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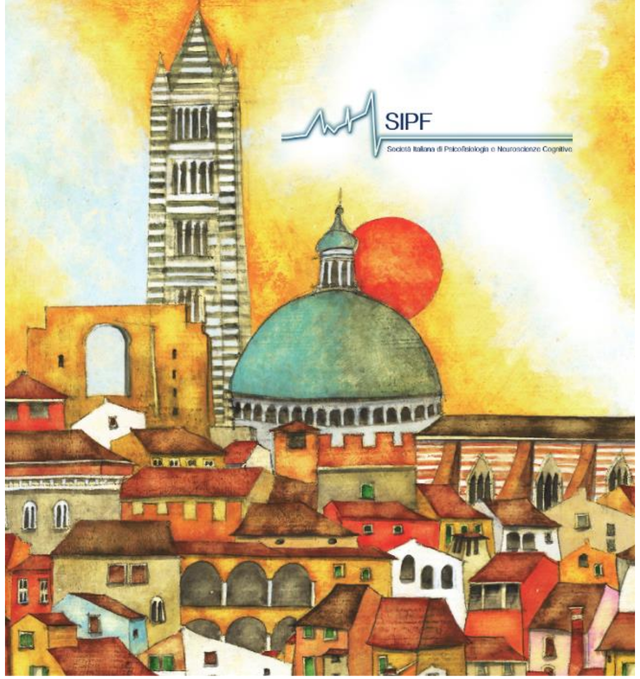


Società Italiana di PsicoFisiologia e Neuroscienze Cognitive (SIPF)
Siena, 9-11 Novembre 2023

Cerebellar tDCS and Pain

Tommaso Bocci, MD
I Unit of Neurology, Department of Health Sciences, University of Milan

Timeline

1)Chronic pain and sensitization: Pathophysiological mechanisms

2) tDCS and cerebellum: clinical evidence

3) tDCS and Cerebellum: neurophysiological evidence

4)How chronic pain and cognition share the same pathways: brain level, spinal pathways and the Cerebellum.

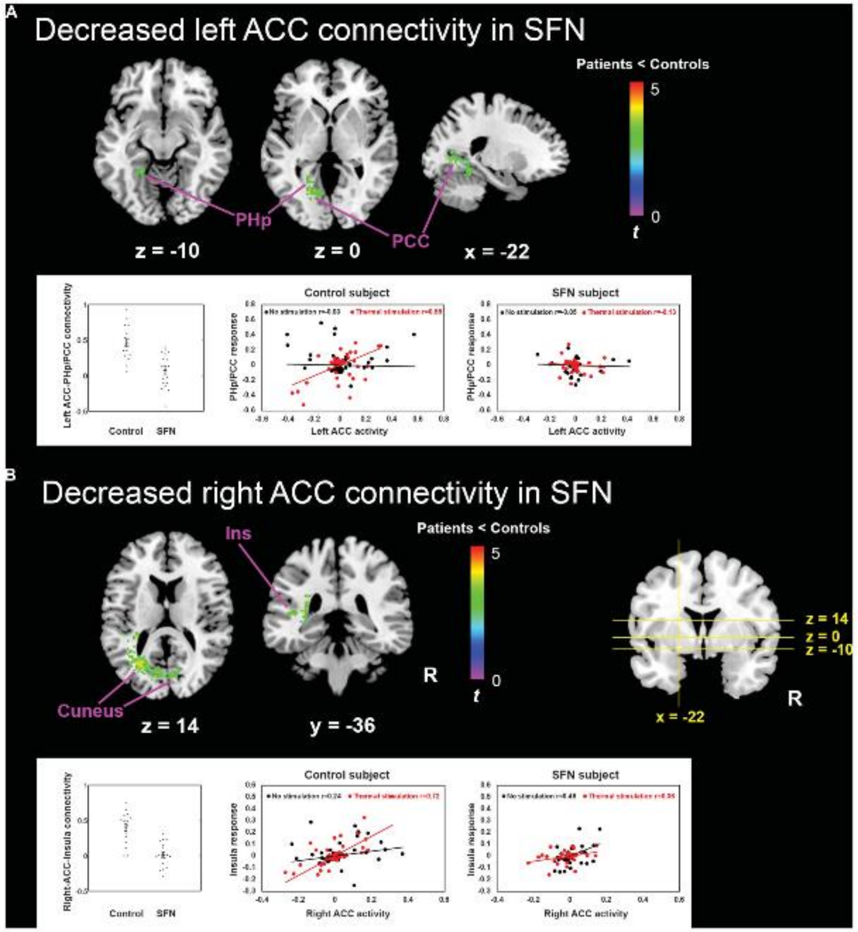
5)Conclusions

«Central Sensitization» and chronic pain: pathophysiological mechanisms part I.

1. Supra-spinal pathways

a. *Functional re-organization of cortical maps*

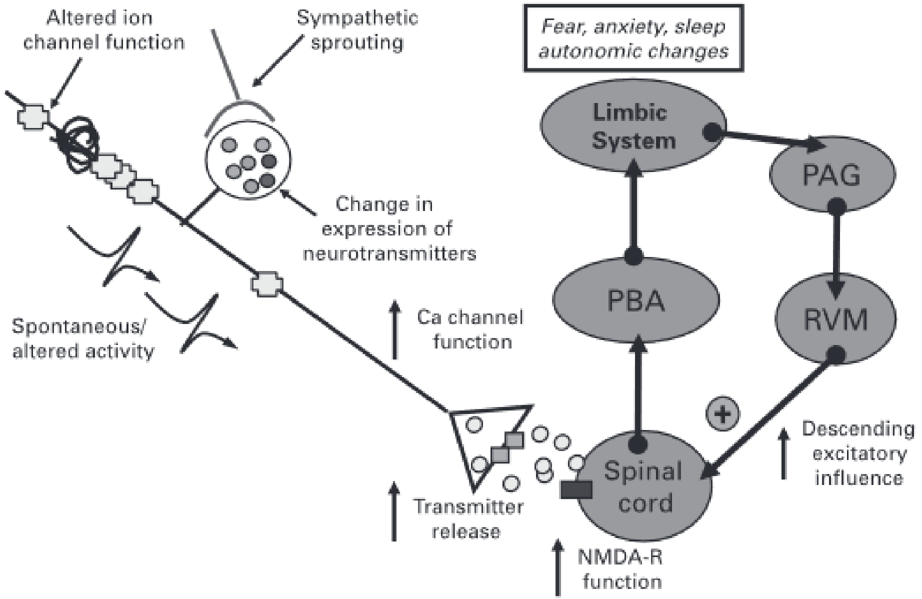
b. *Thalamocortical dysrhythmia*



Hsieh et al., *Pain* 2015

2. Spinal Pathways:

Phenotipic Switch



Suzuki&Dickenson, *Neurosignals* 2006

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ARTICLE

Abnormal thalamocortical network dynamics in migraine

Yiheng Tu, PhD,* Zening Fu, PhD,* Fang Zeng, MD, PhD,* Nasim Maleki, PhD, Lei Lan, MD, PhD, Zhengjie Li, MD, PhD, Joel Park, BA, Georgia Wilson, BA, Yujie Gao, MD, PhD, Mailan Liu, MD, PhD, Vince Calhoun, PhD, Fanrong Liang, MD, MS and Jian Kong, MD, MS, MPH

Neurology® 2019;92:e2706-e2716. doi:10.1212/WNL.0000000000007607

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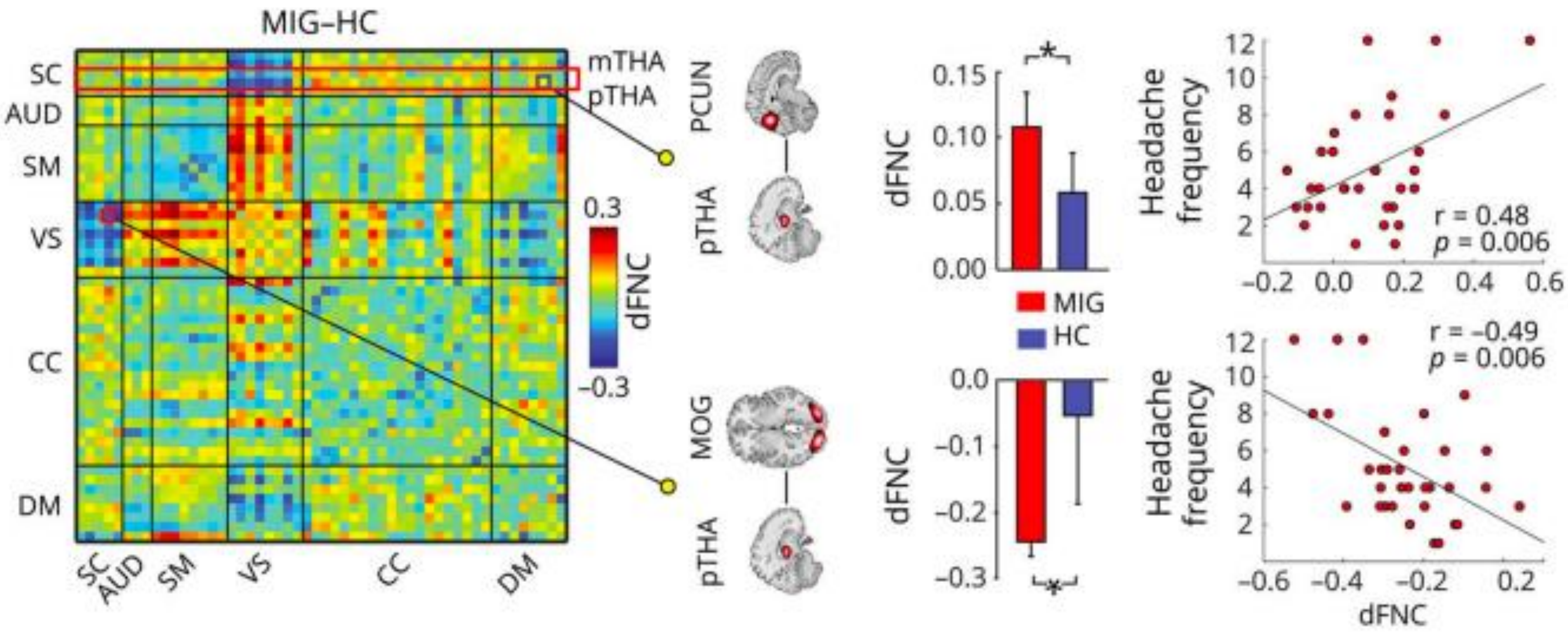
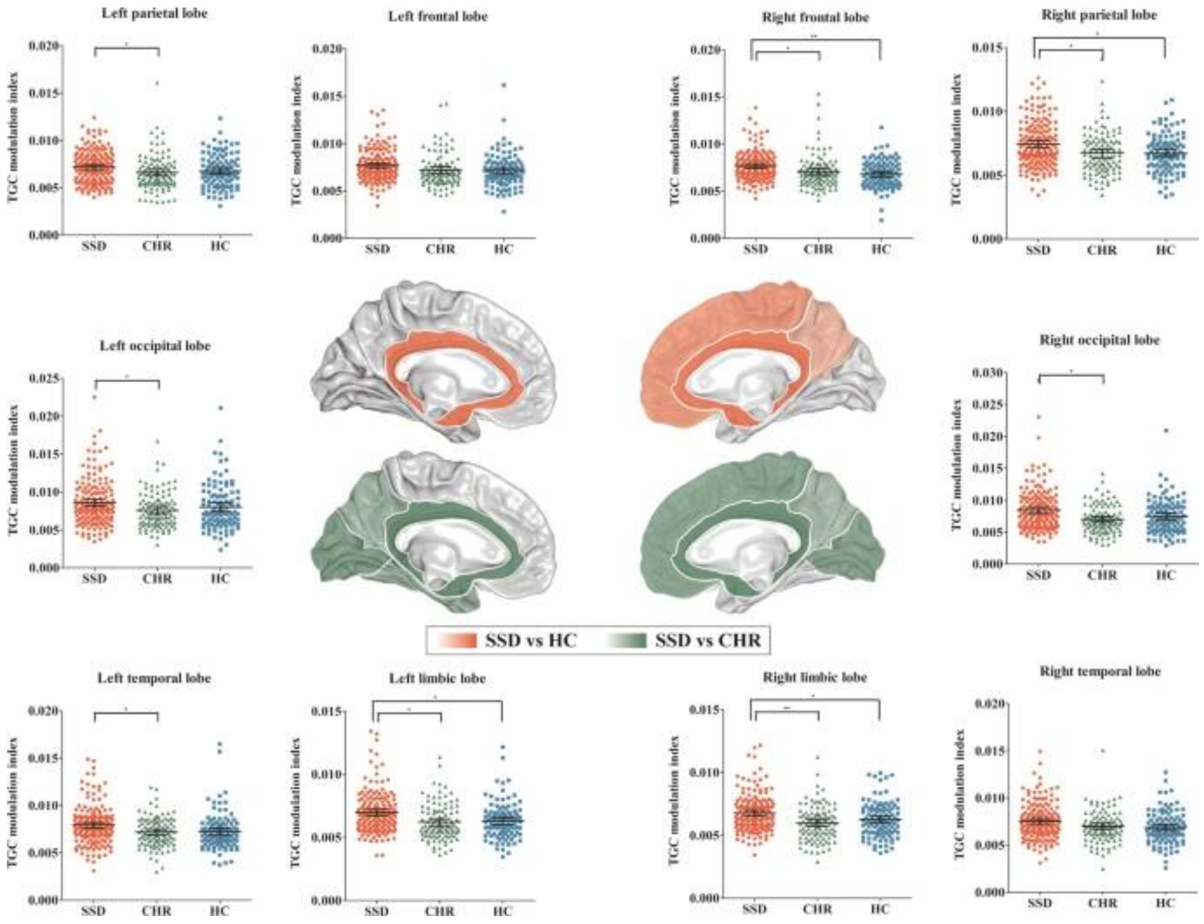
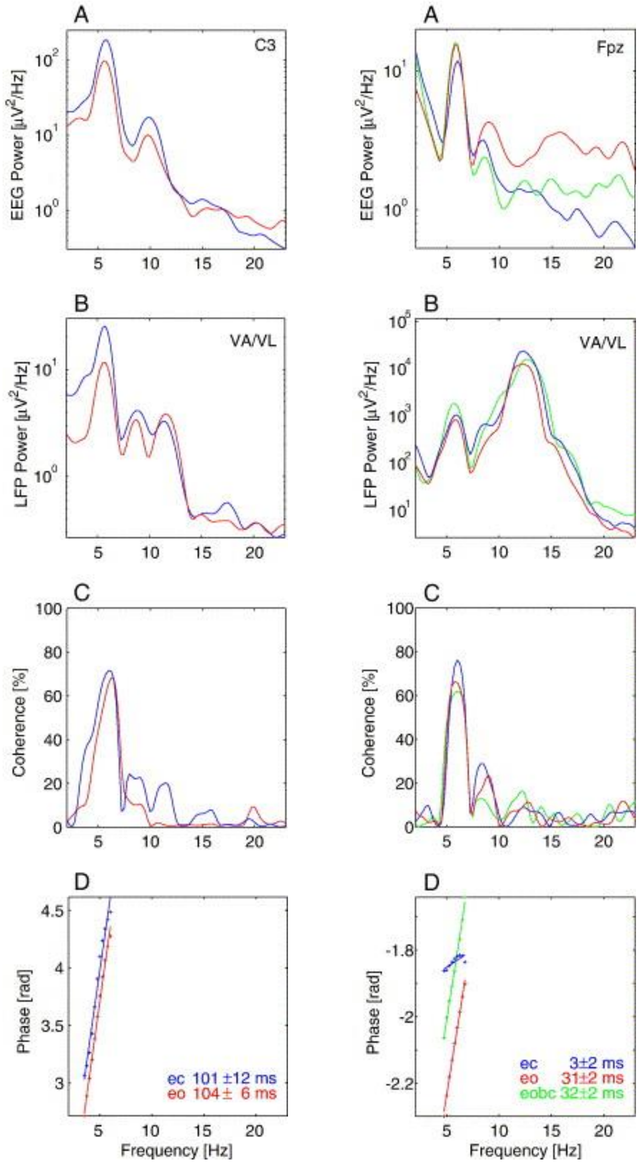


