Moonshot International Symposium,
18th December, 2019 @Tokyo, Japan

# Reproducible computational psychiatry based on data assimilation of multiple-disorder and multi-site database

Mitsuo Kawato

Advanced Telecommunication Research Institute International (ATR), Brain Information Communication Research Group (BICR)

# Unmet medical needs in psychiatry

- Diagnoses such as DSM-V are categorical, and based on symptoms and signs, without biological examination.
- High comorbidities are observed and clear correspondence between categories and medications is lacking.
- No mega-sales psychiatric drug developed in 30 years
- Majority of patients are not fully cured
- NIMH started Research Domain Criteria (RDoC) in 2010

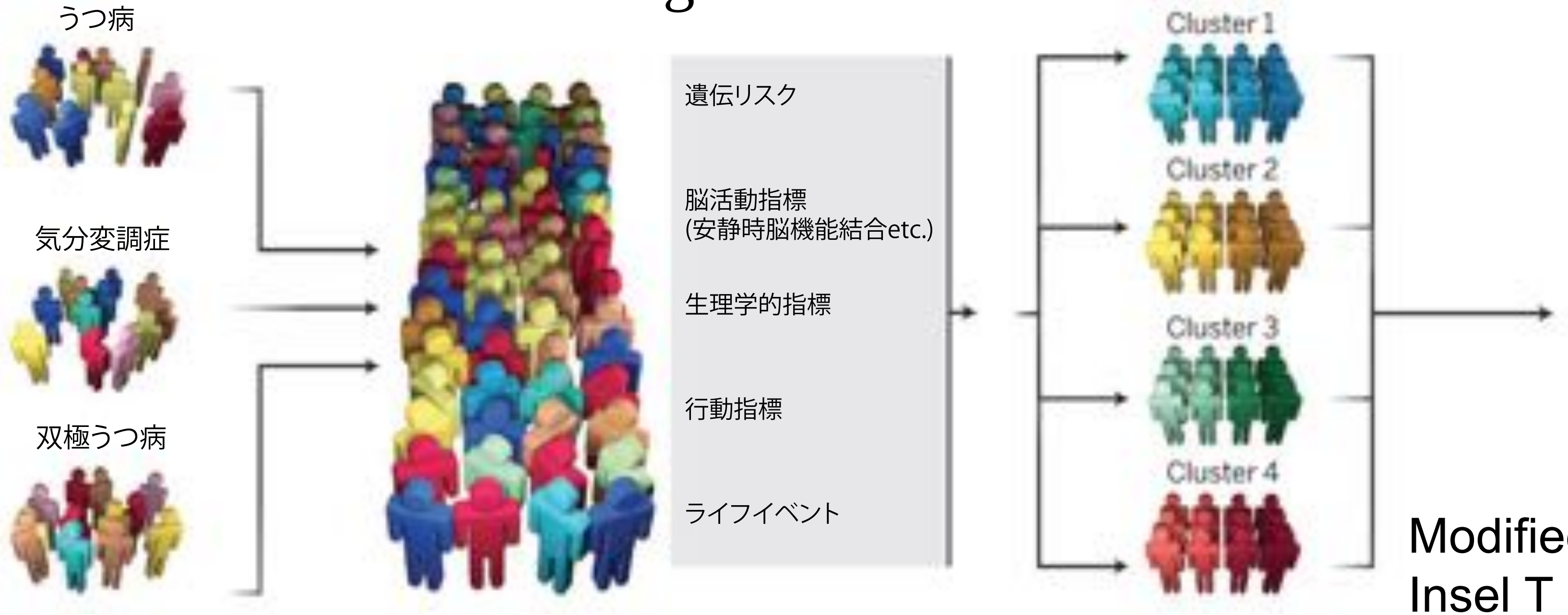
» Clustering based on genetics and neuroscience, but not reproducible!!

» Tom Insel moved to Google in 2015.

