GIORNATE DI

NEUROPSICOLOGIA

DELL'ETÁ EVOLUTIVA

X edizione

21 - 24 gennaio 2015

Brain stimulation

Floriana Costanzo
Deny Menghini

INNOVAZIONI
TERAPEUTICO - RIABILITATIVE
IN ETÀ EVOLUTIVA

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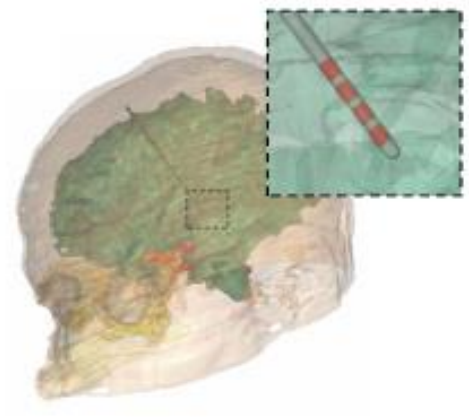
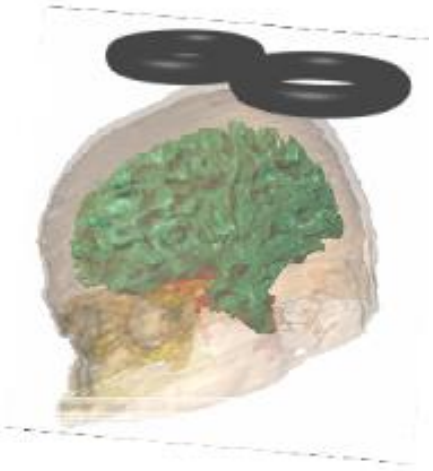
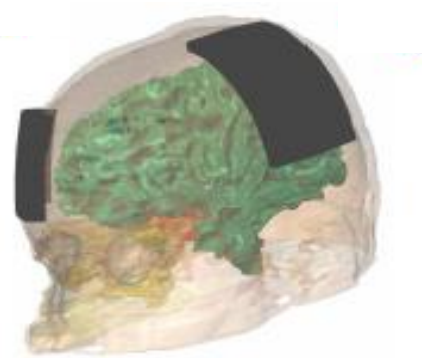
STIMOLAZIONI CEREBRALI



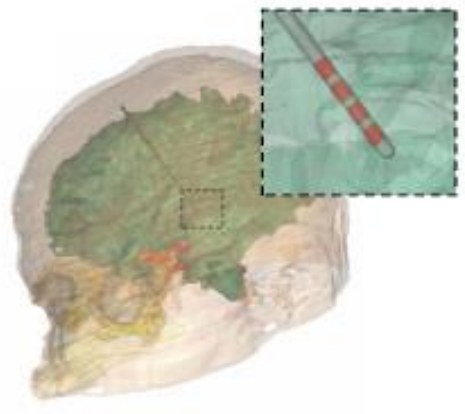
Deep Brain Stimulation



Transcranial Magnetic Stimulation



Transcranial Direct Current Stimulation

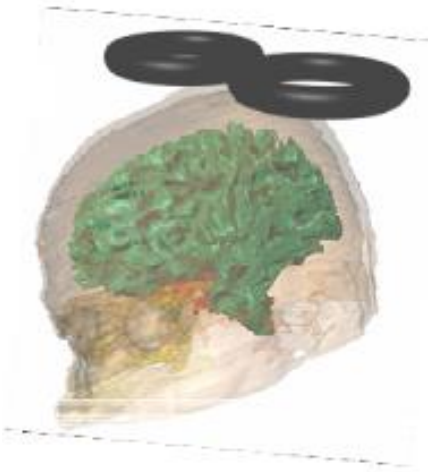


Deep
Brain
Stimulation

Elettrodi impiantati chirurgicamente nel cervello

Parkinson, Depressione, Epilessia, DOC, Autismo

- ✓ Focale
- ✓ Invasiva
- ✓ Problemi di sicurezza
- ✓ Costosa



Transcranial Magnetic Stimulation

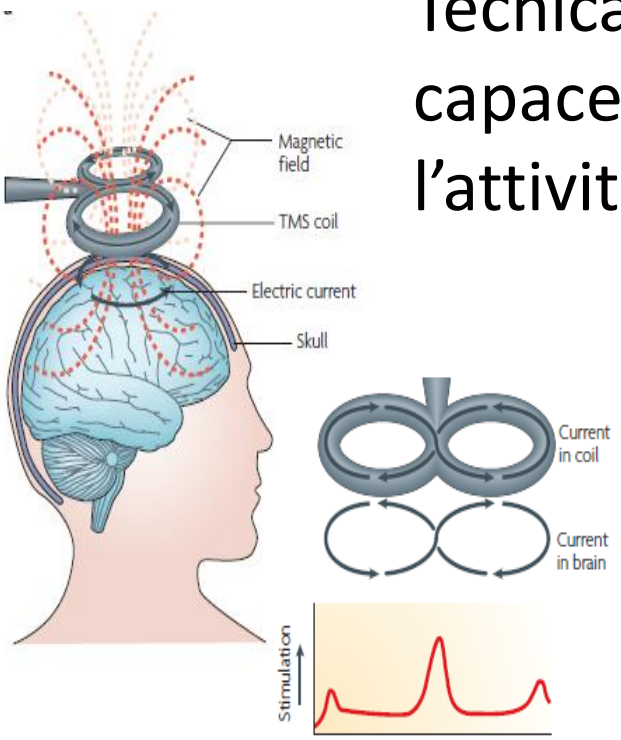
Coil sullo scalpo genera campo magnetico che determina corrente elettrica nel cervello

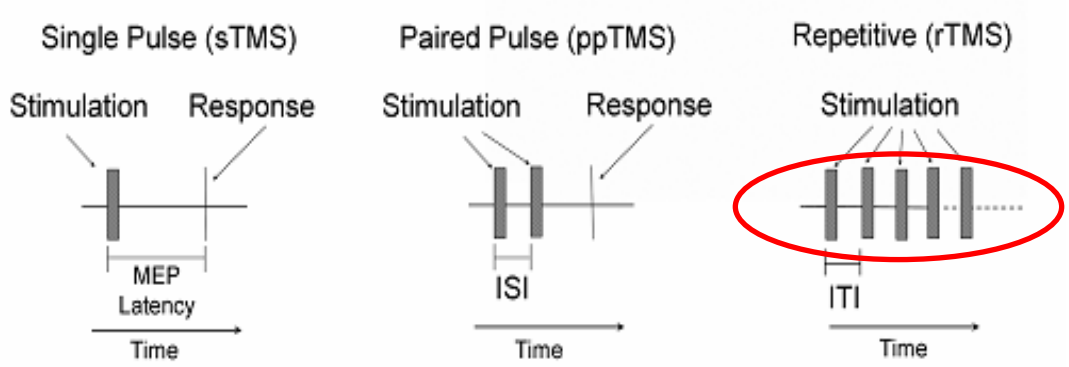
Depressione, Emicrania, Disturbi psichiatrici e cognitivi

- ✓ Abbastanza focale
- ✓ Non invasiva
- ✓ Abbastanza sicura
- ✓ Costosa

TRANSCRANIAL MAGNETIC STIMULATION

Tecnica neurofisiologica
capace di modificare transitoriamente
l'attività corticale





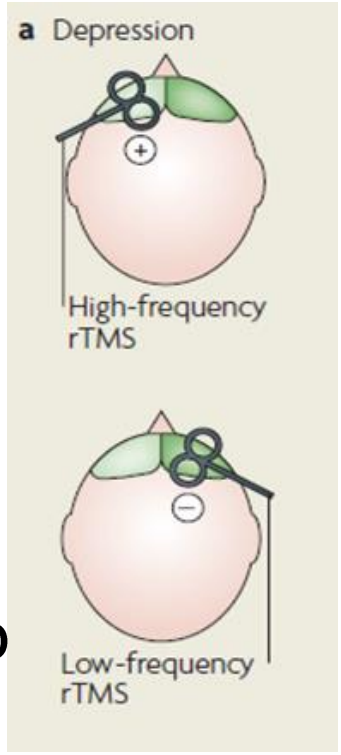
TMS Ripetitiva

Low Frequency (<5Hz):
interferenza inibitoria

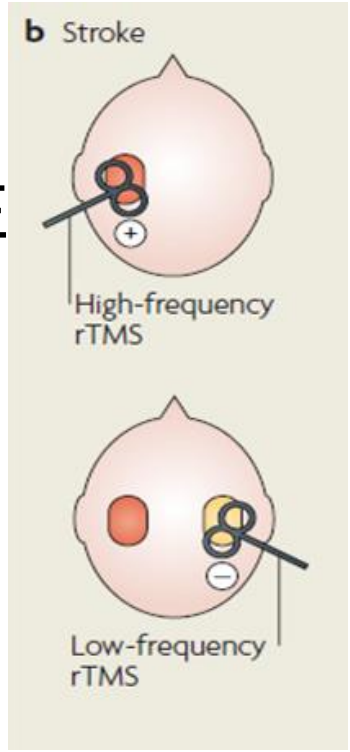
High Frequency (≥5Hz):
facilitazione

APPLICAZIONI TERAPEUTICHE DELLA rTMS

emisfero ipoattivo



FACILITAZIONE

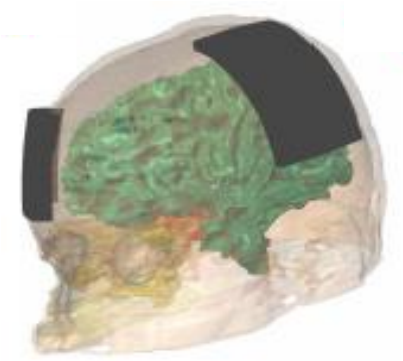


emisfero lesionato

emisfero iperattivo

INIBIZIONE

emisfero sano



Transcranial
Direct
Current
Stimulation

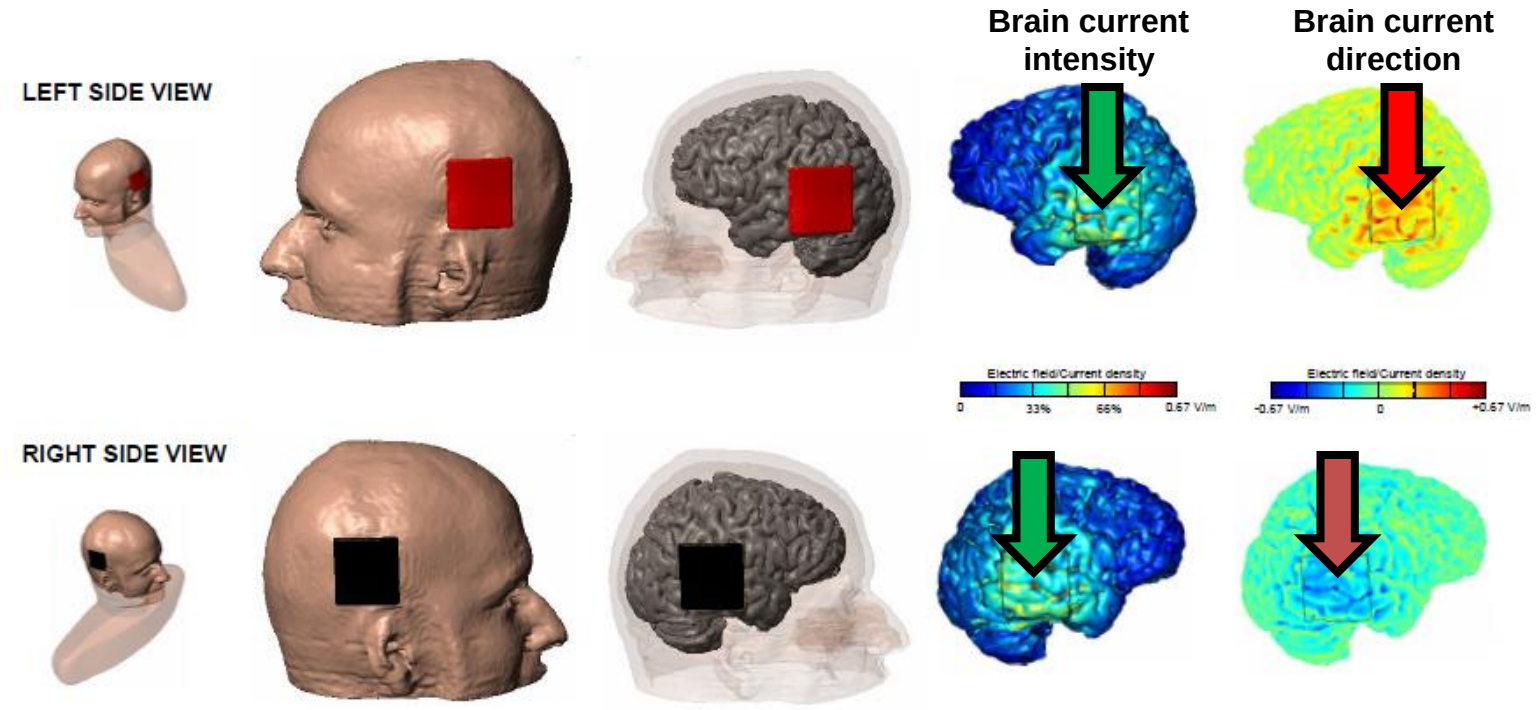
Elettrodi sullo scalpo inviano corrente elettrica debole (tra 1 e 2 mA) nel cervello