Abnormal transient thalamus dynamic functional network connectivity (dFNC) and its association with migraine symptoms

Tu et al., *Neurology* 2019

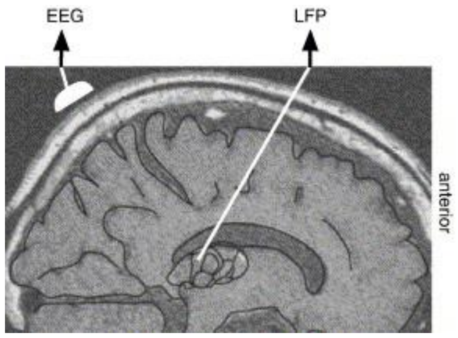
Thalamocortical dysrhythmia AND cognition





Thalamocortical theta coherence in neurological patients at rest and during a working memory task

J. Sarnthein*, A. Morel, A. von Stein*, D. Jeanmonod

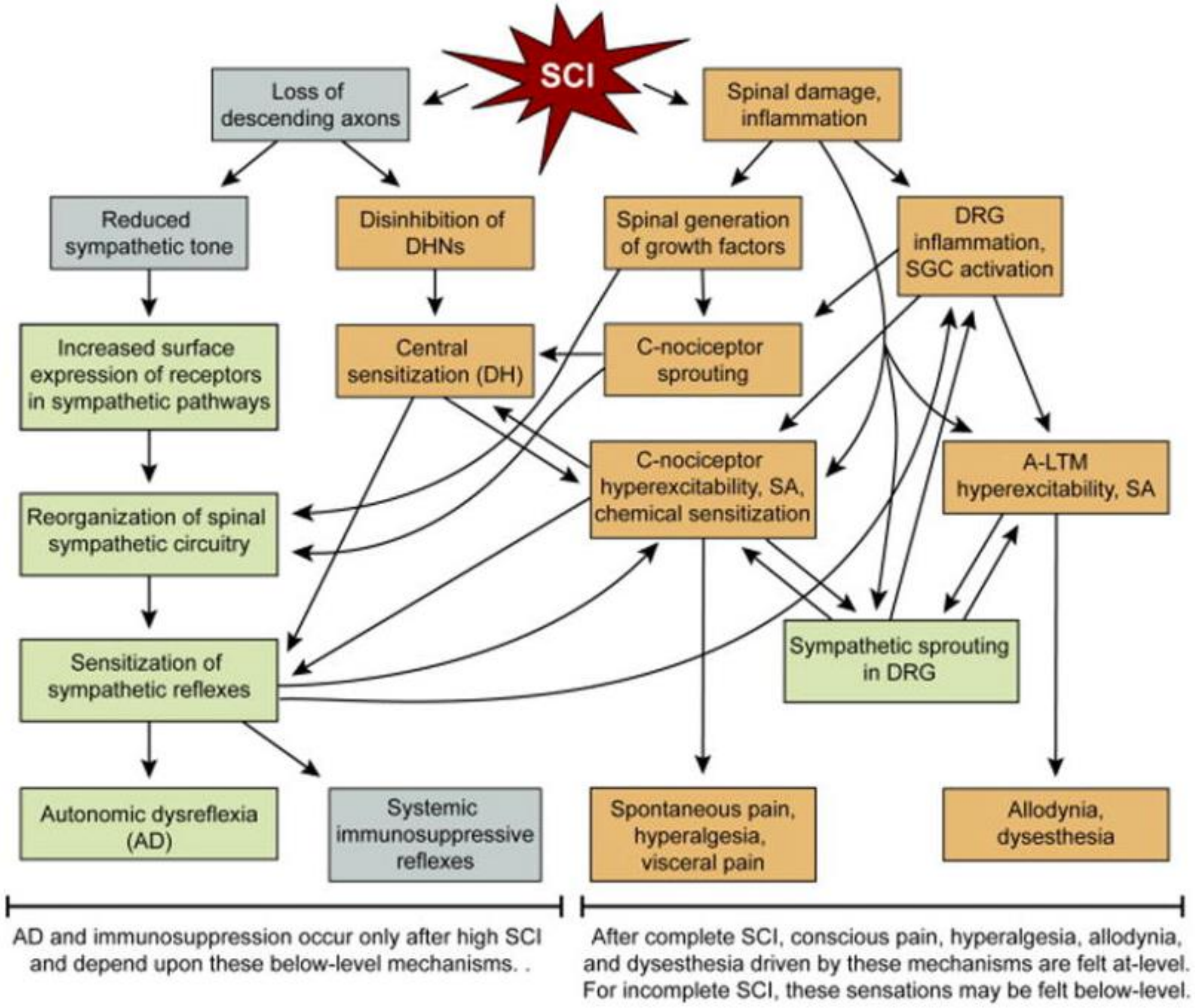


Kim et al., *Neuropsychopharmacology* 2022

Sarnthein et al., *Int J Psychophysiol* 2005

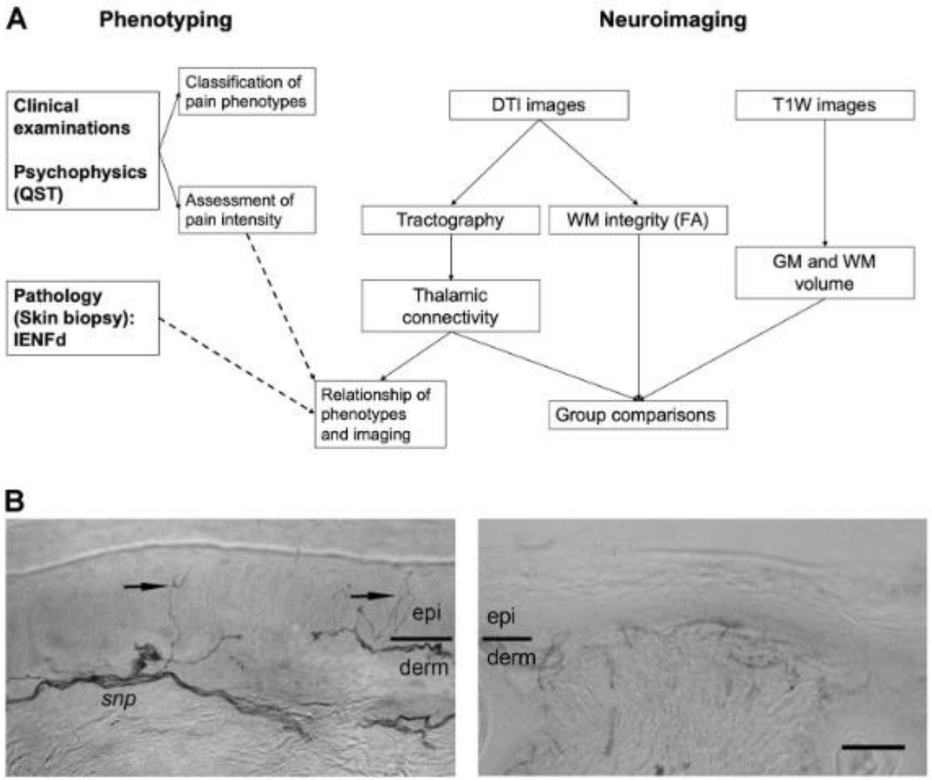
«Central Sensitization» and chronic pain: pathophysiological mechanisms part II.

