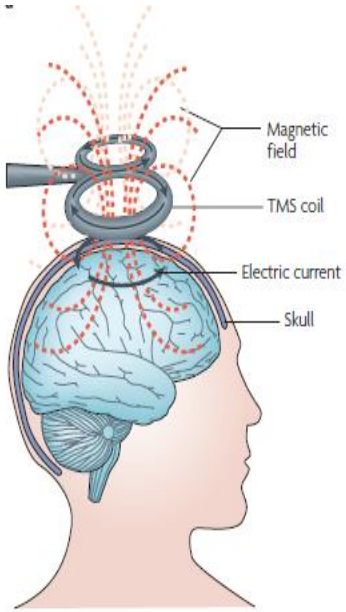
Incontri NPI

La stimolazione cerebrale non invasiva come nuova frontiera terapeutica in Neuropsichiatria



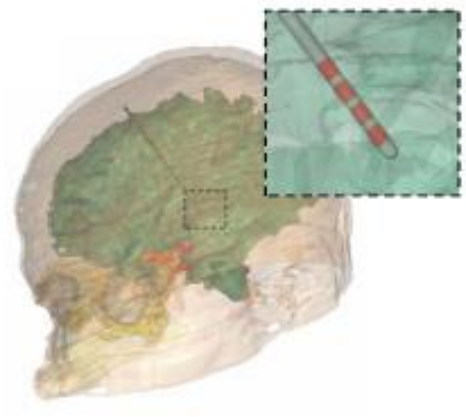
Floriana Costanzo

tDCS Lab

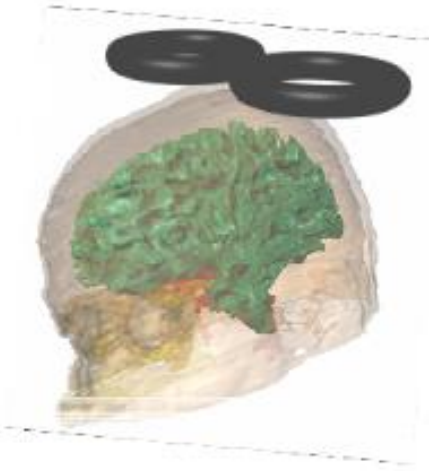
Deny Menghini
Serena Rossi
Cristiana Varuzza
Pamela Varvara

Bambino Gesù
OSPEDALE PEDIATRICO

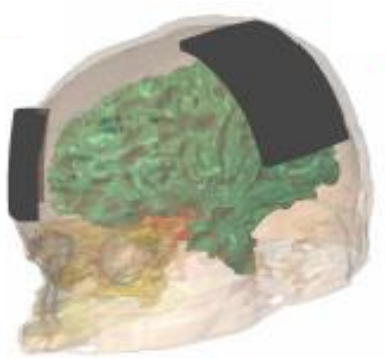
STIMOLAZIONI CEREBRALI



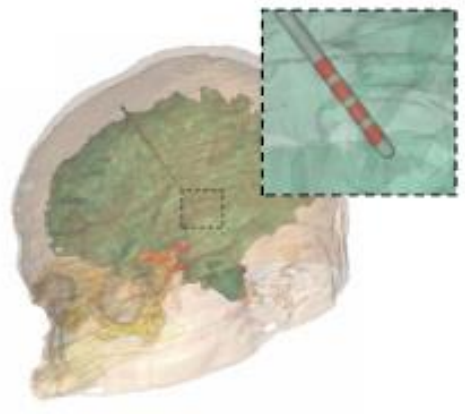
Deep Brain Stimulation



Transcranial Magnetic Stimulation



Transcranial Direct Current Stimulation

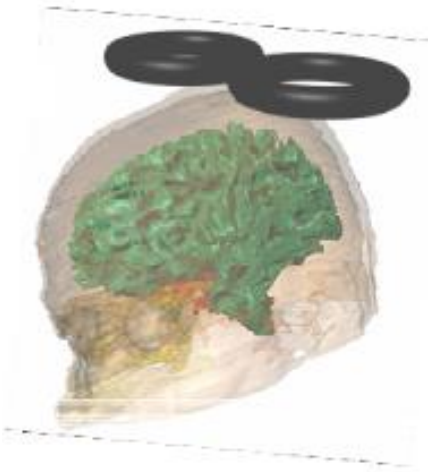


Deep
Brain
Stimulation

Elettrodi impiantati chirurgicamente nel cervello

Parkinson, Depressione, Epilessia, DOC, Autismo

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



Transcranial Magnetic Stimulation

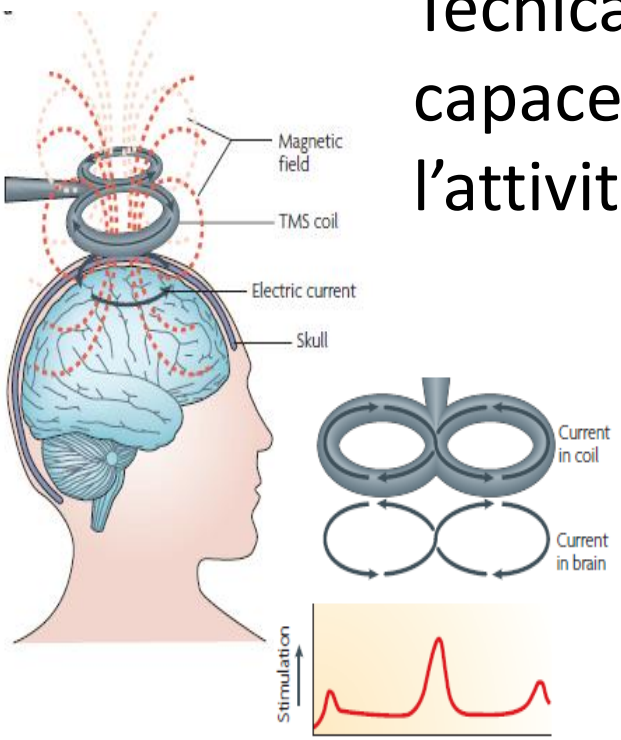
Coil sullo scalpo genera campo magnetico che determina corrente elettrica nel cervello

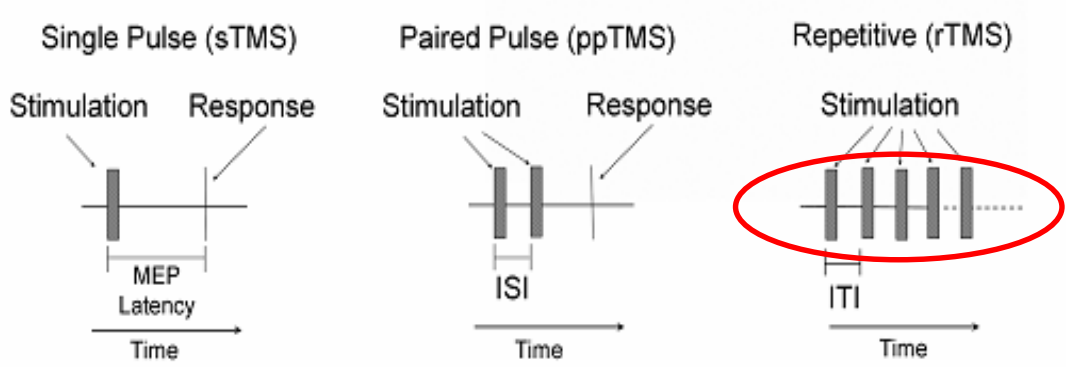
Depressione, Emicrania, Disturbi psichiatrici e cognitivi

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

TRANSCRANIAL MAGNETIC STIMULATION

Tecnica neurofisiologica
capace di modificare transitoriamente
l'attività corticale





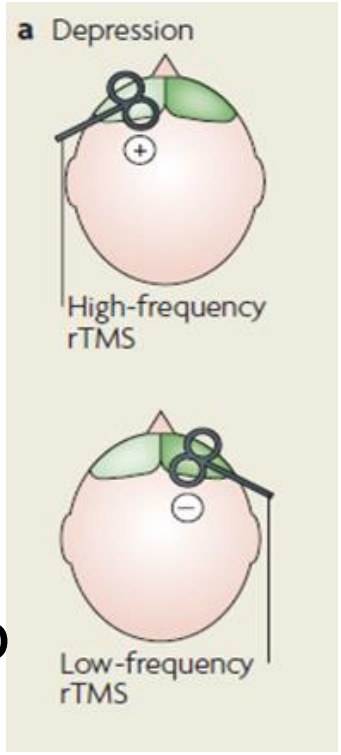
TMS Ripetitiva

Low Frequency (<5Hz):
interferenza inibitoria

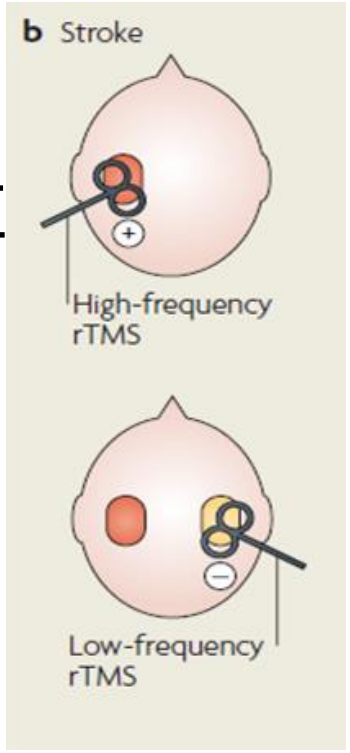
High Frequency (≥5Hz):
facilitazione

APPLICAZIONI TERAPEUTICHE DELLA rTMS

emisfero ipoattivo



FACILITAZIONE

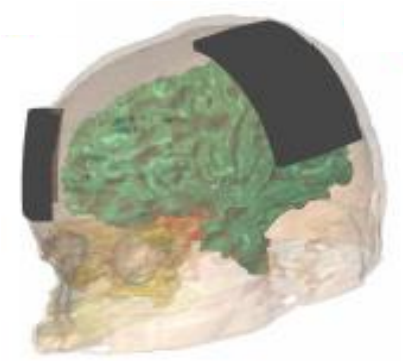


emisfero lesionato

emisfero iperattivo

INIBIZIONE

emisfero sano



Transcranial
Direct
Current
Stimulation

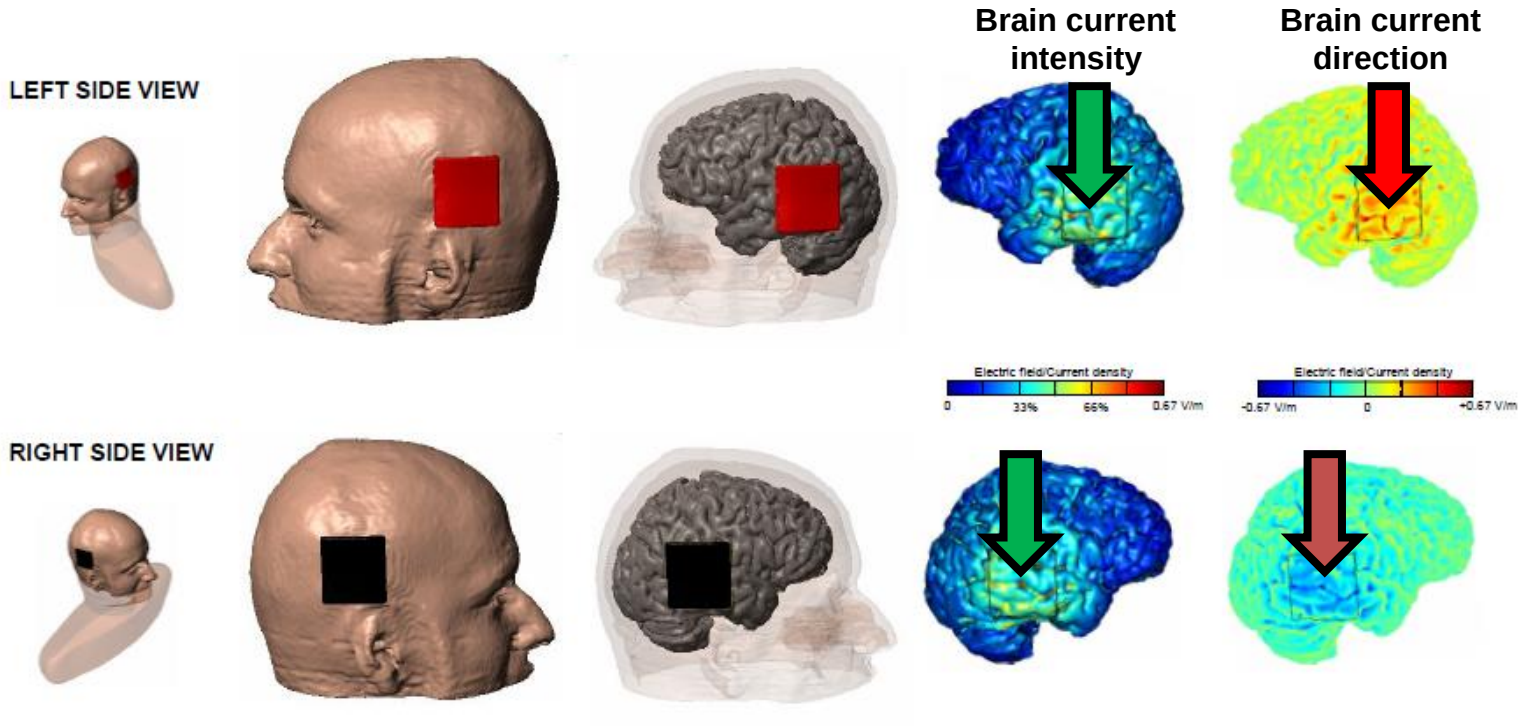
Elettrodi sullo scalpo inviano corrente elettrica debole (tra 0,5 e 2 mA) nel cervello