Abilità cognitive, disturbi psichiatrici, dolore cronico

- ✓ Non focale
- ✓ Non invasiva
- ✓ Sicura
- ✓ Non costosa

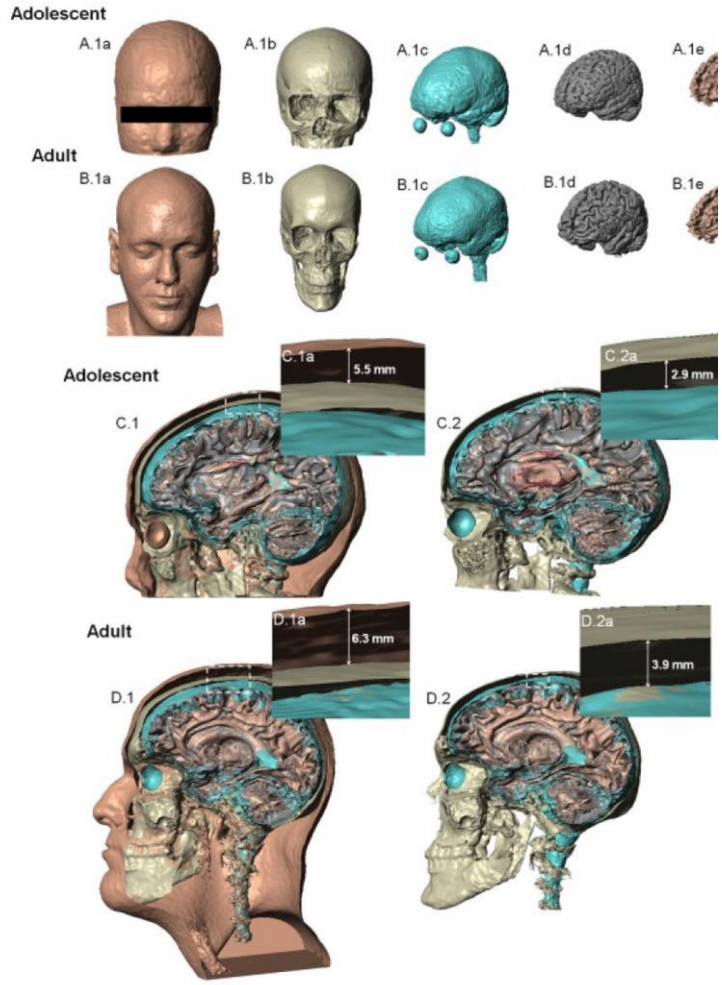
tDCS

- ✓ 2 elettrodi connessi da una stimolatore di corrente continua
- ✓ flusso di corrente fra ANODO (+) e CATODO (-)
- ✓ la corrente verso l'INTERNO sotto l'ANODO
  e verso l'ESTERNO sotto il CATODO



MODELLIZZAZIONI IN ETÀ EVOLUTIVA

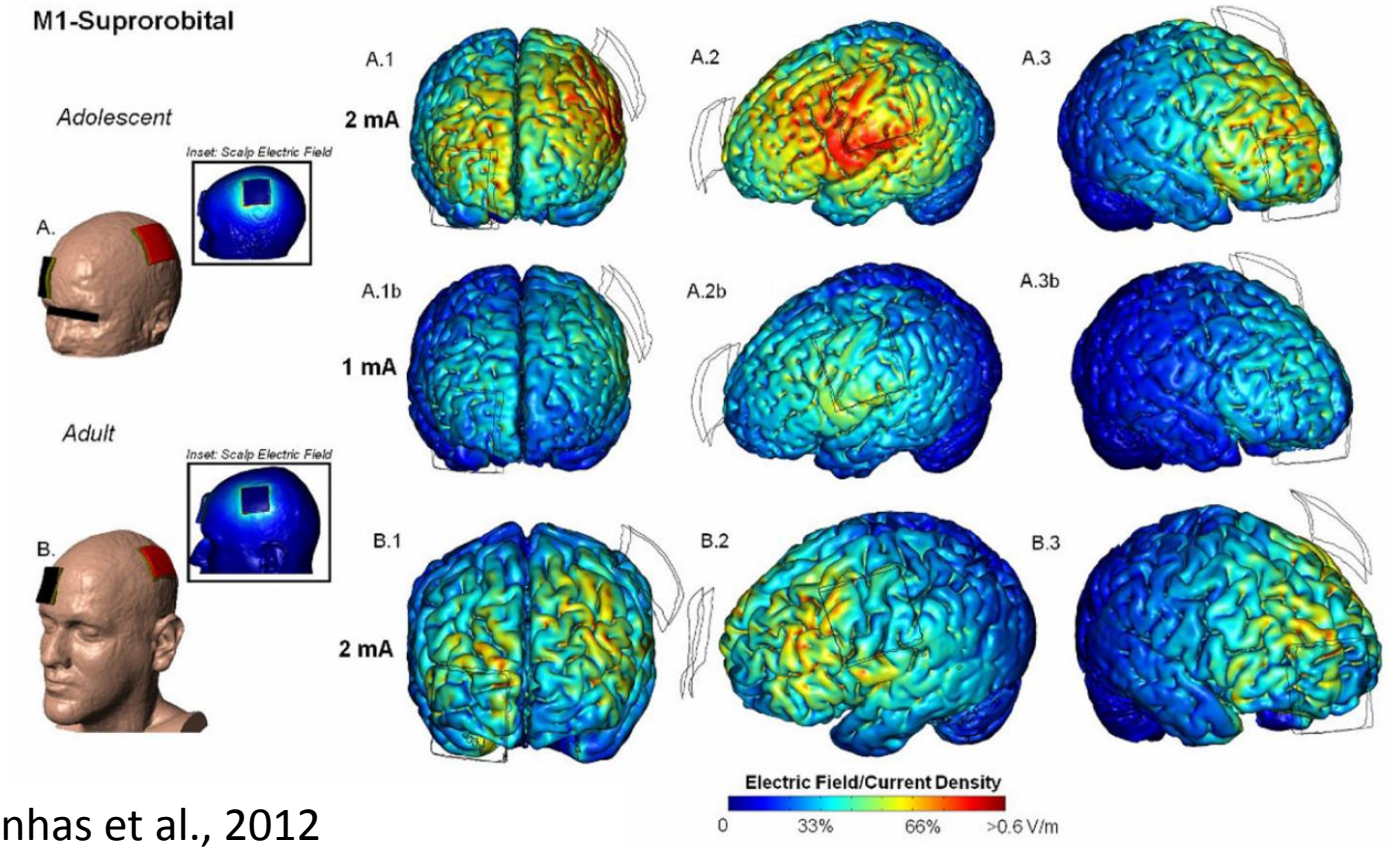
Transcranial Direct Current Stimulation in Pediatric Brain: A computational modeling study



Minhas et al., 2012

MODELLIZZAZIONI IN ETÀ EVOLUTIVA

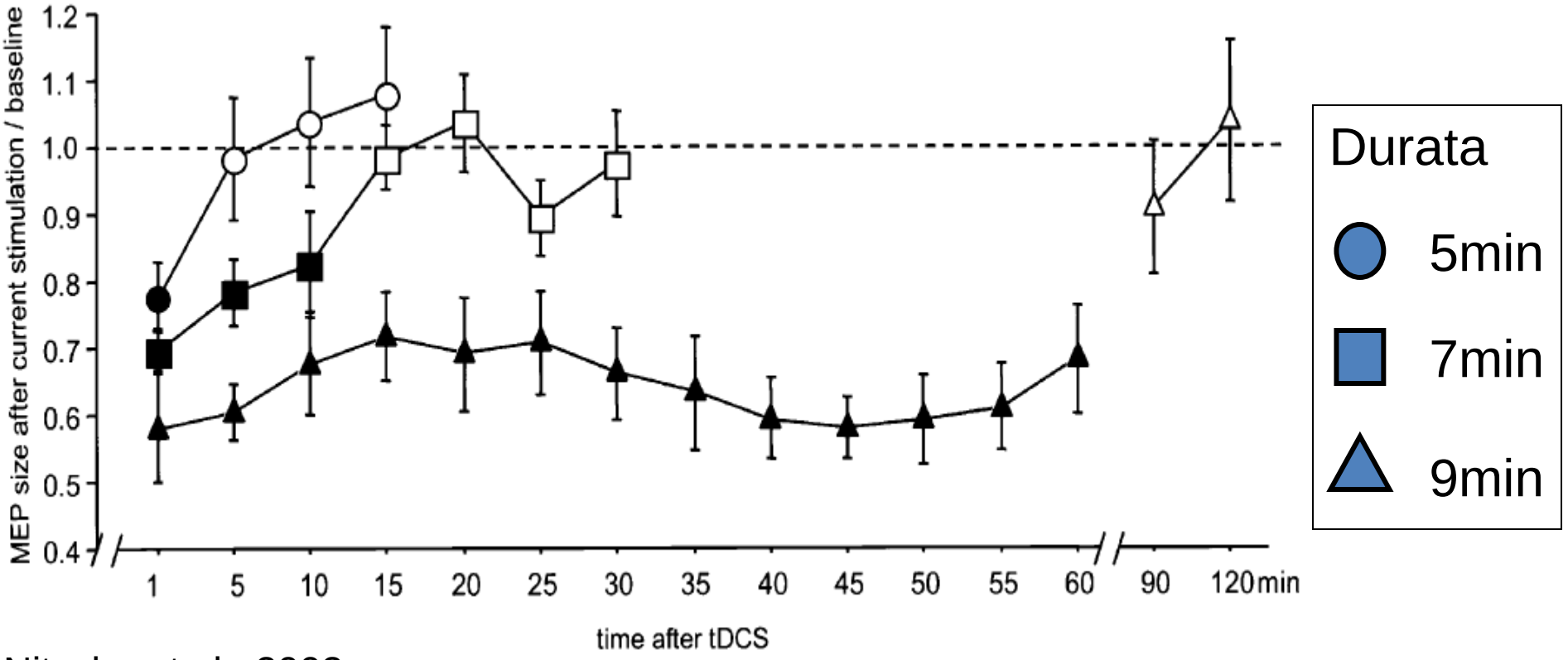
Transcranial Direct Current Stimulation in Pediatric Brain: A computational modeling study



Minhas et al., 2012

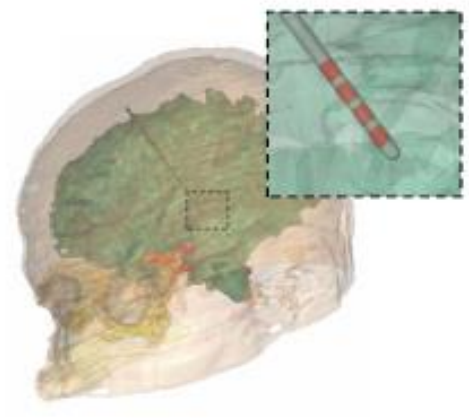
EFFETTO PERSISTENTE

- ✓ L'effetto della tDCS persiste dopo la fine della stimolazione
- ✓ Più lunga è la stimolazione più lento è il ritorno alla baseline

