L'application de la TMS dans l'étude des fonctions cognitives

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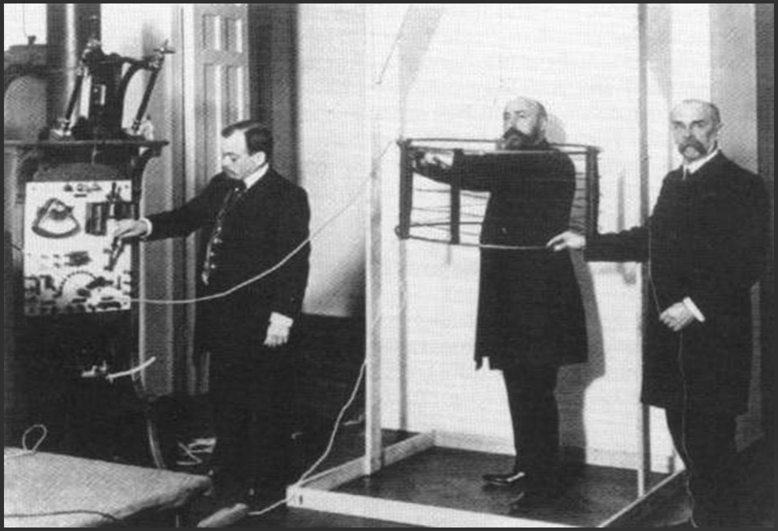
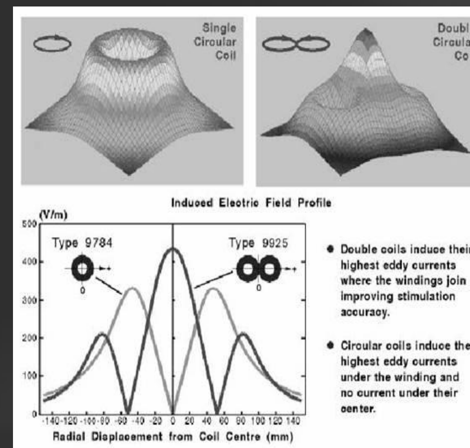
Magnetic stimulation

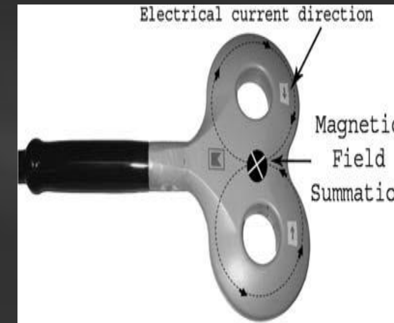


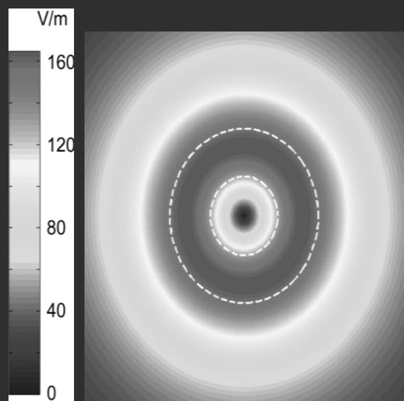
Arsène d'Arsonval (on the right) and two of his assistants are shown demonstrating the effects of the flow of alternating current (1911).
"*an alternating magnetic field with an intensity of 110 volts, 30 amperes and a frequency of 42 cycles per second, gives rise to, when one places the head into the coil, phosphenes and vertigo, and in some persons, syncope*." (d'Arsonval, 1896)

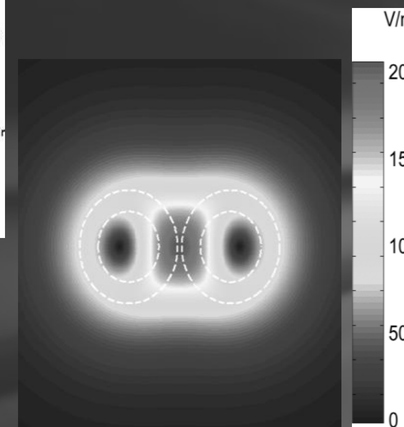
Silvanus P. Thompson: on inserting the head into the interior of the coil, in the dark, or with the eyes closed, there is perceived over the whole region of vision a faint flickering illumination, colourless or of a slightly bluish tint" (1910)

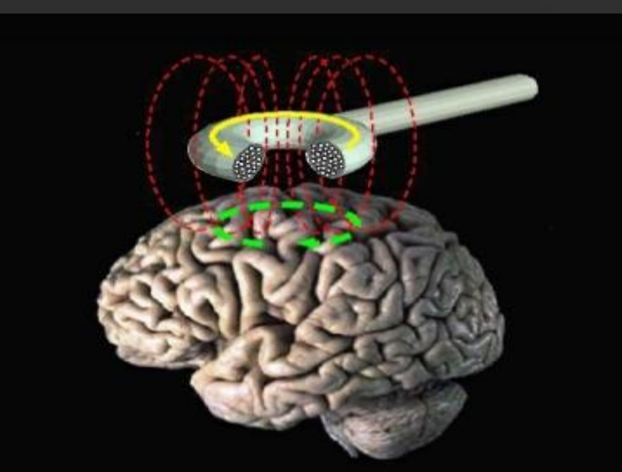
The magnetic coils used by Magnusson and Stevens in 1911,. Additional sections of coils could be energized to increase the magnetic field.











Faraday's principle of electromagnetic induction

"Faraday showed that an electrical current passed through one coil could induce a current in a nearby coil. The current in the first coil produces a magnetic field that in turn causes current to flow in the second coil. In TMS that second coil is replaced by brain tissue and the induced electric field elicits neuronal activity." (Walsh & Cowey, 2000)

TMS and study of cognitive functions

1) Causal relation between cortical activity and behavior

Complement the correlational approaches (fMRI, EEG, MEG)

Virtual lesion or neural noise: change in cortical excitability

Mostly inhibitory but sometimes facilitatory effect

Underlying mechanism is still unclear but the most critical factors are:

***Stimulation parameters*:**

intensity, frequency, timing, coil type/orientation, protocol…

The ***initial state*** of the activated brain region:

rest, active, task-demands…

2) Timing at which activity in a particular cortical region contributes to a given task

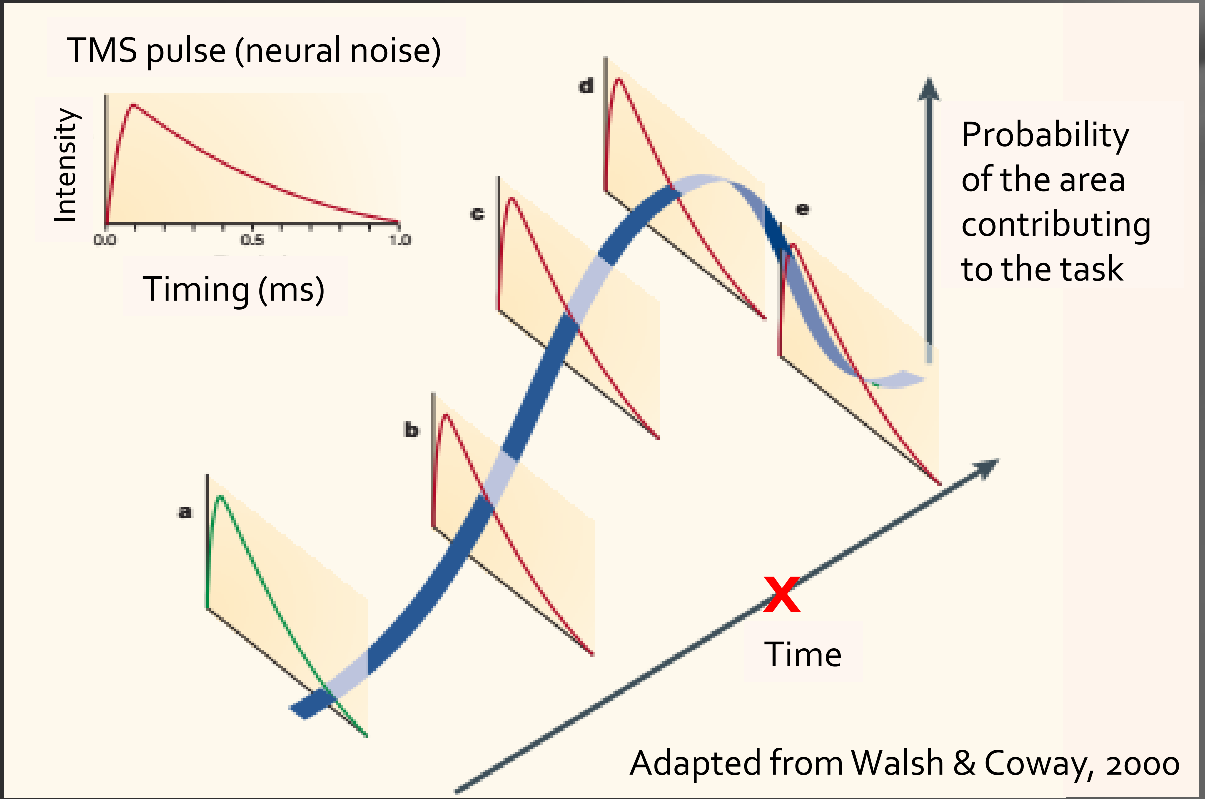
Single-pulse (high temporal resolution…but need to know where & when!)

