



PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga



University of Verona
Department of Neurological,
Neuropsychological, Morphological
and Movement Sciences



REGIONE VENETO
ULSS 20
VERONA



Regione del Veneto - Azienda ULSS 20
Dipartimento delle Dipendenze

Addictio *Group* **Neuroscience**

rTMS over the left DLPFC in a group of patients in treatment for alcohol and/or drug addiction

Paolo Manganotti
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Team



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Aim of the study

To assess the effectiveness of the inclusion of rTMS sessions in a 3 weeks program of hospitalization for the treatment of alcohol and drugs addiction in reducing:

- ***alcohol or drug consumption***
- ***the severity of craving***



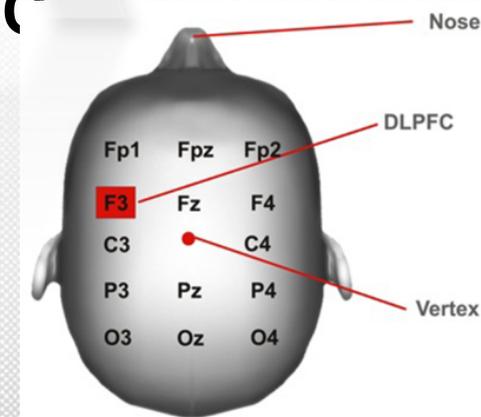
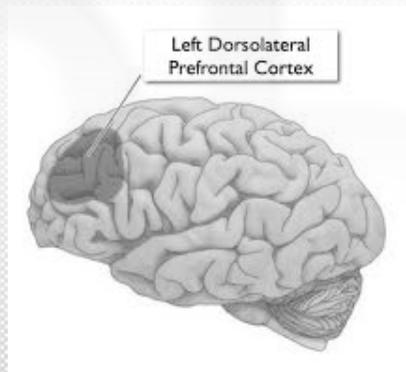
Method 1



SINGLE-BLIND, SHAM-CONTROLLED STUDY



- rTMS by a *Magstim Rapid* stimulator with a figure-8 coil
- **4 sessions** (2 each week) of high frequency (**10 Hz**) rTMS at **100% of MT** over the **left DLPFC**



- Each session consists of **20 trains of 50 pulses**

Method 2

RECRUITMENT AND SCREENING

During the first week at the Unit of hospitalization - Addiction Medicine and Alcoholism Service of the Addiction Department ULSS 20 Verona (Marzana hospital)

INCLUSION CRITERIA

- Men and women aged **18-65 years**
- Individuals who know enough the Italian language to understand and sign the **Informed Consent**
- Persons **in charge** at the Addiction Department ULSS 20 Verona
- Those eligible for treatment are patients with a **SCID** for **DSM-IV diagnosis of alcohol or drug dependence** (heroin, cocaine, amphetamines, cannabis and benzodiazepines)
- Persons who express the **desire to achieve abstinence** or significantly reduce the consumption of at least one substance from which they are dependent
- Persons who declare that **they have used the substance** from which they would like to detox **at least once in the four weeks prior to the assessment** of eligibility for the study

EXCLUSION CRITERIA

- Women during **pregnancy or breastfeeding**
- Persons who present a history with serious **neurological disorders**
- Subjects with unstable **medical conditions**
- Subjects with **cardiac pacemakers and/or hearing aids**
- Subjects with **metallic craniofacial implants**
- Participation in any other clinical trial during the last 60 days



Method 3

DESIGN OF THE STUDY

1° week of hospitalization							2° week of hospitalization							3° week of hospitalization					End hospital	Follow Up
MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED	THU	FRI		1 month after
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19		
GROUP A																				
Recruitment & Assessment							real rTMS			real rTMS				real rTMS			real rTMS			Assessment
							T0											T2		T3
GROUP B																				
Recruitment & Assessment							sham rTMS			sham rTMS				sham rTMS			sham rTMS		Assessment	
							T0											T2	T3	

- **Consumption of the substance of abuse:**
Diary completed by patients + toxicological tests (from T0 to T3)
- **Severity of craving:**
Visual Analogue Scale (VAS) (from T0 to T3)