Abilità cognitive, disturbi psichiatrici, dolore cronico

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

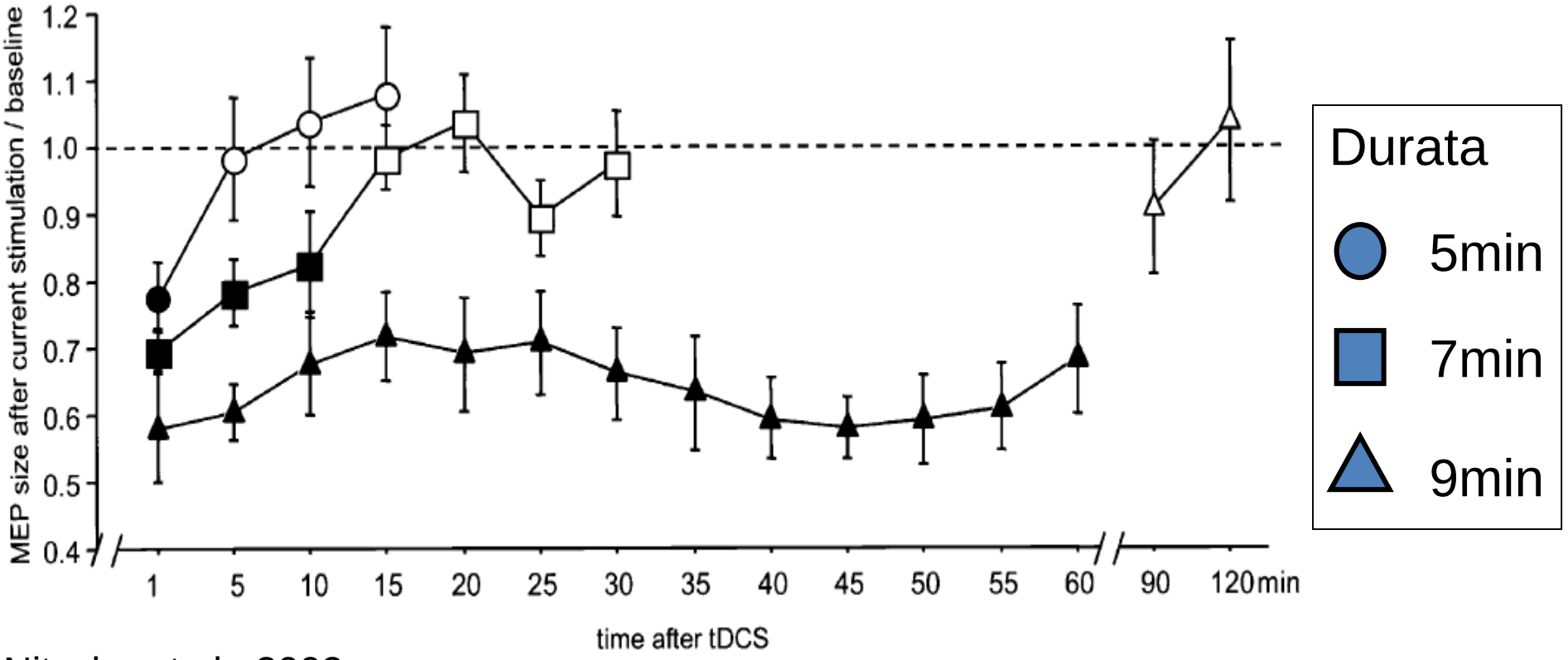
tDCS

- ✓ 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



EFFETTO PERSISTENTE

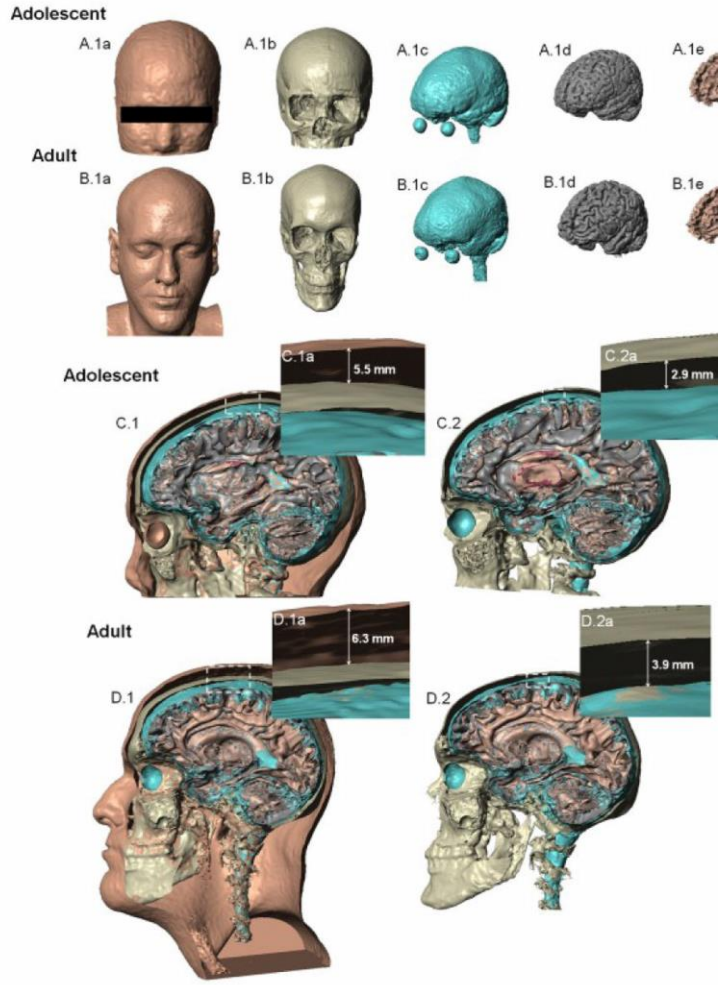
- ✓ L'effetto persiste dopo la fine della stimolazione
- ✓ Più lunga è la stimolazione più lento è il ritorno alla baseline



Nitsche et al., 2003

MODELLIZZAZIONI IN ETÀ EVOLUTIVA

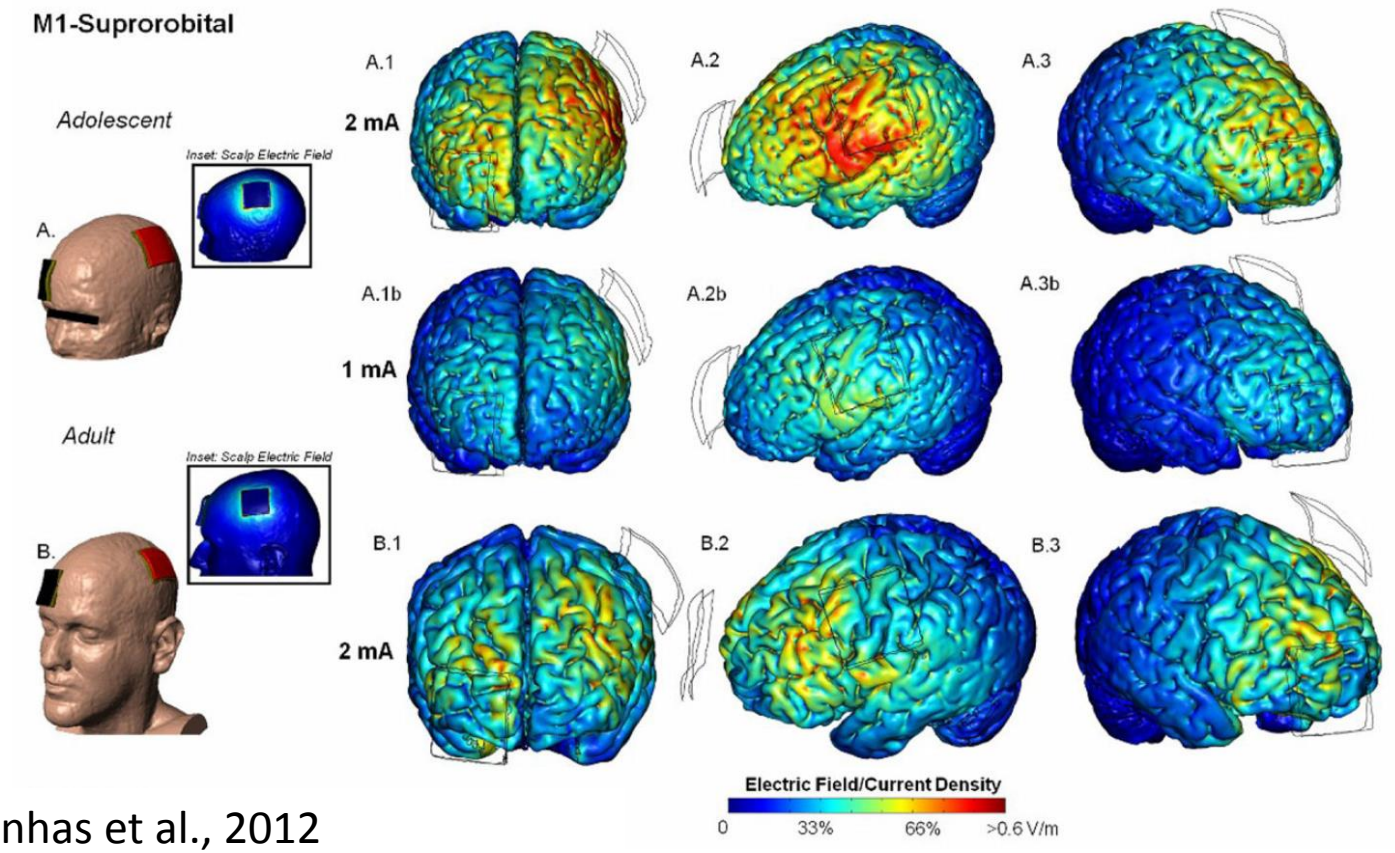
Transcranial Direct Current Stimulation in Pediatric Brain: A computational modeling study



Minhas et al., 2012

MODELLIZZAZIONI IN ETÀ EVOLUTIVA

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



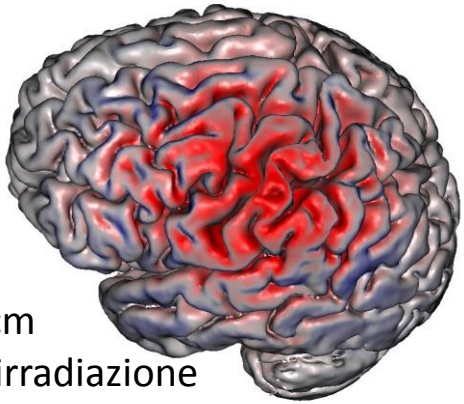
Minhas et al., 2012

tDCS tecniche

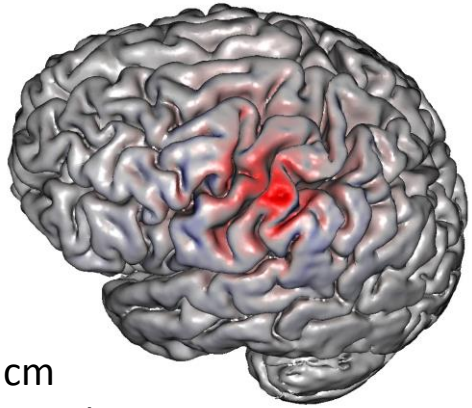
- ✓ tDCS ad alta definizione
- ✓ tACS (transcranial alternating current stimulation) per migliorare la plasticità e sincronizzare i ritmi cerebrali

tDCS AD ALTA DEFINIZIONE

Datta, Bikson, Alam

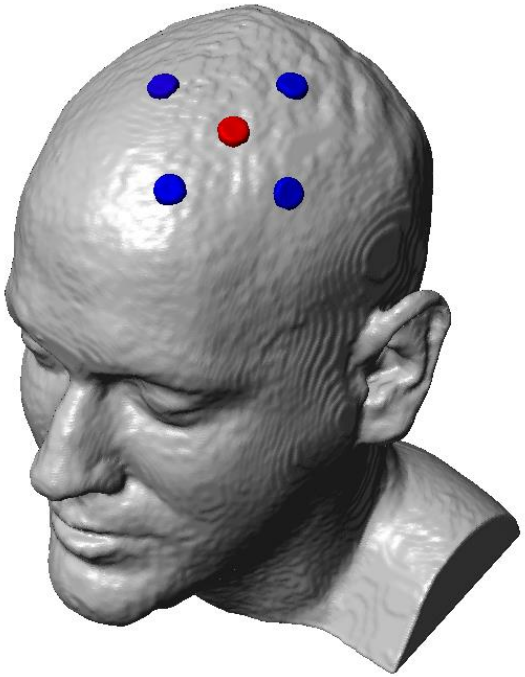


7 cm
di irradiazione

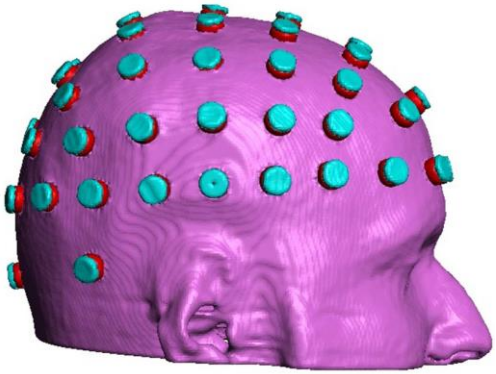


3 cm
di irradiazione

4X1



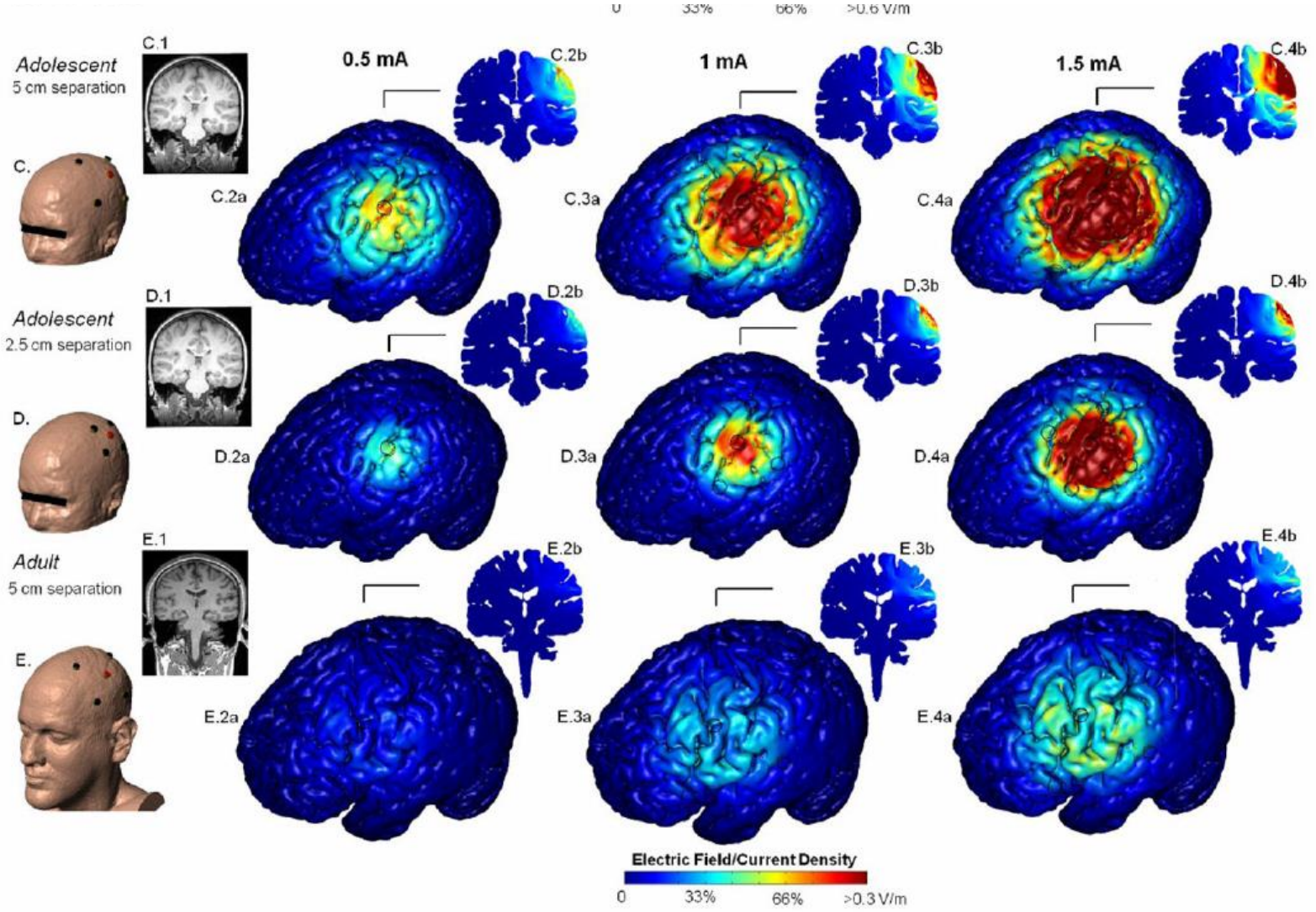
6X6 HD-tDCS
Deep HD-TES



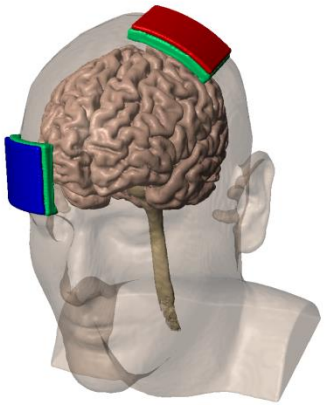
- ✓ Elevato controllo della corrente
- ✓ Focalizzata (target superficiali e profondi)

