TMS in Special Populations

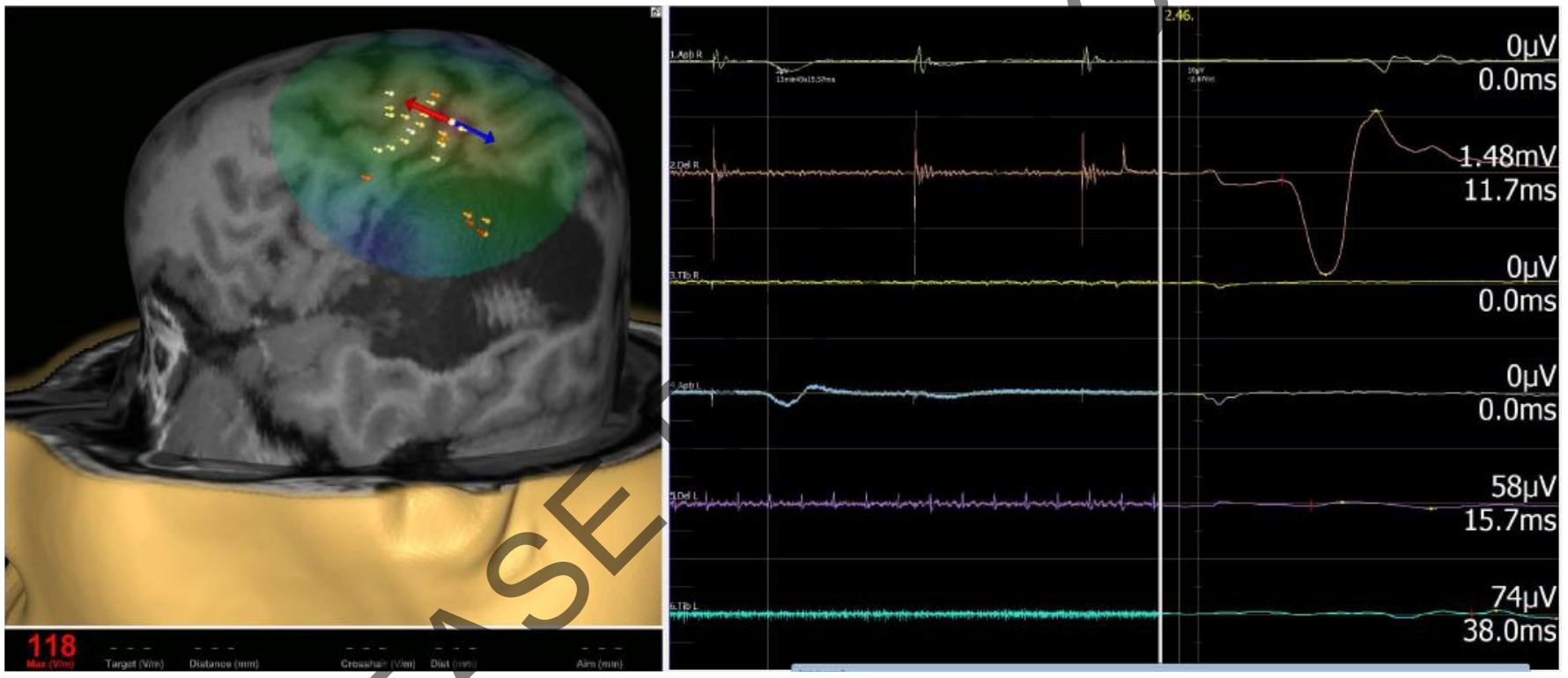
Alexander Rotenberg, M.D., Ph.D.

Professor of Neurology | Joseph J. Volpe Chair in Neurology

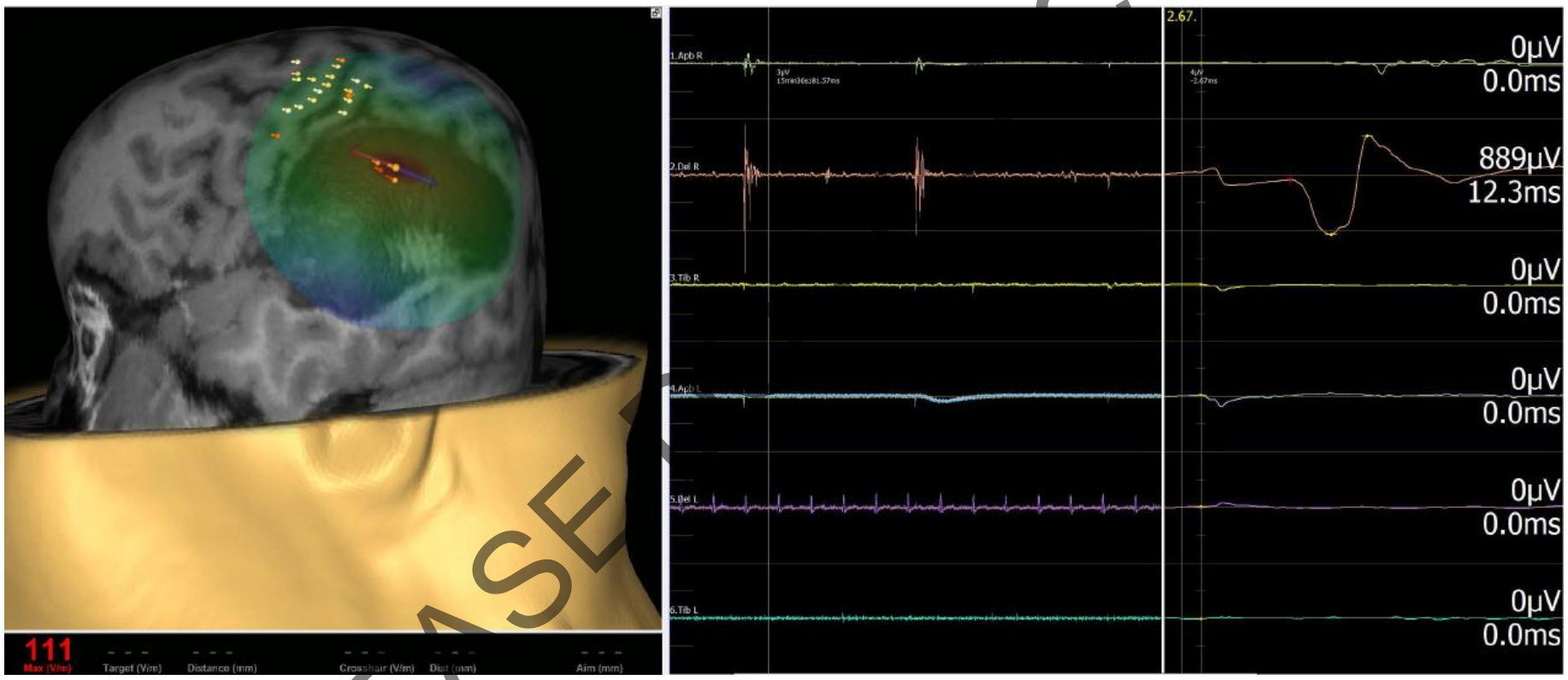
Director, Neuromodulation Program

Unusual brains in TMS

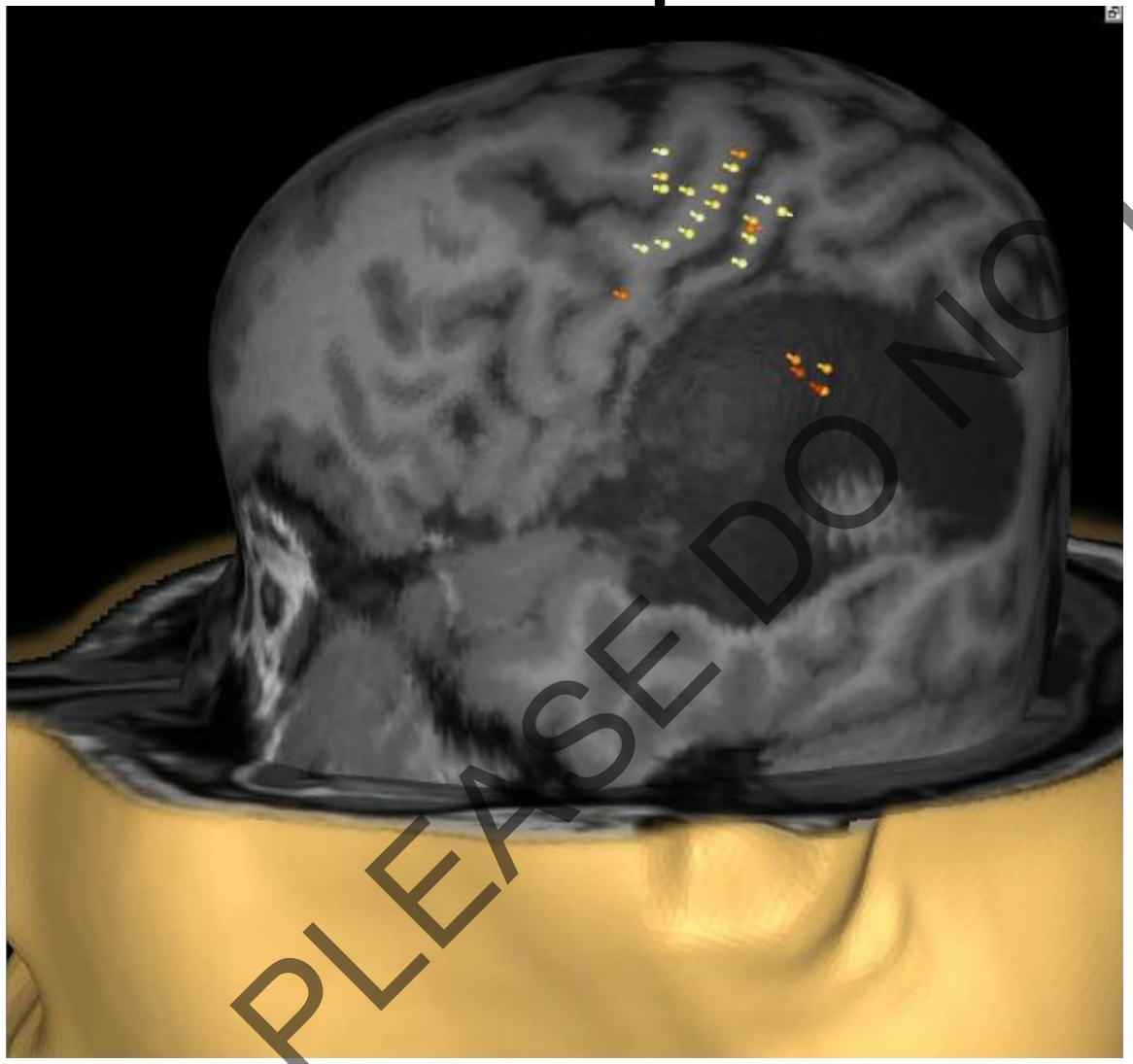
Right deltoid sample

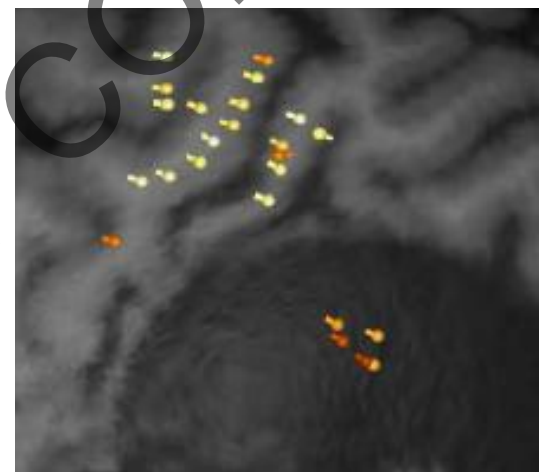


Right Deltoid sample (stim in CSF)



Right deltoid map





Contents lists available at ScienceDirect

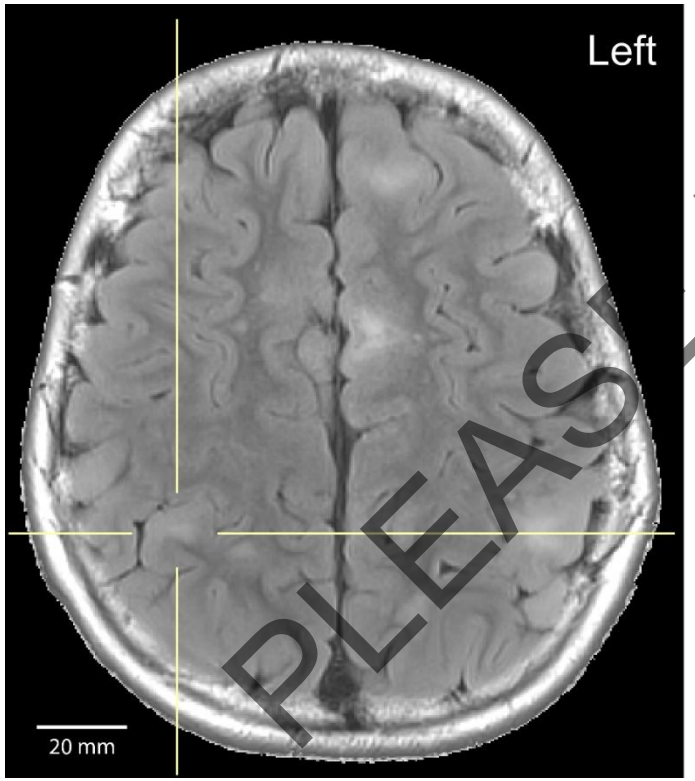
Epilepsy & Behavior Case Reports

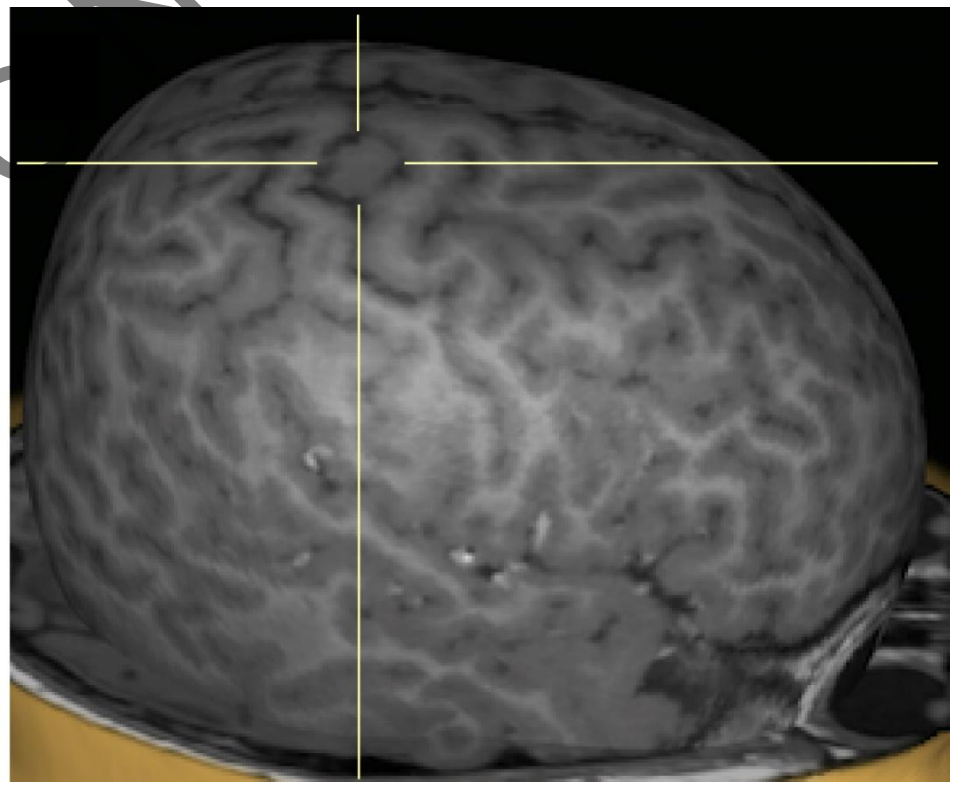
journal homepage: www.elsevier.com

Case Report

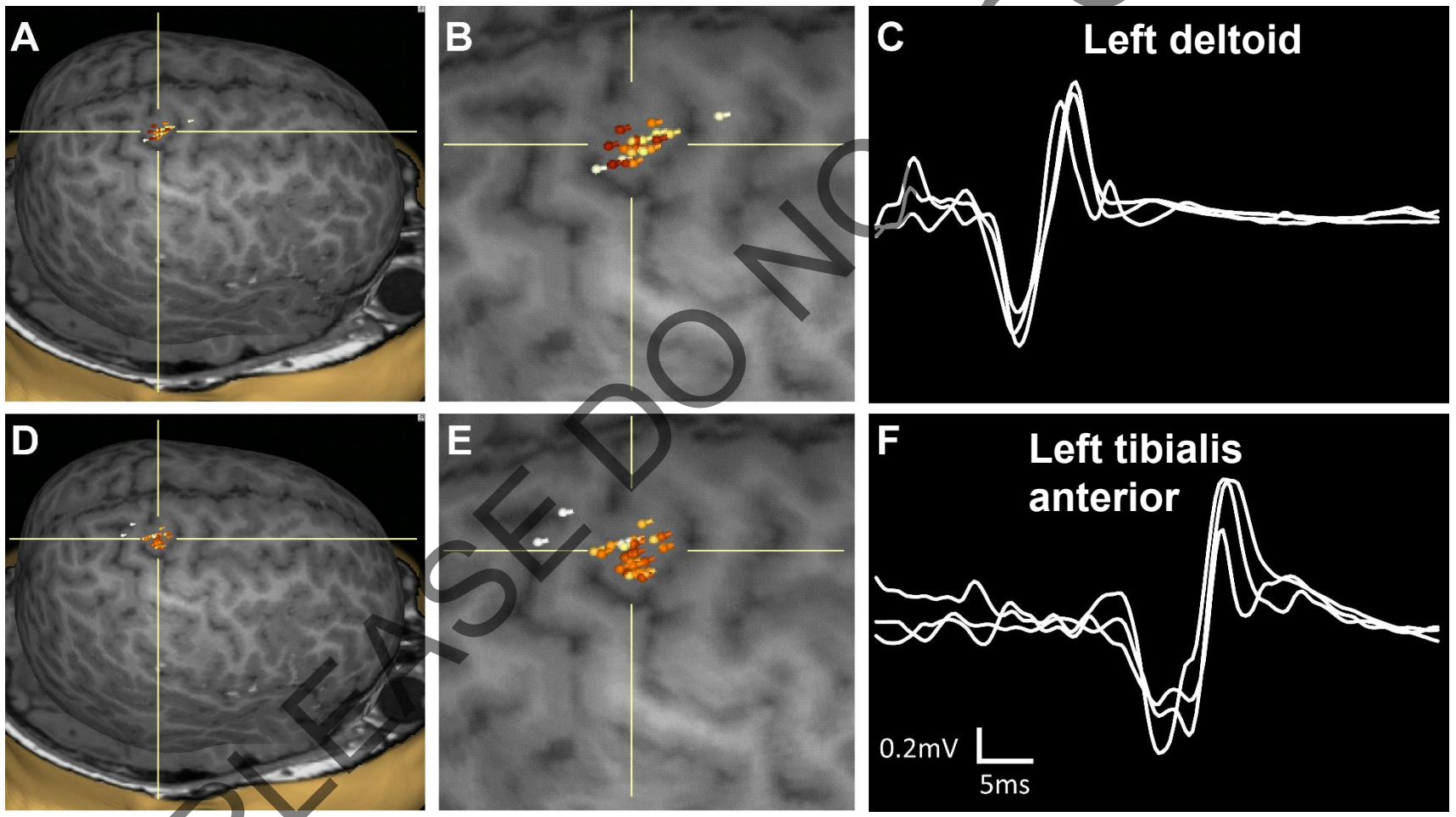
Neurophysiological evidence of preserved connectivity in tuber tissue

Kaye HL [a, b, c, 1], Peters JM [a, c, 1], Gersner R [a, b], Chamberland M [d, e], Sansevere A [a], Rotenberg A [a, b, c, *]





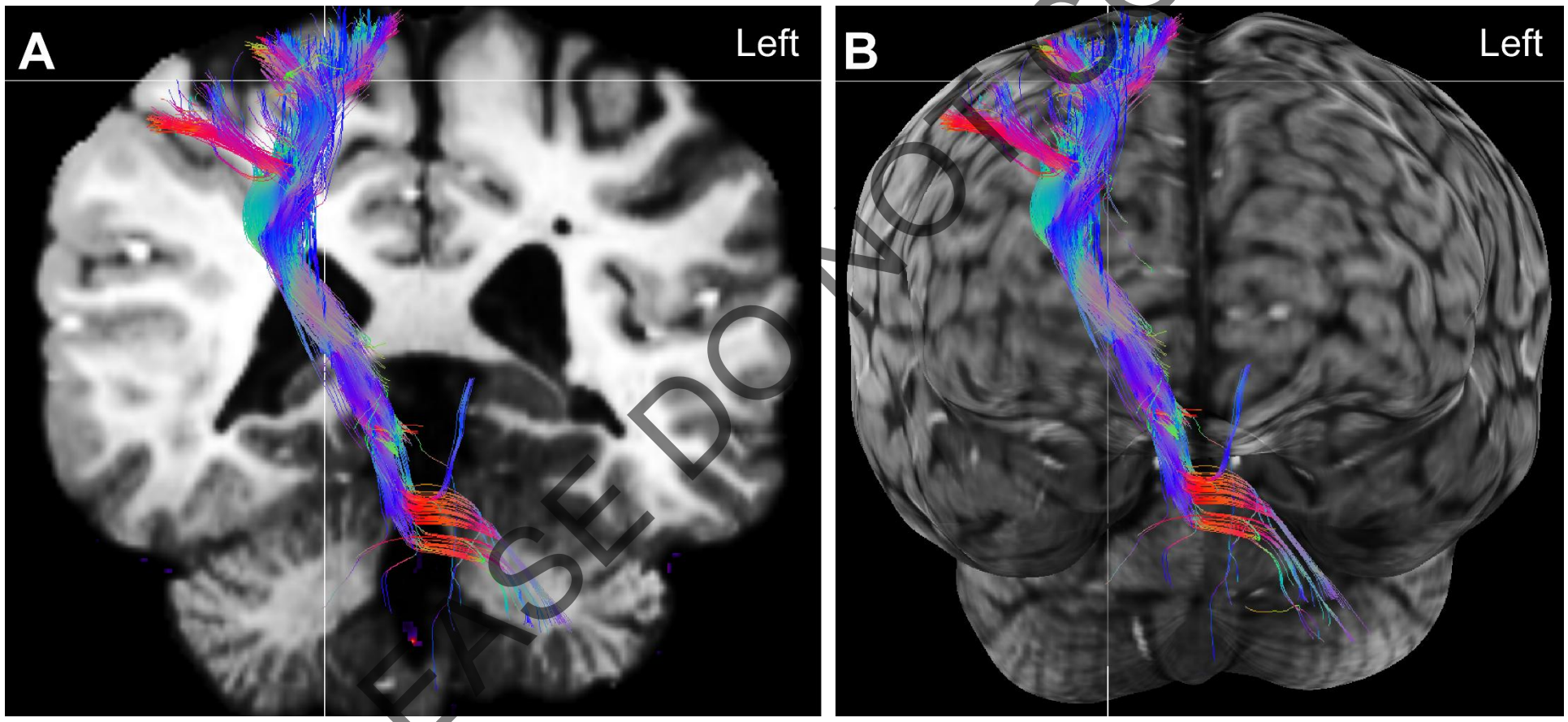
Left deltoid and tibialis anterior Motor Maps



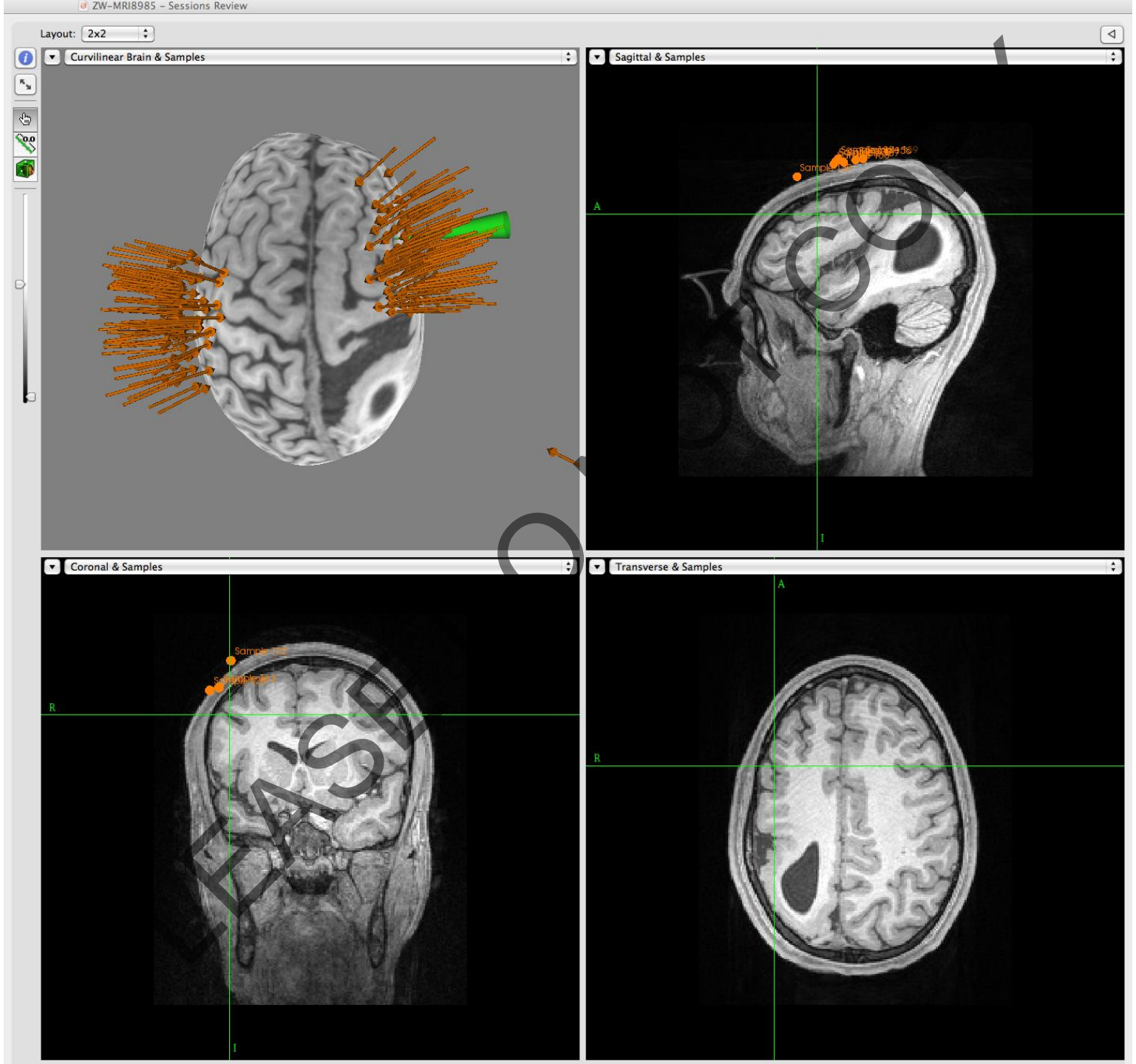
Kaye et al., Epilepsy & Behav. Case Reports

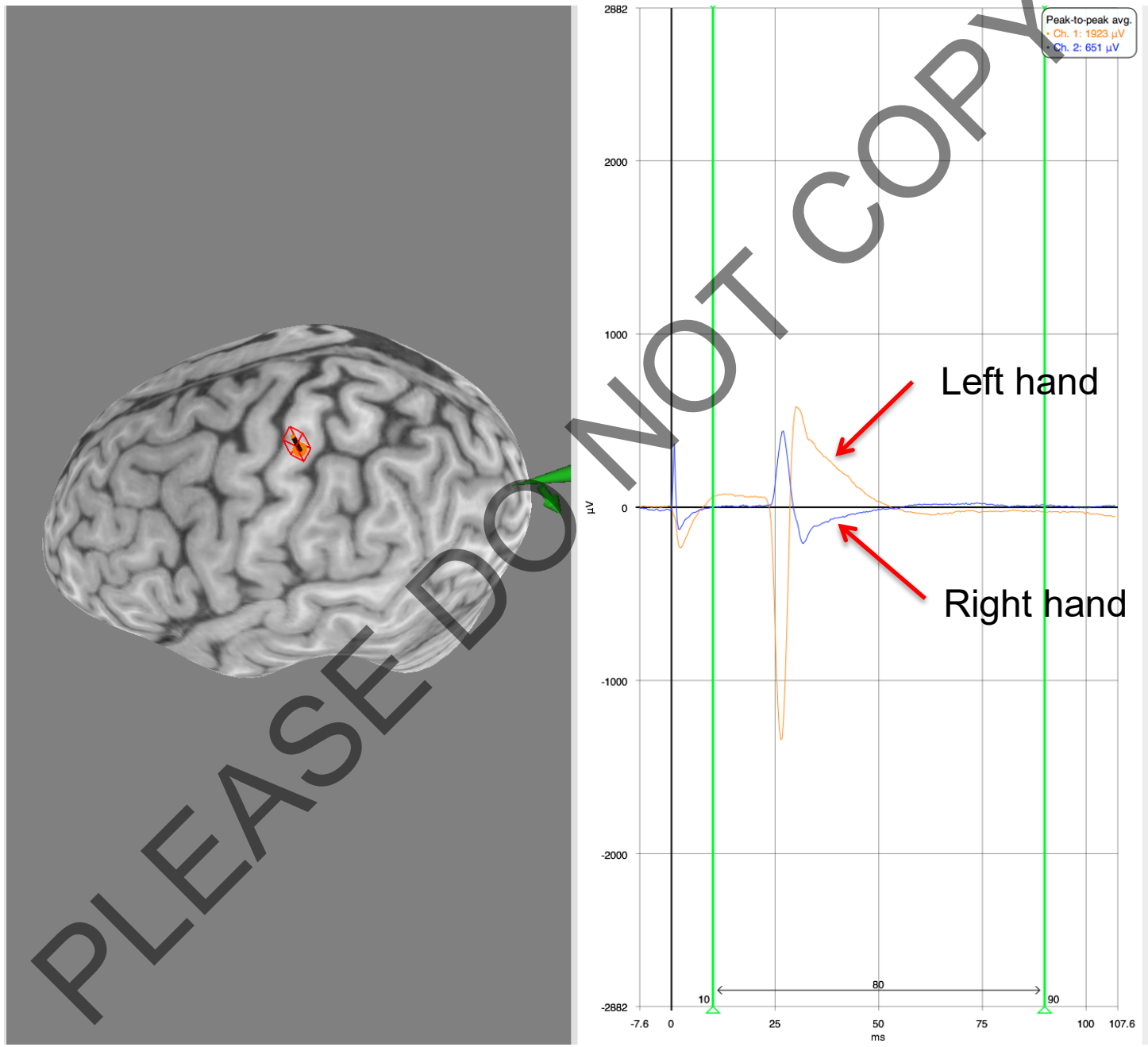
Diffusion Tractography Imaging

corticospinal connectivity within the tuber tissue



Kaye et al., Epilepsy & Behav. Case Reports 2016


ZW-MRI8985 – Sessions Review
Layout: 2x2
Curvilinear Brain & Samples
Sagittal & Samples
Coronal & Samples
Transverse & Samples
A
R
I