Method 4

Further tools used to collect data

- **Mini International Neuropsychiatric Interview (MINI Screen)**
- **SCID-I (for DSM-IV-TR) Substance Related Disorders**
- **Standard Progressive Matrices (SPM)**
- **Temperament and Character Inventory (TCI-R)**
- **Symptom Checklist 90 (SCL-90-R) before and after rTMS treatment**
- **Executive functioning assessment before and after rTMS treatment: i.e., Stroop task**
- **EEG registration before and after rTMS treatment**



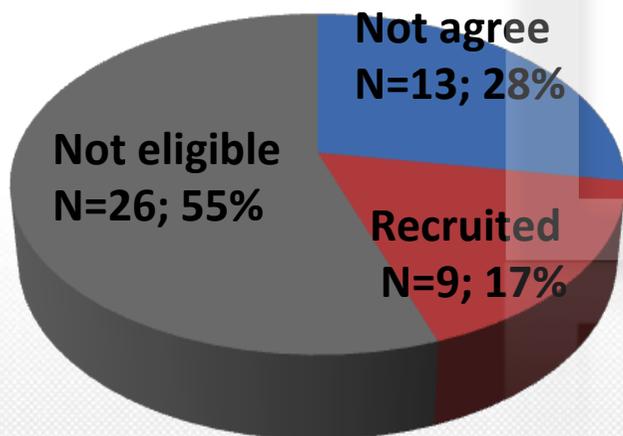
RANDOMIZATION

- **A randomization list generated according to the RANDOM PERMUTED BLOCKS, which assigns subject to one of two treatments (real or sham) in the order of entry into the study**
- **Subjects have equally likely to be assigned to real rTMS or sham rTMS: the relationship between real rTMS group and sham rTMS group is 1:1**
- **The investigators involved in the study do not know which is the treatment of the subject until the beginning of the treatment**
- **Randomization of the subjects already treated: ABAB ABBA**

Results

PRELIMINARY DATA

To date, 9 patients in treatment for alcohol dependence were eligible and agreed to participate in the study



	Real rTMS	Sham
Number of subjects	4	4
Gender	2 M; 2 F	4 M
Age	44.0 ± 9.9	51.0 ± 8.0
Handedness	4 right handed	4 right handed
Educational level	9.3 ± 2.5	10.0 ± 2.4
Mean score SPM (A, B, C, D)	38.17 ± 5.88	37.94 ± 4.29

All patients received pharmacological and psycho-social treatment

TEMPERAMENT AND CHARACTER INVENTORY (TCI-R)

Real rTMS group

	NS	HA	RD	P	sd	coop	st
Mean score (T points)	53,22	57,69	49,57	44,45	40,52	42,88	42,07
sd	5,10	12,13	11,01	10,41	15,02	10,28	24,91

Sham rTMS group

	NS	HA	RD	P	sd	coop	st
Mean score (T points)	49,56	53,95	49,27	50,77	46,41	44,33	40,46
sd	6,18	6,52	5,53	14,63	6,37	6,35	13,00

Symptom Checklist 90 (SCL-90-R) before rTMS treatment

Real rTMS group

	SOM	O-C	INT	DEP	ANX	HOS	PHOB	PAR	PSY	SLEEP
Mean score	1,17	1,47	1,26	1,69	1,47	1,72	0,19	2,11	1,13	2,44
sd	0,55	0,61	0,28	0,47	0,58	0,25	0,09	0,96	0,55	1,17

Sham rTMS group

	SOM	O-C	INT	DEP	ANX	HOS	PHOB	PAR	PSY	SLEEP
Mean score	0,42	0,45	0,45	0,73	0,28	0,34	0,04	0,62	0,15	0,83
sd	0,12	0,61	0,41	0,43	0,22	0,24	0,07	0,34	0,13	0,58