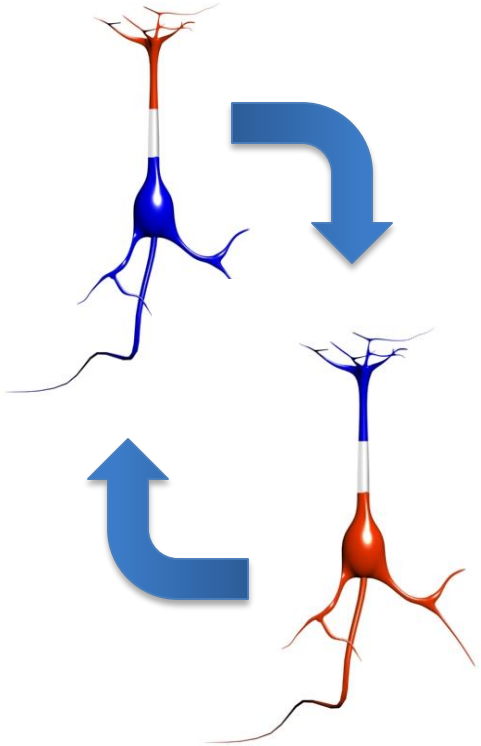
MODELLIZZAZIONI IN ETÀ EVOLUTIVA

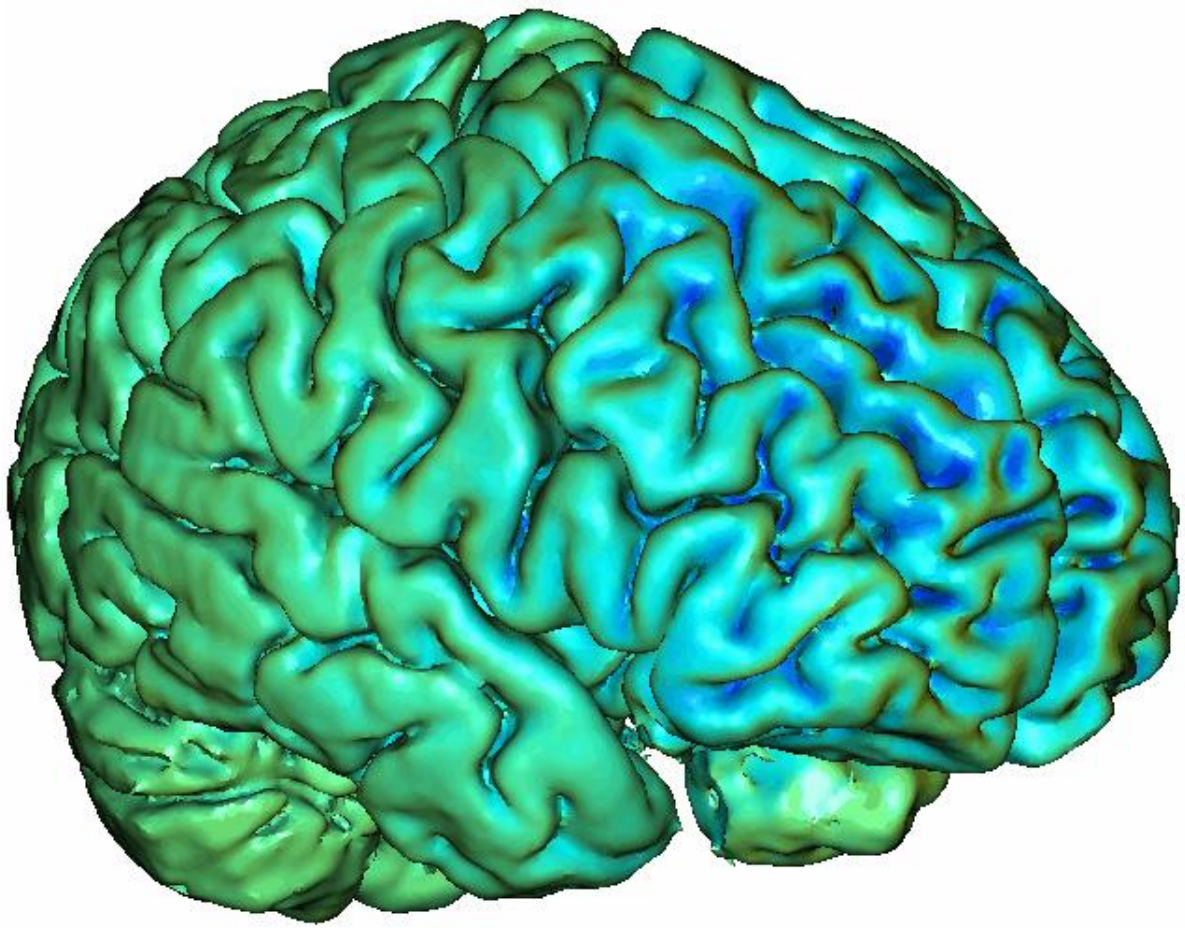
Minhas et al., 2012



tACS



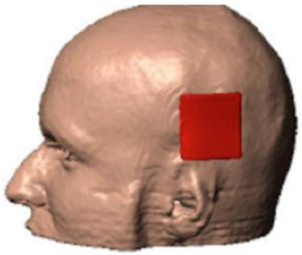


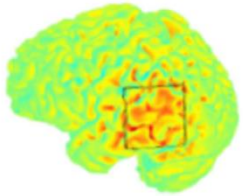


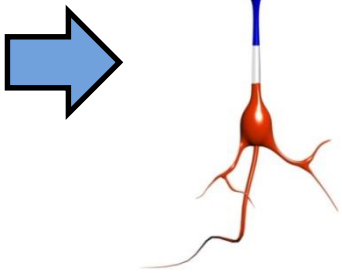
Alterna il flusso di corrente ad una certa frequenza

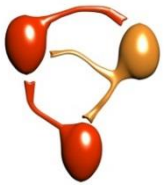
M. Bikson - Practical Course in Transcranial Magnetic and Electrical Stimulation - Gottinga 2014

tACS









tACS

+

TRAINING

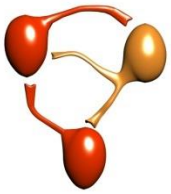
AC flusso di corrente

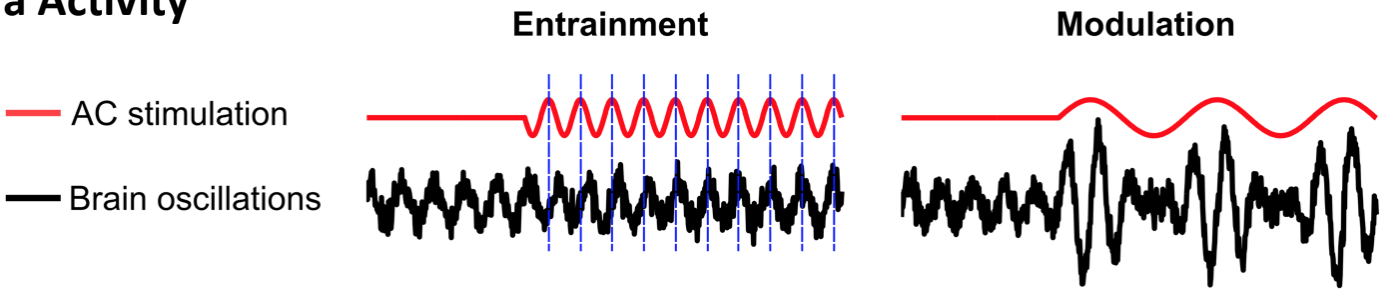
AC polarizzazione cellulare

Aumenta l'attività in corso (oscillazioni)

Meccanismo sinaptico per cambiamenti a lungo termine:
neuroplasticità

Network Gamma Activity

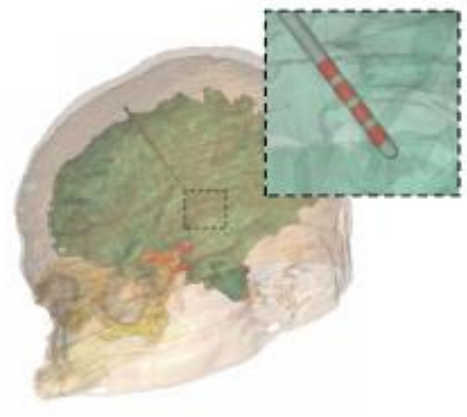




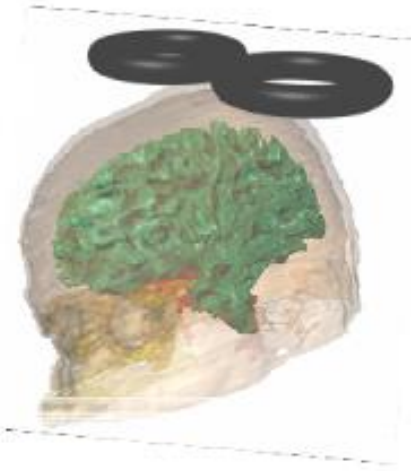
Facilitazione task-specifica: in relazione alla frequenza
target funzionale

Reato et al. 2013

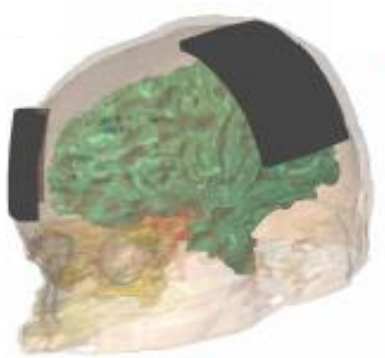
APPLICAZIONI IN ETÀ EVOLUTIVA



Deep Brain Stimulation

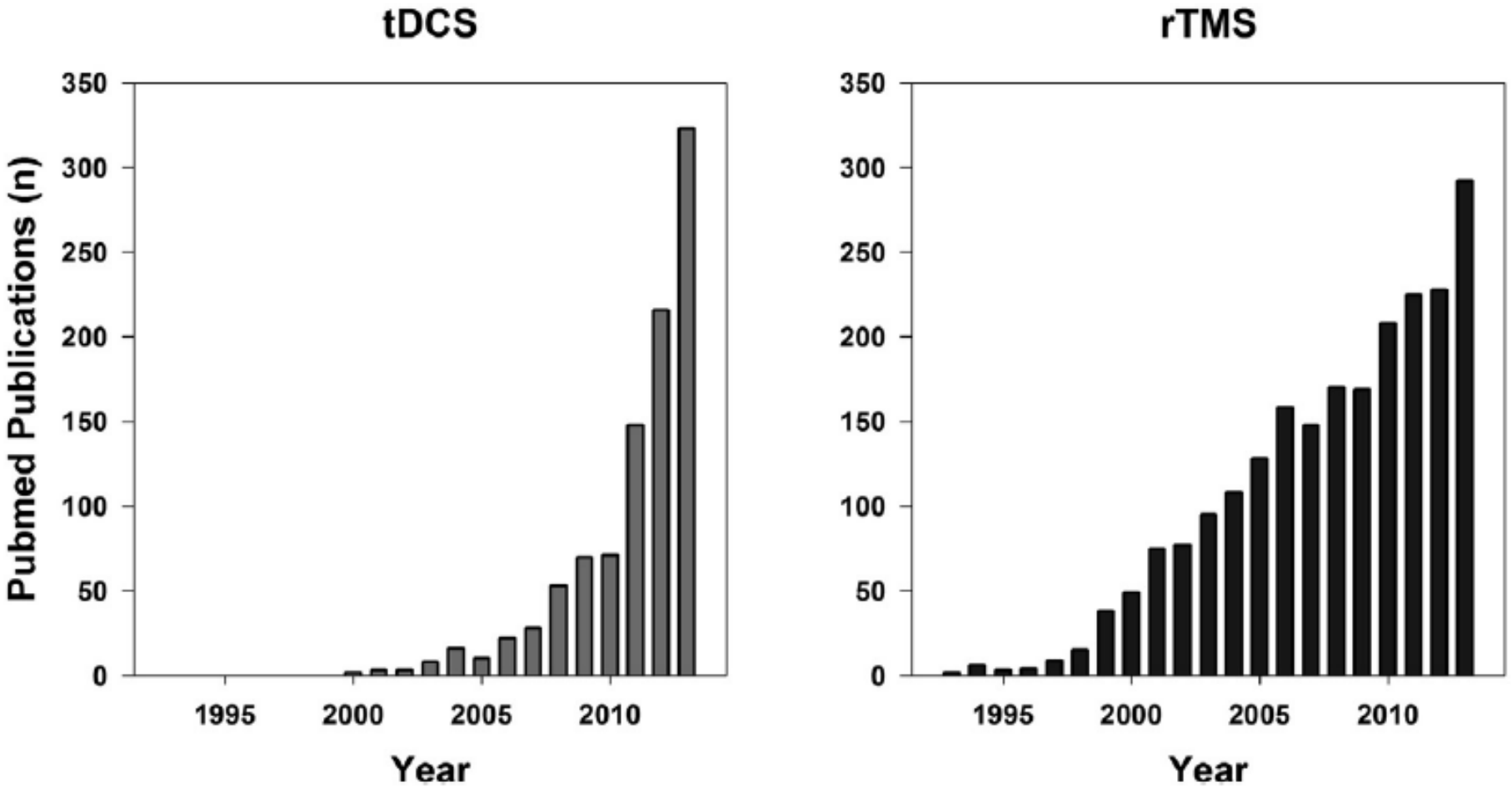


Transcranial Magnetic Stimulation



Transcranial Direct Current Stimulation

CRESCENTE AUMENTO DI STUDI



Krishnan et al., 2015

TOLLERABILITÀ IN ETÀ EVOLUTIVA

Contents lists available at ScienceDirect

Brain Stimulation

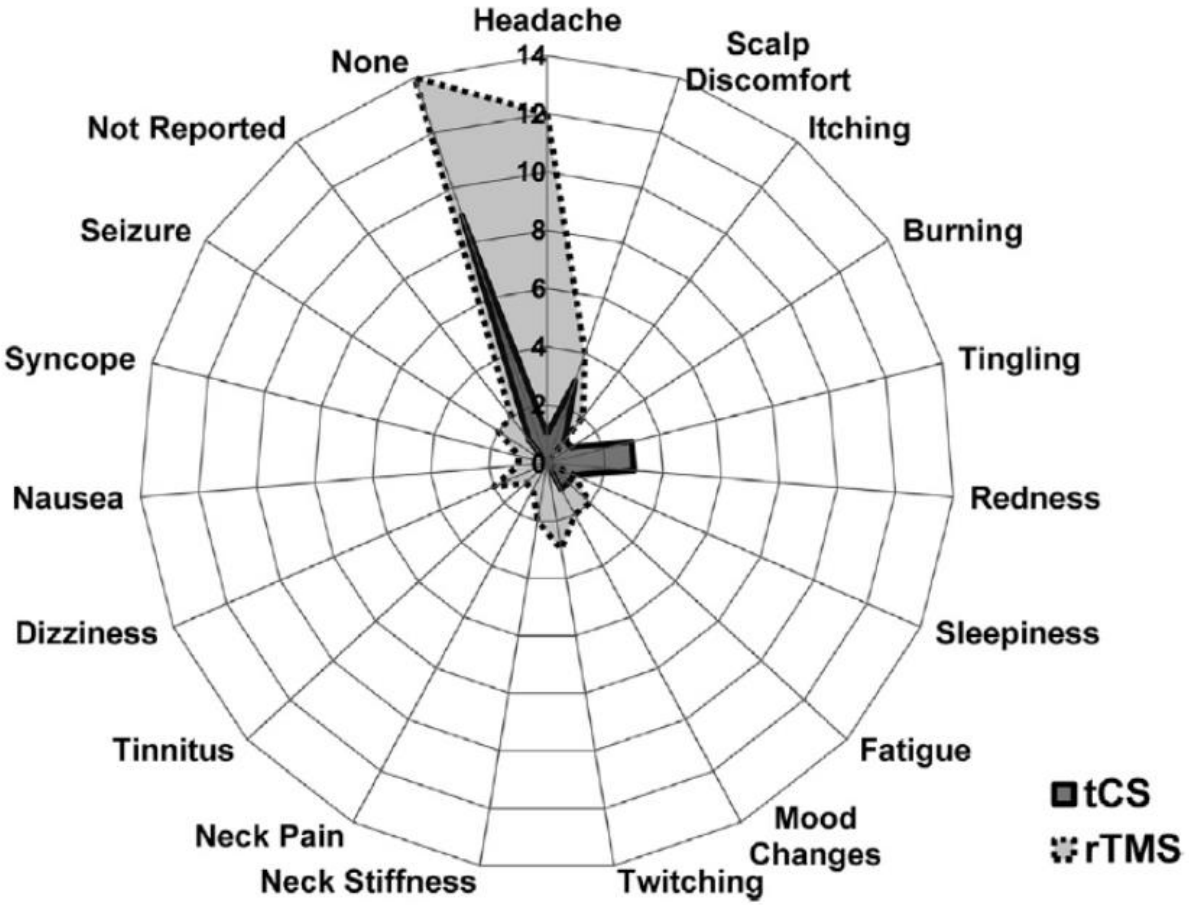
journal homepage: www.brainstimjrnl.com

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)