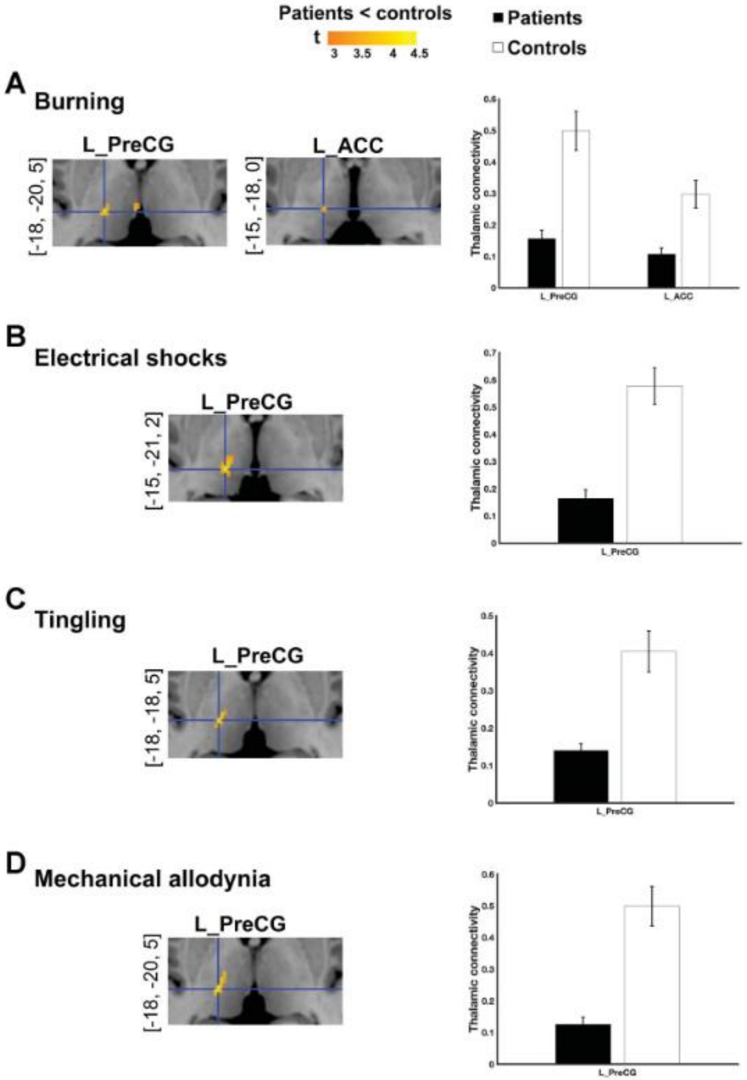
3. Autonomic Dysreflexia



Walters, *Auton Neurosci* 2015

Thalamo-cortical functional connectivity and small fibers Neuropathies

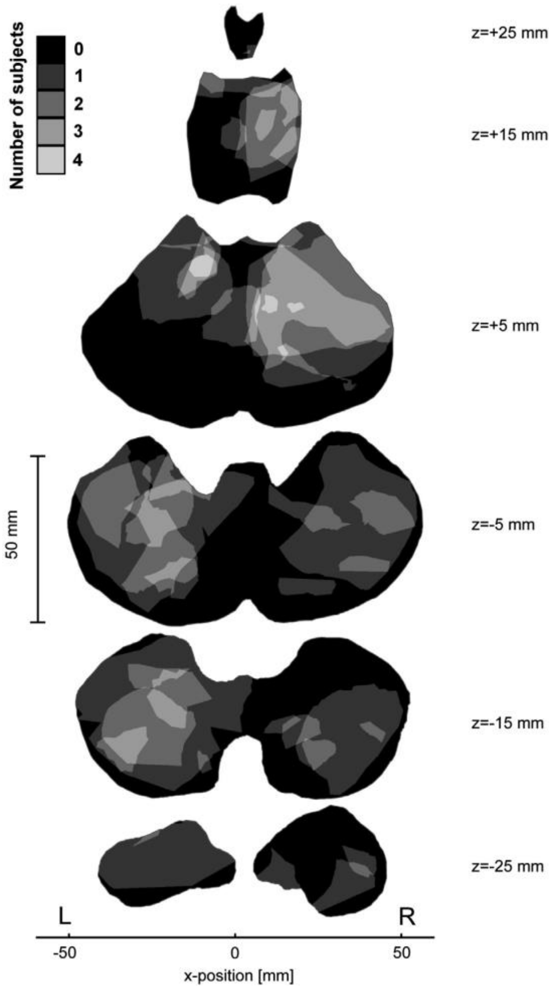




Chao et., *Pain* 2021

tDCS and cerebellum: clinical and neurophysiological evidence. From motor withdrawal to the sensory-discriminative dimension

Clinical Evidence. Stroke



PAIN® 155 (2014) 1303–1312
IASP
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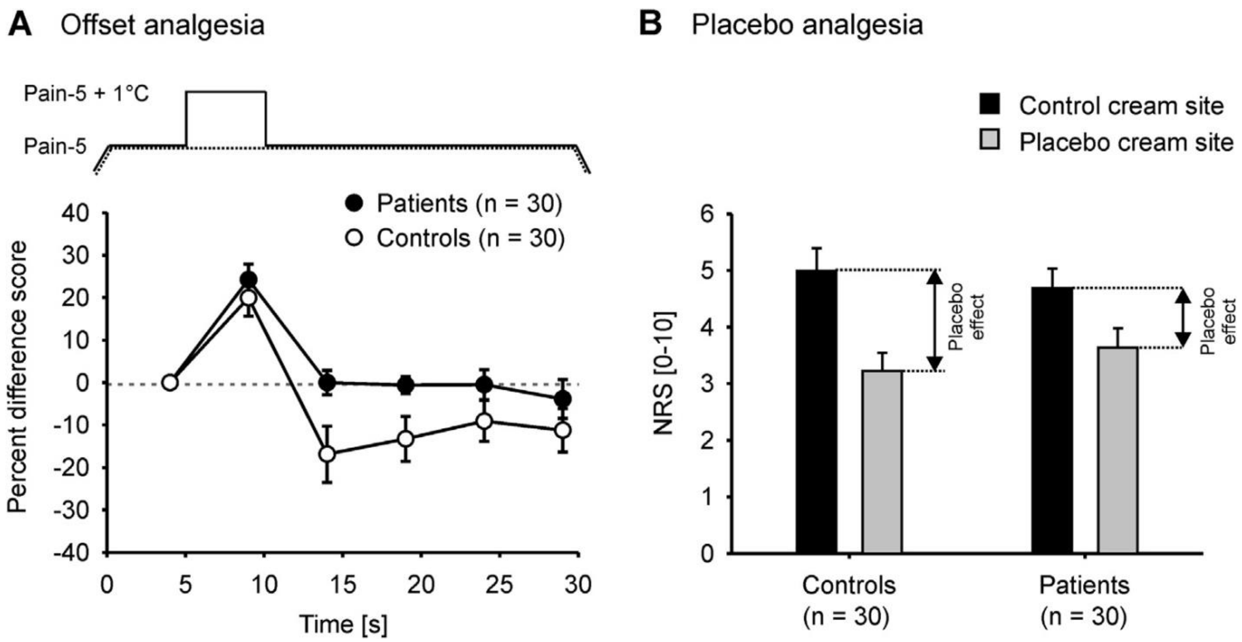
www.elsevier.com/locate/pain

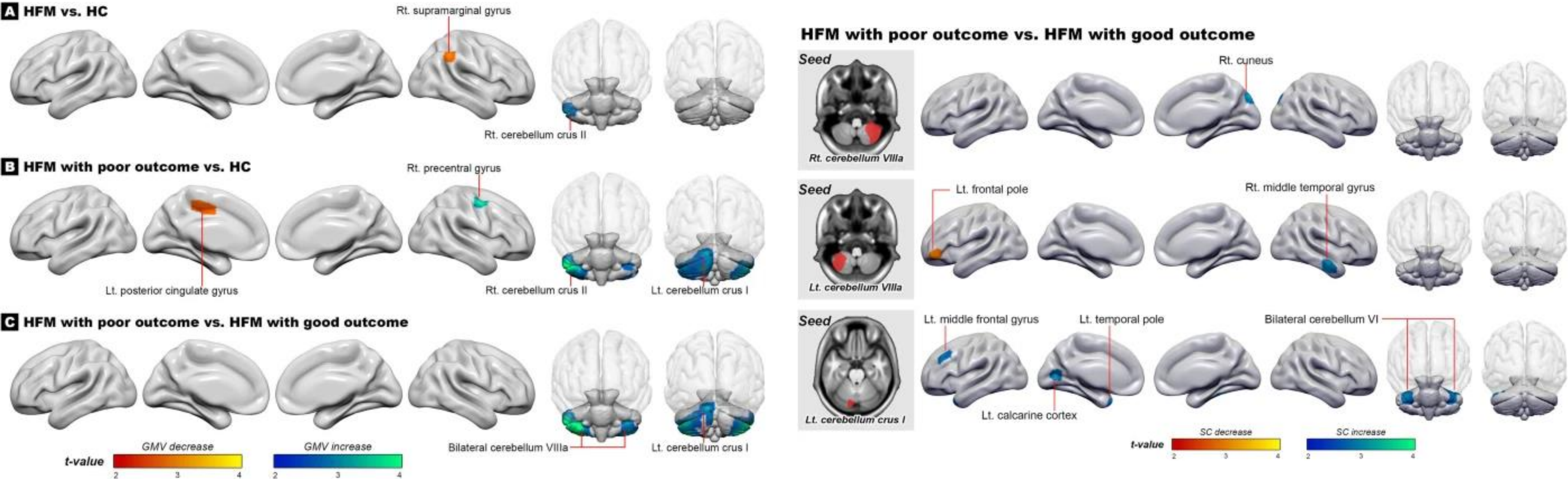
Altered experimental pain perception after cerebellar infarction

Ruth Ruscheweyh *, Maria Kühnel, Filipp Filippopulos, Bernhard Blum, Thomas Eggert, Andreas Straube
Department of Neurology, Ludwig-Maximilians-Universität München, Klinikum Großhadern, Munich, Germany