1° Outcome

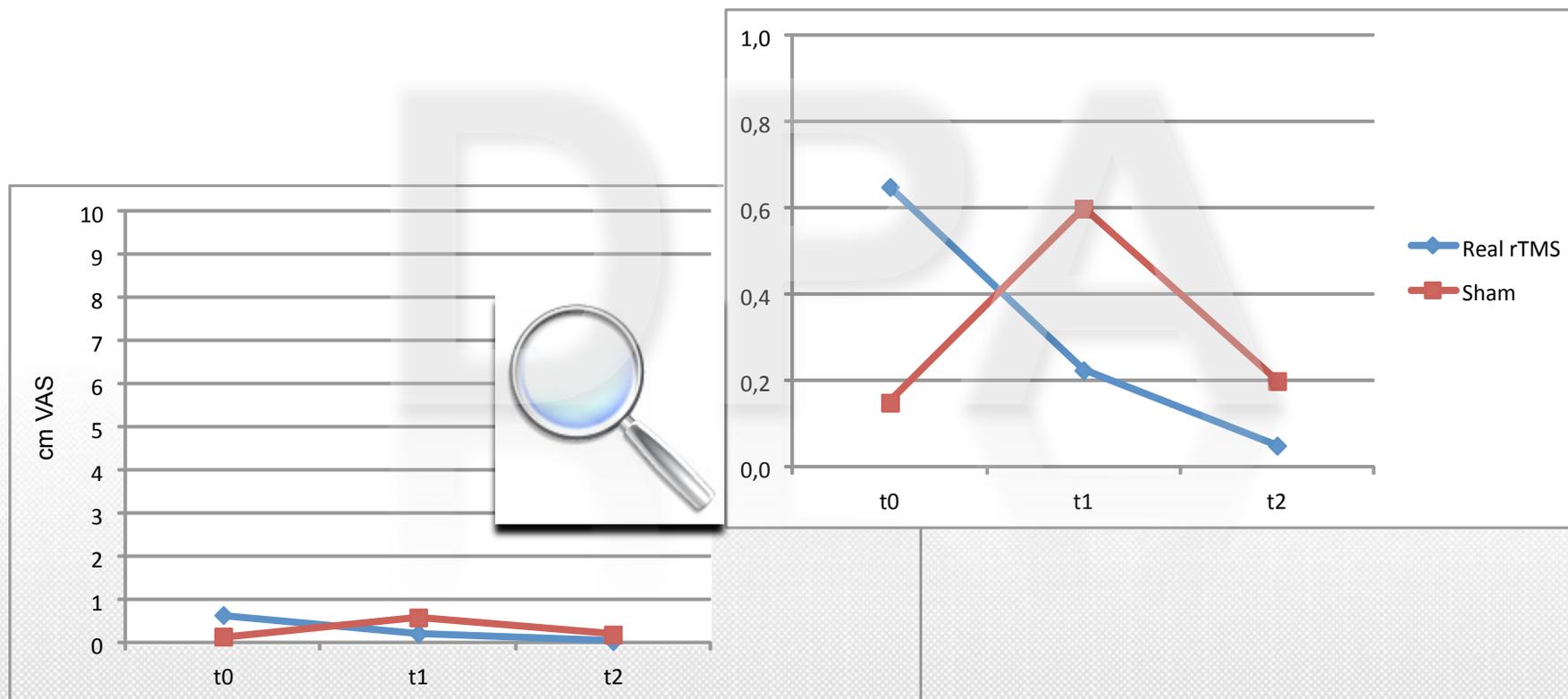
Alcohol consumption before and after rTMS treatment

Until now, 6 subjects have already completed the study (3 received real rTMS and 3 received sham rTMS)

All those who have already completed the study were able to maintain abstinence up to one month after the end of treatment