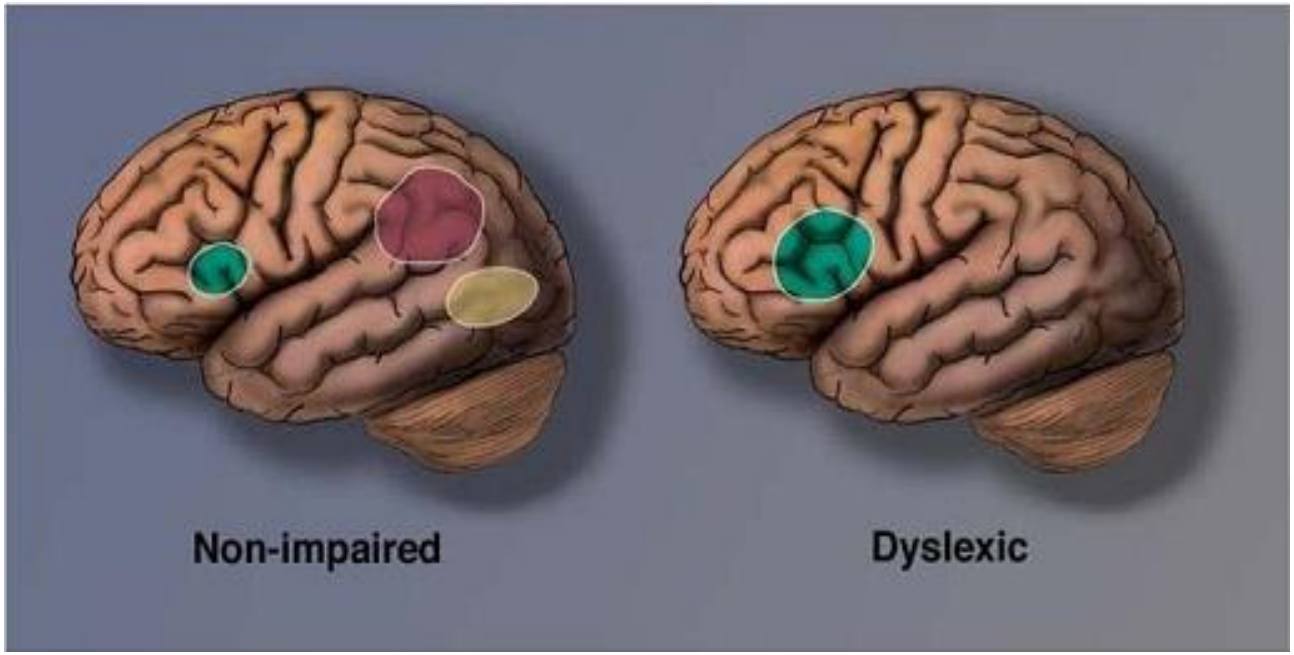
Kinoshita et al. (2005)	7 (1 < 18)	16–33	Extratemporal lobe epilepsy	No adverse effects
Fregni et al. (2006)	27[a]	Mean (SD): 21.6 (7.4) y/20.8 (5.2)	Epilepsy/healthy	Not reported
Loo et al. (2006)	2	16	Depression	No adverse effects
Valle et al. (2007)	17	Mean (SD): 9.1 (3.2)	Cerebral palsy	No adverse 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

STIMOLAZIONE CEREBRALE NON INVASIVA IN POPOLAZIONE PEDIATRICA

- Disturbi di Apprendimento
- Autismo
- ADHD
- Disturbi del comportamento alimentare
- Altri disturbi psichiatrici

STIMOLAZIONE CEREBRALE
E
DISTURBI DI APPRENDIMENTO

Alterazioni cerebrali nei dislessici



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,*]

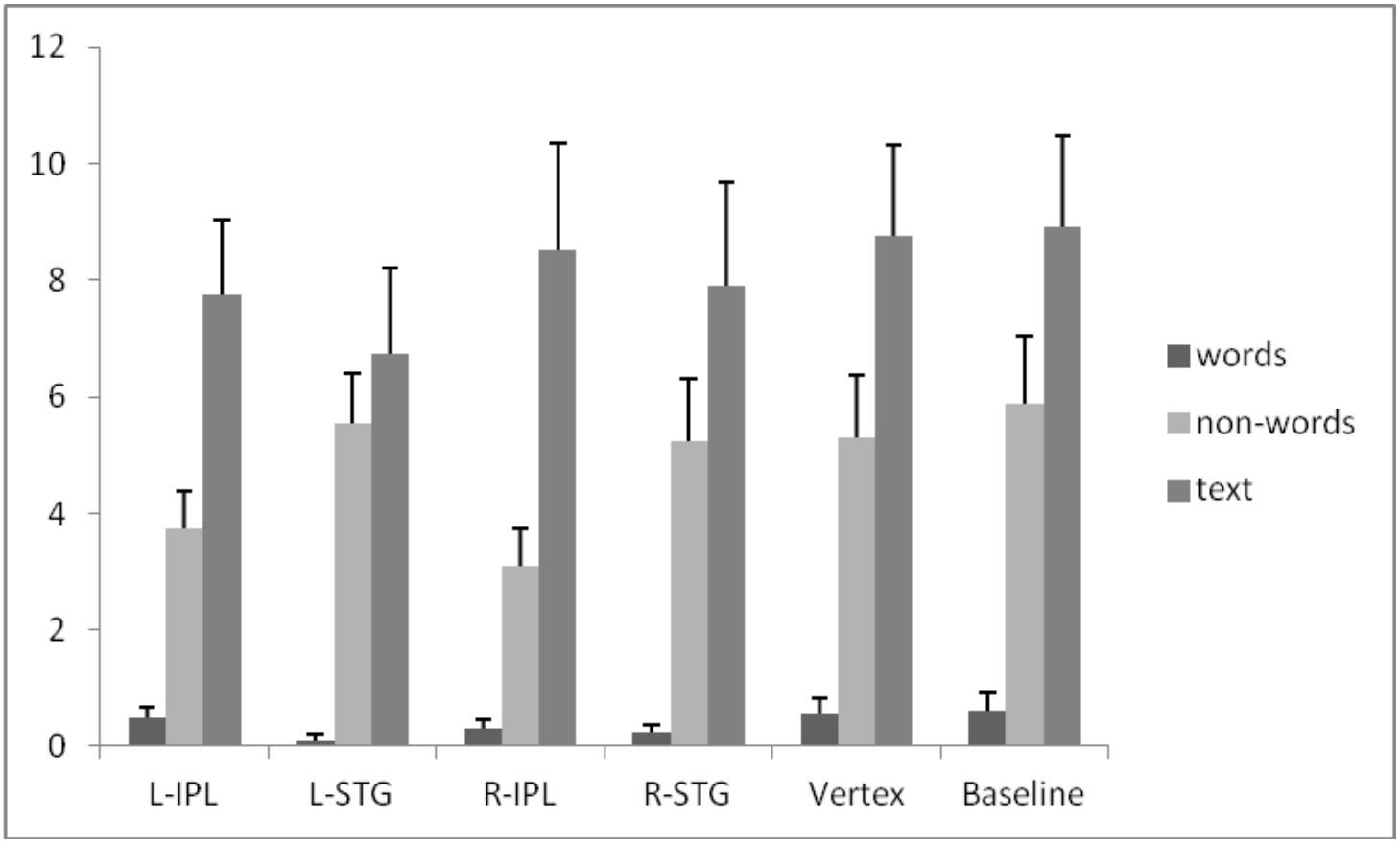
10 dislessici (5M), Età 34 (6,57)

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

TMS E DISLESSIA

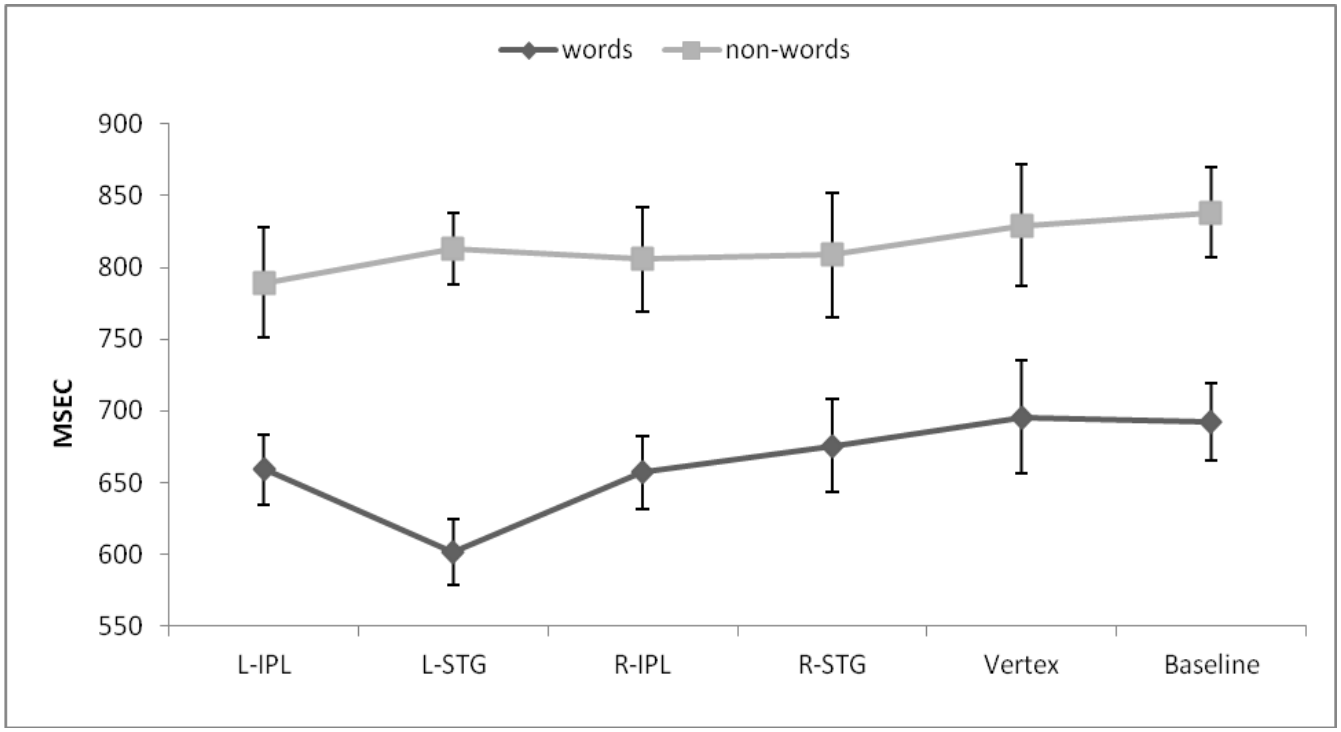
RIDUZIONE ERRORI

Sito e task specifico



TMS E DISLESSIA

RIDUZIONE ONSET Sito e task specifico



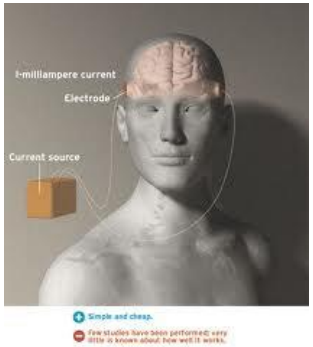
PROSPETTIVE

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*
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TDCS E DISCALCULIA

frontiers in
HUMAN NEUROSCIENCE

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

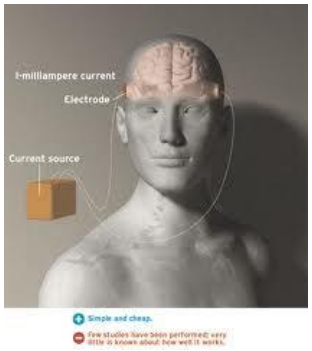
Preliminary evidence for performance enhancement following parietal lobe stimulation in Developmental Dyscalculia

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)

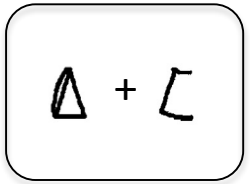
tDCS come training-trattamento 6 sessioni



TDCS E DISCALCULIA

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

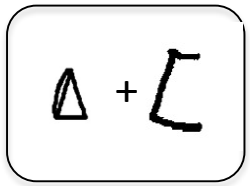
1	2	3	4	5	6	7	8	9
								



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

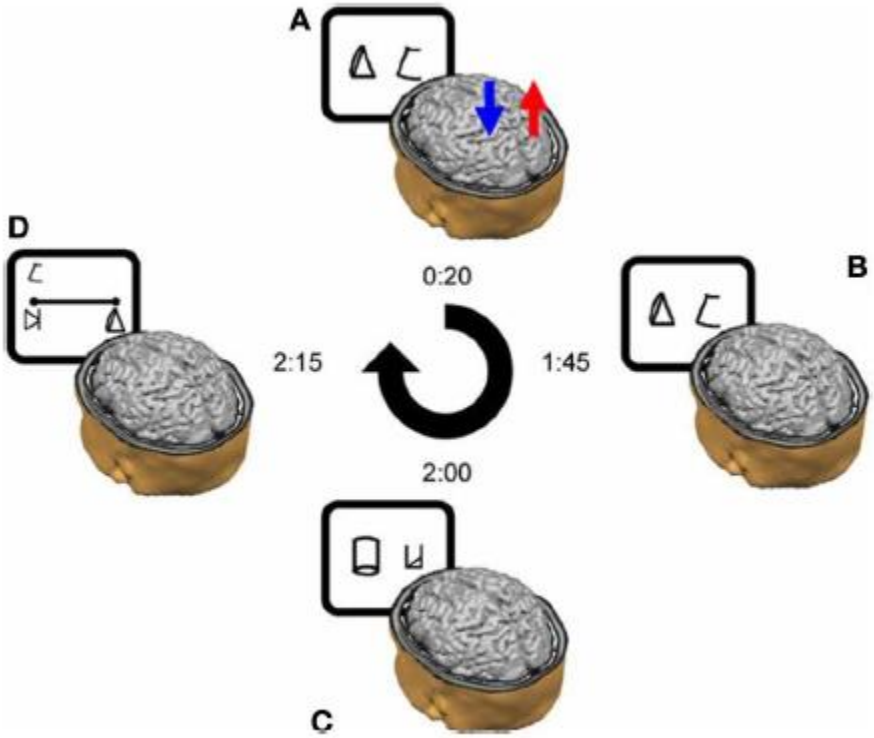
Posizionare il simbolo su una linea orizzontale secondo la grandezza del numero corrispondente.

TDCS E DISCALCULIA

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

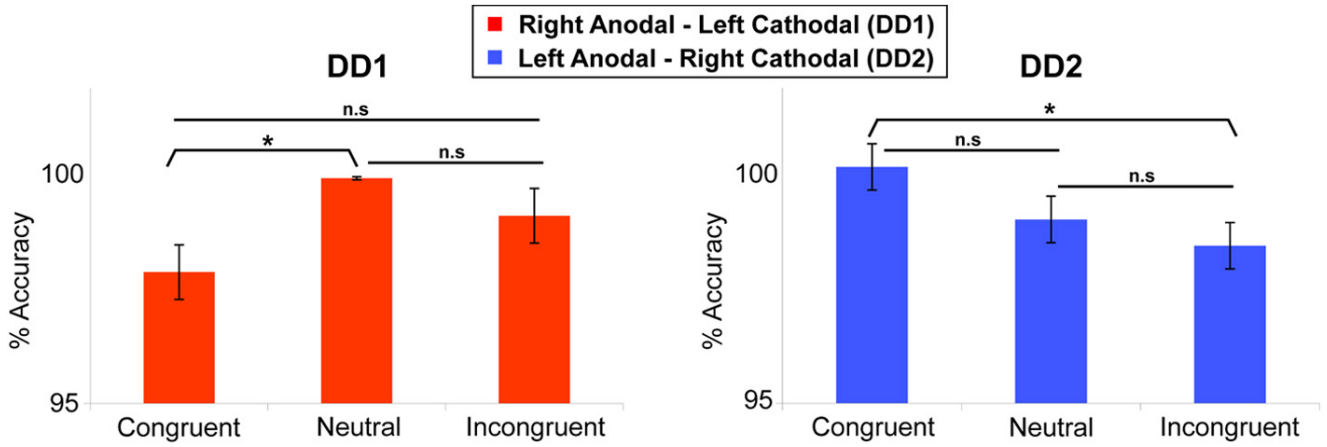
Discalculico1
ANODO a destra
CATODO a sinistra