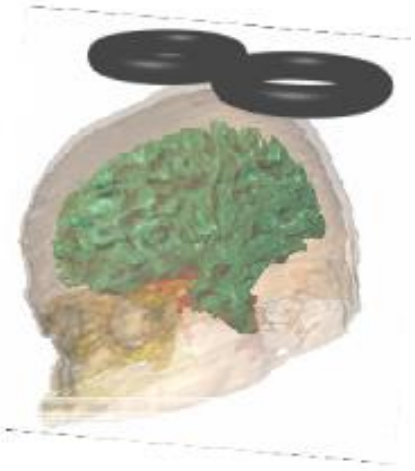


Nitsche et al., 2003

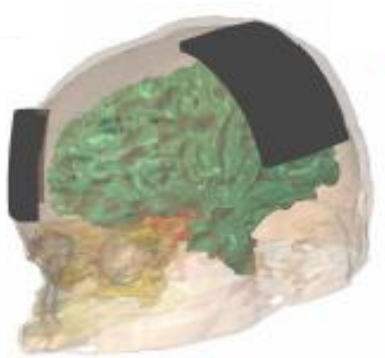
APPLICAZIONI IN ETÀ EVOLUTIVA



Deep Brain Stimulation

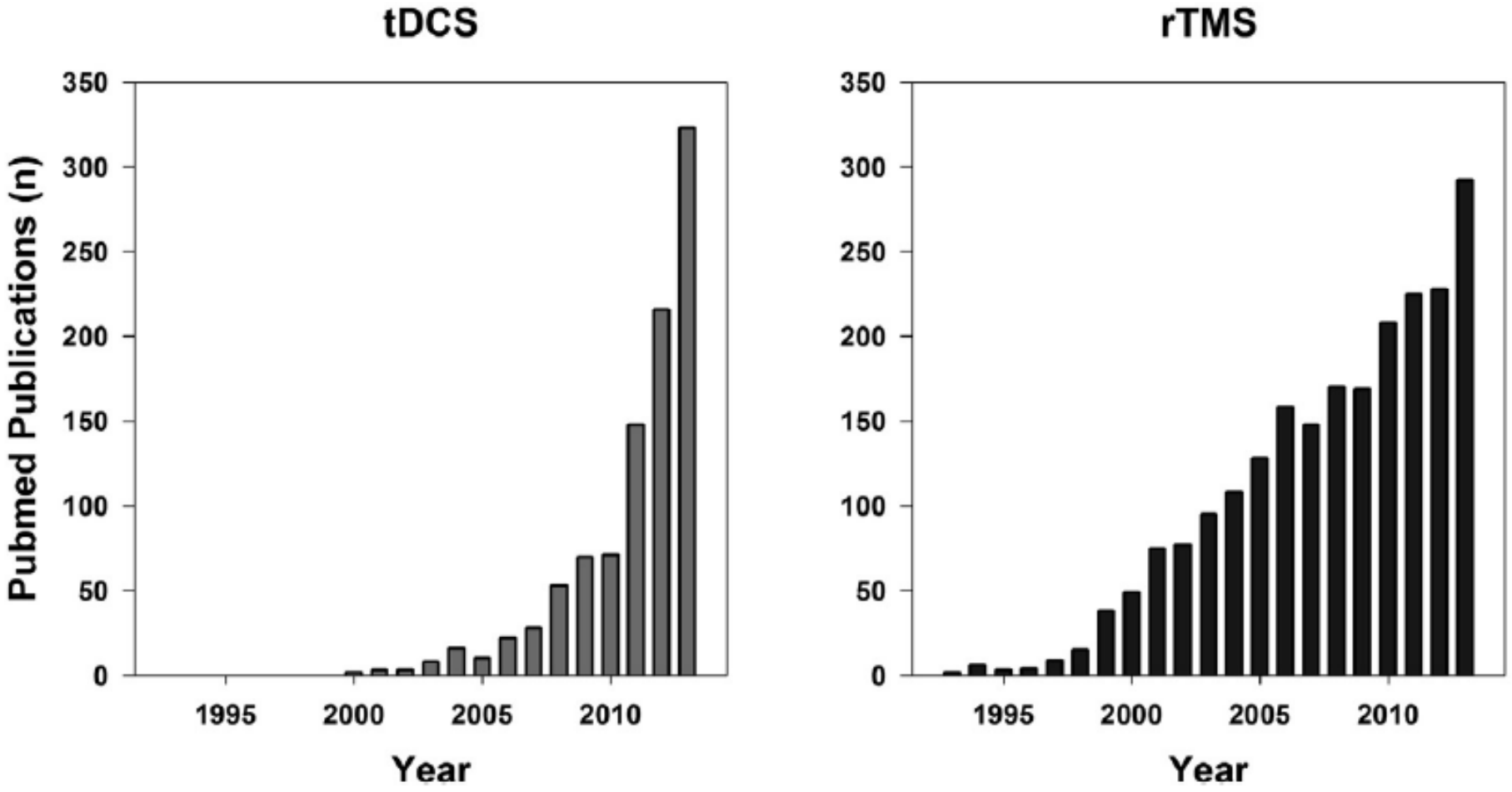


Transcranial Magnetic Stimulation



Transcranial Direct Current Stimulation

CRESCENTE AUMENTO DI STUDI



Krishnan et al., 2015

TOLLERABILITÀ IN ETÀ EVOLUTIVA

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

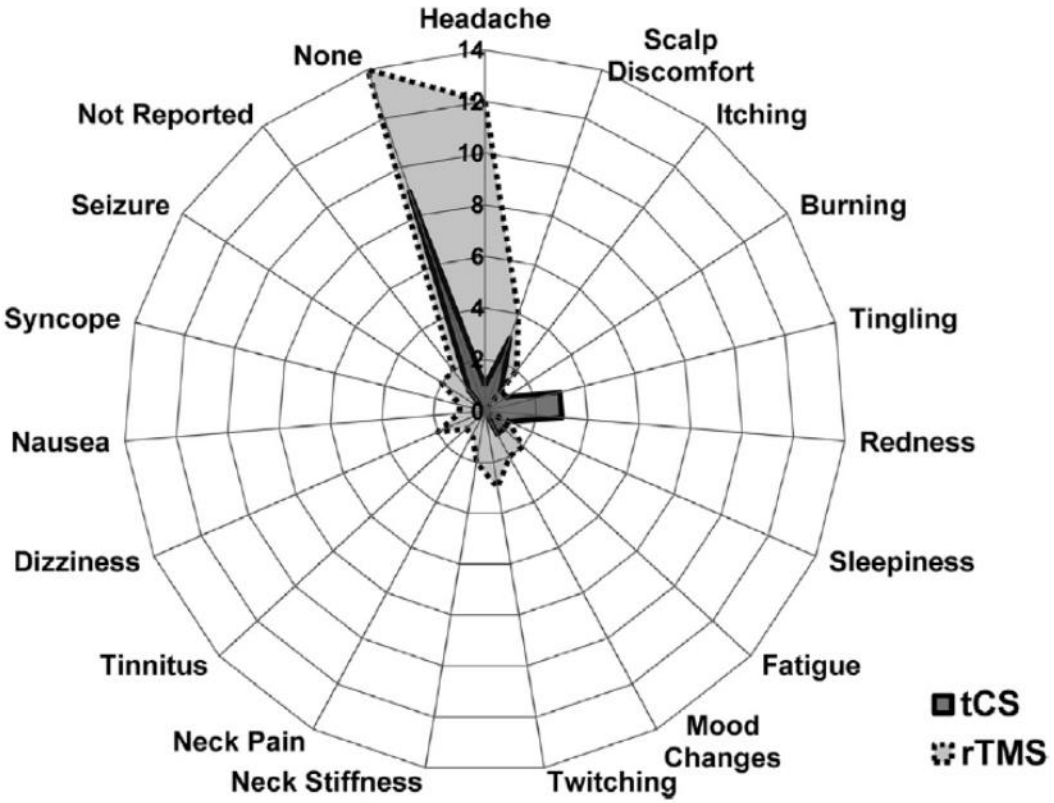
Review Article

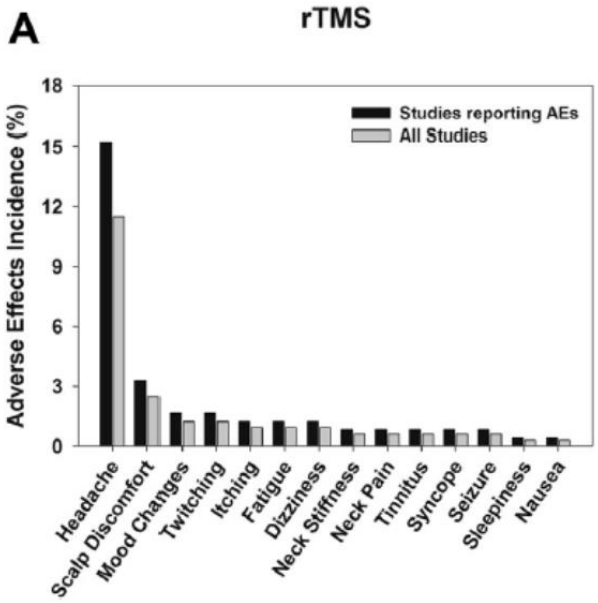
Safety of Noninvasive Brain Stimulation in Children and Adolescents

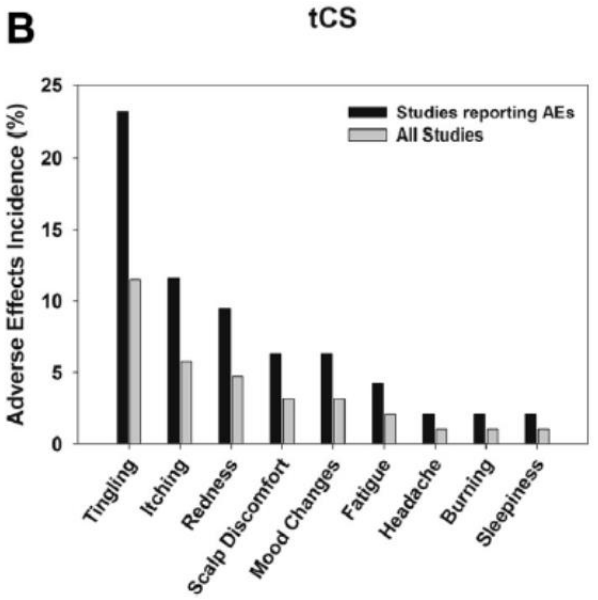
Chandramouli Krishnan*,[1], Luciana Santos [1], Mark D. Peterson, Margaret Ehinger

51 STUDI : 35 rTMS – 16 tDCS

513 bambini – 2,5-17,8 aa







APPLICAZIONI IN ETÀ EVOLUTIVA

References	N ($n < 18$)	Age (y)	Diagnosis	Adverse events[b]
Bogdanov et al. (1994)	21[a]	6–18	Infantile cerebral palsy	Not reported
Alon et al. (1998)	7	2.5–7.5	Cerebral palsy	Well tolerated No reports of seizures, episodes of nausea or vomiting or sleep disruption
Shelyakin et al. (2001)	18	4–8	Infantile cerebral palsy and organic CNS lesions	No negative adverse effects
Ilyukhina et al. (2005)	30	4–6	Delayed neuropsychological development	No adverse effects
San-Juan et al. (2011)	2 (1 < 18)	17 and 31	Rasmussen's encephalitis	No complications or skin injuries
Schneider et al. (2011)	10	6–21	Autism (language disorder)	No adverse effects
Mattai et al. (2011)	13	10.5–17.6	Schizophrenia	Redness, tingling, itching, fatigue
Varga et al. (2011)	5	6.1–11	Epilepsy	No adverse effects
Yook et al. (2011)	1	11	Seizure	No adverse effects
Andrade et al. (2013)	14	5–12	Language disorders	Tingling, burning sensation, scalp pain, local redness, headache, sleepiness, trouble concentrating, mood changes, irritability
Auvichayapat et al. (2013)	36	6–15	Epilepsy	Well tolerated Erythematous rash with no pain or pruritus (one patient)
Young et al. (2013)[c]	11 (8 < 18)	7–18	Dystonia	Uncomfortable at the stimulation electrodes
Grecco et al. (2014)	12	5–10	Cerebral Palsy	No adverse effects
Duarte et al. (2014)	12	Mean (SD): 7.8 (2.0)	Cerebral palsy	Tingling, redness in the supraorbital region No other behavioral changes, headache, or discomfort
Prehn-Kristensen et al. (2014)	12	10–14	ADHD	No effect on mood, alertness, or memory
Young et al. (2014)	14 (12 < 18)	7–19	Dystonia	Skin discomfort
Brasil-Neto et al. (2004)	5 (1 < 18)	6–50	Frontal focal epilepsy	No untoward effects
Graff-Guerrero et al. (2004)[e]	2	11 and 7	Epilepsia Partialis Continua	No major side effects
Morales et al. (2005)	2	8 and 16	Epilepsy	Case A: Well tolerated; no adverse effects Case B: Leg pain and mild headache (resolved after stimulation)