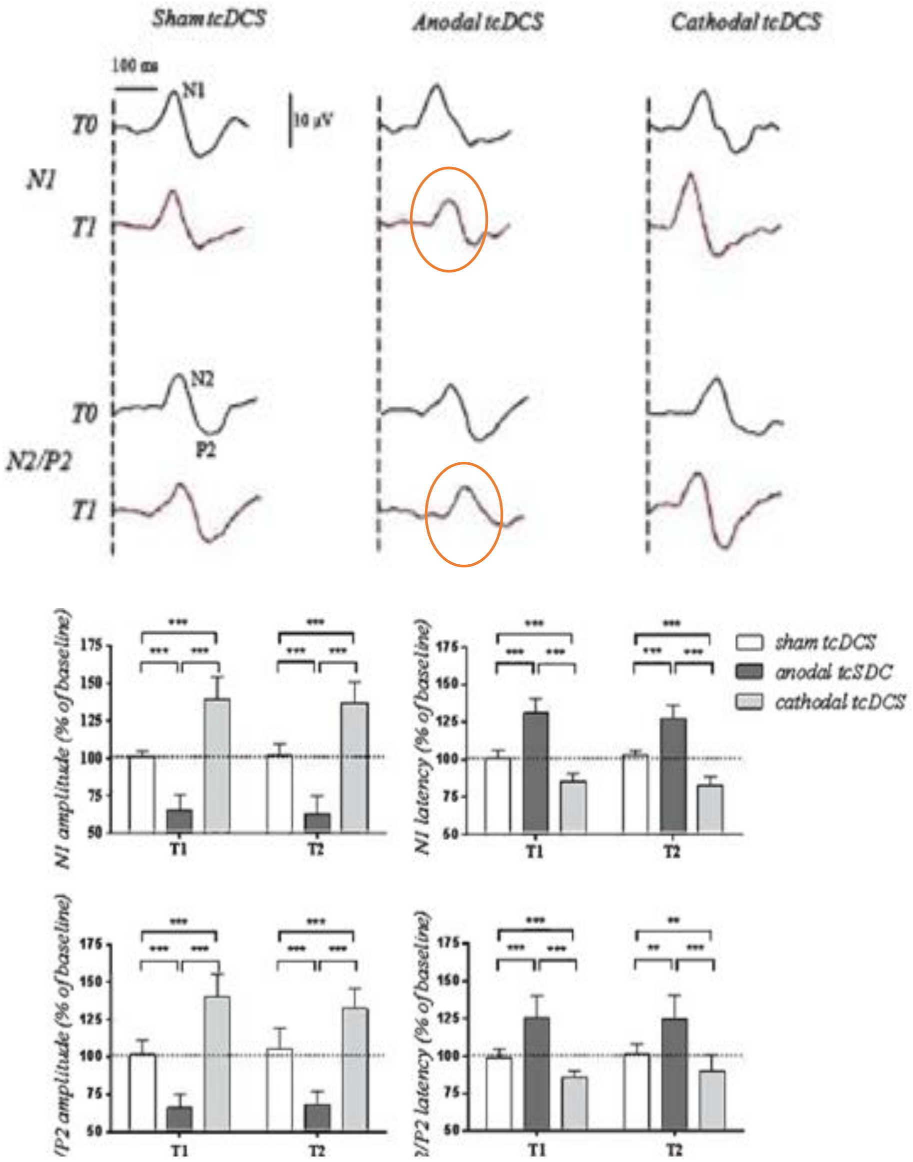
Ruscheweyh et al., *Pain* 2014

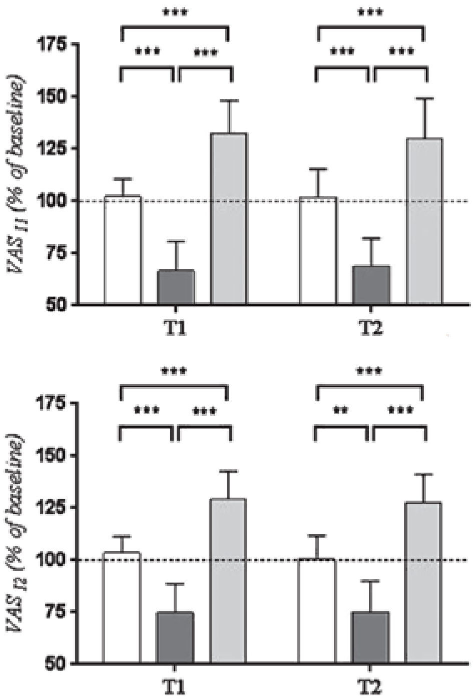
Clinical Evidence. Migraine



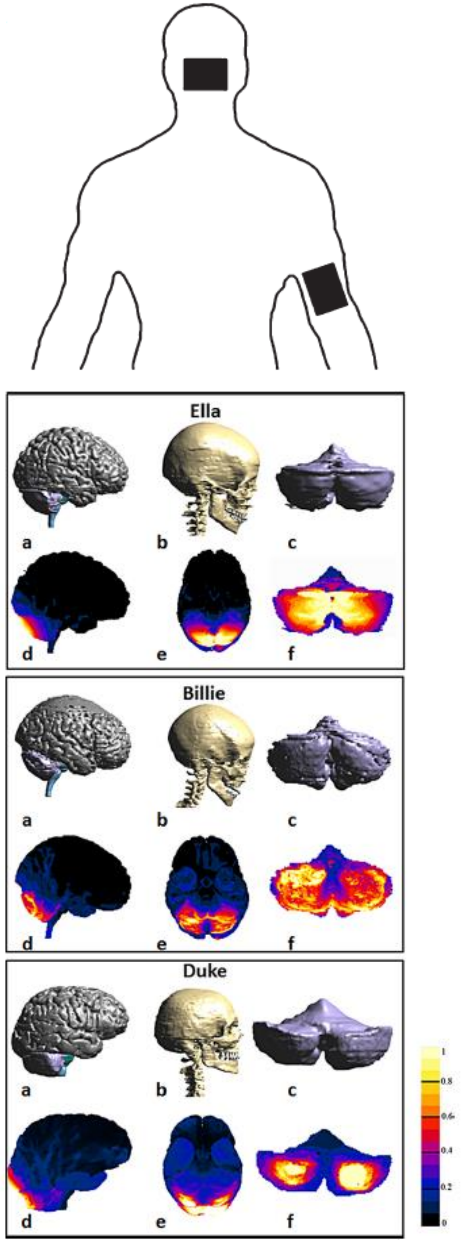
Liu et al., *J Headache Pain 2020*

Neurophysiological evidence in healthy humans. Cerebellar tDCS





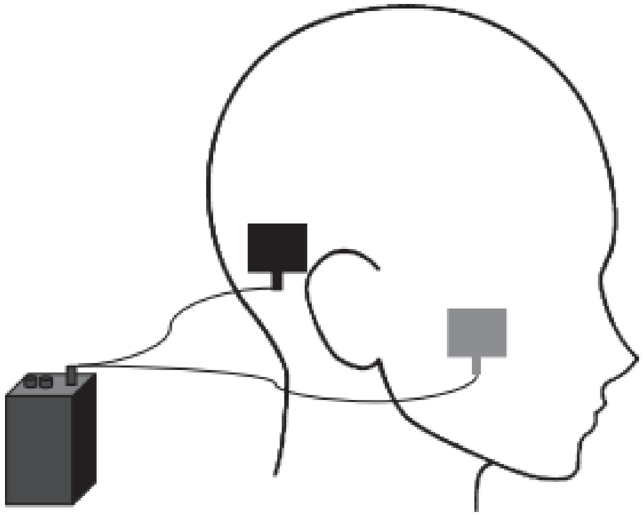
Bocci et al., *Restor Neurol Neurosci* 2015
Bocci et al., *Cerebellum* 2016



Parazzini et al., *Clin Neurophysiol* 2013

Anodal cerebellar tDCS modulates lower extremity pain perception

Manuel Pereira[a], Basil Rafiq[a], Einul Chowdhury[a], Jacqueline Babayev[a], HyunJi Boo[a], Rowan Metwaly[a], Priam Sandilya[a], Eileen Chusid[a] and Fortunato Battaglia[b,*]
[a]*Department of Pre-Clinical Sciences, New York College of Podiatric Medicine, New York, NY, USA*
[b]*Department of Interprofessional Health Sciences & Health Administration, School of Health and Medical Sciences, Seton Hall University, South Orange, NJ, USA*



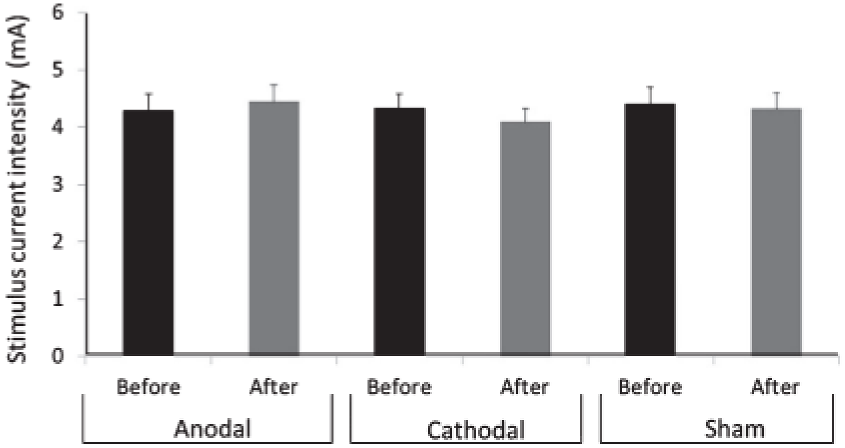


Fig. 2. Anodal, Cathodal and Sham cerebellar tDCS did not modulate the lower extremity sensory threshold. Error bars represent ± 1 standard errors of the mean.

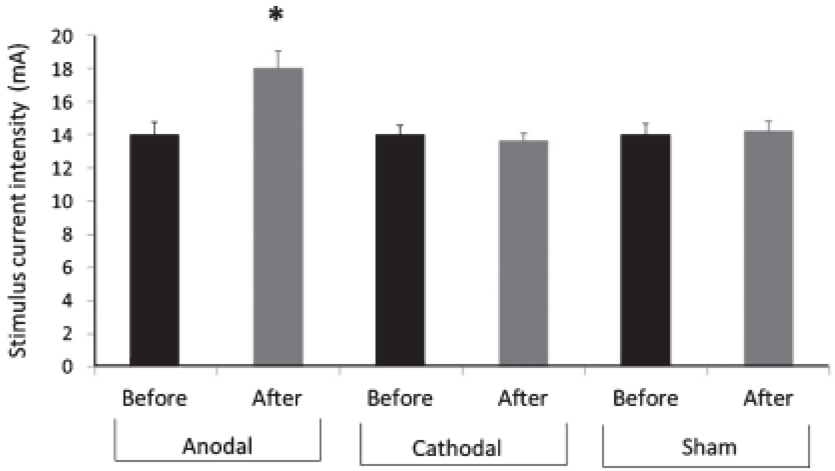
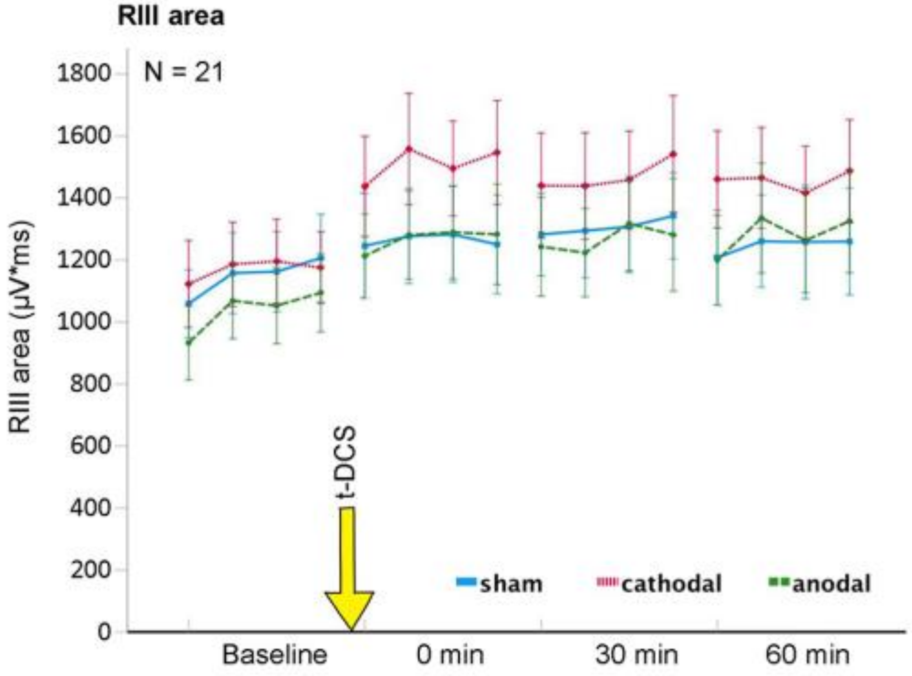
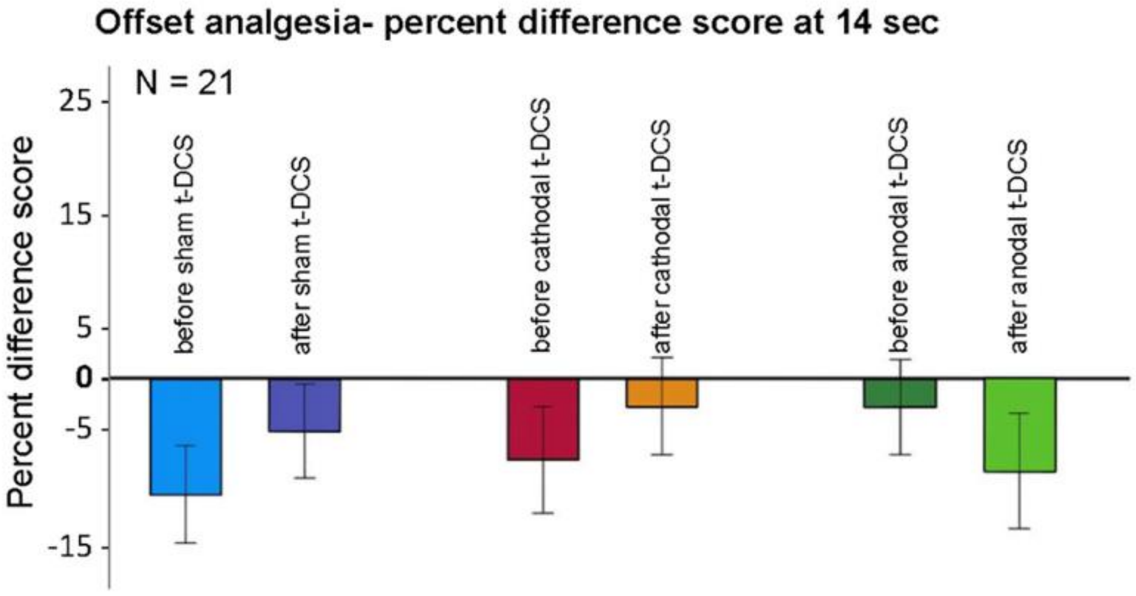


Fig. 3. Anodal cerebellar tDCS induced a significant increase in lower extremities pain threshold. Error bars represent ± 1 standard errors of the mean. $^{*}p < 0.05$.