Begin with repetitive TMS (low temporal resolution but stronger effect -> explore space dimension)

Double-pulse; triple-pulse

TMS temporal resolution depends on: Duration of the TMS pulse effects

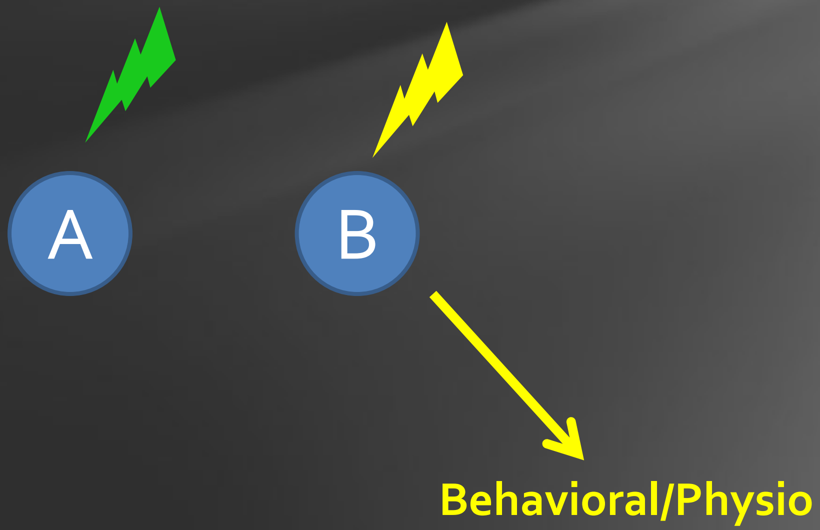
Duration of the area's involvement in the task



3) Connectivity between brain regions

Focal TMS applied to a particular brain region has both local and remote neural effects in the brain.

- Paired-pulse protocol (explore the relation between two areas: how activity changes in one brain area causally impact on activity in connected areas)



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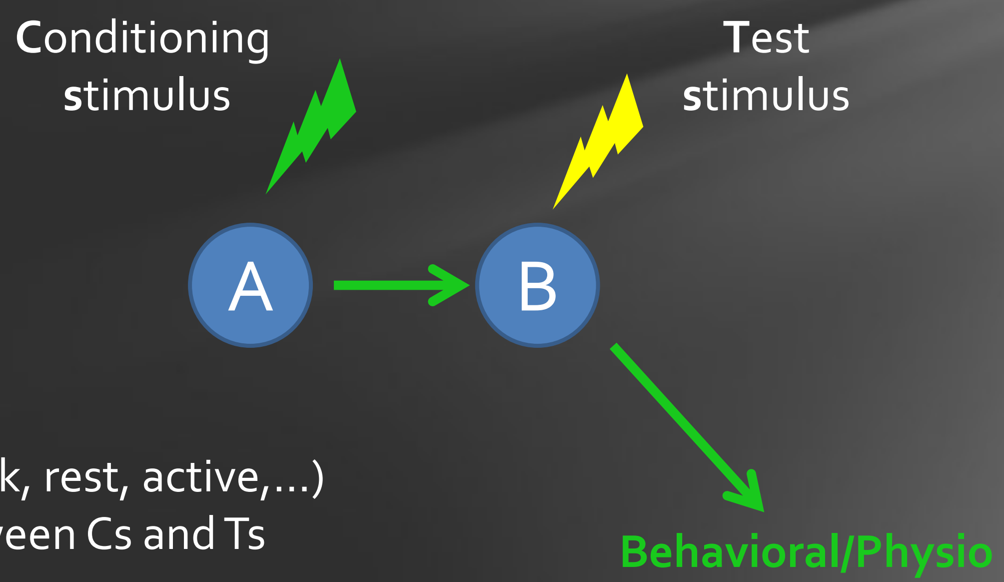
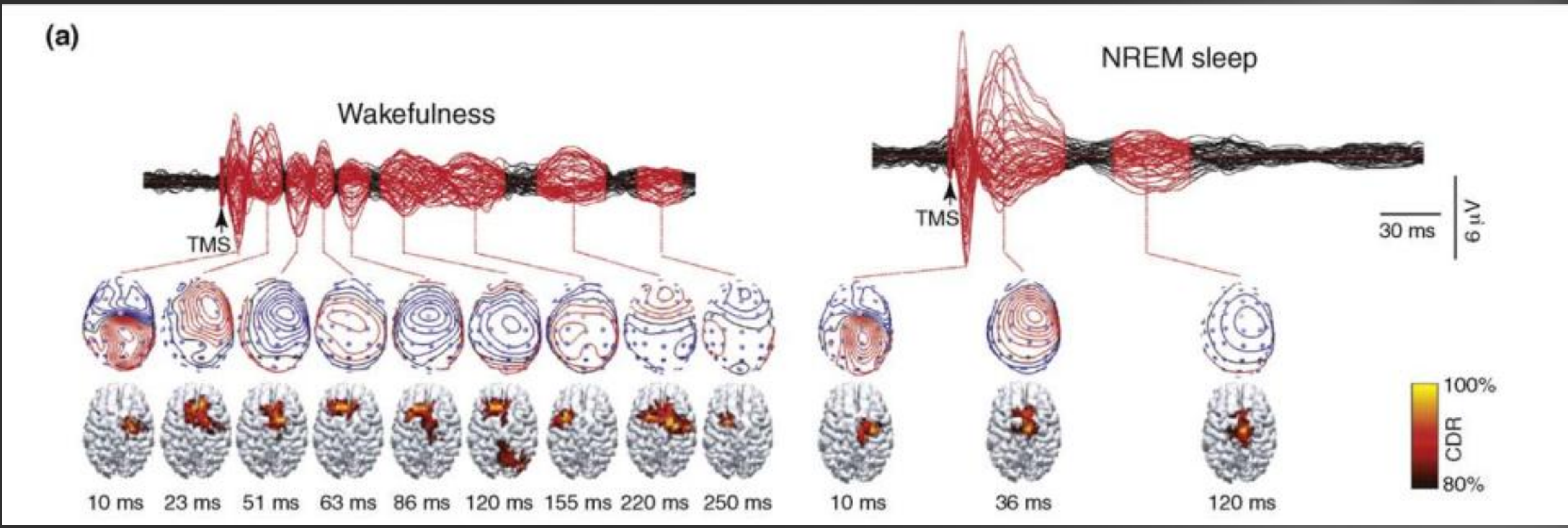


State of the system (task, rest, active,…)
Temporal distance between Cs and Ts
…

3) Connectivity between brain regions

- TMS combined with neuro-imaging (EEG, PET, fMRI)

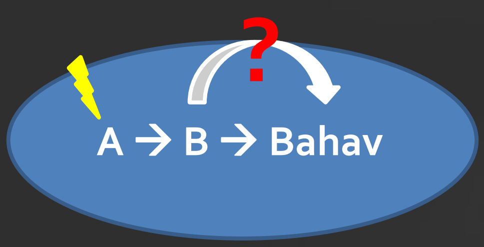


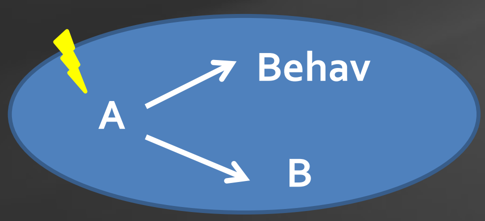
Massimini et al. (2005)

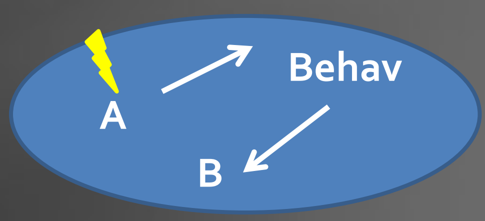
Is the causal inference between ROI and function still valid?