Kinoshita et al. (2005)	7 (1 < 18)	16–33	Extratemporal lobe epilepsy	No adverse effects
Fregni et al. (2006)	27[a]	Mean (SD): 21.6 (7.4) y/20.8 (5.2)	Epilepsy/healthy	Not reported
Loo et al. (2006)	2	16	Depression	No adverse effects
Valle et al. (2007)	17	Mean (SD): 9.1 (3.2)	Cerebral palsy	No adverse effects
Bloch et al. (2008)	9 (5 < 18)	16–18	Depression	Mild headache
Kirton et al. (2008)[d]	5 (4 < 18)	10–16.7	Stroke	Neurocardiogenic syncope, mild headache, nausea, neck stiffness
Rotenberg et al. (2008)	1	14	Rasmussen's encephalitis	Well tolerated with no adverse effects
Jardri et al. (2009)	1	11	Schizophrenia	Well tolerated
Mylius et al. (2009)	1	6	Pantothenate kinase-associated neurodegenerative disease (PKAN)	Not reported
Sokhadze et al. (2009)[e]	8 (5 < 18)	12–27	Autism	No adverse effects
Baruth et al. (2010)[e]	16 (14 < 18)	9–26	Autism spectrum disorder	Itching, mild headache
Kirton et al. (2010)[d]	5 (4 < 18)	10.3–16.7	Stroke	Neurocardiogenic syncope
Sokhadze et al. (2010)[e]	13 (11 < 18)	8–27	Autism spectrum disorder	No adverse effects
Hu et al. (2011)	1	15	Depression	Seizure, hypomania
Kwon et al. (2011)	10	9–14	Tourette's syndrome	Well tolerated No adverse effects or worsening of symptoms
Sun et al. (2011)	17 (8 < 18)	3–32	Epilepsy	Well tolerated; no adverse effects
Wall et al. (2011)	8	14.6–17.8	Depression	Well tolerated
Casanova et al. (2012)	25	Mean (SD): 12.9 (3.1)	Autism	No adverse effects
Croarkin et al. (2012)[c]	8	14–17	Depression	Scalp discomfort
Helfrich et al. (2012)	25	8–14	ADHD	Mild headache; well tolerated
Jardri et al. (2012)[e]	10	Mean (SD): 15.5 (2.3)	Childhood-onset schizophrenia	Scalp discomfort
Sokhadze et al. (2012)[e]	20 (18 < 18)	9–21	Autism spectrum disorder	No adverse effects
Sun et al. (2012)	60[a]	Group 1: Mean (SD): 21.3 (7.5) Group 2: Mean (SD): 19.7 (6.4)	Epilepsy	Mild or moderate headache, tinnitus; well tolerated
Weaver et al. (2012)	9 (4 < 18)	14–21	ADHD	Mild headache, scalp discomfort
Wu et al. (2012)	40	8–17	Tourette's syndrome/healthy	Mild headache, neck stiffness, finger twitching; no reports of seizures
Chiramberro et al. (2013)	1	16	Depression	Seizure
Le et al. (2013)	25	7–16	Tourette Syndrome	Mild sleepness
Wall et al. (2013)	14	13.9–17.8	Depression	Scalp discomfort, no adverse neurocognitive effect
Gillick et al. (2014)[e]	10	8–15	Congenital hemiparesis	Self-limiting headache, dizziness, mood changes, fatigue, abnormal muscle contractions
Gomez et al. (2014)	10	7–12	ADHD	Slight headache, neck pain, slight brief dizziness
Oberman et al. (2014)	19 (17 < 18)	9–18	Autism	Mild headache, mild fatigue; no serious adverse effects

frontiers in
SYSTEMS NEUROSCIENCE

REVIEW ARTICLE
published: 25 November 2013
doi: 10.3389/fnsys.2013.00094

Non-invasive brain stimulation for the treatment of brain diseases in childhood and adolescence: state of the art, current limits and future challenges

Carmelo M. Vicario[1] and Michael A. Nitsche[2]*

Studies	Design		Patients		Stimulation protocol						Outcome	
	Sham controlled	Blinding	Disease	Sample size	rTMS intensity	Stimulation position	Number of sessions/ days	rTMS frequency	Total number of pulses/ session	Duration per session	Effects	Side-effects
ADHD												
Weaver et al., 2008	Yes	Open	ADHD only	4	100% rMT	Right DLPFC	1 session per day/5 days per week/2 weeks	10 Hz	2000 stimuli	N/A	Improved attention in the Sham + active rTMS condition	None

- ✓ Ipoattivazione frontale
- ✓ Si agisce con stimolazione facilitatoria aree frontali (es. R-DLPFC)
- ✓ No studi tDCS

AUTISM SPECTRUM DISORDERS												
Baruth et al., 2010	Control group	Open	Autistic	22	90% rMT	Bilateral DLPFC	1 session per day/1 day per week/12 weeks	•1 Hz	150	N/A	Reduction of irritability and repetitive behavior	None
Sokhadze et al., 2010	No	Open	Autistic	13	90% rMT	Bilateral DLPF cortices	1 session per day/2 day per week/3 weeks	0.5 Hz	150	N/A	Reduced errors % in the oddball task and ritualistic behaviors	None

- ✓ Compromissione frontale
- ✓ Si agisce con stimolazione inibitoria aree frontali (bilaterale)
- ✓ Studio tDCS (Schneider e Hopp, 2011): stimolazione facilitatoria area broca (anodica a sx, 0,8 mA-20 min) → migliora test vocabolario

frontiers in
SYSTEMS NEUROSCIENCE

REVIEW ARTICLE
published: 25 November 2013
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Non-invasive brain stimulation for the treatment of brain diseases in childhood and adolescence: state of the art, current limits and future challenges

Carmelo M. Vicario[1] and Michael A. Nitsche[2]*

TOURETTE												
Kwon et al., 2011	No	Open	TS only	2	100% rMT	SMA	10 daily sessions/10 days	1 Hz	1200	N/A	Tics reduction	None
Le et al., 2013	No	Open	TS only	25	100% rMT	SMA	1 session per day/5 days per week/4 weeks	1 Hz	1200	20 min	Tics reduction	None

- ✓ Iperattivazione SMA
- ✓ Si agisce con stimolazione inibitoria
- ✓ No studi tDCS

											behaviors	
DEPRESSION												
Walter et al., 2001	No	Open	Unipolar major depression	3	Between 90 and 110% of the rMT	Left DLPFC	1 session per day/5 days per week/2 weeks	10 Hz	1600	N/A	Improvement in 2 cases on 3	Tension headache reported in one case with improve-ment
Loo et al., 2006	No	Open	Depression/ ADHD comorbidity	2	110% rMT	Left DLPF cortex	1 session per day/5 days per week/6 weeks	10 Hz	40 trains/5 s per train	N/A	Improvement measured with the CDRS	None

(Continued)

- ✓ Iperattivazione aree frontali di destra
- ✓ Si agisce con stimolazione facilitatoria controlaterale (L-DLPFC)
- ✓ No studi tDCS

BRAIN STIMULATION
e
DISTURBI DI APPRENDIMENTO

TMS E DISLESSIA

Neuropsychologia 51 (2013) 2953–2959

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

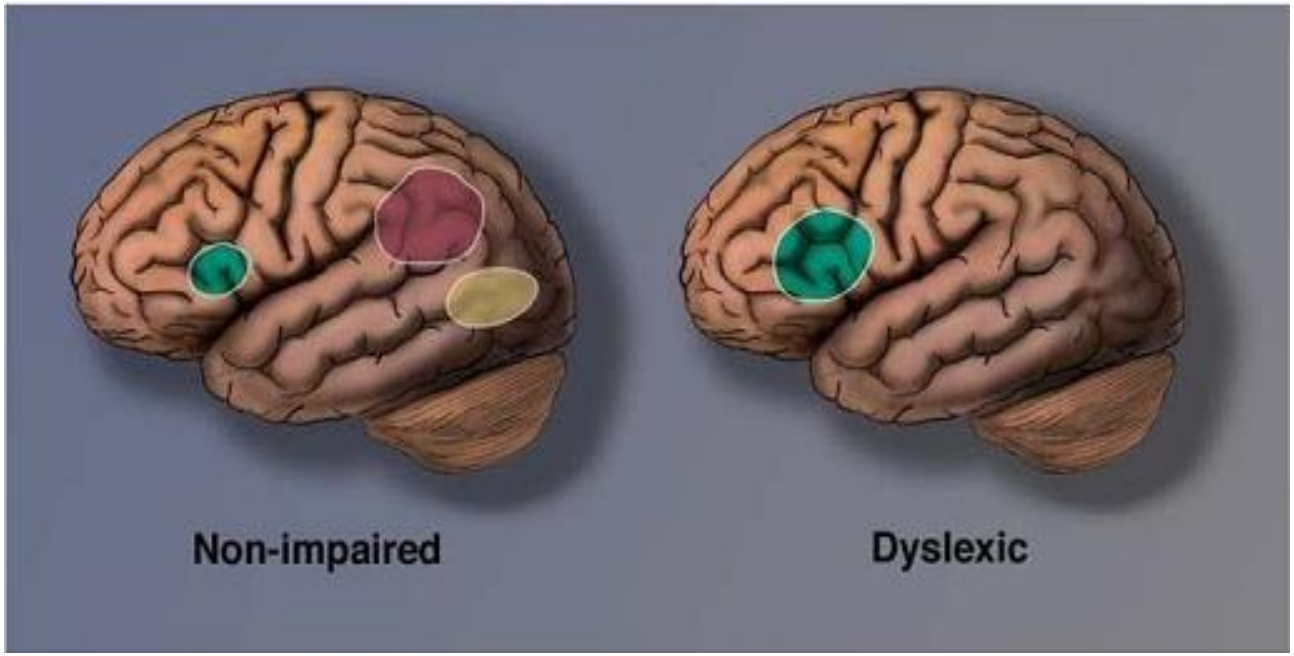
How to improve reading skills in dyslexics: The effect of high frequency rTMS

Floriana Costanzo [a], Deny Menghini [a], Carlo Caltagirone [b,c], Massimiliano Oliveri [b,d], Stefano Vicari [a,*]

10 dislessici (5M), Età 34 (6,57)

rTMS facilitatoria, 5 HZ, off-line, 6 min circa (singola sessione)