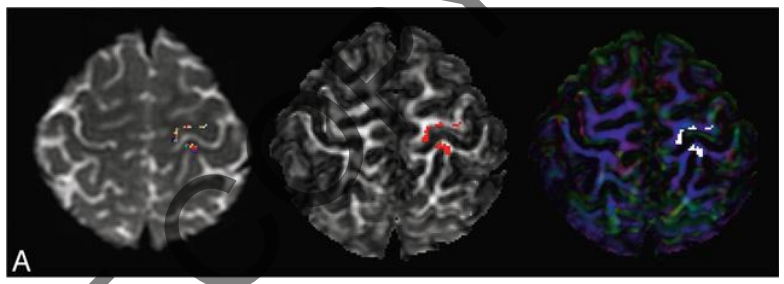


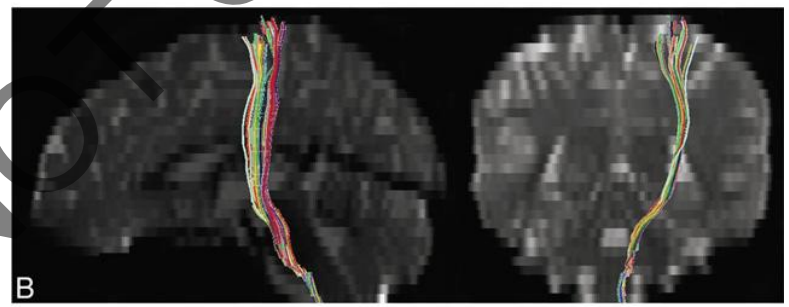
ORIGINAL RESEARCH

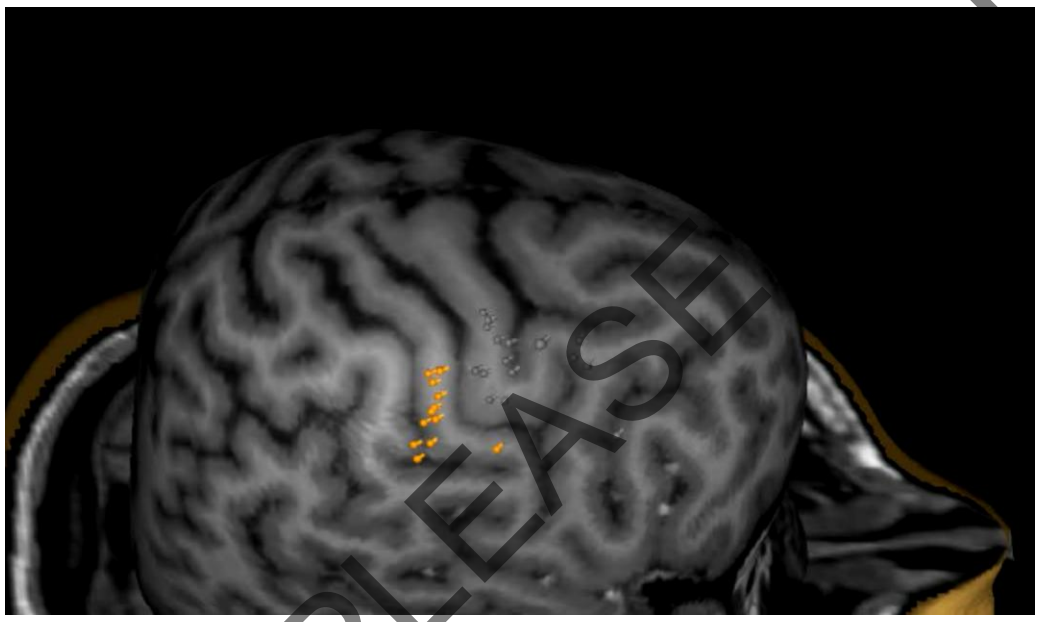
Diffusion Tensor Imaging Study of the Cortical Origin and Course of the Corticospinal Tract in Healthy Children

A. Kumar
C. Juhasz
E. Asano
S.K. Sundaram
M.I. Makki
D.C. Chugani
H.T. Chugani

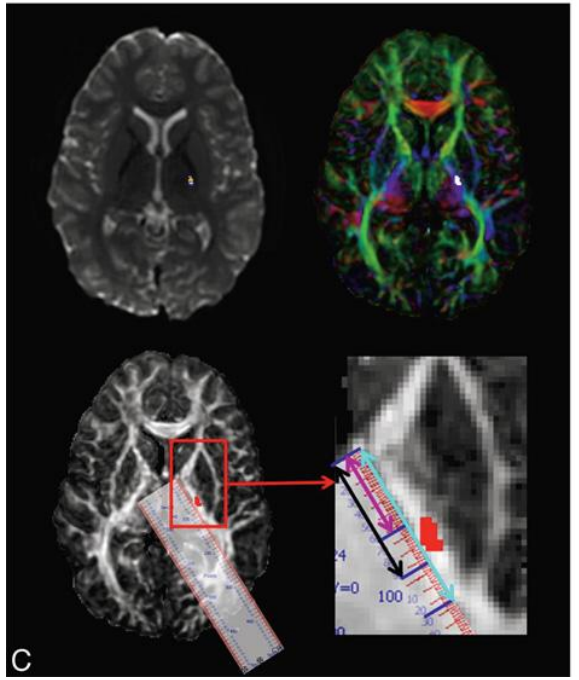
AJNR Am J Neuroradiol 30:1963–70 | Nov-Dec 2009 | www.ajnr.org



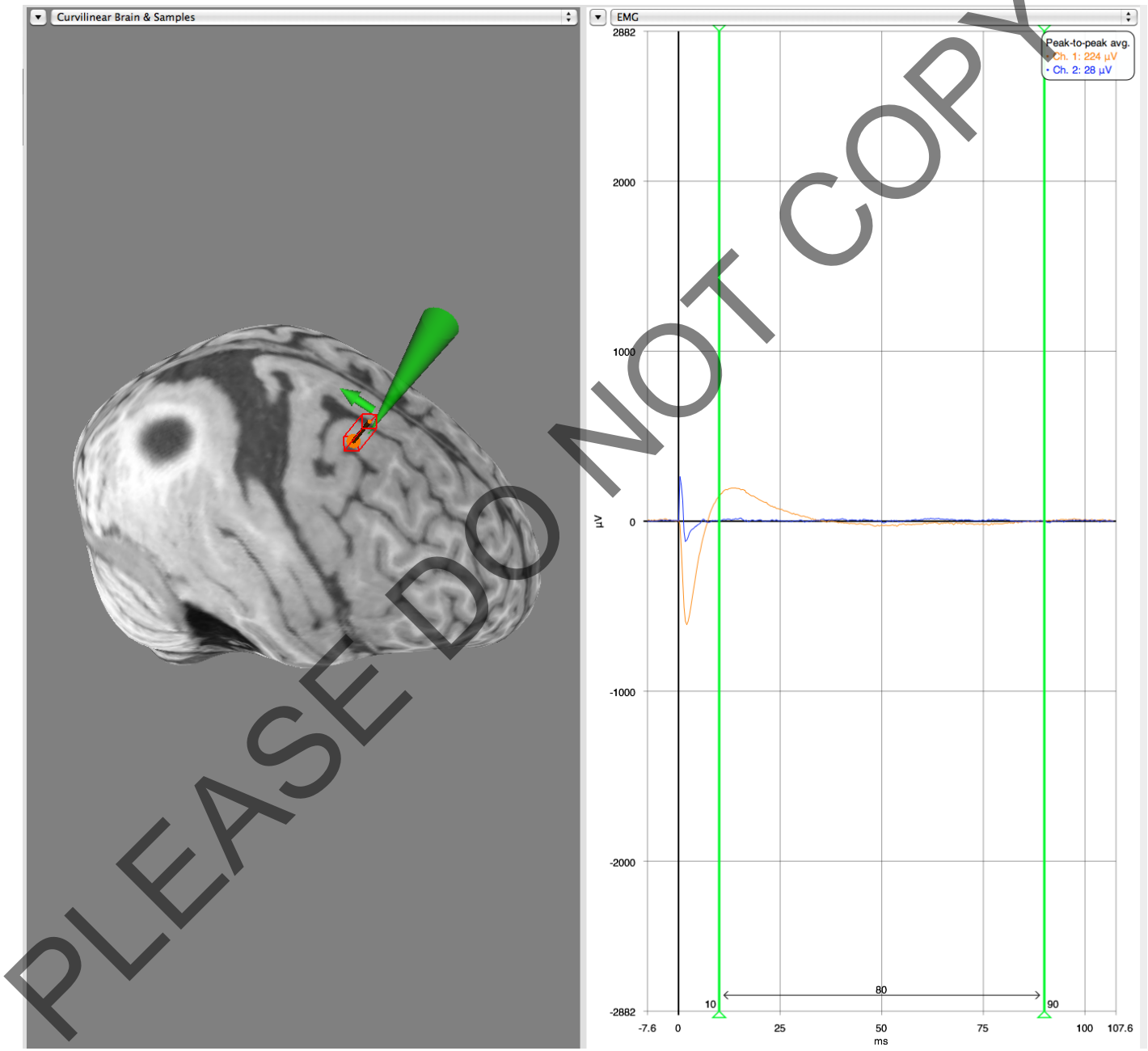




L APB map

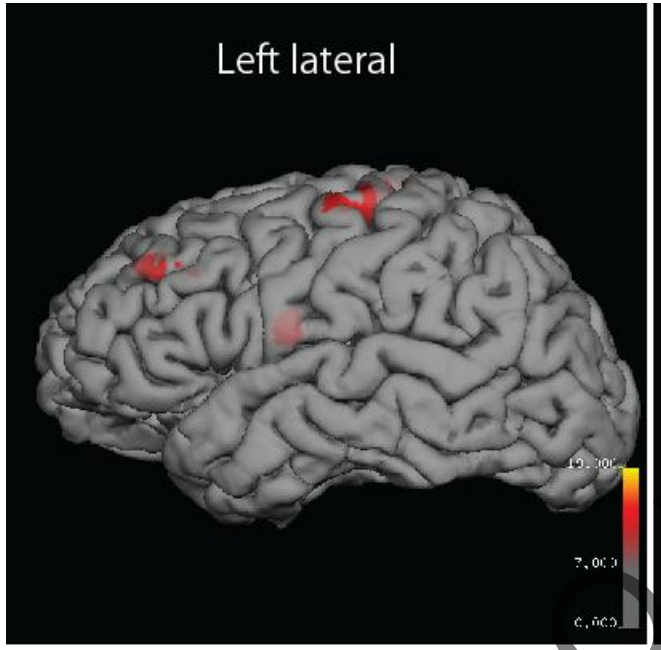


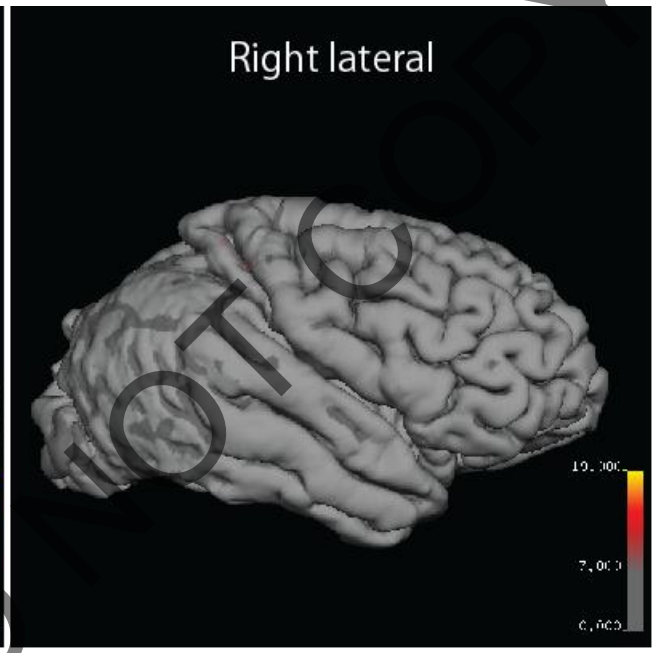
Healthy 12yF



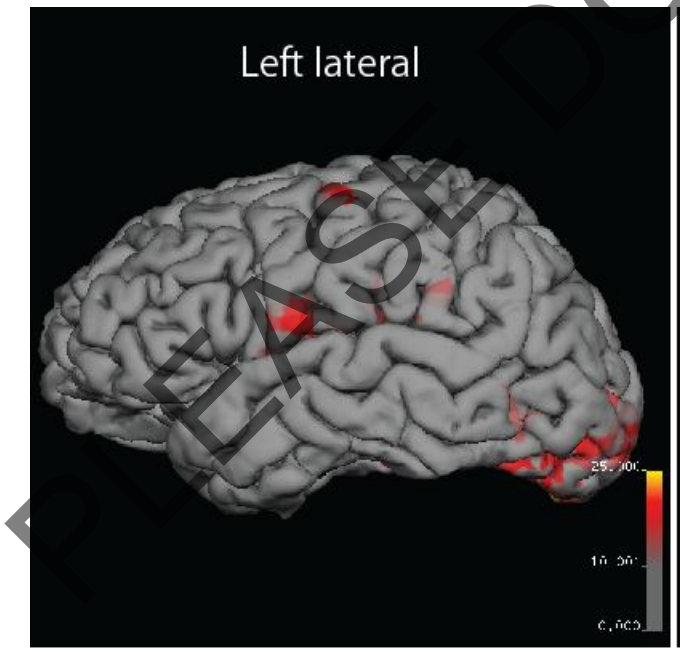
Hand Motor Task - fMRI

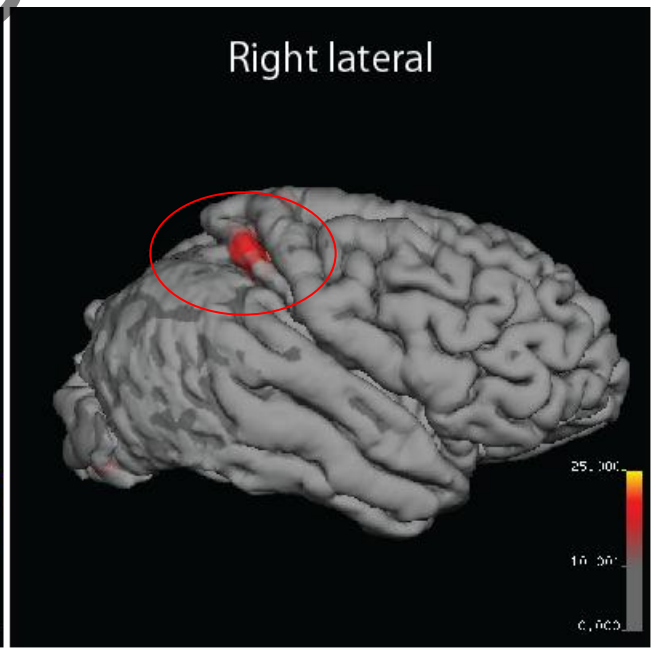
R hand





L hand





Epilepsia, **(*):1–4, 2012
doi: 10.1111/j.1528-1167.2012.03452.x

BRIEF COMMUNICATION

Predicting hand function after hemispherotomy: TMS versus fMRI in hemispheric polymicrogyria

*†‡Andrea Zsoter, ‡Tom Pieper, §Manfred Kudernatsch, and *‡Martin Staudt

*Department of Pediatric Neurology and Developmental Medicine, Children's Hospital, University of Tübingen, Tübingen, Germany; †Experimental Pediatric Neuroimaging, Children's Hospital and Department of Neuroradiology, University of Tübingen, Tübingen, Germany; ‡Clinic for Pediatric Neurology and Neurological Rehabilitation, Epilepsy Center for Children and Adolescents, Schön Klinik Vogtareuth, Germany; and §Clinic for Neurosurgery and Epilepsy Surgery, Schön Klinik Vogtareuth, Germany

N=4 boys with hemispheric polymicrogyria

fMRI: ipsilesional BOLD signal in 3 / 4
nTMS: 0 / 4 crossed lesional corticospinal connections
4 / 4 with preserved grasp in paretic hand after hemispherectomy

ELSEVIER

Clinical Neurophysiology 116 (2005) 2501–2504

www.elsevier.com/locate/clinph

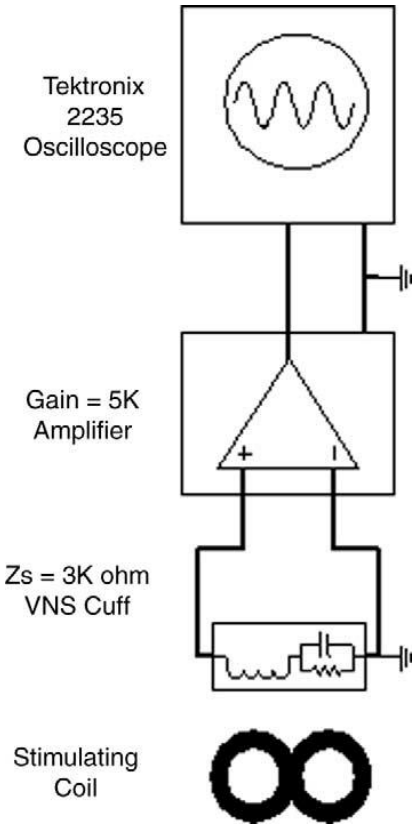
A lack of effect from transcranial magnetic stimulation (TMS) on the vagus nerve stimulator (VNS)

Lara M. Schrader*, John M. Stern, Tony A. Fields, Marc R. Nuwer, Charles L. Wilson

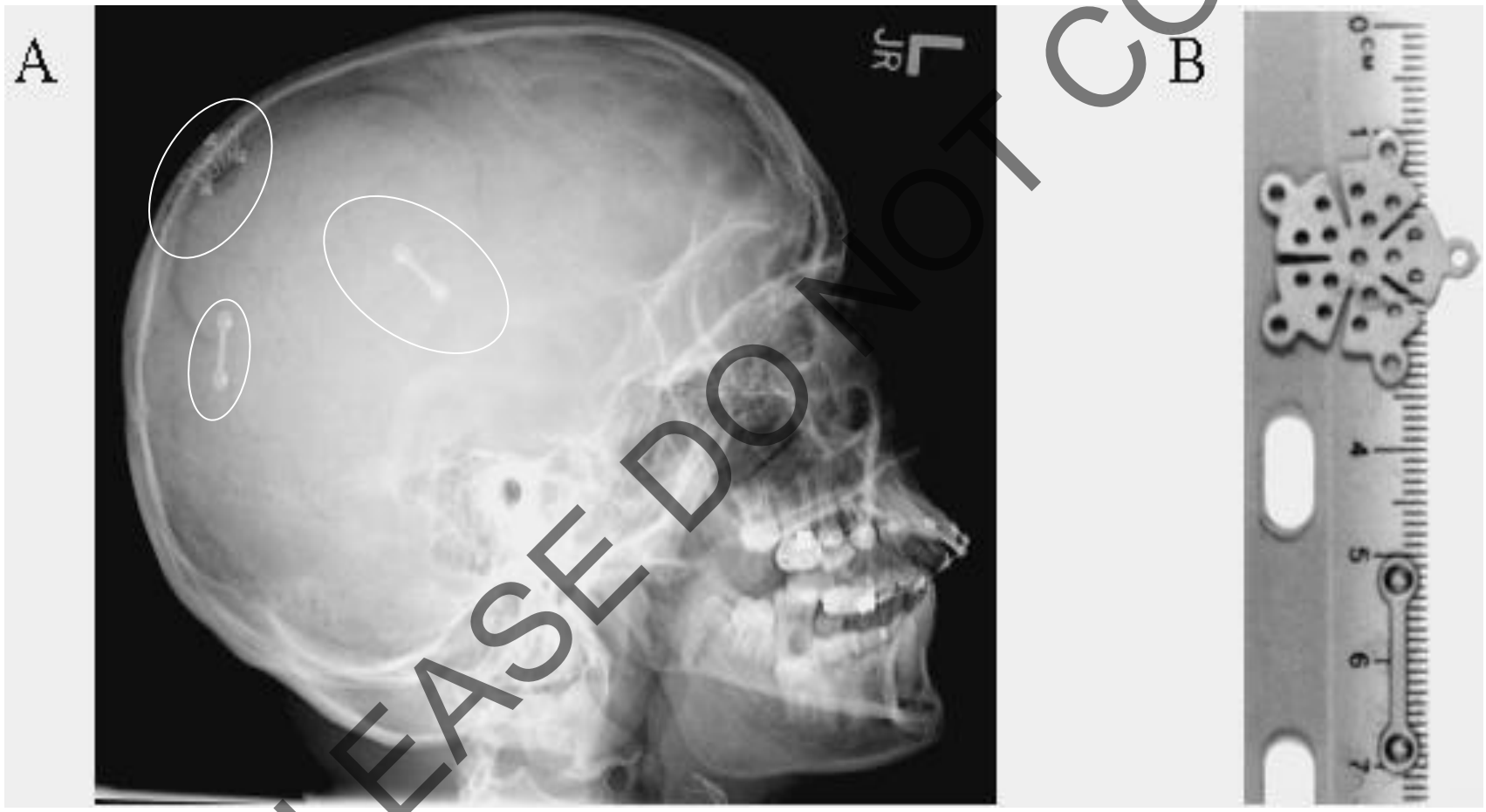
Department of Neurology, Geffen School of Medicine at UCLA, Reed Neurological Research Building, 710 Westwood Plaza, Room 1-194, Los Angeles, CA 90095, USA

Accepted 24 June 2005

- No spurious VNS trigger
- Minimal current (200 nA X 1 ms) induced between the leads

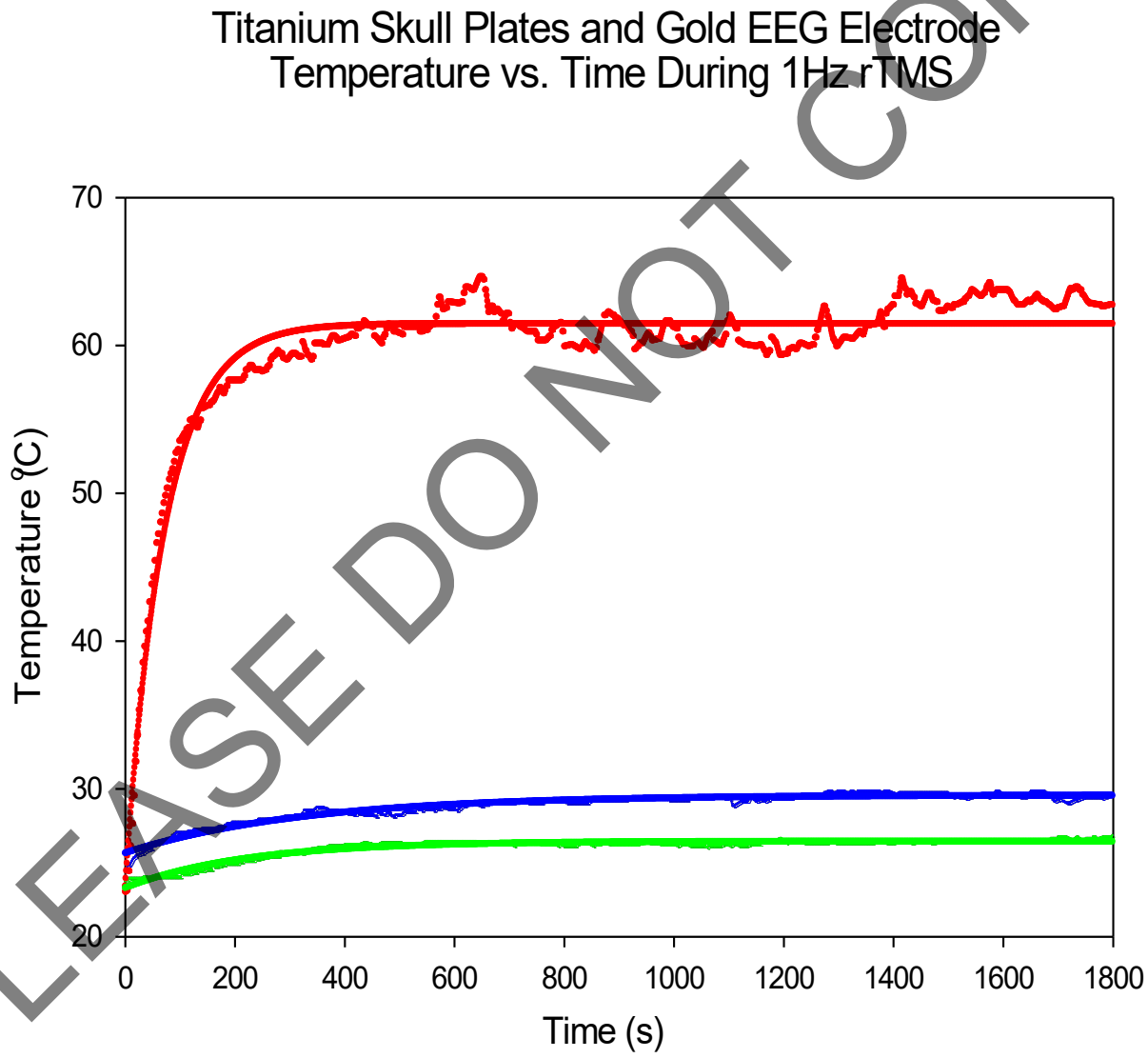


rTMS safety after cranial surgery



Rotenberg et al., 2007
Rotenberg and Pascual-Leone 2009

Ex vivo stimulation

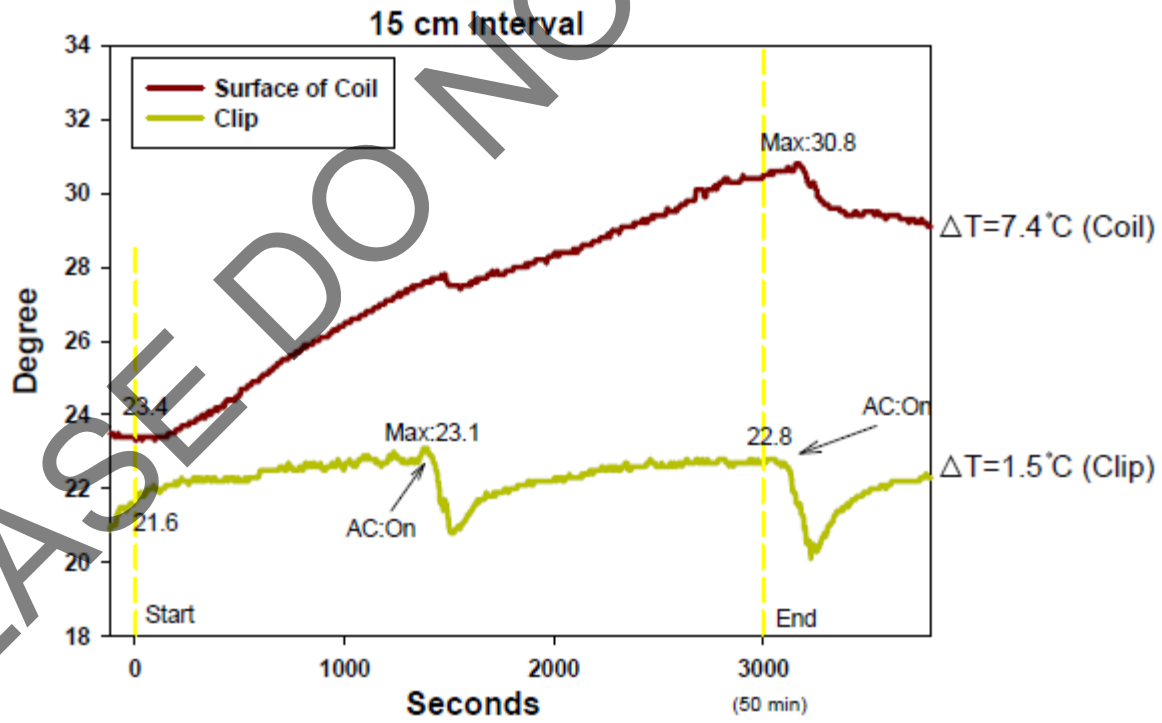


Rotenberg et al., Clin Neirophysiol 2007

Ex vivo stimulation (aneu… clip)

Results (15 cm interval):

We found the temperature of clip increased 1.5 ˚C.
However, it could be due to the changes of room temperature. Please note the difference while AC on
Hence, we added the measurement of room temperature in next trials.