Discalculico2
ANODO a sinistra
CATODO a destra



TDCS E DISCALCULIA

Effetto di congruenza nel compito di Stroop Numerico: Accuratezza



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

TDCS E DISLESSIA

Contents lists available at ScienceDirect

Neuropsychologia

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

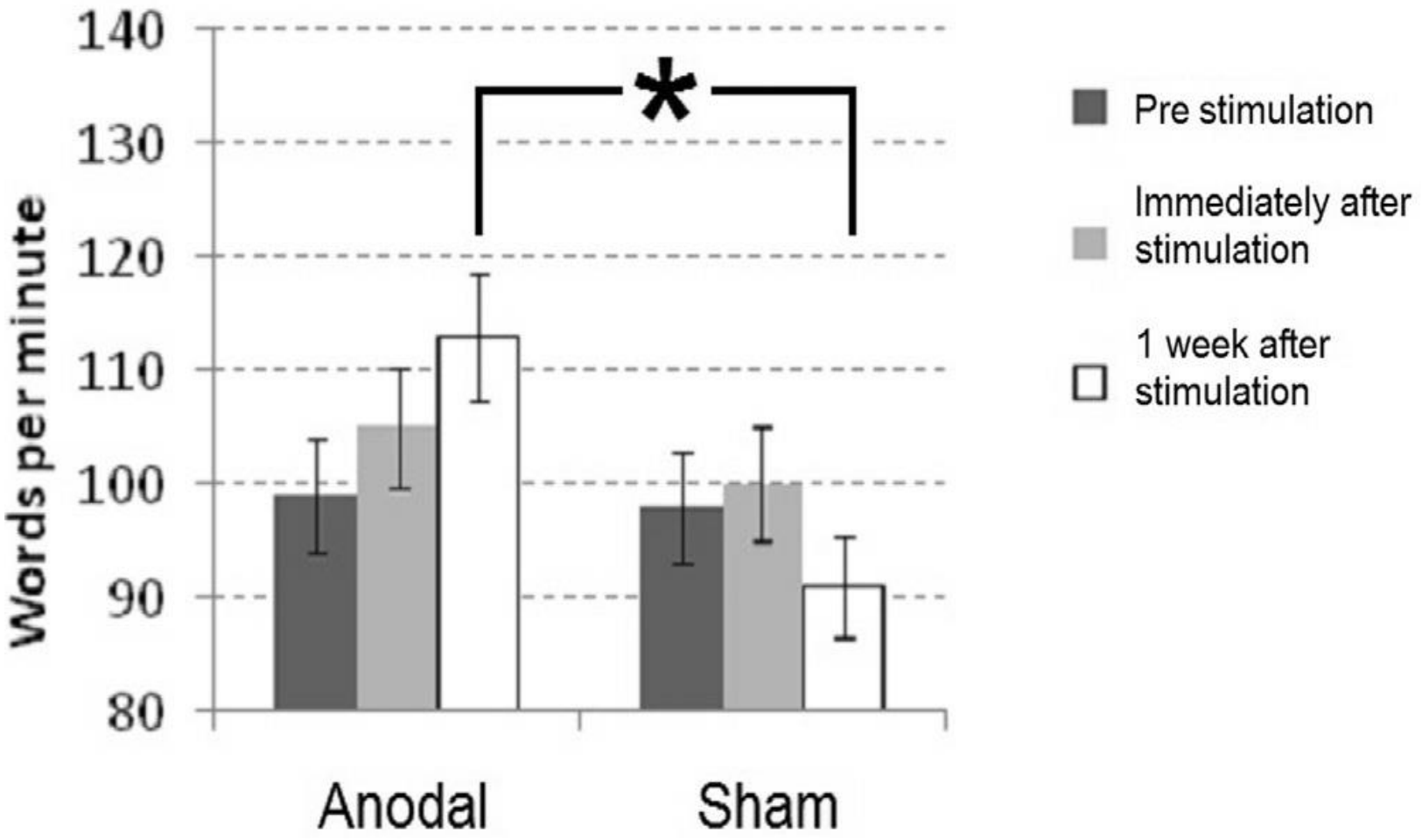
Improved reading measures in adults with dyslexia following transcranial direct current stimulation treatment

Inbahl Heth [a], Michal Lavidor [b,*]

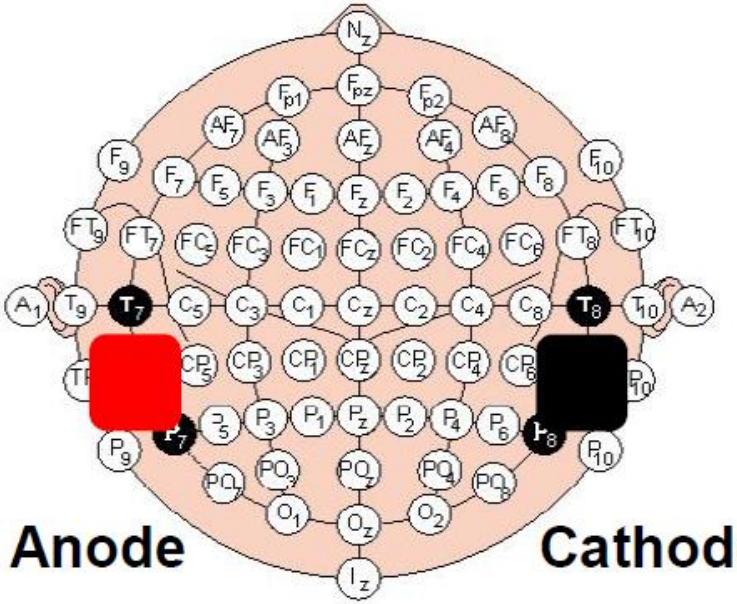
	N	Gender	Age	Years of education
Anodal	10	4 Males	27.2(7.2)	13.8(1.5)
Sham	9	5 Males	24.5(5.2)	13.4(1.3)

1.5 mA corrente per 20 min
Anodica V5/MT
REALE e SHAM
5 giorni consecutivi

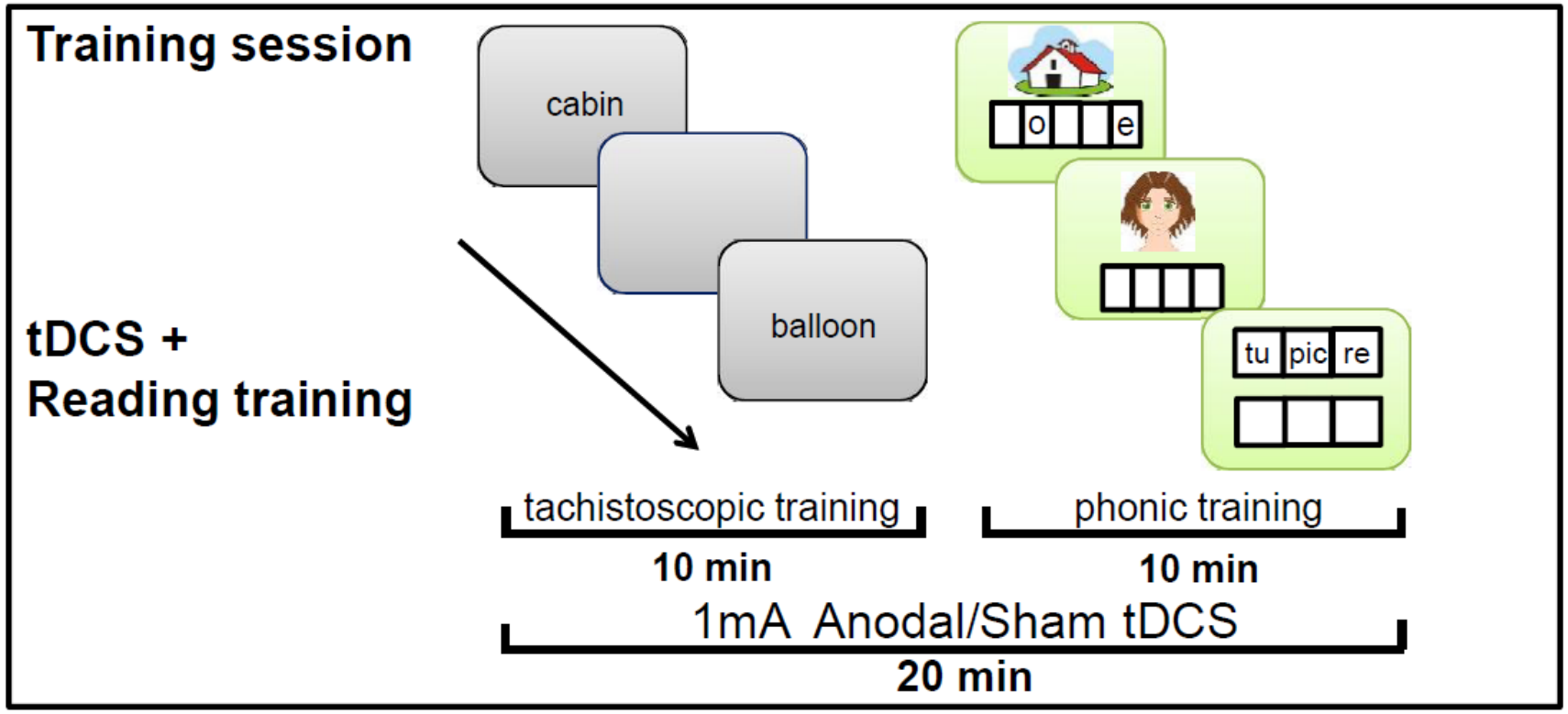
TDCS E DISLESSIA



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

Evidence for reading improvement following tDCS treatment in children and adolescents with Dyslexia

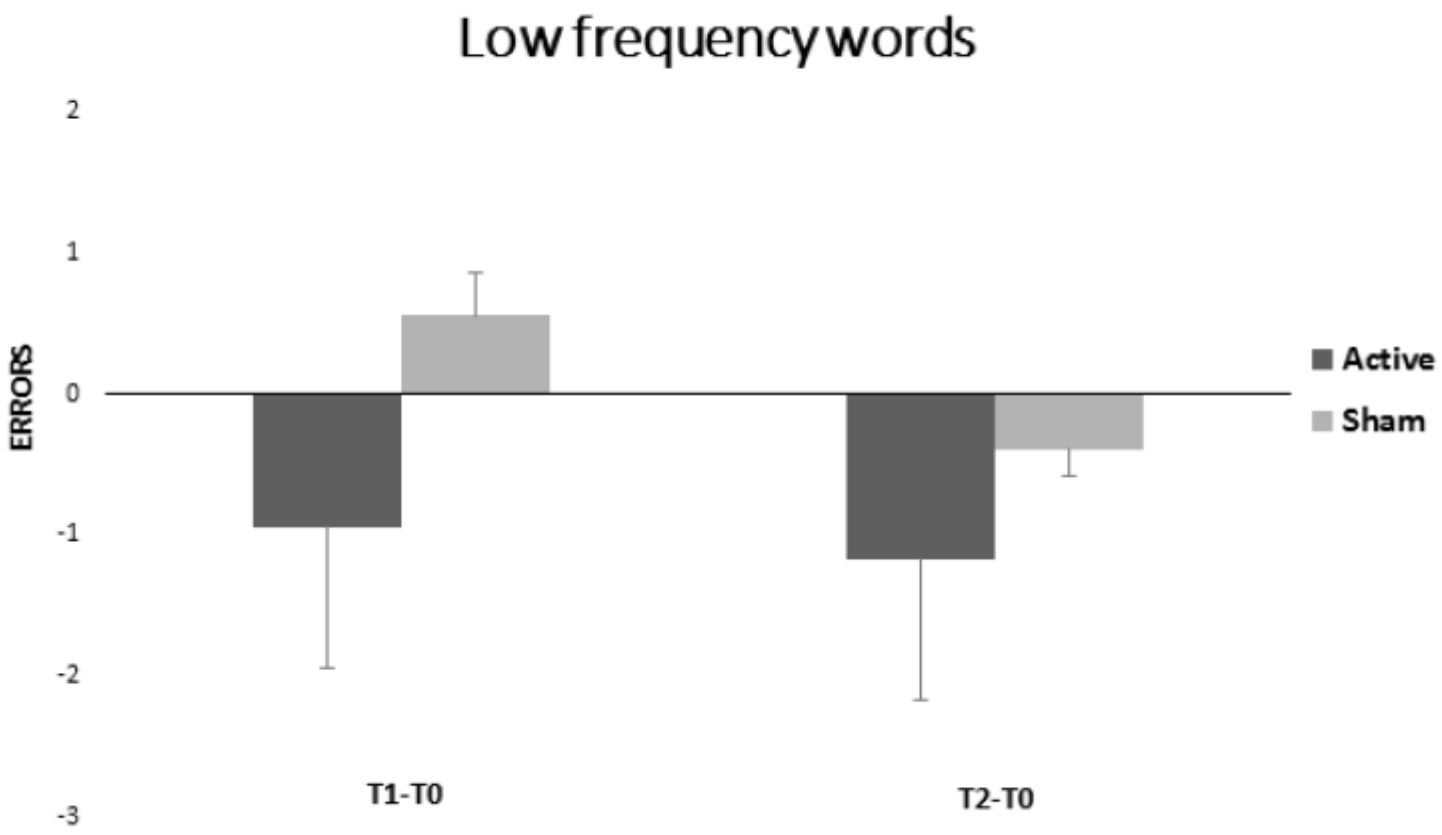
Costanzo F. [1], Varuzza C. [1], Rossi S. [1], Sdoia S. [1], Varvara P. [1], Oliveri M. [2], Koch G. [2], Vicari S. [1] and Menghini D. [1*]

UNDER REVISION

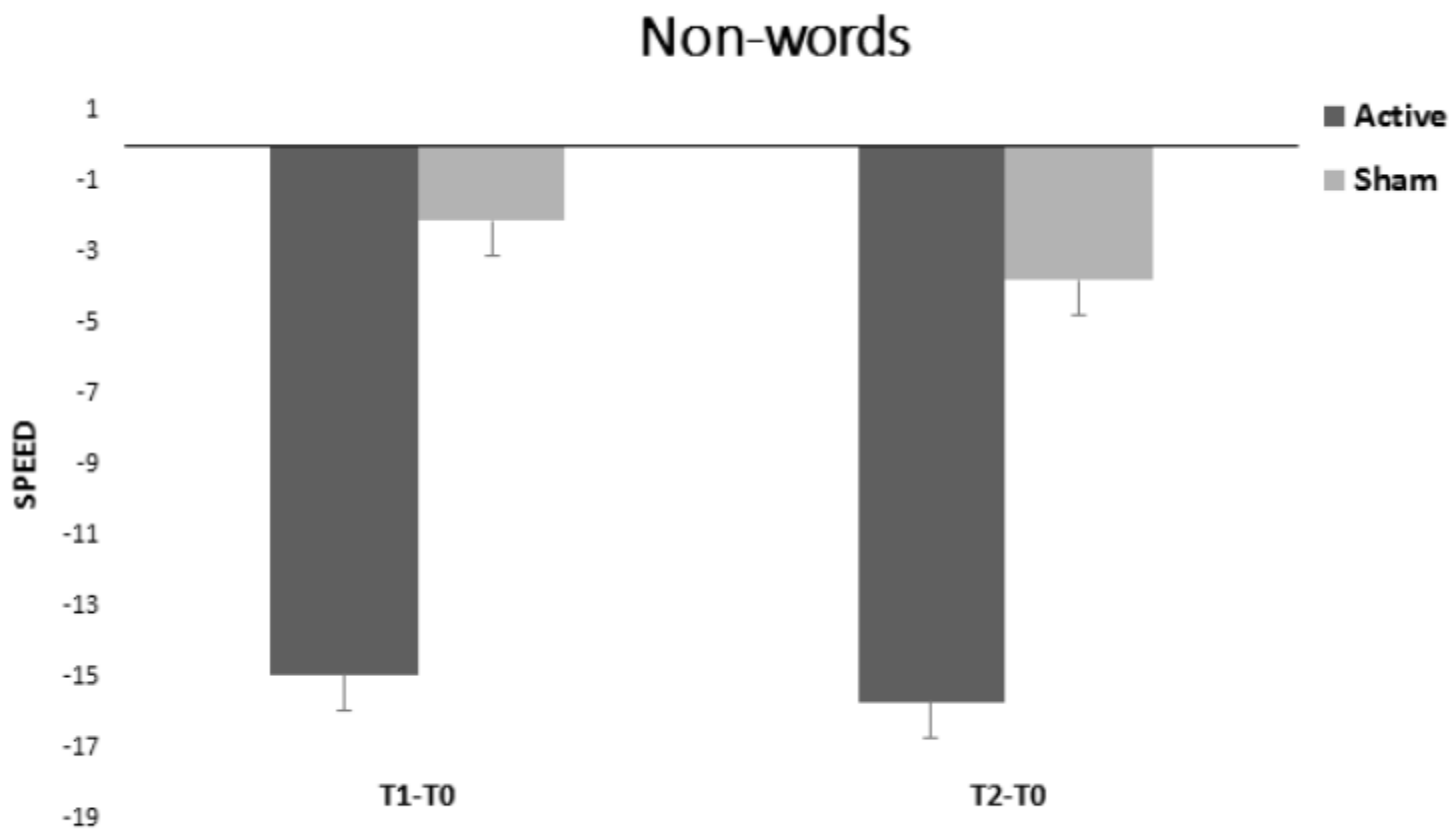
Group	Subject	Sex	Age	IQ[a]	TEXT		HF		LF		NW	
					Err	Spe[a]	Err	Spe[b]	Err	Spe[b]	Err	Spe[b]
Active	1	M	11y9m	102	6	41.4	0.5	23	1.5	26	2	30
Active	2	F	16y8m	136	1	18.2	0	9	2	13	0	18
Active	3	M	10y9m	98	15.5	62.7	2	28	4	48	4	68
Active	4	F	11y11m	110	23.5	43.4	4.5	26	5.5	53	13	89
Active	5	M	11y6m	100	12.5	28	0	11	2.5	20	4	30
Active	6	M	12y6m	110	5.5	48.5	0	20	2	28	0	33
Active	7	F	11y3m	110	16.5	47.3	2	21	2.5	25	6.5	35
Active	8	F	17y1m	118	3	31.2	1	15	1	20	0.5	33
Active	9	F	14y8m	123	5.5	38	0	13.5	0.5	17.2	2.5	29
Sham	10	F	11y1m	120	18.5	32	2	12	2	19	7	27
Sham	11	M	11y1m	110	23.5	76	1.5	30	4	58	9	41
Sham	12	F	12y4m	112	6	26.3	1	11	1.5	1.5	2	18
Sham	13	F	15y6m	94	8	24	0.5	16	0.5	23	0	26
Sham	14	M	12y6m	117	3.5	46	1	15	1	21	2	41
Sham	15	F	16y	100	5	24	1	12	0	10	4	23
Sham	16	F	16y	97	13	34.6	1	18	4	23	2	31
Sham	17	F	15y6m	93	2.5	29.3	0	22	0	23	0	31
Sham	18	F	12y2m	100	19.5	50	3	17	3.5	41	8	34

Note: y = years; m= months; Err = errors; Spe = speed; [a]seconds/sillables x 100; [b]seconds.
TEXT: text; HF: high frequency words; LF: low frequency words; NW: non-words.

