



Non-invasive brain stimulation & Human Brain

Machine Learning Meetup in Korea

Jae-Chang Kim

Ybrain Research Institute

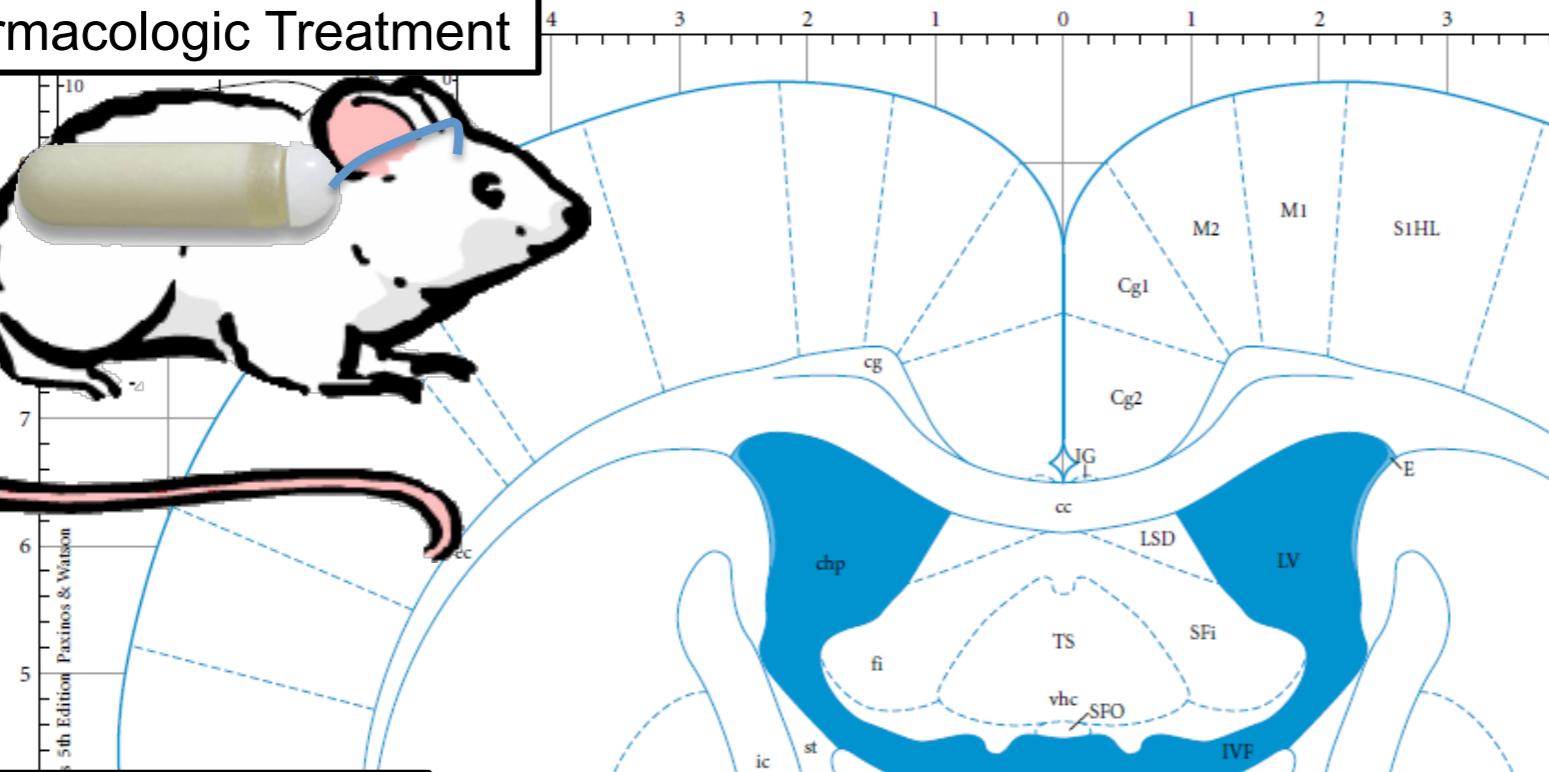
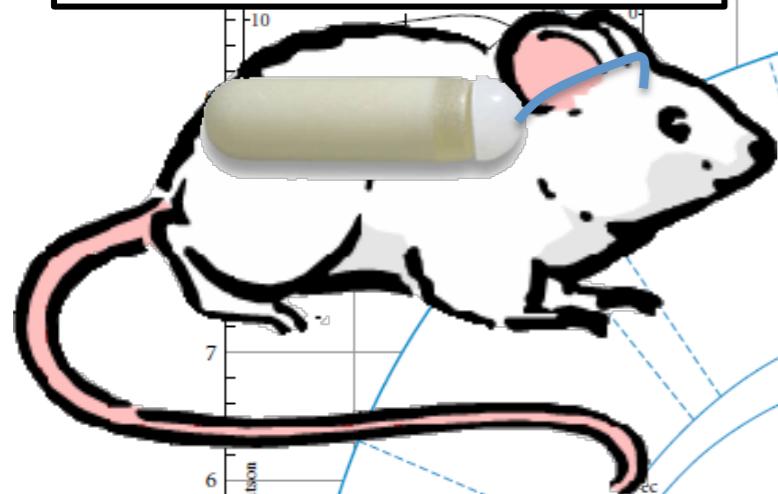
2015.03.12 | TOZ

Contents

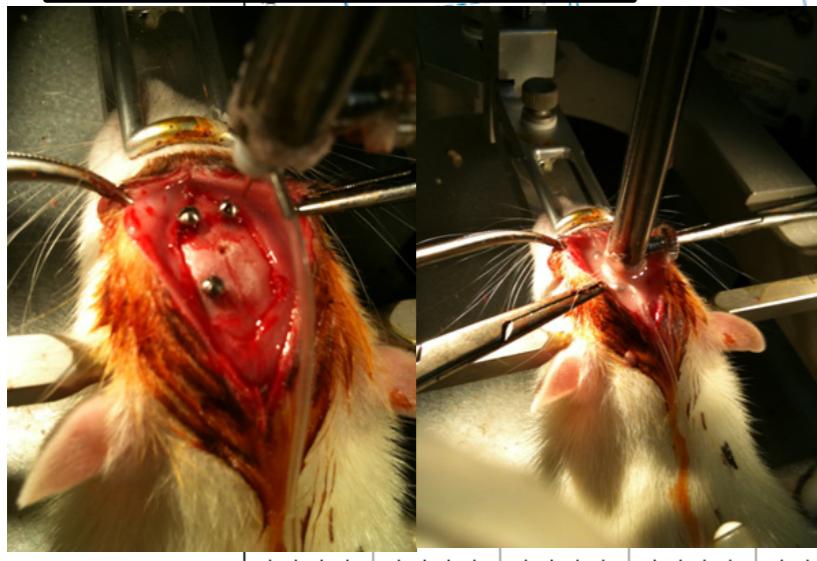
- Brain Stimulation methods
 - Animal study
 - Pharmacology
 - Invasive Brain stimulation - ECT/DBS
 - Non-invasive Brain stimulation - TMS/tDCS
- Applications for decision making

Animal studies

Pharmacologic Treatment



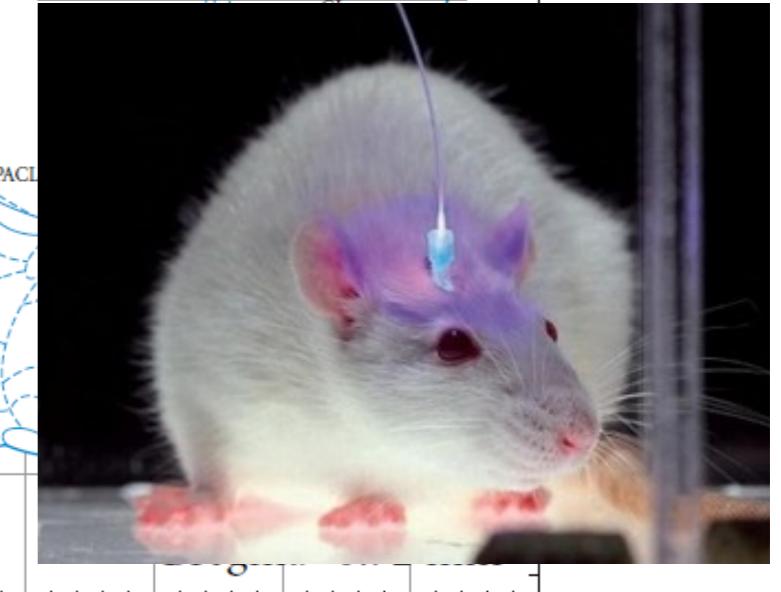
Stereotaxic Surgery



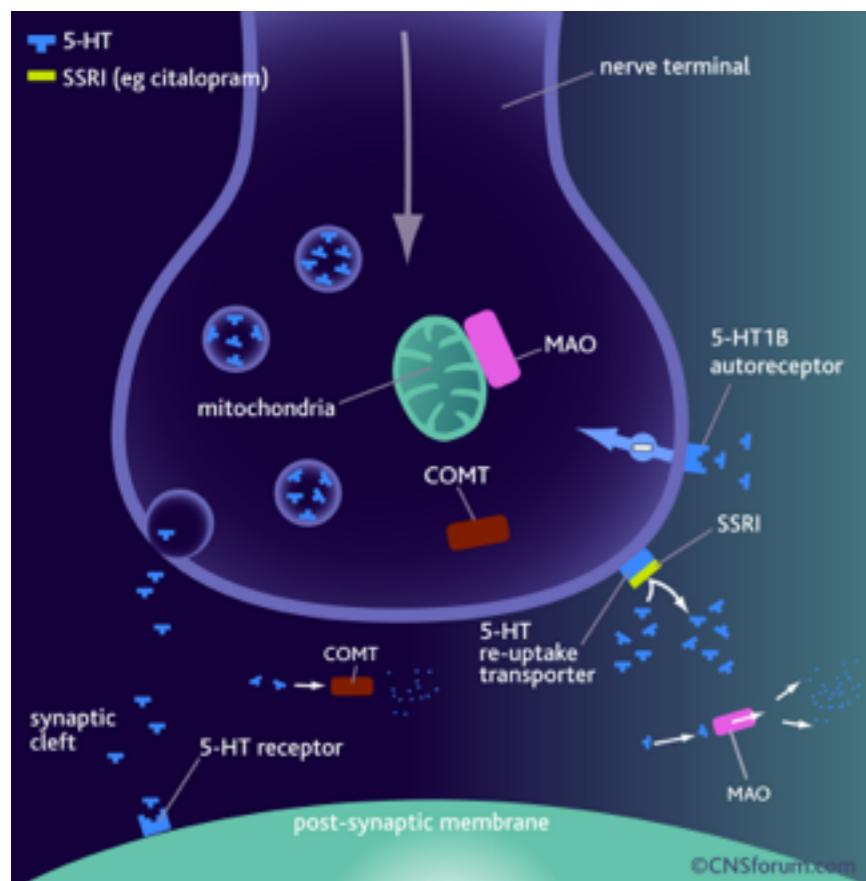
Genetic Modification (Cre/flox, CRISP)



Optogenetics



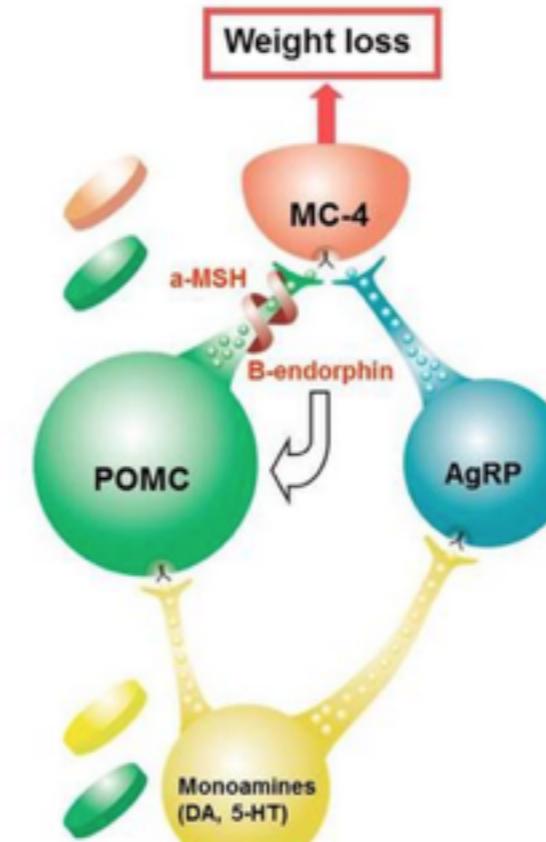
Pharmacology



Naltrexone:
↓β-endorphin-mediated POMC autoregulation leading to:
↑α-MSH release

Bupropion:
↑DA leading to POMC activation:
↑α-MSH release

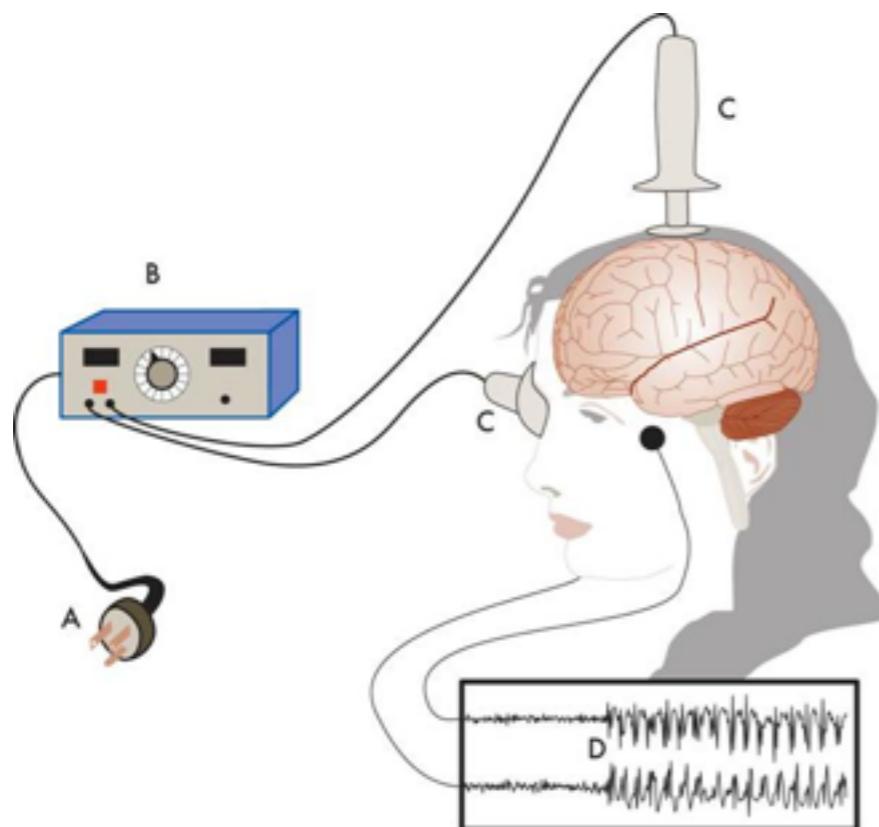
Lorcaserin:
—Serotonin 2C R agonist



Contrave™
(naltrexone SR / bupropion SR)

Qsymia™
(Phentermine / Topiramate ER)

Electroconvulsive Therapy(ECT)

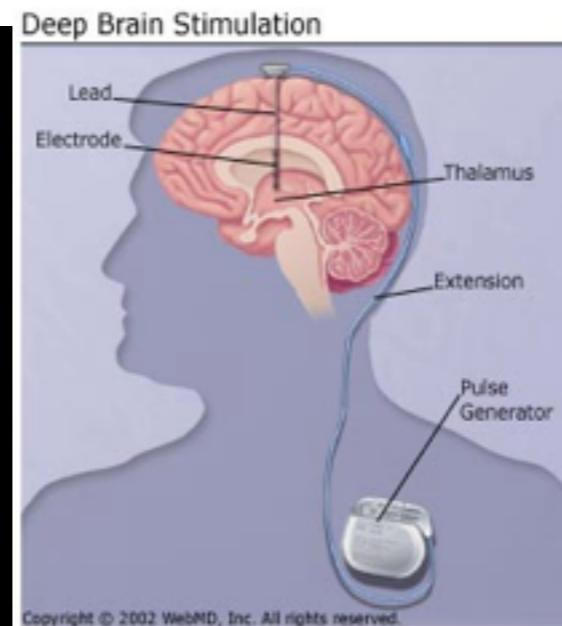
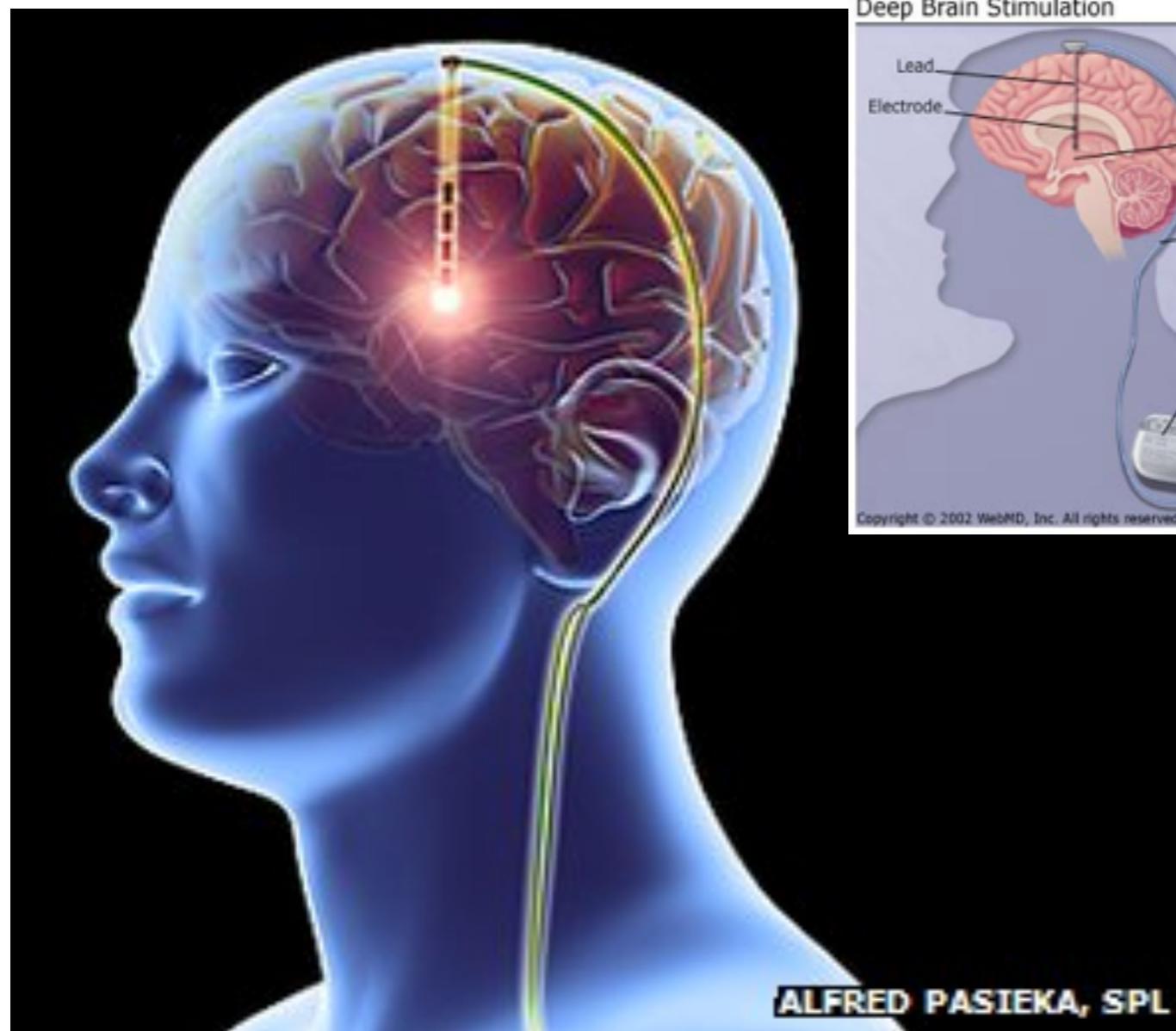


<https://www.youtube.com/watch?v=9L2-B-aluCE>

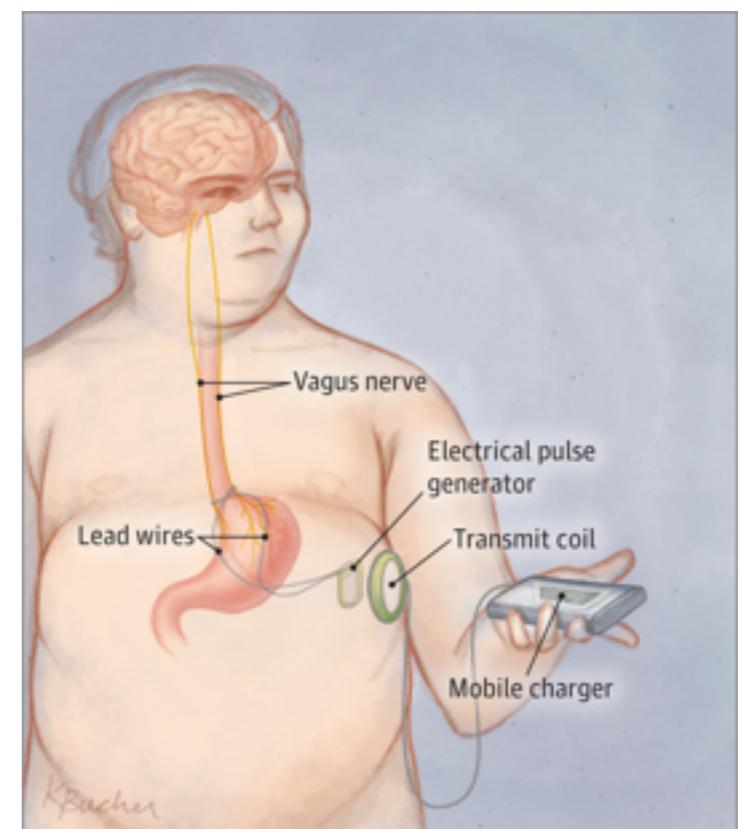
academicdepartments.musc.edu
www.psych.med.umich.edu



Deep brain stimulation(DBS)