2° Outcome

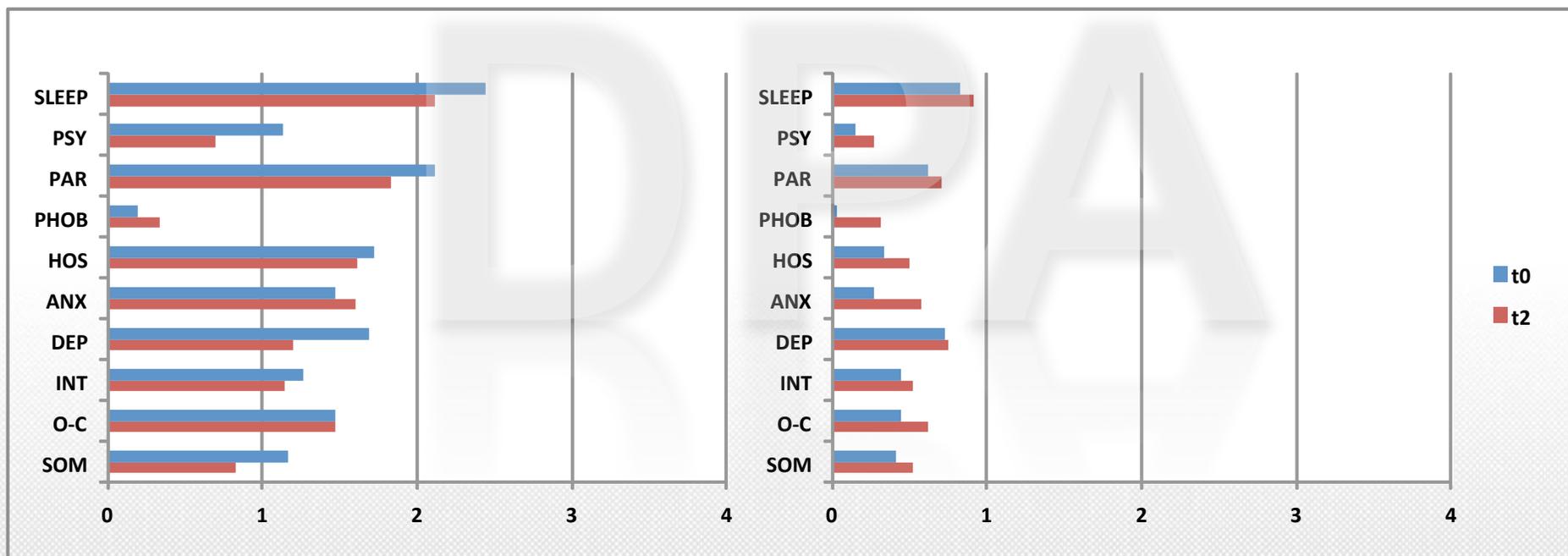
Alcohol craving before and after rTMS treatment