Hsieh et al., Clin Neurophys 2011

Special considerations in pediatric TMS

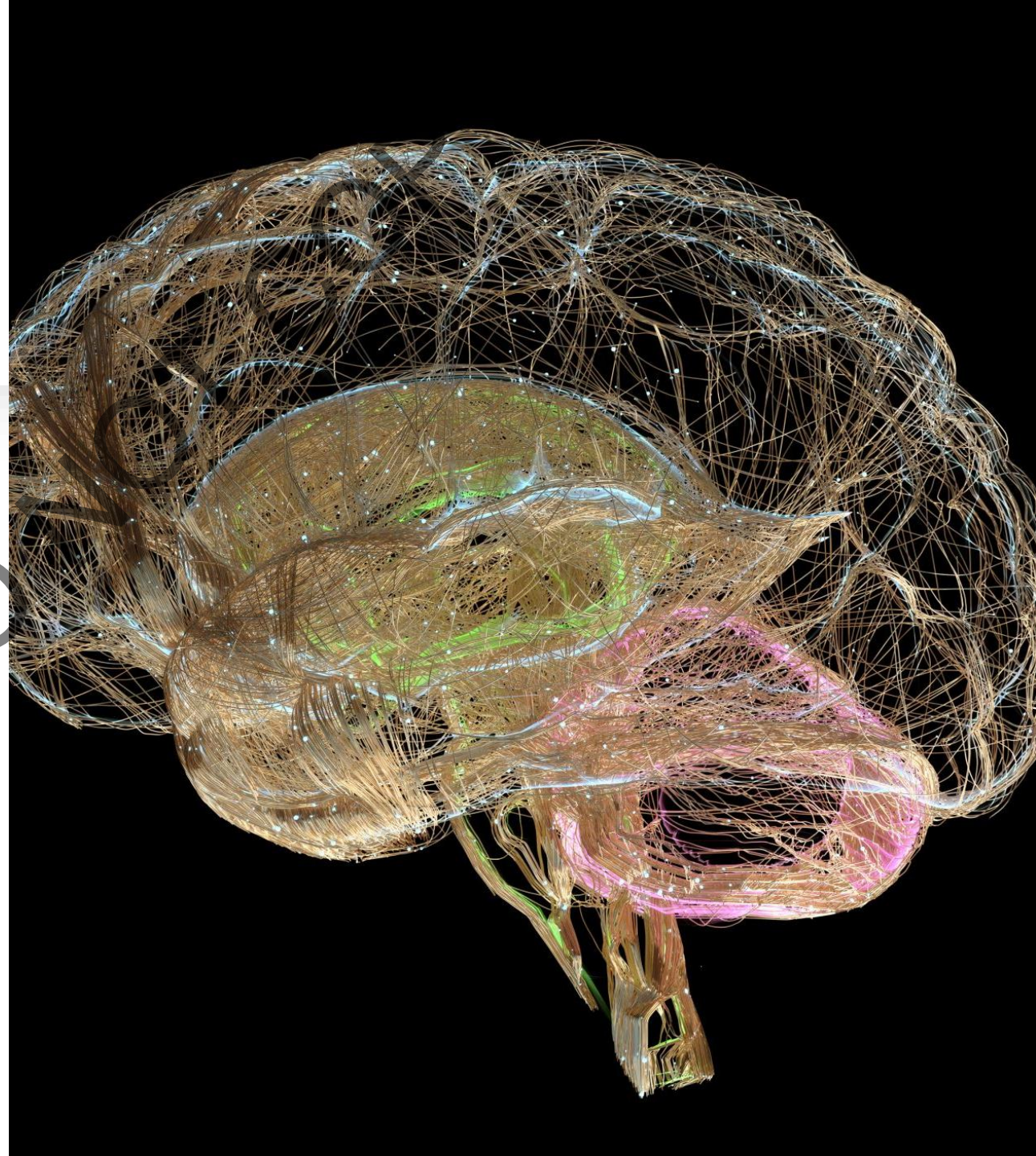
- Head and brain growth
- Developmental regulation of neuronal excitability

Developing brain is a moving target

- Vulnerability (or resistance) to injury likely varies with age
- Studies restricted to narrow age windows are lacking
- Subdivision of the pediatric age group may be necessary

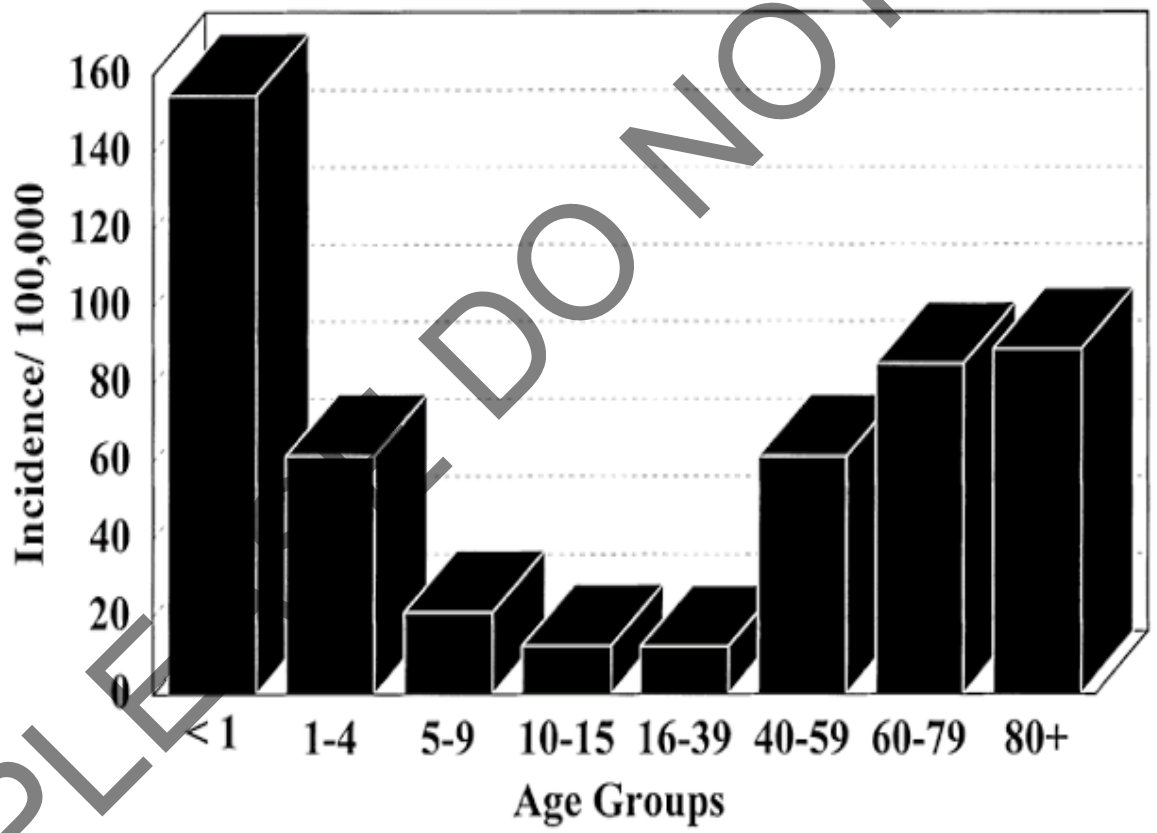
Potential mechanisms for developing brain injury

- Enhanced excitabilty and vulnerability to seizure in early life
  - Risk for excitotoxicity
- Enhanced synaptic plasticity
  - Risk for interference with learning and memory
- Ongoing neurogenesis, synaptogenesis, myelination, etc.
  - Risk of use-dependent structural change



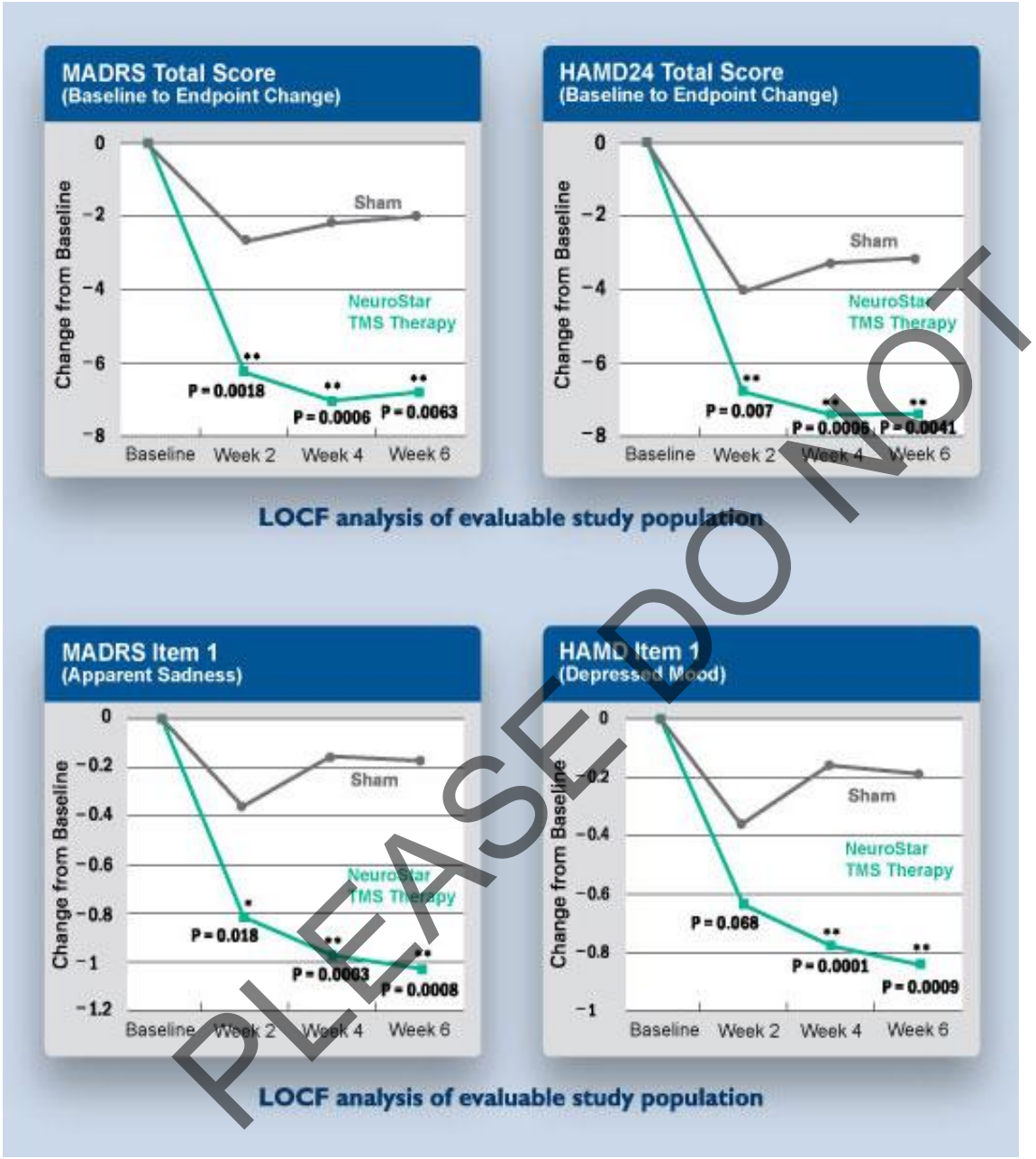
Physiology is reflected in disease …and maybe in TMS risks

Status epilepticus by age



DeLorenzo et al., 1992

Pediatric volume is limited!



Neuronetics Trial

N=164; 23 centers; triple blind

L DLPF 10 Hz rTMS
120% MT
4 sec trains
26 sec ITI
3000 pulses/day
2-3 weeks

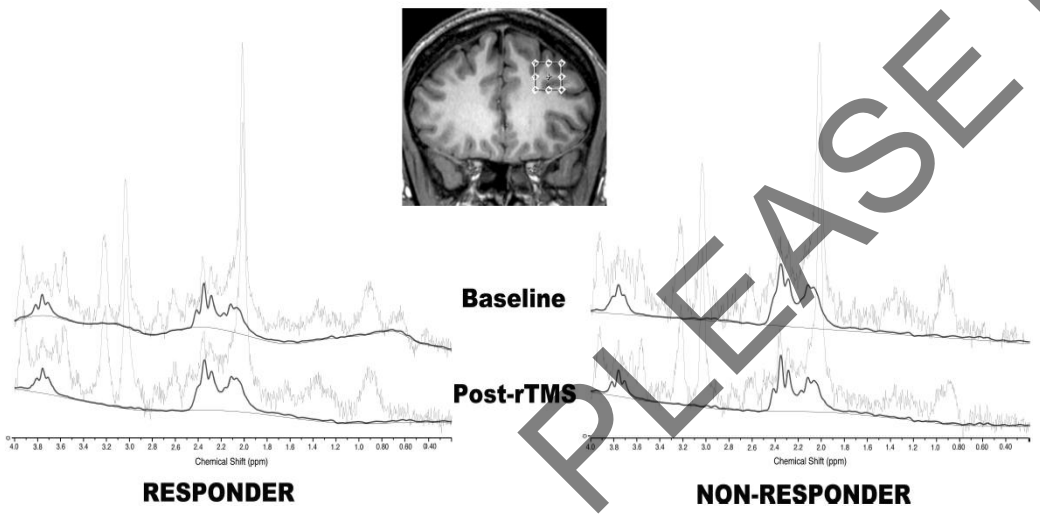
Lisanby et al., 2008

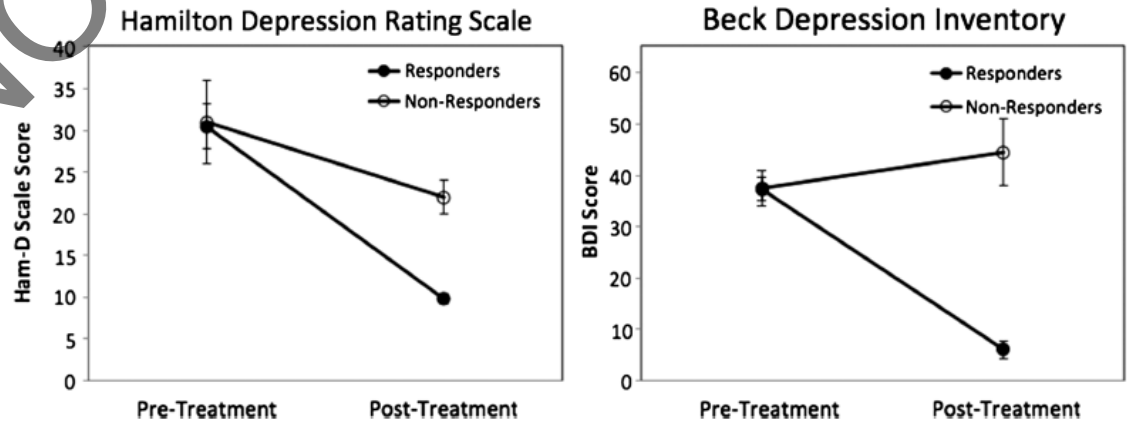
Glutamate Alterations Associated With Transcranial Magnetic Stimulation in Youth Depression

A Case Series

N=6

Xiao-Ru Yang, BSc, Adam Kirton, MD,†‡ Thomas Christopher Wilkes, MD,*† Sarah Pradhan,* Irene Liu, MSc,§ Natalia Jaworska, PhD,* Omar Damji, MSc,†‡ Jamie Keess, BSc,†‡ Lisa Marie Langevin, PhD,* Thilinie Rajapakse, MD,†‡ Robert Marc Lebel, PhD,‖ Mariko Sembo, BSc,* Marilyn Fife, RN,* and Frank P. MacMaster, PhD*†*





Journal of ECT • Volume 30, Number 3, September 2014

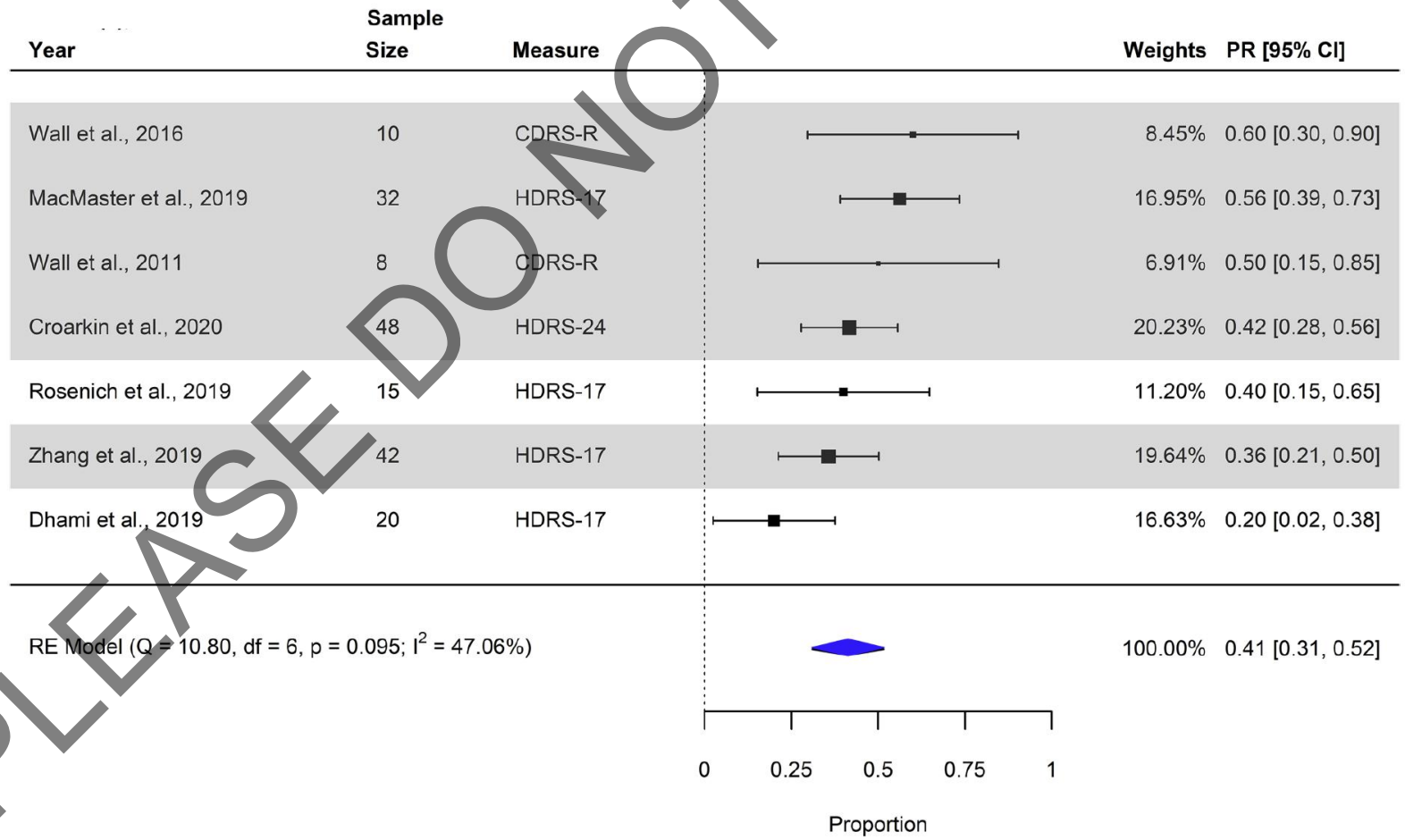
European Child & Adolescent Psychiatry (2022) 31:1501–1525
https://doi.org/10.1007/s00787-022-02021-7

REVIEW

Transcranial magnetic stimulation in the treatment of adolescent depression: a systematic review and meta-analysis of aggregated and individual-patient data from uncontrolled studies

Christine Sigrist[1] · Jasper Vöckel[1] · Frank P. MacMaster[2] · Faranak Farzan[3,8] · Paul E. Croarkin[4] · Cherrie Galletly[5,9,10] · Michael Kaess[6,7] · Stephan Bender[1] · Julian Koenig[1,6,7]

Received: 25 January 2022 / Accepted: 1 June 2022 / Published online: 24 June 2022



Epilepsia, **(*):1–8, 2012
doi: 10.1111/j.1528-1167.2012.03626.x

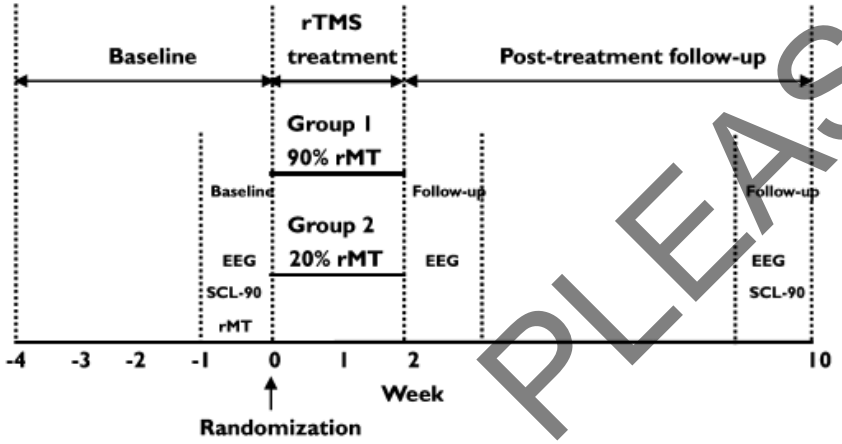
FULL-LENGTH ORIGINAL RESEARCH

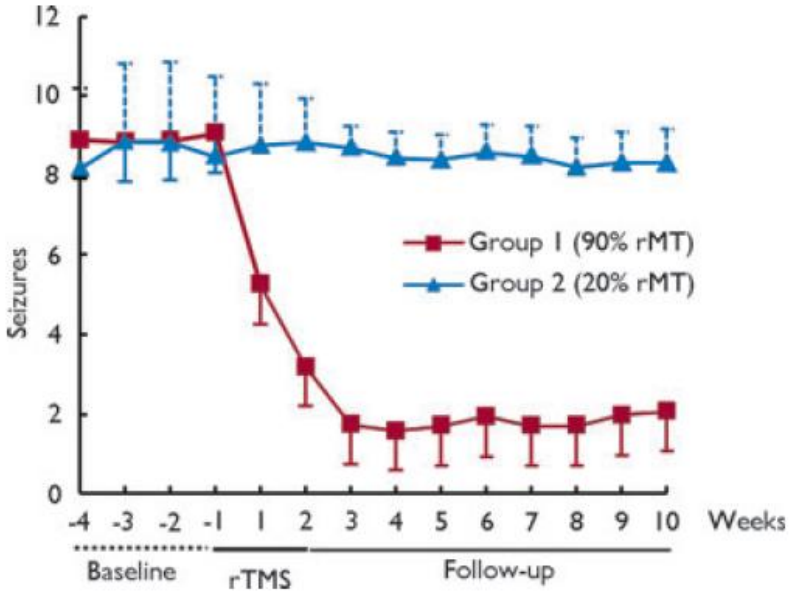
Low-frequency repetitive transcranial magnetic stimulation for the treatment of refractory partial epilepsy: A controlled clinical study

*Wei Sun, *Wei Mao, *Xianghong Meng, *Dequan Wang, †Liang Qiao, †Wei Tao, *Liping Li, *Xiaoying Jia, *Chunyu Han, *Mengmeng Fu, *Xiaoyan Tong, *Xun Wu, and *Yuping Wang

Departments of *Neurology and †Functional Neurosurgery, Xuan Wu Hospital, Capital Medical University, Beijing, China

N=64 (32: 90% RMT; 32: 20% RMT)
0.5 Hz rTMS over seizure focus

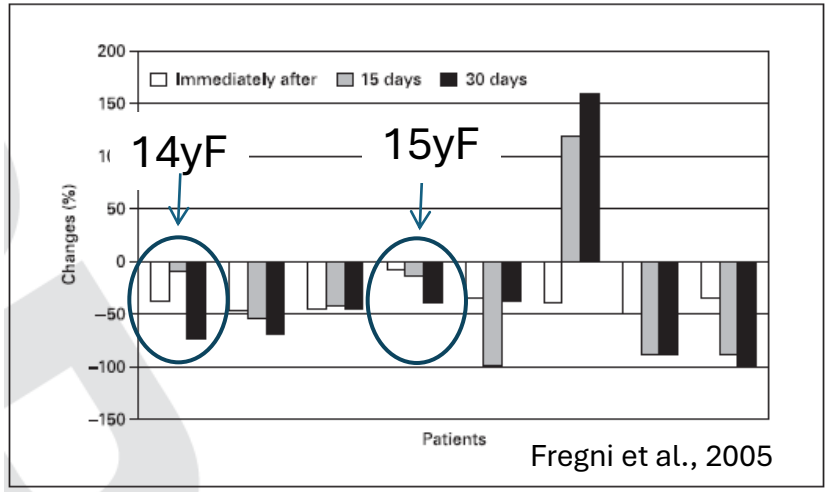




Clinical trials: gaps in knowledge

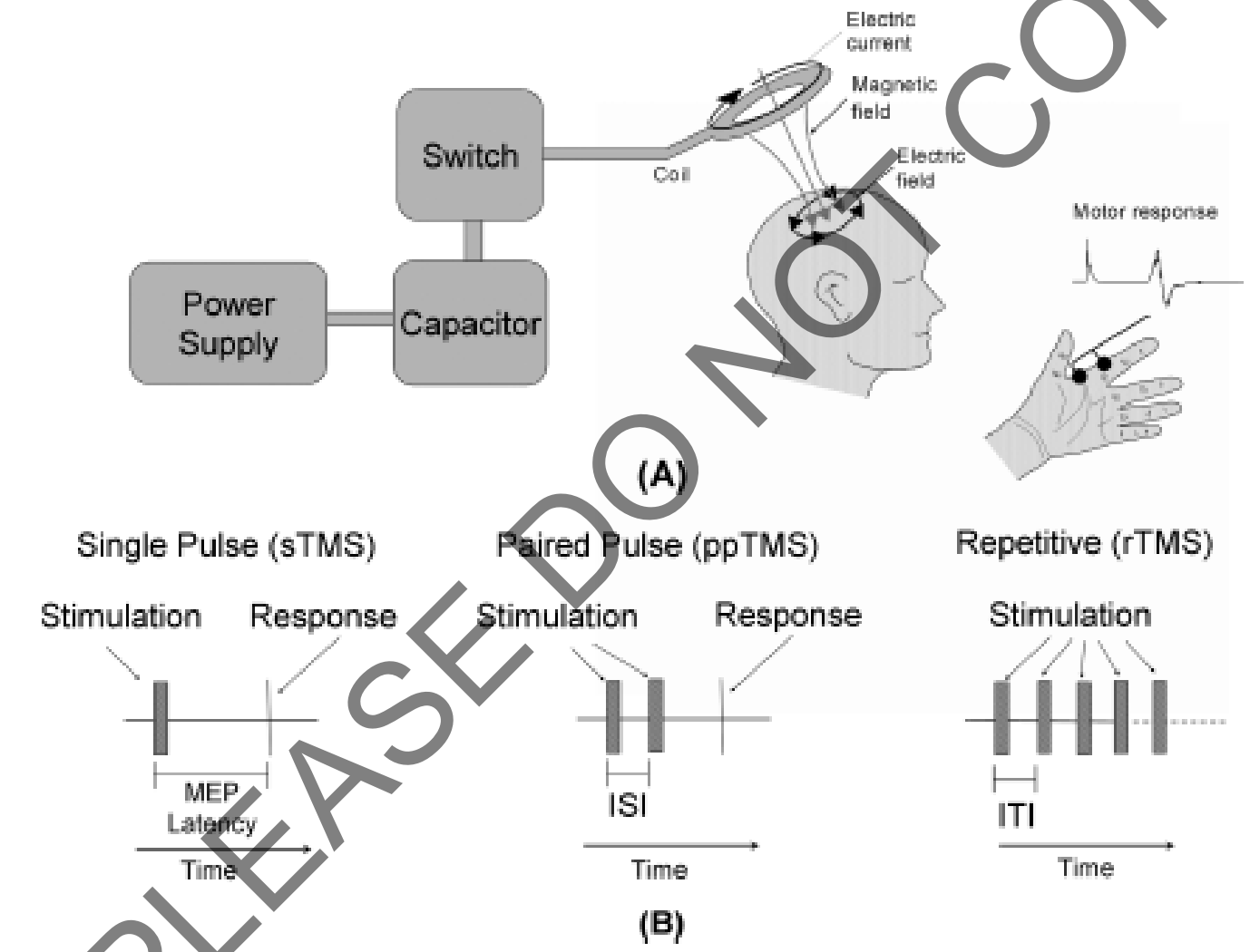
- Limited TMS data in pediatrics
- Few clinical trials segmented by developmental stage
- Fragmented pediatric data available from inclusive prospective trials

N=2?



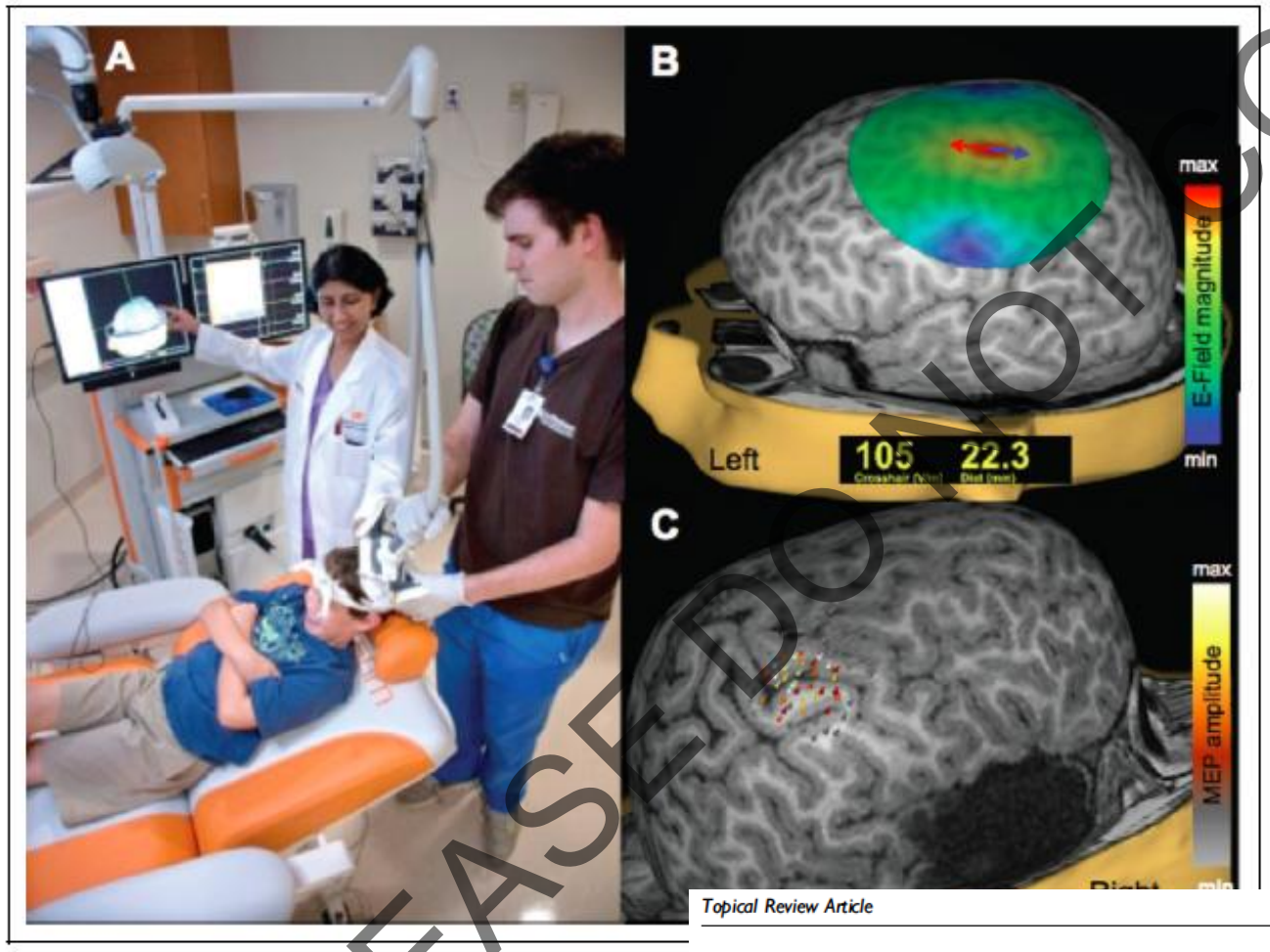
Fregni et al., 2005

Stimulation protocols



Frye, Rotenberg, et al. Child Neurol 2007

Presurgical motor mapping by TMS



Topical Review Article

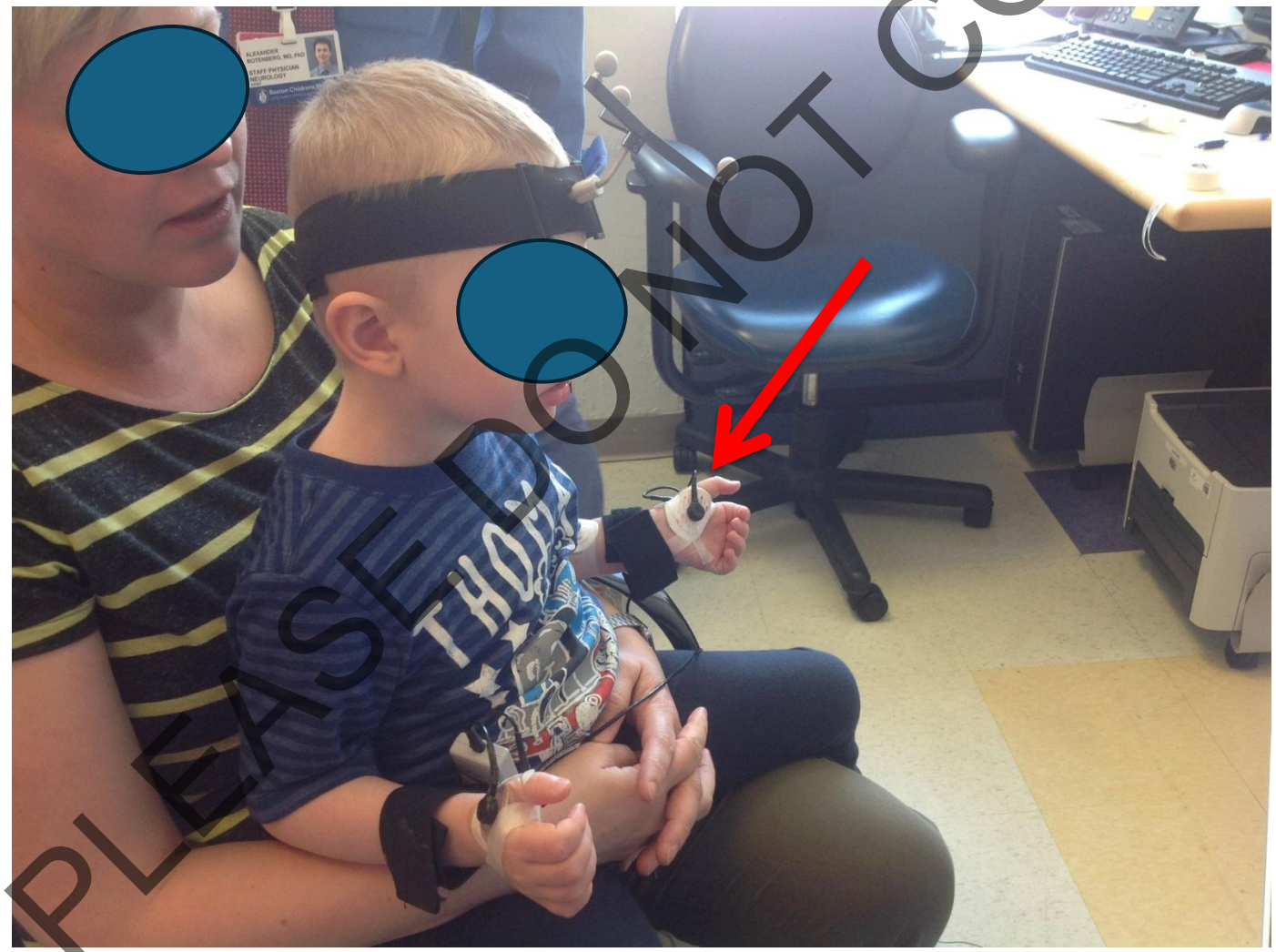
Journal of Child Neurology
1-14

DOI: 10.1177/0883073814553274
jcn.sagepub.com
SAGE

Clinical Applications of Transcranial Magnetic Stimulation in Pediatric Neurology