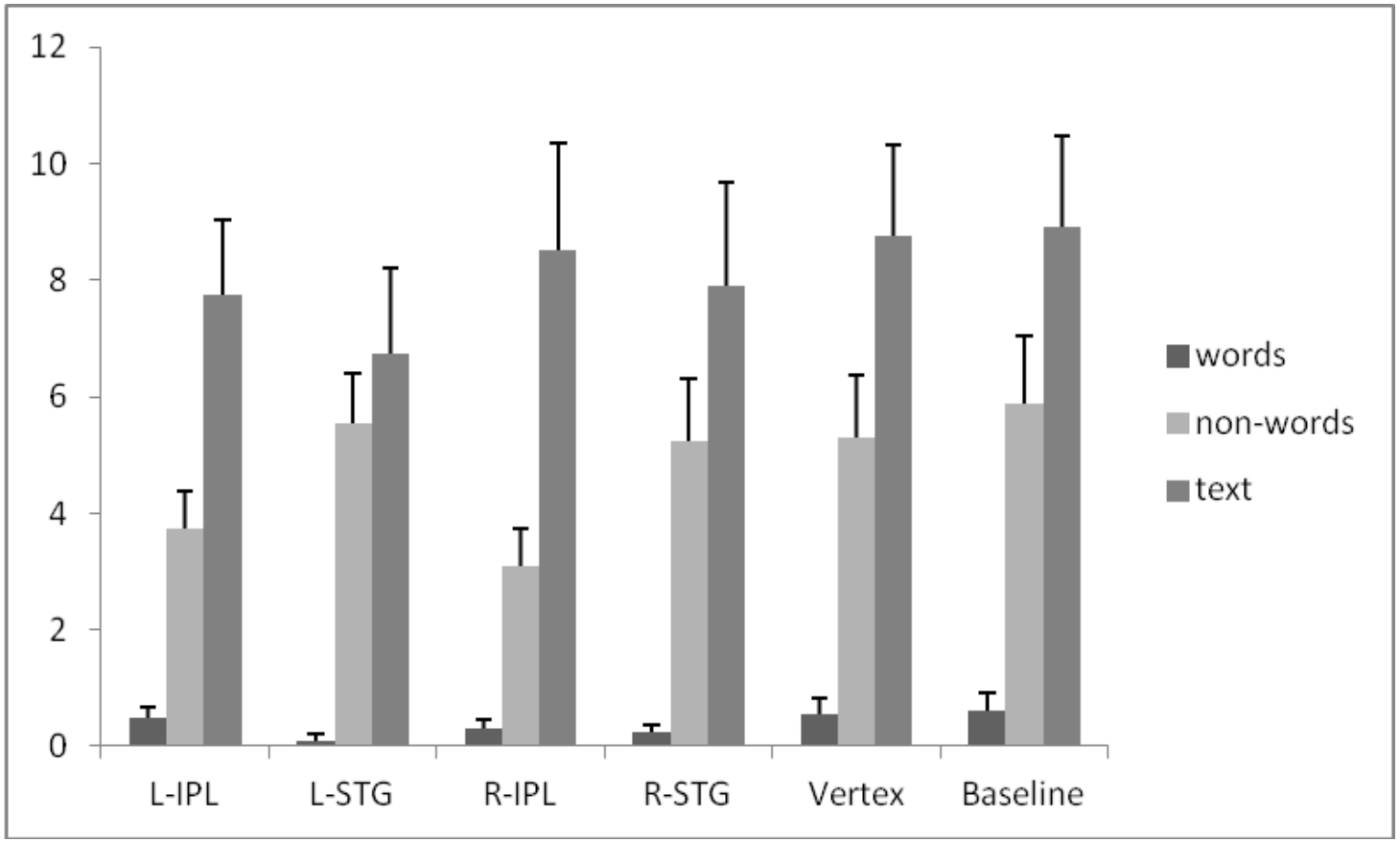
Alterazioni cerebrali nei dislessici



TMS E DISLESSIA

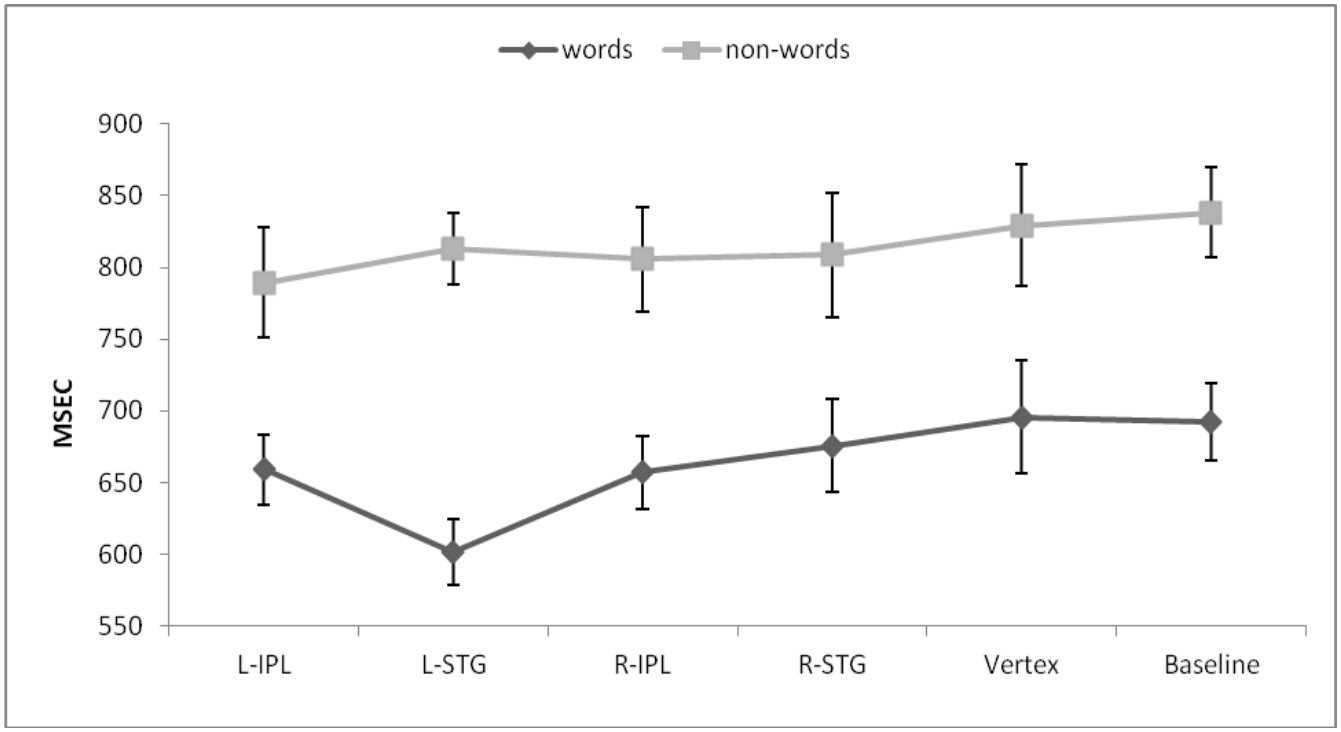
RIDUZIONE ERRORI

Sito e task specifico



TMS E DISLESSIA

RIDUZIONE ONSET Sito e task specifico



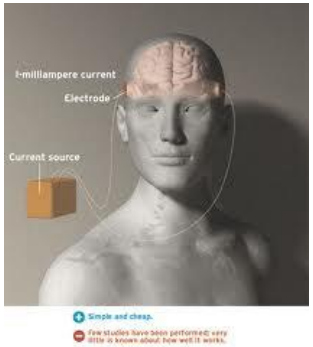
PROSPETTIVE

Finora miglioramenti solo TRANSITORI

Possibile l'applicazione della stimolazione cerebrale
in protocolli TERAPEUTICI
nei disturbi di apprendimento
per miglioramenti a LUNGO TERMINE?

TMS

vs



tDCS?

- ✓ non invasiva
- ✓ + focale
- ✓ - sicura
- ✓ + costosa

- ✓ non invasiva
- ✓ - focale
- ✓ **+ sicura**
- ✓ - costosa

Developmental Cognitive Neuroscience 6 (2013) 176–194

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Review

Can transcranial electrical stimulation improve learning difficulties in atypical brain development? A future possibility for cognitive training

Beatrix Krause*, Roi Cohen Kadosh

Department of Experimental Psychology, University of Oxford, Oxford, UK

frontiers in HUMAN NEUROSCIENCE

OPINION ARTICLE
published: 22 April 2013
doi: 10.3389/fnhum.2013.00139

Transcranial direct current stimulation: a remediation tool for the treatment of childhood congenital dyslexia?

Carmelo M. Vicario[1]* and Michael A. Nitsche[2]

[1] School of Psychology, The University of Queensland, St. Lucia, QLD, Australia
[2] Department of Clinical Neurophysiology, University of Göttingen, Göttingen, Germany
**Correspondence: uqcvicar@uq.edu.au; carmelo.vicario@uniroma1.it*

TDCS E DISCALCULIA

frontiers in
HUMAN NEUROSCIENCE

CLINICAL CASE STUDY
published: 07 February 2014
doi: 10.3389/fnhum.2014.00038

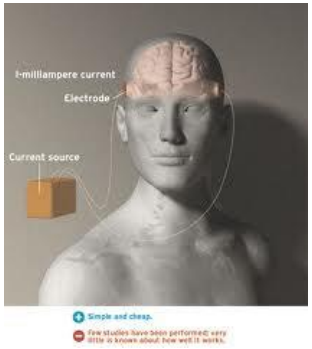
Preliminary evidence for performance enhancement following parietal lobe stimulation in Developmental Dyscalculia

Teresa Iuculano[1,2,3]* *and Roi Cohen Kadosh*[1]

Case series: 2 individui adulti con DD (età 29,5 ± 5)

Primo studio che applica tDCS in pazienti con disturbo di apprendimento evolutivo (adulti)

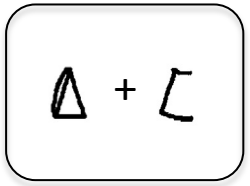
tDCS come training-trattamento 6 sessioni



TDCS E DISCALCULIA

- **Programma di training** (Sessione 1)

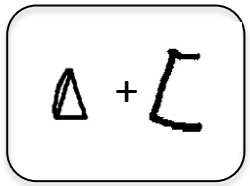
1	2	3	4	5	6	7	8	9
								



Indicare il simbolo corrispondente al numero più grande.

- **Compiti sperimentali** (Sessioni 2-6)

  a. Numerical stroop task



Indicare il simbolo fisicamente più grande.

  b. Number line tasks: 42 trial

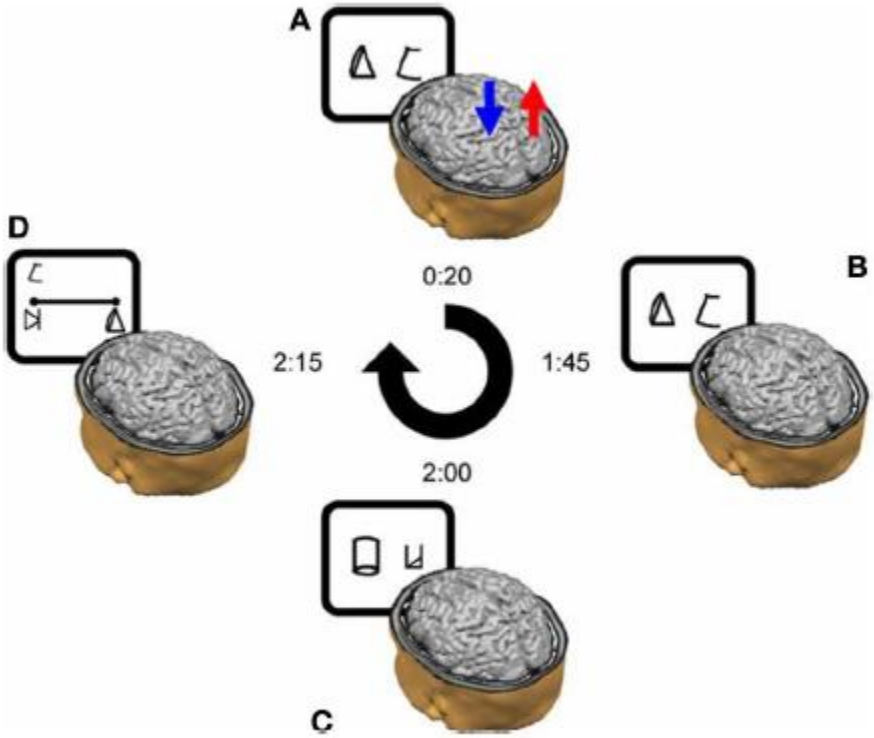
Posizionare il simbolo su una linea orizzontale secondo la grandezza del numero corrispondente.

