997); Juan & Walsh (2003); Muggleton et al (2003); Juan et al (2008); Liu et al (2010); Chao et al (In Press);

Plasticity: Hamilton & Pascual-Leone (1988)

Visual neglect: Fierro et al (2000)

Visual awareness: Cowey & Walsh (2000); Pascual-Leone & Walsh (2001); Juan et al. (2004)

The Ferrier Lecture 2004
What can transcranial magnetic stimulation tell us about how the brain works?

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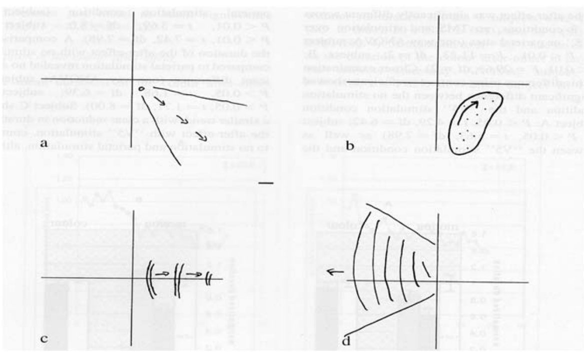
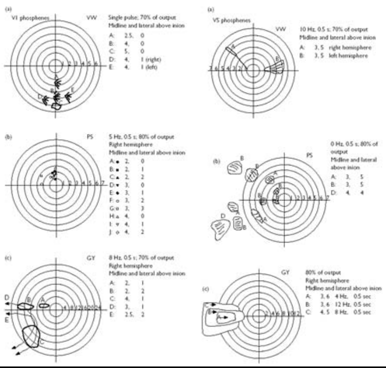
Moving Phosphenes induced by apply TMS over V5/MT



V1 & visual awareness: TMS study on Blindsight patients (Cowey and Walsh, 2000)



Cohen et al (1997); Hamilton & Pascual-Leone (1988): Braille reading

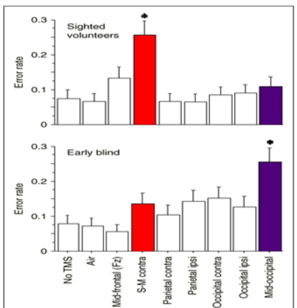


Fig. 2 Proportion of errors made in the discrimination of Braille characters during exposure to repetitive TMS. Results shown for different sites of rTMS application in sighted and early-blind subjects. The asterisks mark significant differences between the two subject groups. (Adapted from Ref. 23.)

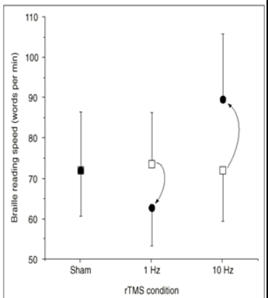
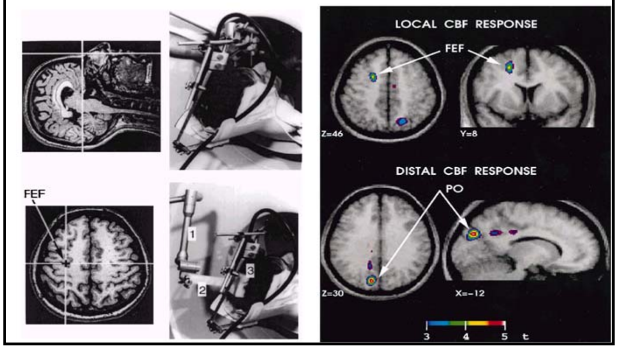
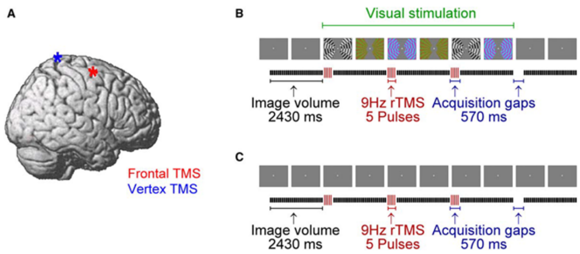


Fig. 3 The effects of rTMS on Braille reading speed. Experimental conditions were either 1 Hz or 10 Hz rTMS stimulation, or 'sham' (a non-stimulating control condition). Open symbols refer to performance prior to rTMS and filled symbols refers to performance immediately following rTMS to the occipital cortex. Symbols display the mean values and error bars the standard deviation values for five early-blind subjects.

Paus (1997) TMS + PET: experiments were designed for anatomical connection studies

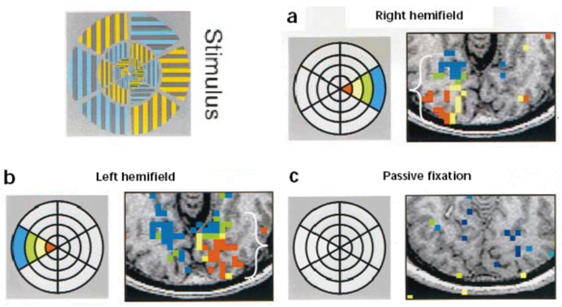


Concurrent TMS-fMRI and Psychophysics Reveal Frontal Influences on Human Retinotopic Visual Cortex Ruff et al., 2006 Current Biology

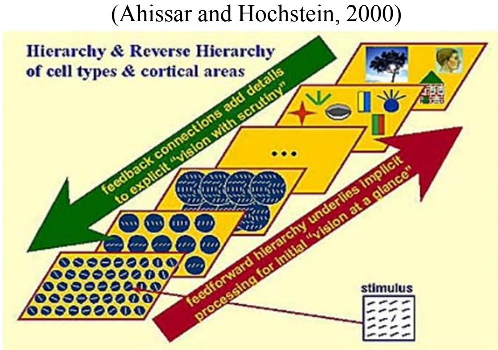


Using TMS to probe the temporal-functional role of V1 in a visual search task

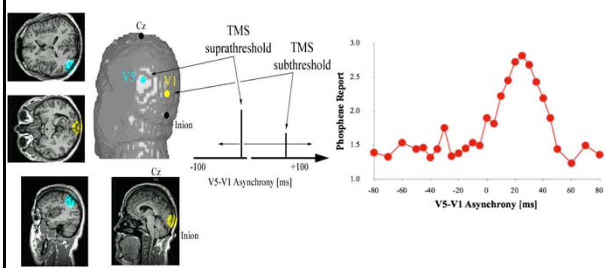
Retinotopic attentional modulation in V1. The locations of covert attention corresponded to the retinotopic locations of the objects. (Brefczynski and DeYoe, 1999).