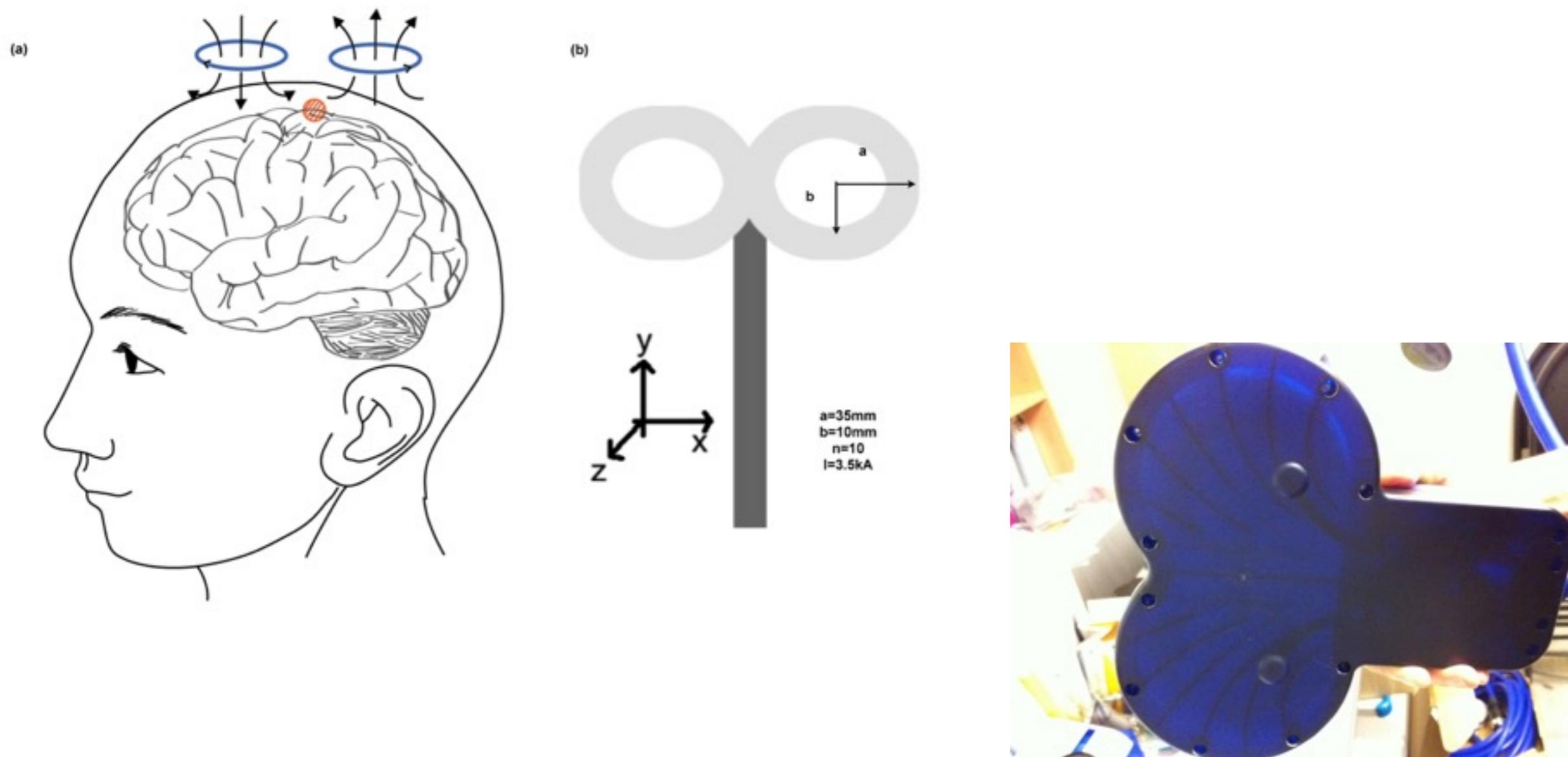


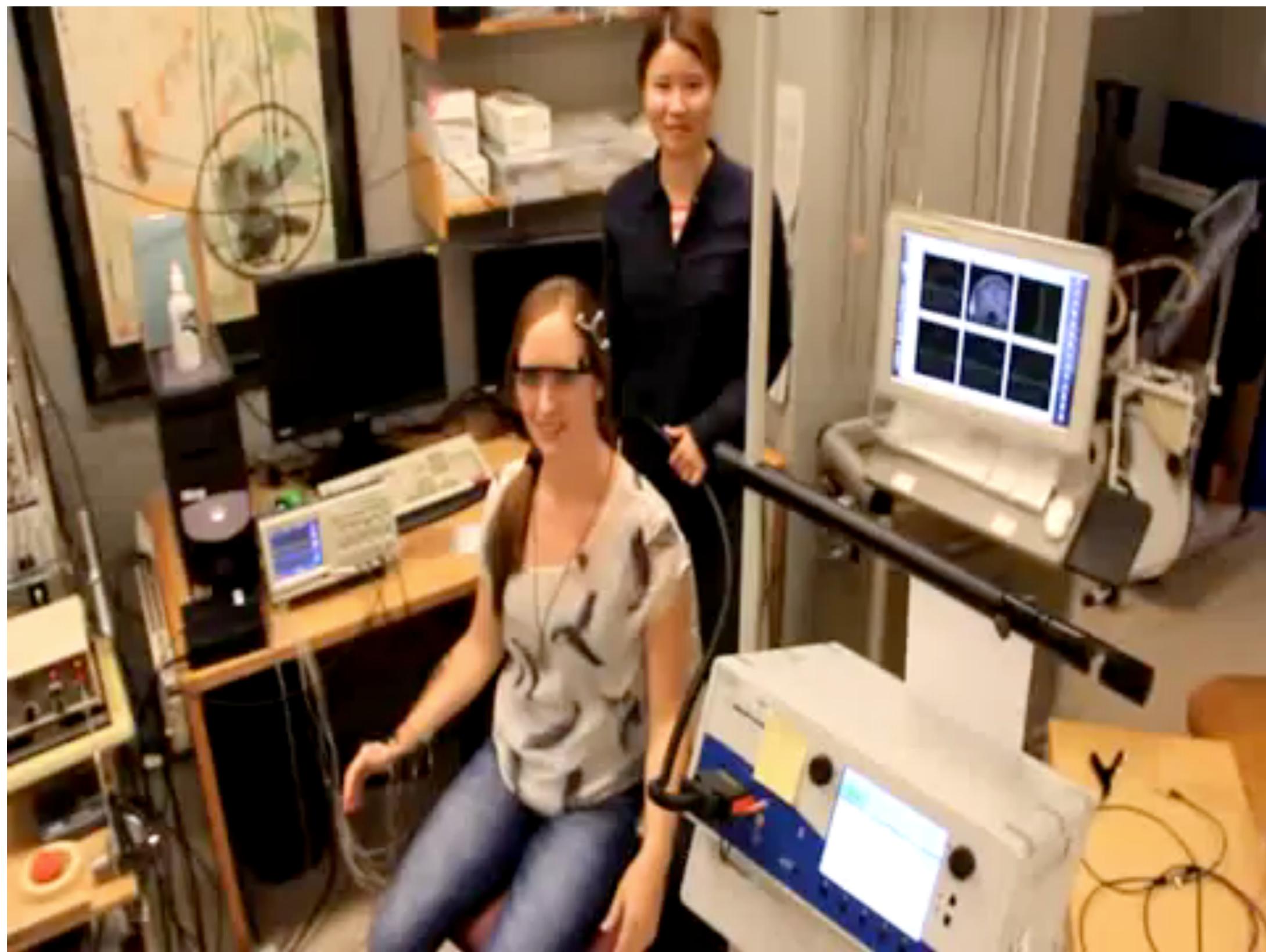
cf.



Non-invasive Brain stimulation

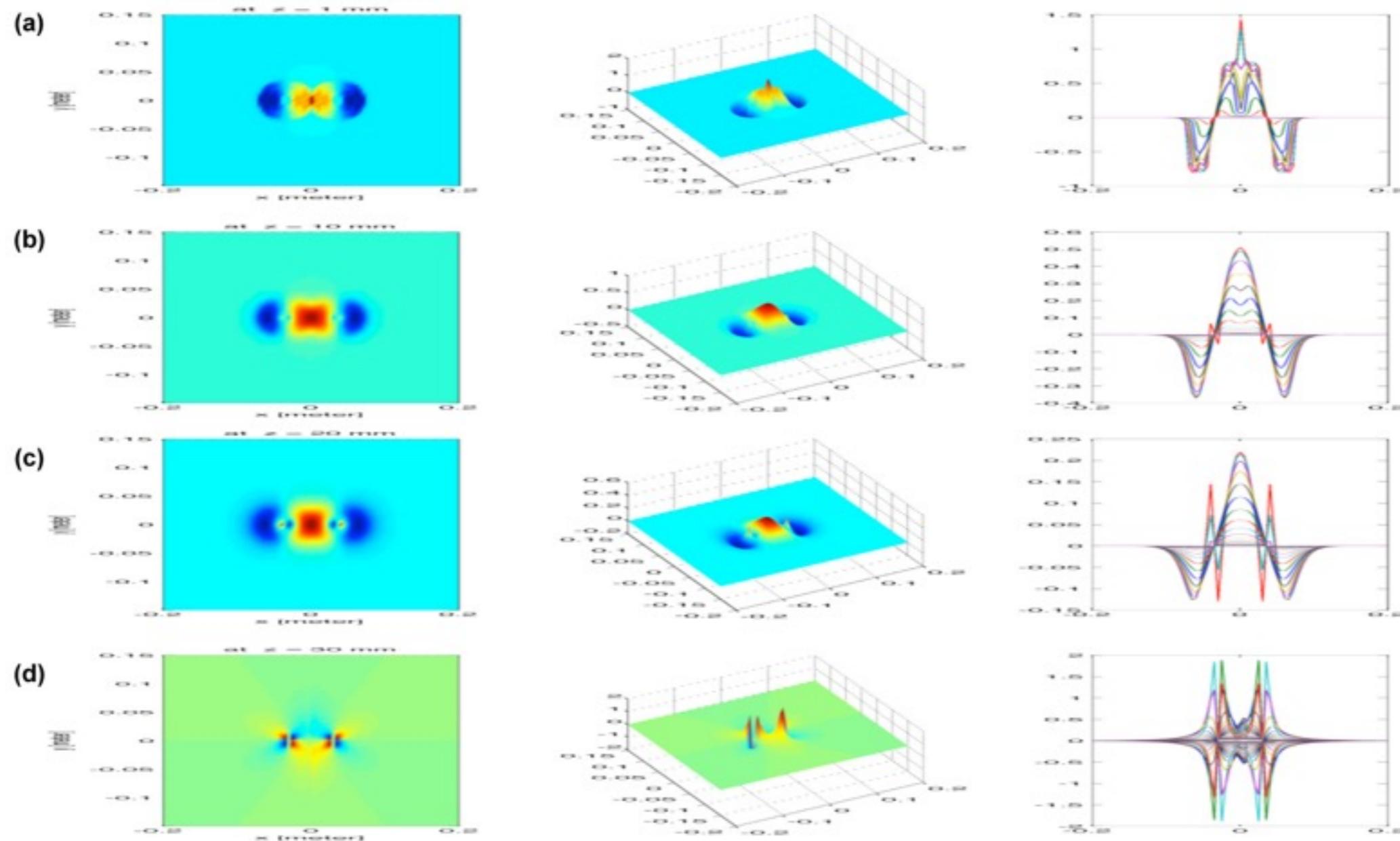
Transcranial Magnetic Stimulation(TMS)





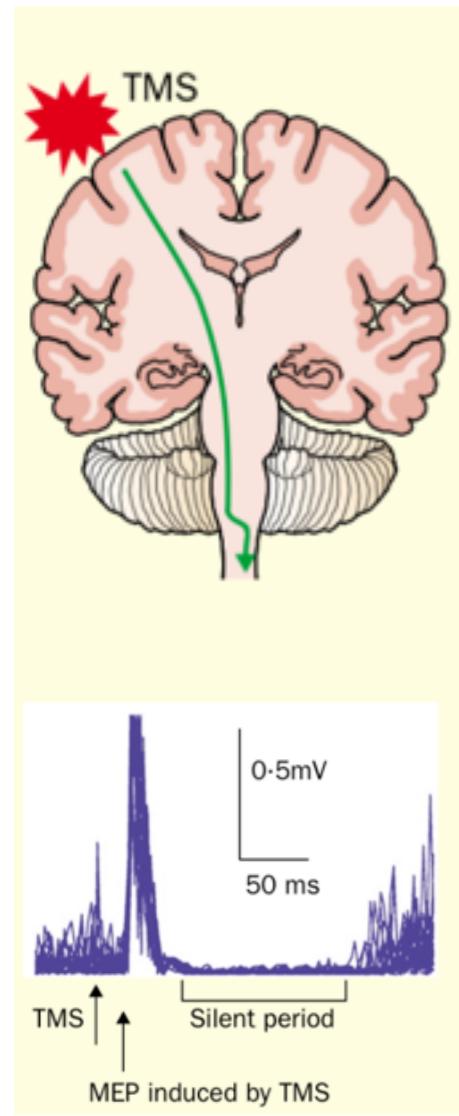
Transcranial Magnetic Stimulation(TMS)

Magnetic field on x-y plane

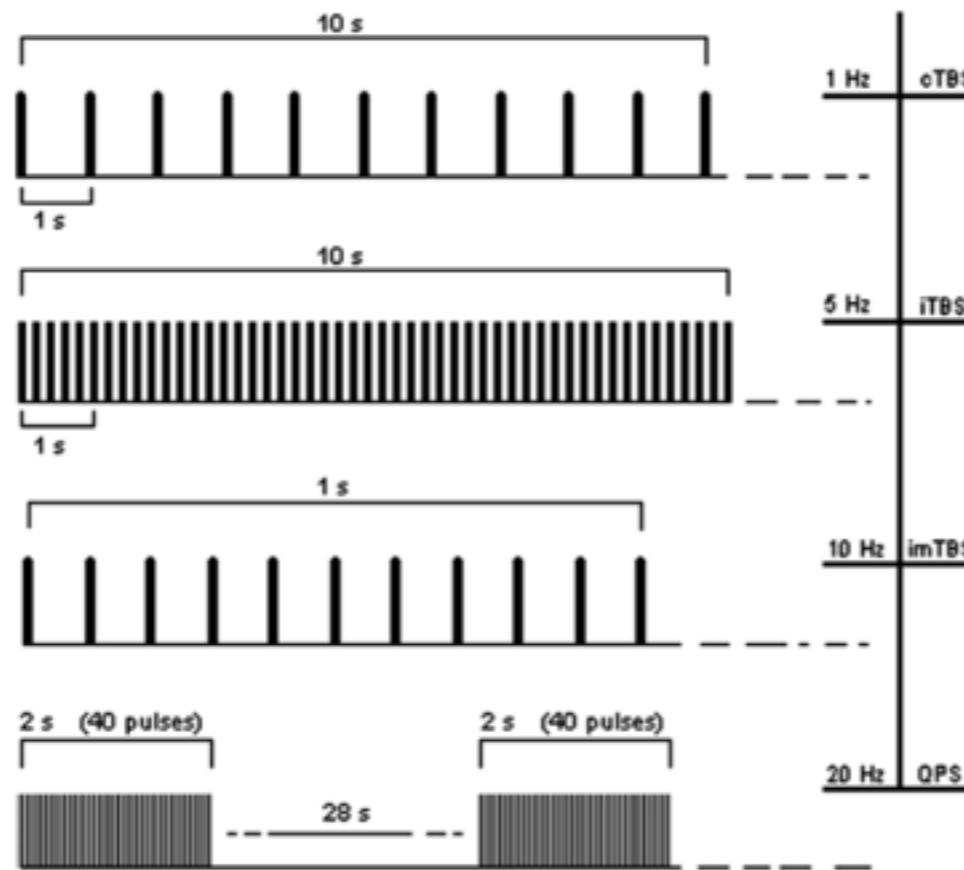


$z=1, 10, 20, 30\text{mm}$

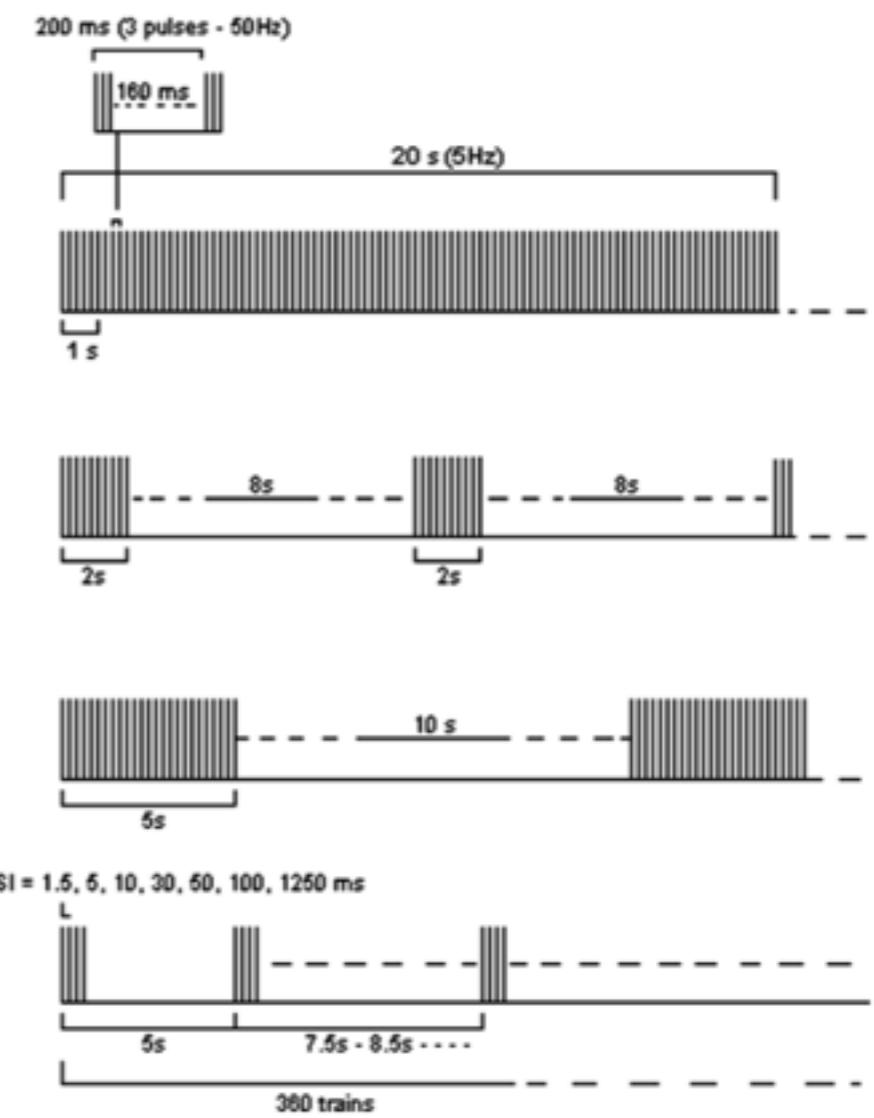
TMS - protocol



Conventional rTMS



Patterned rTMS



Original Article

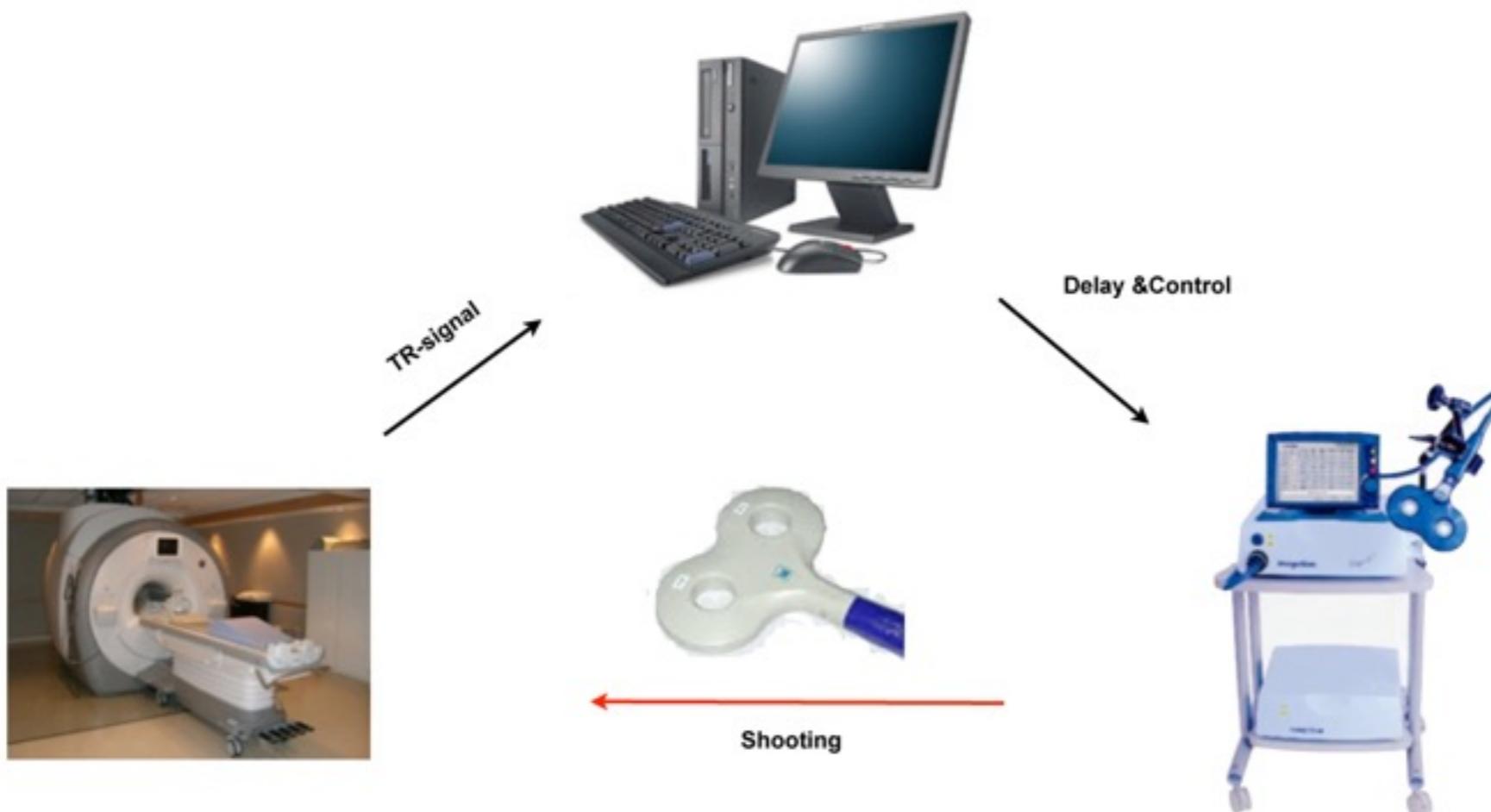
동시 뇌경두개자기자극-기능자기공명영상 시행을 위한 홀더 제작과 시뮬레이션 및 영상 데이터 평가