Pereira et al., *Neurorehabilitation* 2017 cerebellar t-DCS (20 min; 2 mA; sham/anodal/cathodal)

stabilization	baseline	t-DCS	0 min post	30 min post	60 min post	CPM
3 x RIII threshold 3 x pain threshold RIII suprathreshold stim (8 min/ 48 stim) ➢ RIII area ➢ SEP amplitude ➢ Pain intensity	Heat pain intensity (44-48°C) Offset analgesia RIII threshold Pain threshold RIII suprathreshold stim (2 min/ 12 stim) ➢ RIII area ➢ SEP amplitude ➢ Pain intensity		RIII threshold Pain threshold RIII suprathreshold stim (2 min/ 12 stim) ➢ RIII area ➢ SEP amplitude ➢ Pain intensity Heat pain intensity (44-48°C) Offset analgesia	RIII threshold Pain threshold RIII suprathreshold stim (2 min/ 12 stim) ➢ RIII area ➢ SEP amplitude ➢ Pain intensity	RIII threshold Pain threshold RIII suprathreshold stim (2 min/ 12 stim) ➢ RIII area ➢ SEP amplitude ➢ Pain intensity	Pain-6 hot vs. Pain-6 hot + pain-3 cold Blinding check





Stacheneder et al., *Cerebellum* 2022

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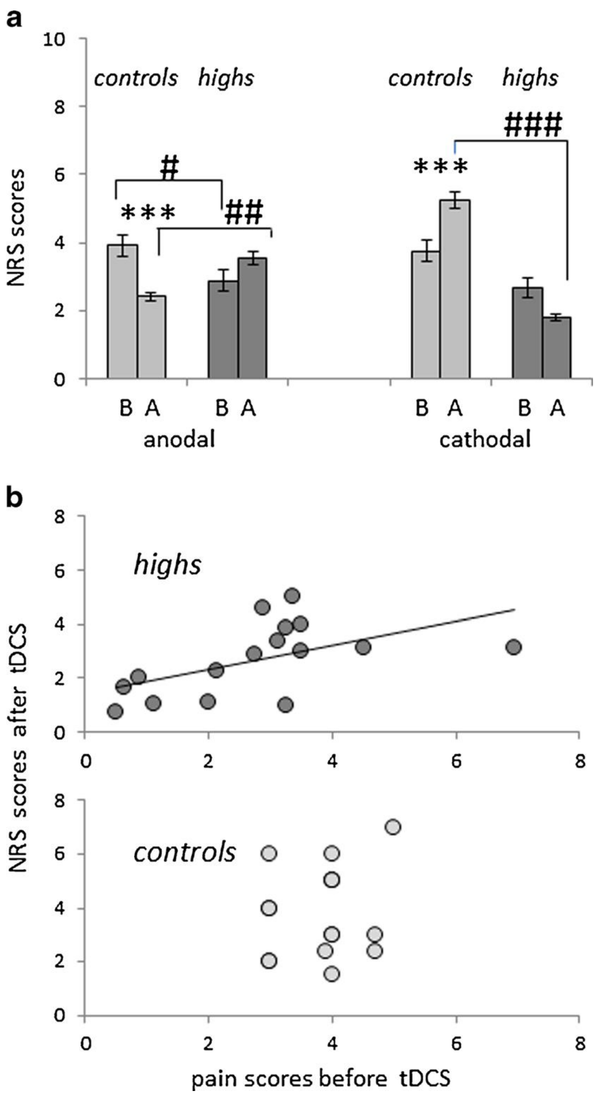
Aldo Ravelli Center for Neurotechnology and Experimental Brain therapeutics

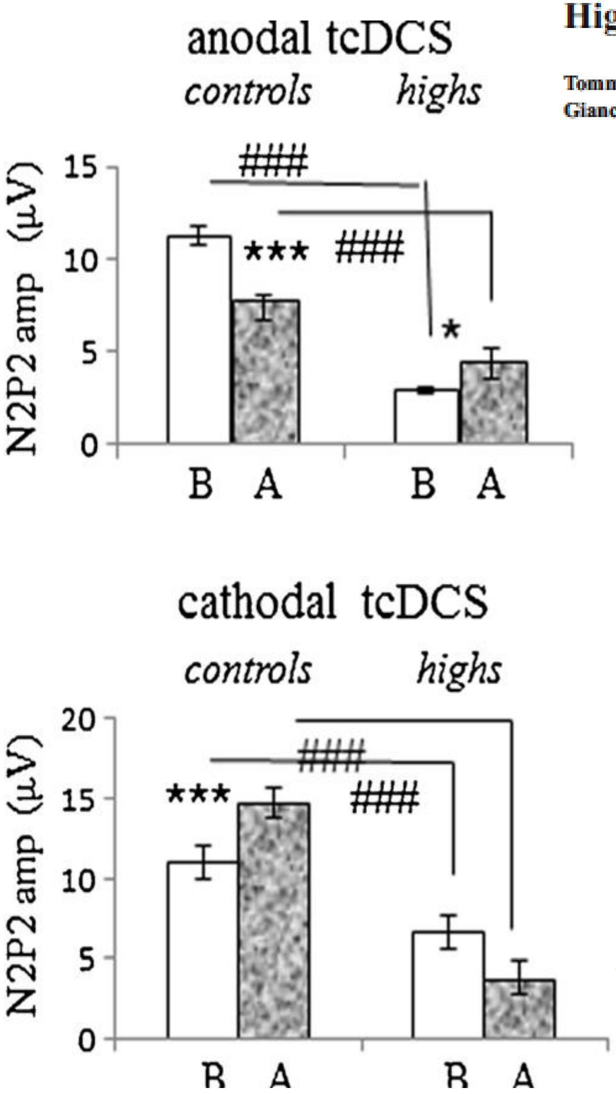
Cerebellum (2017) 16:55–61
DOI 10.1007/s12311-016-0764-2

ORIGINAL PAPER

High Hypnotizability Impairs the Cerebellar Control of Pain

Tommaso Bocci[1] · Davide Barloscio[1] · Laura Parenti[1] · Ferdinando Sartucci[1] · Giancarlo Carli[2] · Enrica L. Santarcangelo[3]





	Controls		Highs		Controls		Highs	
	Anodal				Cathodal			
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD
B, NRS scores	3.91	0.65	2.88	0.95	3.75	0.71	2.66	2.17
A, NRS scores	2.41	0.56	3|54	1.06	5.25	1.04	1.80	0.96
B, N1amplitude (µV)	13.20	3.42	5.12	2.22	11.45	2.67	7.60	3.16
A, N1 amplitude(µV)	9.24	3.64	6.14	2.30	15.19	2.87	6.95	4.09
B, N1 latency(msec)	123.63	12.19	174.85	23.44	127.63	11.45	185.36	26.97
A, N1 latency(msec)	160.73	16.57	168.25	23.91	106.10	7.13	179.16	13.22
B, N2P2 amplitude(µV)	11.23	3.38	2.96	1.01	10.96	1.39	6.62	4.84
A, N2P2amplitude(µV)	7.74	2.90	4.56	1.64	14.76	1.83	3.79	0.83
B,N2 latency(msec)	154.98	13.49	202.31	27.43	153.36	26.05	205.50	19.58
A, N2 latency (msec)	195.65	16.88	211.50	9.76	128.09	20.71	237.24	40.41

B, A before, after cerebellar tDCS

Bocci et al., *Cerebellum* 2017

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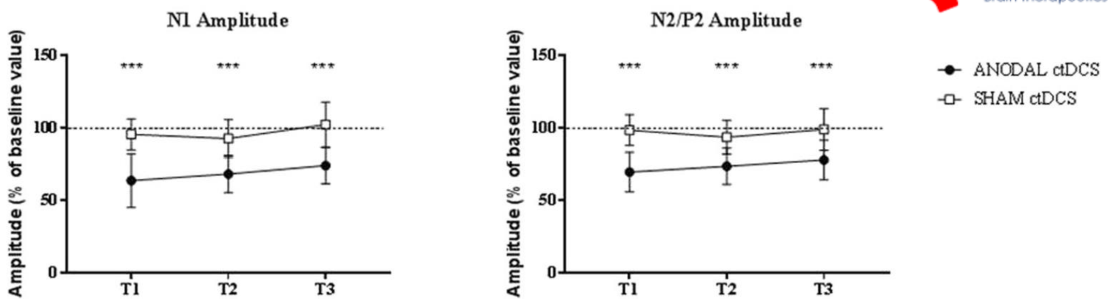
The Cerebellum
https://doi.org/10.1007/s12311-019-01020-w

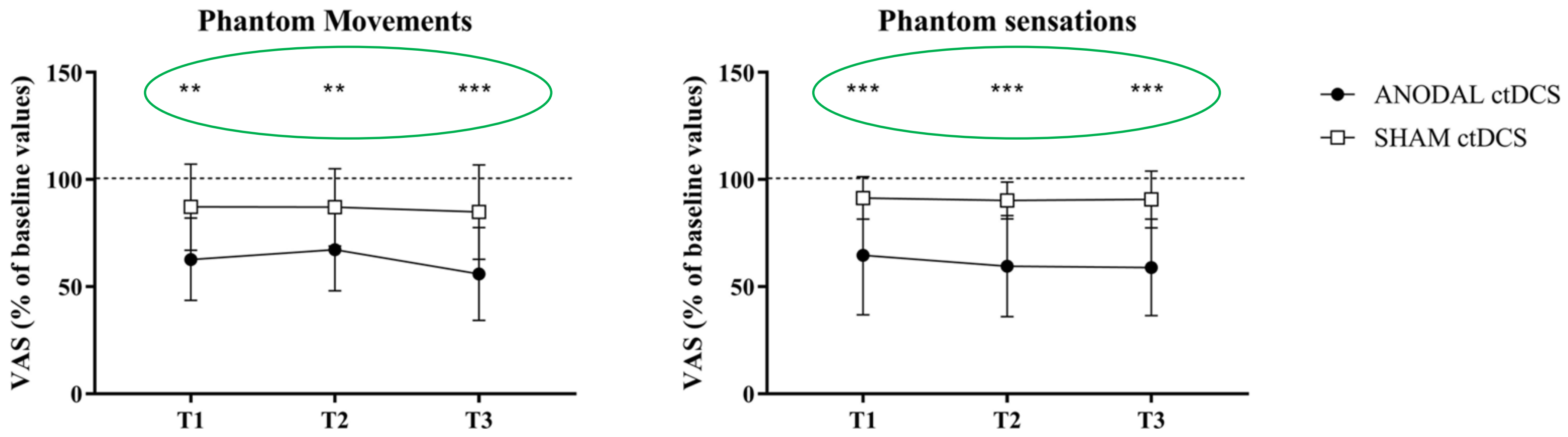
Aldo Ravelli Center for Neurotechnology and Experimental Brain therapeutics

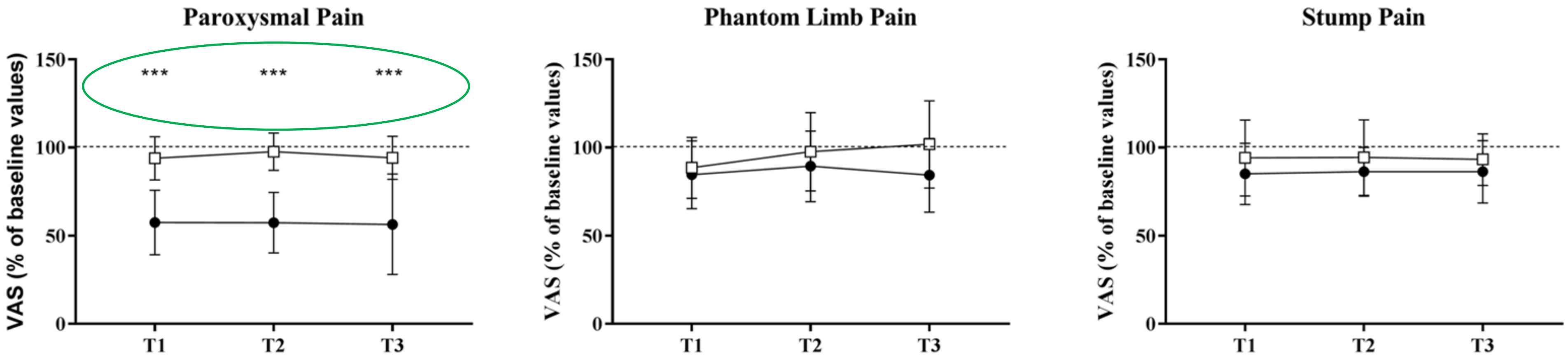
ORIGINAL PAPER

Cerebellar Transcranial Direct Current Stimulation (ctDCS) Ameliorates Phantom Limb Pain and Non-painful Phantom Limb Sensations

Tommaso Bocci[1,2] · Giuliano De Carolis[3] · Roberta Ferrucci[2] · Mery Paroli[3] · Federica Mansani[2] · Alberto Priori[2] · Massimiliano Valeriani[4,5] · Ferdinando Sartucci[1]







tDCS e "Phantom Limb Pain"