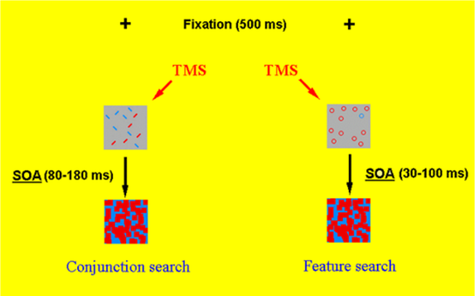
Reverse Hierarchy Theory
(Ahissar and Hochstein, 2000)



V5-V1 back-projection and visual awareness
(Pascual-Lenoe & Walsh, 2001)



Behavioural and TMS paradigm: The conjunction search task (left) and the feature search task (right). The SOA between the stimulus and the mask was adjusted in steps of 10 ms to allow subjects to reach a criterion of 62.5 to 87.5 percent correct in a staircase procedure.



TMS parameters

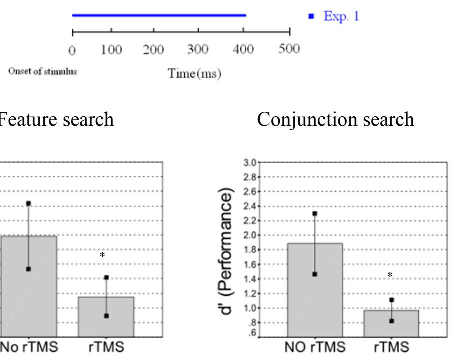
rTMS for Exps 1 & 2: 10 Hz for 400 ms (5 pulses).

Double pulse TMS for Exp 3.

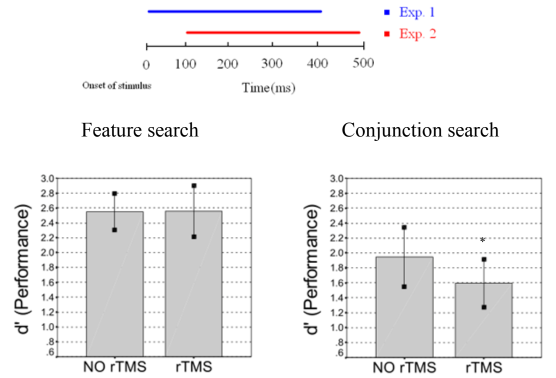
Intensity of stimulation: 65 % of machine output (1.3 Tesla).

Sub-threshold stimulation for generating phosphenes and scotomas.

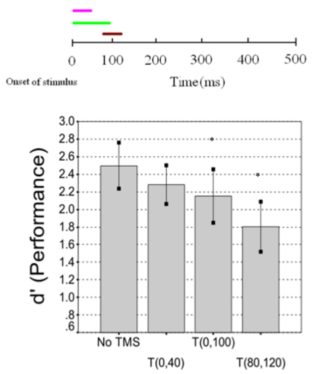
rTMS (0-400) over V1 impairs feature and conjunction search



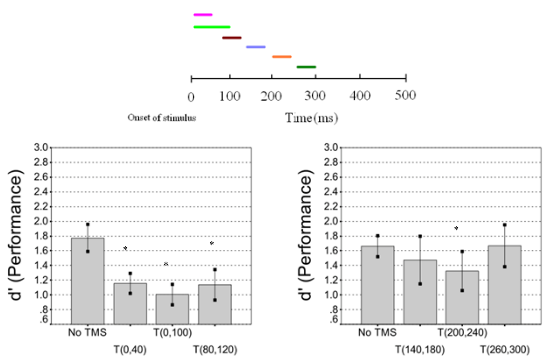
Gap rTMS (100-500) over V1 selectively impaired conjunction search



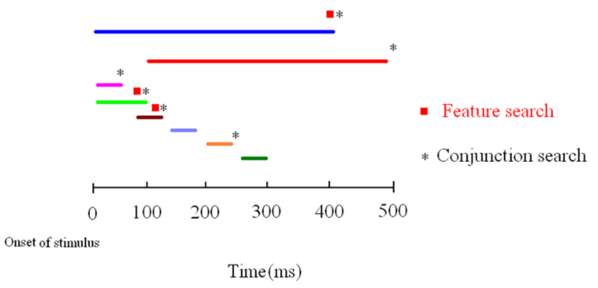
Double pulse TMS (0, 40; 0,100; 80,120)– Feature search



Double pulse TMS (0, 40; 0,100; 80,120) (140,180; 200,240; 260,300) – Conjunction search



Summary of the results



Conclusions

Human V1 is more than a distributor of simple attribute information.

Repeated iterations within V1 or early feedbacks to V1 are necessary for both feature and conjunction search.

Late feedbacks to V1 are essential for conjunction search but not feature search.

Reverse Hierarchy theory is supported in current experiments.

Juan & Walsh, Experimental Brain Research (2003); Juan et al., Progress in Brain Research (2004)

Using TMS to explore the temporal-functional role of FEF in covert attention

How fast can your brain be?