Can behavioural TMS studies without imaging still be considered as valid empirical tools for revealing the functional necessity of the stimulated brain region?

YES… because remote neural effects of TMS is not necessarily functionally relevant!

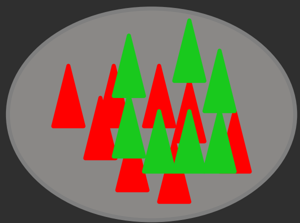






Need TMS interference protocol to prove the causality of the connected regions

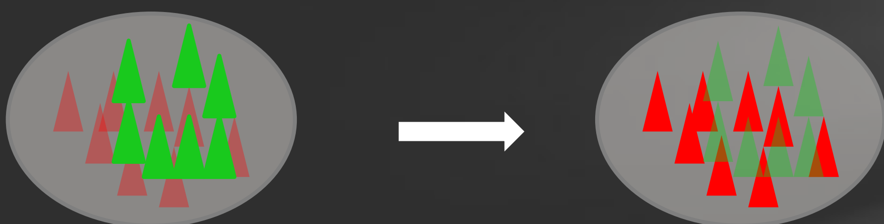
4) State-dependent TMS paradigm/TMS-adaptation paradigm



Reveal some degree of specificity in a region that contains functionally overlapping populations of neurons

Neurons' activation level → State of the system → TMS effect

TMS affects the less active neurons (Silvanto et al., 2008)

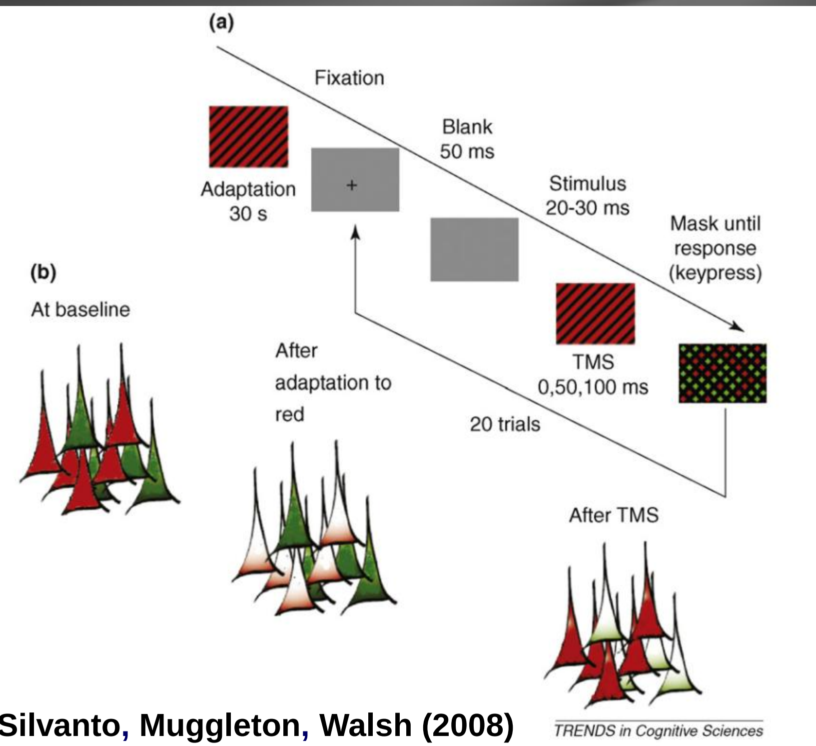


Reduce the excitability of

Increase the (facilitatory) TMS effect on

One can control which neural populations are preferentially affected by TMS

TMS adaptaion paradigm: Induce habituation



Silvanto, Muggleton, Walsh (2008)

How to choose the most appropriate TMS protocol? Pitfalls?
How to control for non-specific TMS effects (artefacts)?

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Review

The use of transcranial magnetic stimulation in cognitive neuroscience: A new synthesis of methodological issues

Marco Sandrini[a,b,*], Carlo Umiltà[c], Elena Rusconi[d,e]

Rev Neurol (Paris). 2011 April 1; 167(4): 291–316. doi:10.1016/j.neurol.2010.10.013.

La stimulation magnétique transcrânienne (SMT) dans la recherche fondamentale et clinique en neuroscience

Antoni Valero-Cabré[1,2,3,4,*], **Alvaro Pascual-Leone**[4], and **Olivier A. Coubard**[5]

Studies in Cognition: The Problems Solved and Created by Transcranial Magnetic Stimulation

E. M. Robertson, H. Théoret, and A. Pascual-Leone

 Journal of Cognitive Neuroscience 15:7, pp. 948–960

The Contribution of writing to reading

A neuronavigated TMS Study

Chotiga Pattamadilok[1], Aurélie Ponz[2], Samuel Planton[1] & Mireille Bonnard[3]

[1]Laboratoire Parole et Langage, [2]Cognitive Neuroscience Experiment and Consulting, [3]Institut de Neurosciences des Systèmes

Pattamadilok, C., Ponz, A., Planton, S., & Bonnard, M. (2016). Contribution of writing to reading: Dissociation between cognitive and motor process in the left dorsal premotor cortex. *Human Brain Mapping, 37, 1531–1543.*

Reading and writing are closely related

Already at the first stage of literacy acquisition, children learn to reproduce the form of written characters that they read.

Writing practice can facilitate reading acquisition

Bara et al., 2004 : Reading training in 5 yrs-old children. Classic Visual training was less efficient than Haptic + Visual training.

Longcamp et al., 2005 : In 3-5 yrs-old children, handwriting training gave rise to a better letter recognition than the typing training.

…

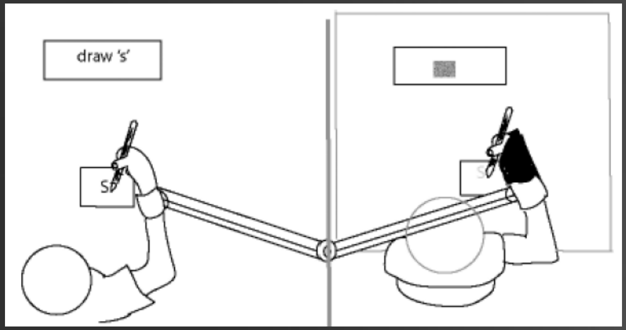
In expert readers, knowledge of how letters are written influences the way in which they are perceived :

Orliaguet et al., 1997: seeing the writing movement of a letter helps to anticipate the identity of a forthcoming letter (while seeing the form does not) ➔ The preparation of the second letter is partly carried out during the production of the first letter.

Bartolomero et al., 2002: tracing out the form of the letter facilitates letter recognition in alexic patients.