PAIN® xxx (2013) xxx–xxx

IASP

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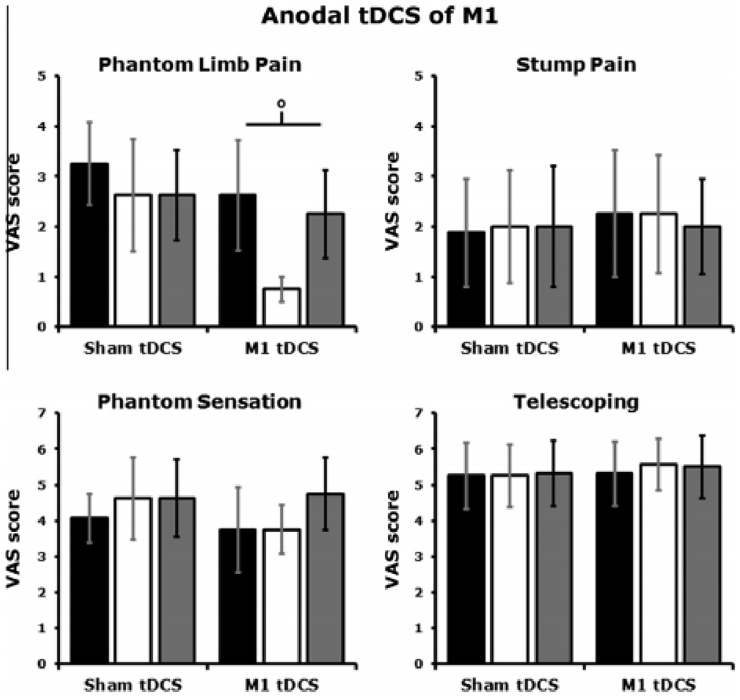
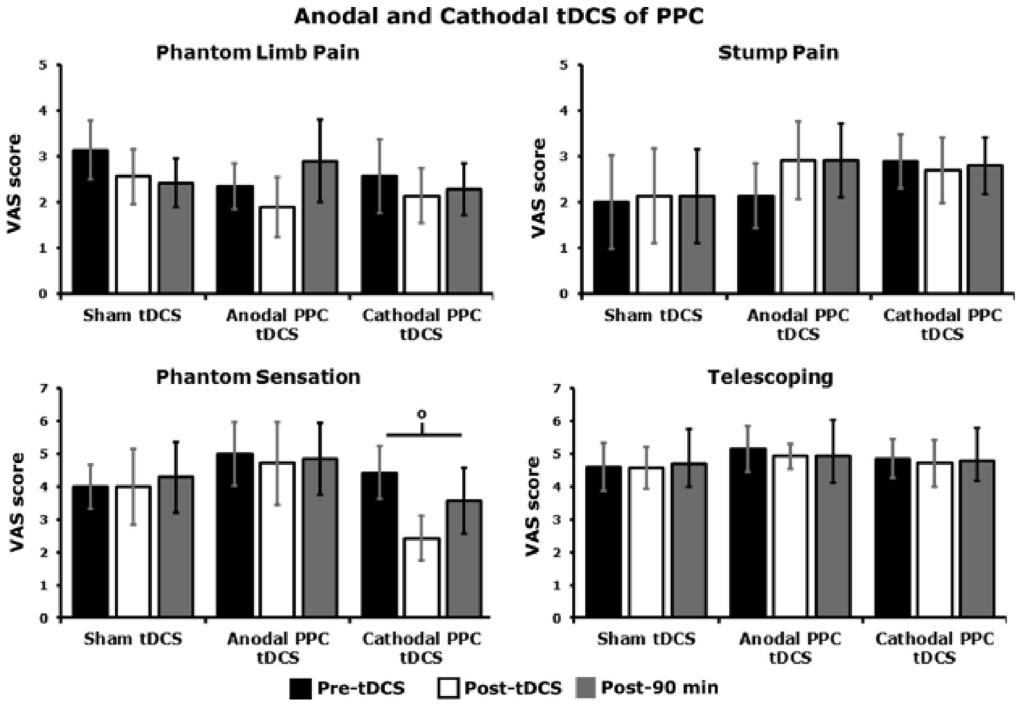
Motor and parietal cortex stimulation for phantom limb pain and sensations

Nadia Bolognini [a,b,*], Elena Olgiati [a], Angelo Maravita [a], Francesco Ferraro [c], Felipe Fregni [d]

[a] Department of Psychology, University of Milano-Bicocca, Milano, Italy
[b] Neuropsychological Laboratory, IRCCS Istituto Auxologico Italiano, Milano, Italy
[c] Department of Rehabilitation, Azienda Ospedaliera Carlo Poma, Mantova, Italy
[d] Laboratory of Neuromodulation, Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, MA, USA



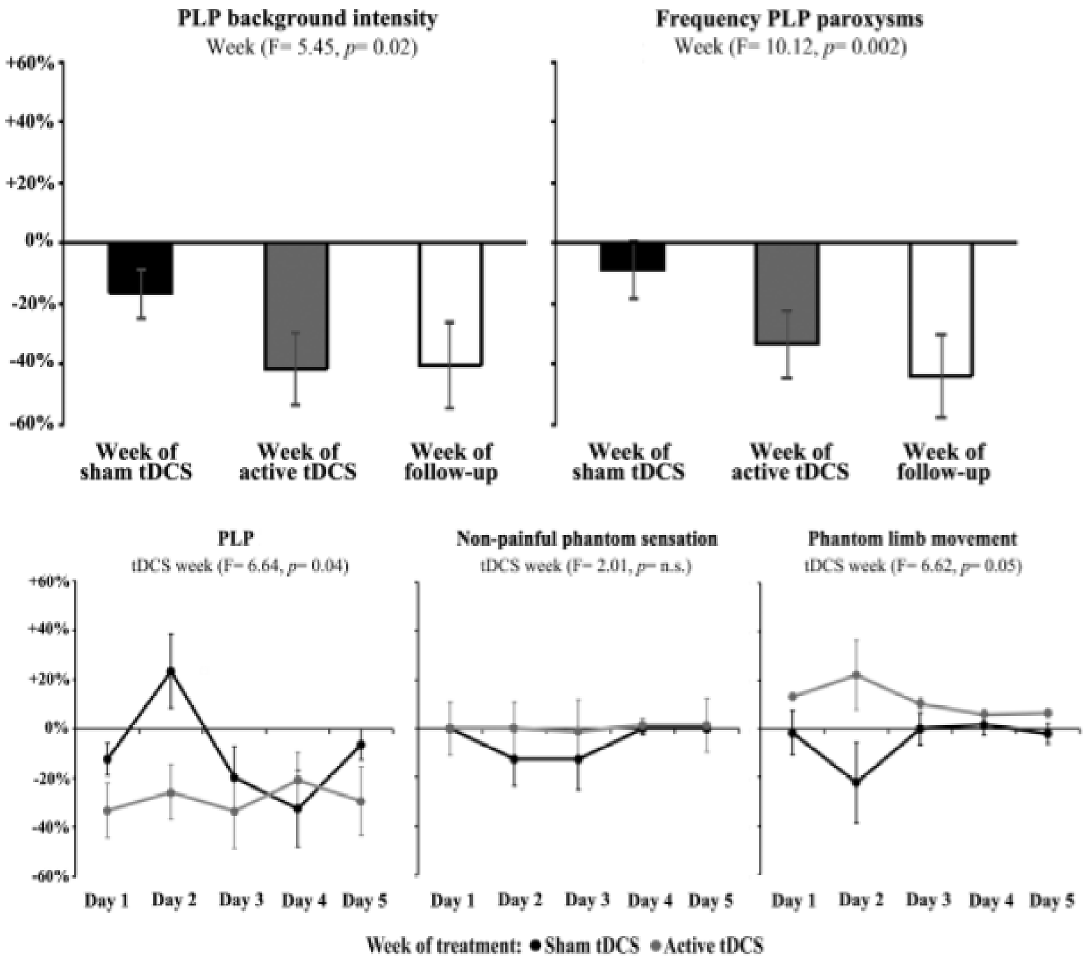


tDCS e "Phantom Limb Pain"

J Pain. 2015 Jul;16(7):657-65. doi: 10.1016/j.jpain.2015.03.013. Epub 2015 Apr 8.

Immediate and Sustained Effects of 5-Day Transcranial Direct Current Stimulation of the Motor Cortex in Phantom Limb Pain.

Bolognini N[1], Spandri V[2], Ferraro F[3], Salmaggi A[4], Molinari AC[5], Fregni F[6], Maravita A[7].



1) 5-day of tDCS over the motor cortex induces a substained phantom limb pain relief
2) An immediate improvement of phantom limb pain and movement is brought about tDCS
3) Phantom limb pain relief is linked to increased movement of the phantom limb
4) Neuromodulation may be helpful for the management of phantom limb pain

The Cerebellum and its role in nociceptive processing. From the sensory dimension to emotional and cognitive aspects

Cerebellum and Cognition: an overview

- «negative bias»
- Stimulus saliency
- Visuomotor tasks

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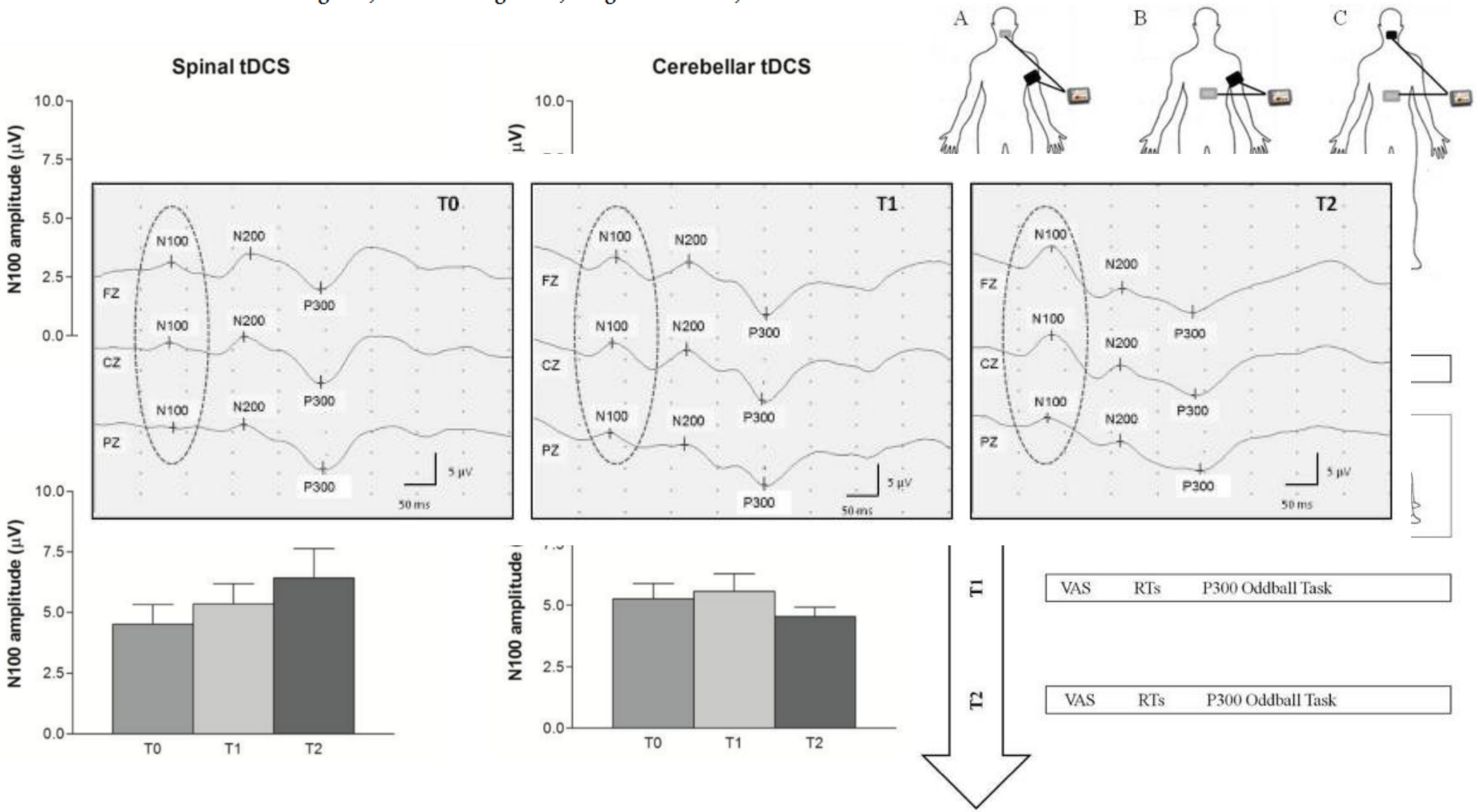
Neuropsychologia

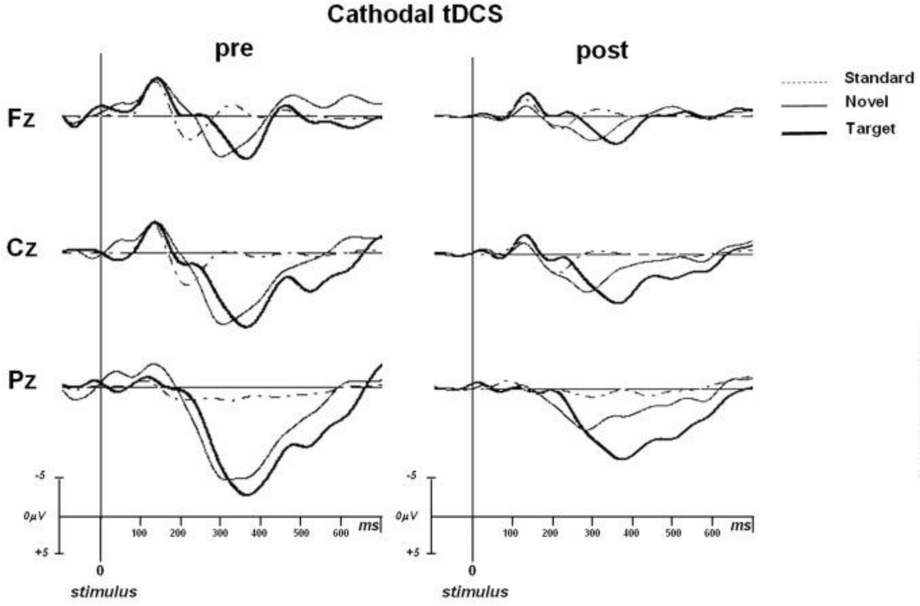
journal homepage: http://www.elsevier.com/locate/neuropsychologia