TDCS E DISCALCULIA

Stimolazione:
1mA aree parietali P3 e P4, 20 min

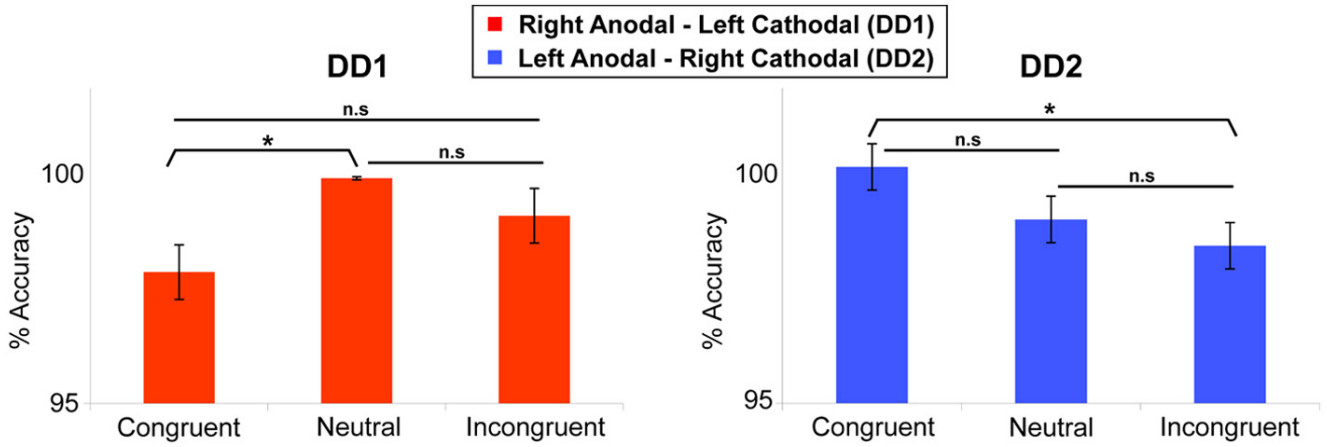
Discalculico1
ANODO a destra
CATODO a sinistra

Discalculico2
ANODO a sinistra
CATODO a destra



TDCS E DISCALCULIA

Congruency effect nel Numerical Stroop Task: Accuratezza



- ✓ indice di elaborazione automatica
- ✓ presente nel soggetto DD2

Bambino Gesù
OSPEDALE PEDIATRICO

Progetto finanziato dal Ministero della Salute (Giovani Ricercatori) 2012

Transcranial direct current stimulation in the treatment of dyslexia: a randomized double-blind study

Deny Menghini
Floriana Costanzo, Cristiana Varuzza, Serena Rossi, Stefano Sdoia, Pamela Varavara, Massimiliano Oliveri, Giacomo Koch, Stefano Vicari

TDCS E DISLESSIA

Intervento nelle aree cerebrali

- ✓ tipicamente ipoattive nella dislessia
- ✓ che si “riattivano” dopo un efficace programma di training

- ✓ Favorire i cambiamenti neurofisiologici che sottostanno al miglioramento comportamentale
- ✓ tDCS strumento complementare per accompagnare i protocolli di trattamento standard?

TDCS E DISLESSIA

Bambini dislessici destrimani (età ≥ 10 anni)

2 gruppi paragonabili per:

- ✓ età cronologica
- ✓ QI
- ✓ difficoltà di lettura
- ✓ variabili sociali

tDCS attiva e training cognitivo
tDCS placebo e training cognitivo

METODO

Partecipanti

- ✓ tDCS attiva +Training di lettura: 8 (5 F); età 13,4 ± 2,4
- ✓ tDCS placebo + Training di lettura: 8 (5 F); età 13,2 ± 2,6

Misure di lettura

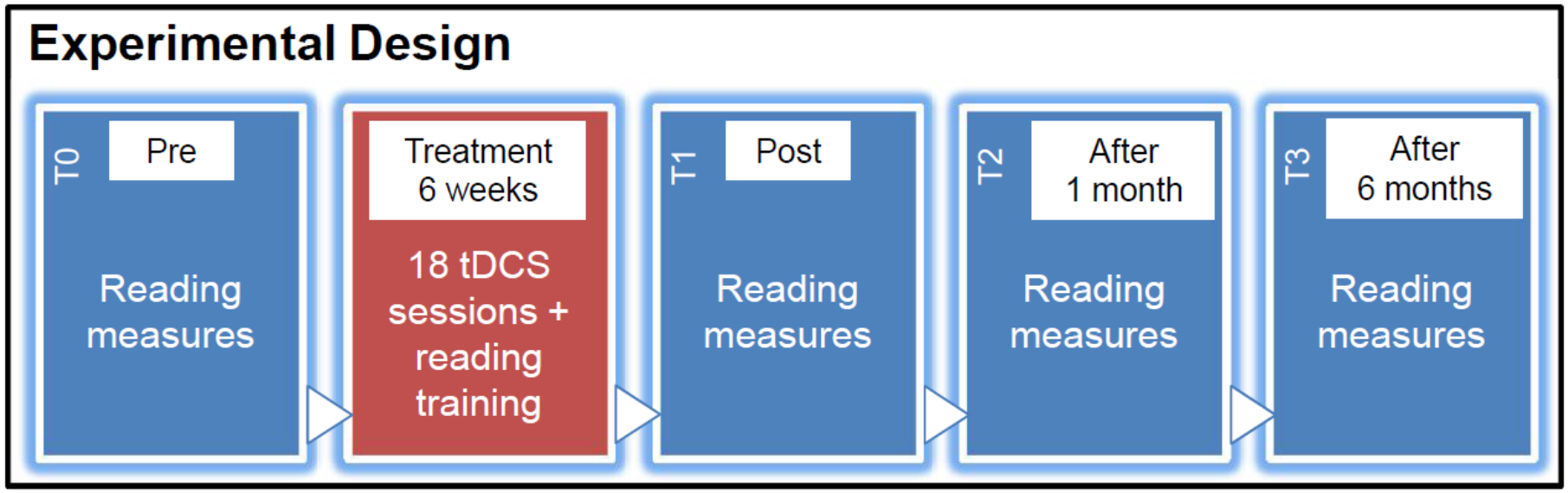
- **Testi** di 400 sillabe (TEXT)
- 20 **parole** ad **alta frequenza**, 10 trisillabiche e 10 bisillabiche (HF)
- 20 **parole** a **bassa frequenza**, 10 trisillabiche e 10 bisillabiche (LF)
- 20 **non parole**, 10 trisillabiche e 10 bisillabiche (NW)

Prima del trattamento

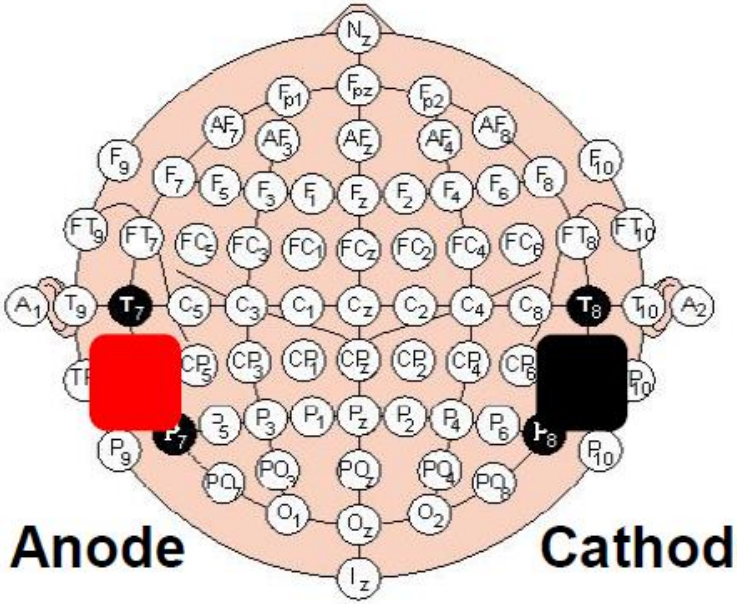
Il gruppo tDCS attiva e tDCS placebo **non differiscono** nelle misure di lettura:

T0 Velocità di lettura:
TEXT U = 18, p = 0.66; HF U = 19, p = 0.77; LF U = 17, p = 0.57; NW U = 20, p = 0.88.

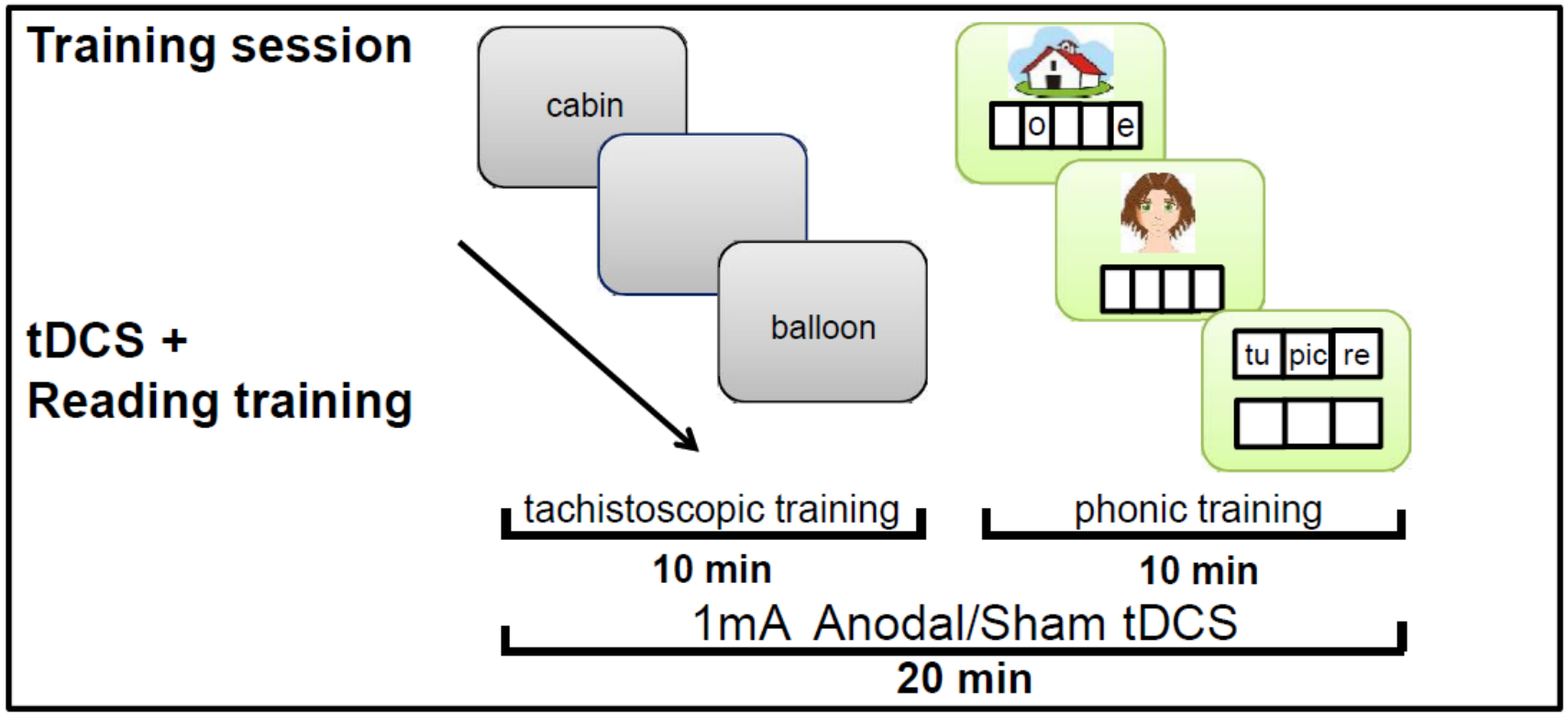
T0 Accuratezza della lettura:
HF U = 19, p = 0.77; LF U = 15, p = 0.39; NW U = 15.5, p = 0.43; TEXT U = 13, p = 0.25.