Wang: 150 km/1hr

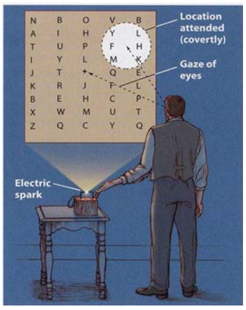
Only 450 ms to reach the batter (18.4 m)

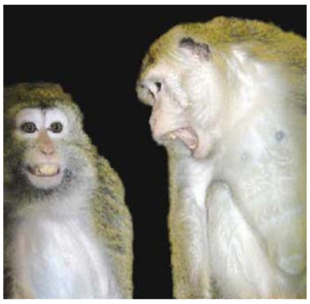
However, it may take more than 200 ms to move your eyes!

How do our brains help us to hit the ball without eye movements?

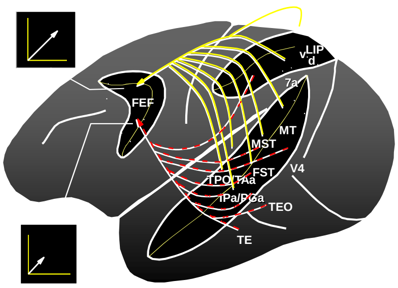
Covert Attention and Eye Movements

Helmholtz's inquiry

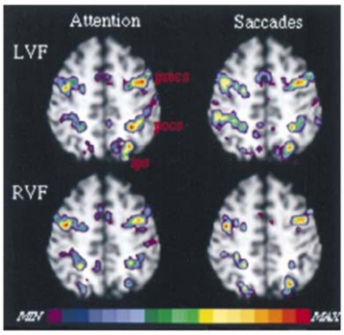




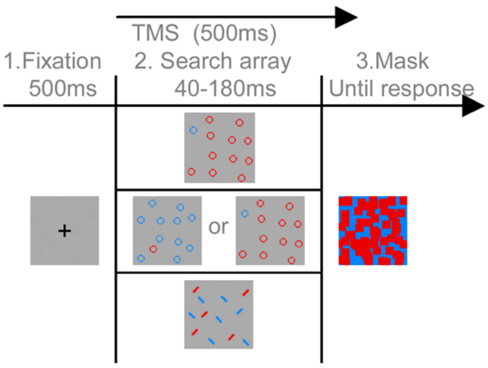
Visual Search with/without Eye Movements and Frontal Eye Field



A common network of functional areas for attention and eye movements (Corbetta et al, 1998)



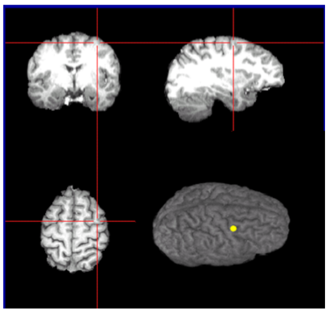
Behavioral and TMS paradigm



The parameters of stimuli & TMS stimulation site

- Search array were 2 x 2 degrees squares.
- Staircase procedure to adjust stimuli presentation time until the performance level of 75% correct was reached.
- 60 trials on one block, rTMS were delivered in half of trials.
- 10 Hz for 500 ms at 65% of stimulator output beginning at the onset of the search array.
- Stimulation sites: FEF (experimental site); V5/MT (control site I); Vertex (control site II)

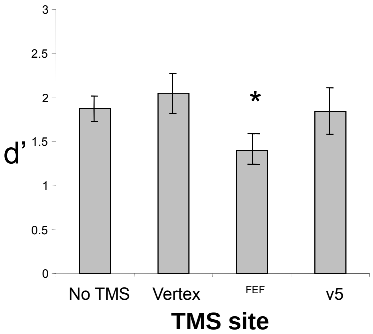
The locations of FEFs were confirmed with structure MRI and Brainsight

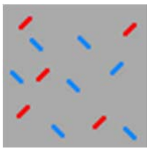


A mean location of 33±3.0, 0±5.1, 65±1.8 (mean ± s.e.m.) was used (MNI co-ordinates).

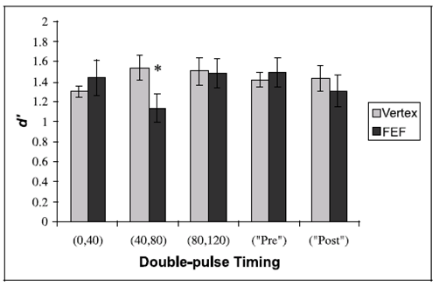
These show good agreement with the location of FEF as reviewed by Paus.

Conjunction search : Subjects' performance were impaired by TMS over FEF

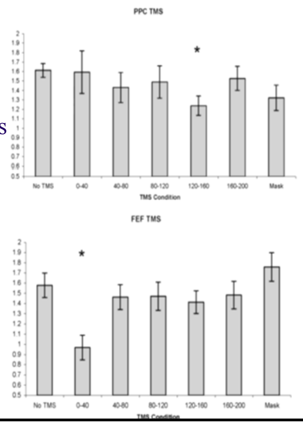




Timing of FEF involvement in visual search (O'Shea et al., 2004)



The functional involvement of FEF is earlier than PPC as revealed in human TMS studies (Kalla, Muggleton, Juan, Cowey and Walsh., 2008, *Neuroreport*)



Intermediate conclusions

Human FEFs are necessary for visual analysis in the absence of eye movements.

The nature of the FEF effect: an increase in false positive responses reminiscent of parietal cortex damage (illusory conjunction).

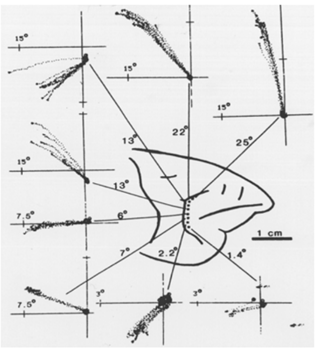
The FEF involvement in visual selection is early and is earlier than posterior parietal cortex.

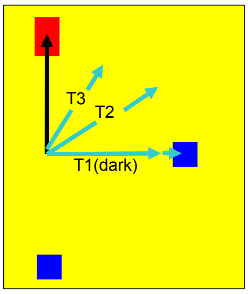
Muggleton, Juan, Cowey & Walsh (2003); Kalla, Muggleton, Juan, et al (2008)

Muggleton, Juan, Cowey & Walsh (2010).