김재창^{1, 2} · 경성현^{1, 3} · 이종두^{1, 2} · 박해정^{1, 2}

¹연세대학교 의과대학 BK21 연세의과학사업단

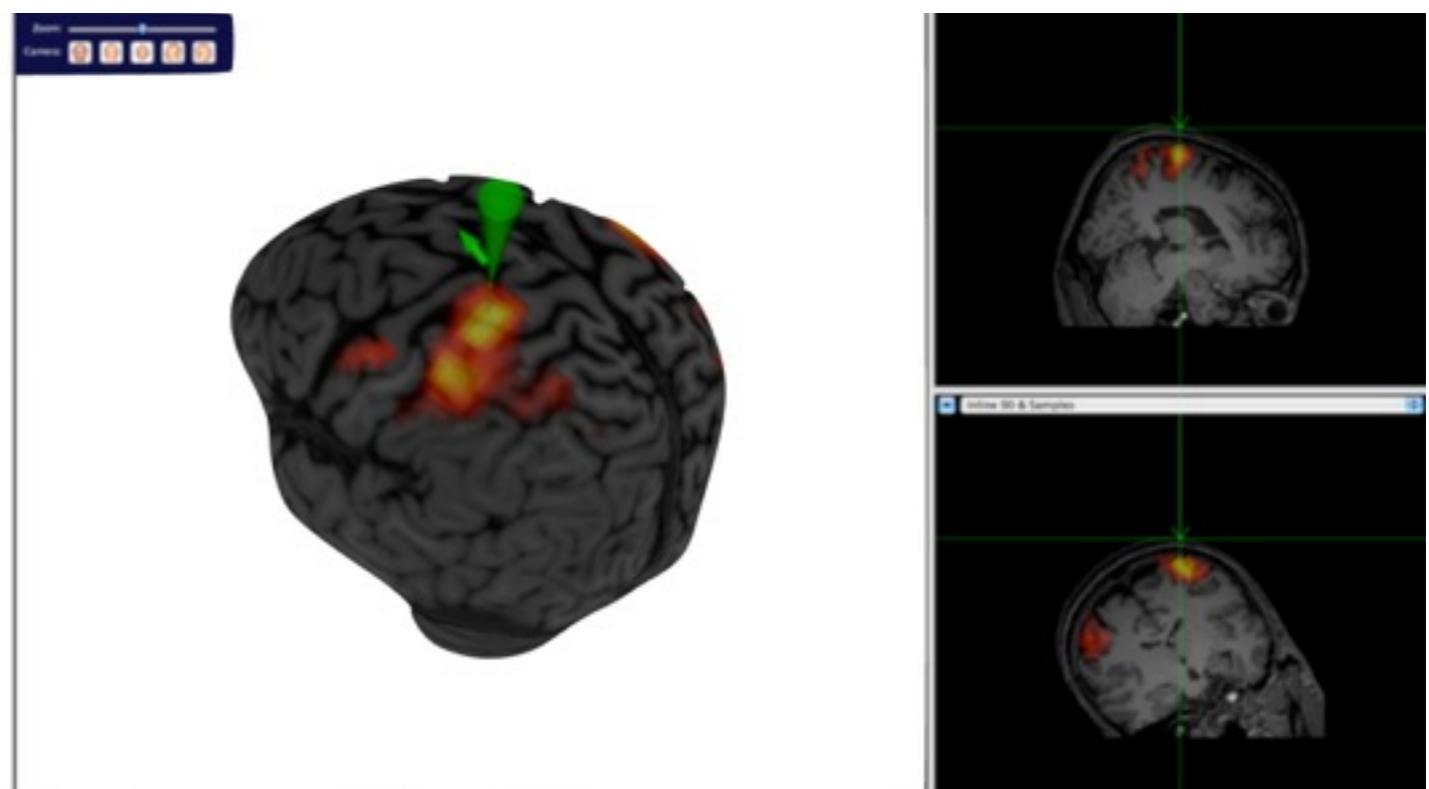
²연세대학교 의과대학 핵의학교실, 의생명과학부

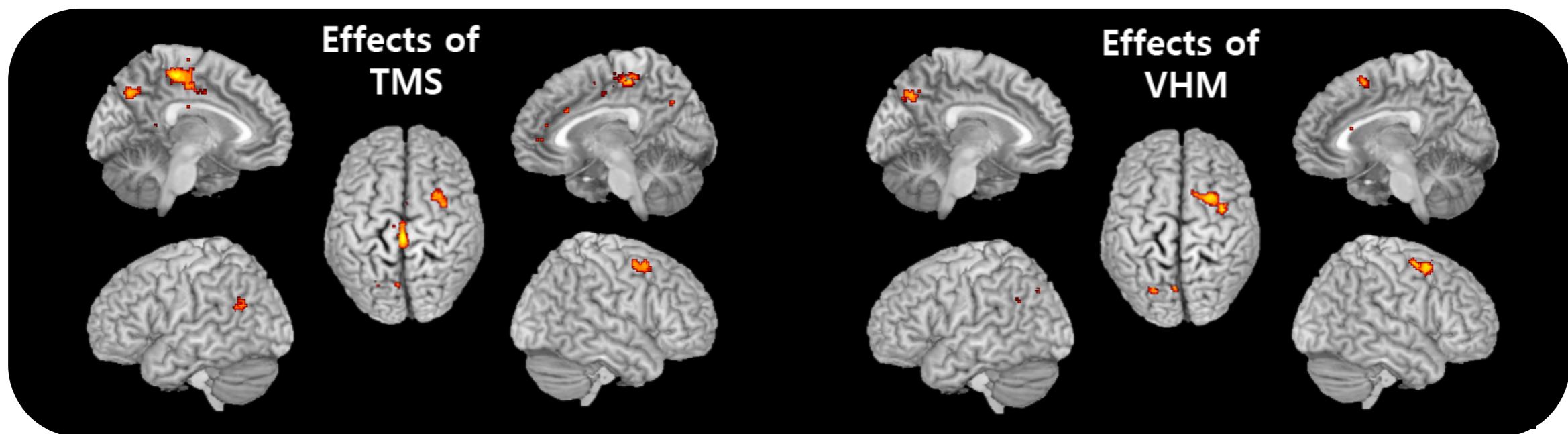
³국가수리과학연구소, 수리모델연구부





Transcranial Magnetic Stimulation(TMS)

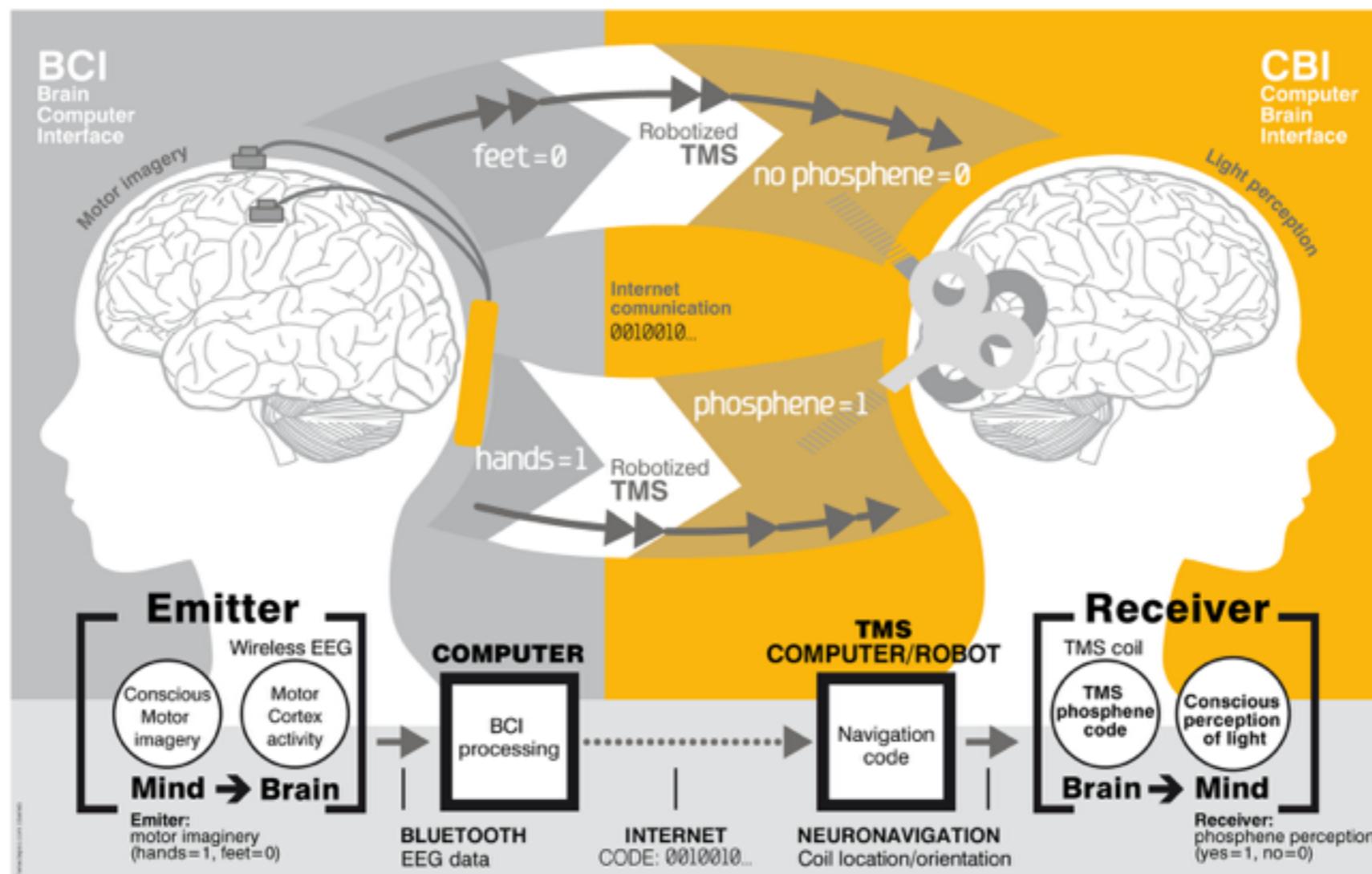




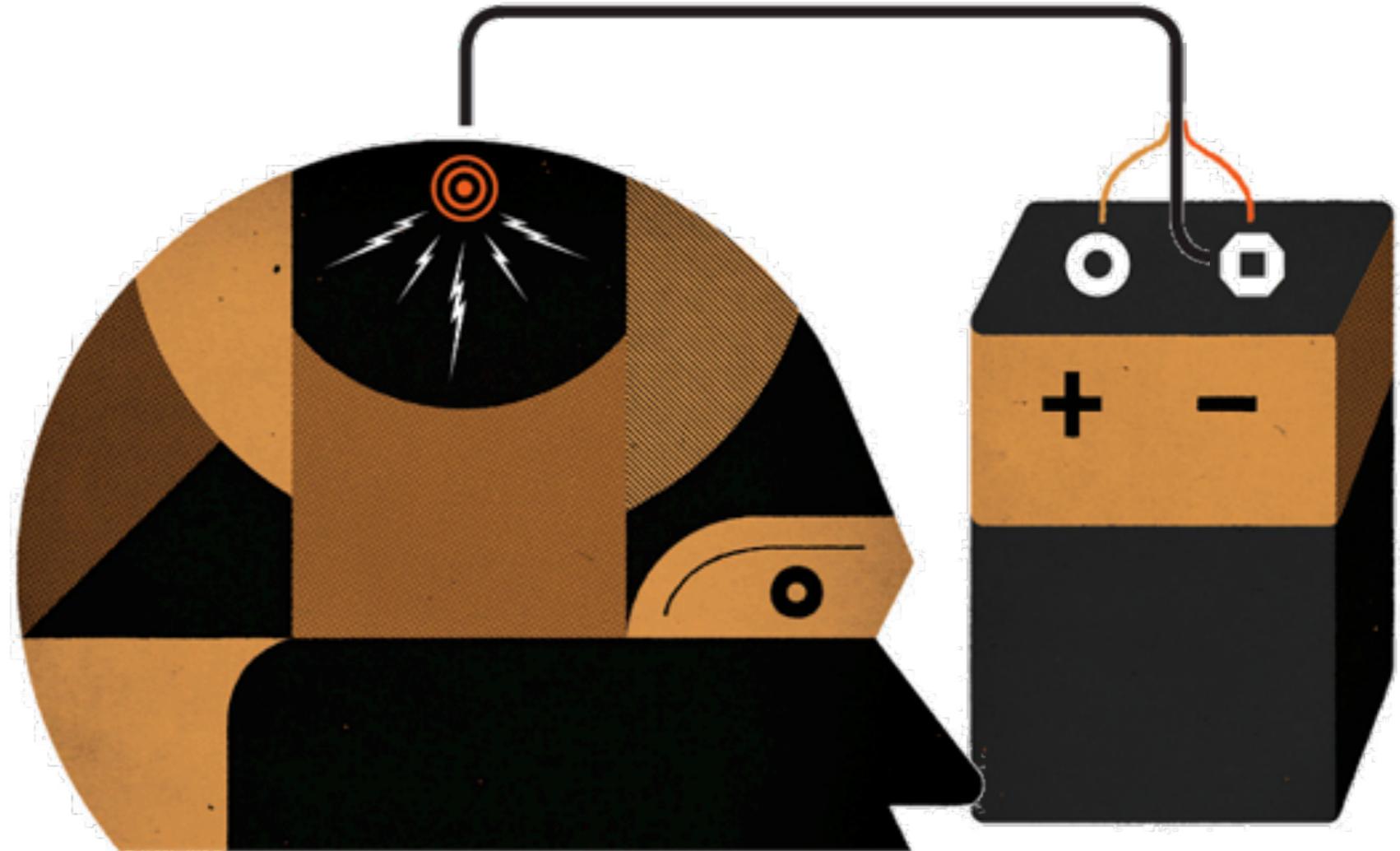
Conscious Brain-to-Brain Communication in Humans Using Non-Invasive Technologies

Carles Grau^{1,2}, Romuald Ginhoux³, Alejandro Riera^{1,4}, Thanh Lam Nguyen³, Hubert Chauvat³, Michel Berg³, Julià L. Amengual⁵, Alvaro Pascual-Leone⁶, Giulio Ruffini^{1,4*}

1 Starlab Barcelona, Barcelona, Spain, **2** Neurodynamics Laboratory, Department of Psychiatry and Clinical Psychobiology, Psychology and Medicine Faculties, University of Barcelona, Barcelona, Spain, **3** Axilum Robotics, Strasbourg, France, **4** Neuroelectrics Barcelona, Barcelona, Spain, **5** Cognition and Brain Plasticity Unit, Department of Basic Psychology, University of Barcelona, Barcelona, Spain, **6** Berenson Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, United States of America



Transcranial direct current stimulation (tDCS) **nature**
Treatment for cravings for alcohol, cigarettes and sweets

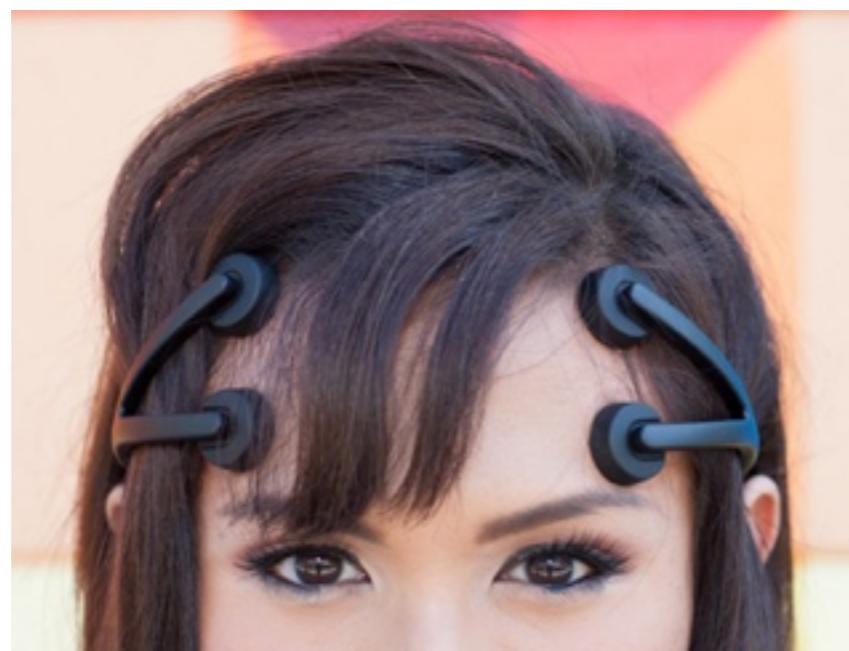
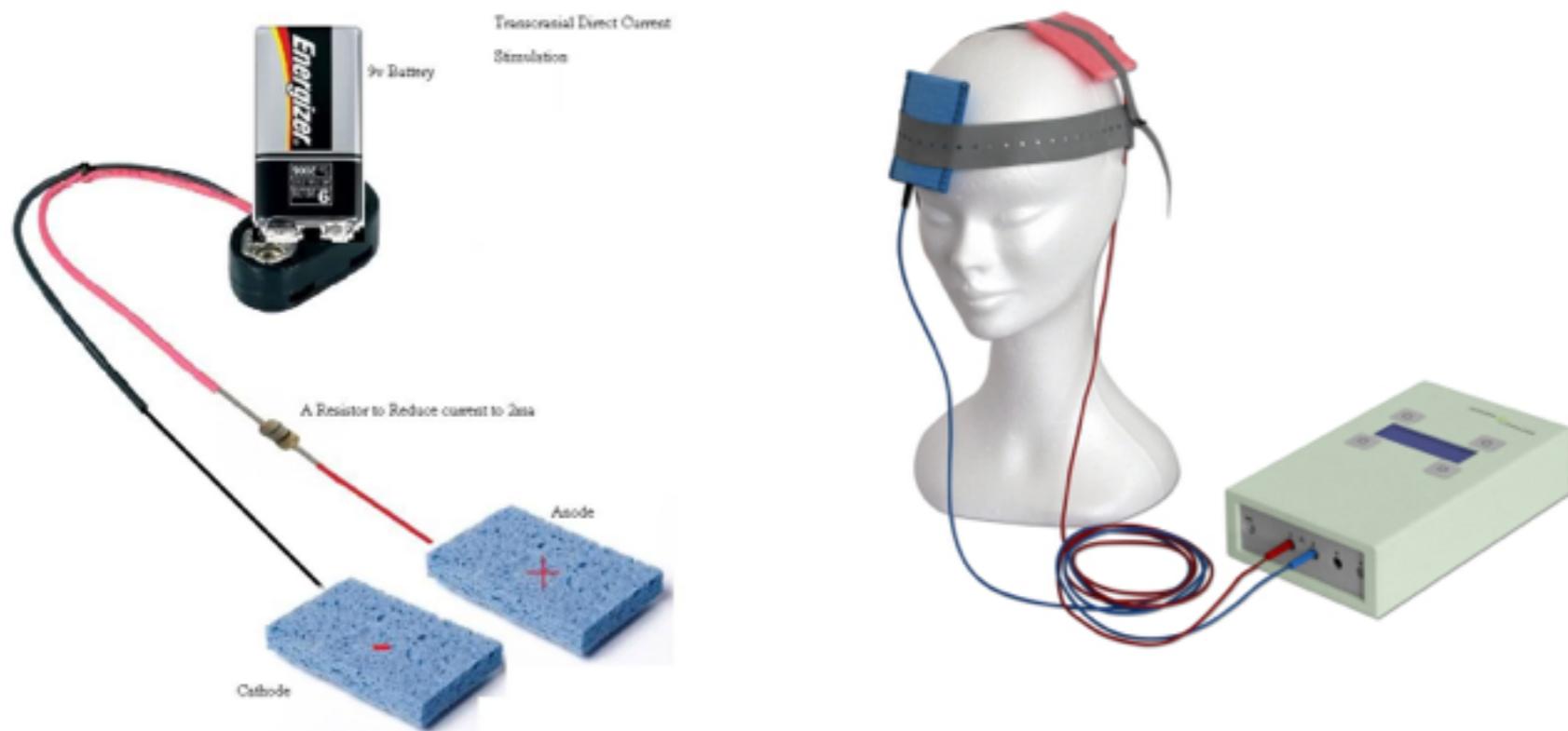