Experimental Design
T0
Pre
Reading measures
Treatment 6 weeks
18 tDCS sessions + reading training
T1
Post
Reading measures
T2
After 1 month
Reading measures
T3
After 6 months
Reading measures

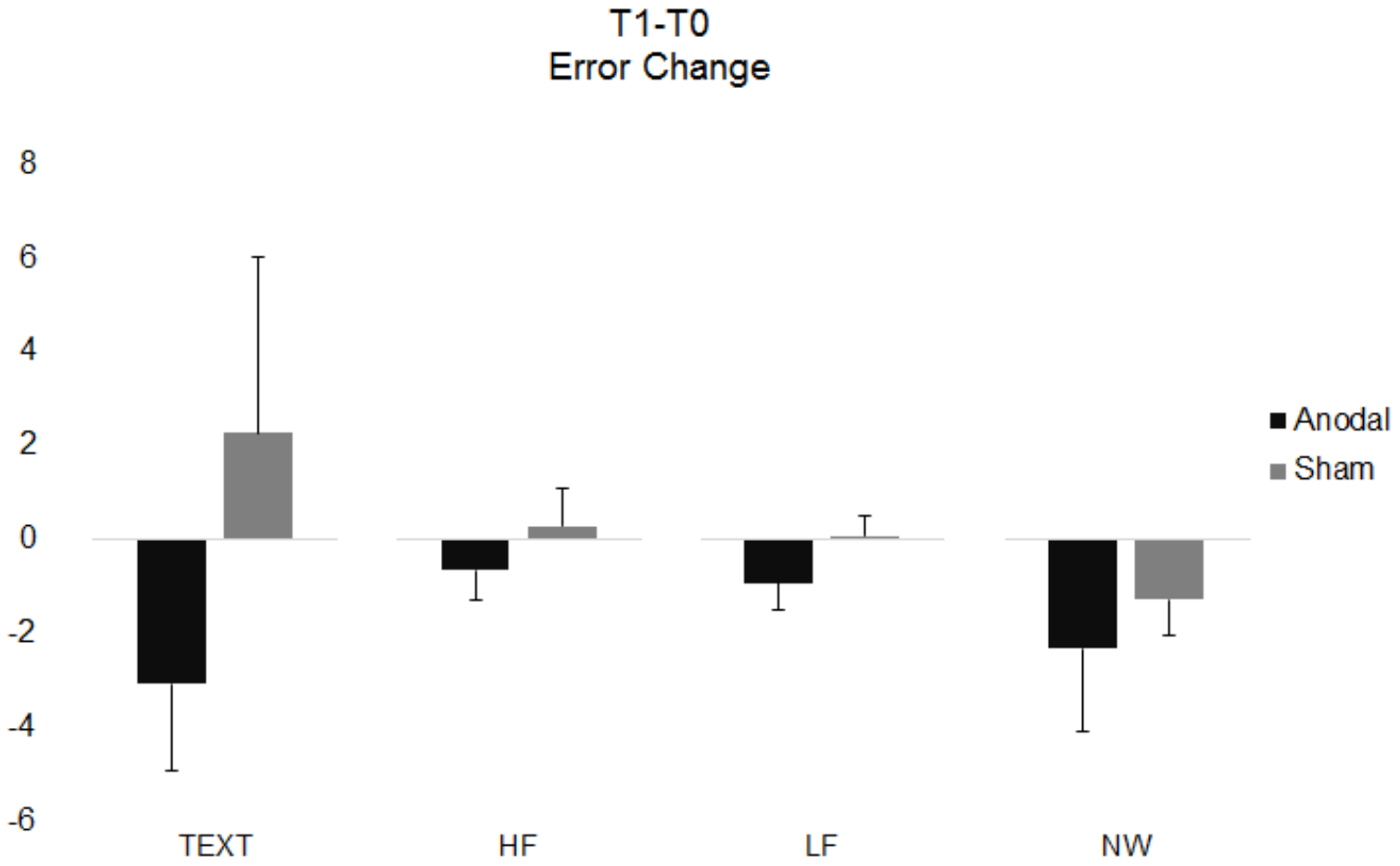
Set-up



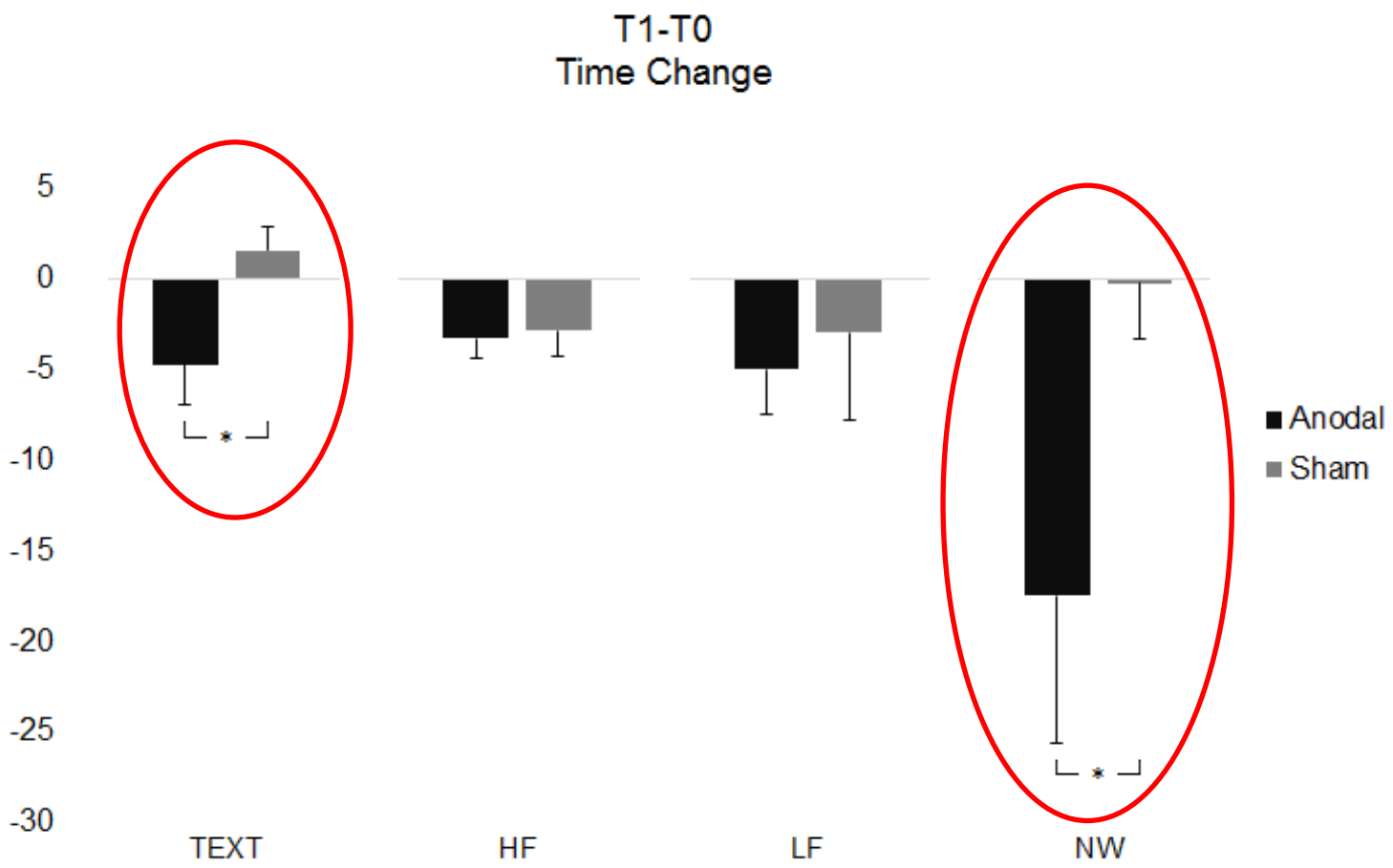
TRAINING


Training session
tDCS +
Reading training
cabin
balloon
o
e
tu
pic
re
tachistoscopic training
10 min
phonic training
10 min
1mA Anodal/Sham tDCS
20 min

RISULTATI



RISULTATI



L'effetto positivo **persiste** dopo 1 mese (T2) e dopo 6 mesi (T3) dalla fine del trattamento

RISULTATI TOLLERABILITÀ

Adverse effect	Mild (%)	Moderate (%)	Severe (%)
Headache	0.0	0.0	0.0
Neck pain	0.0	0.0	0.0
Scalp pain	0.0	0.0	0.0
Tingling	25.0	0.0	0.0
Itching	25.0	0.1	0.0
Burning sensation	12.5	7.7	0.0
Local redness	12.5	0.0	0.0
Sleepiness	0.0	0.0	0.0
Trouble concentrating	0.0	0.0	0.0
Acute mood changes	0.0	0.0	0.0
Irritability	0.0	0.0	0.0

288 sessioni

Questionario di Brunoni et al., 2011

DISCUSSIONE

- ✓ risultati preliminari
- ✓ tDCS è una prospettiva promettente per il trattamento
- ✓ breve training efficace!
- ✓ effetti a lungo termine

PROTOCOLLI IN CORSO

tDCS

NEI DISTURBI DEL COMPORTAMENTO ALIMENTARE

Obiettivo:

- ✓ ridurre l'attività delle aree frontali di destra nell'**anoressia**
- ✓ aumentare l'attività delle aree frontali di sinistra nel **food craving** e **obesità**

Metodo:

1mA (20 min) + psicoterapia (18 sedute)

anoressia: DLPF anodo sn/catodo dx

food craving e obesi: DLPF anodo dx/catodo sn

Misure outcome:

EDI-III, misure fisiologiche e psicopatologiche

PROTOCOLLI IN CORSO

tDCS

NELLA CATATONIA

Caso singolo → bambina di 14 con catatonia farmacoresistente

e disturbo dello spettro autistico

Trattamento alternativo alla TEC (600 mA)

Obiettivo:

ridurre sintomi catatonici ristabilendo le alterazioni funzionali delle aree frontali

Metodo:

1mA (20 min) + trattamento farmacologico (10 sedute)

montaggio di riferimento usato in studi TEC: DLPF anodo sn/catodo dx

Misure outcome:

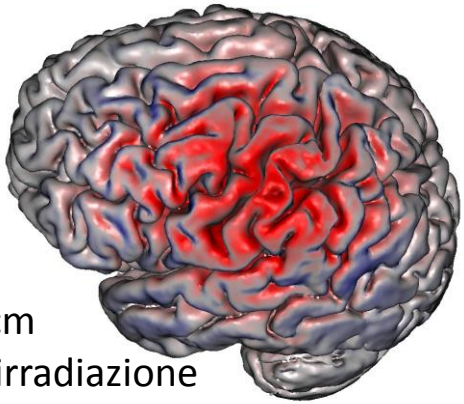
Scala per la catatonia (Kanner-scales), esame neurologico

PROSPETTIVE FUTURE

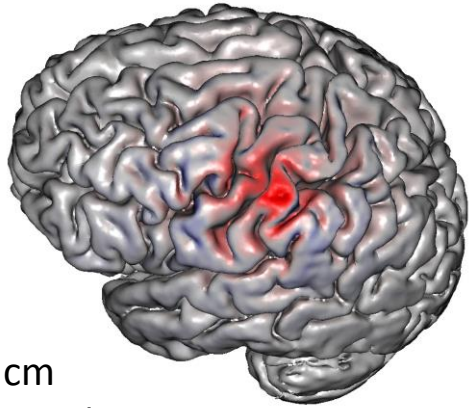
- ✓ tDCS ad alta definizione
- ✓ tACS (transcranial alternating current stimulation) per migliorare la plasticità e sincronizzare i ritmi cerebrali