Dissociation of Spatial Attention

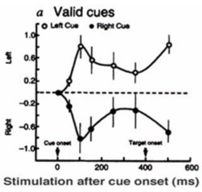
Suprathrehold microstimulation on FEF: stimulating on different parts of FEF systematically induces fixed-vector saccades with variable amplitudes and directions





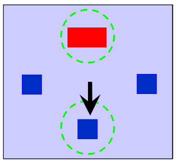
Posner's cueing paradigm

Cue Validity: 80%



Kustov & Robinson (1996, *Nature)*

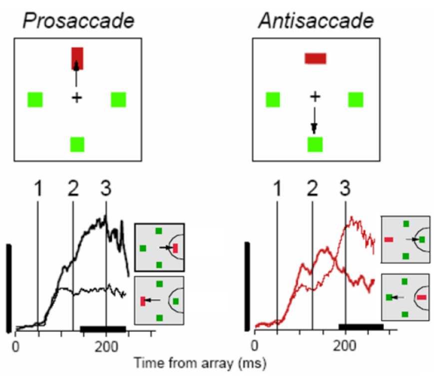
Pro/Anti saccade task



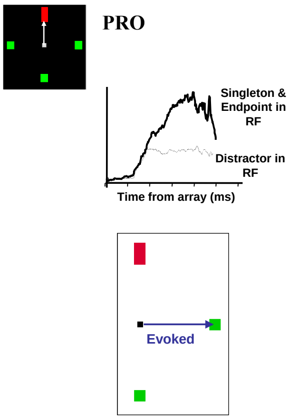
The contingency between the direction of visual selection and that of saccade preparation are low

?

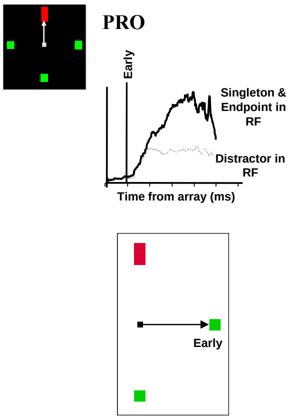
Pro/Antisaccade task to dissociate the locus of attention from the endpoint of a saccade (Sato & Schall, 2003)