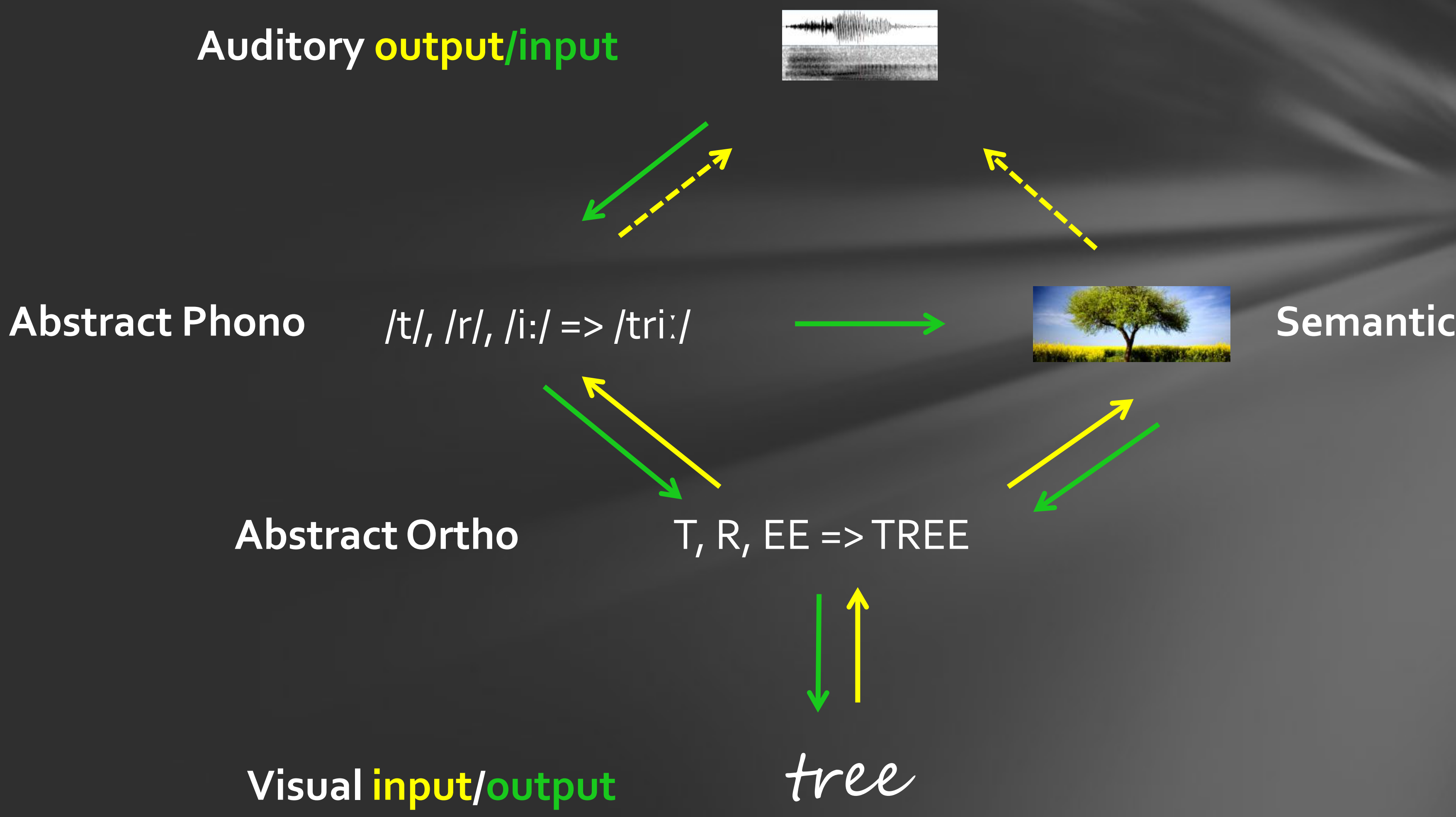
James et al., 2009: Interference of hand movement on letter recognition.

(experimenter)

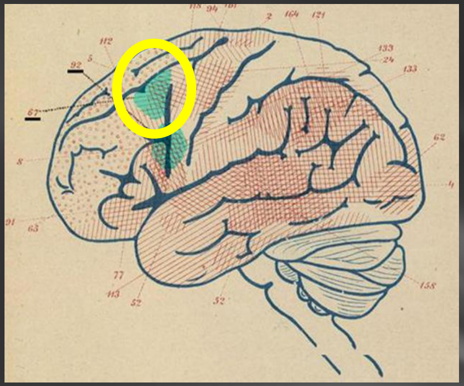


(participant)

Reading and writing share central cognitive processes



Exner’s area as a “writing center”



Exner’s drawings of the localisation of the brain lesions of the patients with agraphia. (Form Roux et al., 2010)

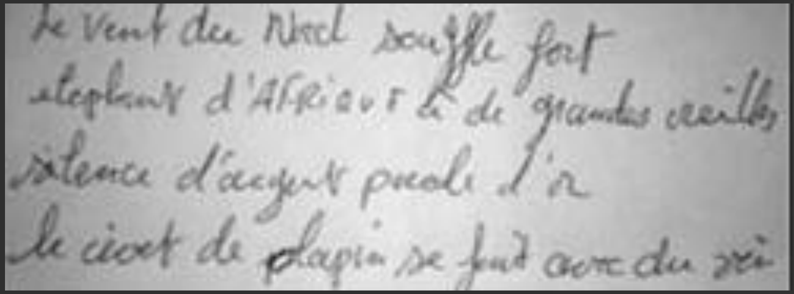
- Sigmund Exner (1881): “the writing center” or” Exner’s area”

  Patients with lesions in the posterior middle frontal gyrus in LH produced writing impairments

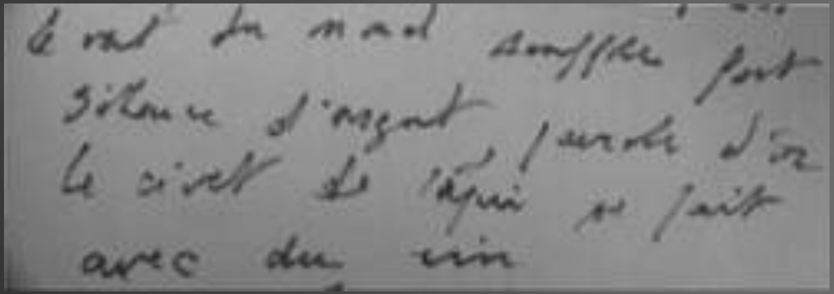
- Infarction in Exner's area produced phonological agraphia (Keller & Meister ,2013)

- Partial removal of the writing area in tumor patients (Roux et al. 2009)

Before surgery



18 days after surgery

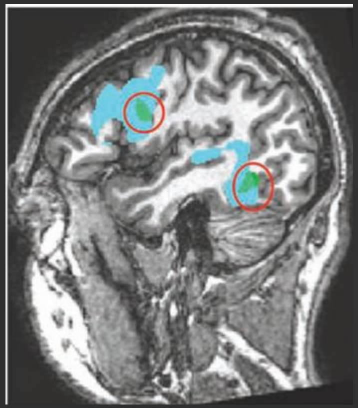


From Roux et al. 2009: *tumor resection necessitated partial removal of the writing area*

- A meta-analysis on fMRI studies showed that Exner’s area’s contribution is specific to writing when it is compared with other motor and language tasks (Planton et al., 2013).

Exner's Area and reading

- In normal readers, an activation of Exner's Area was found during reading tasks (Dehaene et al., 2010; Nakamura et al., 2012, Rapp & Lipka, 2011; Xu et al., 2005; Planton et al., 2013).



Rapp & Lipka, 2011

Activations produced by reading (words > checkerboards) in blue and spelling (spell > case) in green. Indicated with red circles are the regions of overlap between reading and spelling in the left mid-fusiform and the left IFG/IFJ

- Reading difficulties observed in dyslexic children lead to a reduced activity in visual word form area and a greater reliance on Exner's area, suggesting partial compensation through the gesture system (Monzalvo et al., 2012)

Main interpretation: Reading → Writing (Motor representation)

Interpretation of brain imaging data

1) Epiphenomenal (co-activation of the reading and writing systems) or real functional role ?

fMRI

Reading → Writing (Exner's area)

?

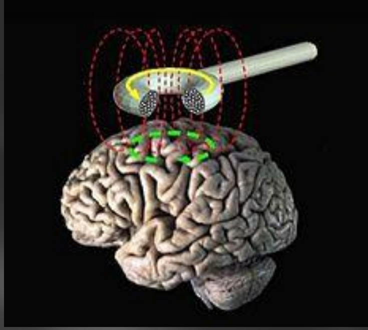
2) If functional role?

Motor: implicit evocation of writing motor processes

Cognitive: shared cognitive components between writing and reading

3) How early?