RISULTATI



RISULTATI



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

324 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

CONFRONTO ANODICA E CATODICA DISLESSIA

Reading changes in children and adolescents with dyslexia after transcranial direct current stimulation

	Baseline	Left anodal/right cathodal	Right anodal/left cathodal	Sham	$F_{3,51}$	*P*	ηp^2
	M ± SD	M ± SD	M ± SD	M ± SD			
High Frequency Word errors	1 ± 1.2	1 ± 1.5	1.3 ± 2.4	1.1 ± 2.6	1.45	0.24	0.08
High Frequency Word times[a]	18.2 ± 8.7	17.2 ± 8.3	17.6 ± 12.1	19.1 ± 12.2	1	0.41	0.06
Low Frequency Word errors	1.9 ± 1.7	2 ± 2.1	2.2 ± 2.9	1.8 ± 2.4	1.96	0.13	0.10
Low Frequency Word times[a]	25.3 ± 12.4	24.7 ± 12.3	26.9 ± 20.3	25.9 ± 13.9	0.68	0.57	0.04
Non-word Reading errors	3.3 ± 3.2	3.5 ± 4.3	3.4 ± 3.5	3.7 ± 4.1	.73	0.54	0.04
Non-word Reading times[a]	36 ± 17.2	32.9 ± 12.5	32.7 ± 13.2	35.5 ± 25.5	.93	0.43	0.05
Text Reading errors	9 ± 6.6	7.7 ± 7.1	10.8 ± 9.2	9.1 ± 8.1	7.21	<.001*	0.30
Text Reading times[b]	37.9 ± 17.1	38 ± 18.3	37.5 ± 19.2	38.9 ± 18.2	0.38	0.77	0.02
Lexical Decision[c]	1393.6 ± 304	1203.4 ± 360.4	1309 ± 414.7	1289.2 ± 351.4	1.37	0.26	0.08
Phoneme Blending accuracy[d]	4.8 ± 2.1	5.3 ± 2.3	5.9 ± 2.1	5.8 ± 2.1	4.12	0.01*	0.20
Phoneme Blending times[a]	34.8 ± 30.7	26.1 ± 15.5	28.2 ± 22.8	30.8 ± 27	3.18	0.03*	0.20
Verbal N-back score	2.4 ± .6	2.5 ± .5	2.7 ± .4	2.6 ± .5	2.79	< 0.05*	0.10
Letter RAN[a]	3.9 ± 1.2	3.4 ± .7	3.7 ± .9	4.1 ± 1.5	1.26	0.30	0.07
Color RAN[a]	5.3 ± 1.5	4.9 ± 1.2	4.9 ± 1.4	5.2 ± 1.7	.77	0.52	0.05

1 sessione 20 min
1mA tDCS

CONDIZIONI:
Baseline
Anodica
Carodica
Sham

	Baseline	Left anodal/right cathodal	Right anodal/left cathodal	Sham	$F_{3,51}$	P	ηp^2
	M ± SD	M ± SD	M ± SD	M ± SD			
Non-word Reading errors	3.3 ± 3.2	3.5 ± 4.3	3.4 ± 3.5	3.7 ± 4.1	.73	0.54	0.04
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Text Reading errors	9 ± 6.6	7.7 ± 7.1	10.8 ± 9.2	9.1 ± 8.1	7.21	<.001*	0.30
Text Reading times[b]	37.9 ± 17.1	38 ± 18.3	37.5 ± 19.2	38.9 ± 18.2	0.38	0.77	0.02

	Baseline	Left anodal/right cathodal	Right anodal/left cathodal	Sham	$F_{3,51}$	P	ηp^2
	M ± SD	M ± SD	M ± SD	M ± SD			
Phoneme Blending accuracy[d]	4.8 ± 2.1	5.3 ± 2.3	5.9 ± 2.1	5.8 ± 2.1	4.12	0.01*	0.20
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Verbal N-back score	2.4 ± .6	2.5 ± .5	2.7 ± .4	2.6 ± .5	2.79	< 0.05*	0.10
Letter RAN[a]	3.9 ± 1.2	3.4 ± .7	3.7 ± .9	4.1 ± 1.5	1.26	0.30	0.07

	Baseline	Left anodal/right cathodal	Right anodal/left cathodal	Sham	$F_{3,51}$	P	ηp^2
	M ± SD	M ± SD	M ± SD	M ± SD			
Color RAN[a]	5.3 ± 1.5	4.9 ± 1.2	4.9 ± 1.4	5.2 ± 1.7	.77	0.52	0.05
Lexical Decision[c]	1393.6 ± 304	1203.4 ± 360.4	1309 ± 414.7	1289.2 ± 351.4	1.37	0.26	0.08

Brain stimulation e Autismo

Promoting social plasticity in developmental disorders with non-invasive brain stimulation techniques

Paulo S. Boggio, Manish K. Asthana, Thiago L. Costa, Cláudia A. Valasek and Ana A. C. Osório*

frontiers in Neuroscience

REVIEW
published: 01 September 2015
doi: 10.3389/fnins.2015.00294

Revisione di studi con tecniche di neuromodulazione
per promuovere la Plasticità Sociale nei disturbi dello sviluppo

AUTISMO → numerosi studi DLPF e TPJ
SCHIZOFRENIA → pochi studi L-DLPF
SINDROME DI WILLIAMS → no studi: ipotesi circuito prefrontale-amigdala

Brain stimulation e Autismo

TABLE 1 | Summary of parameters and results for papers employing TMS or tDCS in developmental disorders.

References	Condition and sample size	Age	Stimulation Parameters	Results
Théoret et al., 2005	ASD = 10	23–58	One session of single-pulse TMS and ppTMS over M1*.	Cortical excitability in ASD group was significantly lower. No group difference in RMT* or response to ppTMS.
Enticott et al., 2012	ASD = 34	M = 26.32	One session of single-pulse TMS over M1*.	Observation of single static hand stimuli don't induce difference in degree of coticospinal excitabilitay in both groups.
Minio-Paluello et al., 2009	ASD = 16	M = 28	One session of single-pulse TMS over M1*.	Observation of painful movements don't induce corticospinal modulation in ASD group.
Puzzo et al., 2009	ASD = 20	ASD—low traits group: M = 23.7 ASD—high traits group: M = 24.5	One session of single-pulse TMS over M1*.	No difference between the groups regarding the images in White screen was observed. In observation of actions videos compared to static images participants with low traits of autism exhibited higher MEP amplitudes. This result wasn't observed in high traits of autism group.
Sokhadze et al., 2009	ASD = 8	12–27	rTMS- 150 pulses at 0.5 Hz and 90% RMT* over left DLPFC* twice per week during 3 weeks.	Normalization in event-related potencial—P300 and was induced gamma frequency eletroencephalography activity. In addition, was observed a reduction in ritualistic behavior.
Sokhadze et al., 2010	ASD = 13	9–27	rTMS- 150 pulses at 0.5 Hz and 90% RMT over left DLPFC* twice per week during 3 weeks.	The post-tests scores showed a reduction in repetitive-ritualistic behavior in the stimulated.
Baruth et al., 2010	ASD = 16	9–26	rTMS- 150 pulses at 1 Hz and 90% RMT over left DLPFC once per week during 6 weeks. The same protocol was applied over the right DLPFC*.	Improvement in repetitive behaviors and irritability reported by their caregivers.
Casanova et al., 2012	ASD = 25	9–19	rTMS- 150 pulses at 1 Hz and 90% RMT over left DLPFC* once per week during 6 weeks. The same protocol was applied over the right DLPFC.	The results showed better accuracy on the selective attention task, improvements in ERP index of visual processing and improvement in repetitive behaviors and irritability reported.
Sokhadze et al., 2012	ASD = 20	9–21	rTMS- 150 pulses at 1 Hz and 90% RMT over left DLPFC* once per week during 6 weeks. The same protocol was applied over the right DLPFC.	The post-test showed improvement in ERP index and better performance in the error monitoring task.
Enticott et al., 2014	ASD = 28	18–59	Deep bilateral rTMS over DMPFC* at 5 Hz during 15 min for 15 consecutive days.	Significant reduction in social relating symptoms. Significant reduction in self-oriented anxiety during difficult and emotional social situations.
Sokhadze et al., 2014	ASD = 27	9–21	rTMS—18 sessions of 1 Hz over DLPFC*, combined with neurofeedback.	Results showed modulation/normalization of many electrophysiological markers and behavioral reaction during executive function test and a decrease in social withdrawal scores.
D'Urso et al., 2015	ASD = 12	18–26	Ten daily sessions of cathodal tDCS over left DLPFC*—20 min/1.5 mA.	Forty-five percentage decrease in social withdrawal scores and a 58% decrease in hyperactivity (as measured in the ABC scale).

(Continued)

Brain stimulation e Autismo

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]*

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 facilitatoria L-DLPC, facilitatoria L-TPJ e inibitoria R-TPJ

Brain stimulation e Autismo

frontiers in
HUMAN NEUROSCIENCE

OPINION ARTICLE
published: 06 January 2015
doi: 10.3389/fnhum.2014.01034

Transcranial magnetic stimulation (TMS) therapy for autism: an international consensus conference held in conjunction with the international meeting for autism research on May 13th and 14th, 2014

Lindsay M. Oberman[1], Peter G. Enticott[2], Manuel F. Casanova[3], Alexander Rotenberg[4,5], Alvaro Pascual-Leone[5] and James T. McCracken[6]*

Enticott et al.,2014→ TMS ad alta frequenza per aumentare l'eccitabilità corticale nella corteccia prefrontale mediale migliora ansia sociale e self-report relazione sociale

Conclusione della conferenza → **entusiasmo sull'uso potenziale della TMS nella clinica dell'autismo**

tDCS e Autismo

Primo studio tdCS:

The use of the Bilingual Aphasia test for assessment and transcranial direct current stimulation to modulate language acquisition in minimally verbal children wtith Autism.

Schneider e Hopp
Clin Linguist Phon 2011, 25 (6-7):640-54

Stimolazione facilitatoria area broca (anodica a sx)
(0,8 mA, 20 min) → migliora test vocabolario

Concludono → **tDCS anodica trattamento sintassi in autismo**

Brain stimulation e Autismo

Clinical Study

Behavioural Neurology
Volume 2015, Article ID 928631, 11 pages

The Short-Term Effects of Transcranial Direct Current Stimulation on Electroencephalography in Children with Autism: A Randomized Crossover Controlled Trial

Anuwat Amatachaya,[1] Mark P. Jensen,[2] Niramol Patjanasoontorn,[3] Narong Auvichayapat,[4] Chanyut Suphakunpinyo,[4] Suparerk Janjarasjitt,[5] Niran Ngernyam,[1] Benchaporn Aree-uea,[1] and Paradee Auvichayapat[1]

Ridotta attività alfa → anomala mturazione e plasticità corticale nell'ASD
Obiettivo: effetto tDCS sul picco di frequenza Alfa e valutazione autismo (ATEC).

20 bambini con autismo M -> età 5-8 aa
1 sessione tDCS attiva/sham (1mA 20 min)
L-DLPF anodica (F3), mastoide per elettrodo referente

Brain stimulation e Autismo

Channel	Active condition					Sham condition				
	Baseline	Immediately	24 hours	48 hours	72 hours	Baseline	Immediately	24 hours	48 hours	72 hours
Fp1	8.98	9.34*	9.05	8.84	9.17	8.96	8.98	8.99	8.95	8.95
Fp2	8.93	8.80	9.02	9.03	9.50*	8.96	8.98	8.98	8.95	8.98
F7	8.88	9.39**	9.19	9.08	9.19	8.85	8.86	8.83	8.87	8.85
F3	8.47	9.01***	9.09**	8.69	8.54	8.51	8.49	8.60	8.58	8.55
Fz	8.94	9.34*	9.18	9.04	9.23	8.88	8.89	8.89	8.89	8.91
F4	8.83	9.09	8.81	9.00	9.08	8.82	8.84	8.83	8.83	8.84
F8	8.77	9.01	9.02	8.84	9.15	8.76	8.78	8.82	8.77	8.79
T3	8.83	9.08	8.91	8.97	9.09	8.82	8.86	8.83	8.83	8.82
C3	8.98	9.17	9.07	9.11	9.21	8.87	8.84	8.93	8.97	8.90
C4	9.39	9.29	9.24	9.44	9.42	9.35	9.27	9.28	9.32	9.35
T4	9.01	8.98	8.98	9.18	9.24	8.99	8.97	8.95	9.00	9.09
T5	9.49	9.00	9.16	9.17	9.36	9.40	9.36	9.35	9.24	9.35
P3	9.49	9.14	9.21	9.27	9.60	9.40	9.38	9.34	9.38	9.43
Pz	9.12	9.25	9.25	9.19	9.36	9.12	9.14	9.13	9.14	9.23
P4	9.43	9.19	9.20	9.55	9.33	9.30	9.24	9.20	9.30	9.30
T6	9.23	9.48	9.07	9.08	9.24	9.17	9.22	9.09	9.10	9.12
O1	9.70	9.39	9.41	9.54	9.54	9.65	9.62	9.57	9.59	9.55
O2	9.53	9.40	9.26	9.70	9.59	9.50	9.47	9.45	9.49	9.52