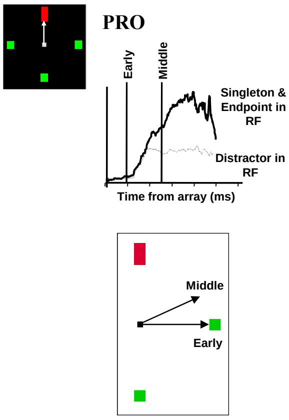
PRO

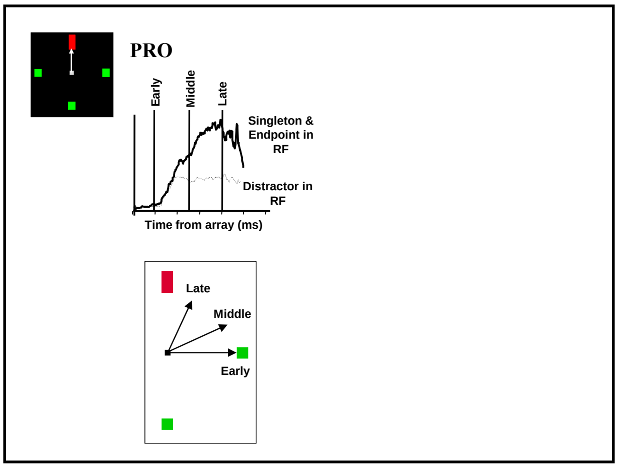

Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Evoked

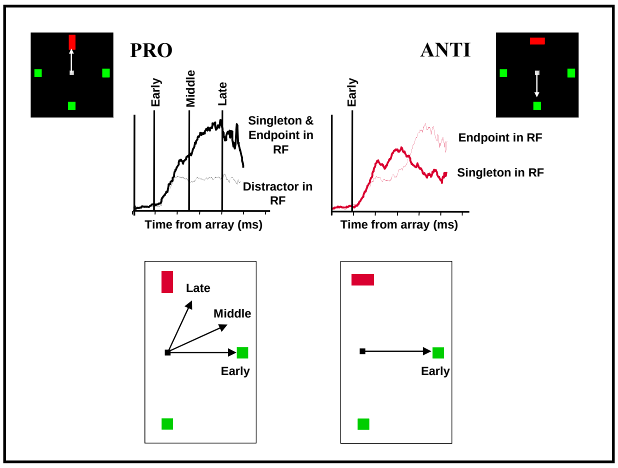
PRO

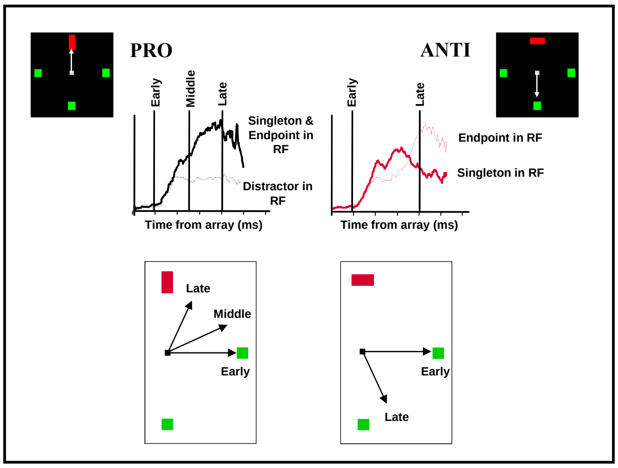

Early
Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Early

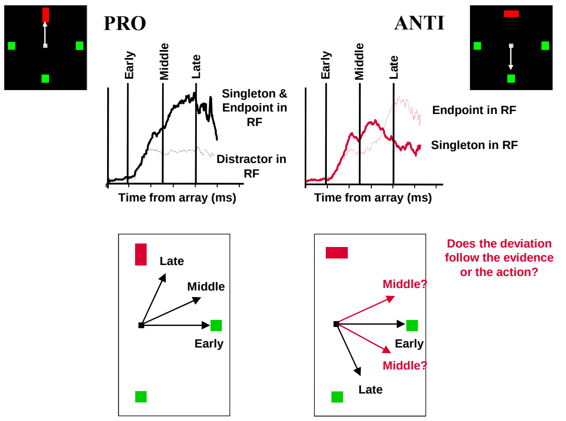
PRO


Early
Middle
Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Middle
Early

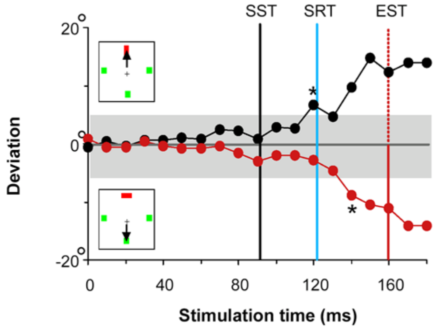

PRO
Early
Middle
Late
Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Late
Middle
Early


PRO
ANTI
Early
Middle
Late
Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Early
Endpoint in RF
Singleton in RF
Time from array (ms)
Late
Middle
Early
Early

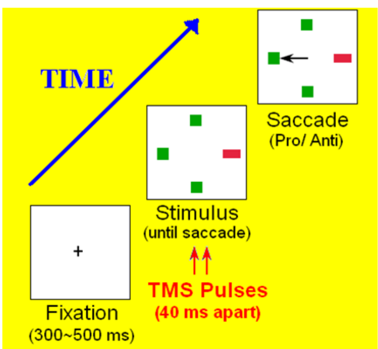

PRO
ANTI
Early
Middle
Late
Singleton & Endpoint in RF
Distractor in RF
Time from array (ms)
Early
Late
Endpoint in RF
Singleton in RF
Time from array (ms)
Late
Middle
Early
Early
Late



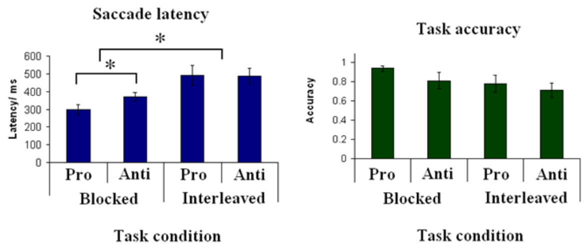
The summary of the microstimulation effects on the deviation of saccades across times



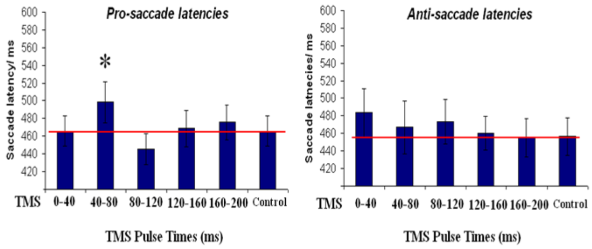
Are there two separate time stages for visual selection and saccade preparation in Human FEFs?



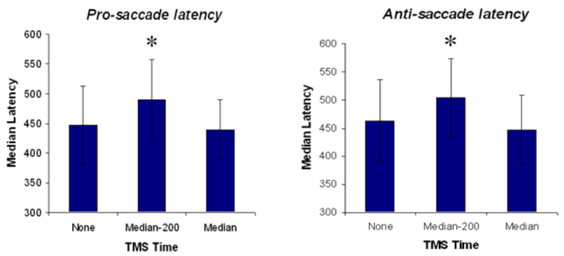
Behavioral data showed two different strategies may be used in blocked versus interleaved trials.



TMS effects on Pro-saccade latencies in early visual selection stage



TMS effects on both pro/ anti saccade latencies in saccade preparation stage



Intermediate conclusions

Prosaccades are faster than antisaccades only when they are presented as blocks.

When they are mixed there is no difference. This suggests there is little benefit of moving your eyes to the location processed (or "attended"), when the predictability of the trial type is low.

TMS effects on two time periods suggest that two separate stages of visual processing and saccade generation in human FEFs.

Juan et al (Cerebral Cortex, 2008)

The application of TMS and tDCS in the investigation of human inhibitory control

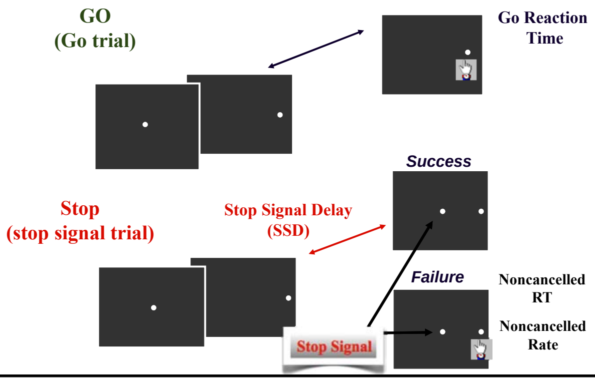
What is inhibitory control and its importance

The dilemma zone

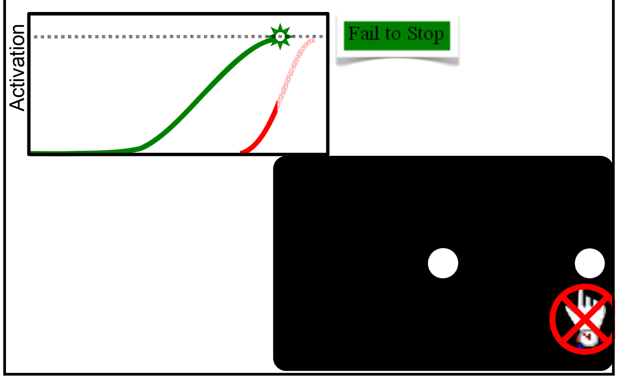
- ADHD
- Conduct Disorder
- Impulsive-Violent Offenders
- Cocaine-dependent men

Animals Use Inhibitory Control for Flexible Behavior Too!