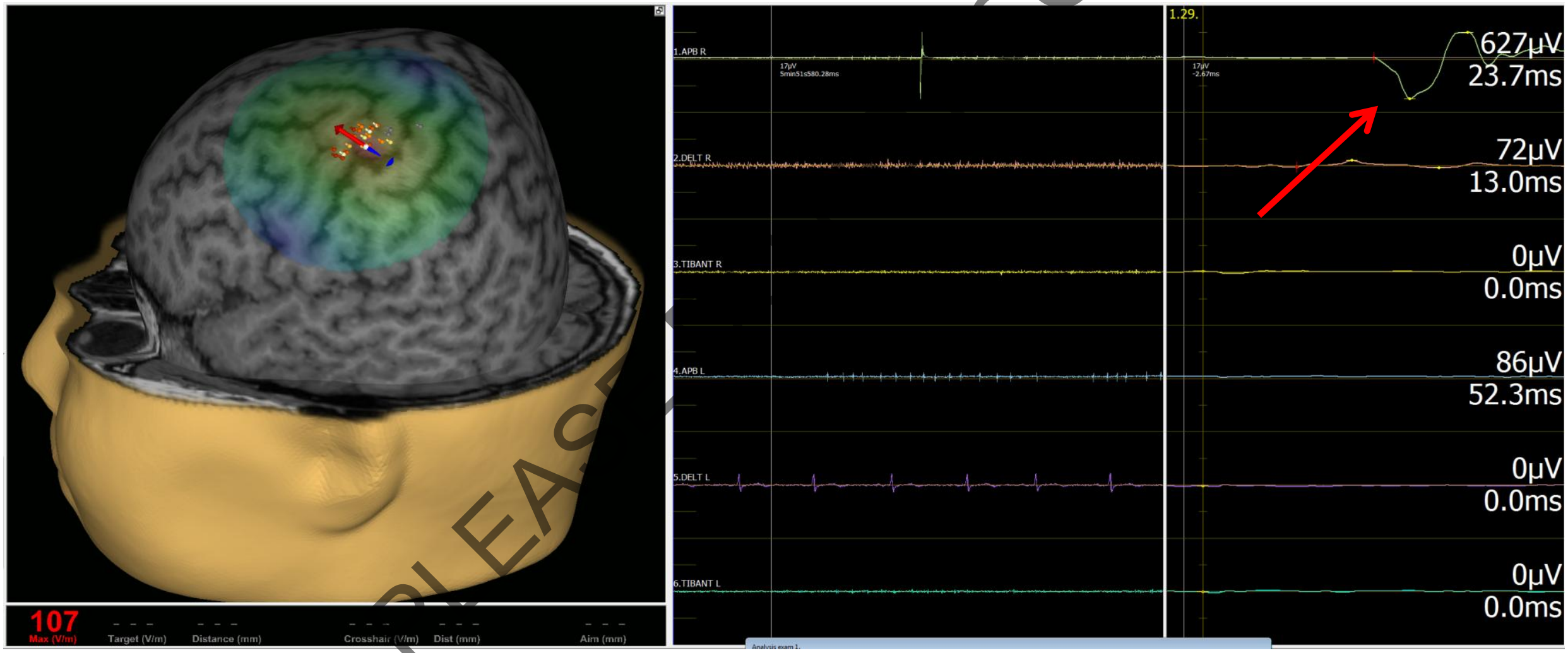
Shalini Narayana, PhD[1,2,3], Andrew C. Papanicolaou, PhD[1,2,3], Amy McGregor, MD[2,4], Frederick A. Boop, MD[2,5], and James W. Wheless, MD[2,4]

TMS is feasible in children (with accommodations)

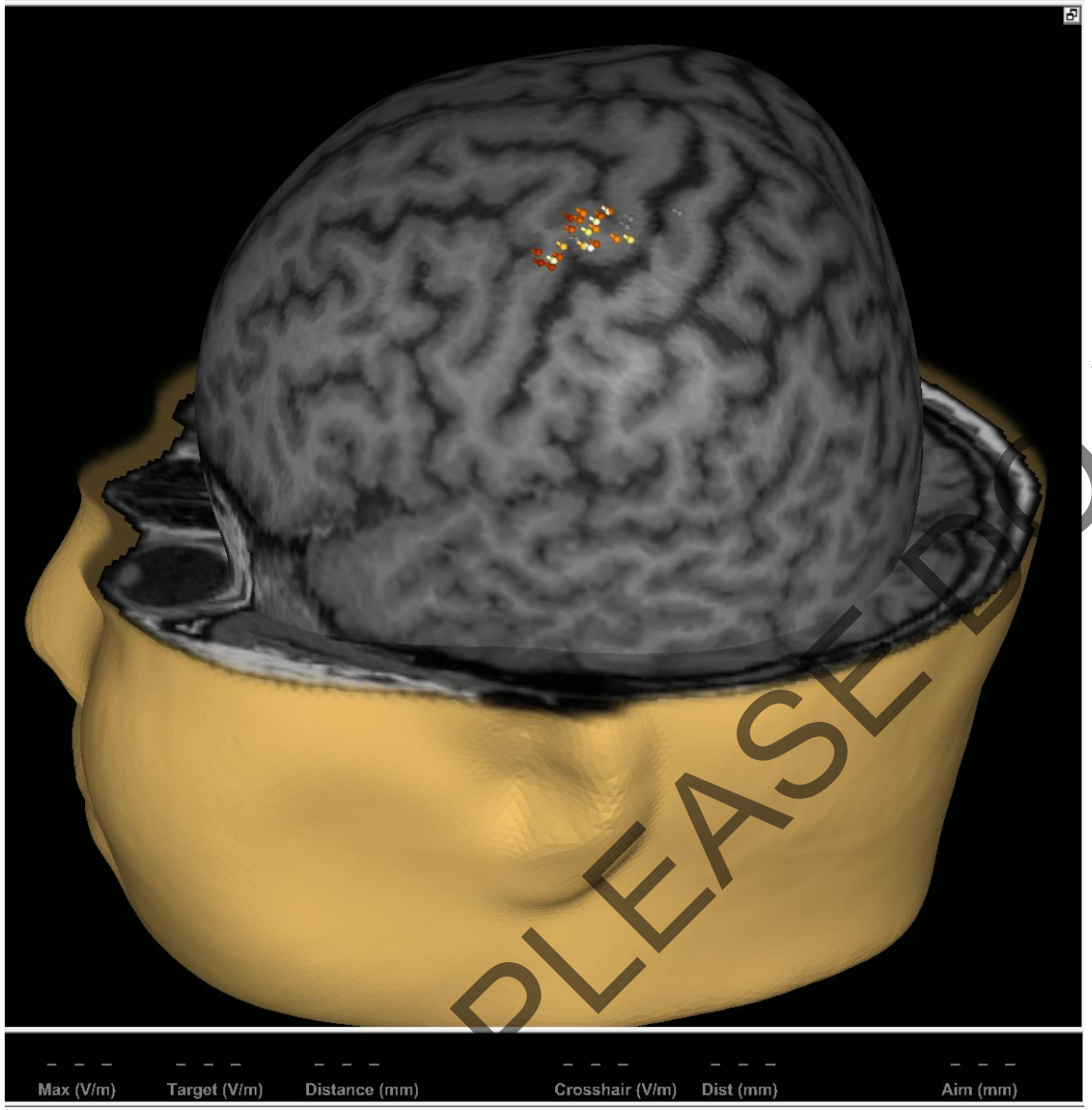


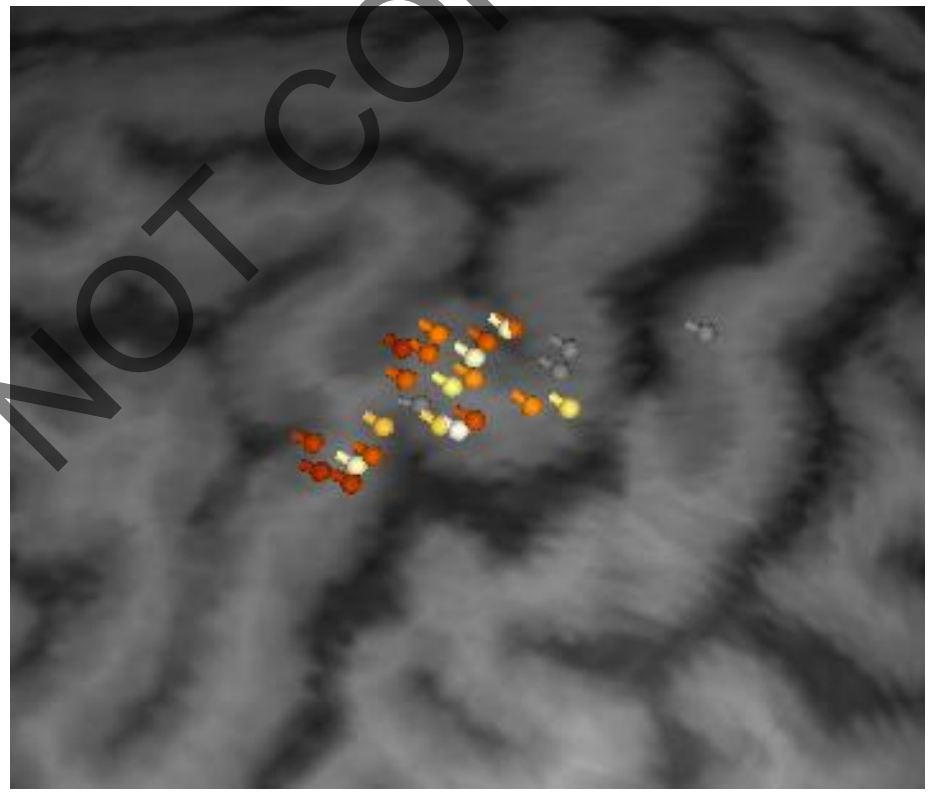
TMS is feasible in children (with accommodations)

Motor TMS example

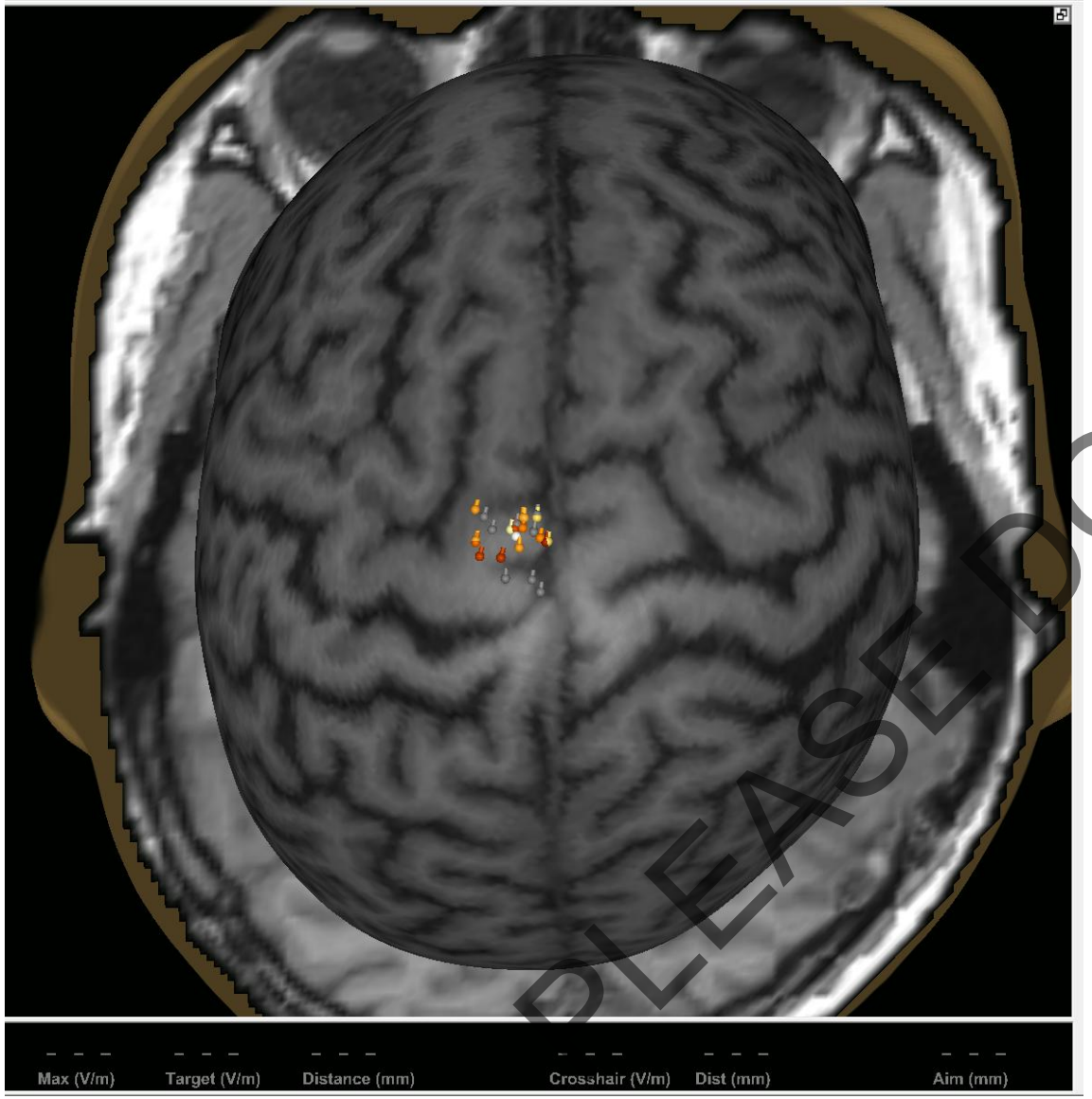


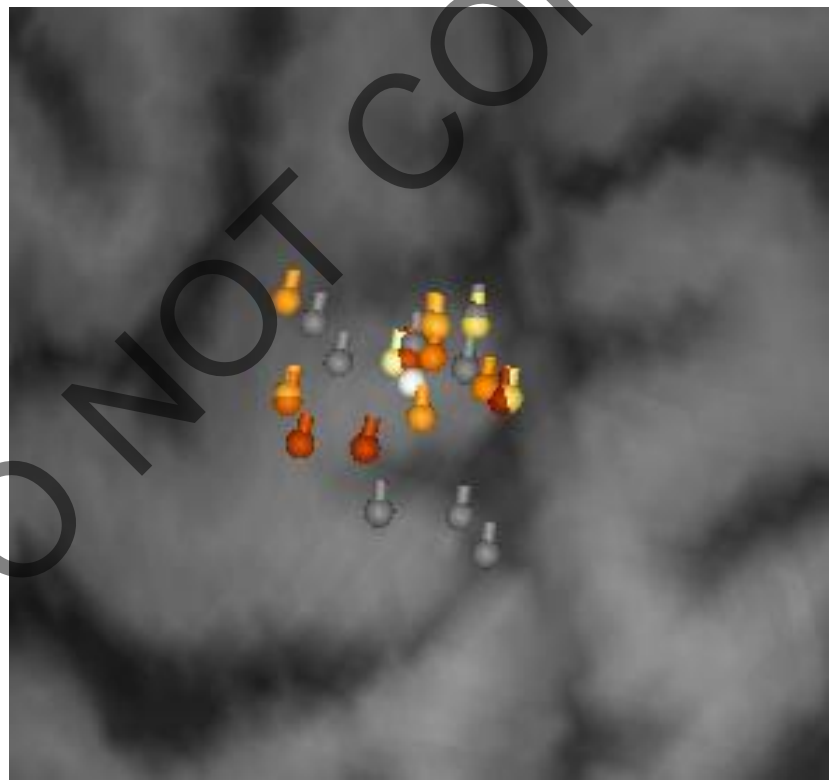
Right hand (APB) map





Right foot (TA) map



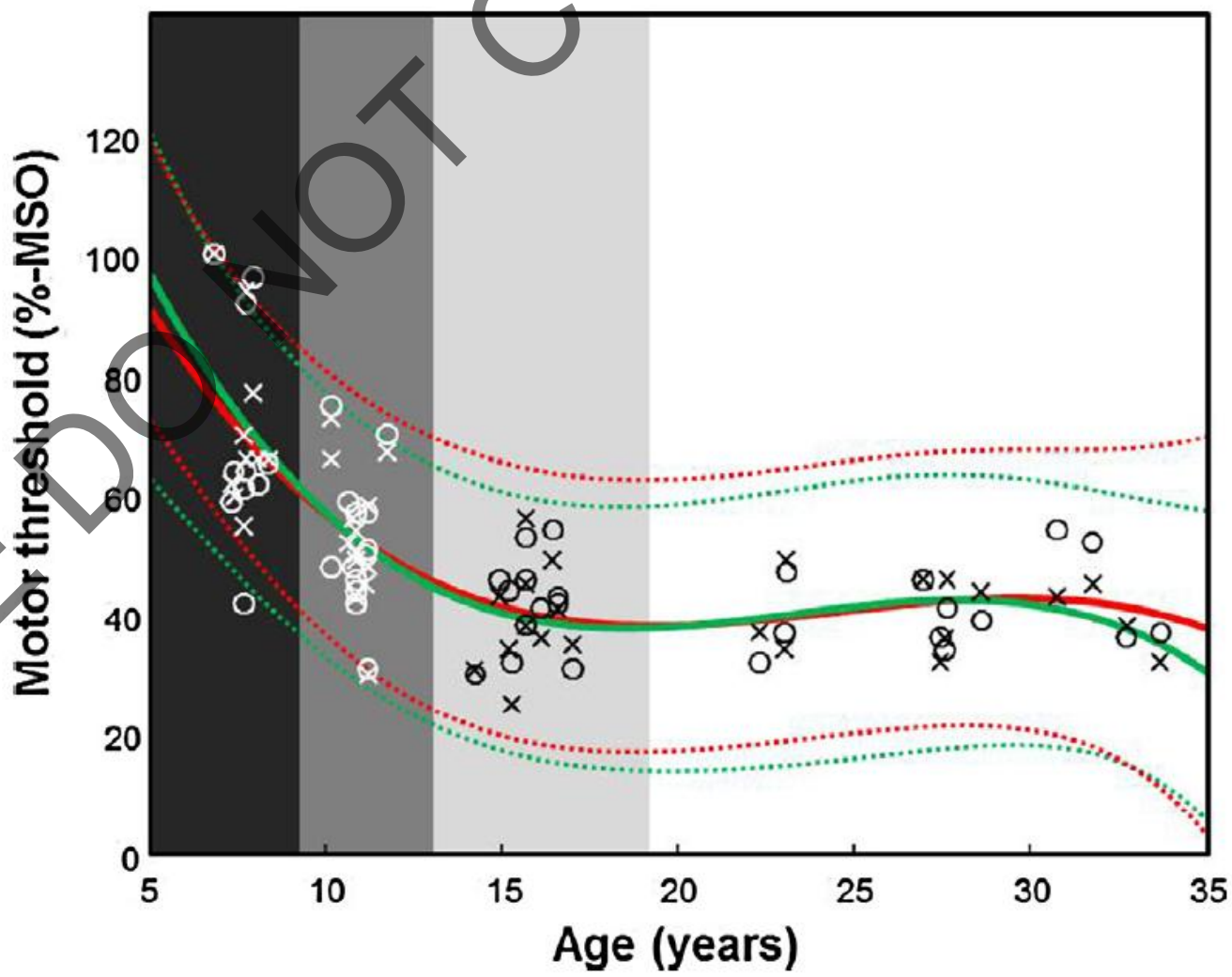


ORIGINAL ARTICLE

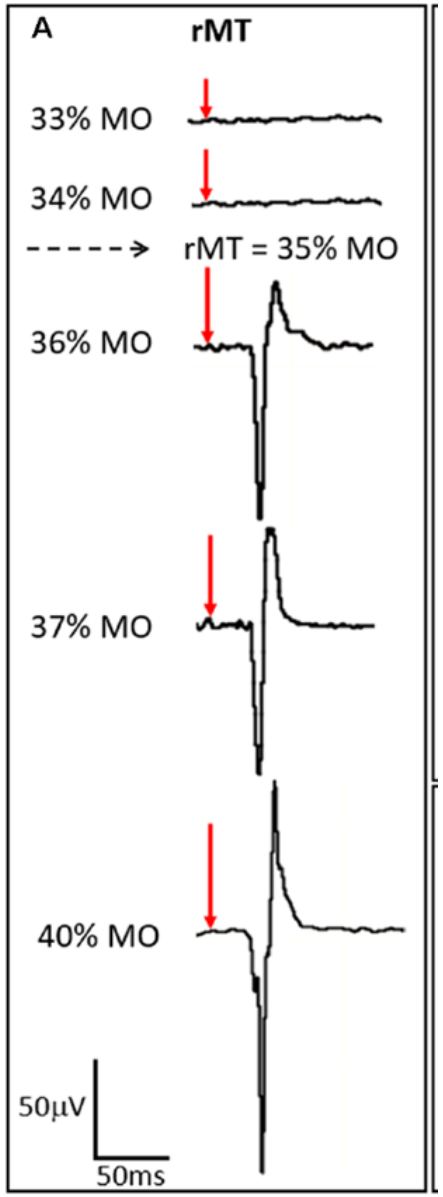
Development of corticospinal motor excitability and cortical silent period from mid-childhood to adulthood — a navigated TMS study

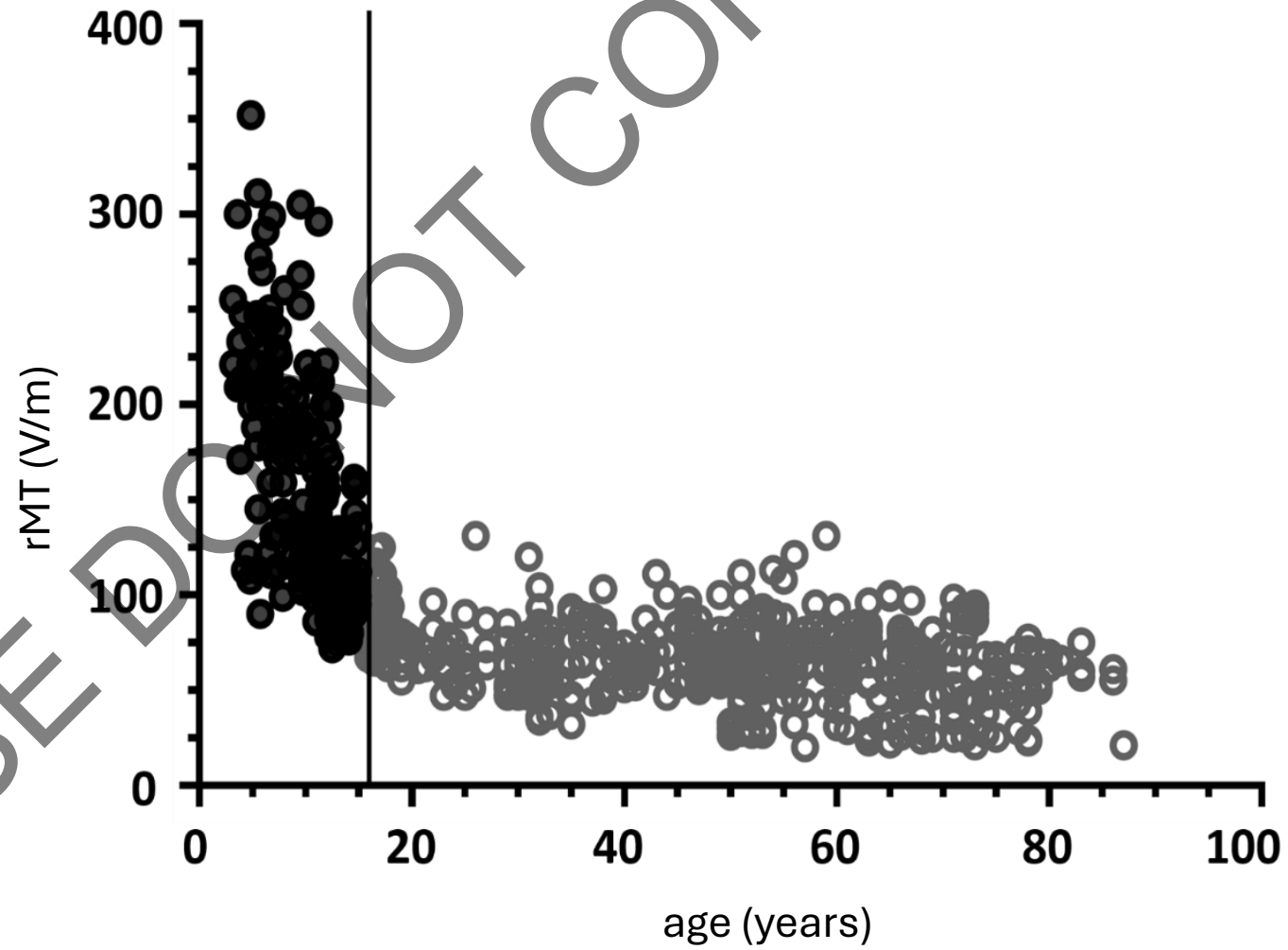
Laura Säisänen[a,b,*], Petro Julkunen[b,c], Timo Lakka[d,e,f], Virpi Lindi[c], Mervi Könönen[b,g], Sara Määttä[a,b]