BRAIN BUZZ

BY DOUGLAS FOX

2011 Nature. Brain buzz

Transcranial direct current stimulation (tDCS)



neuroconn, foc.us, sorterix

TMS - FDA approval



Neurostar - depression

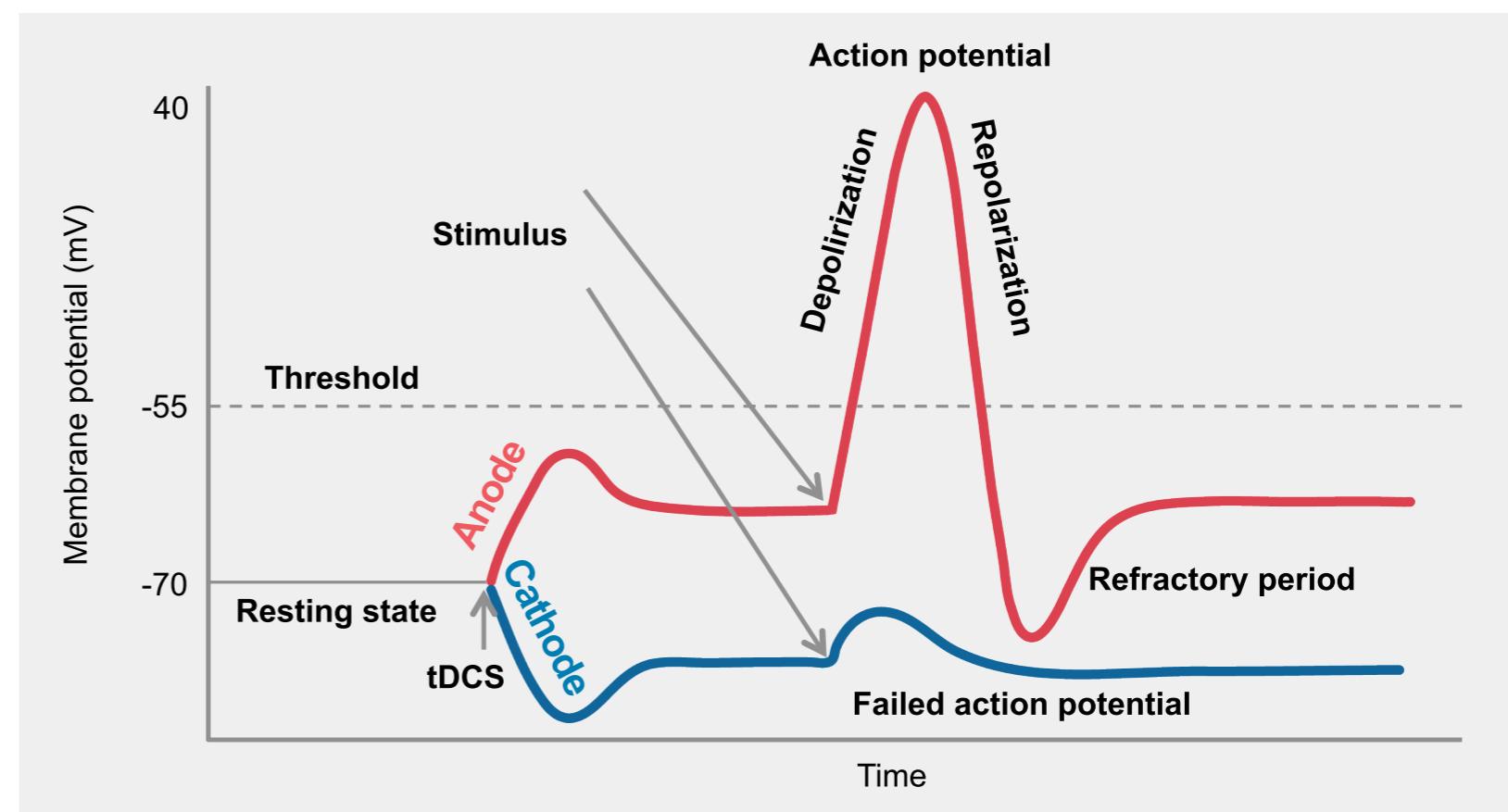


eNeura - migraine

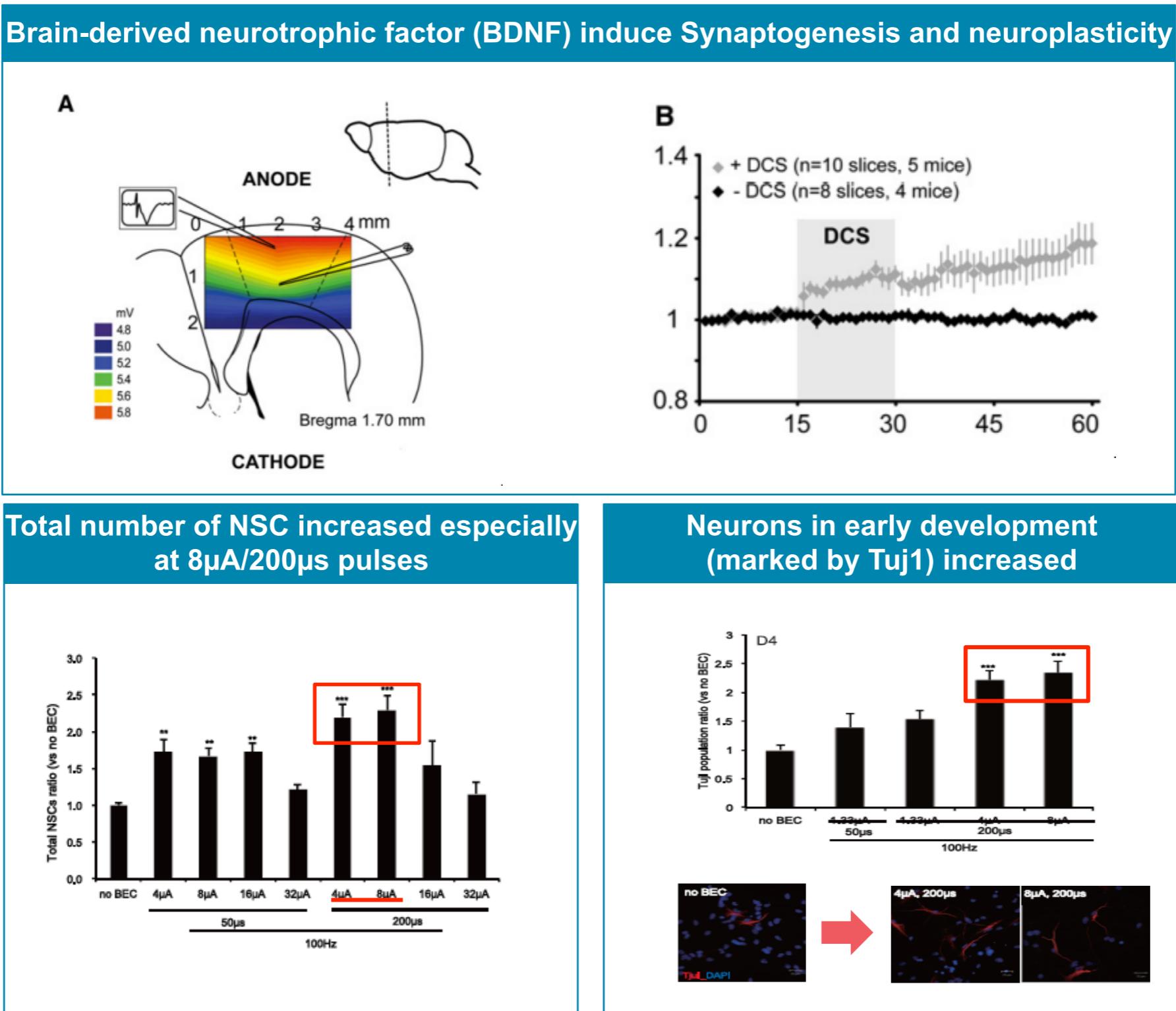
TMS - Safety

| Side effect | Single-pulse TMS | Paired-pulse TMS | Low frequency rTMS | High frequency rTMS | Theta burst |
|---|------------------|---|--------------------------------------|--|---|
| Seizure induction | Rare | Not reported | Rare (usually protective effect) | Possible (1.4% crude risk estimate in epileptic patients; less than 1% in normals) | Possible (one seizure in a normal subject during cTBS) (see para 3.3.3) |
| Transient acute hypomania induction | No | No | Rare | Possible following left prefrontal stimulation | Not reported |
| Syncope | | Possible as epiphomenon (i.e., not related to direct brain effect) | | | Possible |
| Transient headache, local pain, neck pain, toothache, paresthesia | Possible | Likely possible, but not reported/addressed | Frequent (see para. 3.3) | Frequent (see para. 3.3) | Possible |
| Transient hearing changes | Possible | Likely possible, but not reported | Possible | Possible | Not reported |
| Transient cognitive/neuropsychological changes | Not reported | No reported | Overall negligible (see Section 4.6) | Overall negligible (see Section 4.6) | Transient impairment of working memory |
| Burns from scalp electrodes | No | No | Not reported | Occasionally reported | Not reported, but likely possible |
| Induced currents in electrical circuits | | Theoretically possible, but described malfunction only if TMS is delivered in close proximity with the electric device (pace-makers, brain stimulators, pumps, intracardiac lines, cochlear implants) | | | |
| Structural brain changes | Not reported | Nor reported | Inconsistent | Inconsistent | Not reported |
| Histotoxicity | No | No | Inconsistent | Inconsistent | Not reported |
| Other biological transient effects | Not reported | Not reported | Not reported | Transient hormone (TSH), and blood lactate levels changes | Not reported |

Transcranial direct current stimulation (tDCS)



tDCS & Neurophysiology



tDCS & Neurophysiology

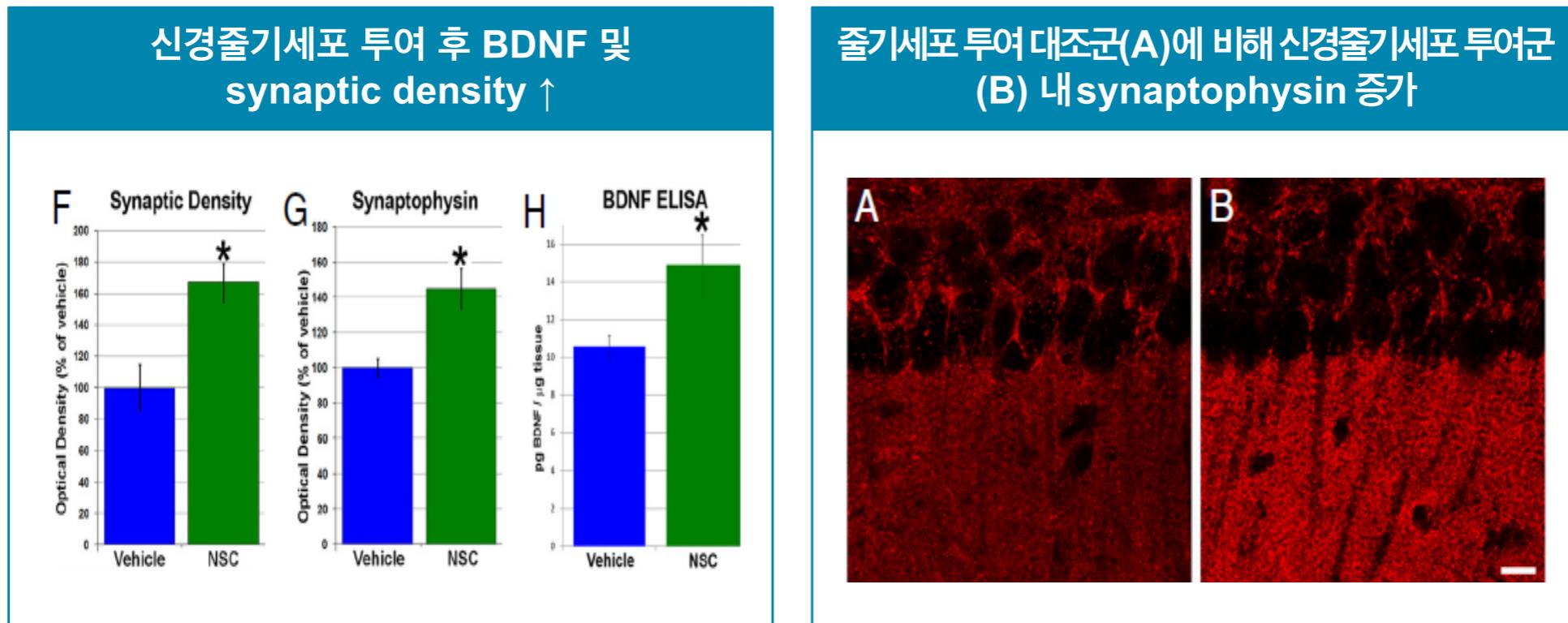
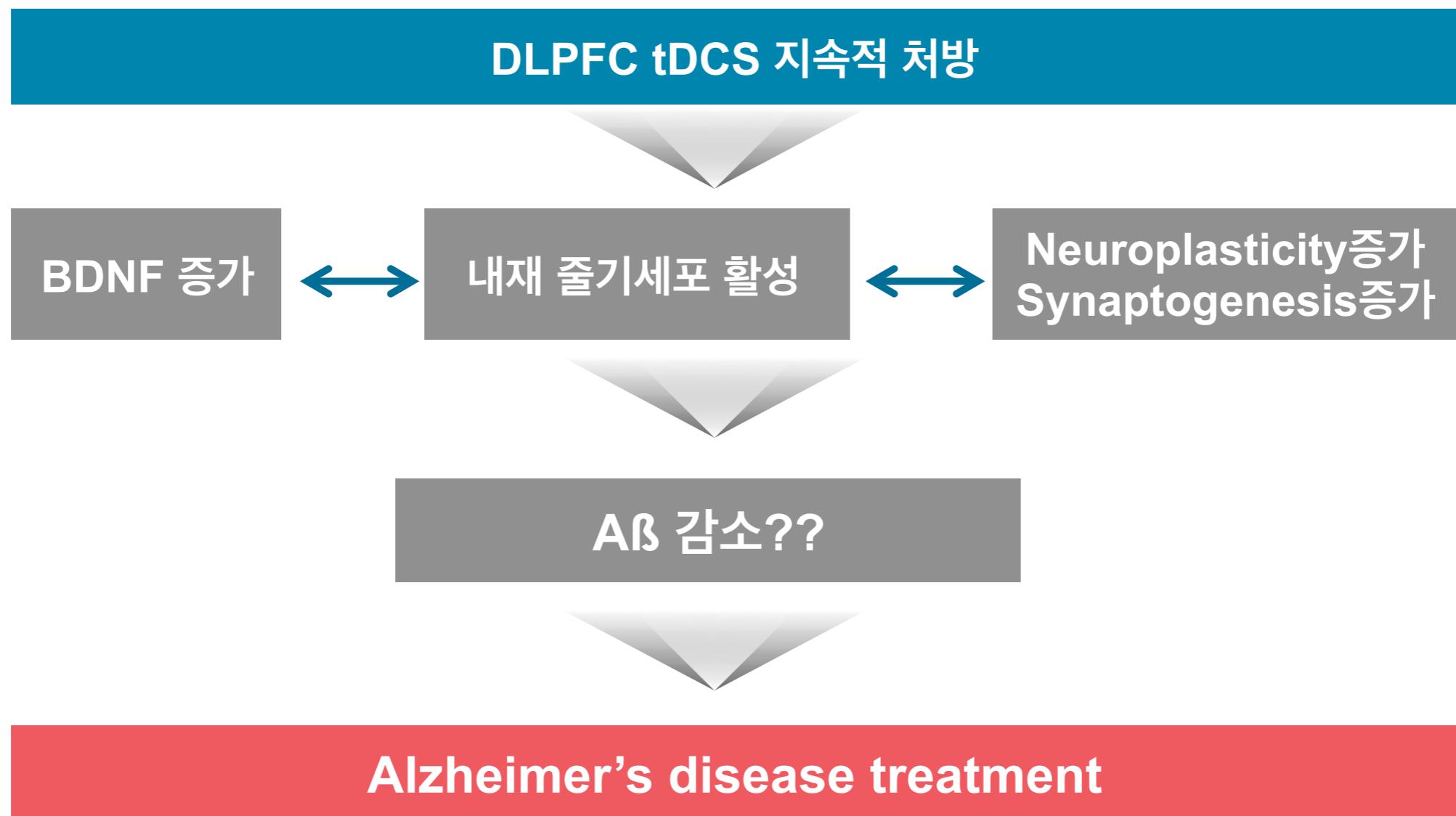


Table 1 | Clinical studies of tDCS in dementia.

| Study | Design | n | Age (years) | Disease diagnosis | MMSE | Medication | Parameters | Brain target | Effect |
|----------------------------|-----------------------------|----|-----------------|--------------------------|----------------|-----------------|--------------------------------------|----------------|---|
| ALZHEIMER'S DISEASE | | | | | | | | | |
| Boggio et al. (2009) | Cross over, sham controlled | 10 | 79 ± 9 | NINCDS, ADRADA | 17 ± 5 | AChEIs + others | Anodal/sham, 2 mA, 30 min | Left DLPFC | Improved visual recognition memory after atDCS |
| Boggio et al. (2011) | Sham controlled | 15 | 78 ± 7, 81 ± 10 | Adas-Cog, VRT, VAT, ADAS | 21 ± 3, 19 ± 3 | No data | Anodal, sham 2 mA, 30 min | TC bilateral | Improved visual recognition memory after atDCS |
| Ferrucci et al. (2008a) | Cross over, sham controlled | 10 | 75 ± 7 | DSM-IV, NINCDS-ADRADA | 23 ± 2 | AchEI | Anodal/cathodal/sham, 1.5 mA, 15 min | Left/right TPC | Accuracy of the word-recognition memory increased after atDCS |

AD mechanism

tDCS의 지속적인 처방으로 퇴화되고 있는 뇌세포간의 연결성을 증가시켜
치매의 원인이라고 알려져있는 물질(Amyloid beta)의 감소를 유도



Depression Mechanism

JAMA PSYCHIATRY

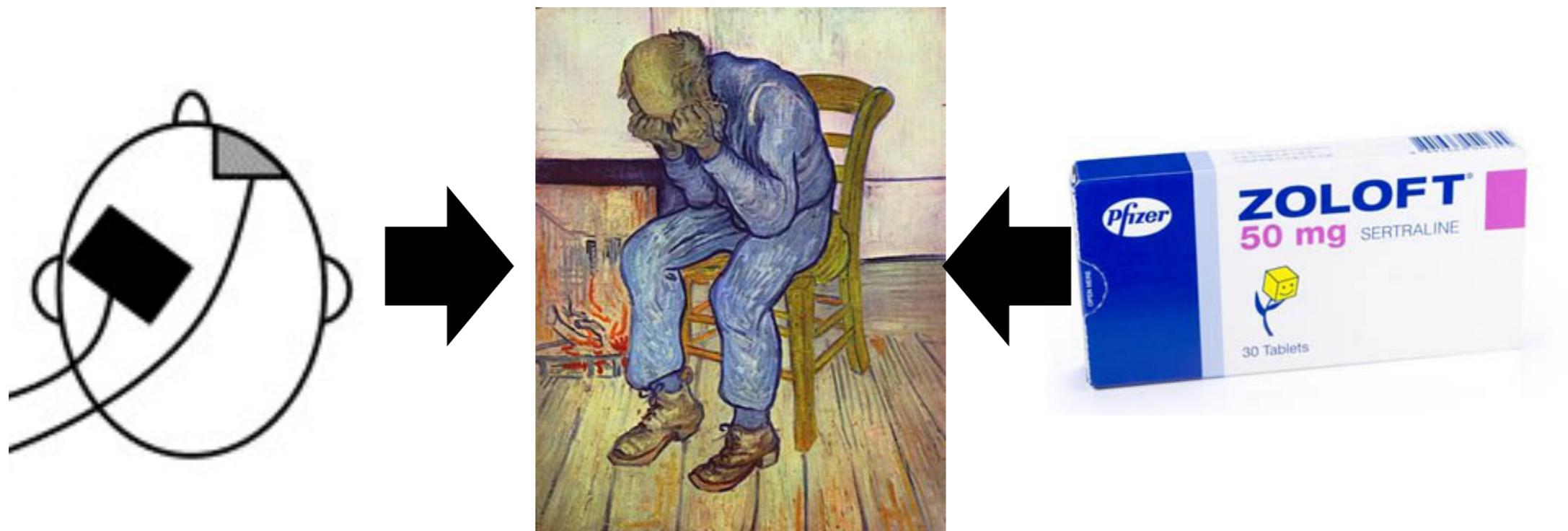
PUBLISHED ONLINE FEBRUARY 6, 2013

ORIGINAL ARTICLE

HM,.ONLINE FIRST

The Sertraline vs Electrical Current Therapy for Treating Depression Clinical Study

Results From a Factorial, Randomized, Controlled Trial

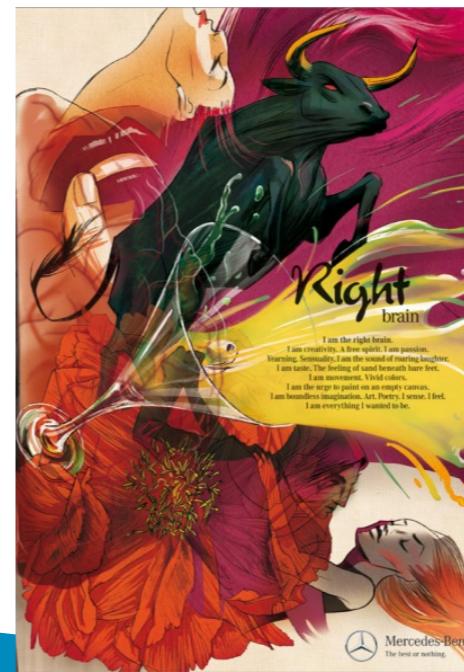


Depression Mechanism

Depression Mechanism

Depression is associated with an inter-hemispheric imbalance; a hyperactive right-hemisphere and a relatively hypoactive left-hemisphere.

processing pleasurable experiences, decision making



negative emotion, anxiety, stress, pain, vigilance, arousal

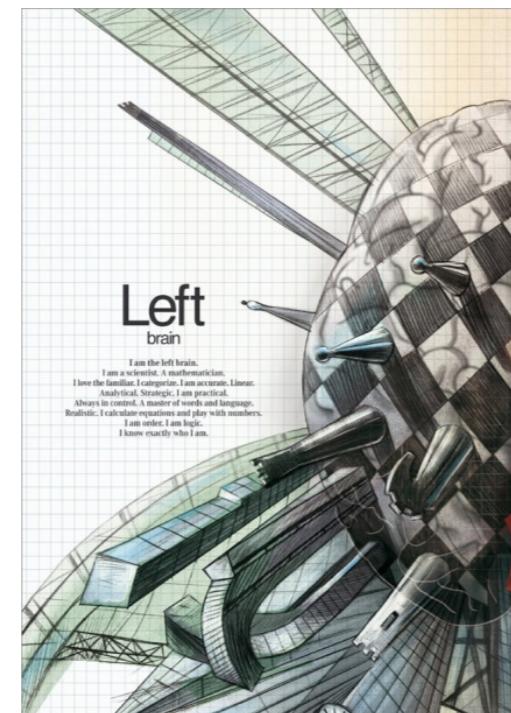
Depression Mechanism

Depression is associated with an inter-hemispheric imbalance; a hyperactive right-hemisphere and a relatively hypoactive left-hemisphere.