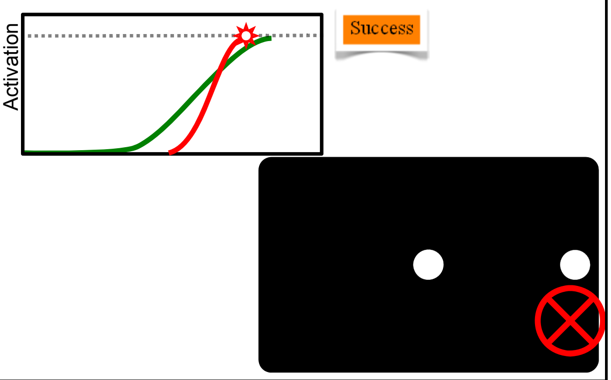
The inhibitory control can be measured
with the stop signal (countermanding) task



Stop signal trial: Fail to stop



Stop signal trial: Success to stop

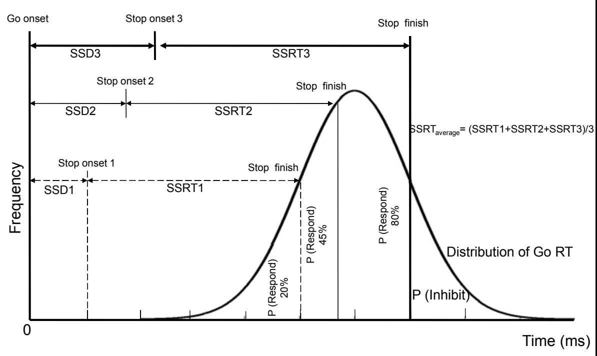


Dependent Measures of the Stop Signal Task

- Go reaction time (Go RT)
- Noncancelled rate
- Noncancelled RT
- Stop Signal Reaction Time (SSRT)

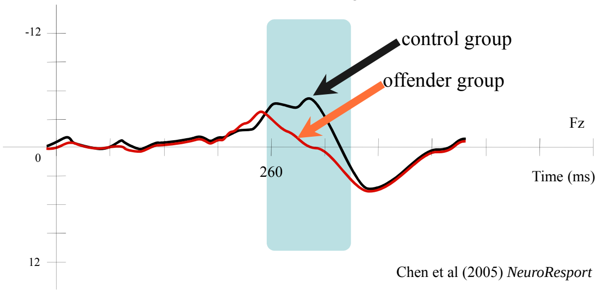
81

Measuring stop signal reaction time (SSRT)



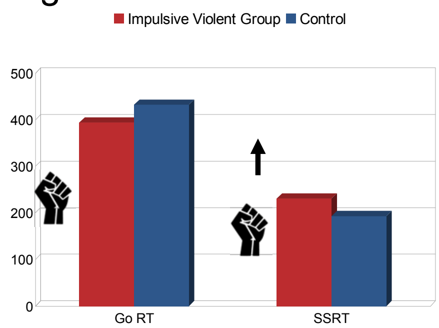
Recap our previous studies

A go/no-go task was used to investigate impulsive violent offenders' and normal subjects' inhibitory processes. The N200 ERP component was associated with response inhibition and the amplitude of this component was lower in an impulsive violent group than for normal controls.

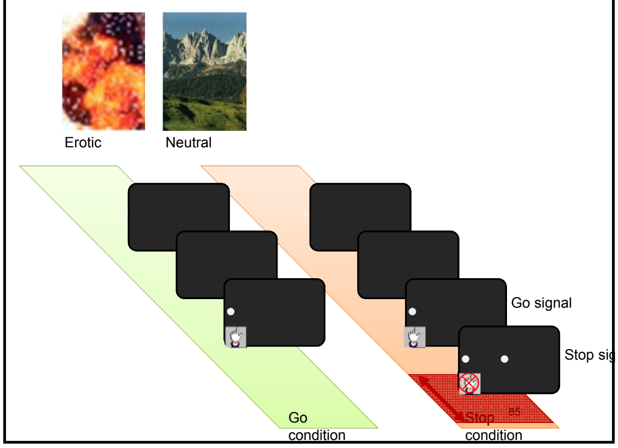


Chen et al (2005) *NeuroResport*

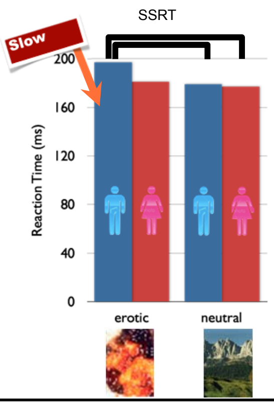
Impulsive violent offenders have longer SSRT than controls