Neurophysiologie Clinique/Clinical Neurophysiology (2017)



rMT across ages





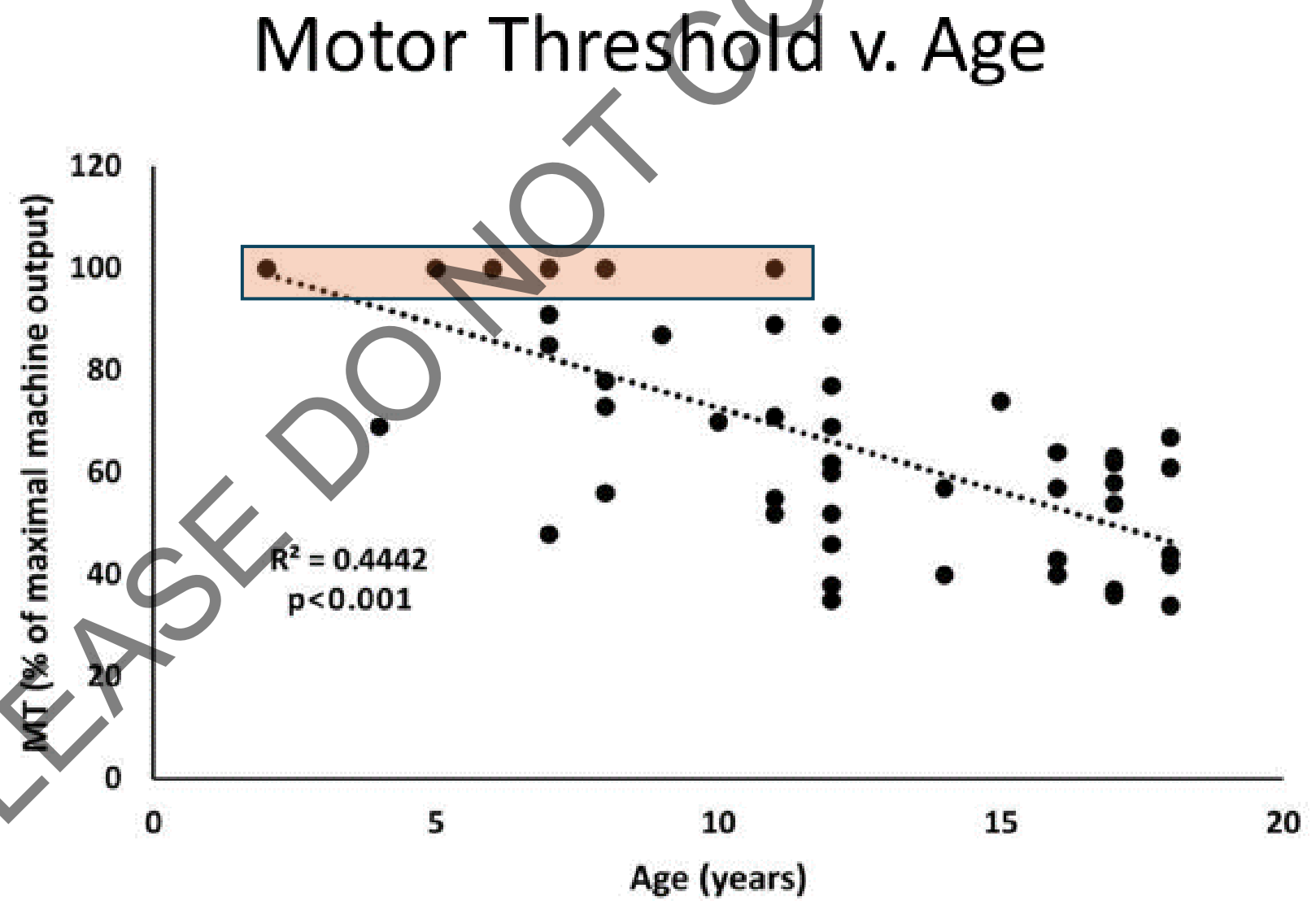
Kaye, Krieg, et al., in prep

Curr Neurol Neurosci Rep (2017) 17:11
DOI 10.1007/s11910-017-0719-0

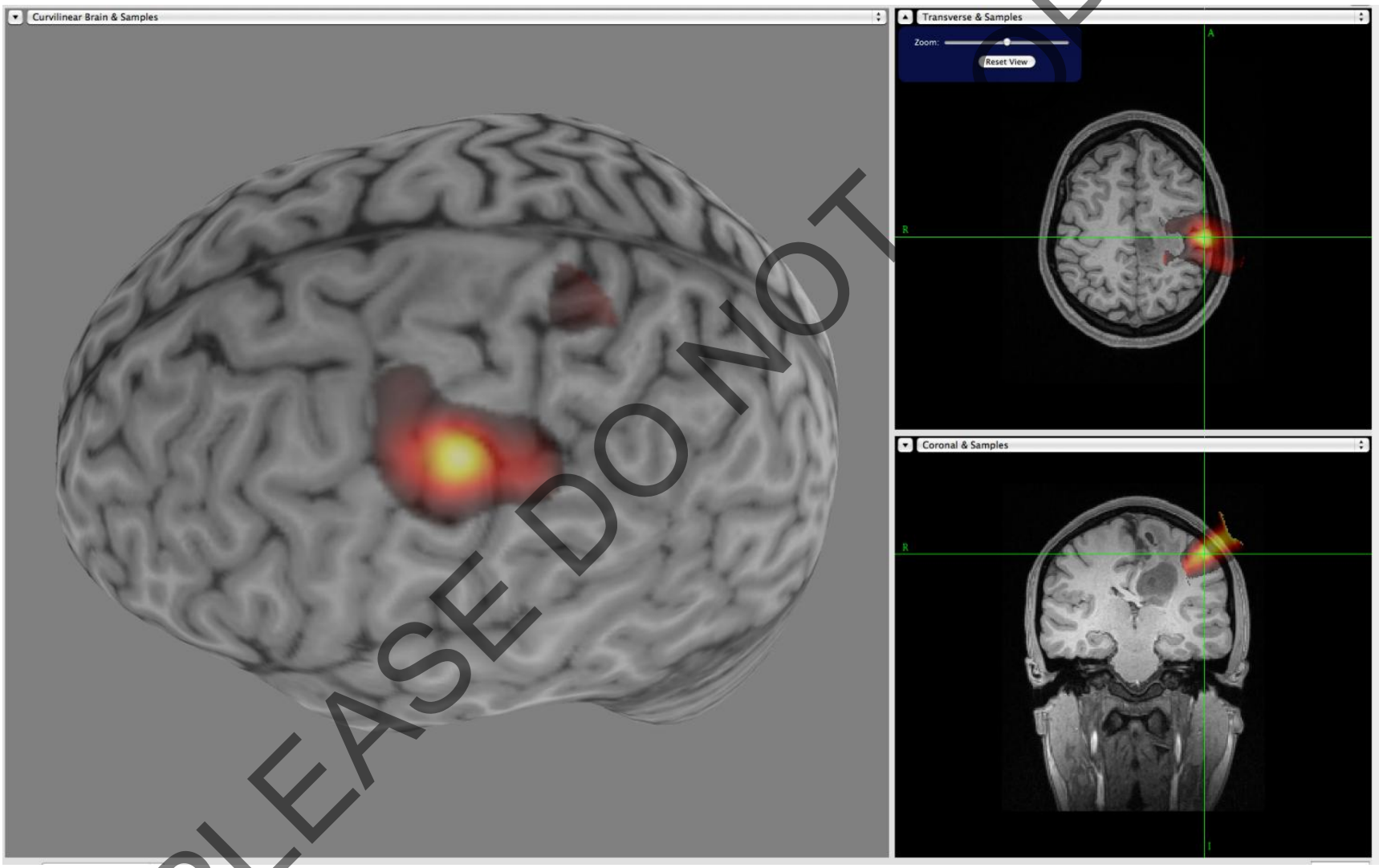
PEDIATRIC NEUROLOGY (WE KAUFMANN, SECTION EDITOR)

Transcranial Magnetic and Direct Current Stimulation in Children

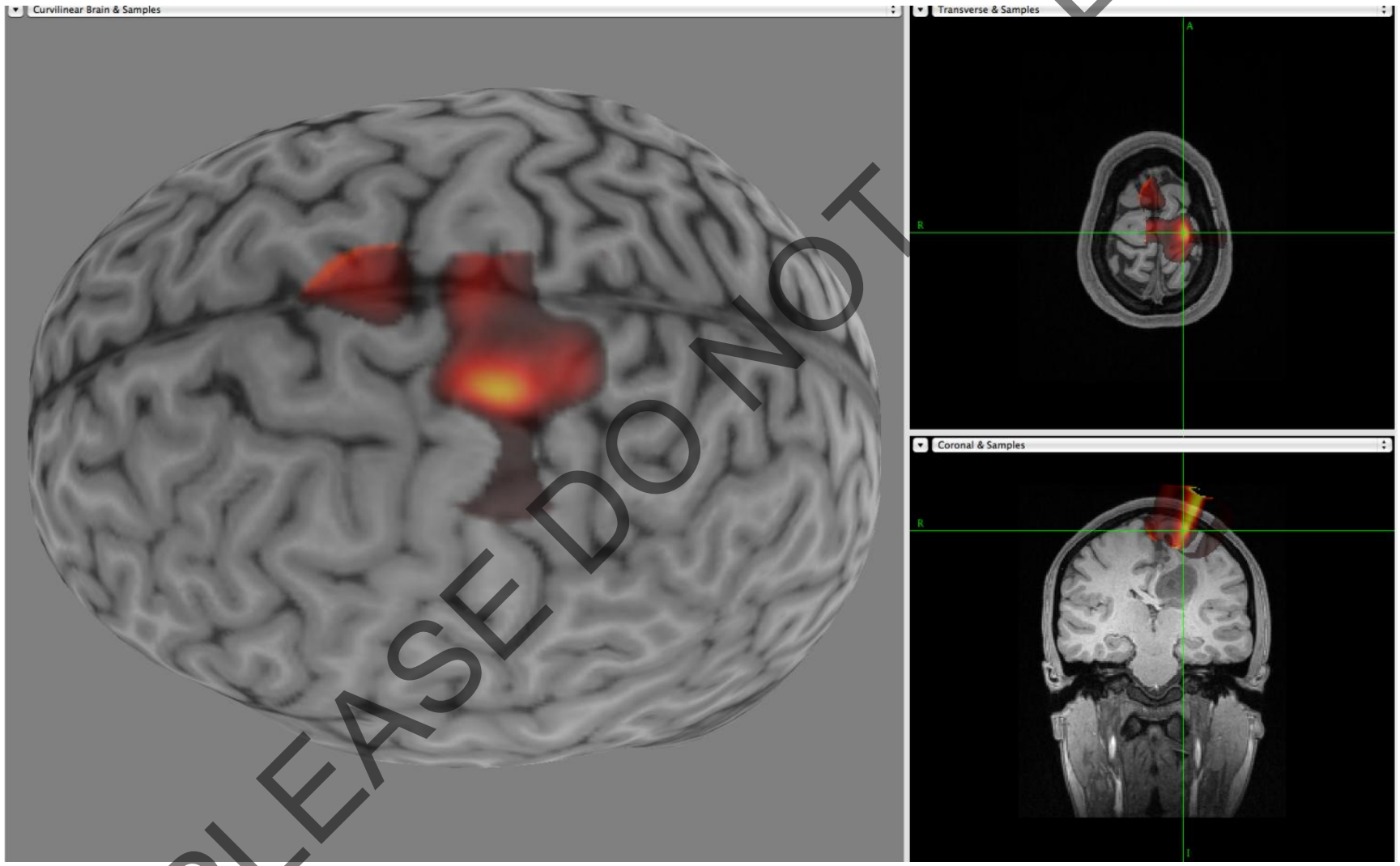
Mustafa Q. Hameed[1,2,3] · Sameer C. Dhamne[1,2] · Roman Gersner[1,2] · Harper L. Kaye[1,2] · Lindsay M. Oberman[4] · Alvaro Pascual-Leone[5,6] · Alexander Rotenberg[1,2]



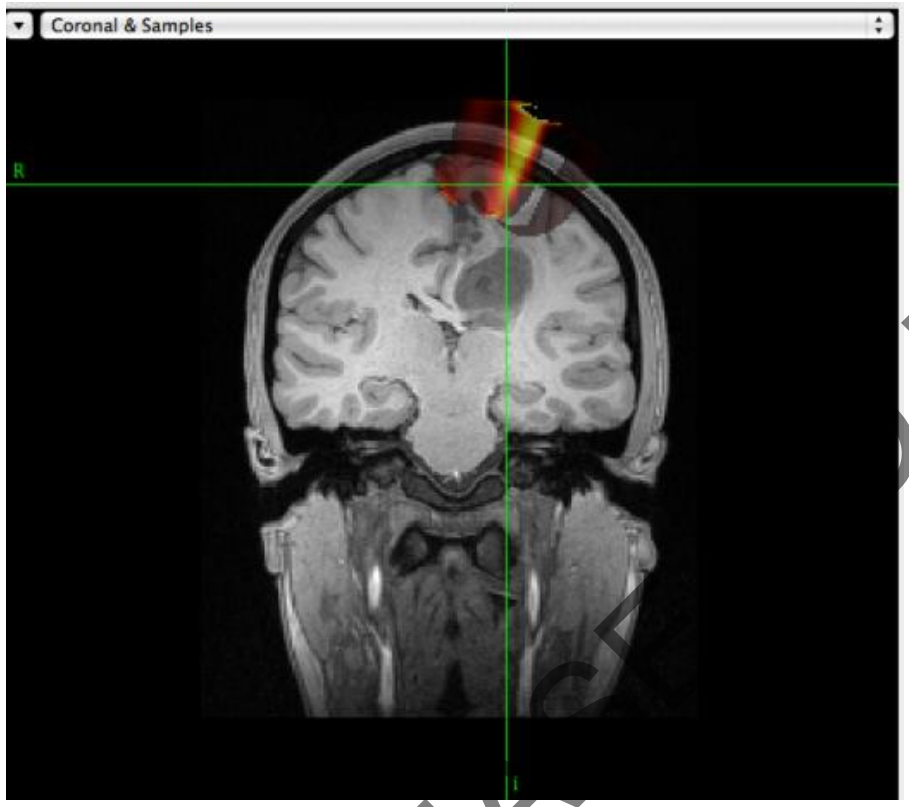
Motor map relative to lesion (hand; FDI)

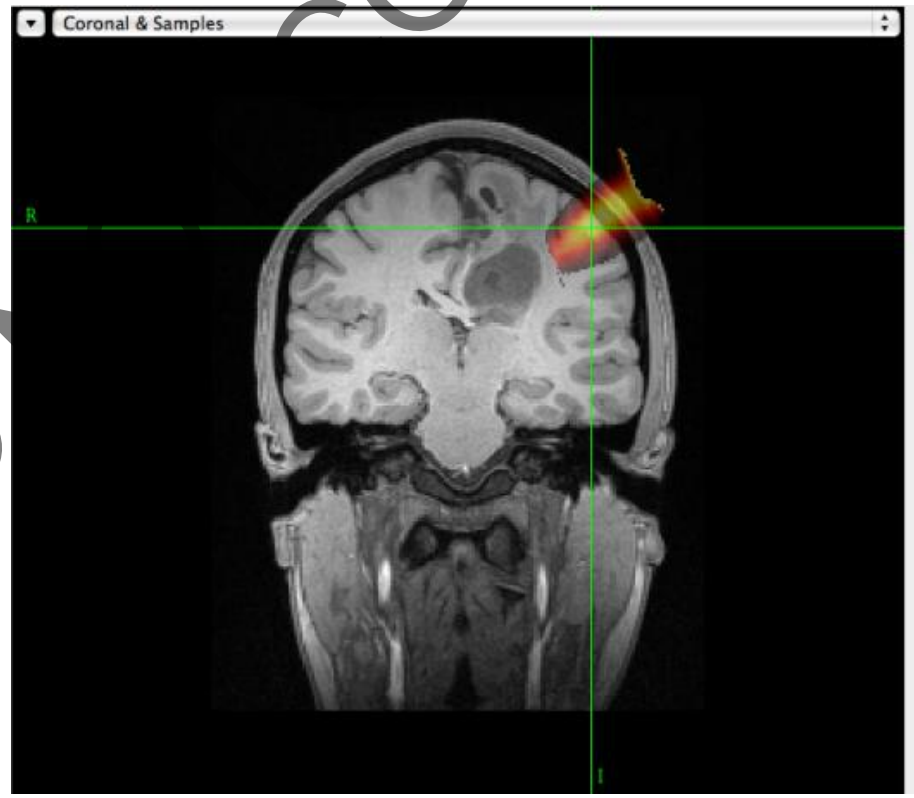


Motor map relative to lesion (foot; TA)

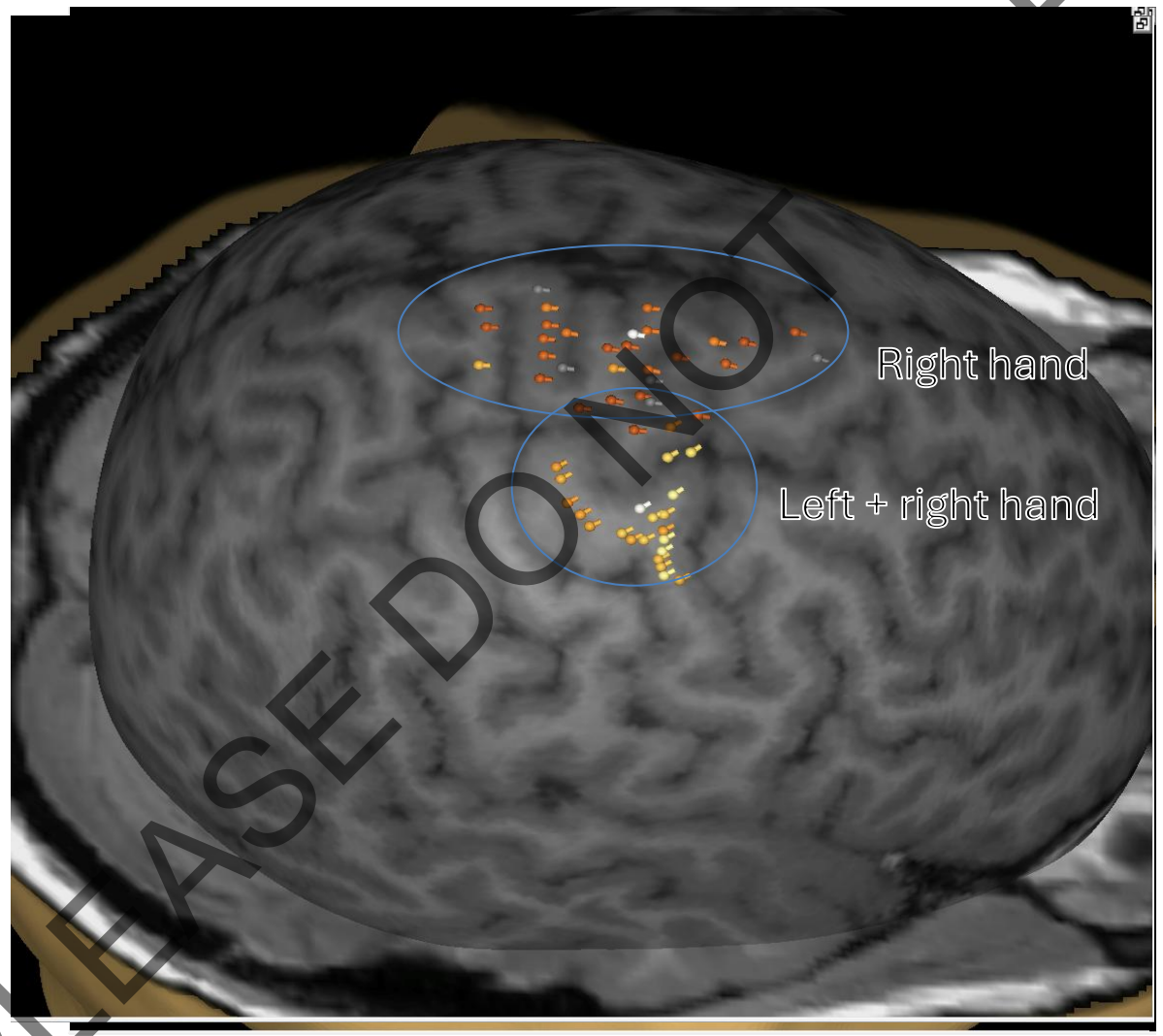


Map identifies surgical access



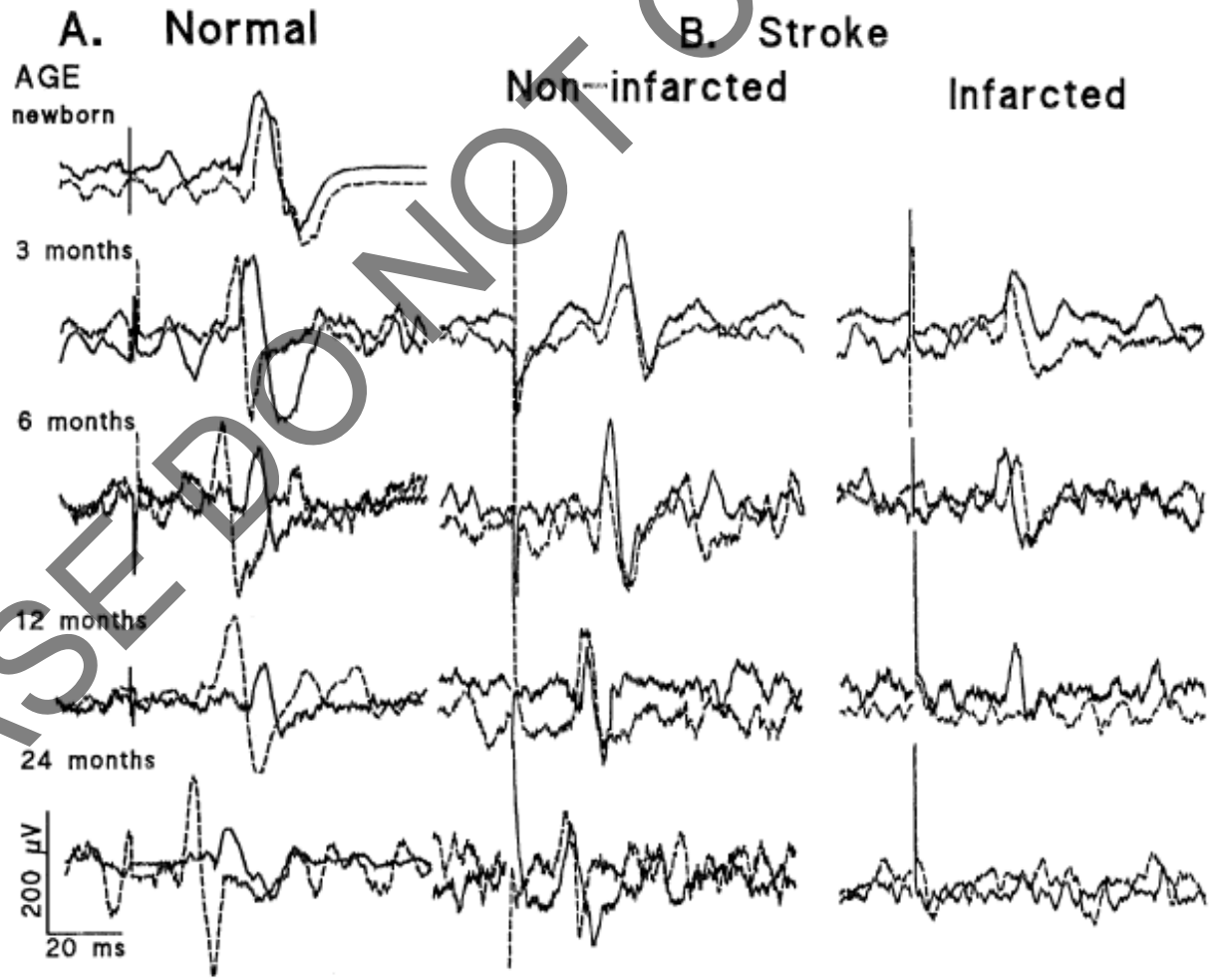


Presurgical motor mapping by TMS



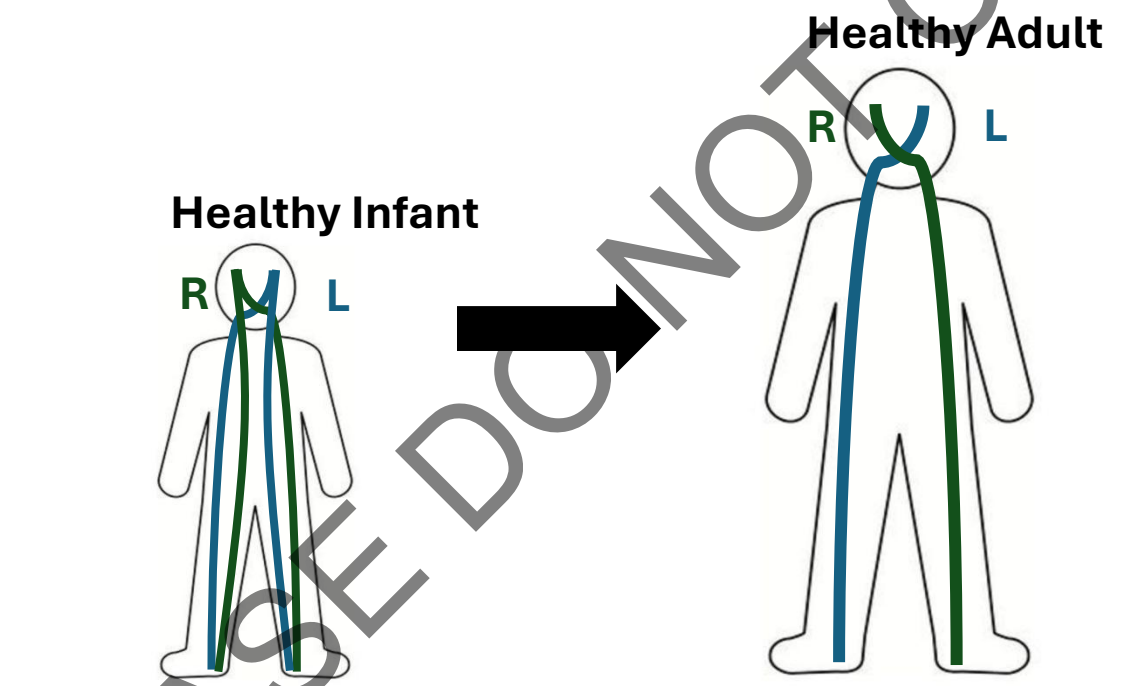
Development and Plasticity of the Corticospinal System in Man

J.A. Eyre



Dashed: contra
Solid: ipsi

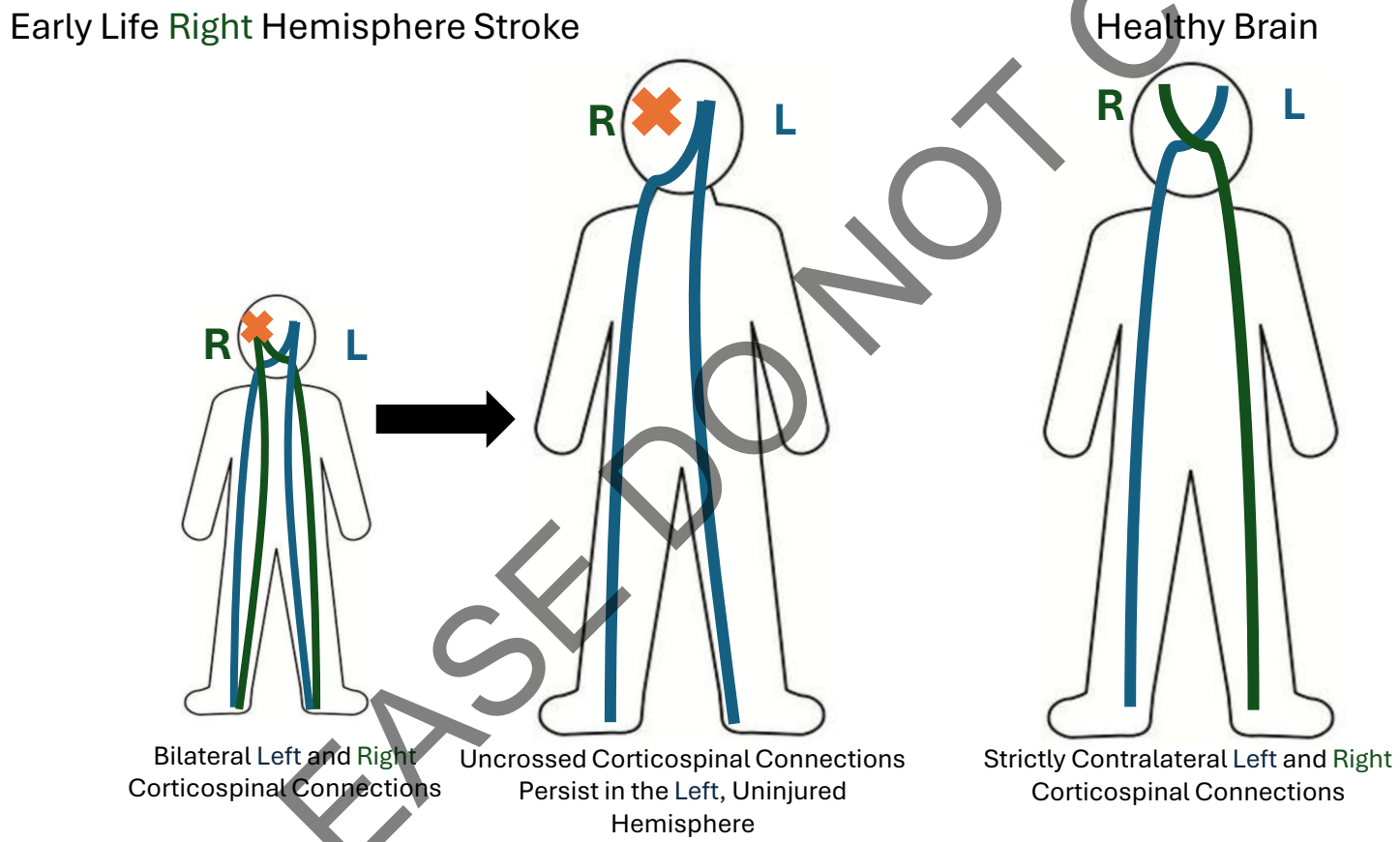
Corticospinal Tracts Bilateral at Birth



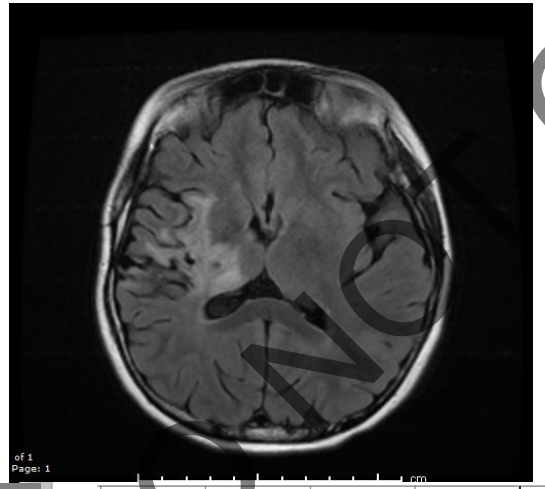
Bilateral Left and Right Corticospinal Connections

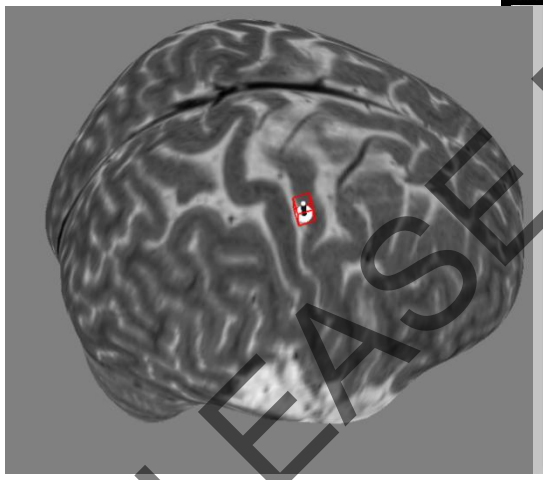
Strictly Contralateral Left and Right Corticospinal Connections