Anode
stimulation



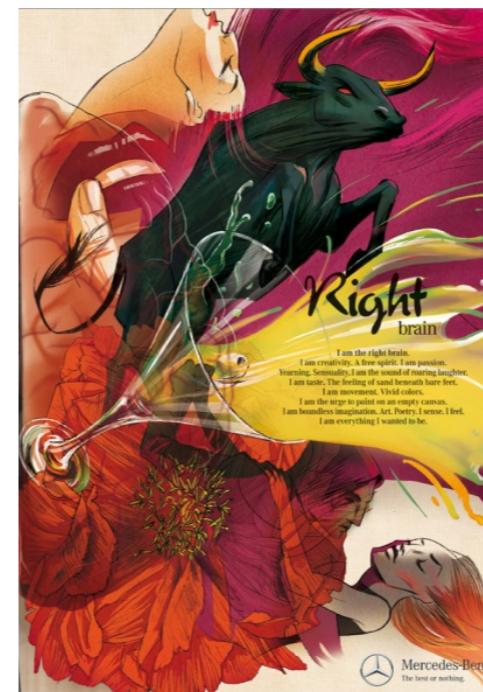
processing pleasurable experiences, decision making



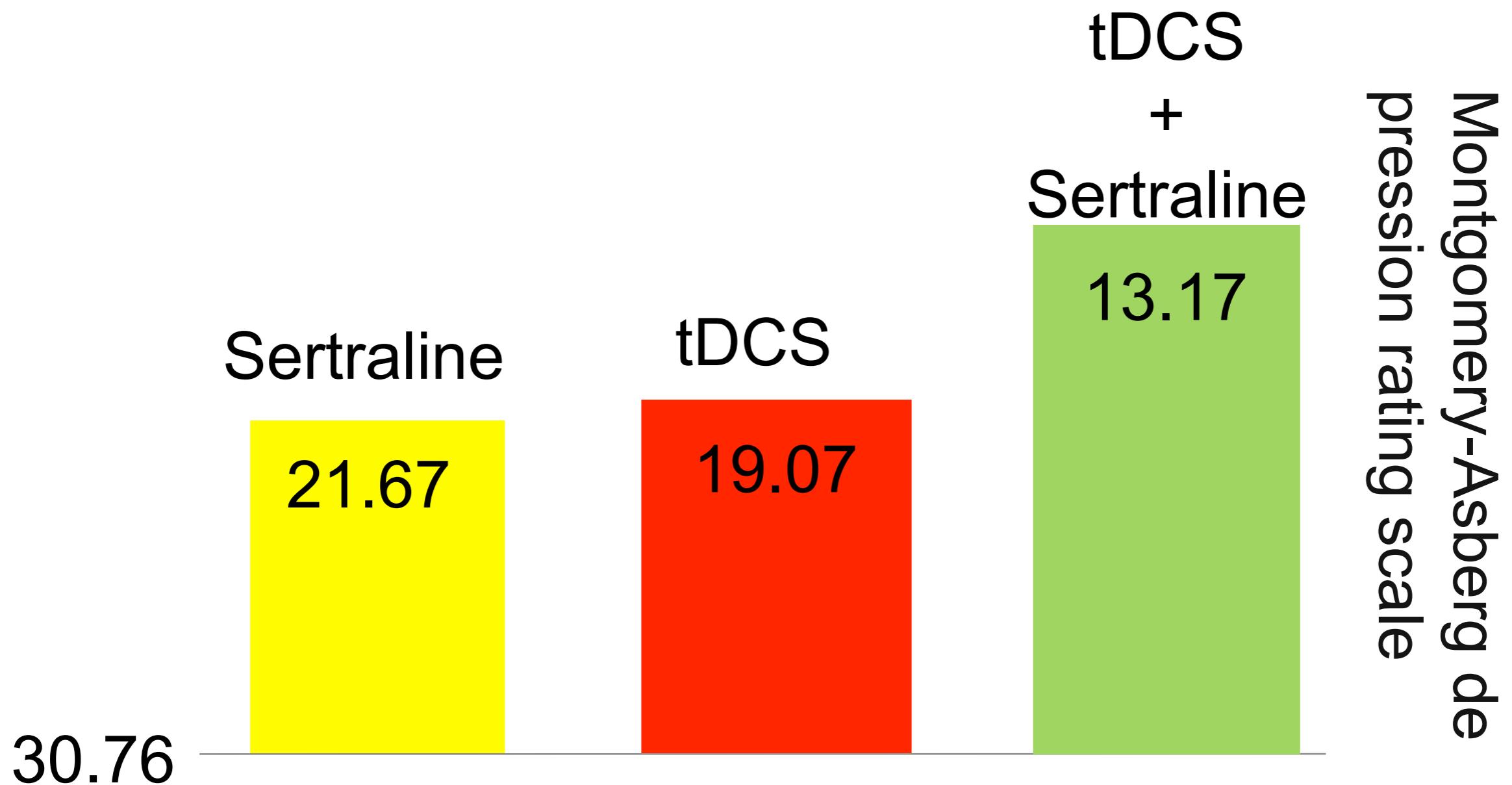
Cathode
suppression



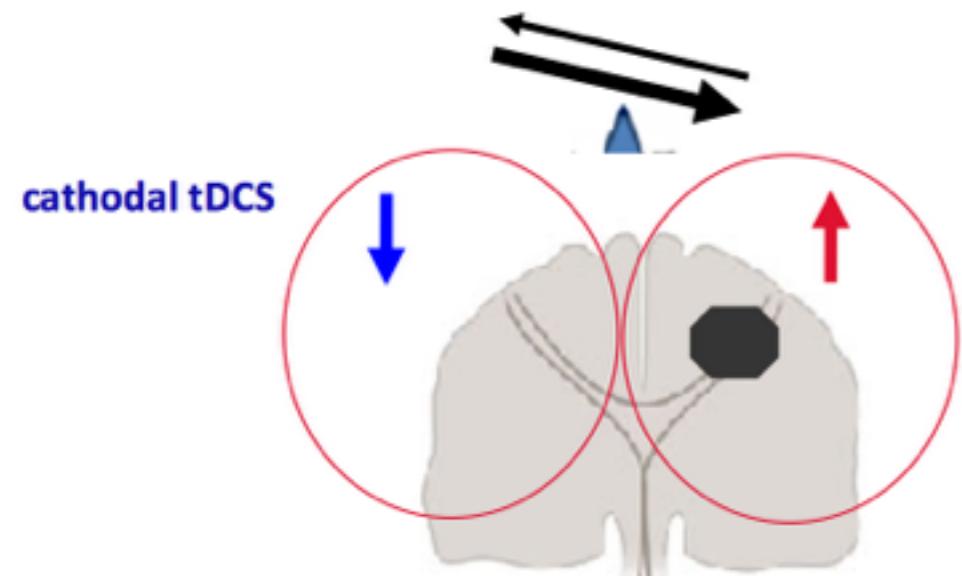
negative emotion, anxiety, stress, pain, vigilance, arousal



Synergistic effect of sertraline and tDCS



Stroke

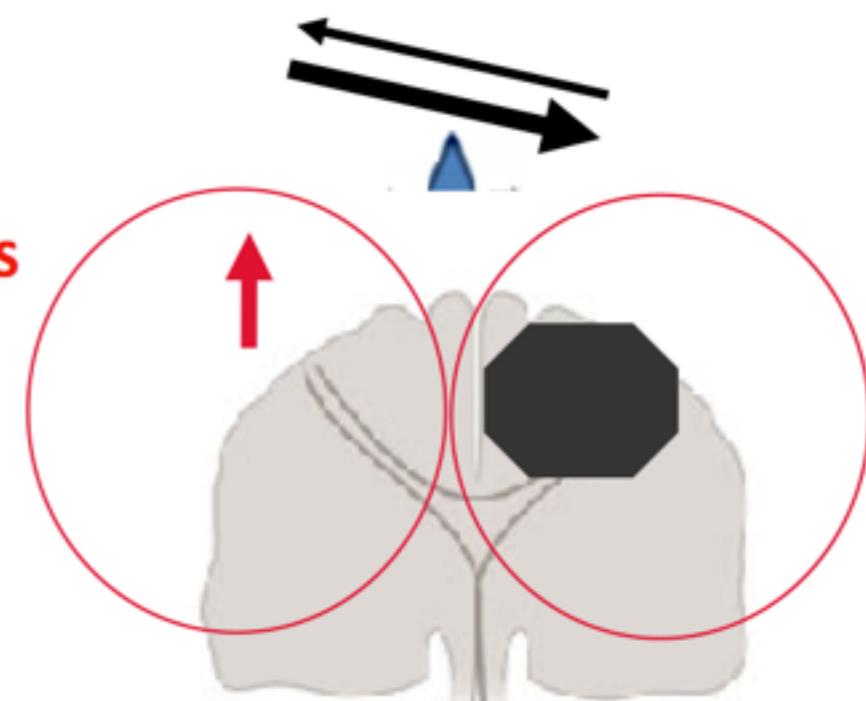


adapted from Flöel et al, Ann Neurol 2004,
Schlaug et al, Arch Neurol 2008

cathodal tDCS

anodal tDCS
Up-regulation of NMDA-receptor
dependent signaling, BDNF release,
cortical oxidative metabolism

anodal tDCS
Up-regulation of NMDA-receptor
dependent signaling, BDNF release,
cortical oxidative metabolism



tDCS Disease Treatment Indications

tDCS technology



Brain
Disease
Treatment

Depression

Dementia

Parkinsonism

ADHD

frontiers in
HUMAN NEUROSCIENCE

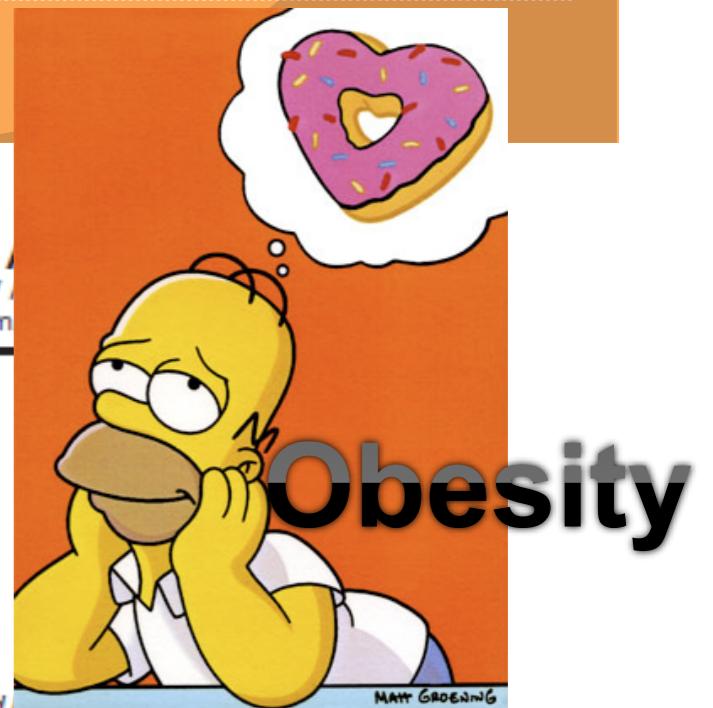
Translating tDCS into the field of obesity:
mechanism-driven approaches

Miguel Alonso-Alonso^{1,2*}

¹ Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

² Center for the Study of Nutrition Medicine, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

MINI REVIEW
published: 27 A
doi: 10.3389/fnhum



Safety

| 증상 | Active | Sham |
|-------|------------|------------|
| 가려움 | 46 (39.3%) | 27 (32.9%) |
| 따가움 | 26 (22.2%) | 15 (18.3%) |
| 두통 | 17 (14.8%) | 13 (16.2%) |
| 열감 | 10 (8.7%) | 8 (10%) |
| 불편감 | 12 (10.4%) | 11 (13.4%) |
| Total | 117편 | 82편 |

TMS/tDCS - Pros & Cons

Pros.

TMS

- Non-invasive
- Good focality (~ 1cm x 1cm)

tDCS

- Non-invasive
- Small device(= Portable)
- Less side effects

Cons.

- Some side effects induced by high B-field
- Relatively huge device

- Bad focality (5cm x 5cm)
- Hard to modulate sub-cortical area

Applications for decision making

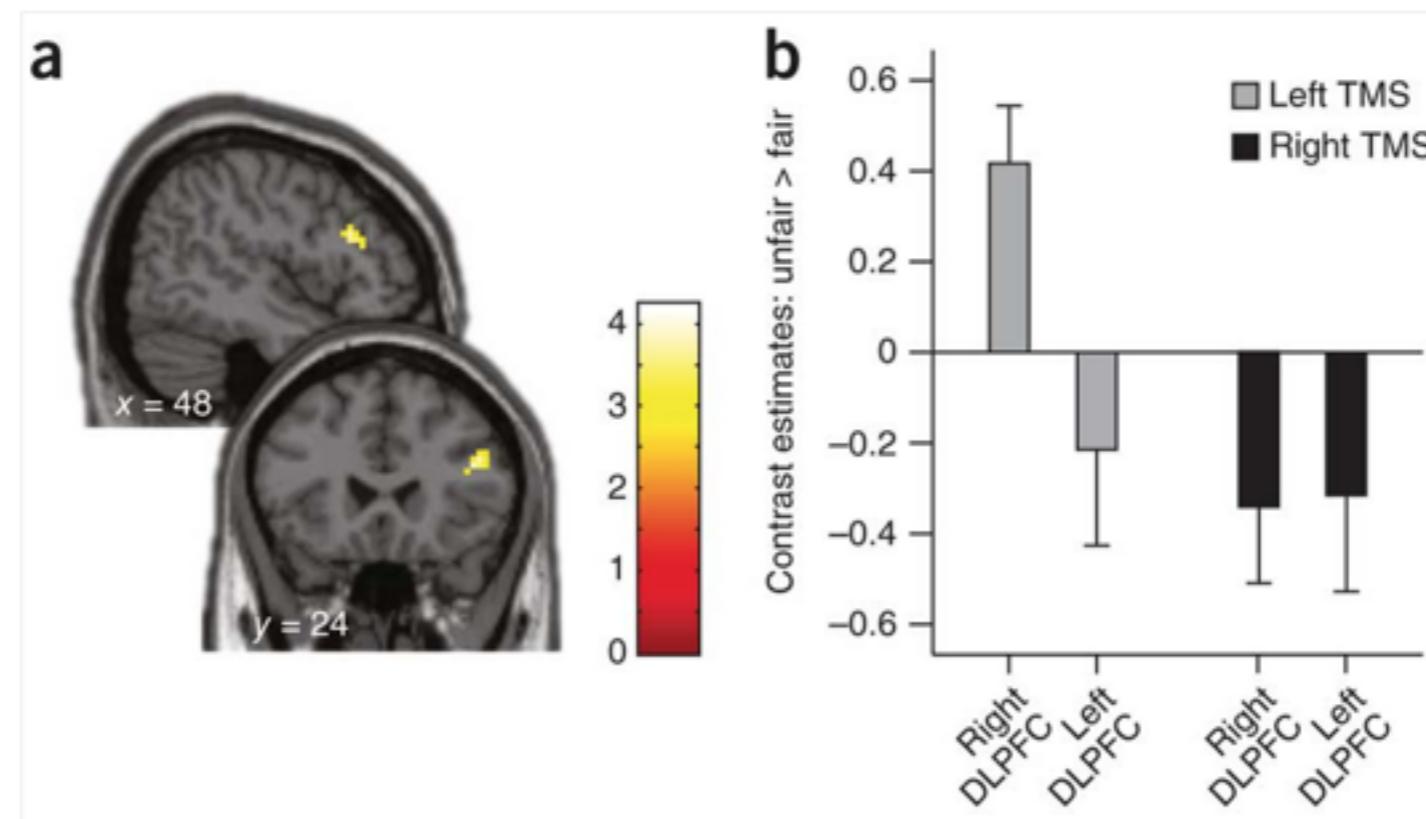
TMS

ORIGINAL RESEARCH ARTICLE

Front. Neurosci., 13 February 2014 | doi: 10.3389/fnins.2014.00018

TMS affects moral judgment, showing the role of DLPFC and TPJ in cognitive and emotional processing

 Danique Jeurissen^{1,2,3*},  Alexander T. Sack^{2,4},  Alard Roebroeck^{2,4},  Brian E. Russ⁵ and  Alvaro Pascual-Leone¹



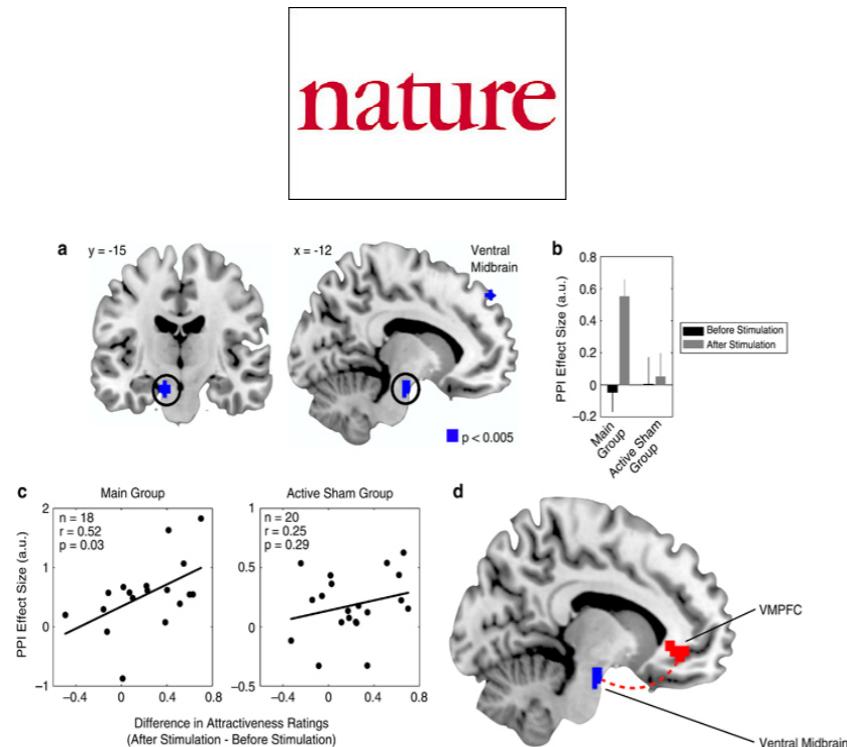
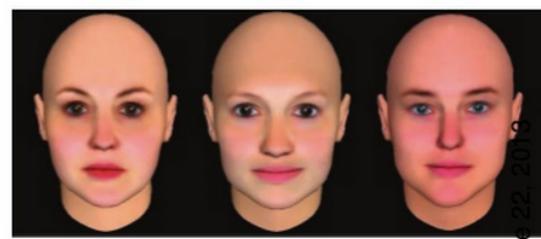
tDCS and Decision making



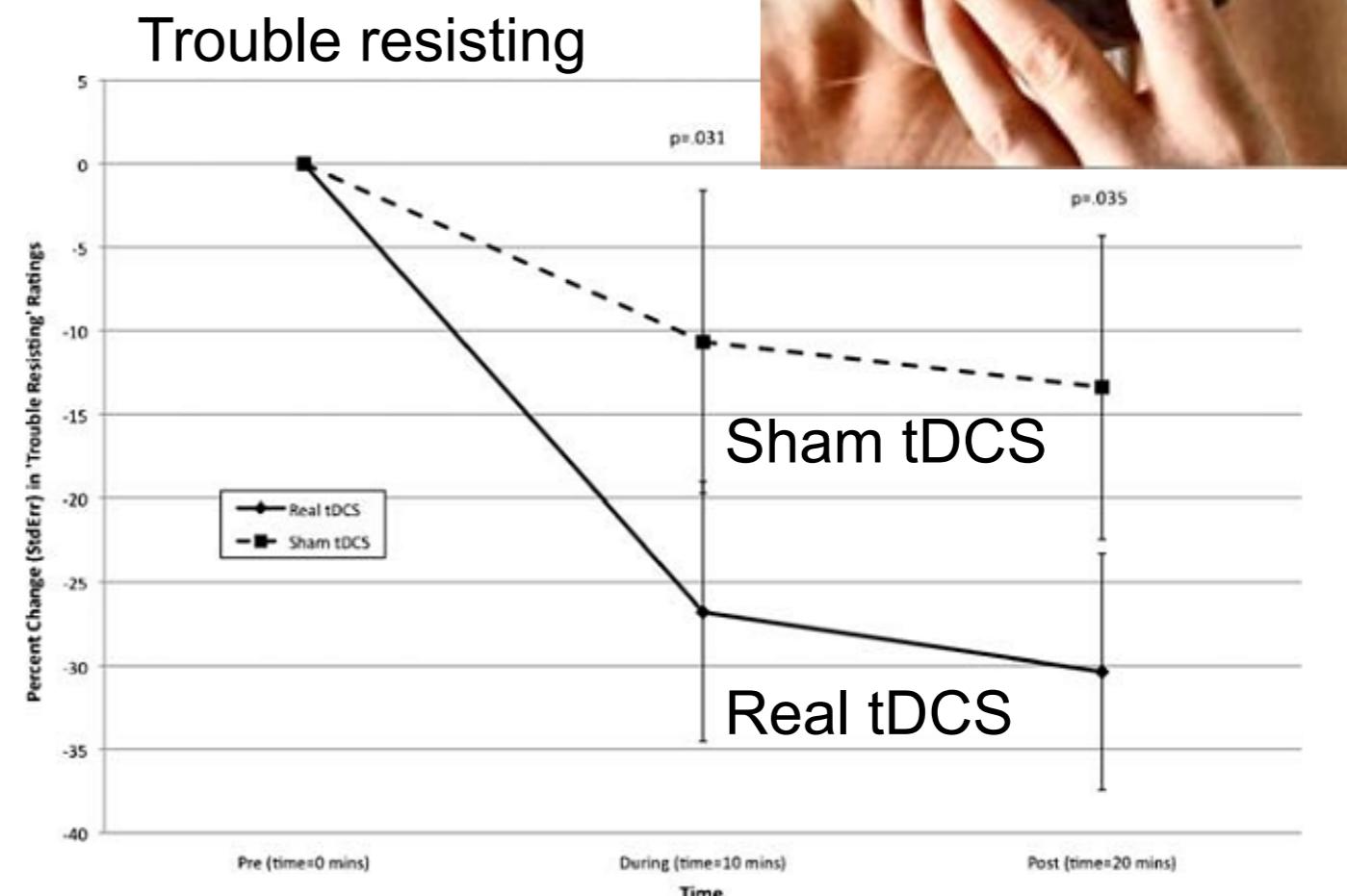
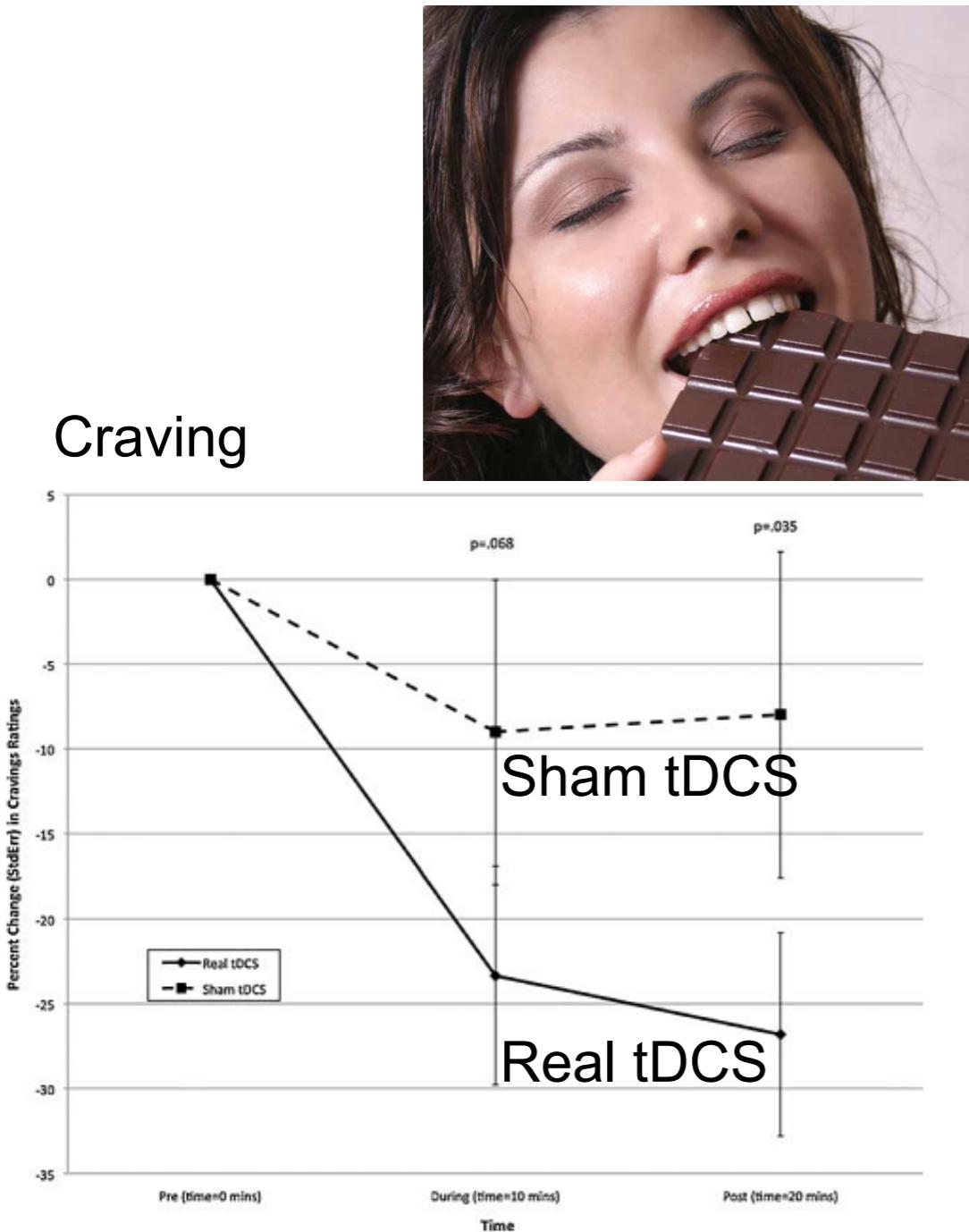
FINDINGS

Beer Goggles for Your Brain

Hot? Or not? The lightning-quick spark that triggers desire when you see an attractive face is kindled within the ventral midbrain, associated with processing reward. Now, researchers have discovered a way to stoke that fire ... with 2 millamps of electrical current.