The Contribution of Exner's Area to reading



Aim: Disruptive effect of transcranial magnetic stimulation applied on Exner's area

Task: Lexical decision

Stimuli: **Words vs. Pseudowords**

(global vs. sequential process)

"Cognitive" hypothesis

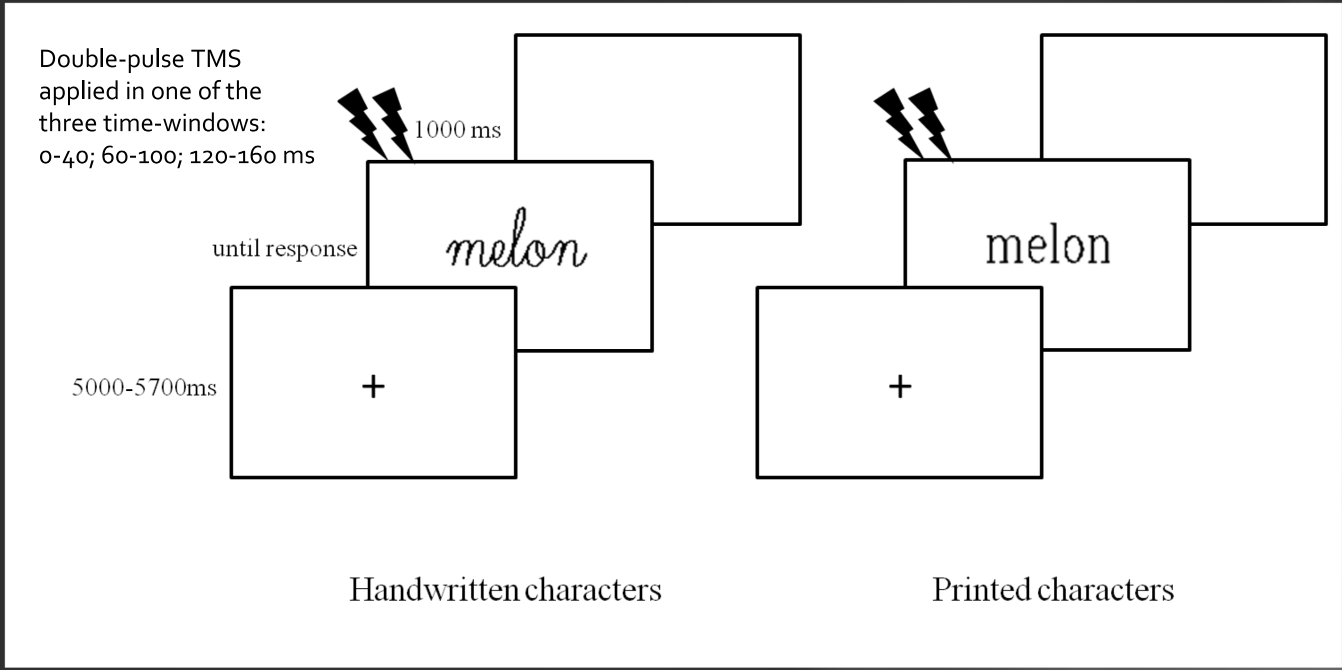
Characters: **Handwritten vs. Printed characters**

(handwritten character is more related to motor knowledge => embodiment of the perception of handwritten letters)

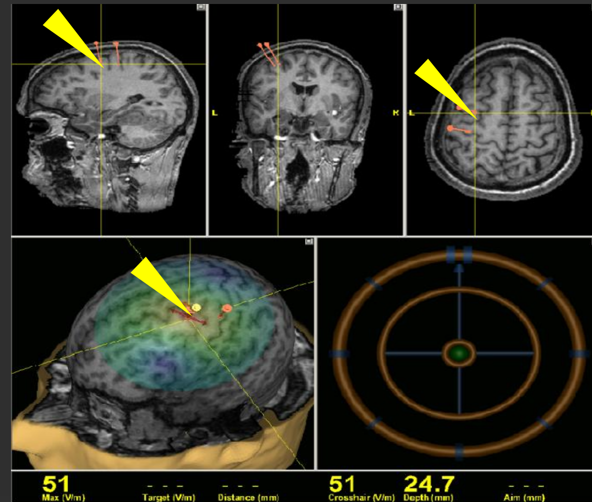
"Motor" hypothesis

TMS stimulation: double-pulse TMS in 3 time-windows

0/40 ms (baseline)
60/100 ms
120/160 ms



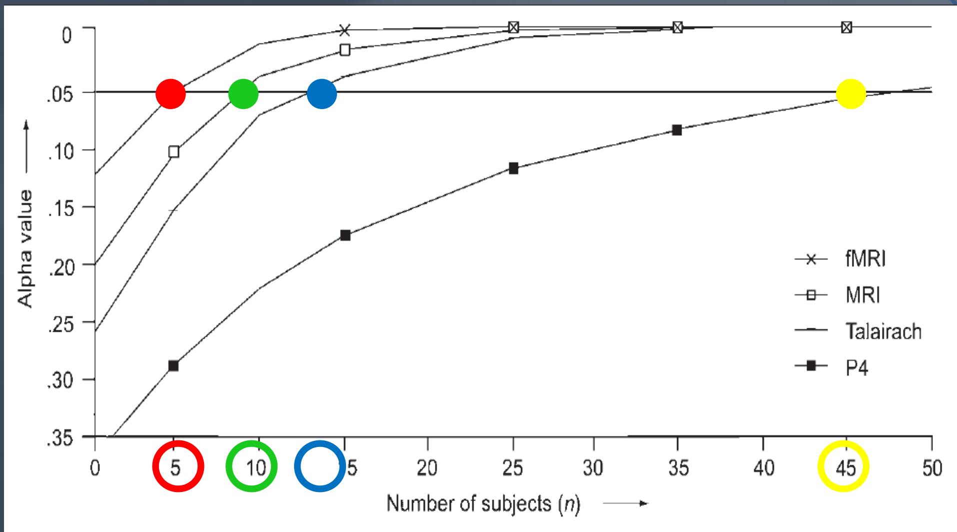
Participants: 15 Right-handed French speakers
Responded with the **left hand** to avoid interference with the right hand
RT & ACC were collected



Localization: Individual MRI (Sack et al. 2009) Posterior middle frontal gyrus at the junction between the precentral sulcus and the superior frontal sulcus in LH

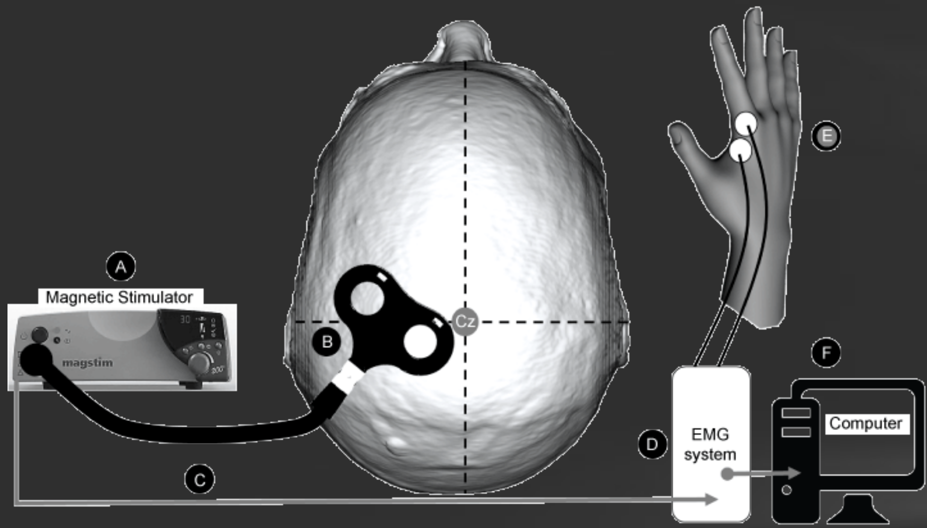
Visualization: image-guided frameless stereotaxic neuronavigation system