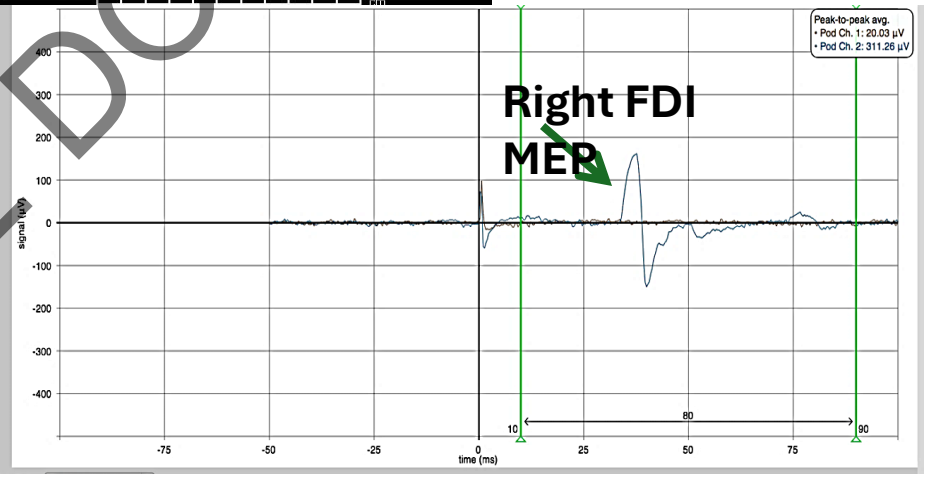
Contralesional bilateral CST in stroke



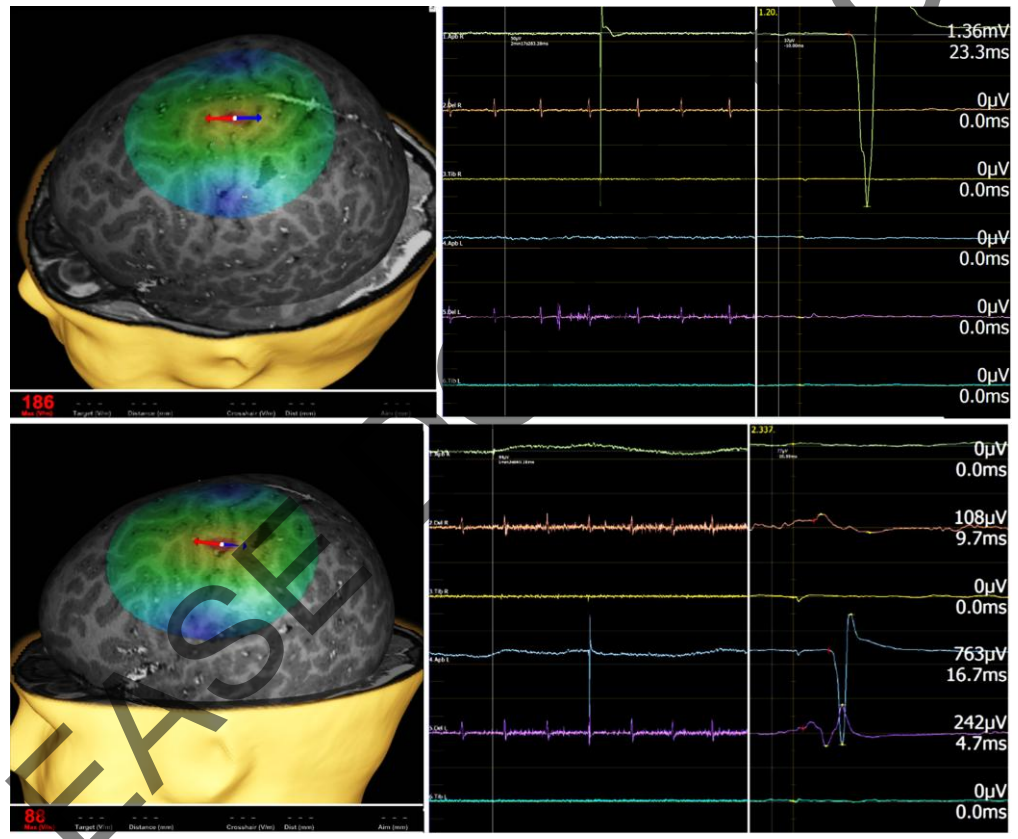
Right-sided tumor and right arm tonic seizures







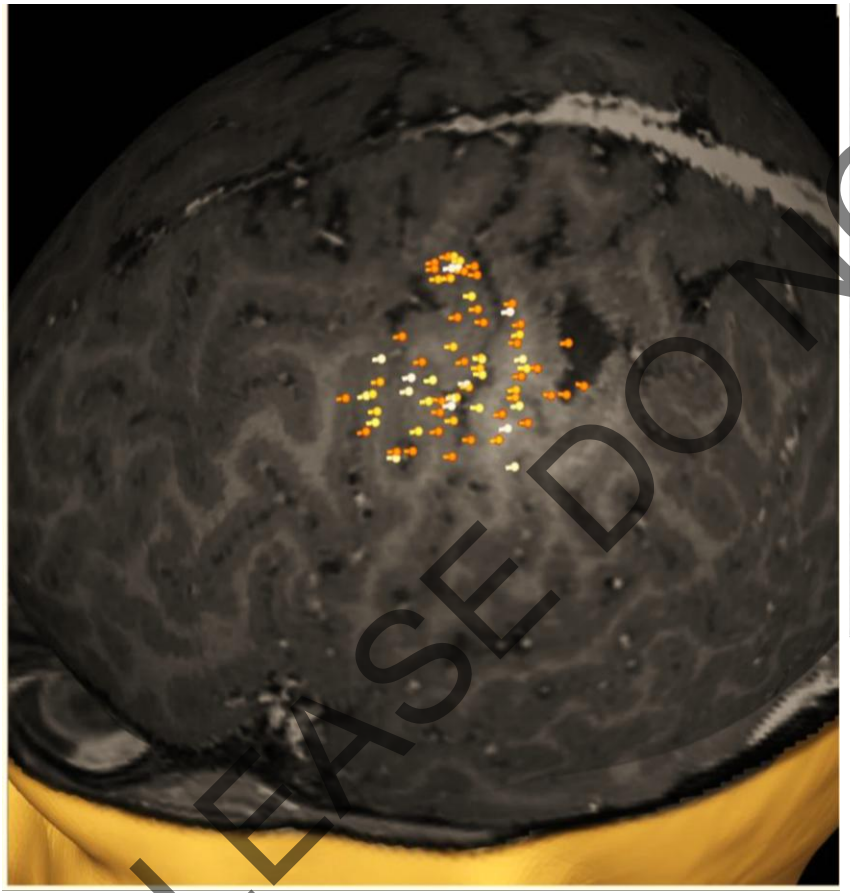
Ipsilateral hand connectivity in epileptic hemisphere

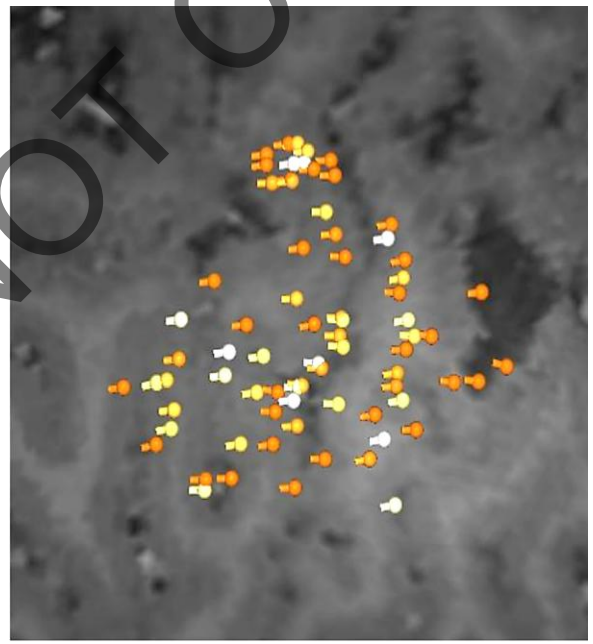


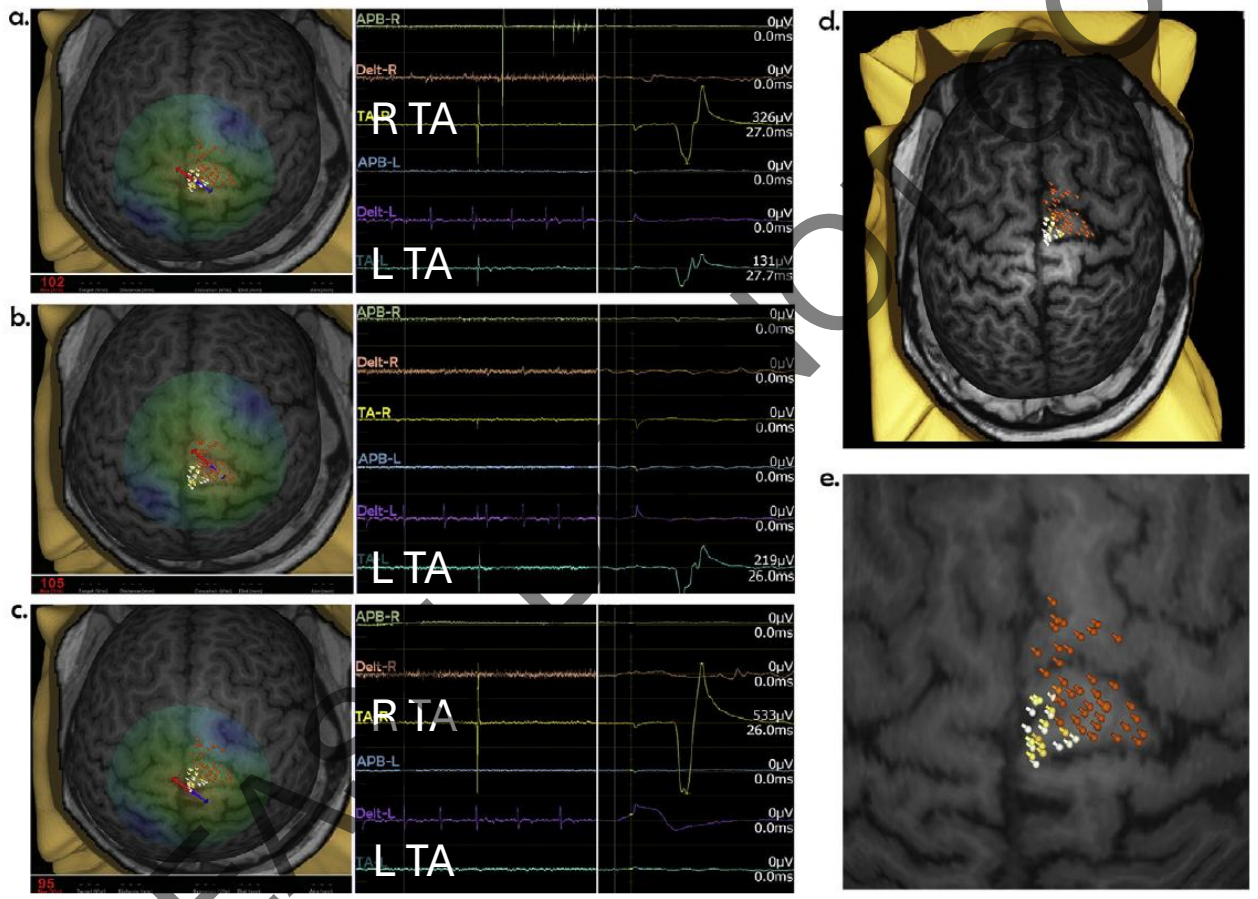
Right APB

Left APB

Color Coded Map of Left, Right, & Bilateral APB MEP's

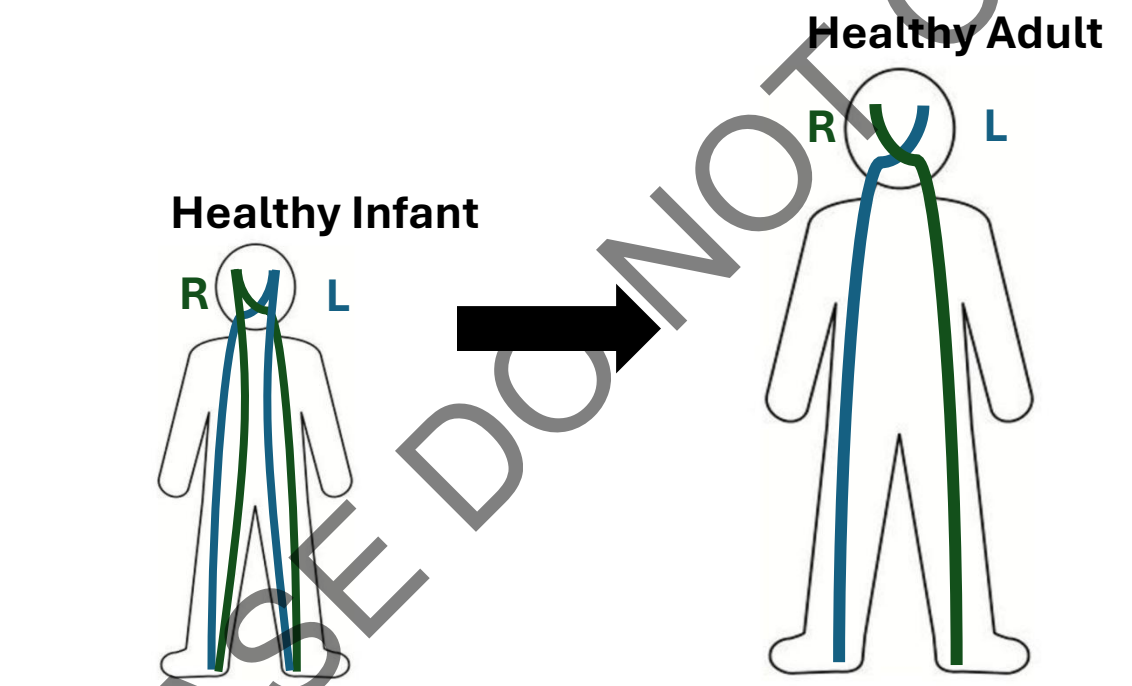






95% with b/l TA map in lesional hemisphere (chi sq $p<0.01$)

Corticospinal Tracts Bilateral at Birth



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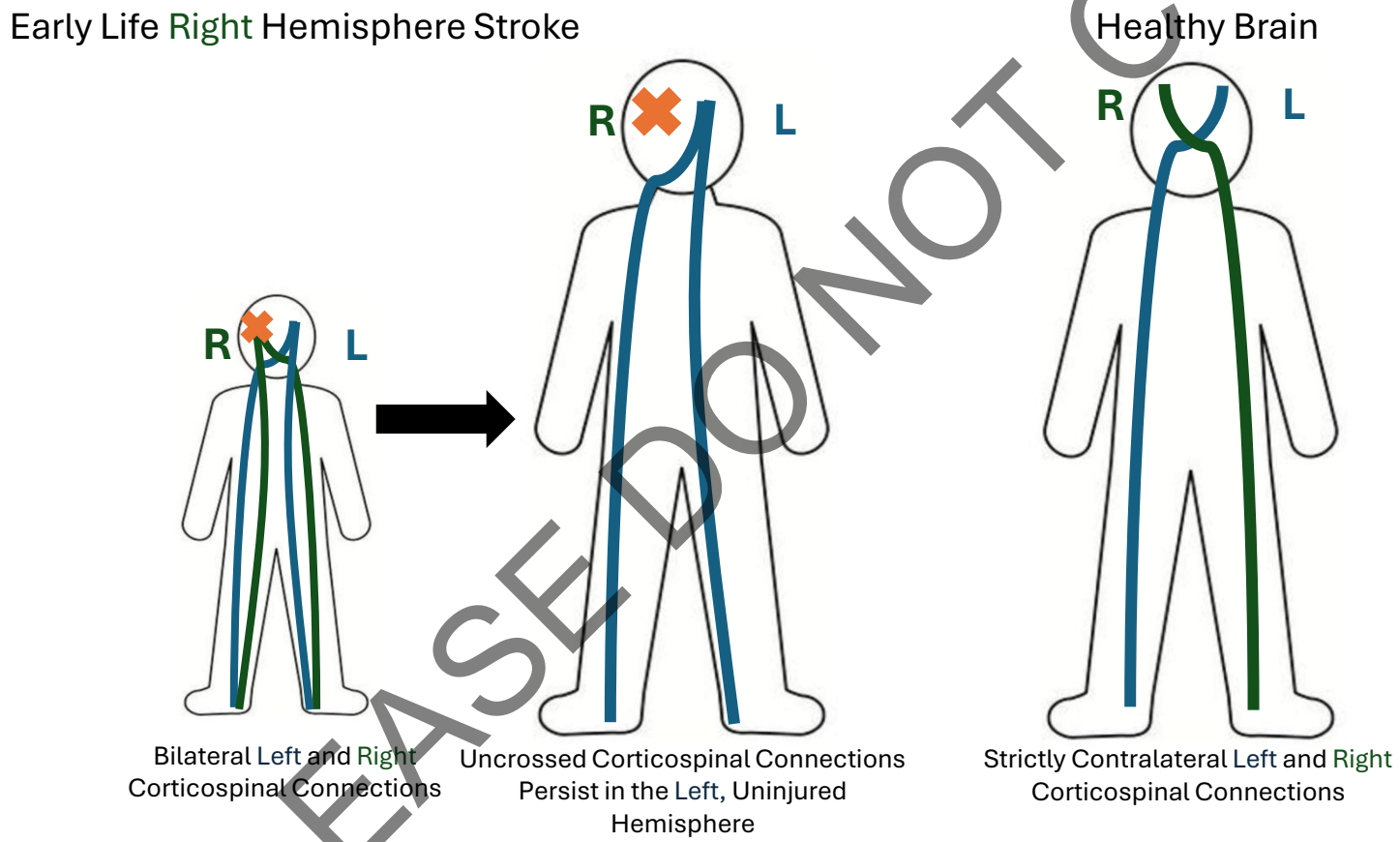
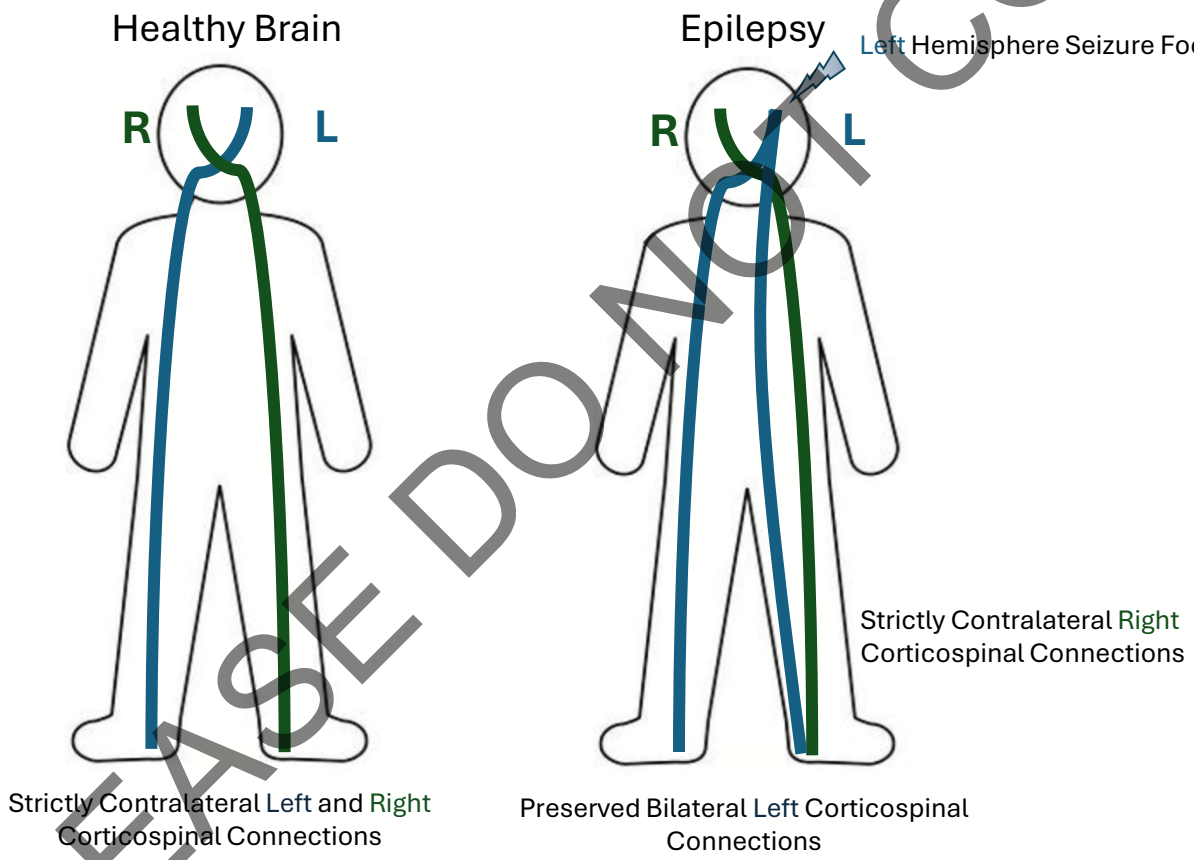
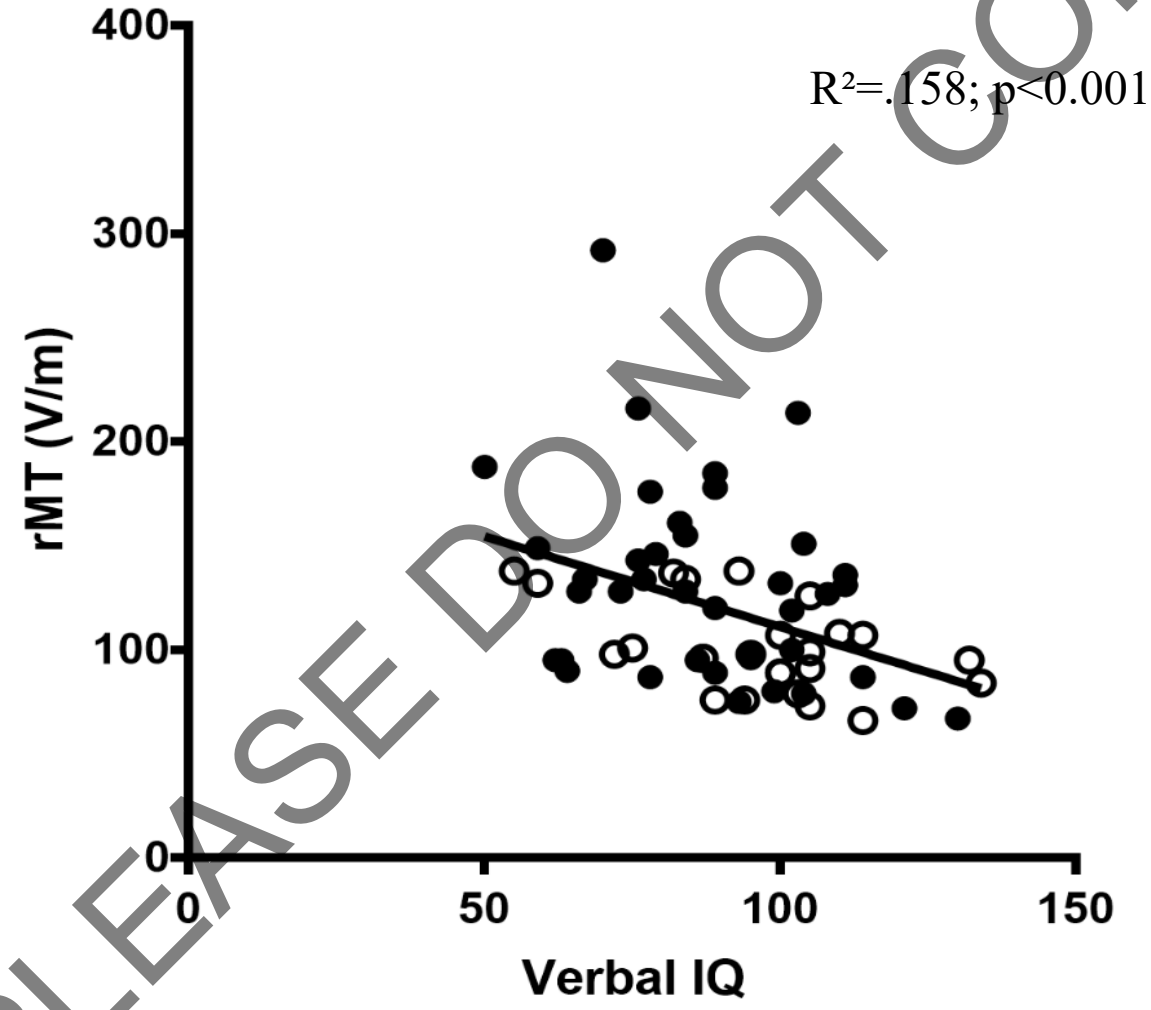


Lesional bilateral CST in epilepsy



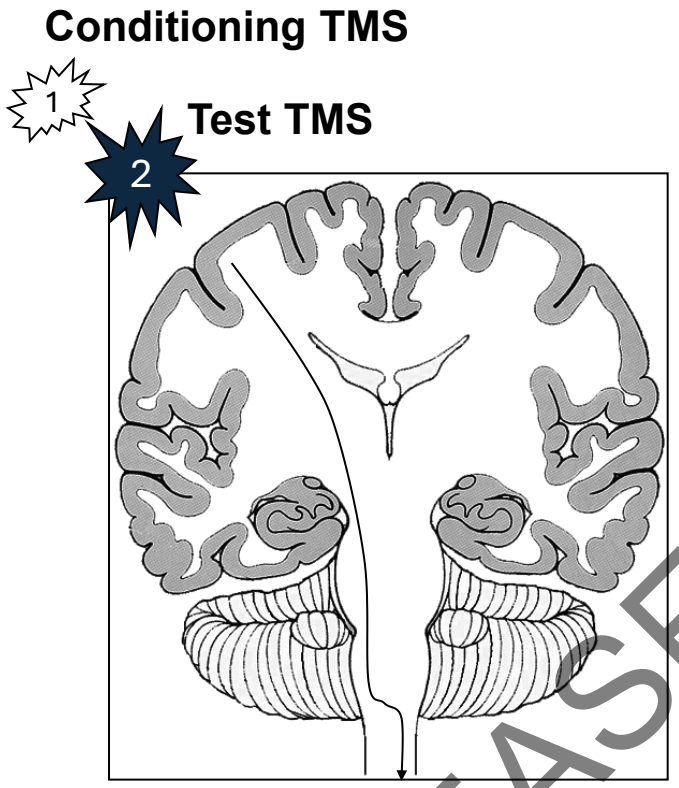
IQ v. rMT

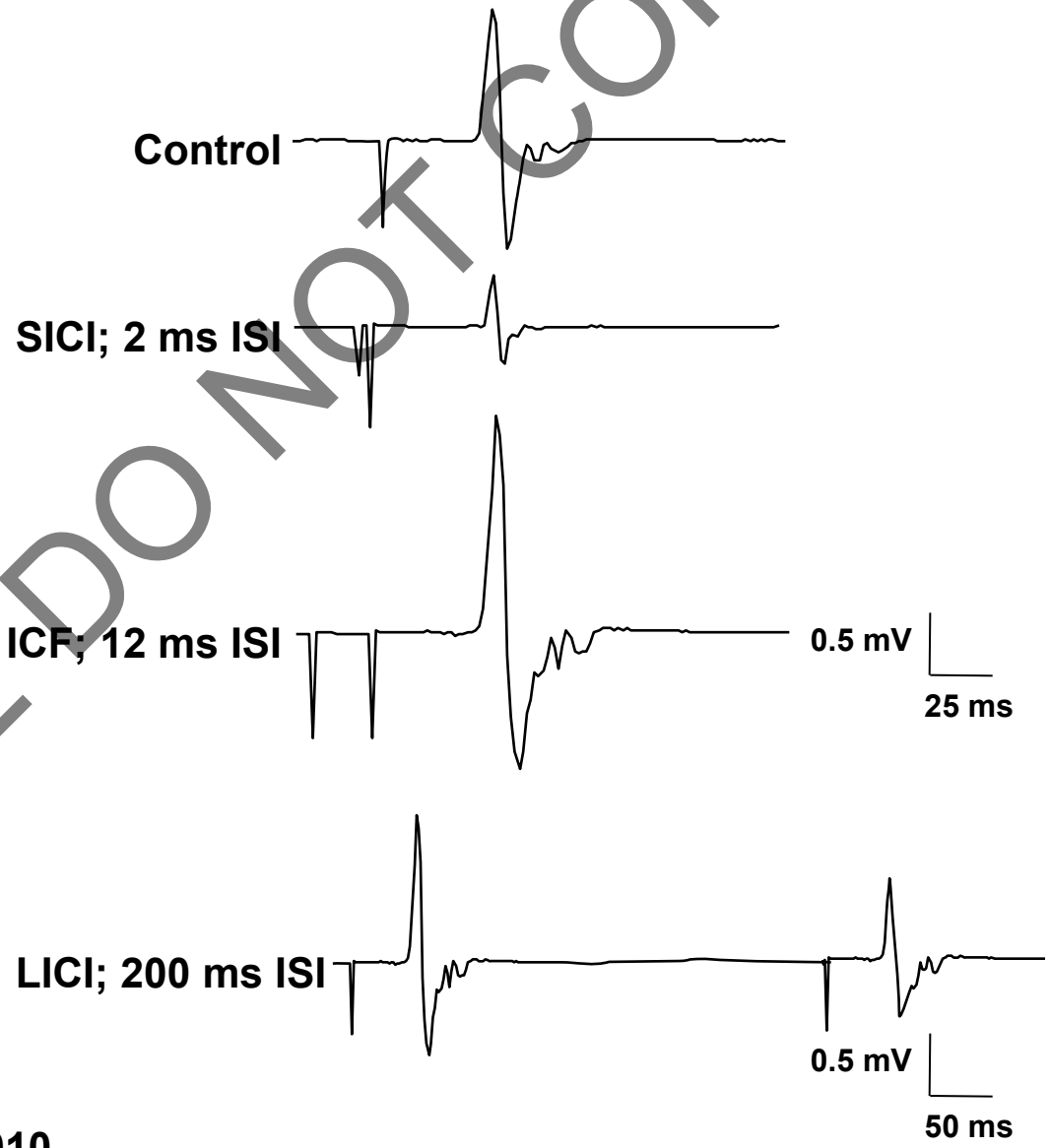


R^2=.158; $p<0.001$

Kaye et al., in prep

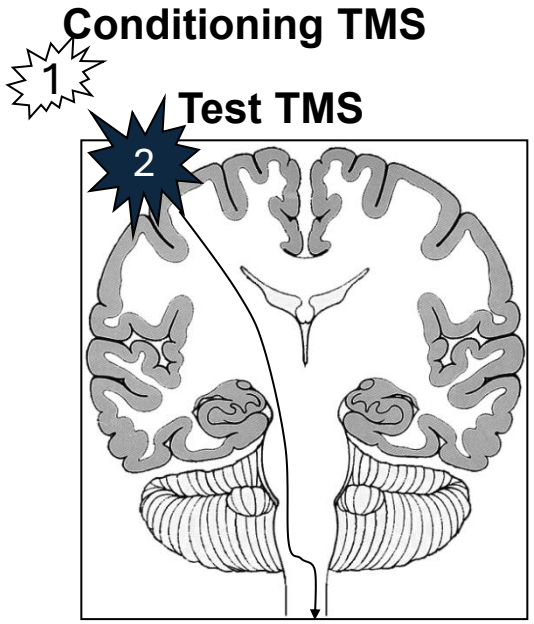
Measures of Cortical Excitability by Paired-Pulse TMS (ppTMS)



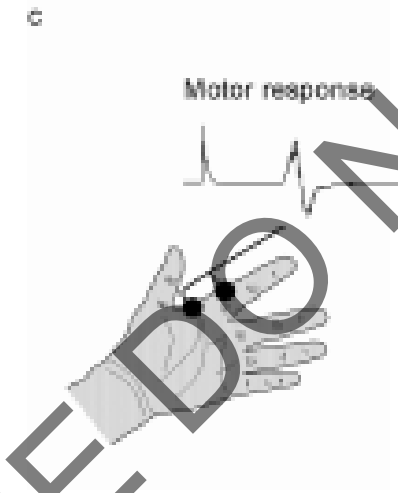


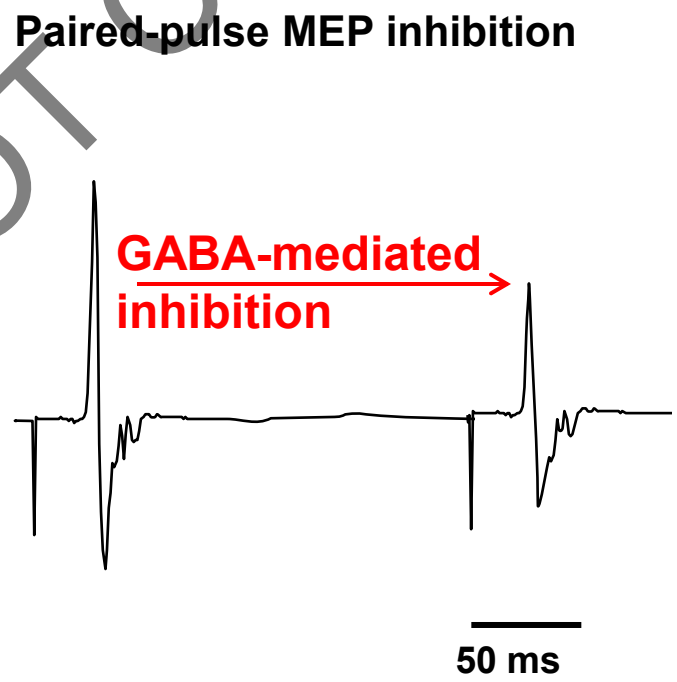
Rotenberg and Pascual-Leone, 2010

GABAergic cortical inihibition measures by paired-pulse TMS (ppTMS)