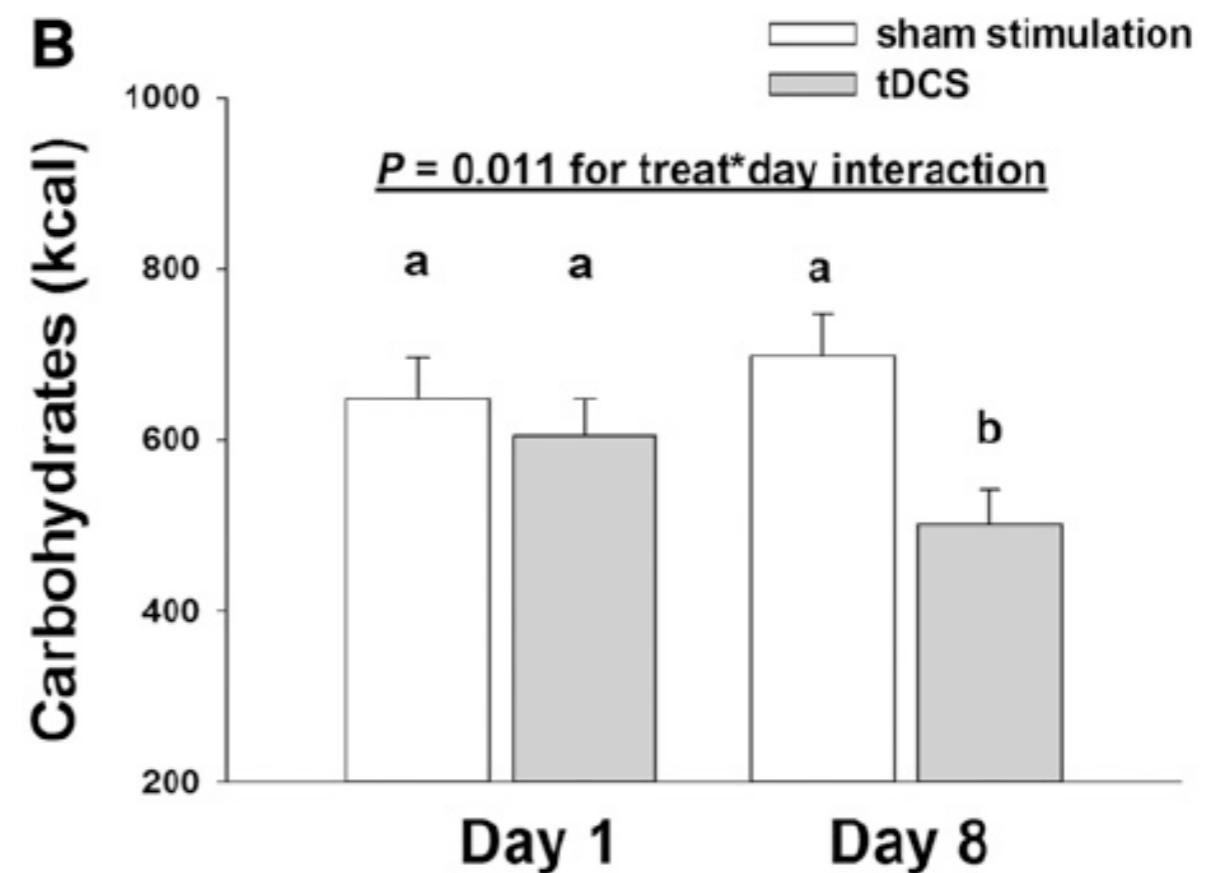
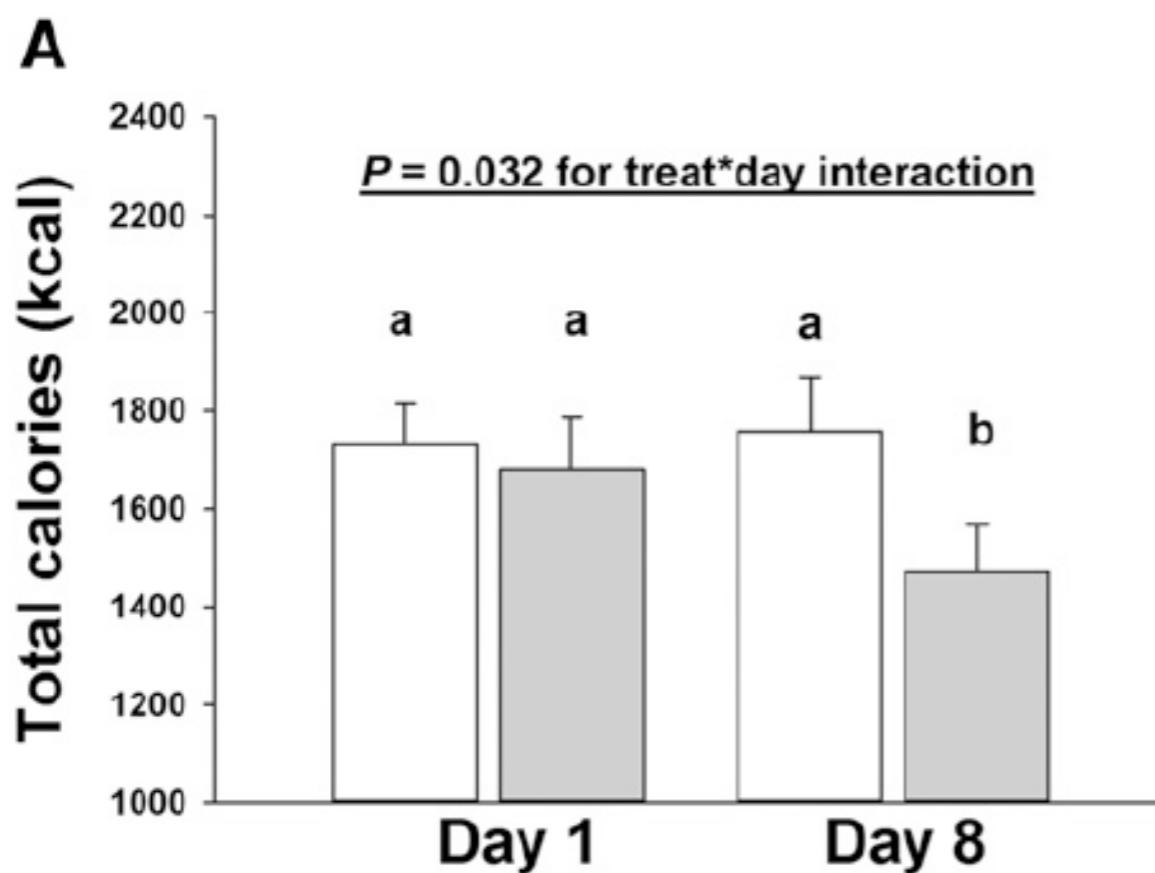


tDCS Decreases Food Craving



2011 Appetite. Prefrontal cortex transcranial direct current stimulation (tDCS) temporarily reduces food cravings and increases the self-reported ability to resist food in adults with frequent food craving

Long-term tDCS Treatment Decreases Food Intake



2014.3.21. 하나뿐인 지구
<치명적인 유혹, 지방> EBS

우리는 왜 먹고 싶어 하는가?

하나뿐인 지구

치명적인 유혹, 지방

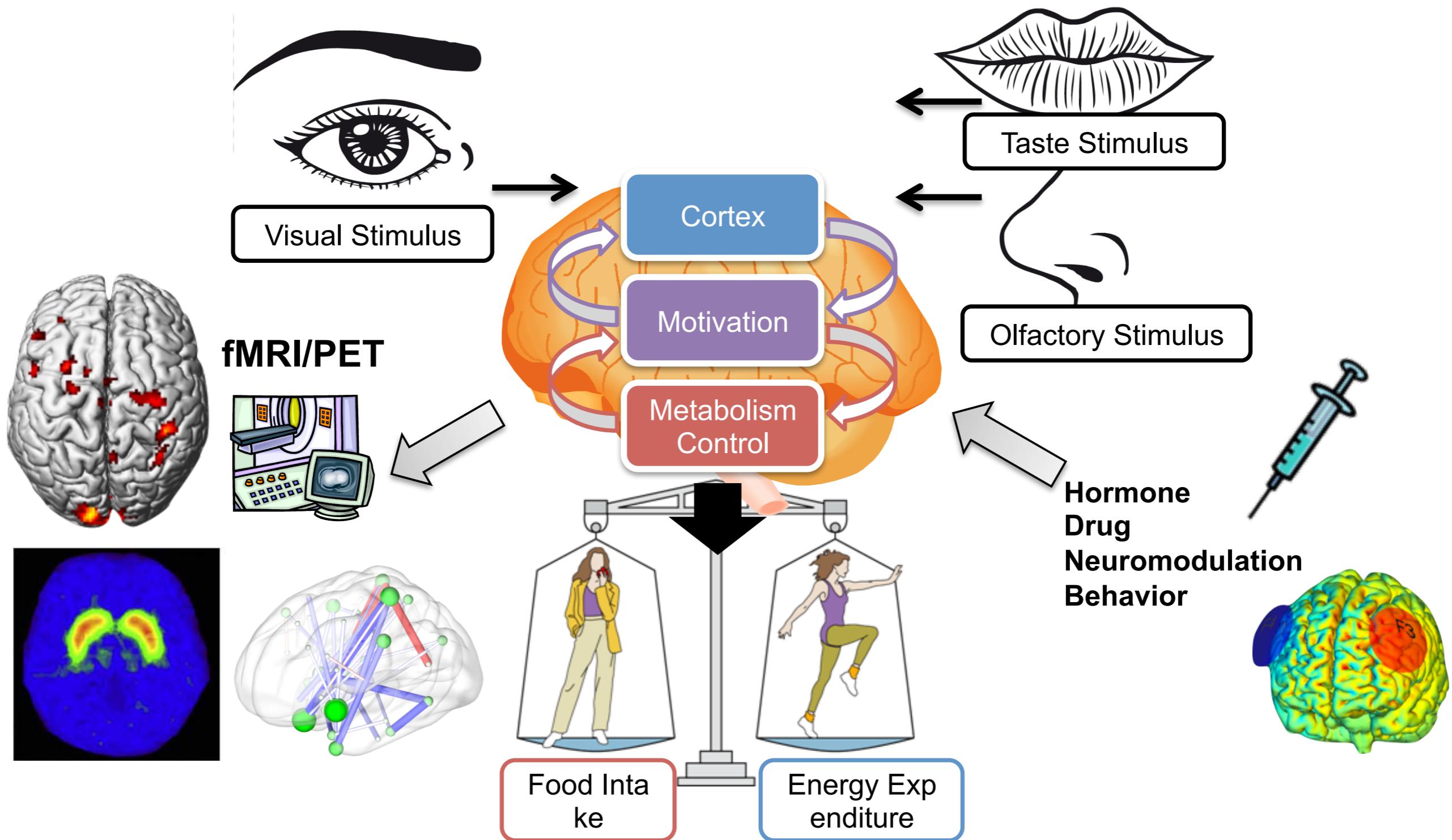
EBS

최형진 교수

충북대학교 내분비내과

설탕이나 지방과 같은 맛있는 음식에 대한 반응이
담배, 마약처럼 쾌감 중추에서

Functional Neuro-Anatomy for Metabolism Regulation



Study protocol

Food presentation m

ax 4sec

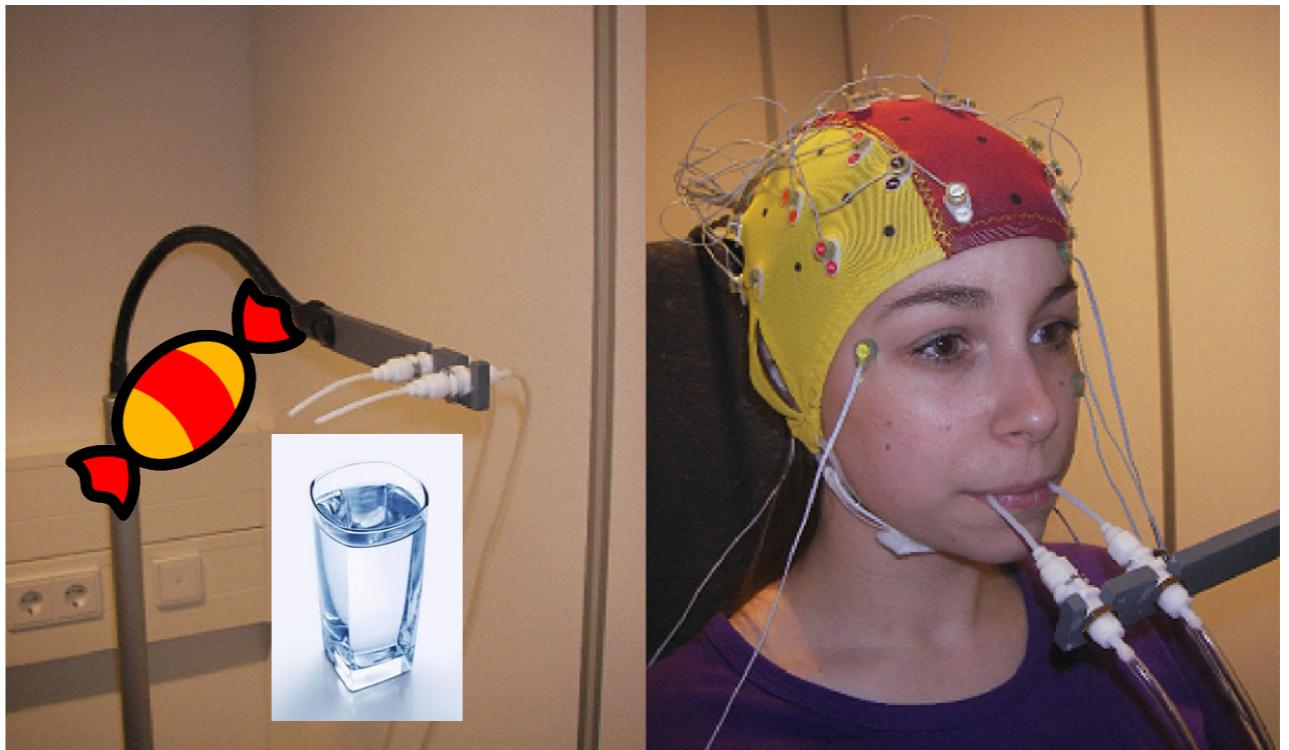


Feedback 1
sec

3

Fixation
1~10sec

+



May I ask...

USA

\$100 million



EU

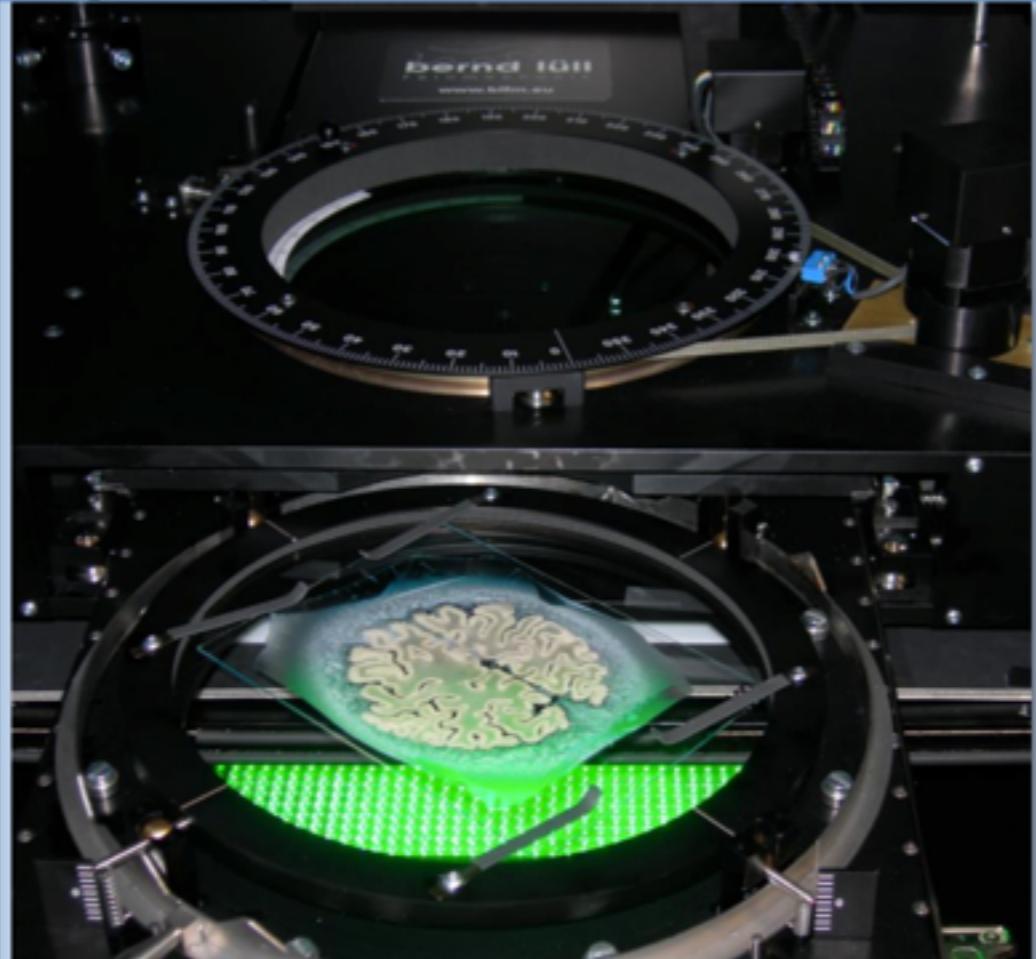
€1 billion



Human Brain Project

Data acquisition for PLI on 2 spatial scales

Large-area polarimeter



Data traffic:

single-shot image

Size: 3.000×3.000 pixel

Resolution: $60\mu\text{m} \times 60\mu\text{m}$

Scan time: 15min/section

4.4 GByte per section → 11TByte per brain

PLI microscope

Data traffic:

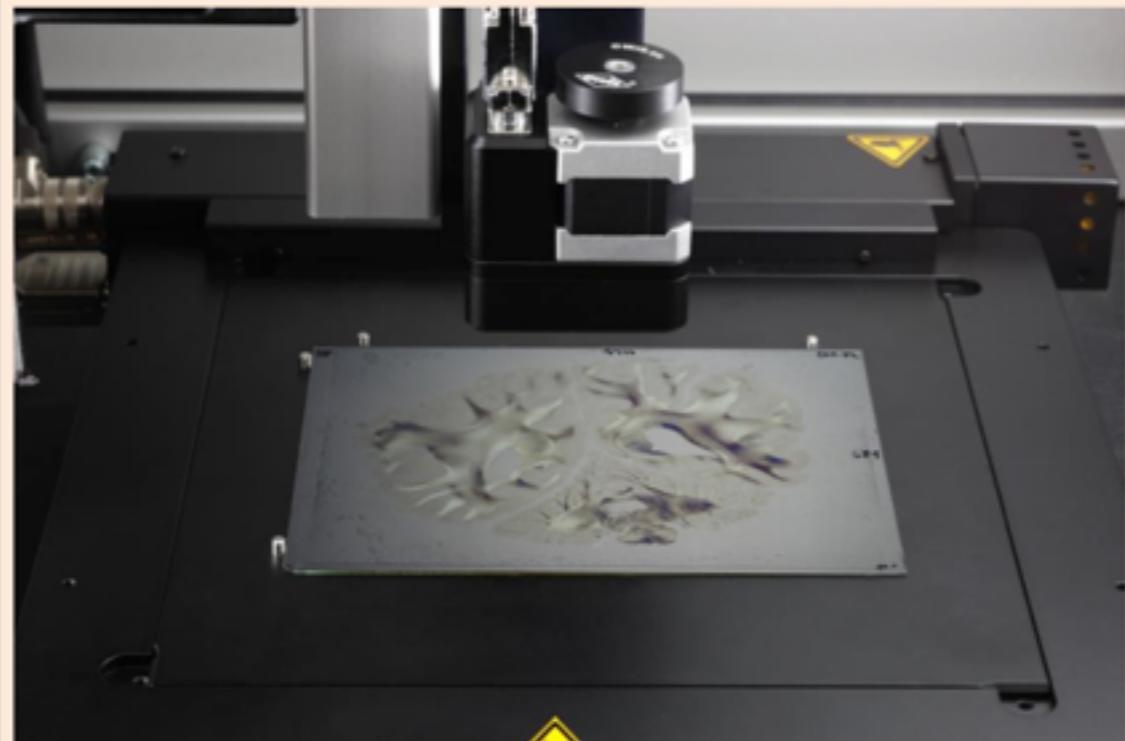
Tiled image acquisition

Total size: 100.000×100.000 pixel

Resolution: $1,6\mu\text{m} \times 1,6\mu\text{m}$

Scan time: 6h/section

1.5 TByte per section → 3.8 PByte per brain



Axer et al. (2011) *NeuroImage* 54: 1091-1101 &
(2011) *Frontiers Neuroinformatics* 5:34



Human Brain Project

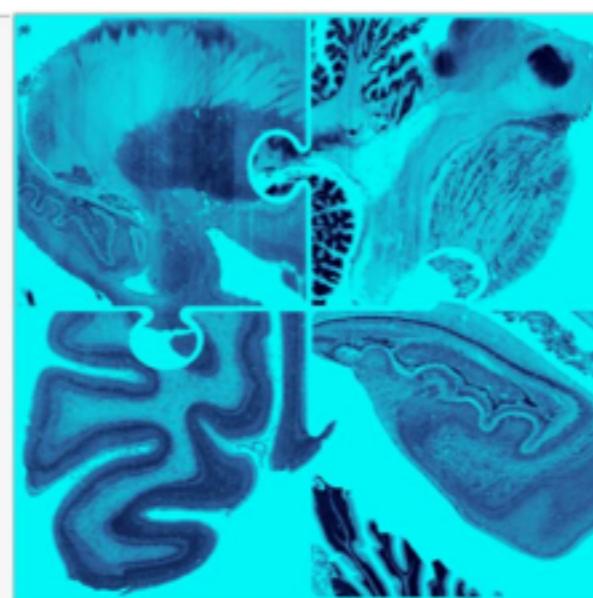
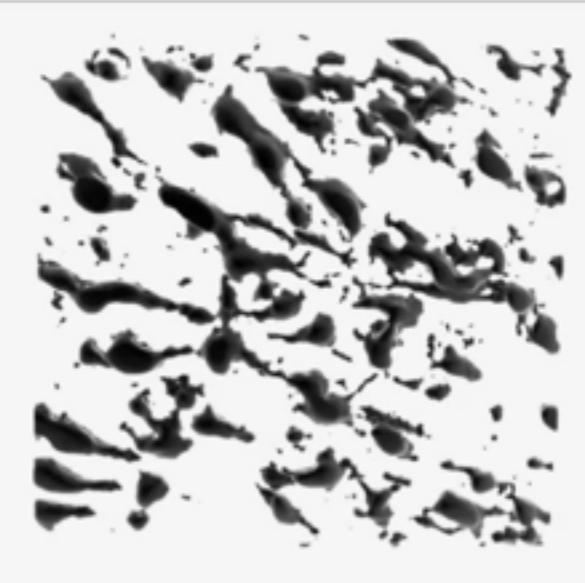
BigBrain → BigData challenge @ 1 micron