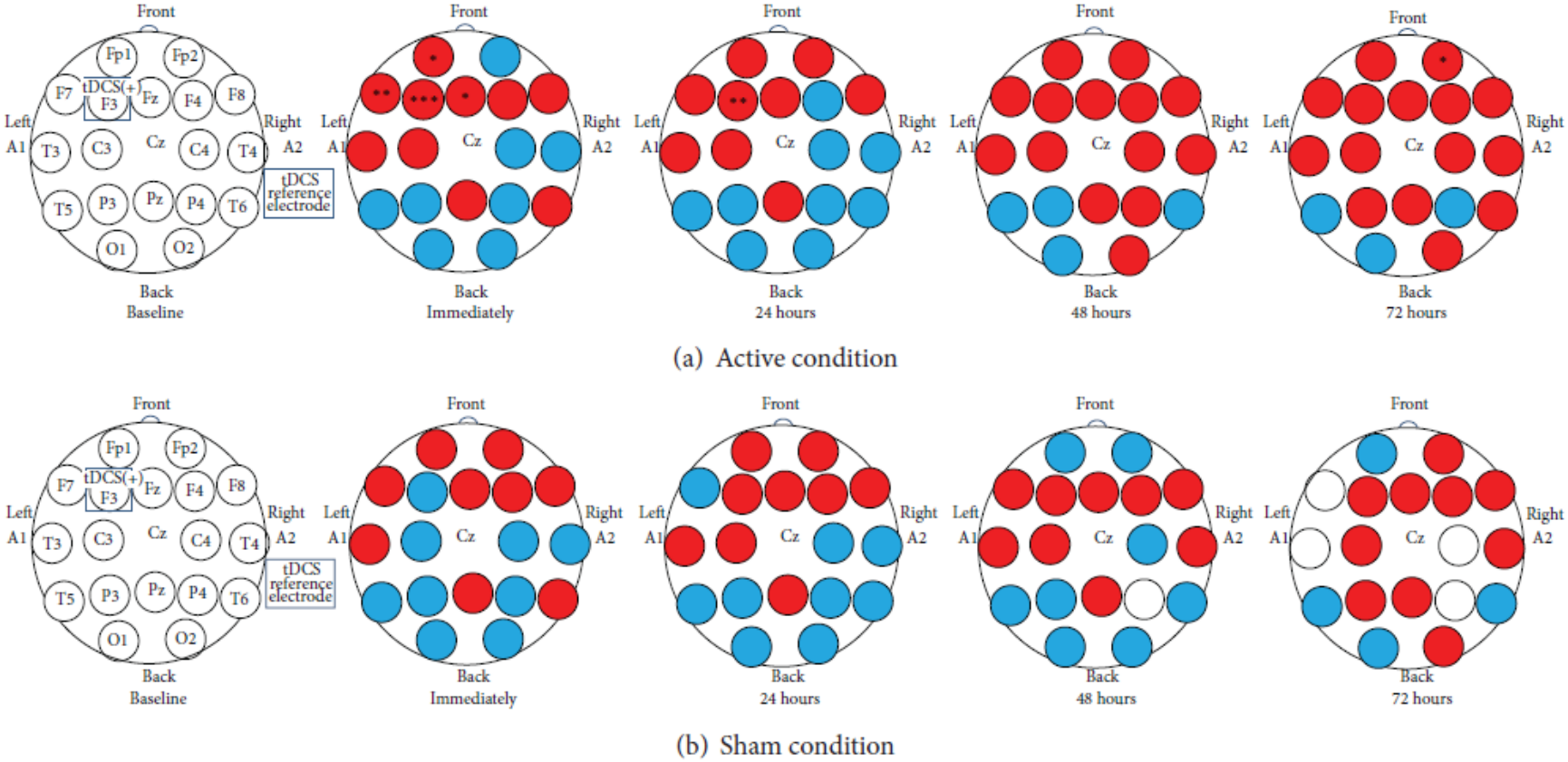
Significant difference when compared with baseline indicated by $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

Significant Condition × Time interactions when compared between active and sham condition indicated by $^{\dagger}P < 0.05$; $^{\dagger\dagger}P < 0.01$.

Miglioramento in 2 domini ATEC (sociale e comportamento) dopo attiva

Frequenza Alfa aumenta nel sito di stimolazione

Brain stimulation e Autismo



Associazione tra aumento frequenza Alfa e miglioramento ATEC

Concludono → **tDCS anodica su F3 per miglioramento clinico relato a freq Alfa**

tDCS Autismo e Catatonia

BRAIN
STIMULATION
Basic, Translational, and Clinical Research in Neuromodulation

Article in Press

Transcranial Direct Current Stimulation Treatment in an Adolescent with Autism and Drug-Resistant Catatonia

F. Costanzo, D. Menghini, L. Casula, A. Amendola, L. Mazzone, G. Valeri, S. Vicari

tDCS Autismo e Catatonia

- ✓ Ragazza di 14 anni con diagnosi di autismo e catatonia
- ✓ QI 58
- ✓ Buon funzionamento scolastico sociale e relazionale
- ✓ A 11 anni→ evento traumatico → regressione emotiva/comportamentale
- ✓ Benzodiazepine, antipsicotici e stabilizzatori dell'umore
- ✓ Nessun effetto e progressivo peggioramento

tDCS Autismo e Catatonia

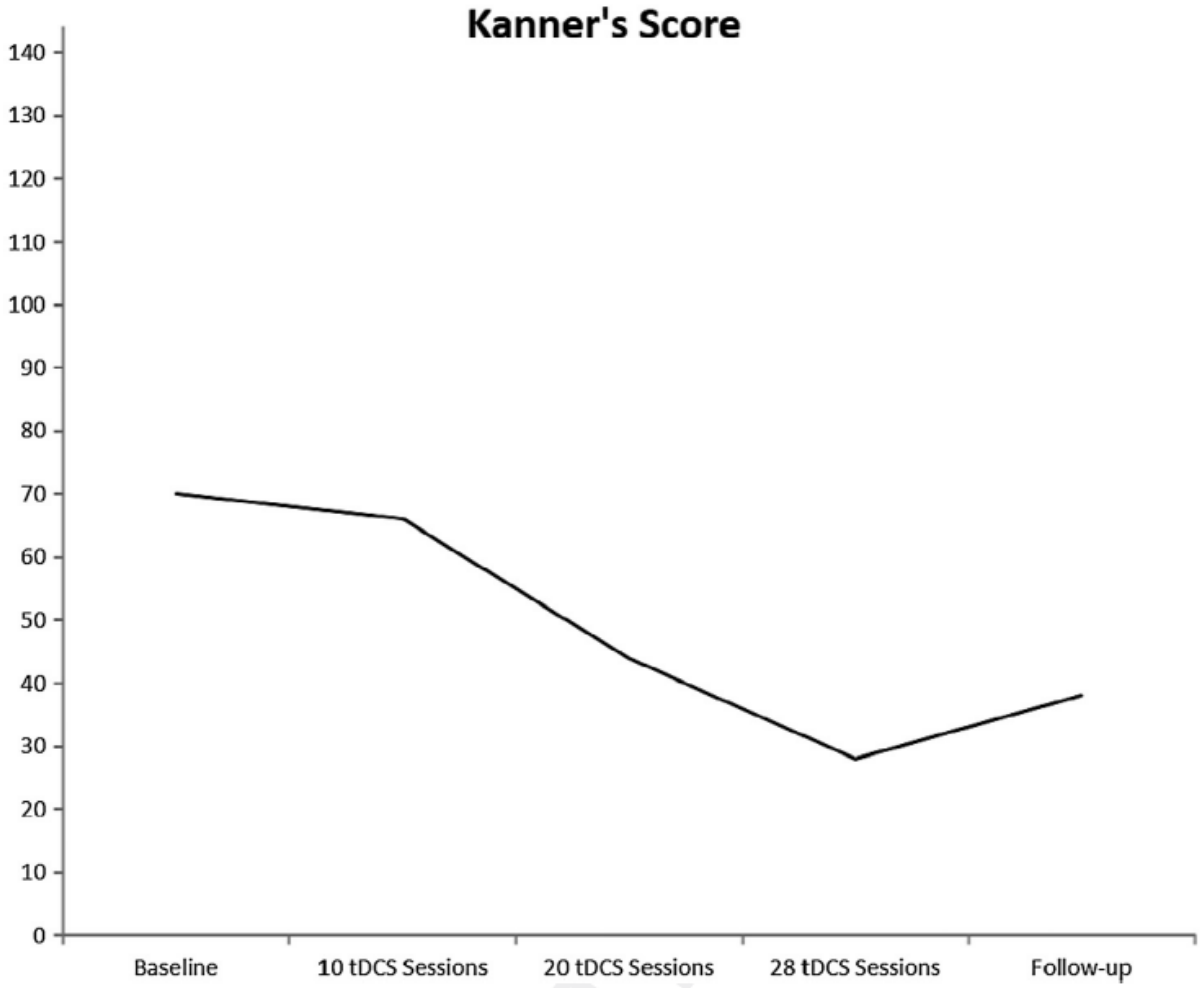


Figure 1. Time course of catatonic symptoms, as assessed by the total score of the Kanner Catatonia Rating Scale, before starting the tDCS treatment, after 10, 20 and 28 tDCS sessions and after 1-month follow-up.

tDCS Autismo e Catatonia

Table 1
Specific catatonic symptoms as assessed by the Kanner Catatonia Rating Scale. Asterisks indicate symptoms that fully recovered during the treatment course.

Symptom	Baseline	10 tDCS sessions	20 tDCS sessions	28 tDCS sessions	1 month follow-up
Excitement	6	2	2	0*	0*
Immobility	6	6	6	6	6
Stupor	2	4	2	2	4
Mutism	8	8	6	6	8
Staring	6	8	2	2	4
Posturing	4	4	6	6	6
Grimacing	6	6	2	0*	2
Stereotypy	6	4	0*	0*	0*
Mannerism	2	0	2	2	2
Rigidity	6	0*	0*	0*	0*
Flaccidity	0	0	0	0	0
Negativism	8	6	6	2	2
Refusal to eat	2	6	2	0*	0*
Refusal to drink	2	4	2	0*	0*
Impulsivity	2	2	0	0*	2
Nudism	0	2	4	0	0
Incontinence	0	0	0	0	0
Combativeness	4	4	2	2	2

tDCS a ADHD

Neuropharmacology. 2013 January ; 64: 566–578. doi:10.1016/j.neuropharm.2012.06.020.

CAN NONINVASIVE BRAIN STIMULATION ENHANCE COGNITION IN NEUROPSYCHIATRIC DISORDERS?

Asli Demirtas-Tatlidede, MD[1], Andrew M. Vahabzadeh-Hagh, MD[2], and Alvaro Pascual-Leone, MD, PhD[2]

ADHD Target: circuito fronto-striato-cerebellare

Studi con TMS e adulti:

Niederhofer, 2008 → 5 sessioni 1 Hz rTMS nelle area M1 → miglioramenti cognitivi

Bloch et al. (2010) → singola sessione di 20 Hz rTMS sulla R-DLPFC → migliora attenzione (PANAS e self-report)

tDCS a ADHD

Brain Stimulation 7 (2014) 793–799

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Transcranial Oscillatory Direct Current Stimulation During Sleep Improves Declarative Memory Consolidation in Children With Attention-deficit/hyperactivity Disorder to a Level Comparable to Healthy Controls

Alexander Prehn-Kristensen [a,*], Manuel Munz [a], Robert Göder [b], Ines Wilhelm [c,d], Katharina Korr [a], Wiebke Vahl [a], Christian D. Wiesner [a], Lioba Baving [a]

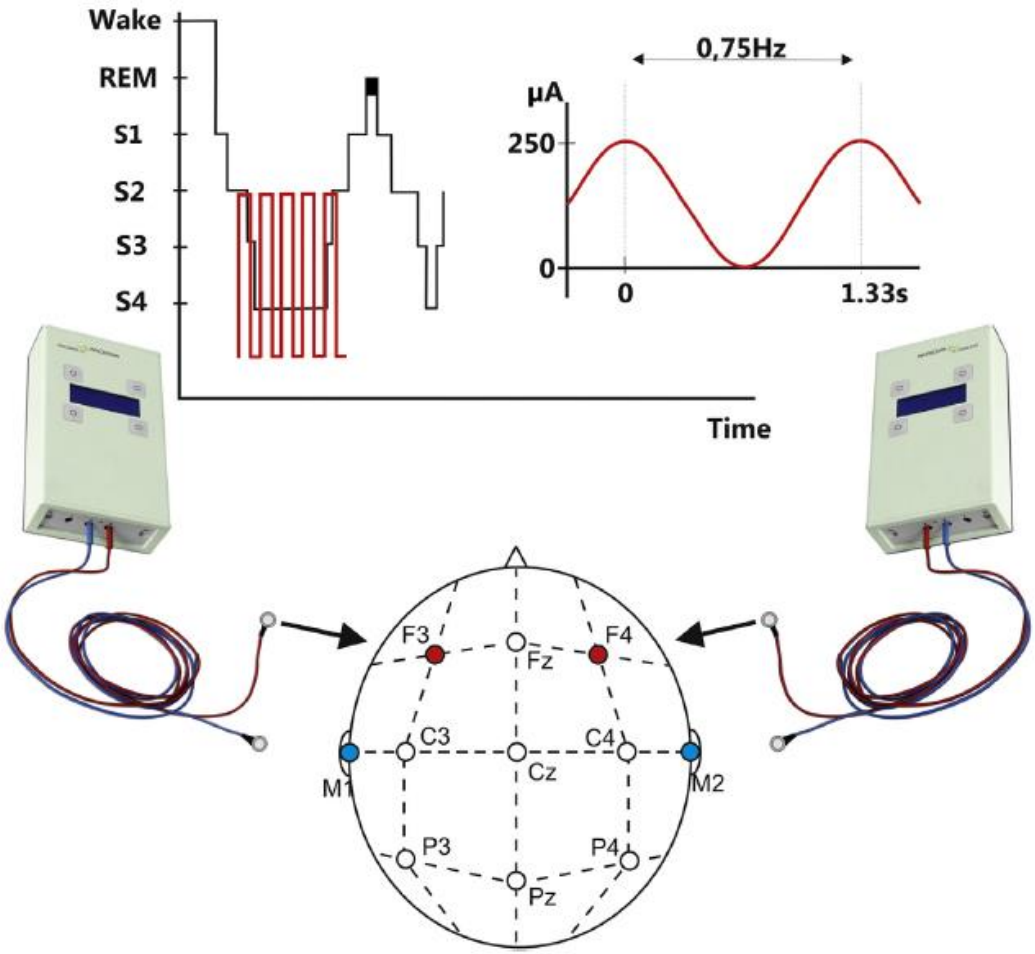
Participant characteristics.

	ADHD	Controls	ADHD vs. controls
	Mean (SD)	Mean (SD)	*P*
Age	12.1 (1.4)	11.9 (1.4)	.678
IQ	105 (7.0)	105 (8.1)	.915
Figural memory	65.4 (24.4)	75.7 (19.4)	.267
Attention problems (CBCL)	68.6 (7.9)	50.4 (1.4)	<.001

SD, standard deviation; CBCL, child behavior checklist.

tDCS a ADHD

A. Prehn-Kristensen et al. / Brain Stimulation 7 (2014) 793–799



Corrente Anodica da 0 a 250 mA → frequenza 0.75 Hz.
Stimolazione monofasica sinusoidale
Massima densità di corrente 0.497 mA/cm2.
La stimolazione iniziava 4 min dopo l'entrata nello stato 2 del sonno non-REM

tDCS a ADHD

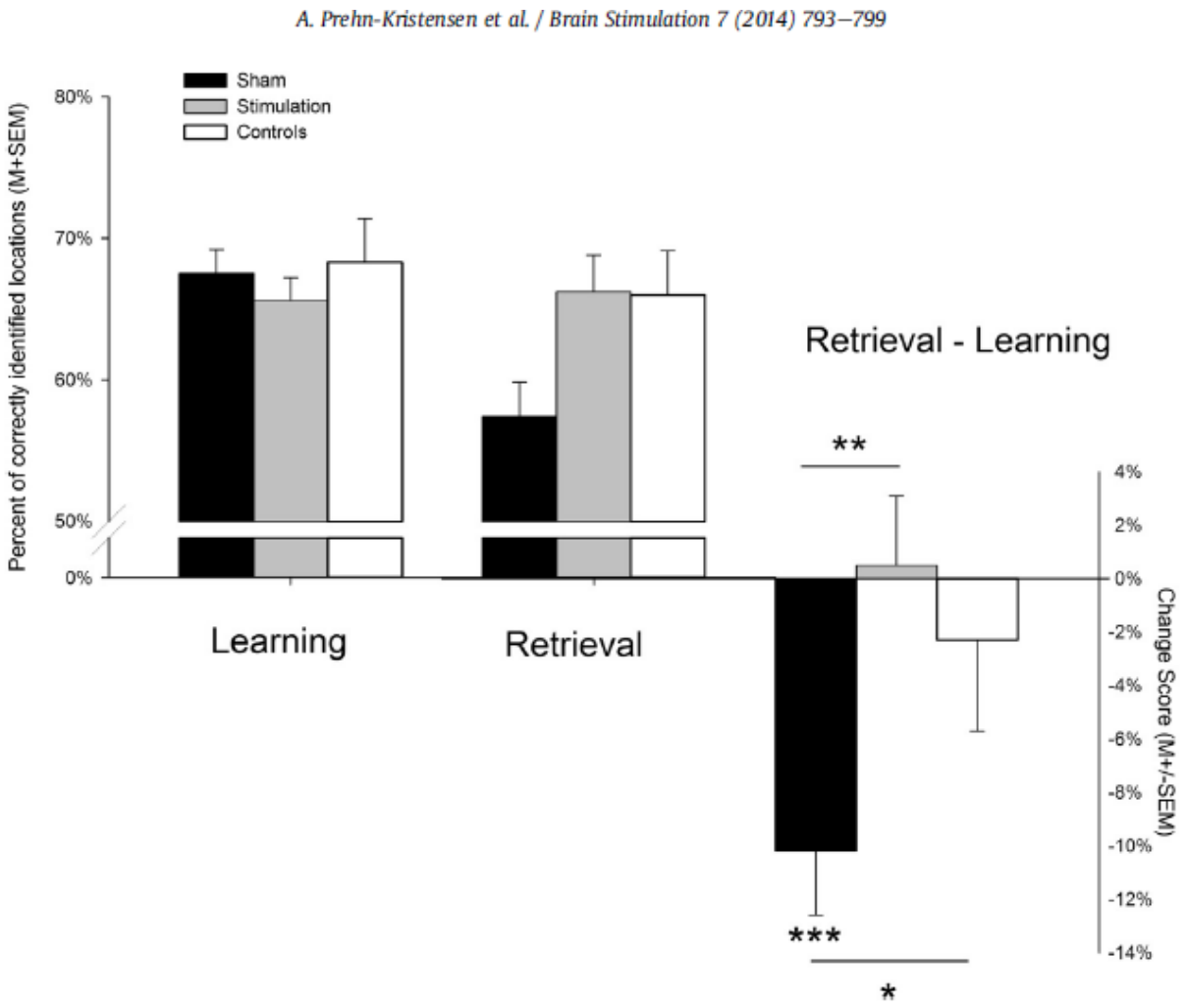


Figure 2. Memory performance; * $P < .036$ (one-tailed); ** $P = .004$ (one-tailed); *** $P = .001$.