Rotenberg and Pascual-Leone, 2010





Motor cortex inhibition

A marker of ADHD behavior and motor development in children

D.L. Gilbert, MD, MS
K.M. Isaacs, BA
M. Augusta, BA
L.K. MacNeil, BA
S.H. Mostofsky, MD

Figure 1 Transcranial magnetic stimulation (TMS) data from one typically developing child

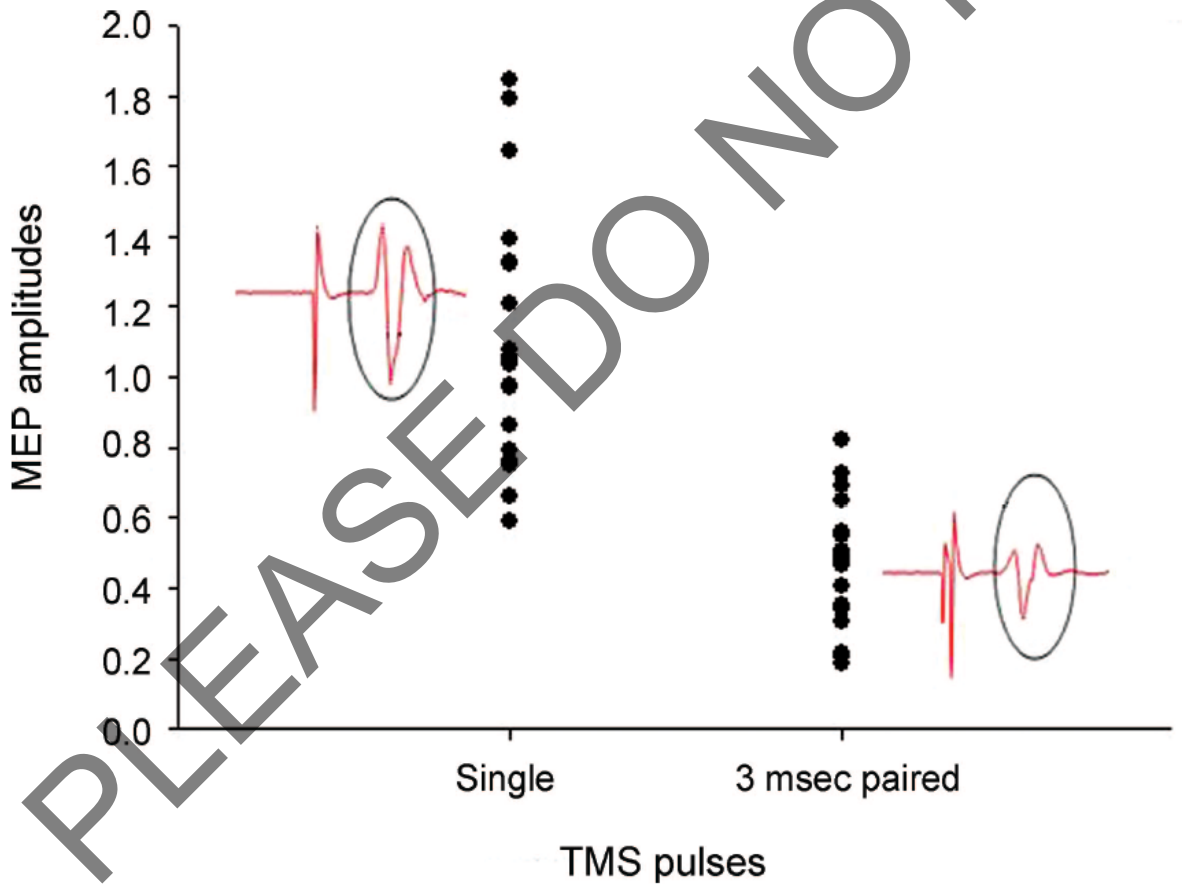


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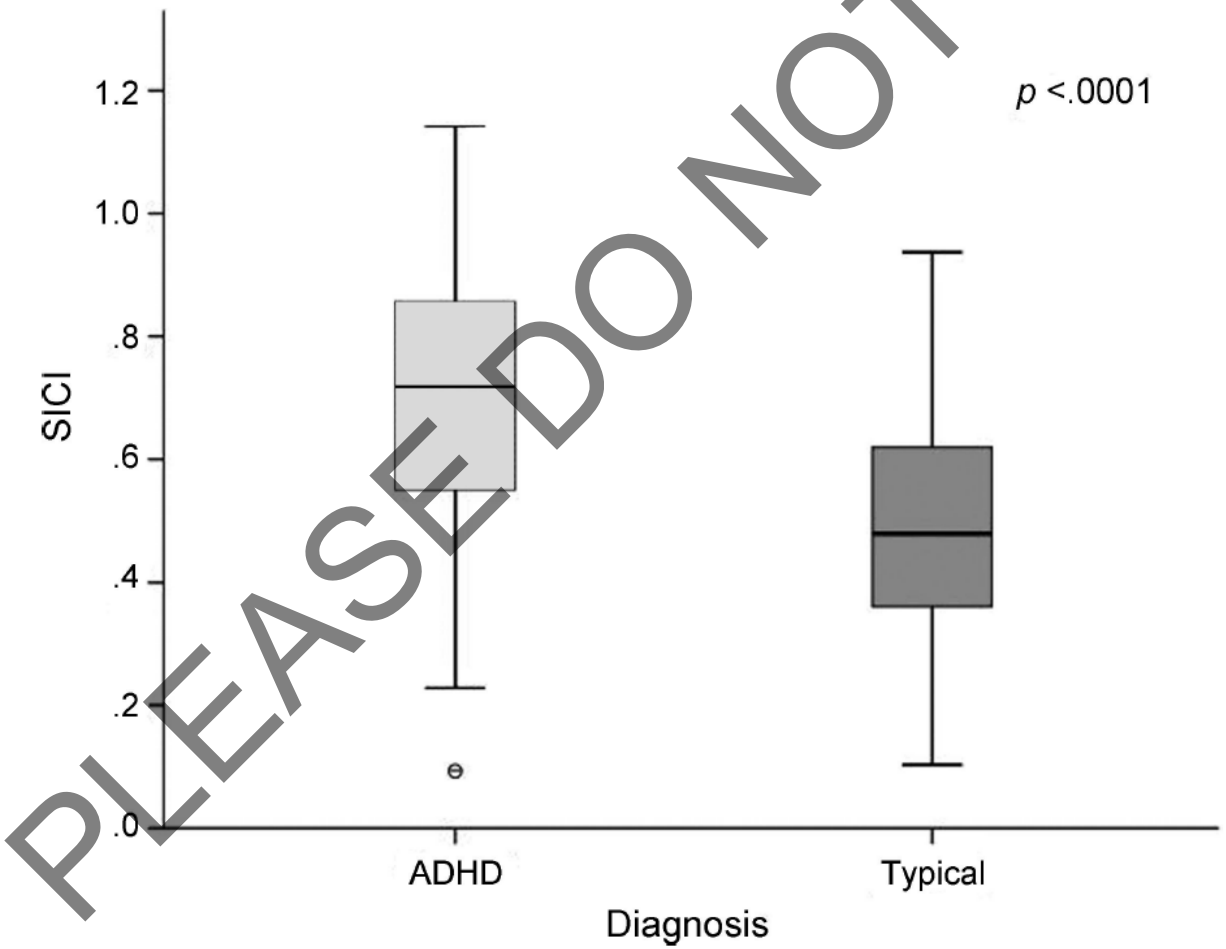
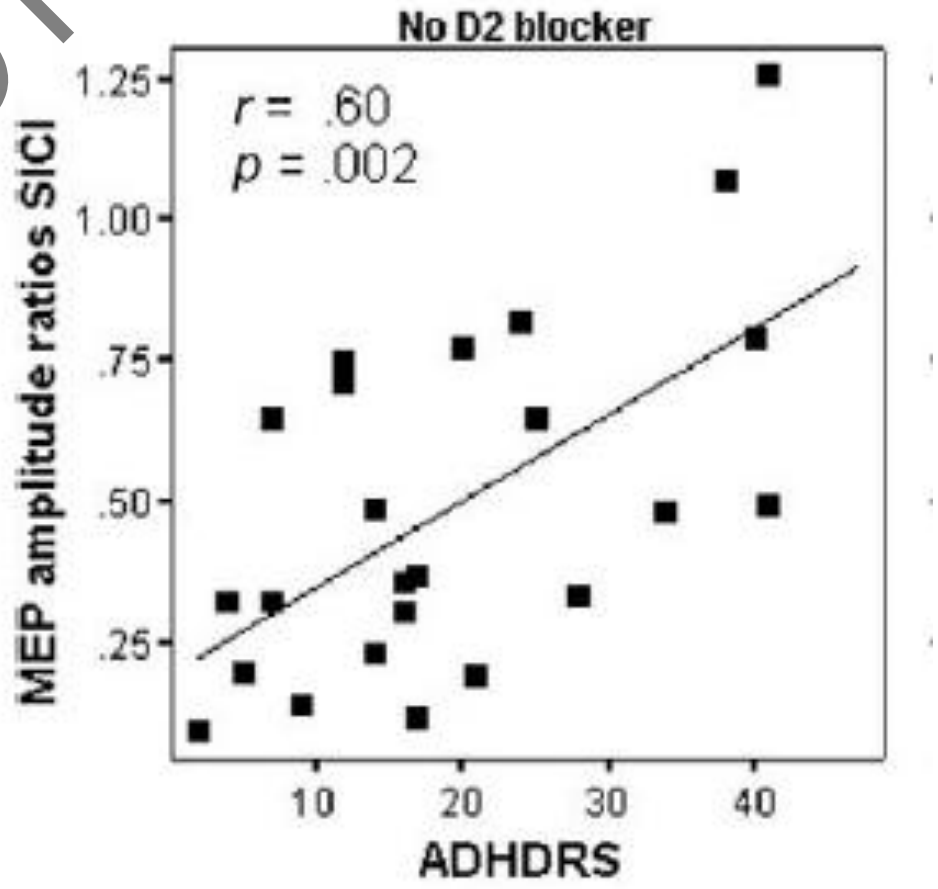
Figure 2 **Short interval cortical inhibition (SICI) is significantly reduced in children with attention-deficit/hyperactivity disorder (ADHD) vs typical children**



Transcranial Magnetic Stimulation-Evoked Cortical Inhibition: A Consistent Marker of Attention-Deficit/Hyperactivity Disorder Scores in Tourette Syndrome

Donald L. Gilbert, Floyd R. Sallee, Jie Zhang, Tara D. Lipps, and Eric M. Wassermann



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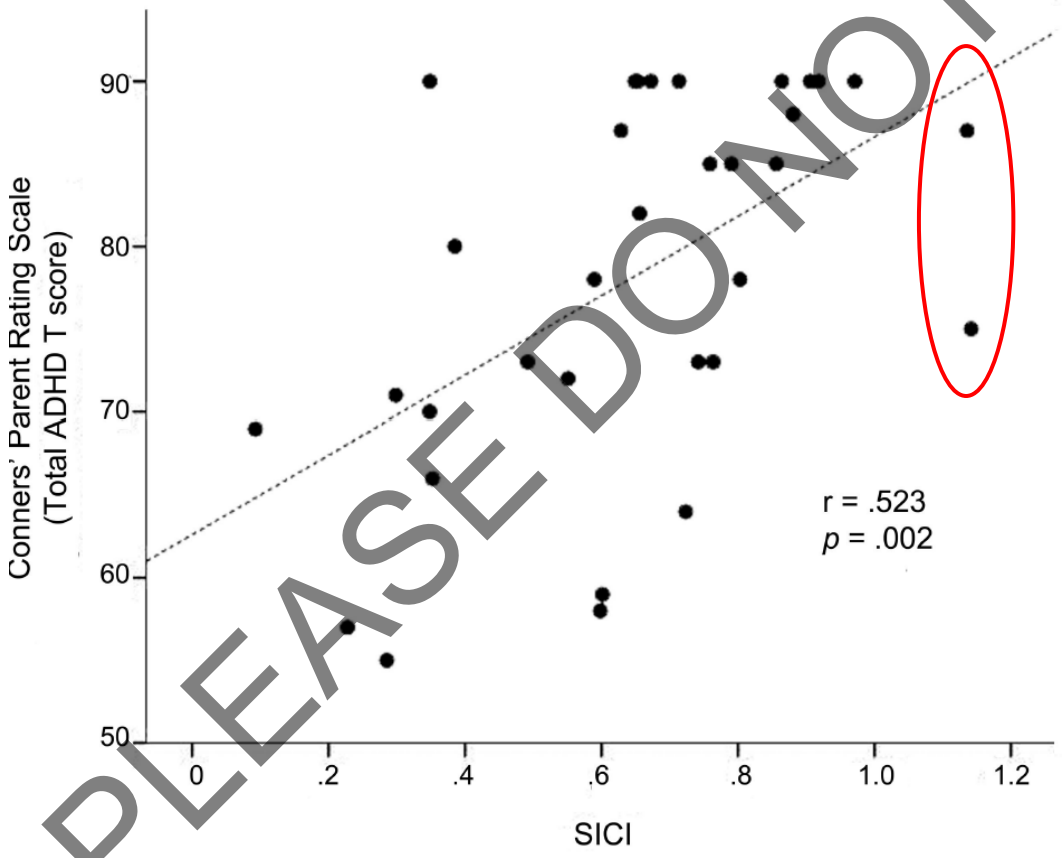
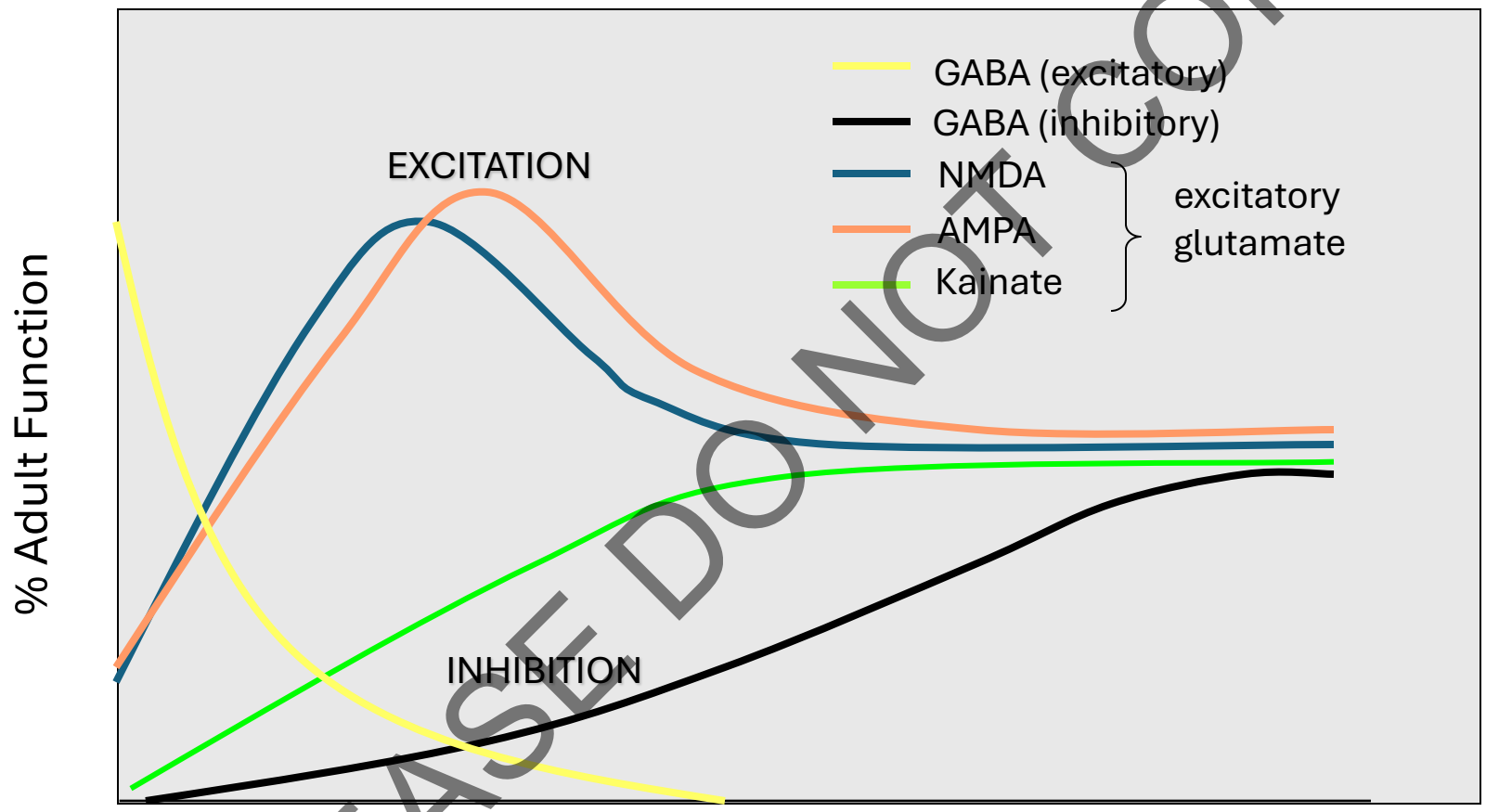
S.H. Mostofsky, MD

Figure 3 **Short interval cortical inhibition (SICI) correlates with behavioral ratings in children with attention-deficit/hyperactivity disorder (ADHD)**

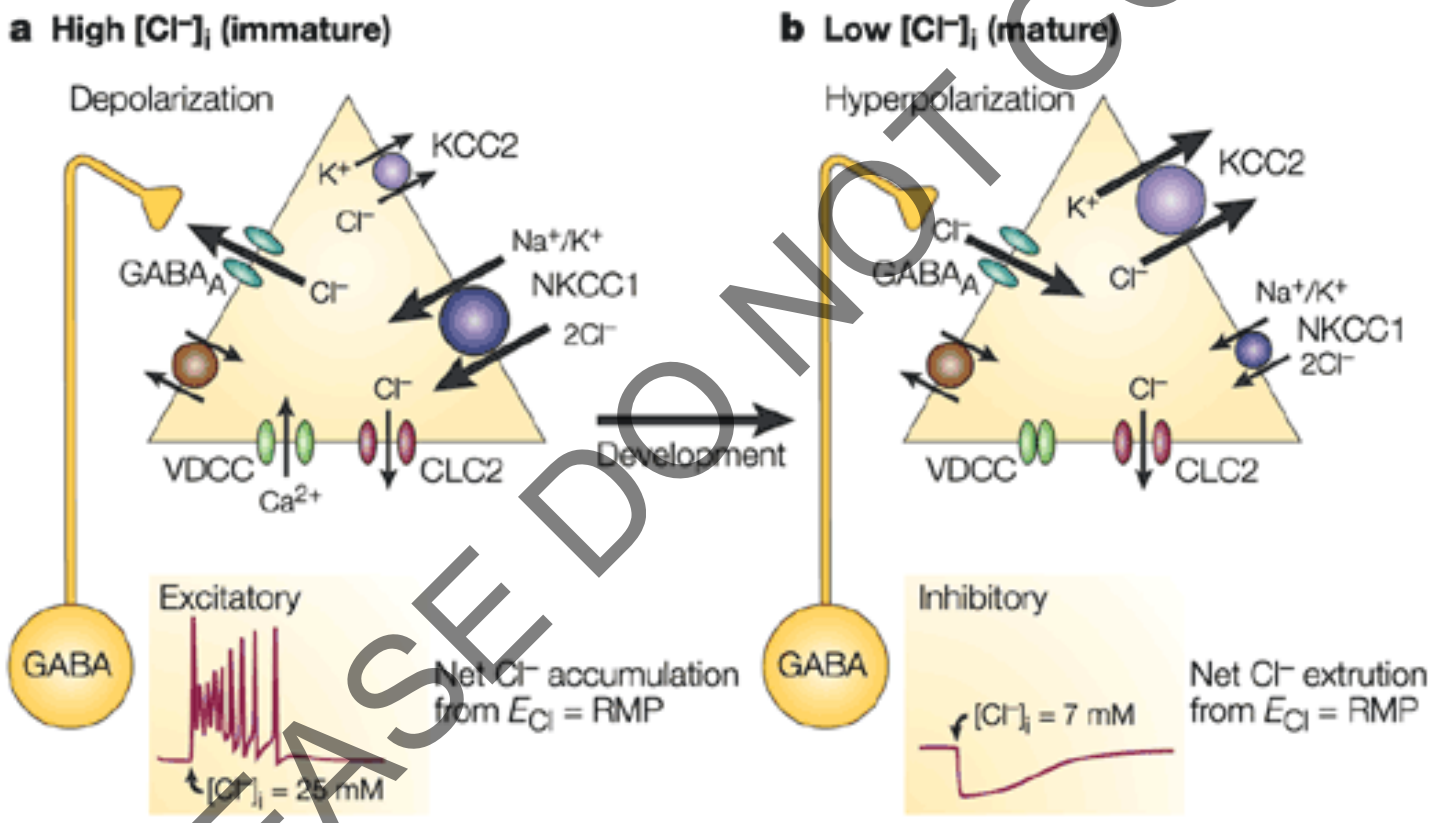


Neuronal Receptor Expression vs Age



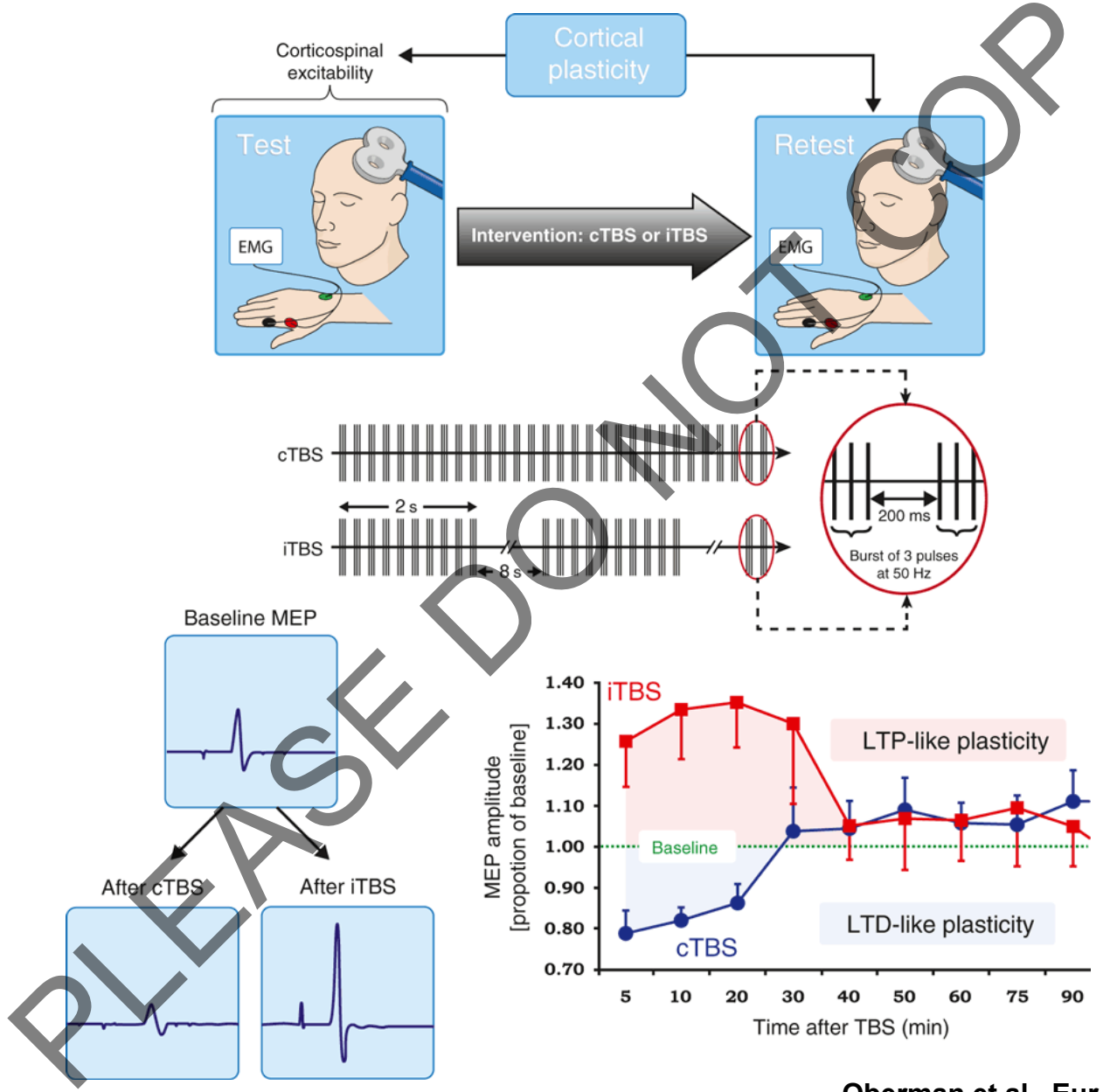
Silverstein and Jensen, *Ann Neurol*, 2007
Rakhade and Jensen, *Nature Rev.*, 2010

Chloride homeostasis in the immature brain



Ben-Ari 2002

Theta burst stimulation and synaptic plasticity



Oberman et al., Eur. J. Neuroscience, 2012

J Neurophysiol 101: 2872–2877, 2009.
First published April 1, 2009; doi:10.1152/jn.91060.2008.

Neurochemical Effects of Theta Burst Stimulation as Assessed by Magnetic Resonance Spectroscopy

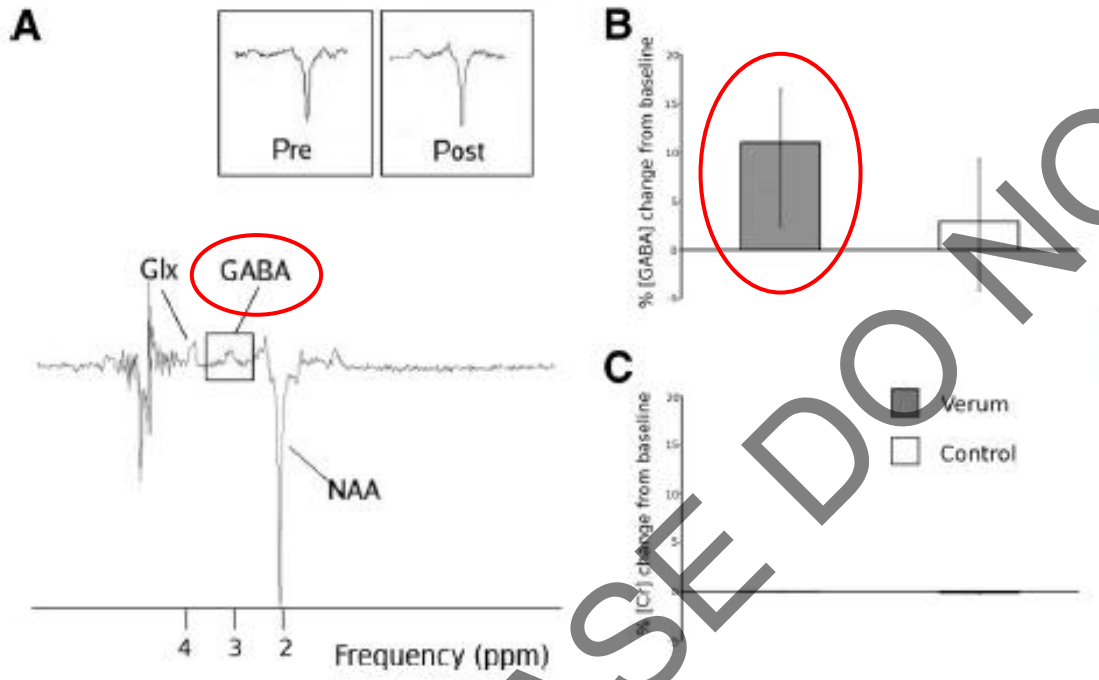
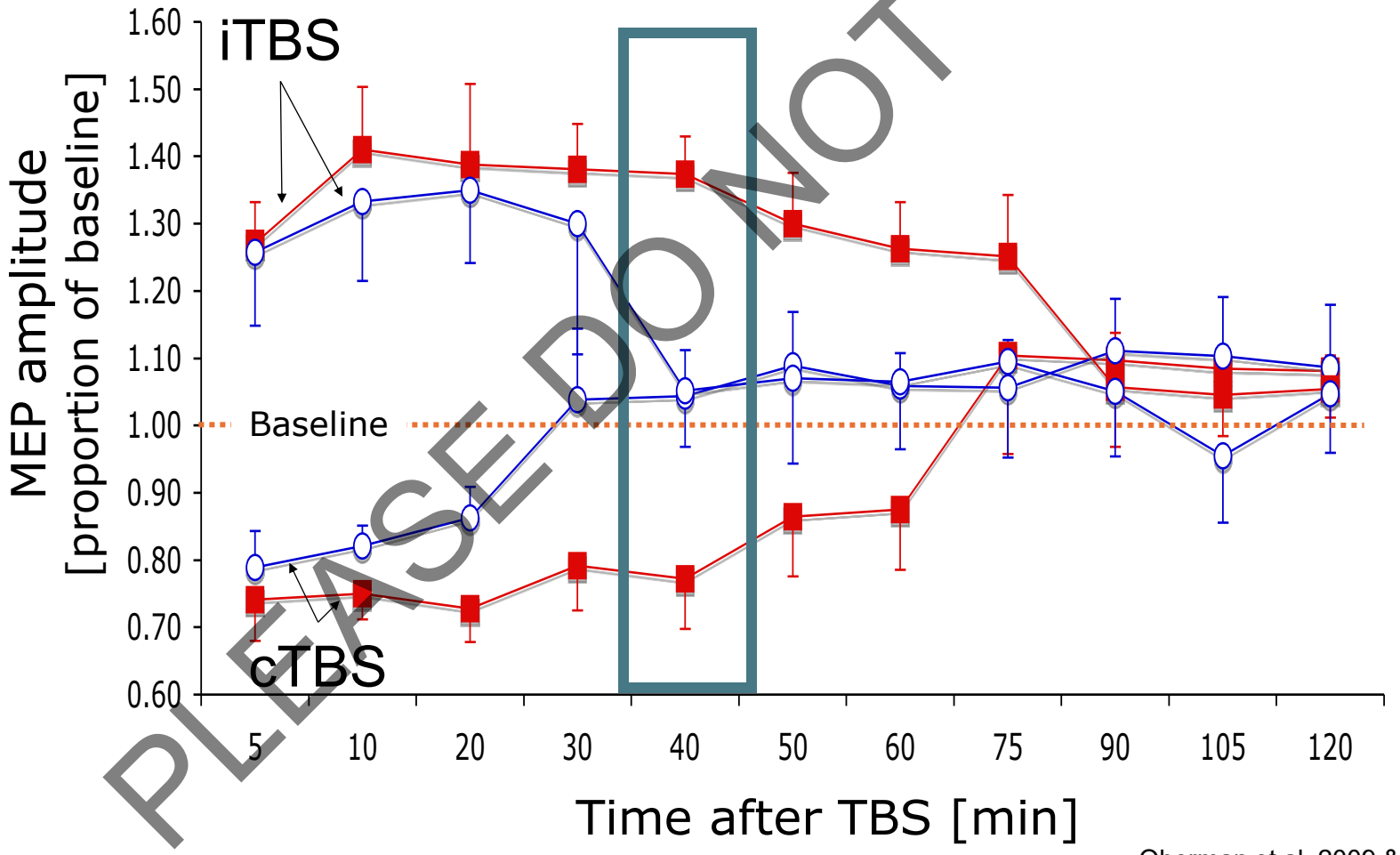


FIG. 3. *A*: typical γ-aminobutyric acid (GABA)–optimized spectrum acquired. *Insets* show representative GABA and *N*-acetylaspartate (NAA) peaks before and after stimulation in the same subject. Glx, composite measure of glutamate and glutamine. *B*: percentage change in GABA:NAA ratio from baseline. Verum stimulation leads to a significant increase in GABA:NAA ratio, compared with control. *C*: percentage change in creatine signal for baseline. There is no significant change with either stimulation condition.