Data intensive analytics:

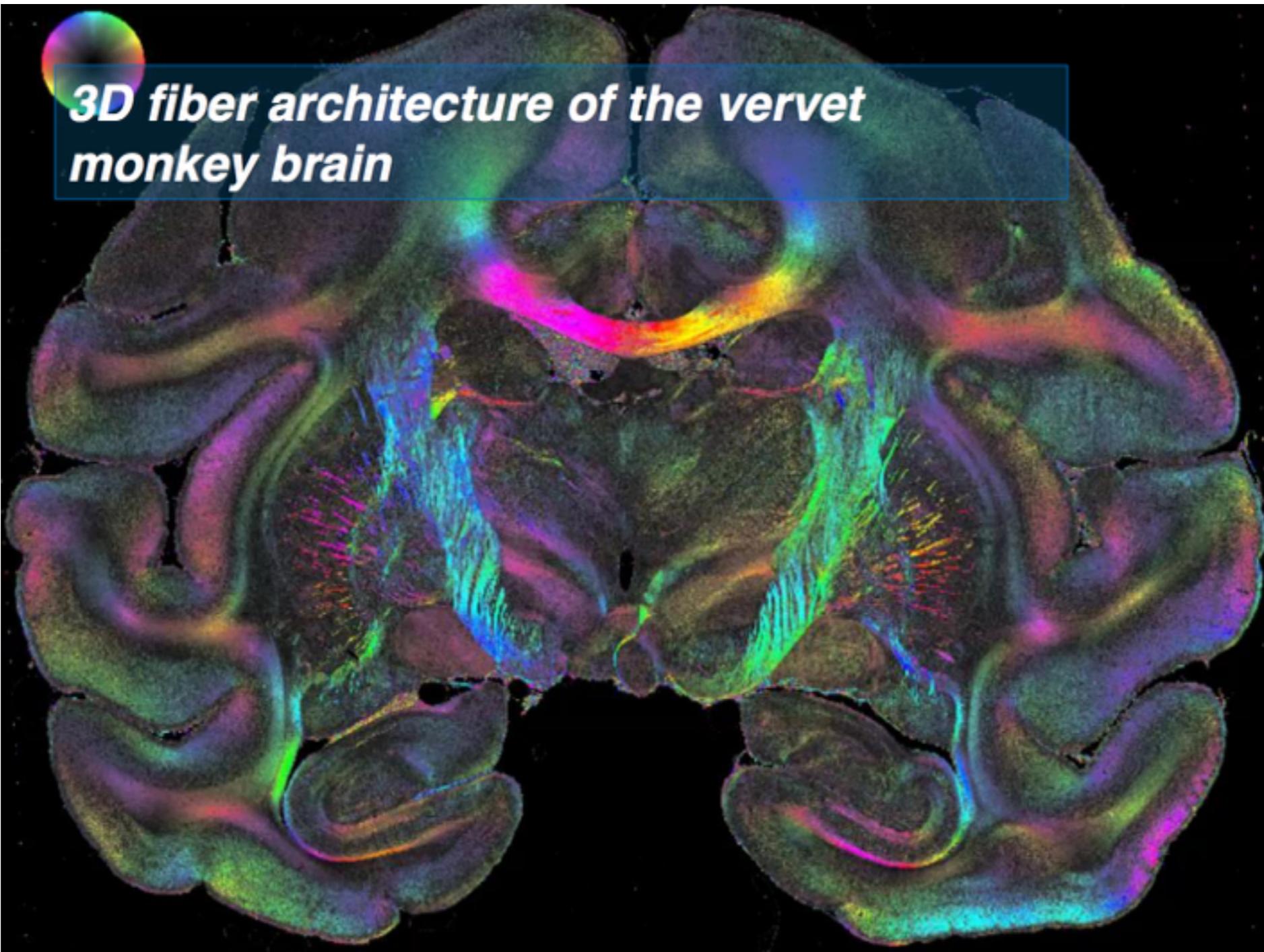
- „BigBrains“ (H 20 PByte at cellular resolution per brain)
- High requirements for memory
- Fast, parallel I/O
- Novel tools on CPU, GPU, CPU+GPU
- Interactive visualization and supercomputing
- Upload and download of modified versions (protocols, versions)
- Fusion and comparison with other data sets

COMPLEXITY:
≈100 billion nerve cells
each with 10^4 synapses
2 states for each synapse
 $= 2^{10^{15}}$



**Image acquisition with a
confocal laserscanner with
integrated autoloader**

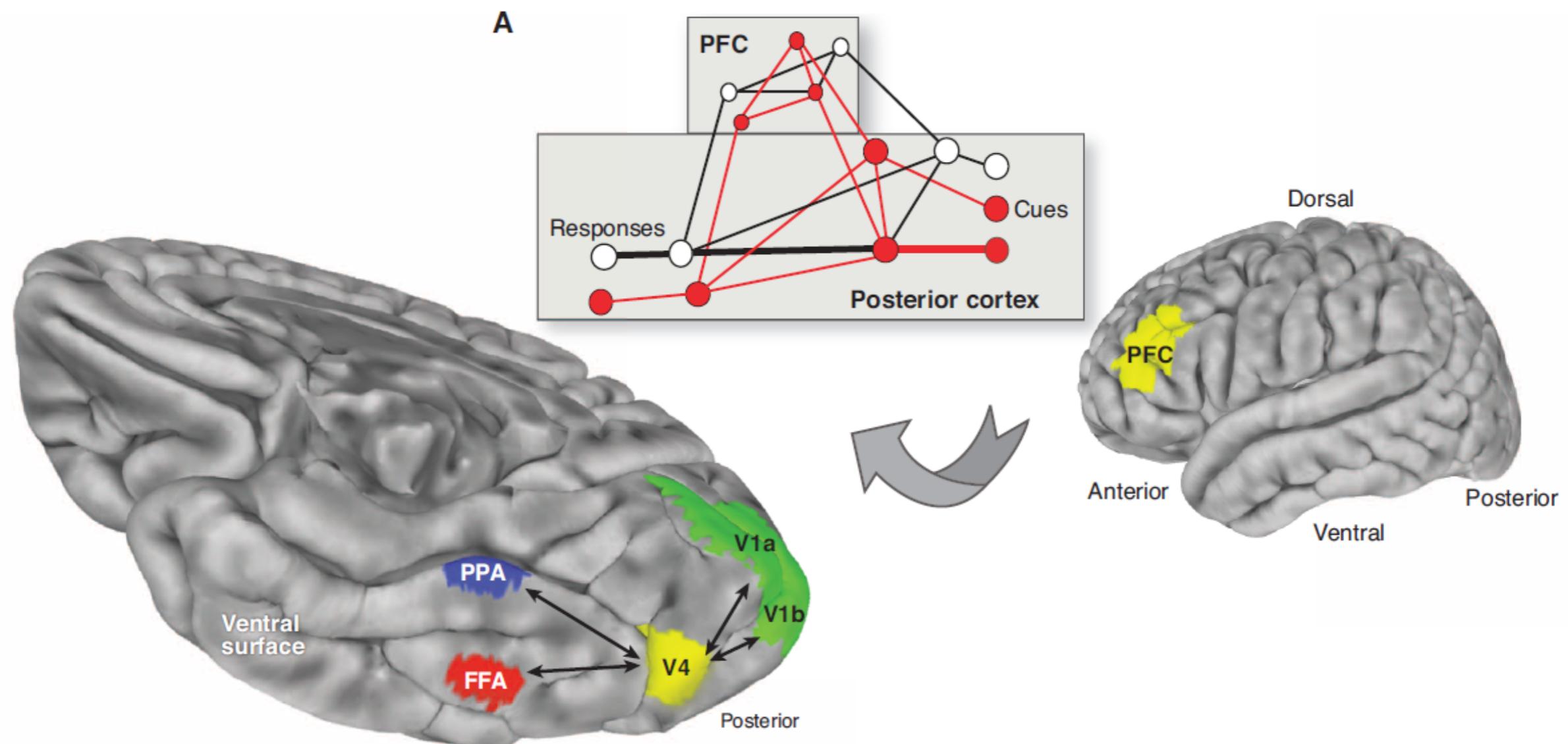
3D fiber architecture of the vervet monkey brain



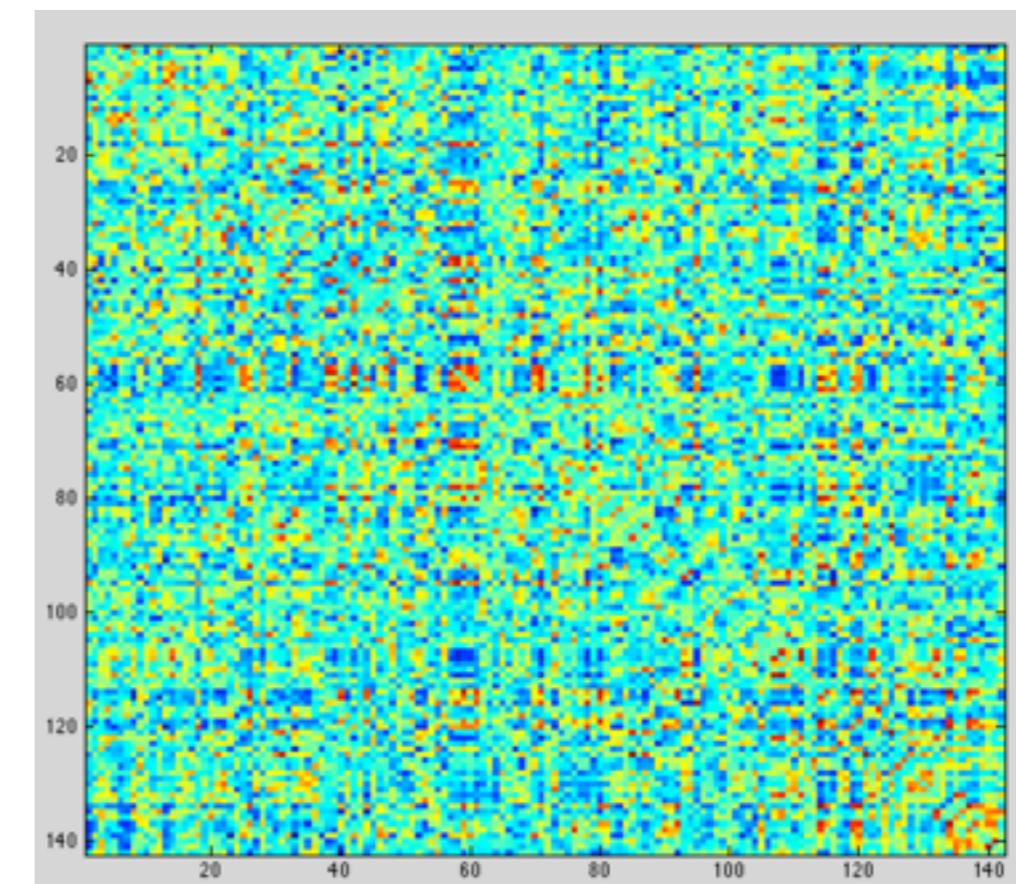
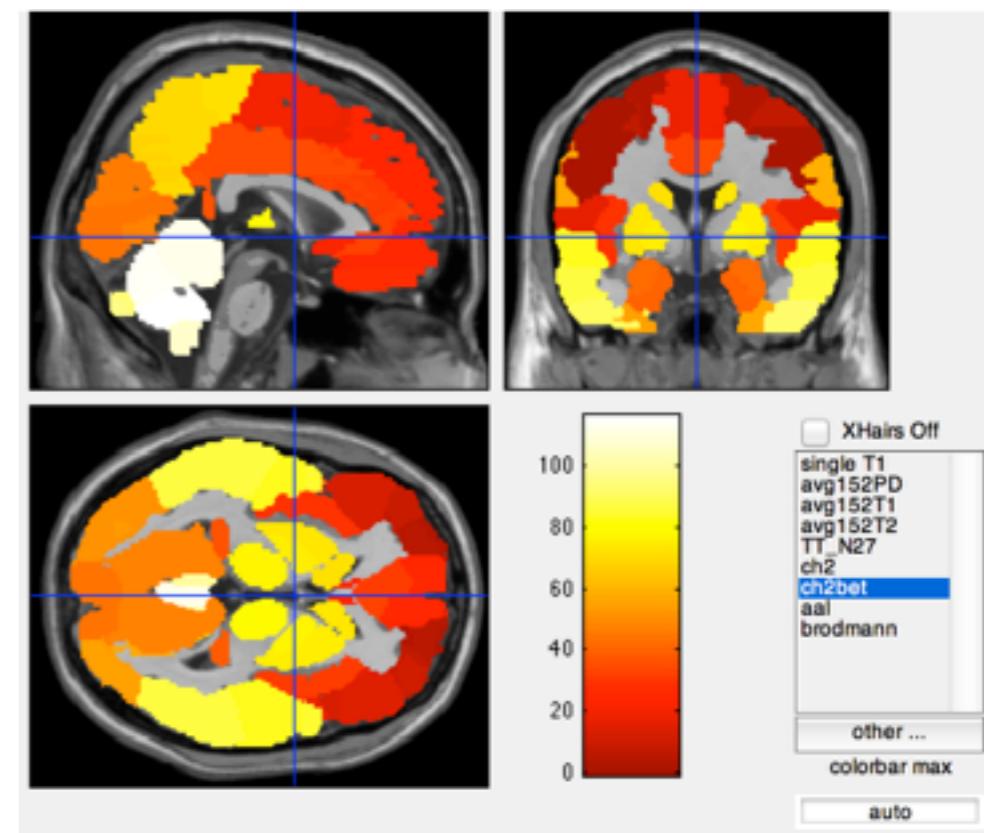
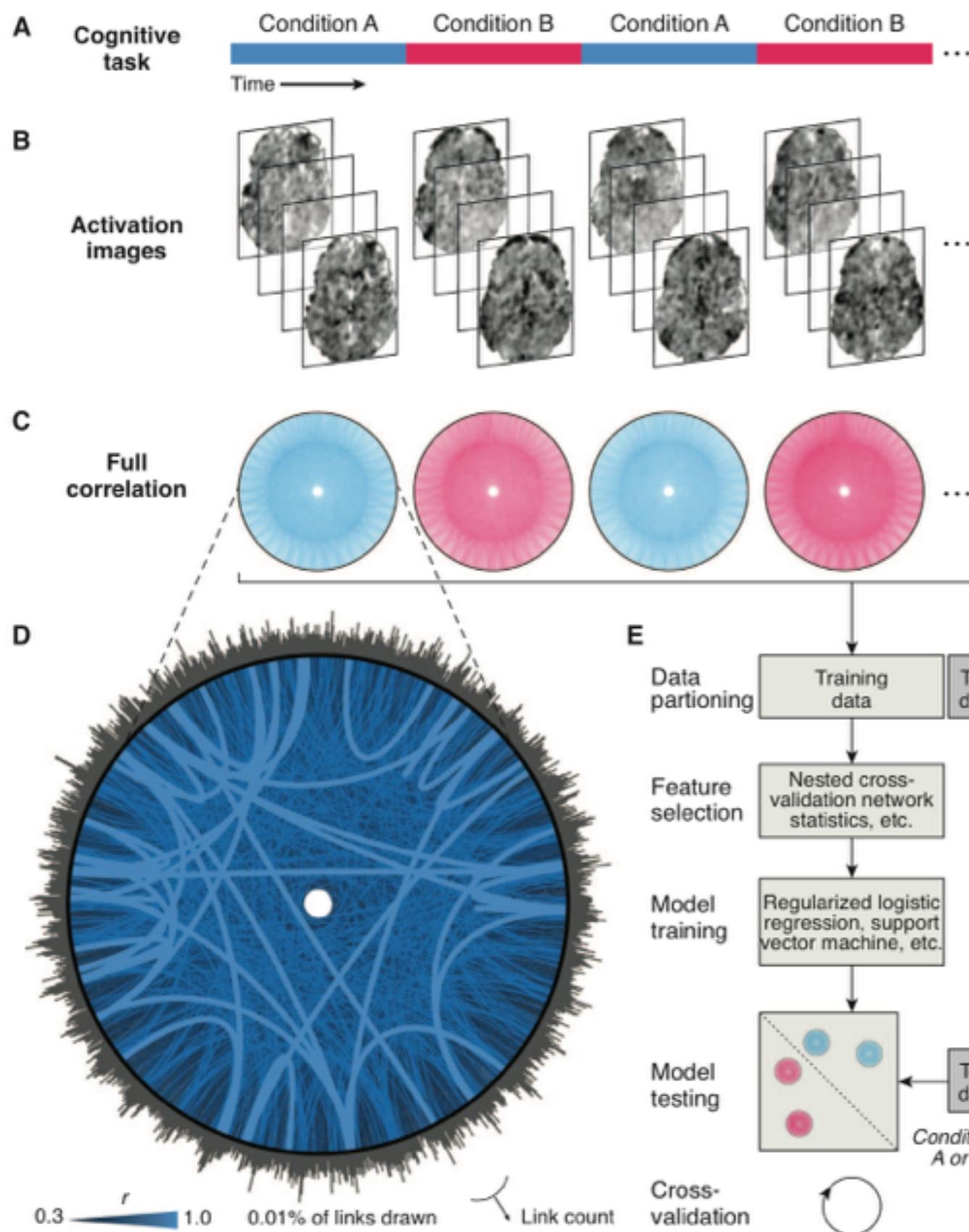
REVIEW

Science

Functional Interactions as Big Data in the Human Brain



Continued



Genome Big Data + Brain Big Data

NEUROGENOMICS

REVIEW

nature
neuroscience

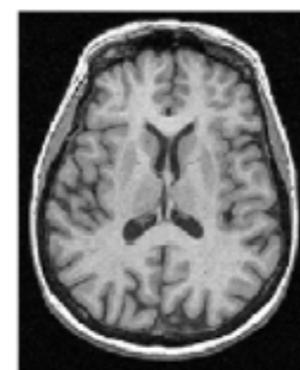
Whole-genome analyses of whole-brain data:
working within an expanded search space

Sarah E Medland^{1,13}, Neda Jahanshad^{2,3,13}, Benjamin M Neale^{4–6} & Paul M Thompson^{2,3,7–12}

Published online
21 January
2015

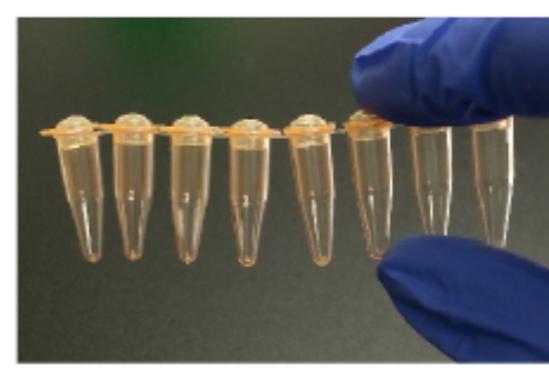
Imaging Protocols

Participant 1



Participant N

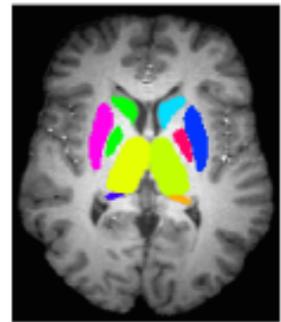
T_1 -weighted structural images

Genetics Protocols

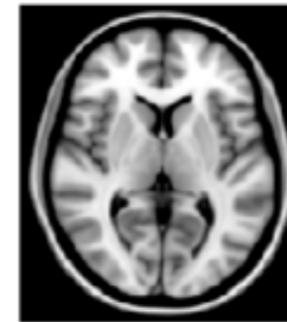
Biological specimens
collected for genotyping

MRI Image Processing**Genotyping using commercially available platforms**

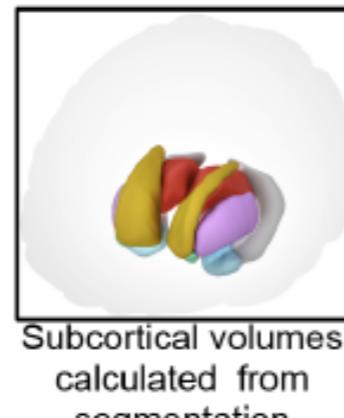
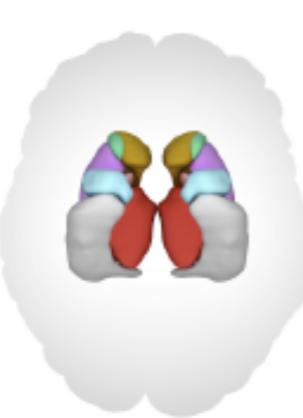
Freesurfer or FSL



Subcortical
segmentation



Registration to
template to
calculate ICV



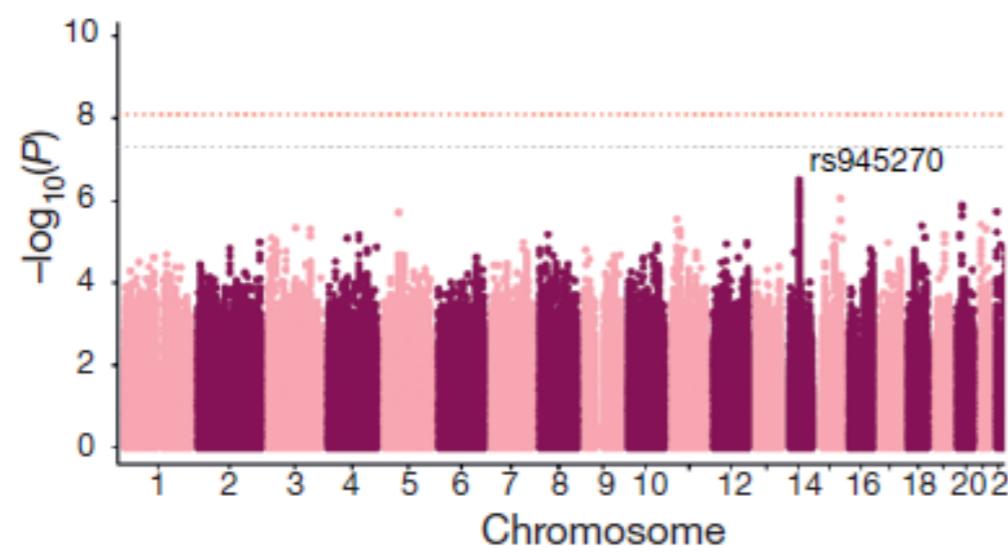
Subcortical volumes
calculated from
segmentation