tDCS AD ALTA DEFINIZIONE

Datta, Bikson, Alam

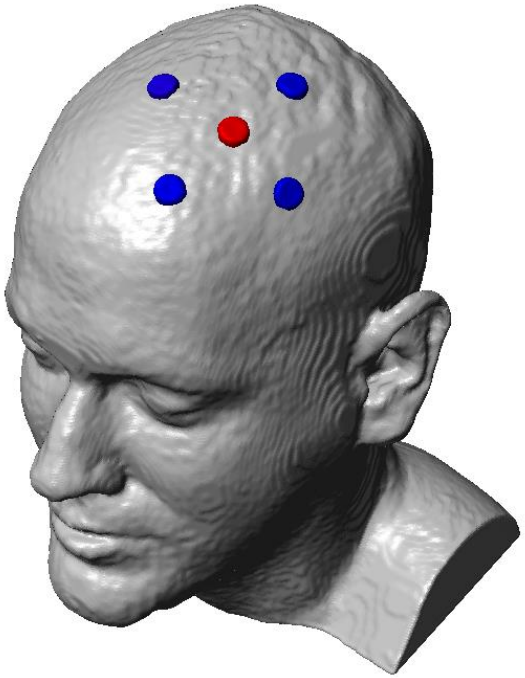


7 cm
di irradiazione

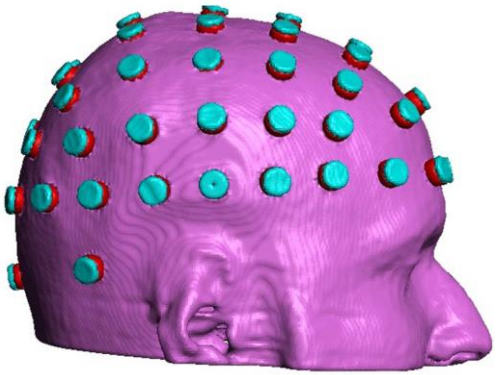


3 cm
di irradiazione

4X1



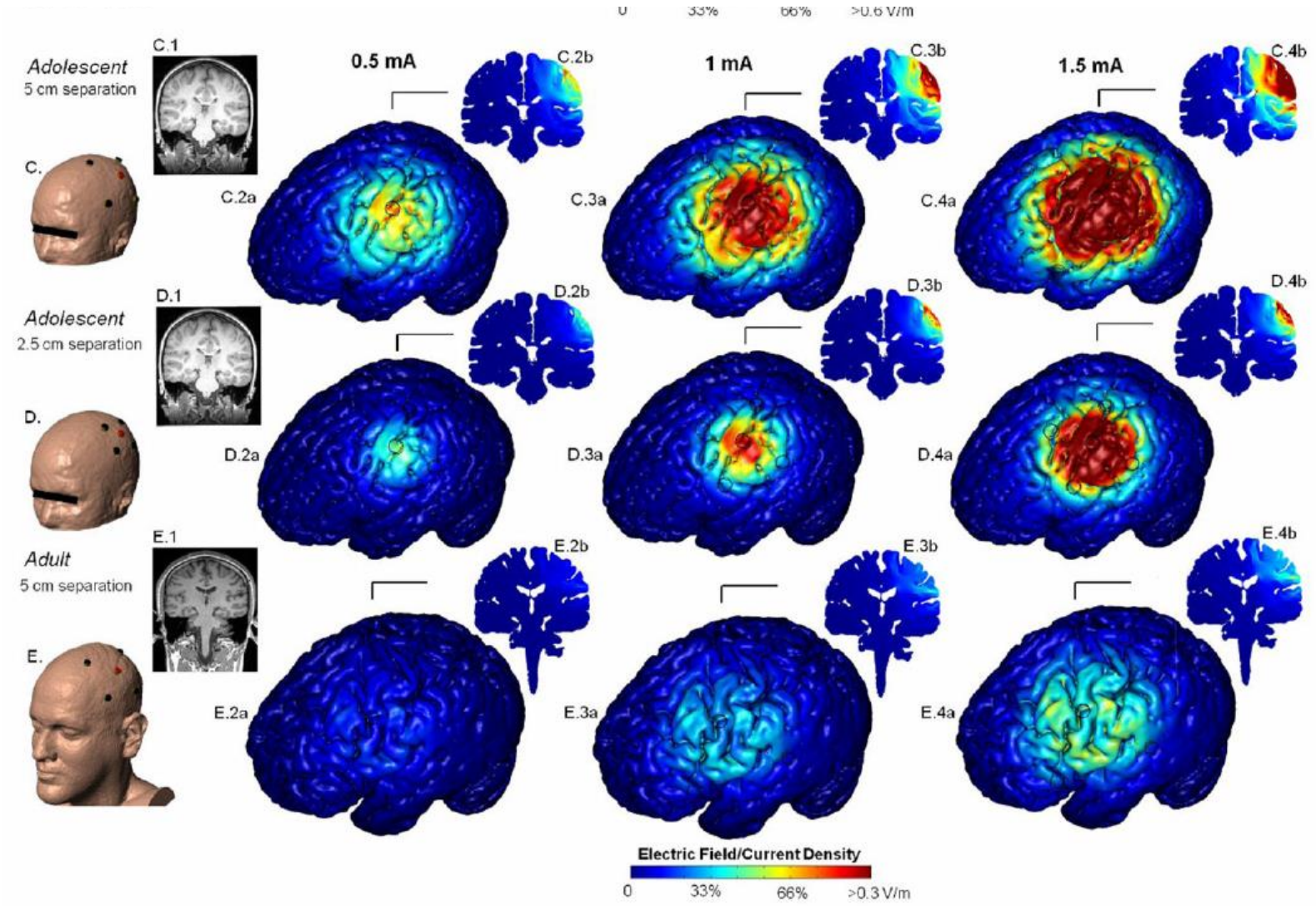
6X6 HD-tDCS
Deep HD-TES



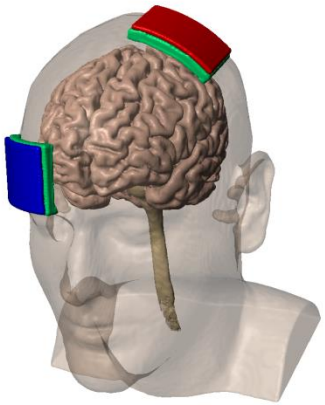
- ✓ Elevato controllo della corrente
- ✓ Focalizzata (target superficiali e profondi)

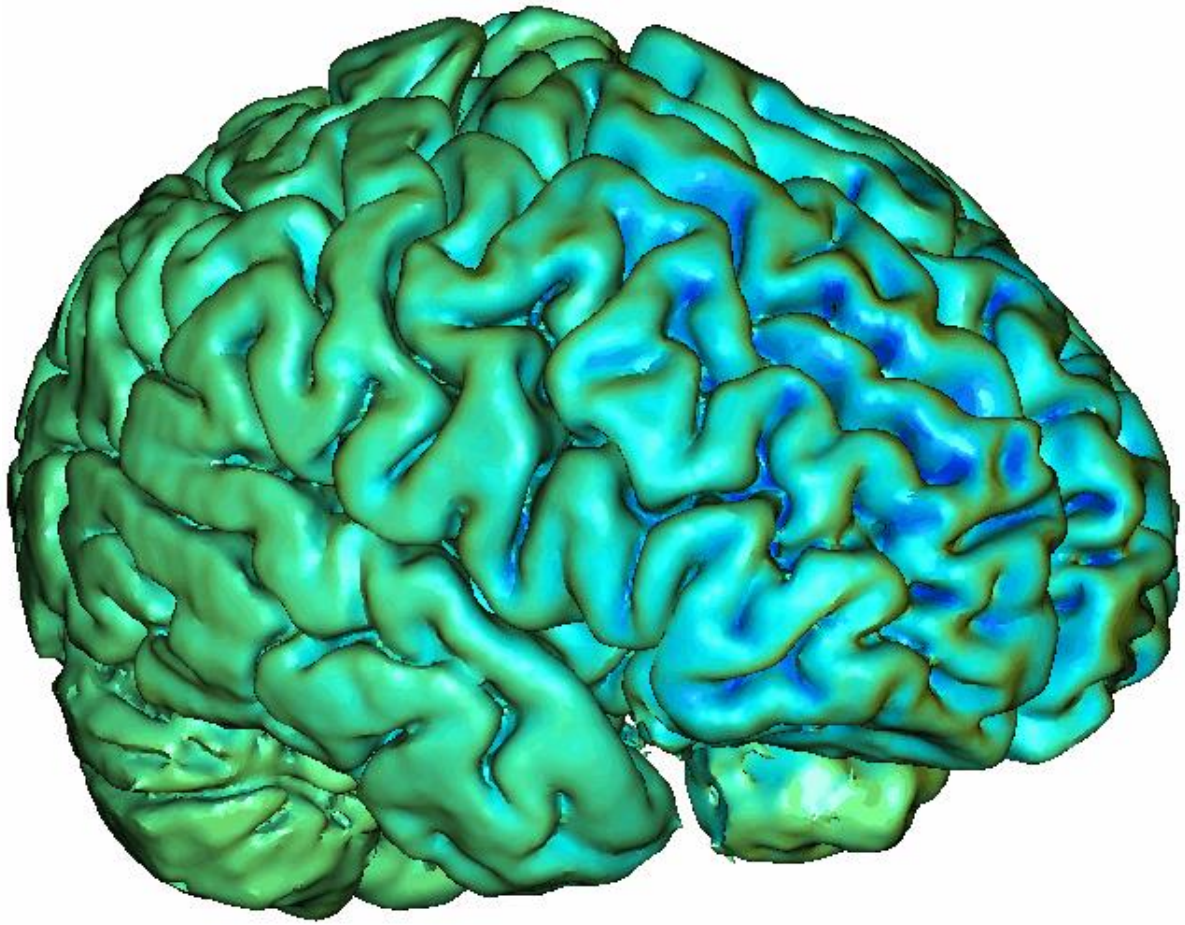
MODELLIZZAZIONI IN ETÀ EVOLUTIVA

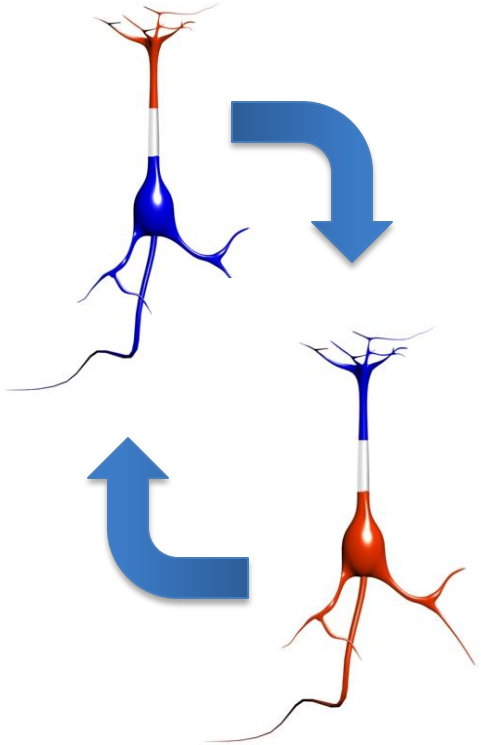
Minhas et al., 2012



tACS



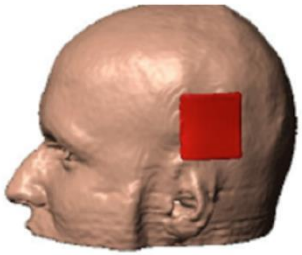


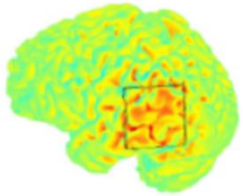


Alterna il flusso di corrente ad una certa frequenza

M. Bikson - Practical Course in Transcranial Magnetic and Electrical Stimulation - Gottinga 2014

tACS



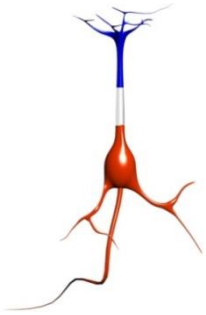


tACS

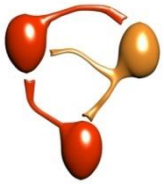
+

TRAINING

AC flusso di corrente



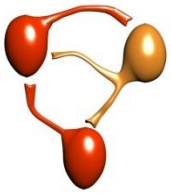
AC polarizzazione cellulare

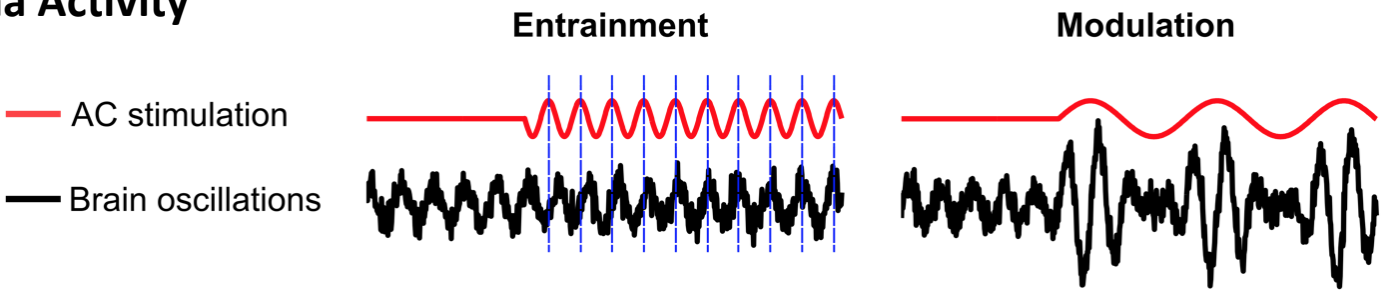


Aumenta l'attività in corso (oscillazioni)

Meccanismo sinaptico per cambiamenti a lungo termine:
neuroplasticità

Network Gamma Activity





Facilitazione task-specifica: in relazione alla frequenza
target funzionale

Reato et al. 2013

CONCLUSIONI

- ✓ La stimolazione cerebrale non invasiva è una prospettiva di riabilitazione nei disturbi evolutivi

- ✓ In combinazione, può ottimizzare l'effetto dei trattamenti cognitivi e psicologici

Ann Neurol. 2013 September ; 74(3): . doi:10.1002/ana.24002.

New Innovations: Therapeutic opportunities for Intellectual disabilities

Jonathan D. Picker, MBChB, PhD[1,2] and **Christopher A. Walsh, MD, PhD**[1,3]

CONCLUSIONI

- ✓ E’ necessario tarare i protocolli di stimolazione per le caratteristiche del cervello in età evolutiva
- ✓ Prevedere protocolli di stimolazione specifici partendo dalle alterazioni cerebrali di ciascun disturbo
- ✓ Monitorare i protocolli e prevedere follow-up a lungo termine

UOC Neuropsichiatria Infantile

www.specchioriflesso.net