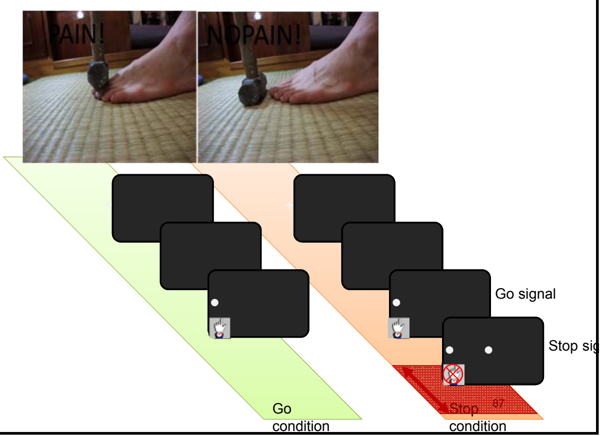


Chen et al (2008) *Behavioral Brain Research*

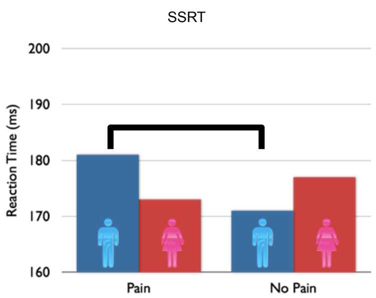


Gender differences in the inhibitory control and emotion



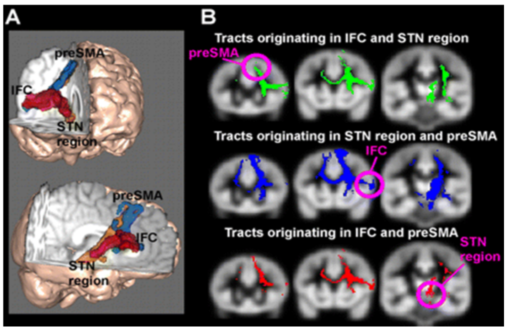


Gender differences in the inhibitory control and pain



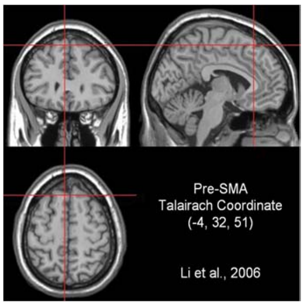
Yu et al (2012) *Cognition*

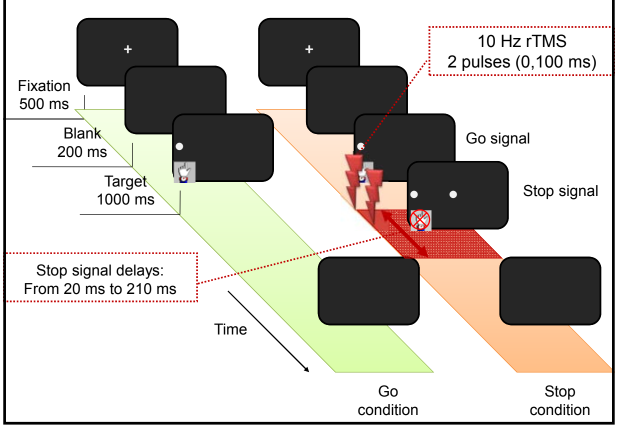
The possible neural network of inhibitory control



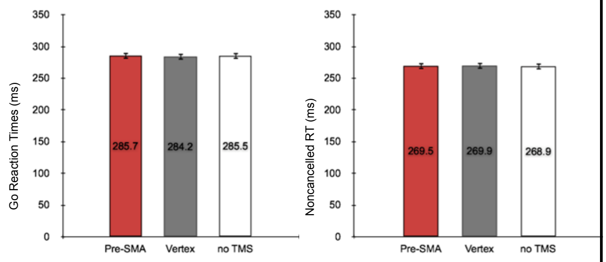
Courtesy of Aron et al., 2007

TMS over pre-supplementary area to probe the neural mechanism of inhibitory control

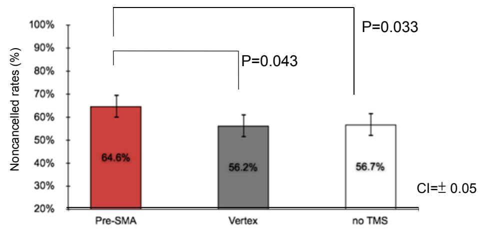




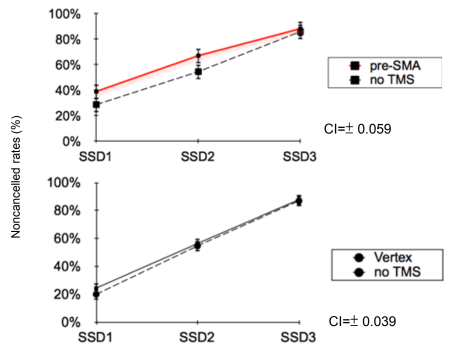
Go RT Noncancelled RT



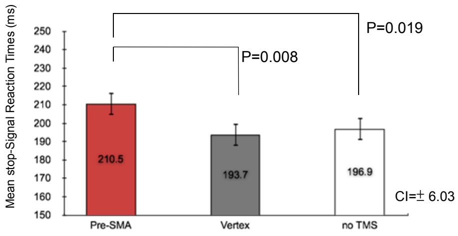
The mean noncancelled rates



The inhibition function of the three SSDs for the three TMS conditions



The mean stop signal reaction times of averaging the first and second sub-sessions across three conditions



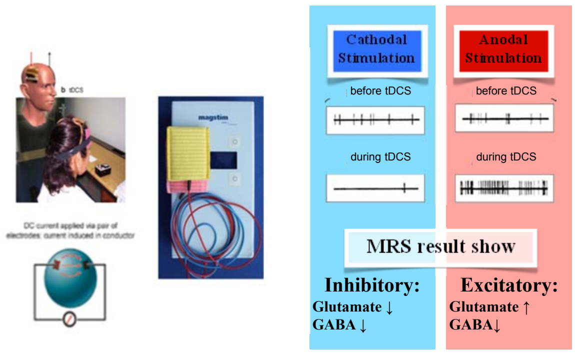
Intermediate conclusions

TMS delivered over left Pre-SMA (rFEF) resulted in effects consistent with the hypothesis that the Pre-SMA (rFEF) is necessary for the inhibitory control, producing both elevated SSRTs and increased error rates compared to control stimulation.

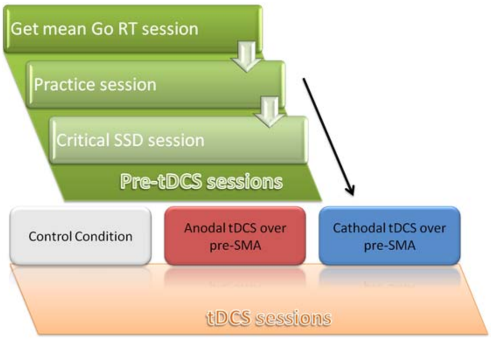
A casual link between Pre-SMA (rFEF) and inhibitory control in normal subjects is established in current studies.