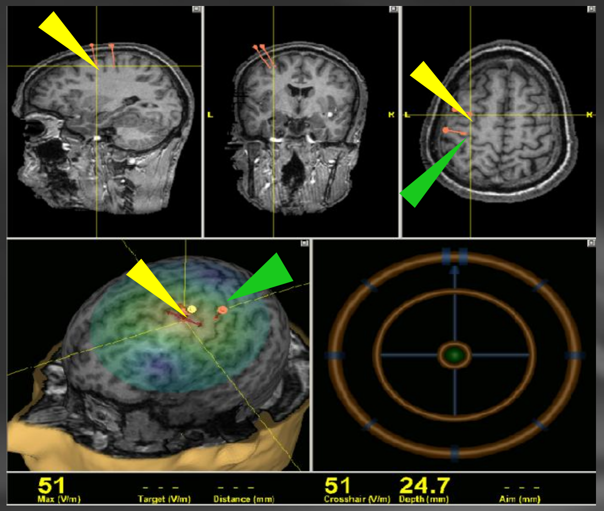
- 10–20 EEG (e.g., P4 : **+/-** right parietal sulcus)
- Individual MRI-guided TMS neuronavigation
- Group functional Talairach coordinates
- **fMRI-guided TMS neuronavigation**
- Individual TMS-guided (localizer task)



Different methods can be combined. The choice of the method depends on: time, budget, precision required, number of subjects, equipment, security, …

Sack et al. 2009





Intensity: Adjusted Motor Threshold* (primary motor cortex =)

*(MT: the lowest stimulation intensity capable of producing changes of MEP or overt muscle twitch)

- At least two factors influence the susceptibility of a brain area to stimulation: **magnetic field strength** and **excitability of the cortex**

↓ The distance between the center of the coil and the cortex

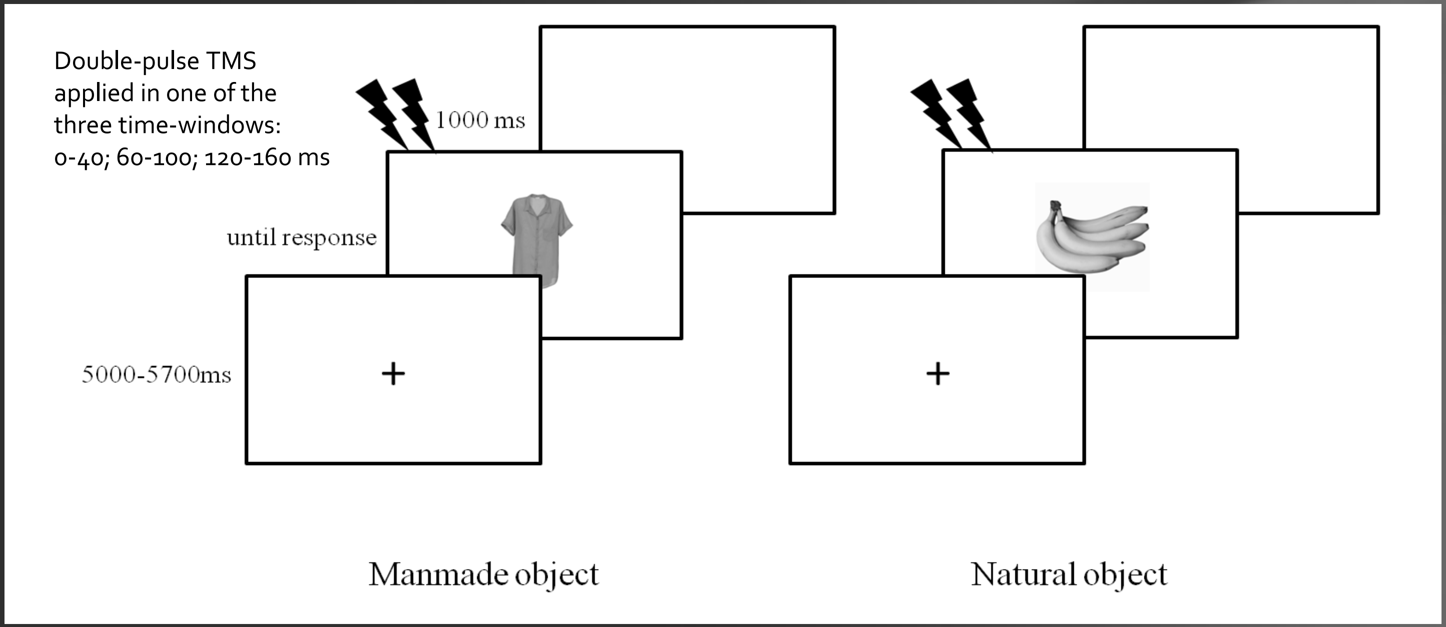
↘ Unknown for most areas
Depend on the state of the system (e.g., task, active vs. rest, ...)

- Solutions: Motor Threshold; Adjusted MT; Constant intensity (50%-70%).

Control for artifacts

→ non-specific TMS effects due to click sounds and muscle twitches (online protocol)

- Sham coil (same click sound but no scalp sensation), placebo coil (more satisfactory?)…but need naive subjects!
- Control site (vertex? homologous area? …)
- Control task or control condition within the same task
- Double dissociation (sites * tasks)
- Control time-window (here, baseline = 0/40ms)
- Combination of different methods



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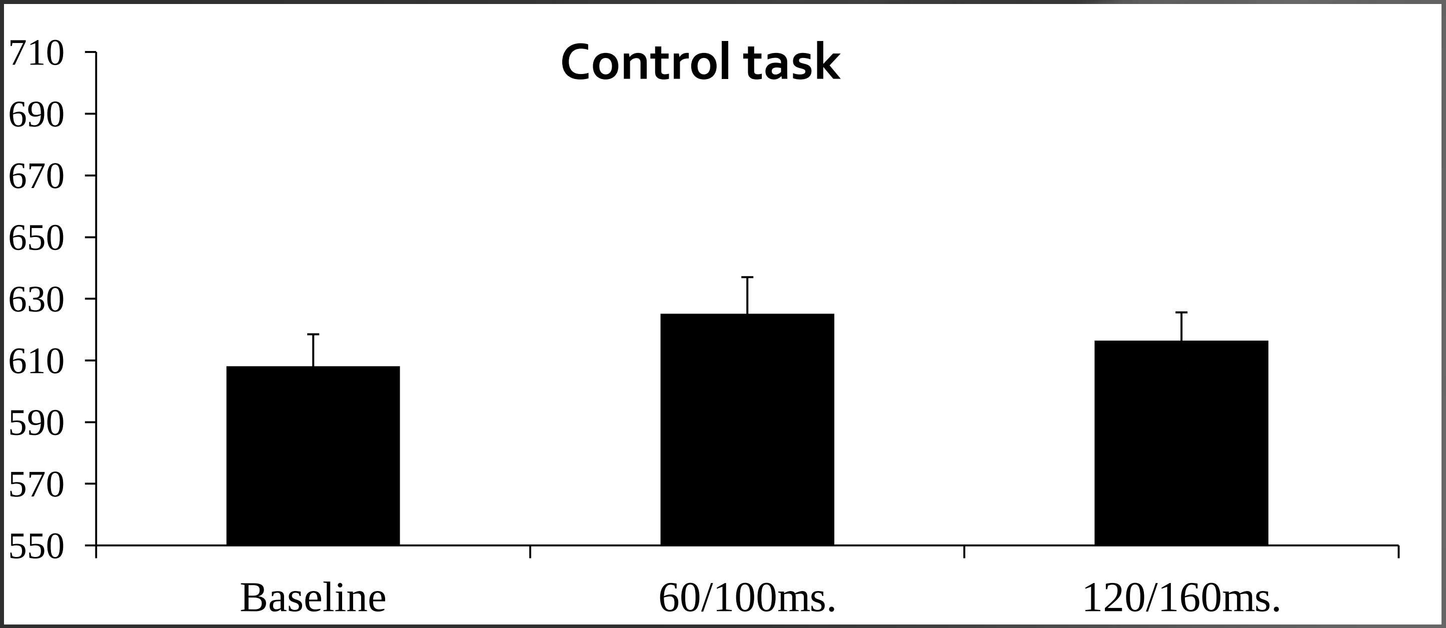
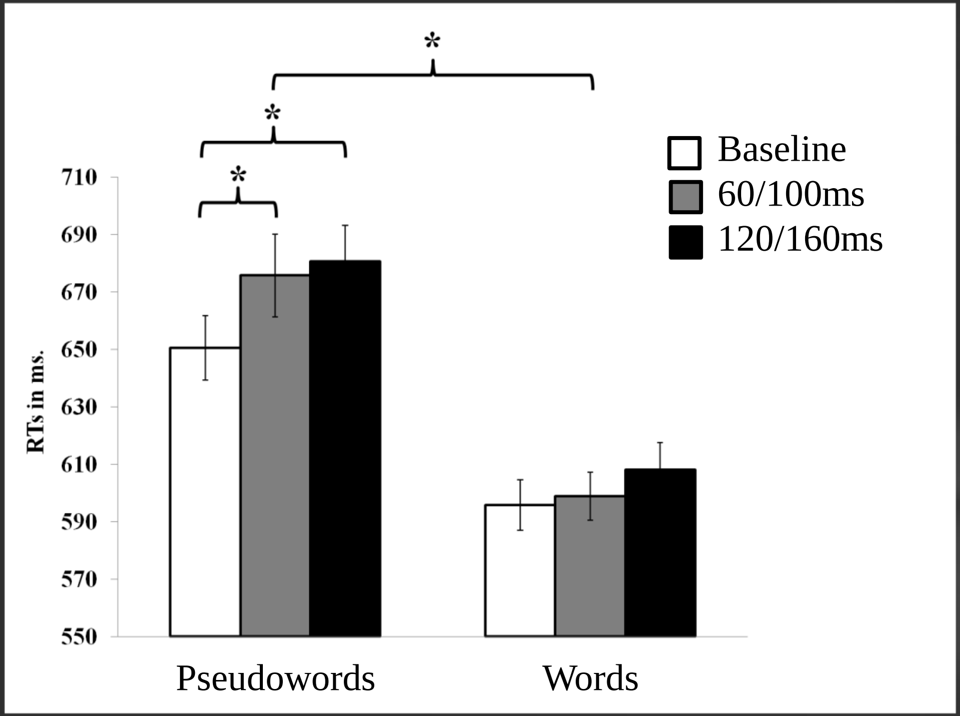
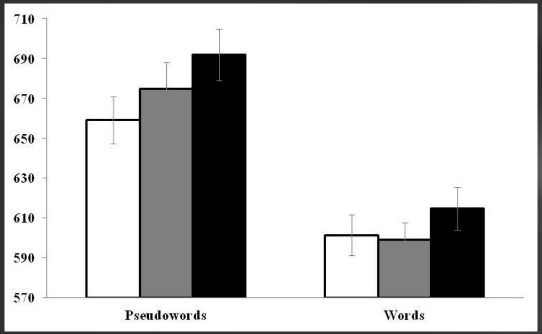
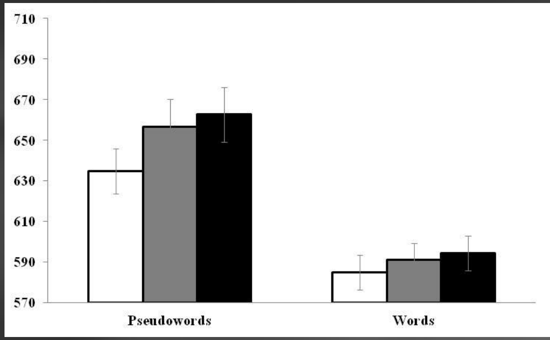