Compito memoria di oggetti 2D

tDCS a ADHD

frontiers in Cellular Neuroscience

ORIGINAL RESEARCH
published: 11 August 2015
doi: 10.3389/fncel.2015.00307

14 M con ADHD (10–14 aa)

so-DCS, frequency=0.75Hz) durante il non-REM (I o II notte)

Compito: Go-NoGo

Slow oscillating transcranial direct current stimulation during non-rapid eye movement sleep improves behavioral inhibition in attention-deficit/hyperactivity disorder

Manuel T. Munz[1], Alexander Prehn-Kristensen[1], Frederieke Thielking[1], Matthias Mölle[2], Robert Göder[3] and Lioba Baving[1]*

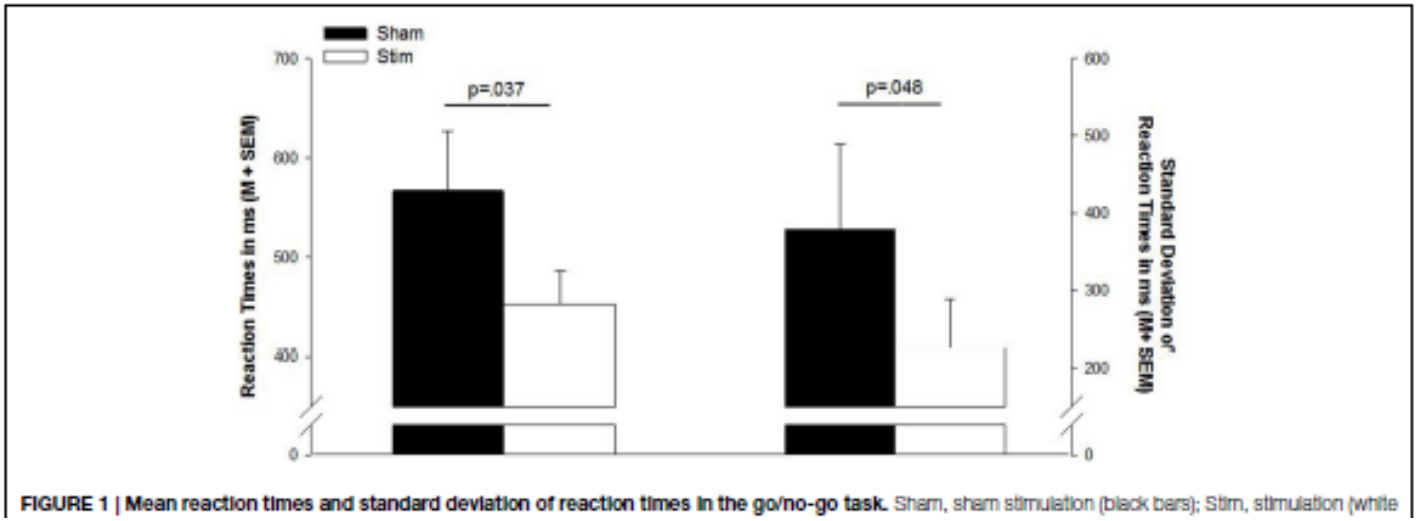


FIGURE 1 | Mean reaction times and standard deviation of reaction times in the go/no-go task. Sham, sham stimulation (black bars); Stim, stimulation (white

Brain stimulation disturbi del comportamento alimentare

REVIEW

A Systematic Review of the Effects of Neuromodulation on Eating and Body Weight: Evidence from Human and Animal Studies

Jessica McClelland*, Natali Bozhilova, Iain Campbell & Ulrike Schmidt

Section of Eating Disorders, Institute of Psychiatry, King's College London, London, UK

Eur. Eat. Disorders Rev. **21** (2013) 425–427

EDITORIAL

Treatment of Eating Disorders can not Remain 'Brainless': The Case for Brain-Directed Treatments

- Numerosi studi suggeriscono un'efficacia della stimolazione cerebrale
- Il trattamento non può rimanere "Brainless"

Aree target della stimolazione cerebrale

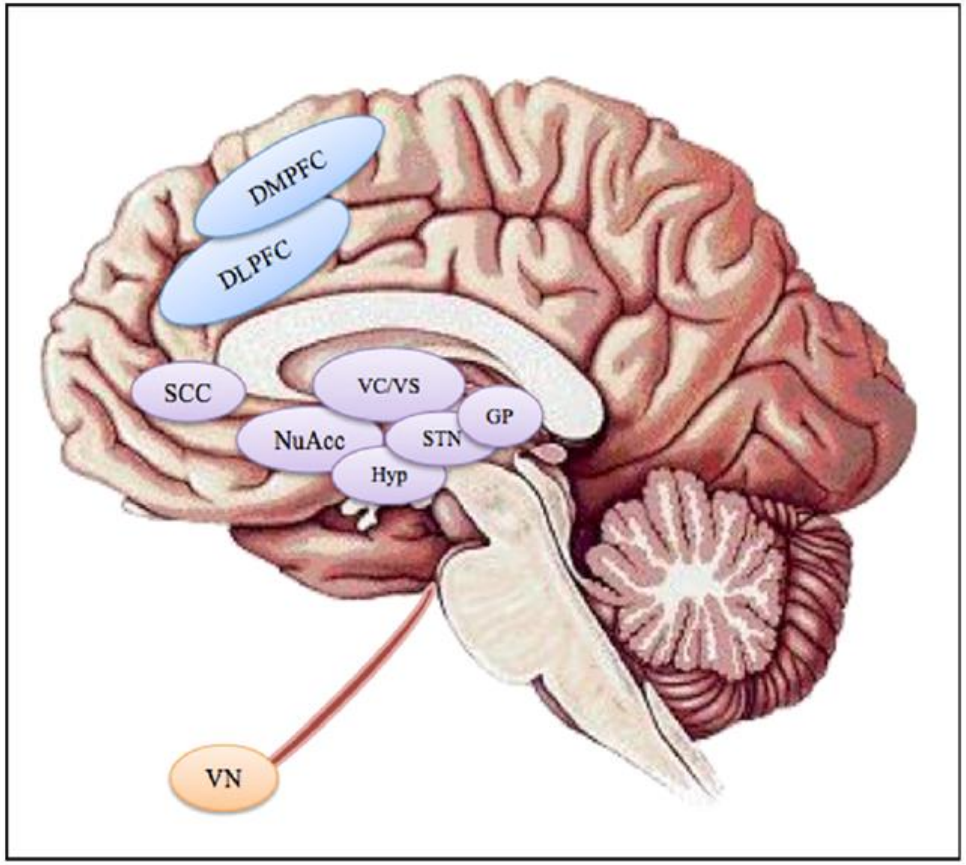
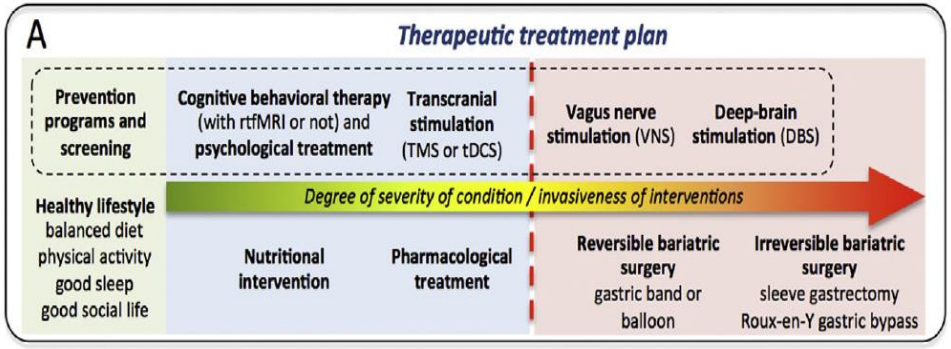
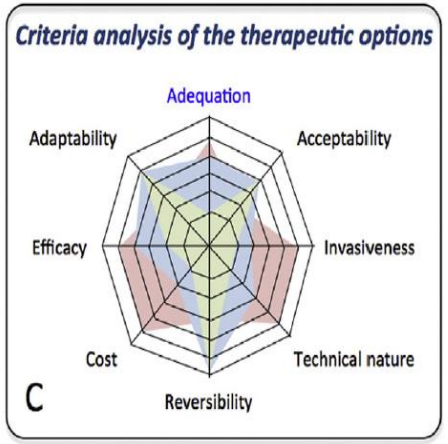
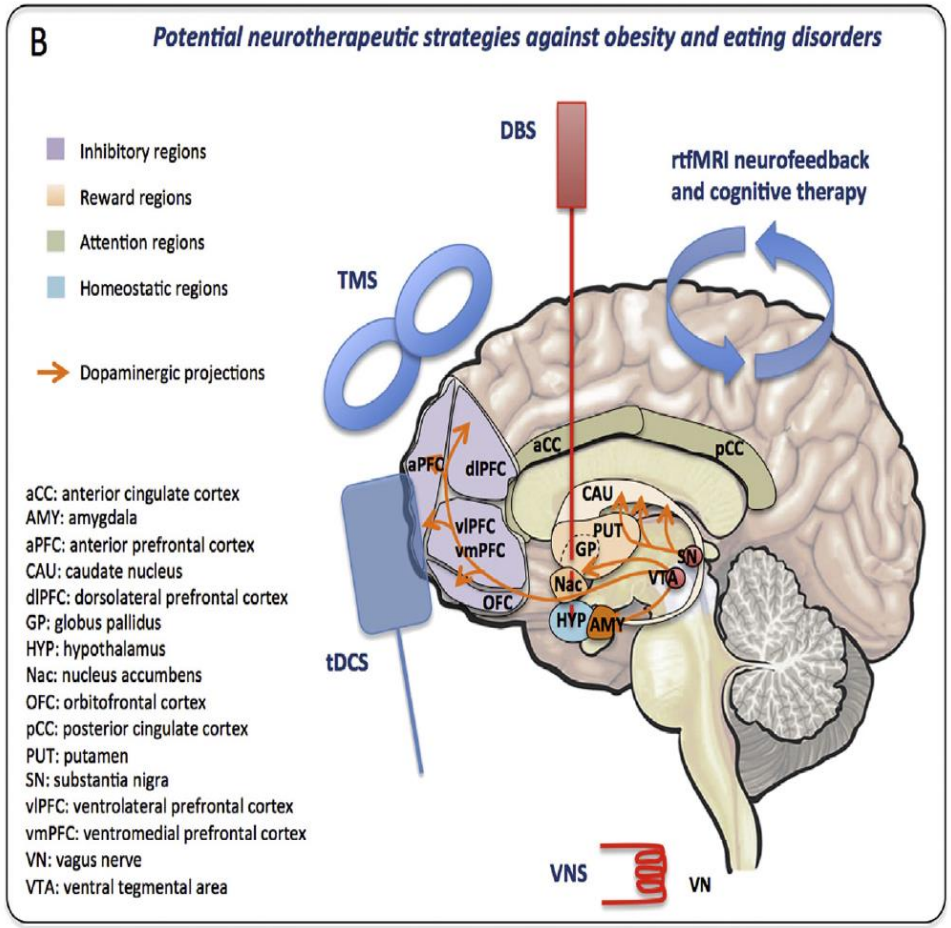


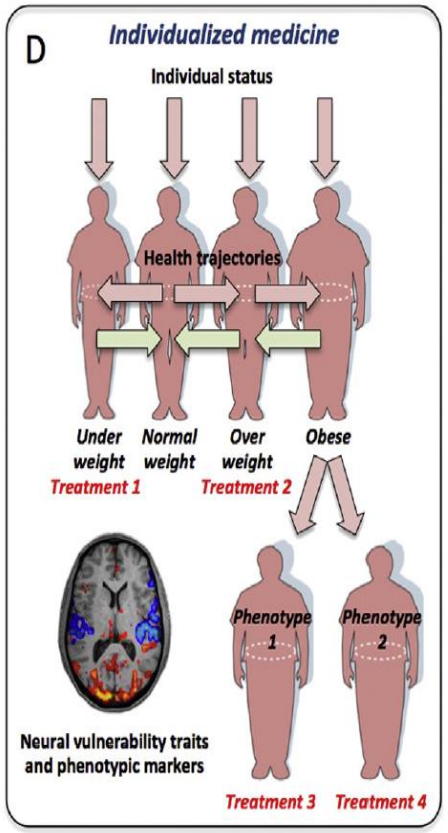
Figure 2. Brain areas targeted in reviewed studies. TMS and tDCS (blue): DMPFC, dorsomedial prefrontal cortex; DLPFC, dorsolateral prefrontal cortex. DBS (purple): SCC, subgenual cingulate cortex; NuAcc, nucleus accumbens; VC/VS, ventral capsule/striatium; Hyp, hypothalamus; STN, sub-thalamic nucleus; GP, globus pallidus. VNS (orange): VN, vagus nerve

Aree target della stimolazione cerebrale









Val-Laillet et al., 2015

Nei disturbi del comportamento alimentare

Medical Hypotheses 74 (2010) 1044–1047

Contents lists available at ScienceDirect

Medical Hypotheses

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

Transcranial direct current stimulation in the treatment of anorexia

David Hecht *

Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London WC1N 3AR, UK
Department of Psychology, University of Hull, Cottingham Road, Hull HU6 7RX, UK

Brain Stimul. 2014 Jan-Feb;7(1):149-50.

rTMS as a treatment for anorexia nervosa

Bainbridge K, Brown A

Oudijn *et al. BMC Psychiatry* 2013, **13**:277
http://www.biomedcentral.com/1471-244X/13/277

BMC Psychiatry

REVIEW **Open Access**

Is deep brain stimulation a treatment option for anorexia nervosa?

Marloes S Oudijn[1], Jitschak G Storosum[1], Elise Nelis[1] and Damiaan Denys[1,2*]

Nei disturbi del comportamento alimentare

PROTOCOLLO tDCS IN CORSO

Obiettivo: ridurre l'attività a destra ed aumentare a sinistra DLPF

Metodo:

1mA (20 min) + psicoterapia (18 sedute; 3v/sett)

anoressia: DLPF anodo sn/catodo dx

food craving e obesi: DLPF anodo dx/catodo sn

Outcomes:

EDI-III, misure fisiologiche e psicopatologiche

Brain Stimuation in altri disturbi psichiatrici

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]*

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

CONCLUSIONI

- ✓ La stimolazione cerebrale non invasiva è una prospettiva di riabilitazione nei disturbi dell'apprendimento e in altri disturbi dello sviluppo

- ✓ 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