Chen et al (2009, Neuroimage); Muggleton et al (2010, JOCN)

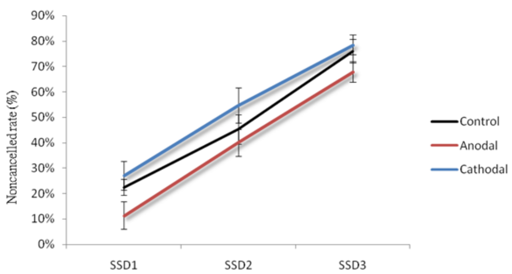
Transcranial Direct Current Stimulation



tDCS over PreSMA to modulate the inhibitory control bidirectionally



Inhibition function across SSDs



Intermediate conclusions

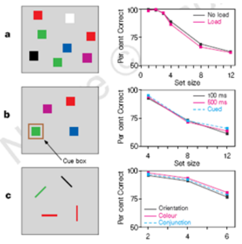
Pre-SMA tDCS can modulate the inhibitory control bidirectionally which may offer some potential intervention programs for people with deficit in this domain.

Hsu et al (2011, Neuroimage)

Why are we so bad at CB?

- Limitation in visual working memory
  a. Storage and retrieval difficulties
- Visual working memory (VWM)
  a. Synchronized neural firings
  b. Fast formation (50 ms per item)
  c. Very transient
  d. Limited in capacity
- On average 4 items
  a. Huge variance in individual differences

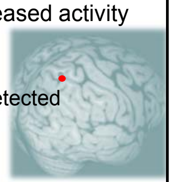
(Cowan and colleagues, 1999, 2001; Vogel and colleagues, 2004, 2005, 2008)



Luck & Vogel (1997) *Nature 390*:279-281

Neural Correlates

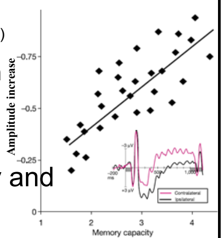
- Most neuroimaging studies report increased activity in posterior parietal cortex (PPC)



- –Increased PPC activity when change is detected
  - **fMRI**: Beck et al. (2001)
  - **ERP**: Fernandez-Duque et al. (2003)
- –PPC activity level is correlated with encoding load
  - **fMRI**: Todd & Marois (2004, 2005)
- Causal evidence reveals the timing of PPC involvement
  - **TMS: Encoding & Maintenance**: Tseng et al. (2010)
  - **TMS: Retrieval & Comparison**: Olson & Berryhill (2009)

More on PPC

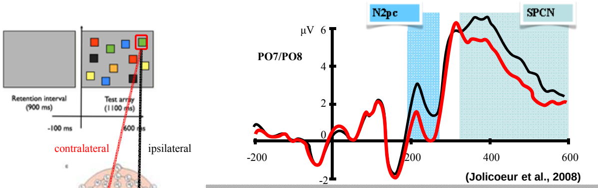
- Vogel & Machizawa (2004, 2005): ERP
  - PPC activity can be indicative of VWM capacity
  - Contralateral delay activity (CDA)
  - Sustained parietal contralateral negativity (SPCN)
  - Individual differences in VWM can be predicted by parietal activation
- Can we increase PPC activity and improve VWM performance?



Vogel & Machizawa (2004) *Nature 428, 748-751*

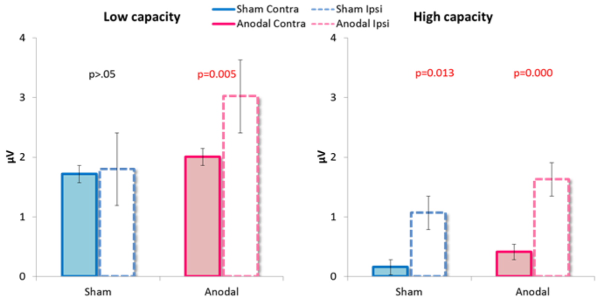
Indexes from ERP for VWM task

N2pc (N2 posterior contralateral scalp sites) is apparent in hemisphere that's contralateral to the visual target, and is an accurate indicator of the deployment of covert visual attention



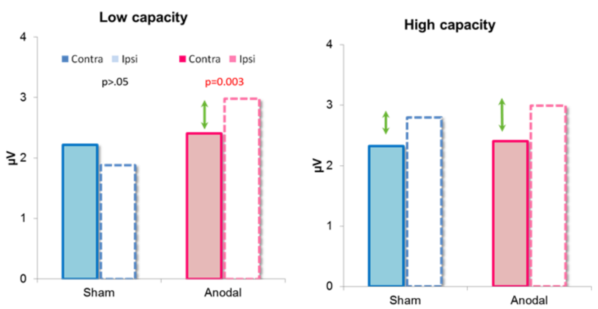
SPCN increases in amplitude when the number of to-be-remembered items increases, thus it serves as an electrophysiological marker of maintaining and accessing representation in WM

Summary-N2PC



Low and high performers showed different performance.
Only the low performers were affected by anodal tDCS.
Anodal tDCS increased the amplitude of N2pc and behavior performance.
However, Anodal tDCS did not improve high performers' performance.

Summary-SPCN



The results of SPCN showed the same pattern with N2pc.
Only low performers were affected by anodal tDCS.

Conclusions

- Anodal tDCS over rPPC can potentially improve VWM performance in low performers
- ERP results suggest that rPPC tDCS facilitated one's deployment of attention (N2pc) and enhanced access to VWM information (SPCN)
- First study to simultaneously demonstrate tDCS-induced behavioral improvement that can be indexed by electrophysiological measures
- Also, first study to document the interaction between tDCS and one's natural ability

Tseng & Hsu et al, *J Neurosci.*, 2012

References

http://icn.ncu.edu.tw/g_01.aspx?faculty_id=10