Symptom Checklist 90 (SCL-90-R) before and after rTMS treatment

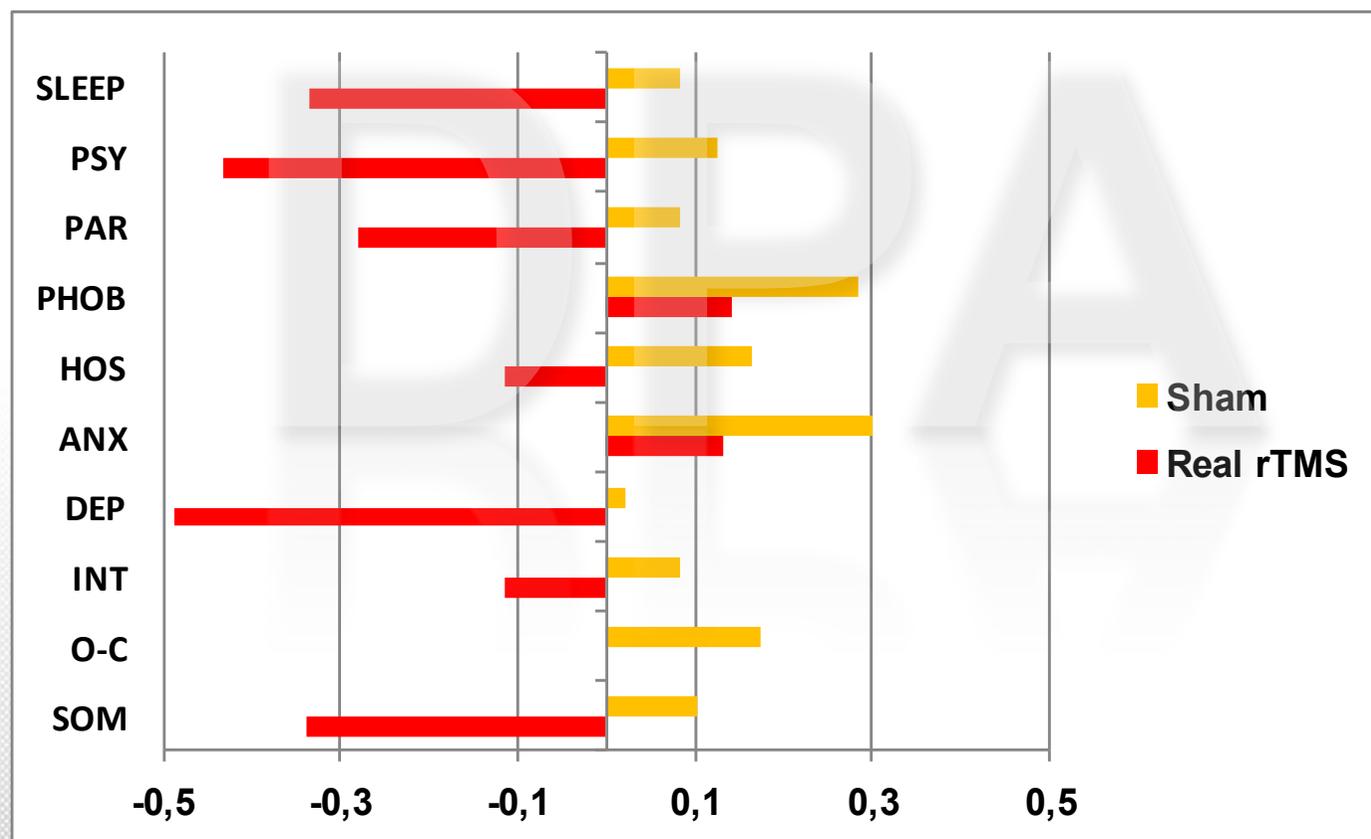
Real rTMS group

Sham rTMS group



Assessment of the psychopathological symptoms related to craving

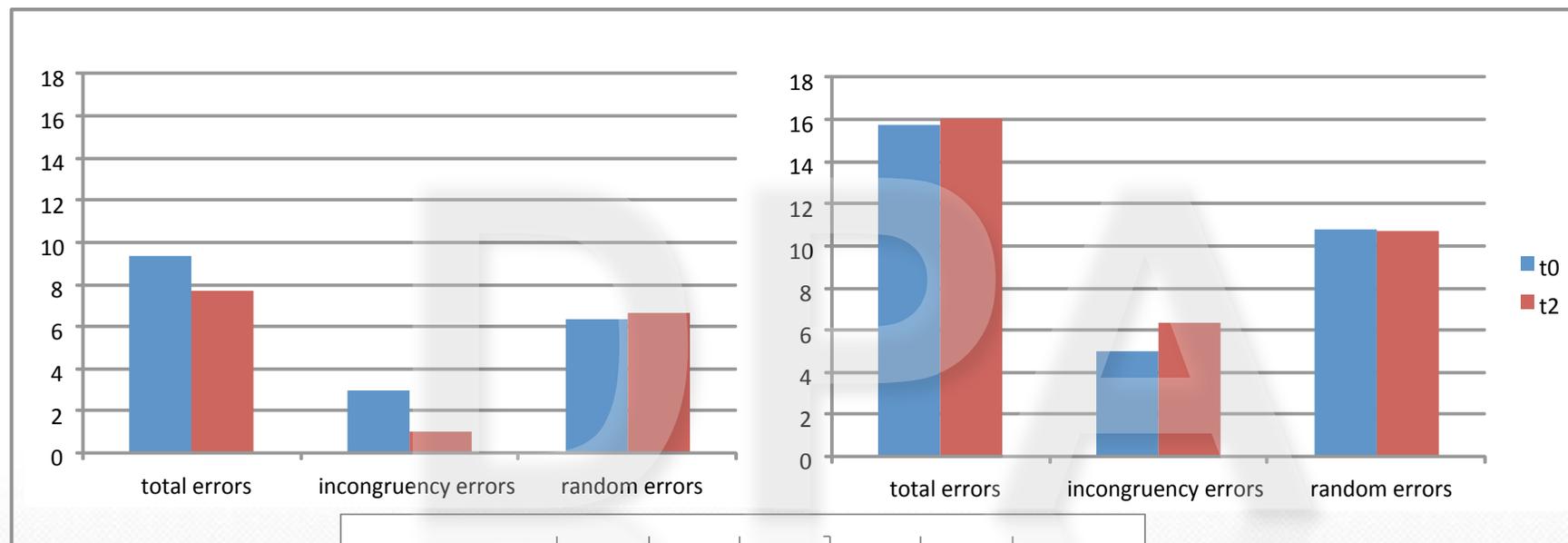
Difference between SCL-90 at t2 and SCL-90 at t0