Main task: Reaction times





Handwritten



Printed

ANOVA: Character * Lexicality * TMS

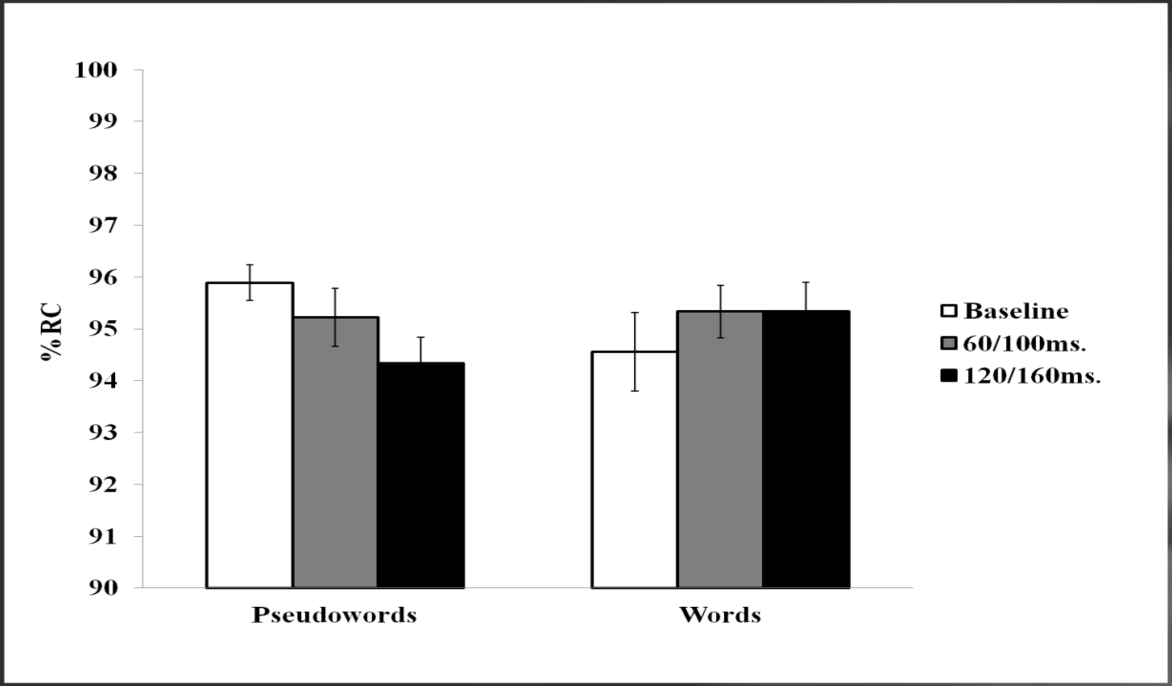
Lexicality x TMS

~~Character x TMS~~

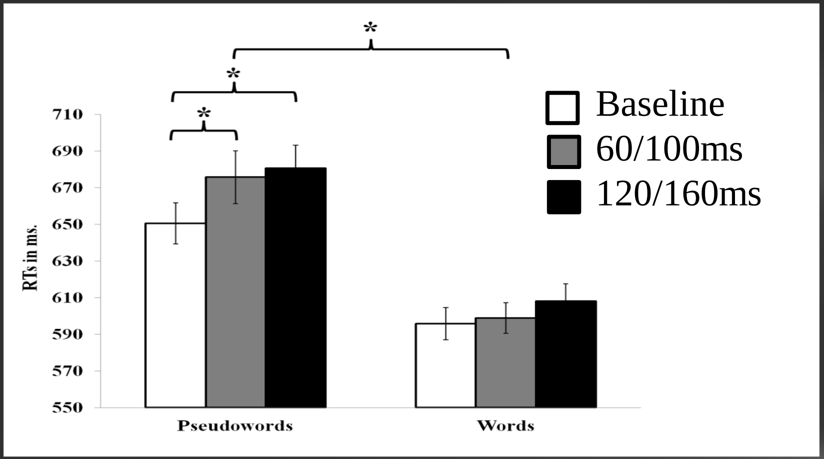
~~Character x Lexicality x TMS~~

TMS effect on pseudowords only

Main task: Accuracy



Same tendency but no significant result



Does Exner's area contribute to reading?

Yes

How early?

