Clinical and fundamental applications of robotized cortical excitability mapping procedure

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# Ongoing studies

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Cortico-spinal excitability

Cortical excitability: cortex’s ability to produce a response following a stimulation

TMS: non-invasive cortical stimulation

Assessment:
- Stimulating the motor cortex allows for a remote and quantifiable observation of the stimulation effect recorded by electromyography – Motor Evoked Potential (PEM)
- Stereotypical response

Applications:
- Motor system integrity
- Plasticity and neurotransmitter markers
Cortical Excitability

**EEG**: measure of the electric activity of the cortex

**Applications**:
- Cortical tissue integrity
- Measure of dynamical characteristics of different cortical areas
- Biomarkers MP?

**Evaluations**:
- Power of the evoked response (TMS Evoked Potential TEP)
- Dynamic of the response to the stimulation through the time (Time-frequency analysis)
Cortical excitability and Neurotransmitters

Neurotransmitters and TEP:

**GABA** increases the **earliest** components of the TEP

**GABAB** increases the **later** components of the TEP
Study aim:
• Imaging of whole cortex cortical excitability through EEG
• Assess dynamical properties associated with each area
• Extract response modes: cortical areas sharing similar dynamical properties

Method: robotized TMS stimulation of 18 cortical sites & EEG recordings

Harquel et al., 2016
Regression quality score: new quantifier of cortical excitability

\[ s_j(t) = \beta * x_i(t) + \varepsilon(t) \]

- Single trial \( S_j \)
- More **reliable** and **robust** quantifier of cortical excitability

Raffin, Harquel, Passera, Chauvin, Bougerol, David (*HBM, under review*)
Regression quality score: new quantifier of cortical excitability

\[ s_j(t) = \beta \cdot x_i(t) + \varepsilon(t) \]

Regression quality score - Sensitivity of the measure
- Dynamic response
- Amplitude
- Latency

Trials 80% rMT

Local TEP M1 120% rMT
Participant 18

Trials intensity (% rMT)

Raffin, Harquel, Passera, Chauvin, Bougerol, David (HBM, under review)
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**Study 3:** Exploring the effect of **deep brain stimulation** on **motor control** in **PD patients** using non-invasive brain stimulation

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Spatial resolution of TMS/EEG coupling

Motor cortex spatial resolution:

Two cortical targets spaced by 7 mm can evoke different MEP amplitudes

Stimulating two different sites of the motor cortex can induced evoked responses in different muscles

Following the shape of the motor cortex allows for a more accurate mapping of different muscles

Harquiel,... Passera, ... et al., Neuroimage,2017

Raffin et al., Neuroimage,2015
Aim of the study
• Assess the spatial resolution of TMS/EEG

Method:
9 stimulation sites, 3 per gyrus
  Premotor
  Primary Motor Cortex
  Primary Sensory motor cortex

Material: robotized and neuronavigated TMS, 128-electrodes EEG cap

Harquel et al., 2016
Protocol and hypotheses

Hypothesis 1: $S_1 \neq M_1 \neq PM$

Hypothesis 2: $S_1 = M_1 \neq PM$

Hypothesis 3: $S_1 \neq S_2 \neq S_3 \neq M_1...$

Gyrus level resolution (fine)

Gyrus level resolution (coarse)

Target specific resolution
Preliminary results

18 participants

#2 Gyrus level resolution (low)
#3 Target specific resolution
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Modulation of dynamic characteristics

Motor cortex dynamic characteristics

2. Are modulated by Levodopa (Casula et al., 2017, Casarotto et al., 2019)
3. Seem to be PD specific (Casula et al., 2017)

HC

OFF/OFF

OFF/ON

ON/ON

Cz

ALPHA (10Hz)

Casula et al., 2017

Casarotto et al., 2019
EXCIPARK Protocol

EEG cap set-up
Estimated: 30min

TMS set-up
Estimated: 15min

TMS Stimulation
Estimated: 60min

Material:
128 active electrodes EEG cap
Robotized and neuronavigated TMS

1 mapping per year
4 years follow up study
30 patients
30 controls
The aim of the Action Parkinson is to identify:

Early signatures of PD could be used to predict the pathology’s evolution according to the different subtypes of PD.

The evolution of these signatures will be studied longitudinally over the course of 4 years.

EXCIPARK aims to identify the cortical areas maximizing the Cortical Excitability markers of PD.
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PARKMOTEUR Protocol TMS/EEG

**EEG cap set-up**
Estimated: 30min

**TMS set-up**
Estimated: 15min

**TMS stimulation**
Estimated: 60min

- Mapping ON/OFF
- Paired pulse stimulation IFG
  - M1: ISI 4ms 18ms
  - 150ms (control ISI)

**Material:**
- 128 active electrodes EEG cap
- Robotized and neuronavigated TMS
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rTMS and visual hallucinations

Neurology®

October 04, 2016; 87 (14)  ARTICLE

rTMS reduces cortical imbalance associated with visual hallucinations after occipital stroke

Sara A. Rafique, John R. Richards, Jennifer K.E. Steeves

First published September 2, 2016, DOI: https://doi.org/10.1212/WNL.0000000000003180
Case description

The hallucinations content was very structured at the beginning (objects, humans, rain or snow) then degraded (bodyparts: mouth and eyes) and now are constituted mainly of geometrics shapes, shifting in content and in movement.

Current form of the hallucinations:

34 y/o woman
Resection following brain tumor in the occipital cortex in 2014

Suffers from continuous visual hallucinations following the surgery -2014

**Protocol**

**SESSION 1**

- **Anatomical MRI and DTI**
- **TMS Mapping**
  - Single Pulse Burst TMS: 5Hz (speech arrest)
  - 20Hz (phosphene)
- 3 pulses per cortical site
- **Visual analog scale**
  - Oral description after each site
  - VAS report
  - Drawing of TMS induced modifications

**SESSION 2**

- **TMS mapping**
  - Single Pulse Burst 20Hz
  - Hallucinatory threshold estimation
- **1Hz rTMS (inhibitory)**
  - 1 session 1200 pulses

*Phosphene: Dugué et al, 2011, Plos One
Speech arrest: Krieg et al (2014)*

*Passera B., Harquel S., Dojat M., Vercueil L., David O., Chauvin A., OHBM Meeting 2019 ROME; Passera et al., (in prep)*
Session 2 – Mapping

- Systematic apparition
- Apparition
- Change
- No response

- Stimulation target
- Hallucinatory hotspot

Single Pulse

Session 2 - rTMS

Reduction of hallucinations

Hallucinations of lower intensities and more focal

“There are lines, arrows, both vertical and horizontal. Not too intense, moving, lines, dots, as usual…”

“So, there is as much flashes. But less intense, less bright. Also, they are slower. Everything is calmer.”

“So, it’s a bit more intense than right after [rTMS ed.] but very localized in the top right corner. And, right now, there is an area, in the middle which is blank”

“So, it’s a bit more intense than right after. There are even waves of lines… like this morning. And it’s moving faster”

“It’s stable compared to earlier. I’d say it’s equivalent in terms of intensity, and of quantity… But there are once more a few flashes in the middle”

Thanks for your attention