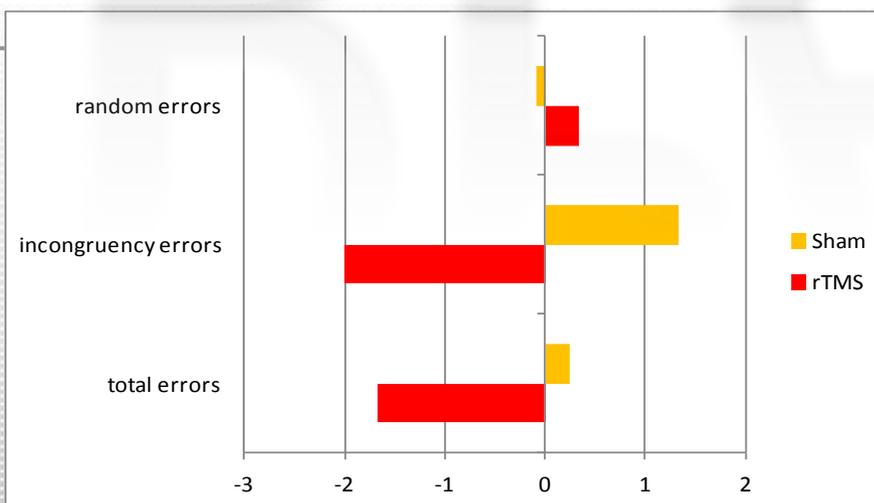
Stroop task before and after rTMS treatment

Real rTMS group

Sham rTMS group



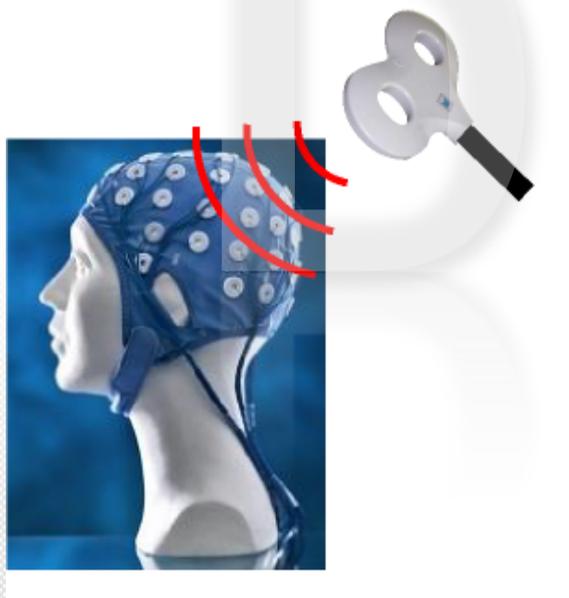
**Difference between
Stroop task at t2 and
Stroop task at t0**



**Inhibition capacity of an
automatic response**

Further opportunities to investigate neurophysiological correlates

▪ **EEG – rTMS**
coregistration



▪ **fMRI**
before and after rTMS treatment





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**Thanks for
your attention**