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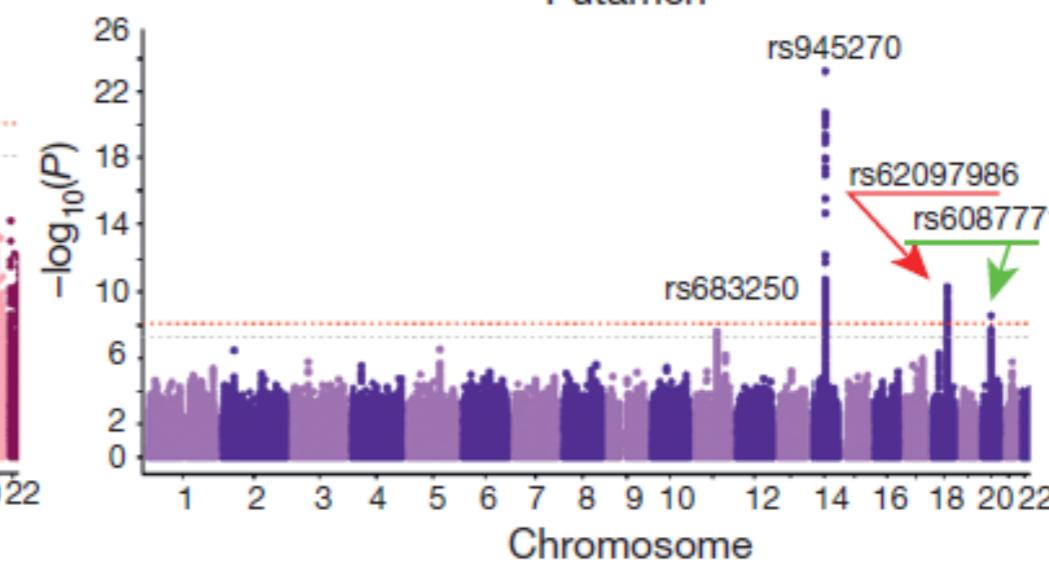
Genome-wide genotypes were imputed to EUR reference panel from the 1000 Genomes Project (Phase 1 Version 3) following standardized protocols



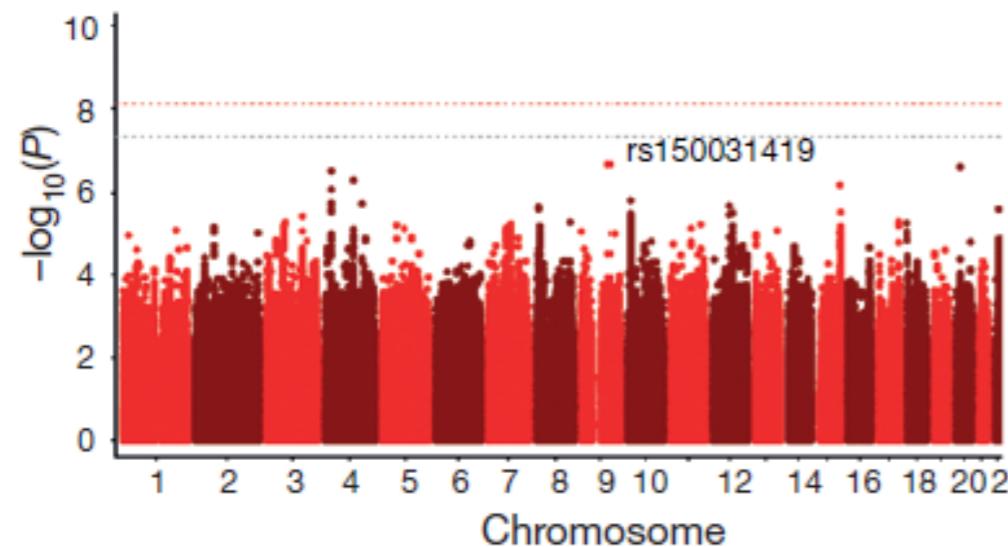
Pallidum



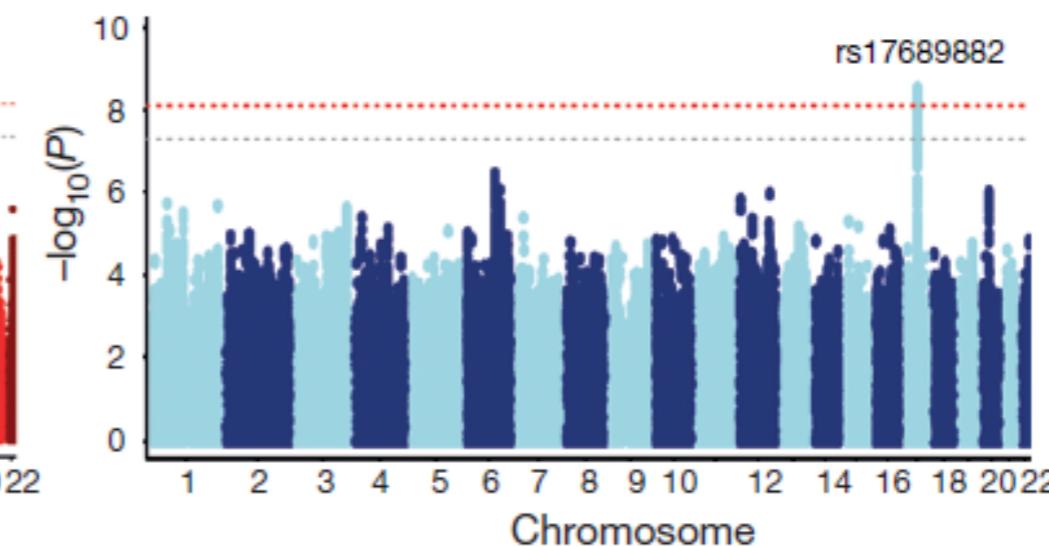
Putamen

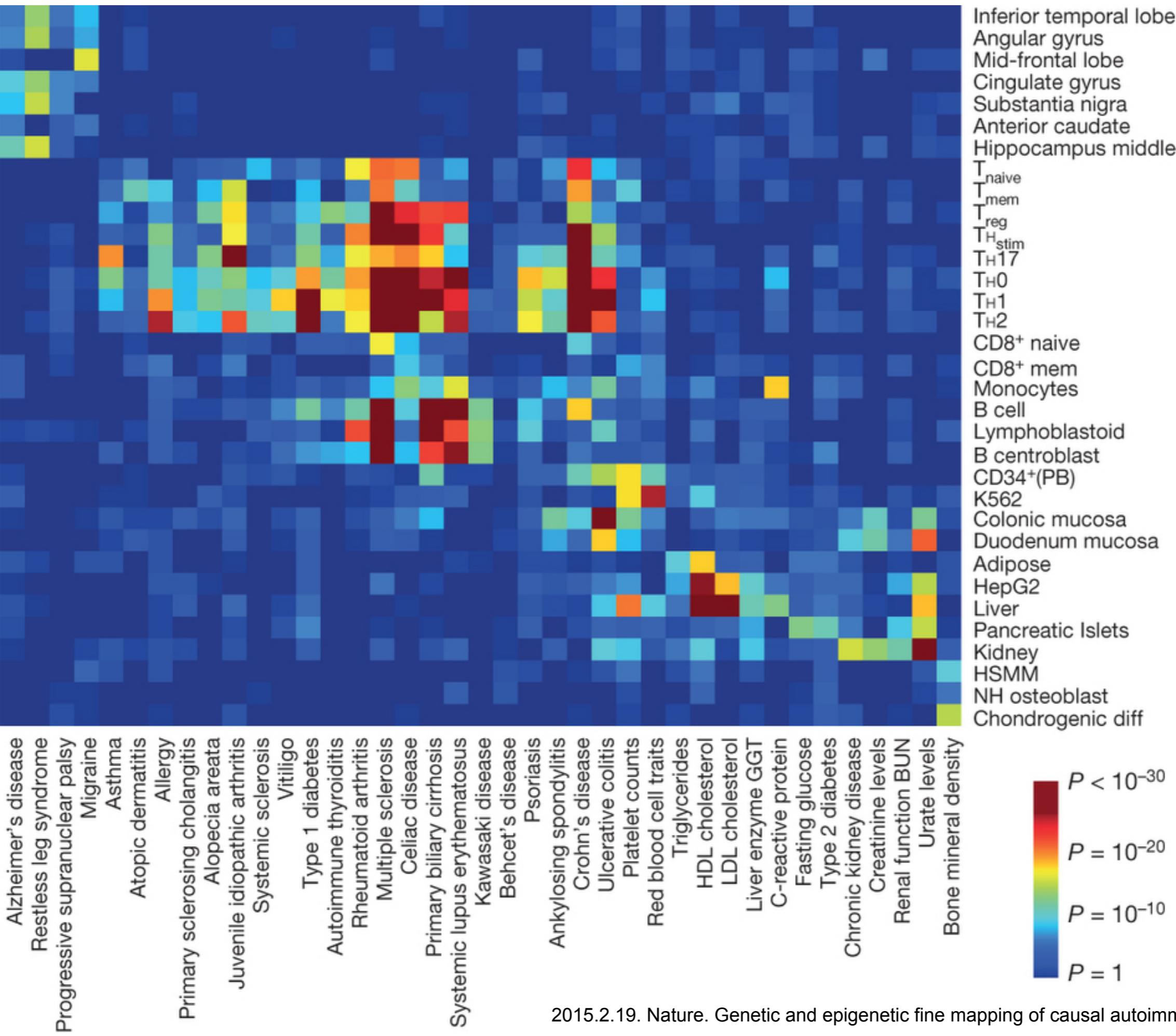


Thalamus

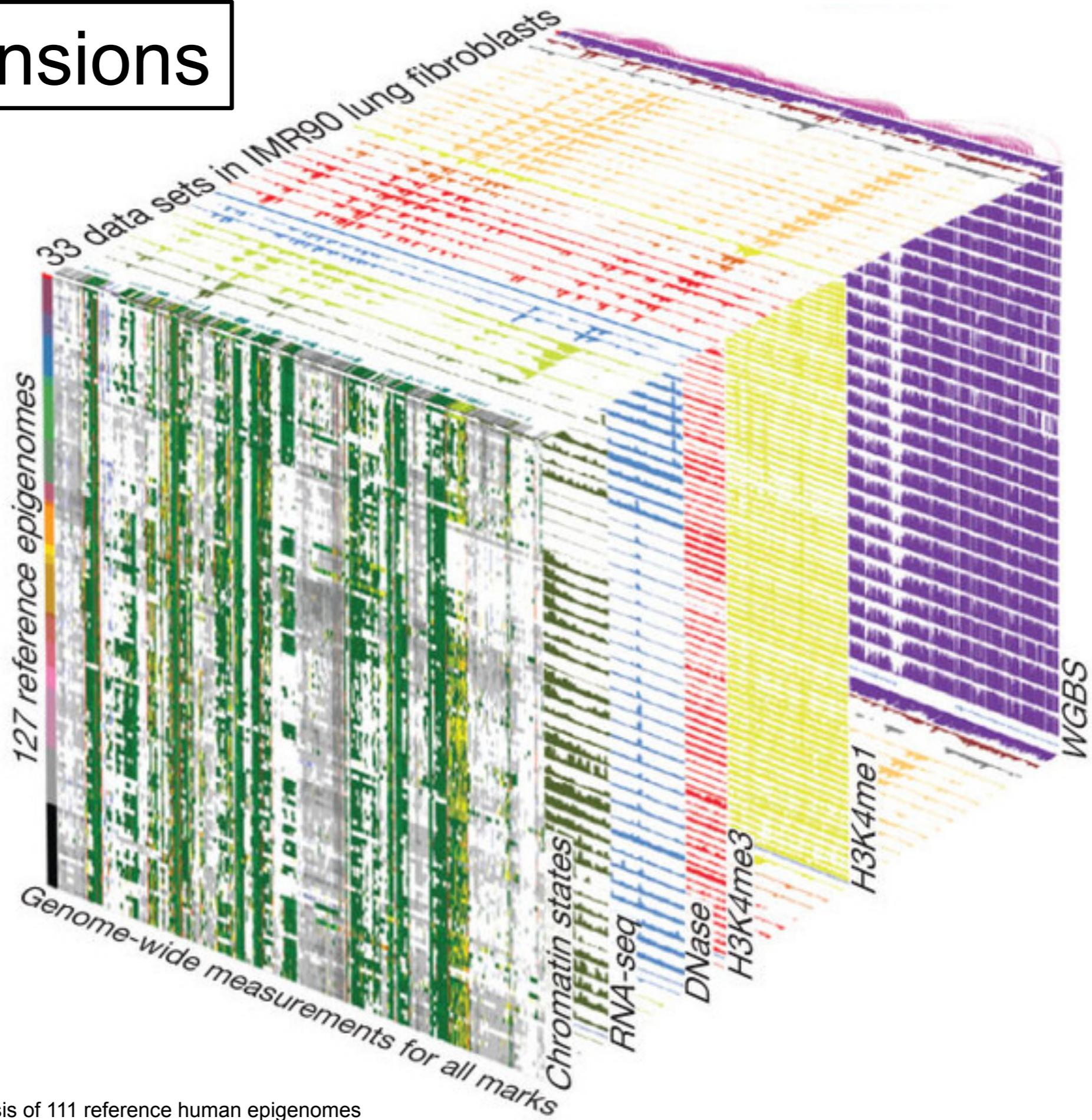


ICV

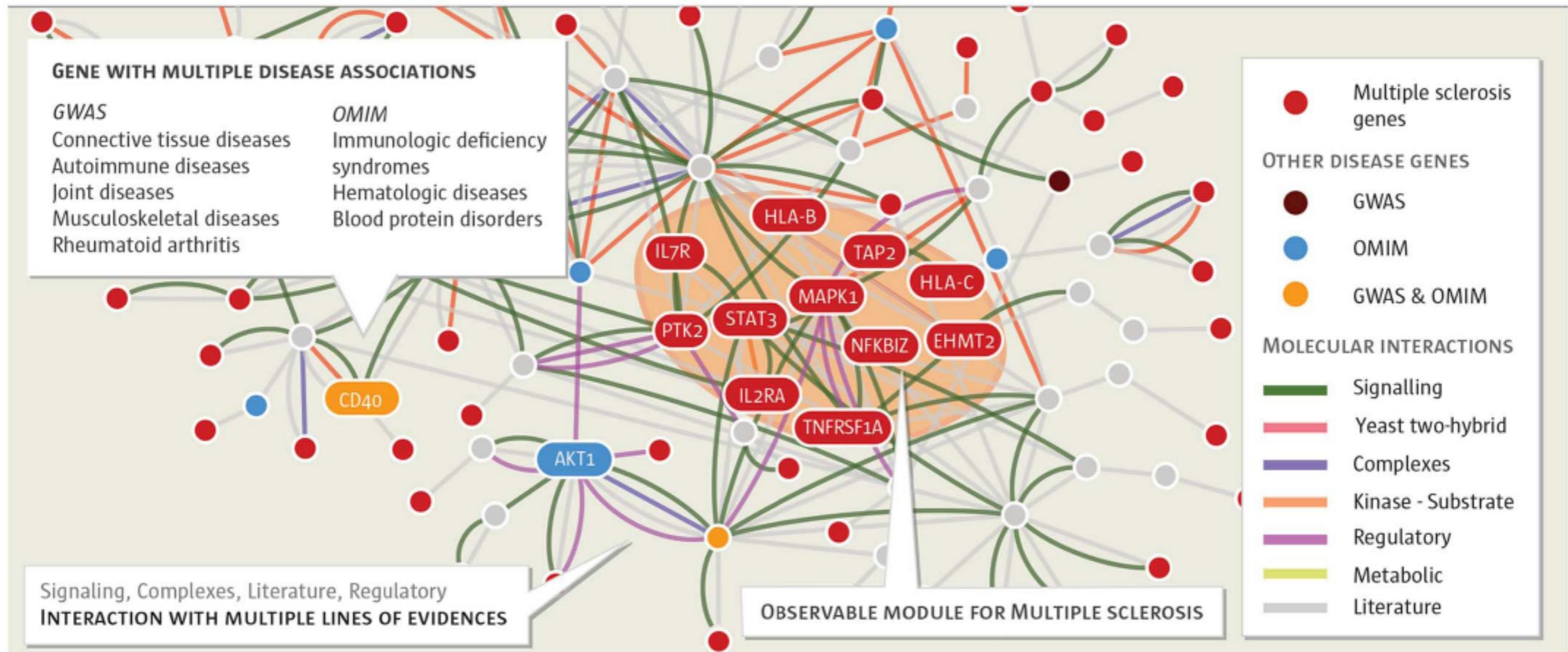




Data Dimensions

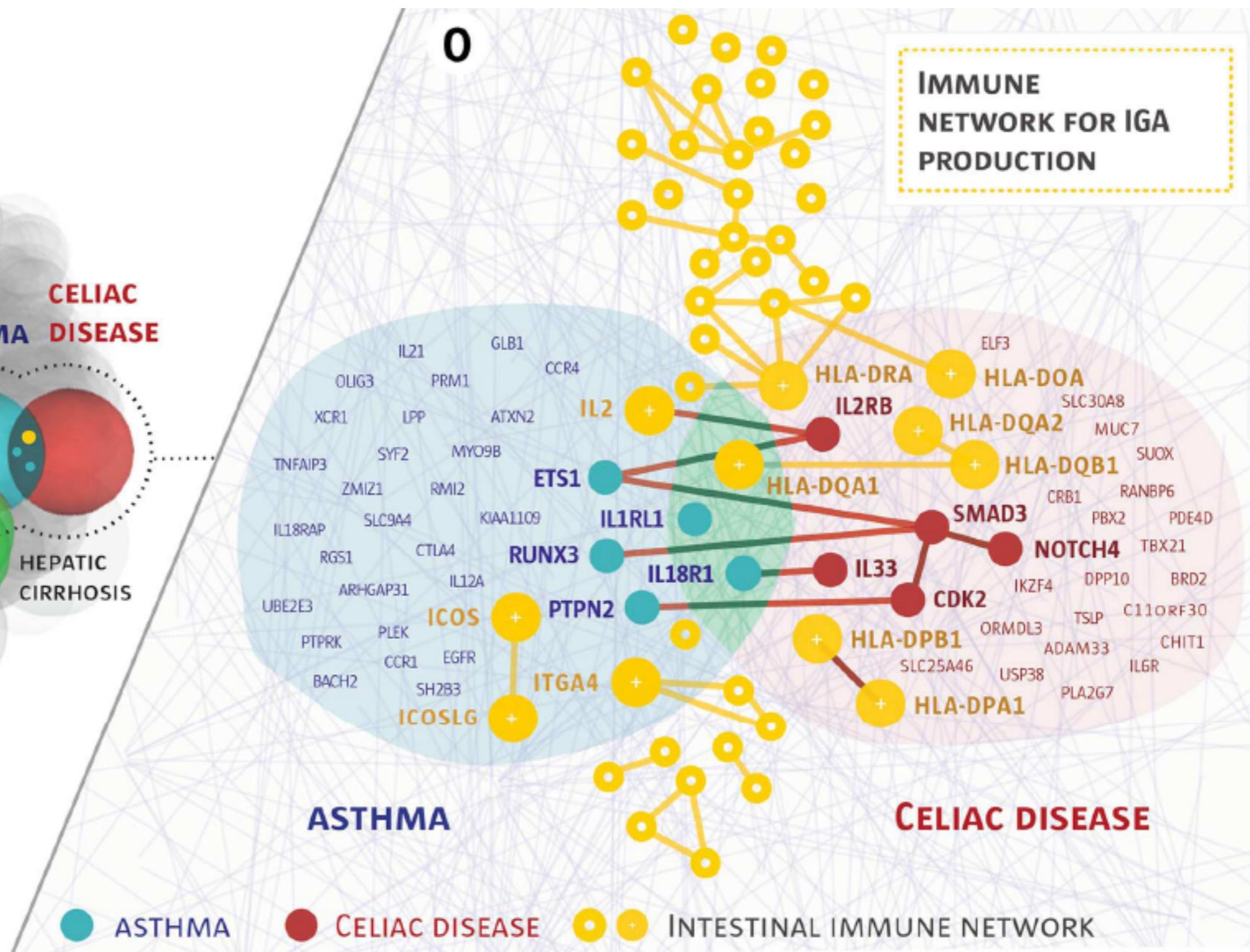
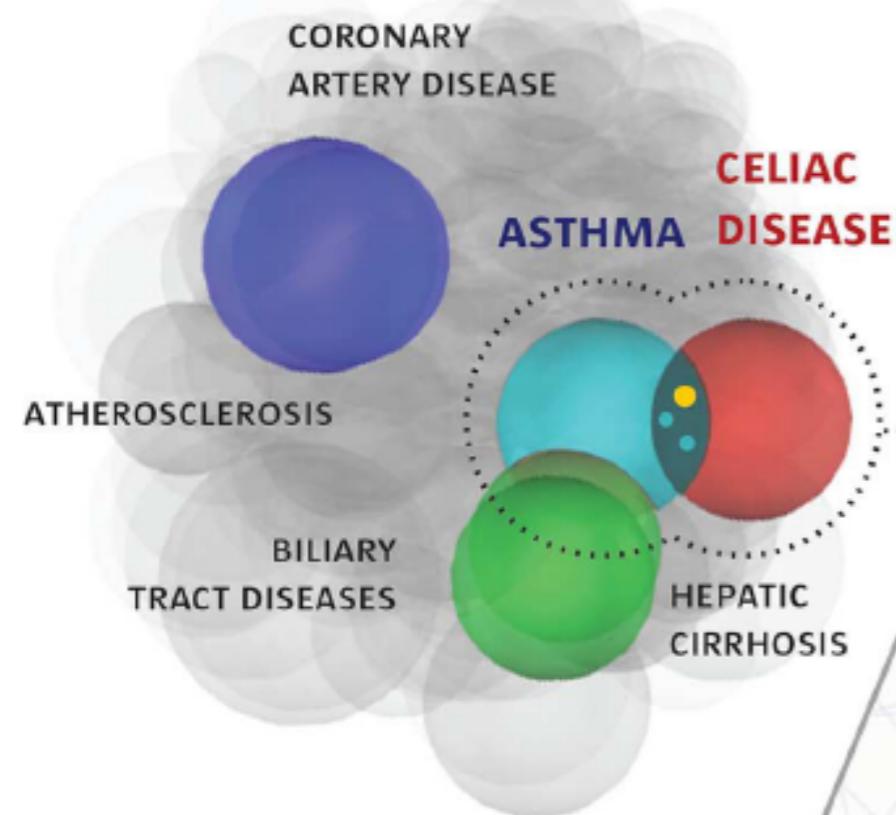


Building the Interactome



Network-based Model of Disease-disease Relationship

N



Thank you!