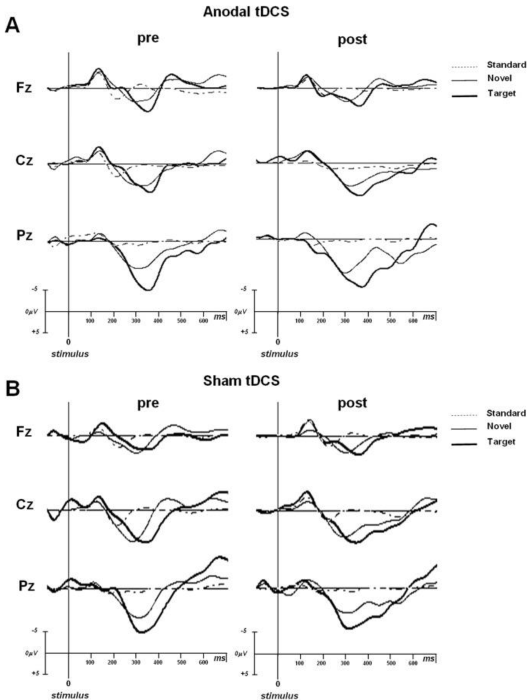
ELSEVIER

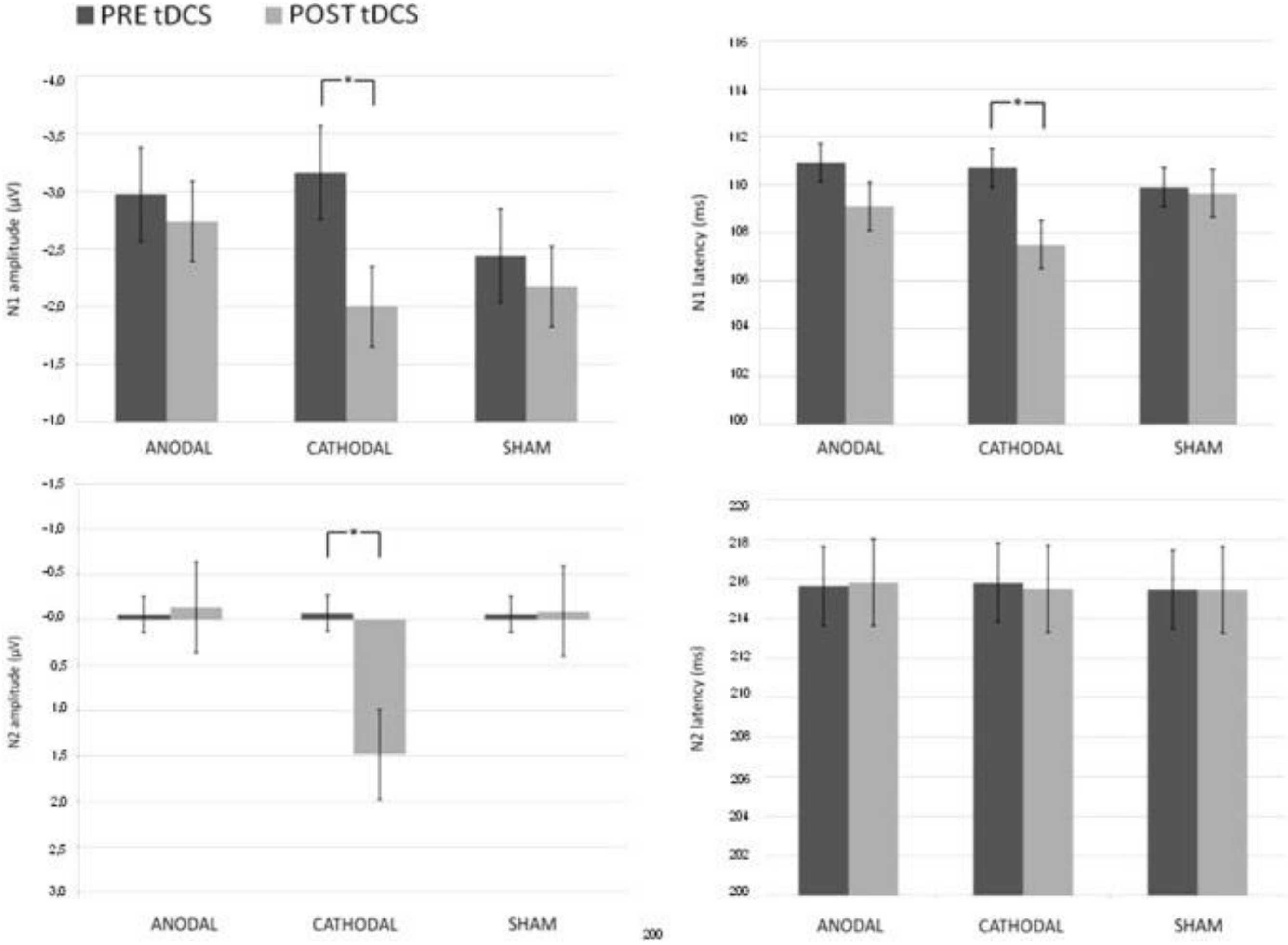
Spino-cerebellar tDCS modulates N100 components of the P300 event related potential

Fabiana Ruggiero [a], Roberta Ferrucci [a,b,c], Tommaso Bocci [b,c], Martina Nigro [a], Maurizio Vergari [a], Sara Marceglia [a,d], Sergio Barbieri [a], Alberto Priori [b,*]









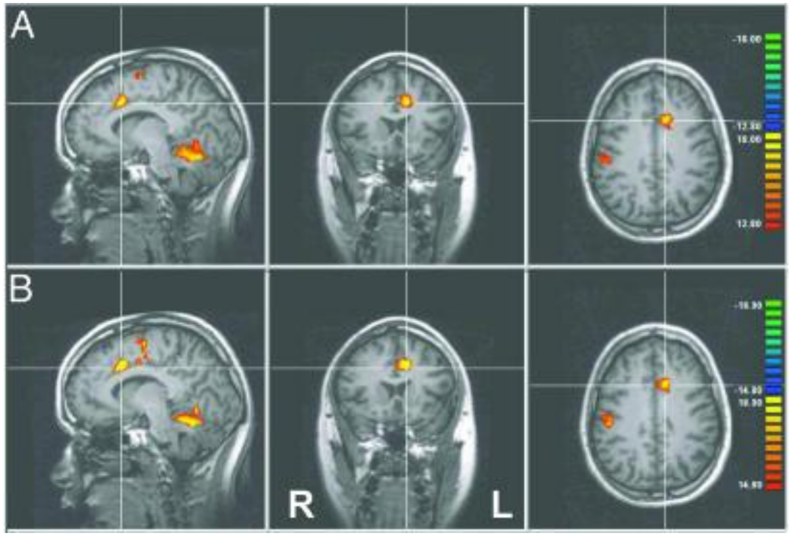
Mannarelli et al., *Neuropsychologia* 2016

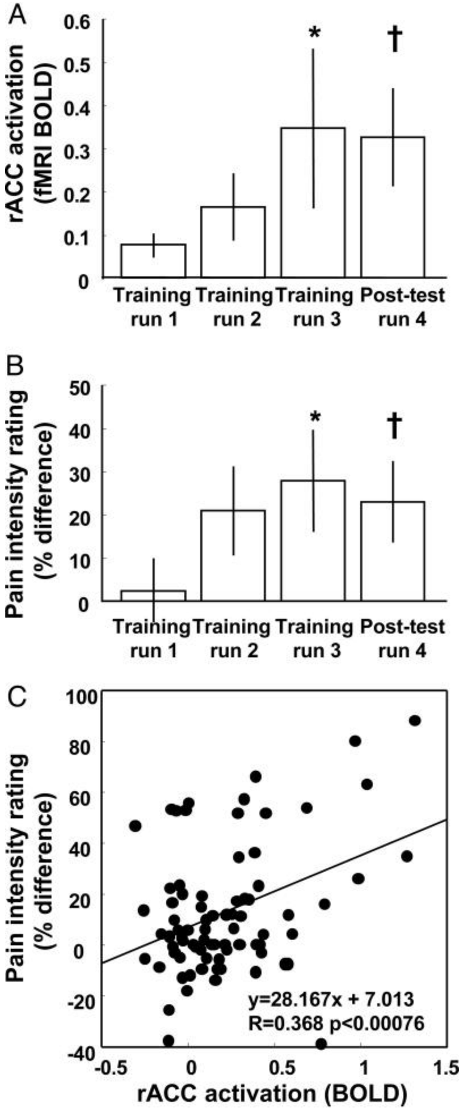
Pain and cognition: what did we learn from meditation and Mindfullness training?

Control over brain activation and pain learned by using real-time functional MRI

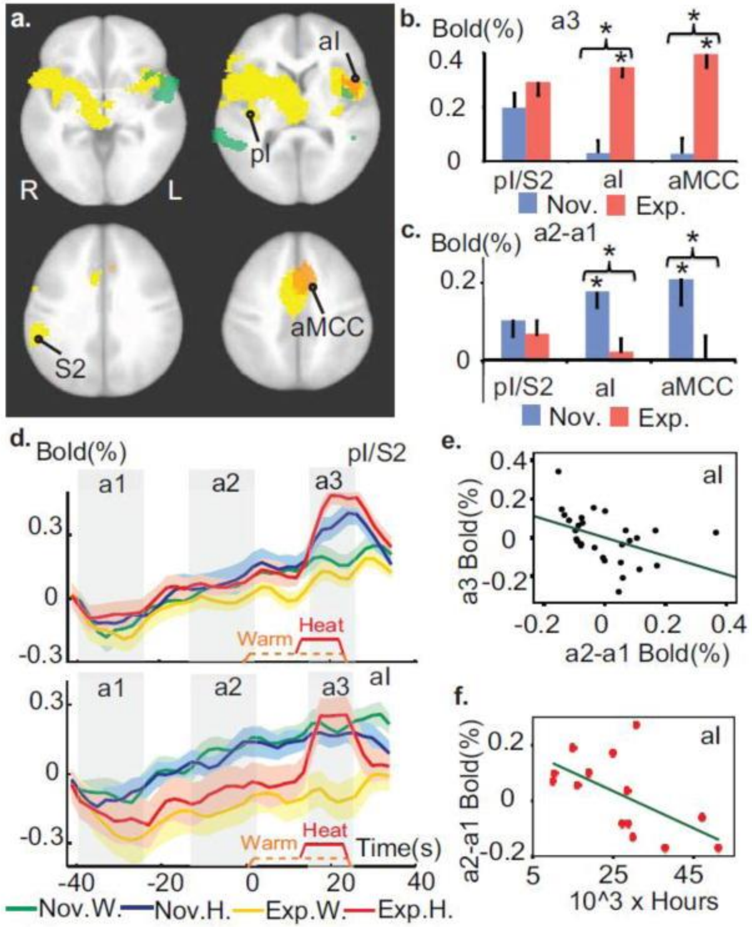
R. Christopher deCharms[†‡], Fumiko Maeda[§¶], Gary H. Glover[||], David Ludlow[††], John M. Pauly[‡‡], Deepak Soneji[††], John D. E. Gabrieli[§,§§], and Sean C. Mackey[††]

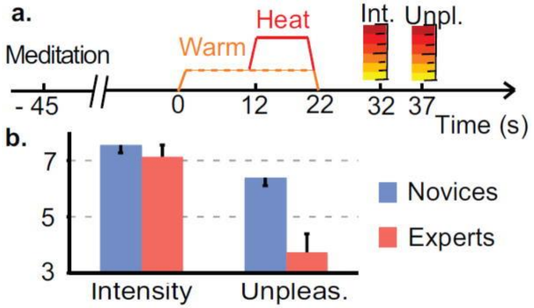
[†]Omneuron, Inc., 99 El Camino Real, Menlo Park, CA 94025; Departments of [§]Psychology, [¶]Psychiatry, [||]Radiology, and [‡‡]Electrical Engineering and [††]Department of Anesthesia and Division of Pain Management, Stanford University, Stanford, CA 94305; and [§§]Department of Brain and Cognitive Sciences, Harvard–MIT Division of Health Sciences and Technology, Cambridge, MA 02139