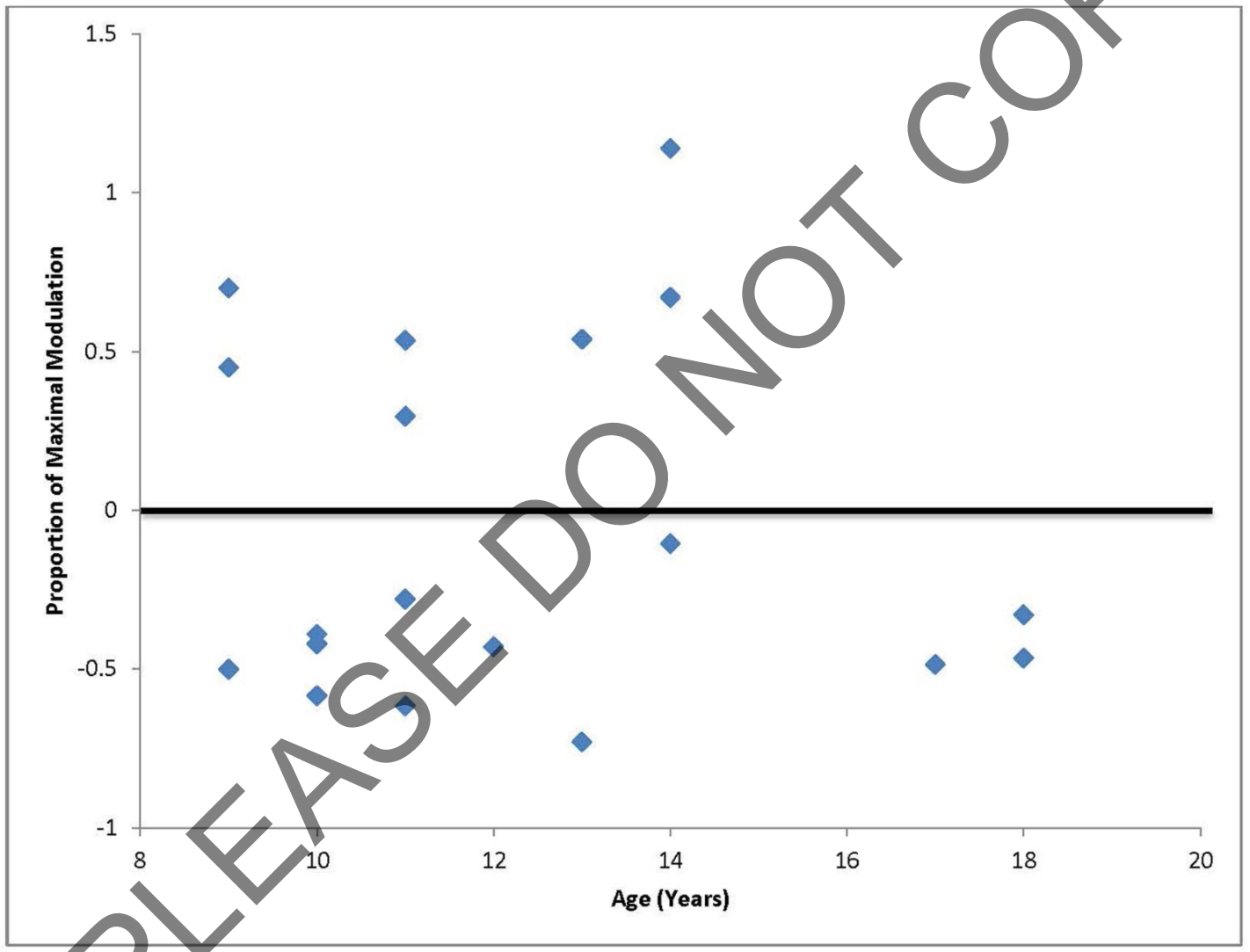
Stagg et al., *J Neurophysiol*, 2009

Hyperplasticity in Autism Spectrum Disorders



Oberman et al. 2009 & in press

Paradoxical facilitation in children with ASD



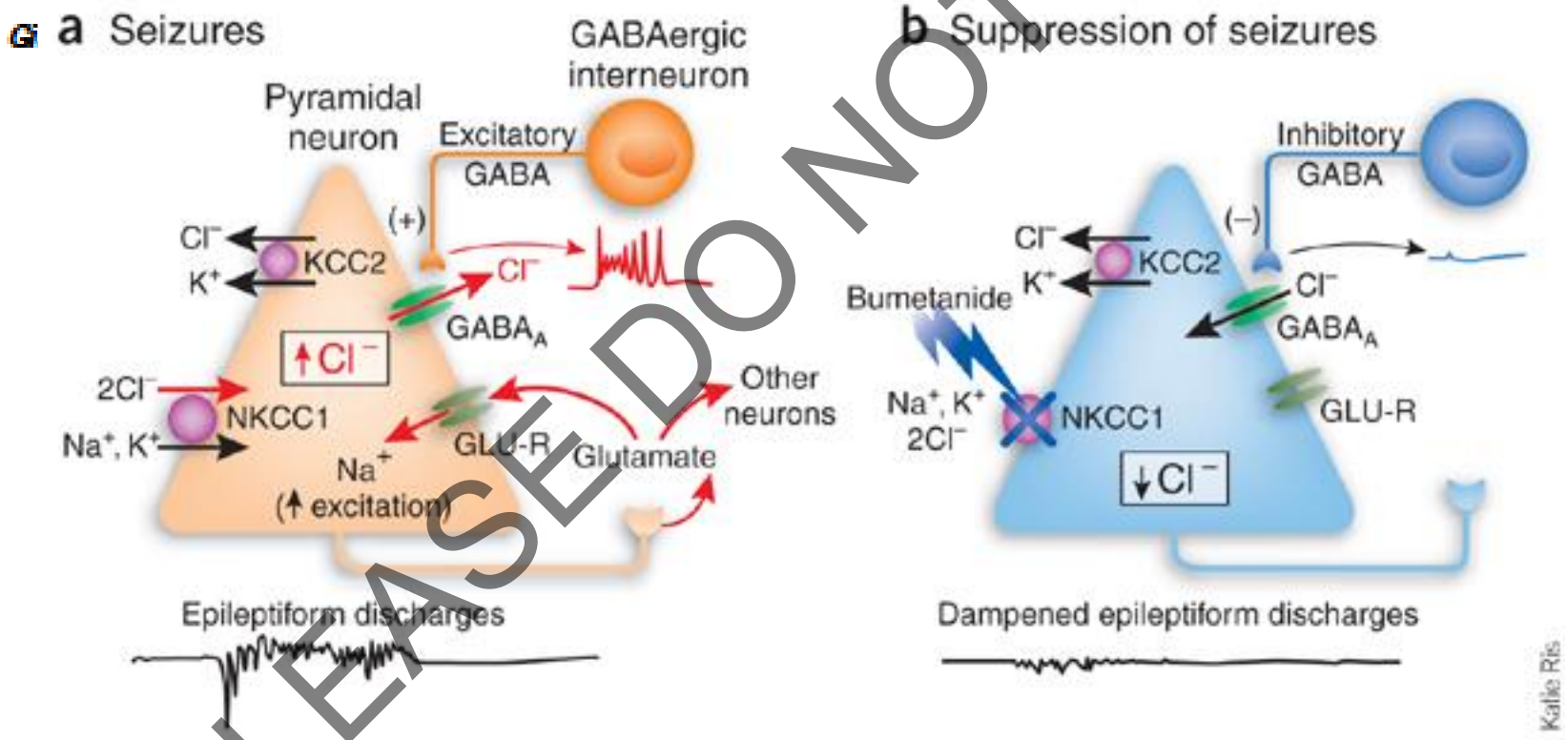
Oberman et al., 2014

Why is this interesting?

frontiers in PEDIATRICS

REVIEW ARTICLE
published: 08 July 2014

GABAergic signaling as therapeutic target for autism spectrum disorders



Chloride homeostasis may be dysmature in the ASD brain, and NKCC1 block may rescue the ASD phenotype

Citation: Transl Psychiatry (2012) 2, e202; doi:10.1038/tp.2012.124

www.nature.com/tp

A randomised controlled trial of bumetanide in the treatment of autism in children

E Lemonnier[1,2], C Degrez[1], M Phelep[1], R Tyzio[3], F Josse[1], M Grandgeorge[1,2], N Hadjikhani[4,5] and Y Ben-Ari[3]

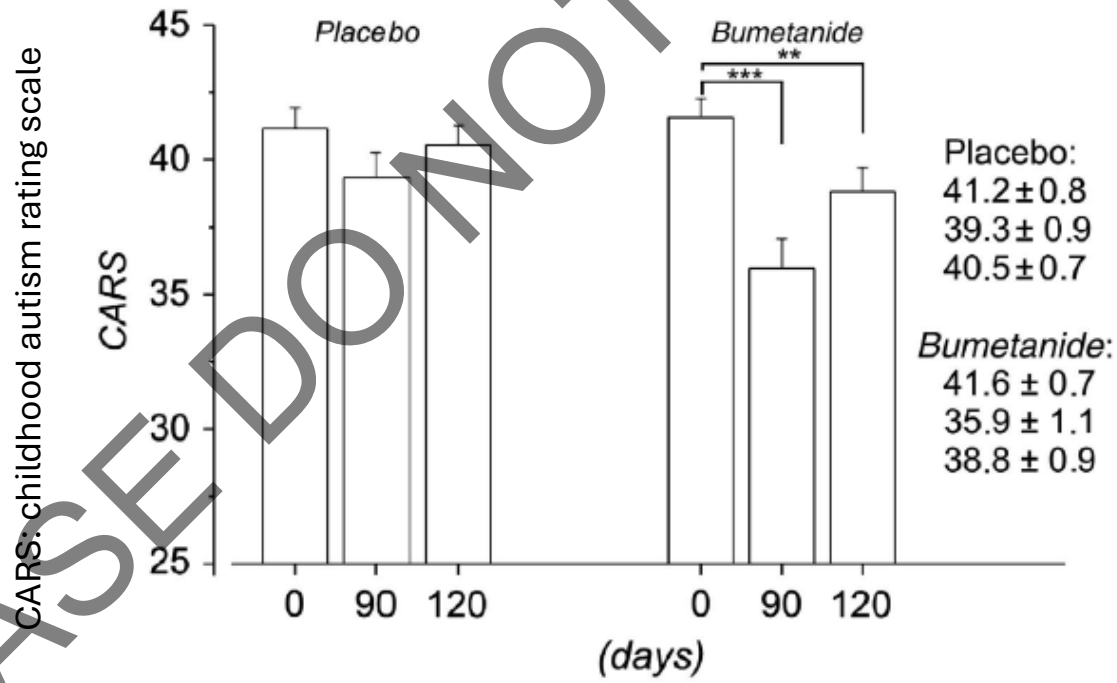


Figure 2 All the values obtained with CARS are depicted. Note the significant differences between placebo and bumetanide treated patients and a partial return to pretreatment values after 1-month wash-out period. The number of items >3 was also significantly reduced as shown at the right side of the figure (number corresponding to D0, D90 and D120; ***$p<0.005$ for D90 and **$p<0.05$ for D120).

Pediatric Neurology 68 (2017) 3–17

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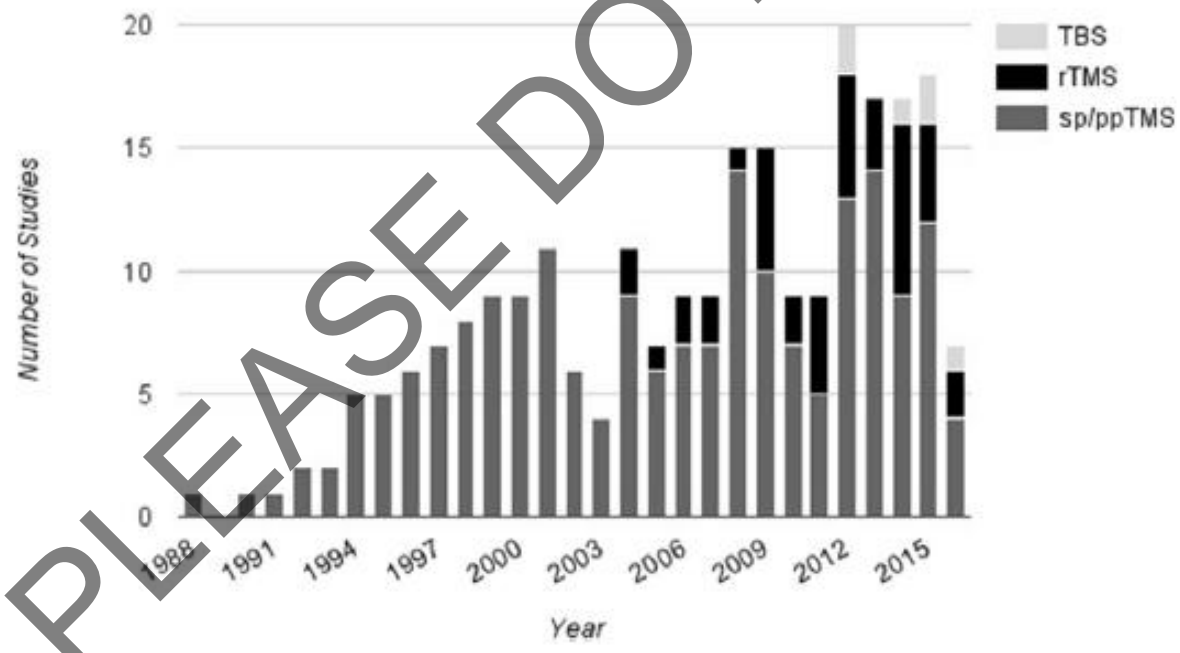
journal homepage: www.elsevier.com/locate/pnu

Topical Review

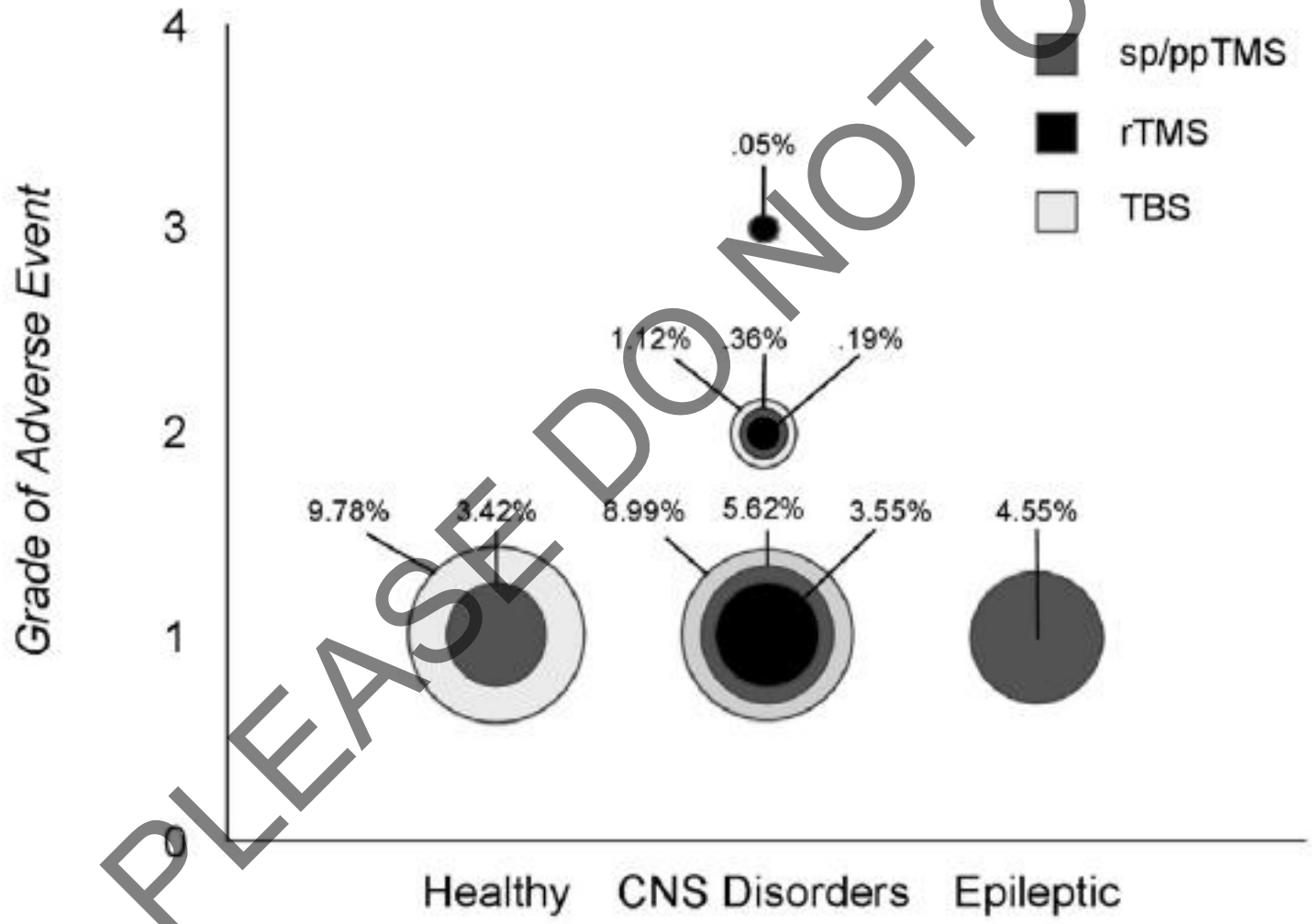
Safety of Transcranial Magnetic Stimulation in Children: A Systematic Review of the Literature

Corey H. Allen BS [a], Benzi M. Kluger MD, MS [b], Isabelle Buard PhD [b,*]

[a] *Neuroscience Institute, Georgia State University, Atlanta, Georgia*
[b] *Department of Neurology, University of Colorado-Anschutz Medical Campus, Aurora, Colorado*



Grade 1: mild event that needs no intervention
Grade 2: moderate event with noninvasive intervention needed
Grade 3: severe event, but not life-threatening, that calls for hospitalization.



Original Article

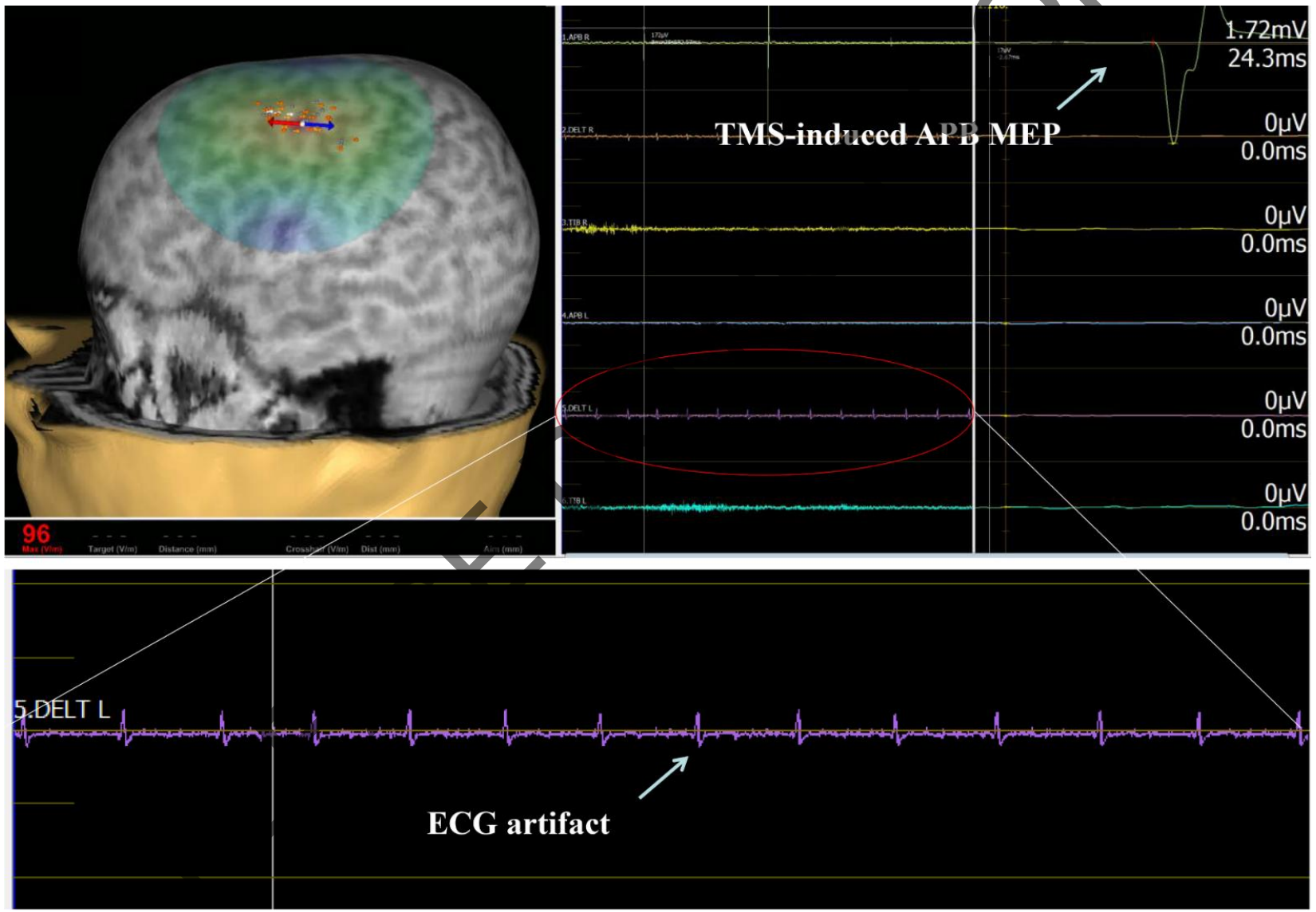
J Child Neurol, 2001

Subjective Reactions of Children to Single-Pulse Transcranial Magnetic Stimulation

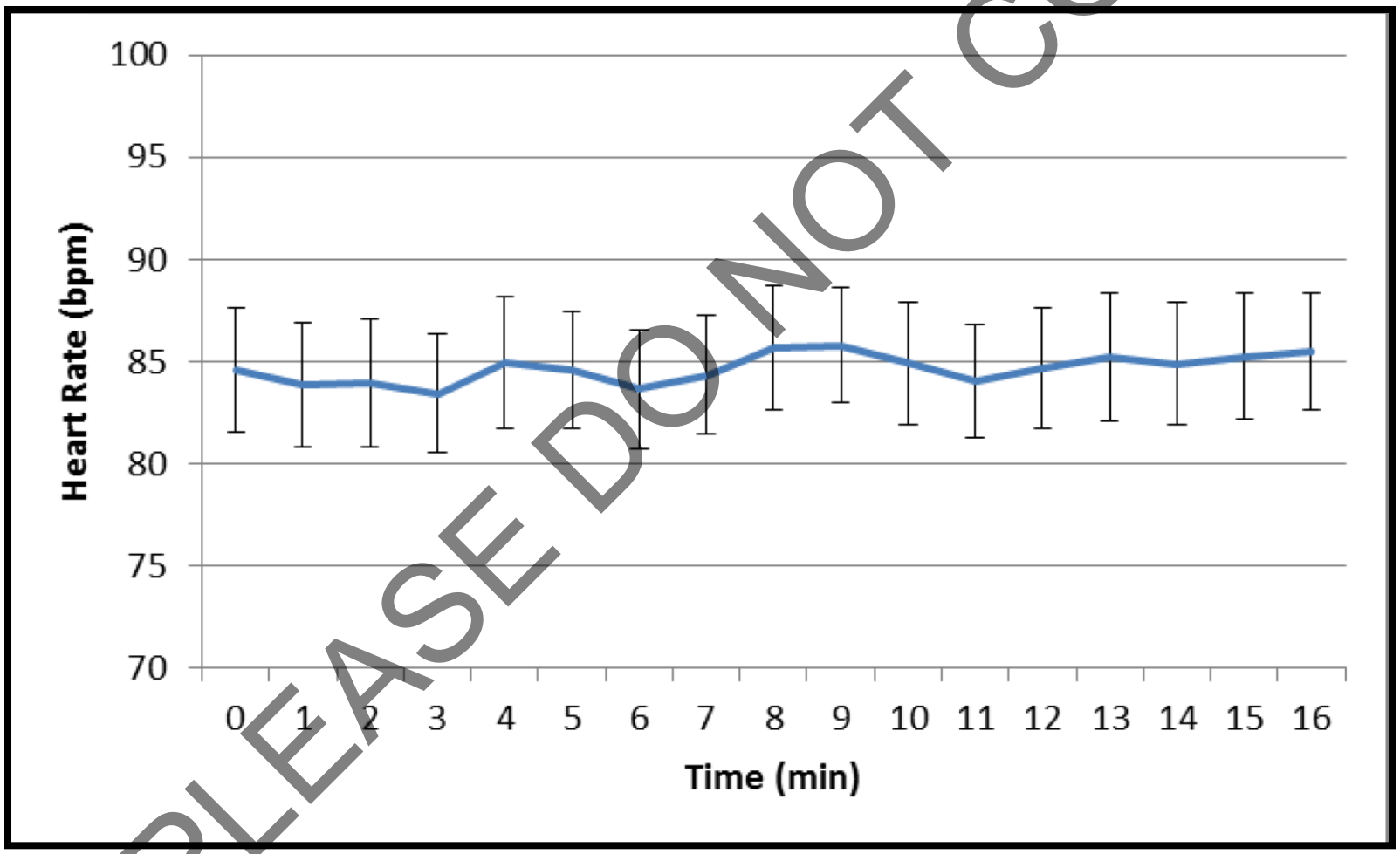
Marjorie A. Garvey, MD; Karen J. Kaczynski, BA; Danielle A. Becker, BS; John J. Bartko, PhD

more enjoyable than “a long car ride”

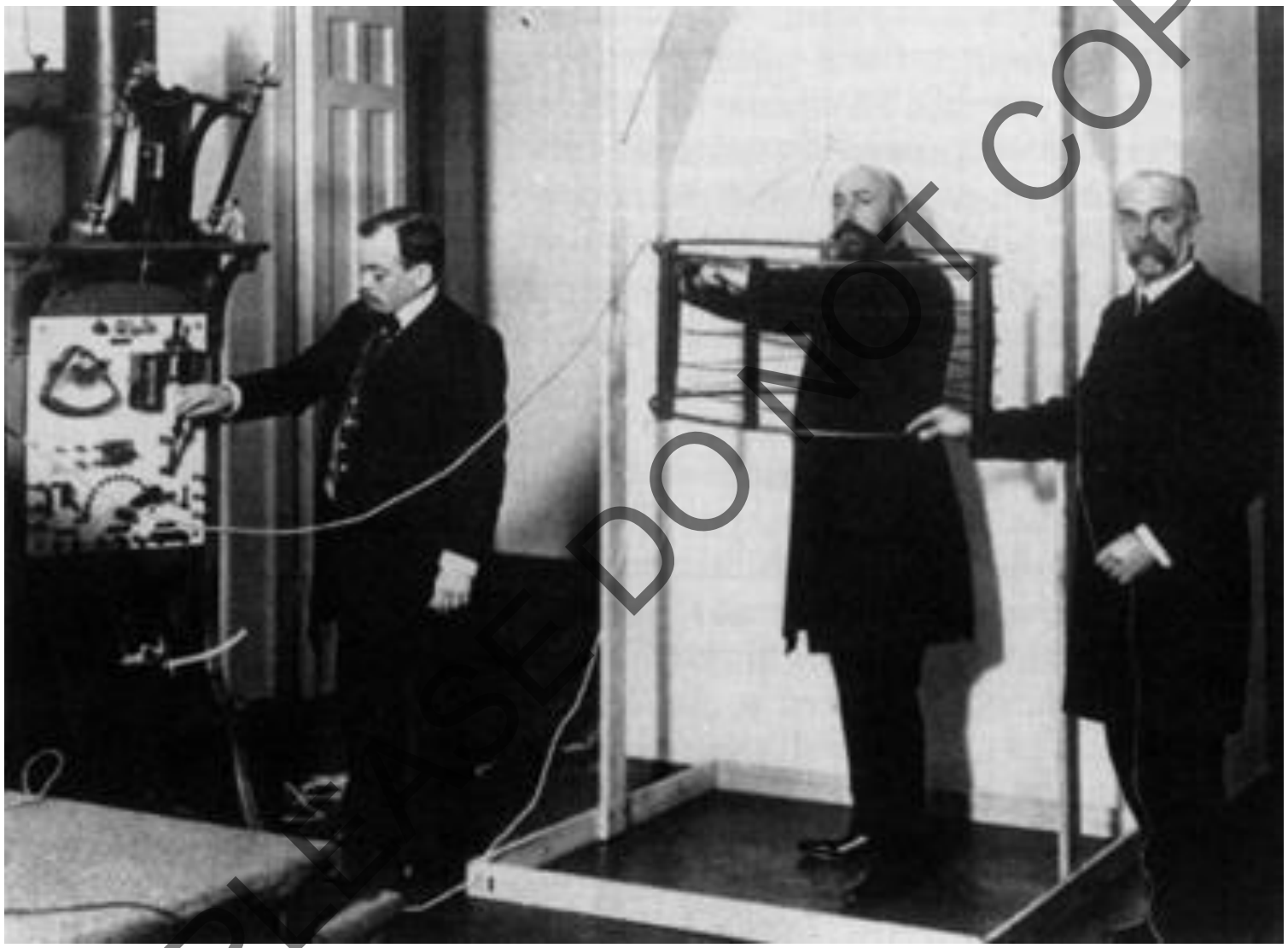
Heart Rate Measures



Heart Rate Stability During nTMS



Who’s doing the heavy lifting?



Jacques-Arsène d'Arsonval (1851 – 1940)

Thanks!