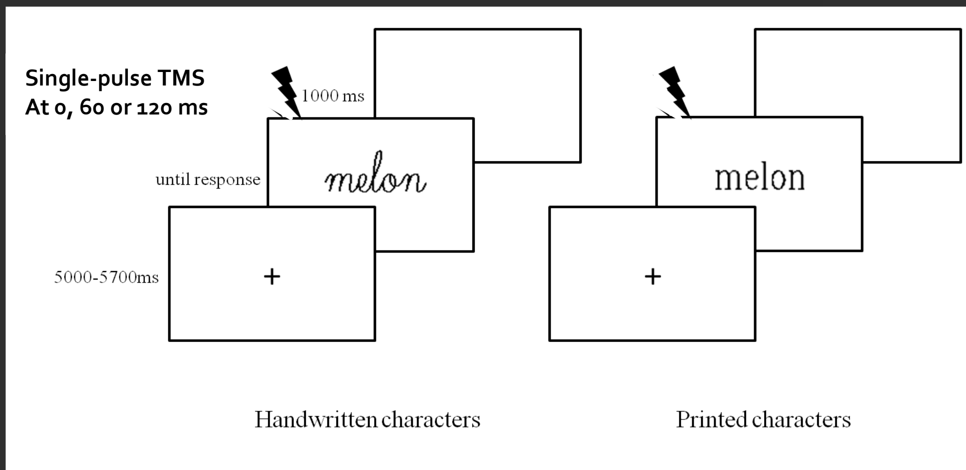
Already within the first 100-150 ms

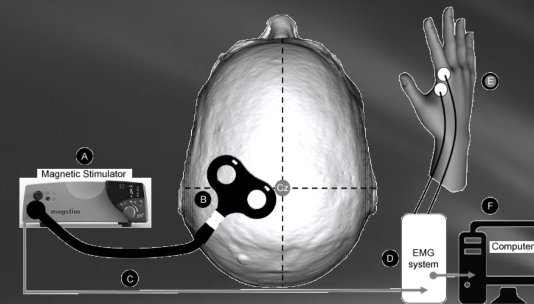
Does it depend on the type of stimulus or character?

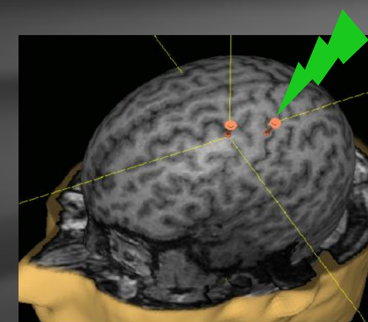
Only for pseudoword decision regardless of the type of character. ➔ rule out the "motor" hypothesis?

BUT…Did handwritten characters elicit motor representations as expected?

TMS as a tool to investigate the causal role of a given cognitive task on the activation state of the motor cortex.

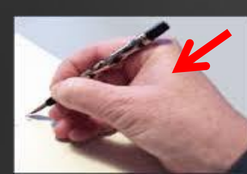






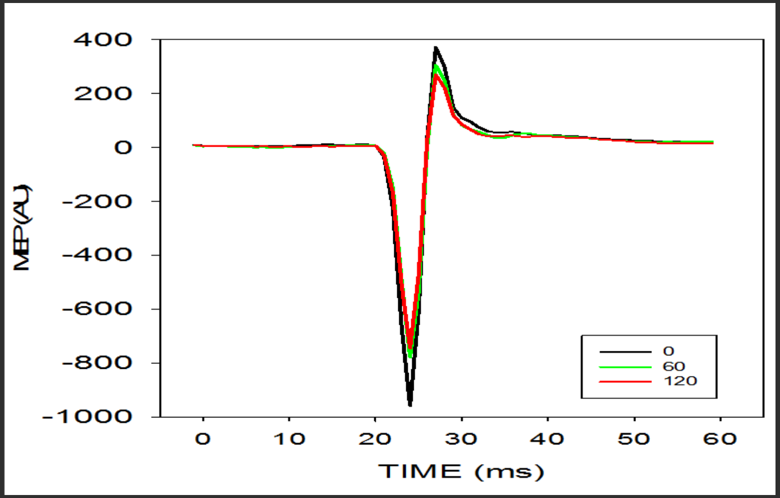
Stimulation protocol

TMS stimulation: single-pulse in 3 time-windows
0 ms (baseline), 60 ms, 120 ms
Site of stimulation: Motor cortex (first dorsal interosseous)
Intensity: 110% of the resting motor threshold
EMG recording: First dorsal interosseous muscles of the right hand (participants responded with their left hand)

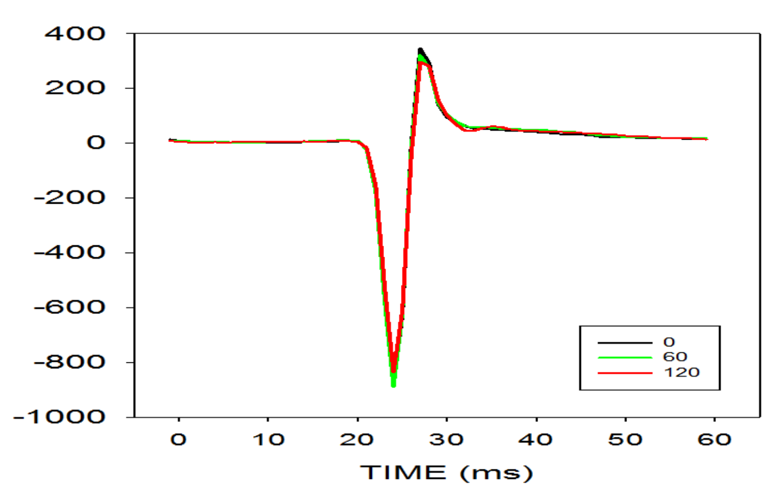


Why single-pulse?

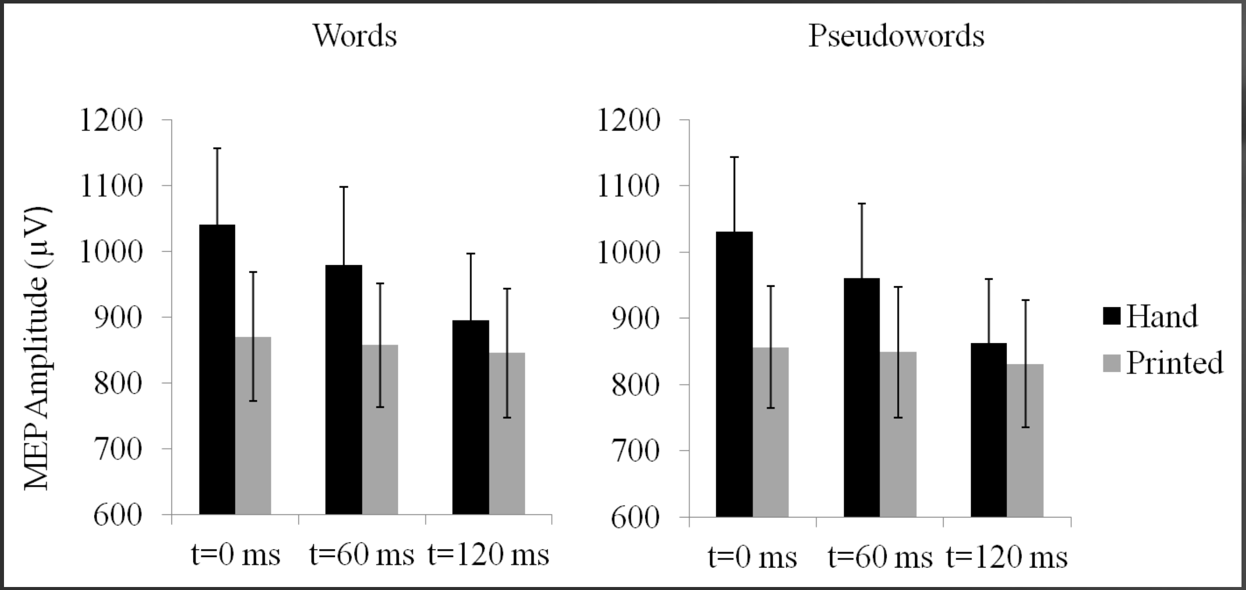
- Probe a modulation of cortico-spinal excitability of digit muscles during reading handwriting vs. printed character
- Minimize artifacts on electric muscle responses
- No need to disrupt the performance



Handwritten



Printed



Character x TMS

~~Lexicality x TMS~~
~~Character x Lexicality x TMS~~

Printed: MEP amplitudes remained stable across the different time-points

Hand: MEP amplitudes decreases from T= 0 to T = 160

Handwritten but not printed character induced changes in cortico-spinal excitability of the hand muscles involved in writing gestures

Discussion

The TMS finding show the contribution of the Exner's area during reading. Coherent with lesion studies (e.g., Anderson et al., 1990: Lesion in the left premotor cortex (BA6) led to pure agraphia and alexia)

Dissociation between the "motor" and "cognitive" hypothesis.

- Reading handwritten characters induced changes in cortico-spinal excitability of the hand muscles involved in writing gestures
- But the contribution of the Exner's area in reading seems to be explained by the shared cognitive processes between reading and writing, i.e., sequential or sublexical process