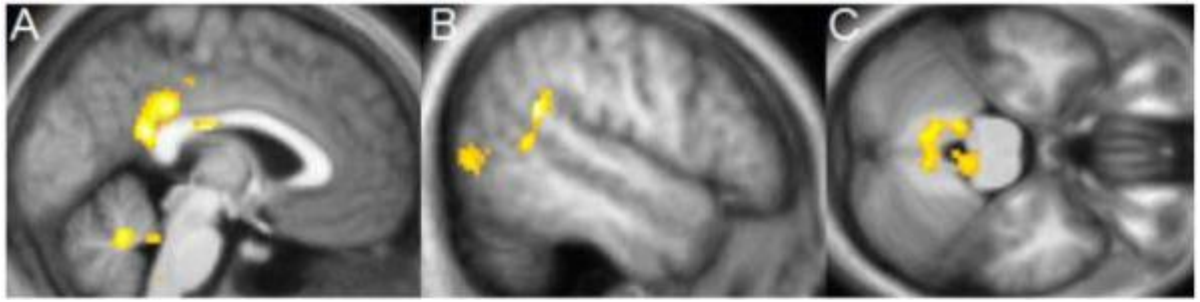


deCharms et al., PNAS 2005





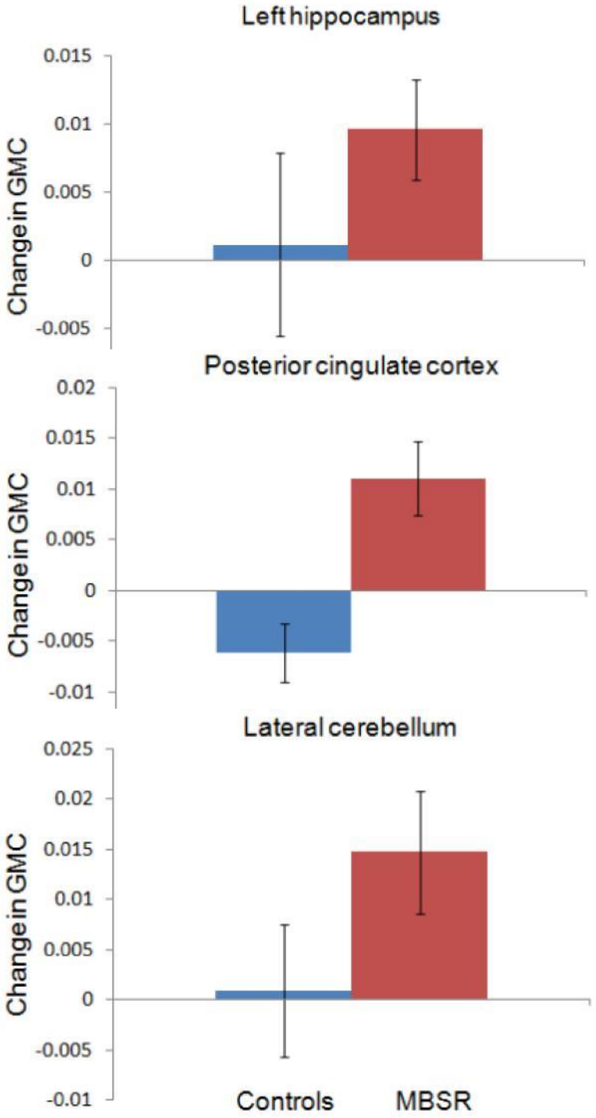
Lutz et al., NeuroImage 2013



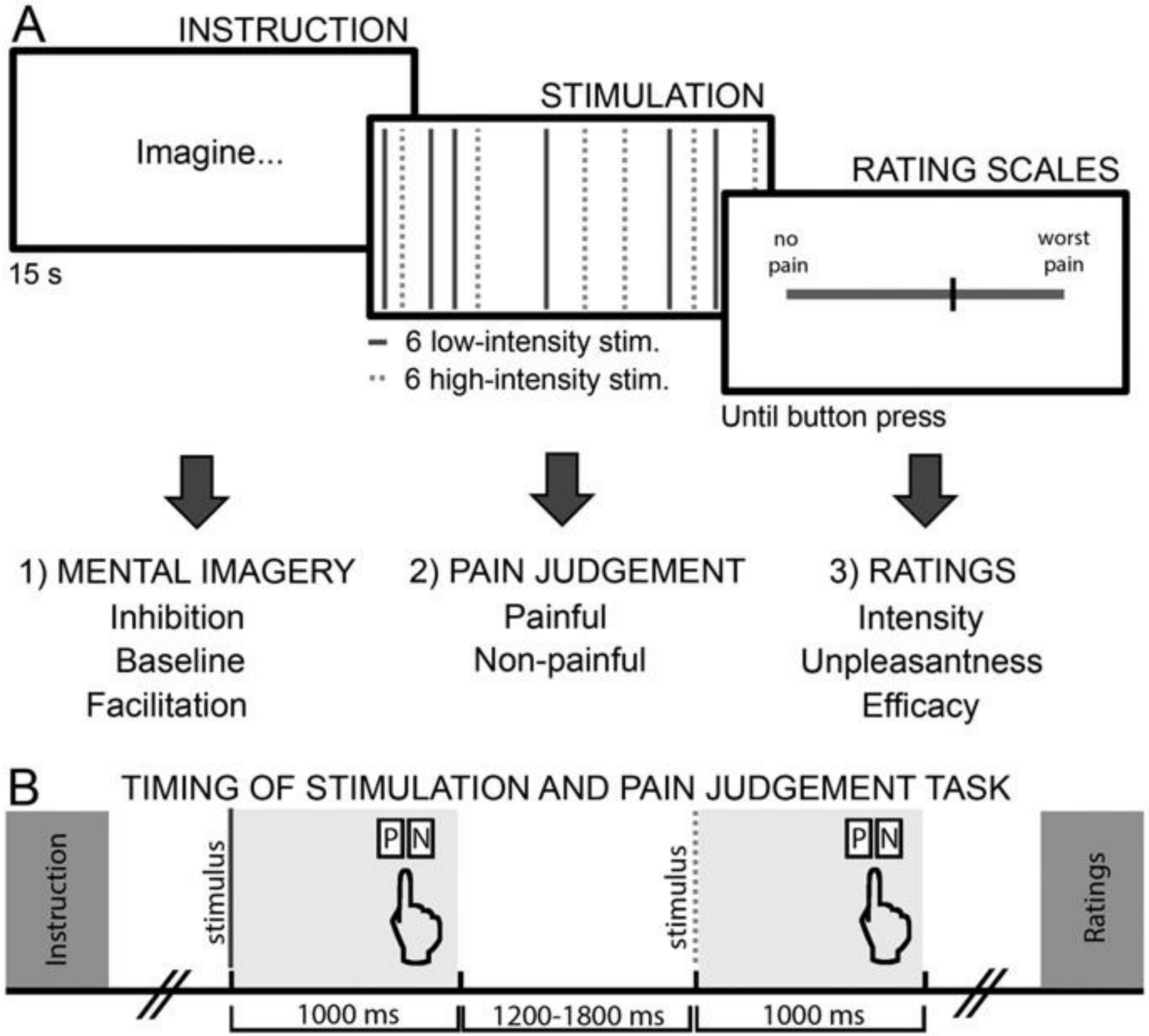
Overview of morphometric studies on meditation

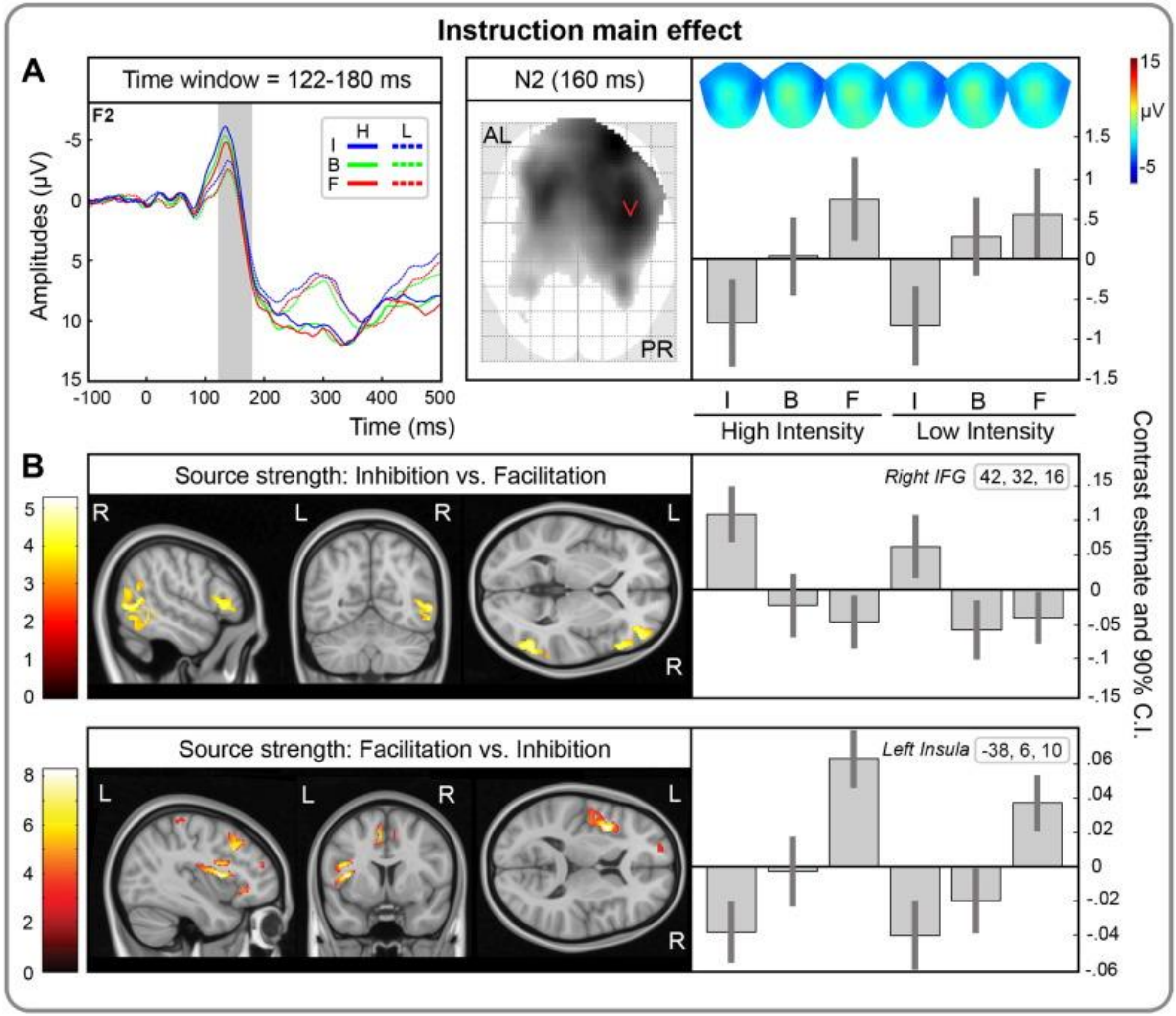
Study	Meditation tradition	N Meditators/ Controls	Morphological measures	Regions identified greater in meditators than controls
Lazar et al. (2005)	Insight	20 / 15	Cortical thickness	Right anterior insula and right middle and superior frontal sulci
Pagnoni & Cekic (2007)	Zen	13 / 13	Gray matter volume (VBM in SPM5)	Meditators showed no age-related decline in the left putamen as compared to controls
Hölzel et al. (2008)	Insight	20 / 20	Gray matter density (VBM in SPM2)	Left inferior temporal lobe, right insula, and right hippocampus
Vestergaard-Poulsen et al., (2009)	Tibetan Buddhist	10 / 10	Gray matter density & volume (VBM in SPM5)	Medulla oblongata, left superior and inferior frontal gyri, anterior lobe of the cerebellum and left fusiform gyrus
Luders et al. (2009)	Zazen, Vipassana, Samatha & others	22 / 22	Gray matter volume (VBM in SPM5)	Right orbito-frontal cortex, right thalamus, left inferior temporal lobe, right hippocampus
Grant et al. (2010)	Zen	19/20	Cortical thickness	Right dorsal anterior cingulate cortex, secondary somatosensory cortex

VBM: voxel-based morphometry (Gaser), SPM: Statistical Parametric Mapping, (Wellcome Department of Cognitive Neurology, London)



Hölzel et al., *Psychiatry Res* 2011





Fardo et al., *NeuroImage* 2015

Conclusions

- The Cerebellum is involved in the modulation of both ascending and descending pathways, engaged in the sensory-discriminative, as well as affective-emotional and cognitive dimensions of pain processing
- cerebellar tDCS has recently provided interesting data about pain treatment
- a polarity-specific effect has been described in three (out of three) articles, with anodal stimulation driving an overall analgesic effect
- As a proof of concept, the combination with either tsDCS or mindfulness training may improve its effects as a potential non-pharamcological tool


Thank You for your kind attention!