» In Japan SRPBS 2008~2013, 2013~2018, and Brain/MINDS Beyond 2018~

# Research Domain Criterion (NIMH)

Traditional classes　　Biological data　　Data-driven classification

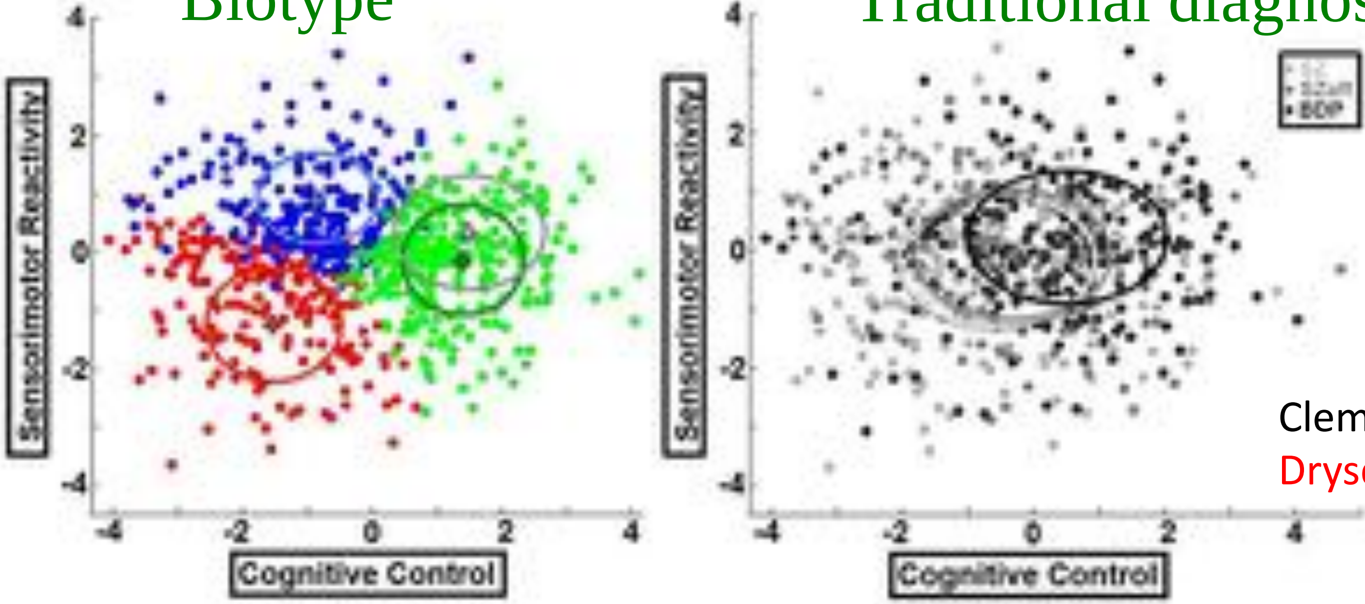



再現性確認

バイオマーカー
に基づく治療

Modified from
Insel T et al. 2015
*Science*

Biotype　　Traditional diagnosis




- Schizophrenia
- Schizoaffective disorders
- Bipolar disorders

Clementz BA et al. *Am J Psych* 2016

Drysdale AT et al. *Nat Med* 2017

# Difficulty of AI in psychiatry

- Huge site differences in MRI
- Over-training and poor generalization
- Clustering is more difficult than classification
- Until recently, neither classification or stratification was generalizable for perfectly independent cohort
- No reproducibility in science and no practical utility in diagnoses or interventions
- Harmonization and multi-site database essential

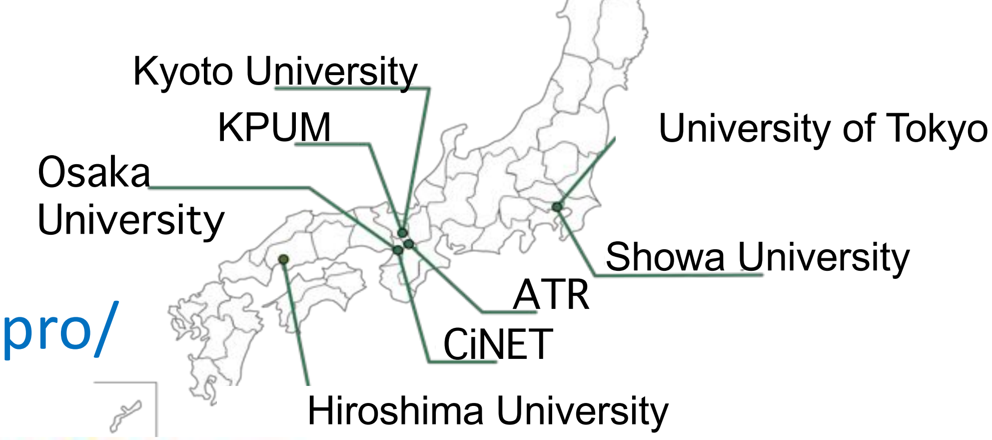
Yamashita A, Yahata N, Itahashi T, Lisi G, Yamada T, Ichikawa N, Takamura M, Yoshihara Y, Kunimatsu A, Okada N, Yamagata H, Matsuo K, Hashimoto R, Okada G, Sakai Y, Morimoto J, Narumoto J, Shimada Y, Kasai K, Kato N, Takahashi H, Okamoto Y, Tanaka SC, Kawato M, Yamashita O, Imamizu H: Harmonization of resting-state functional MRI data across multiple imaging sites via the separation of site differences into sampling bias and measurement bias, *PLoS Biology*, **17(4)**: e3000042. (2019)

# DecNef database project

Strategic Research Program for Brain Sciences (SRPBS)

The mental and neurological disease treatment group

https://bicr-resource.atr.jp/decnefpro/




## Details of the multi-site multi-disorder database

| Institute | MRI scanner | ASD | Depression | Schizophrenia | OCD | Chronic pain/Back pain | Others | Healthy and typically developed controls | Sum |
|---|---|---|---|---|---|---|---|---|---|
| University of Tokyo | Philips, GE | 10 | 103 | 36 | | | 32 | 170 | 351 |
| Osaka University | Siemens | | | | | 43 | 10 | 29 | 82 |
| Showa University | Siemens | 115 | | 19 | | | | 110 | 244 |
| Kyoto University | Siemens | | 20 | 104 | | | | 244 | 368 |
| Hiroshima University | Siemens, GE | | 318 | | | 40 | | 468 | 826 |
| ATR Brain Information Communication Research Laboratory Group | Siemens | | 4 | | 5 | | | 271 | 280 |
| Kyoto Prefectural University of Medicine (KPUM) | Philips | | | | 105 | | | 90 | 195 |
| Center of Information and Neural Networks (CiNet) | Siemens | | | | | 24 | | 39 | 63 |
| Sum | | 125 | 445 | 159 | 110 | 107 | 42 | 1421 | 2409 |

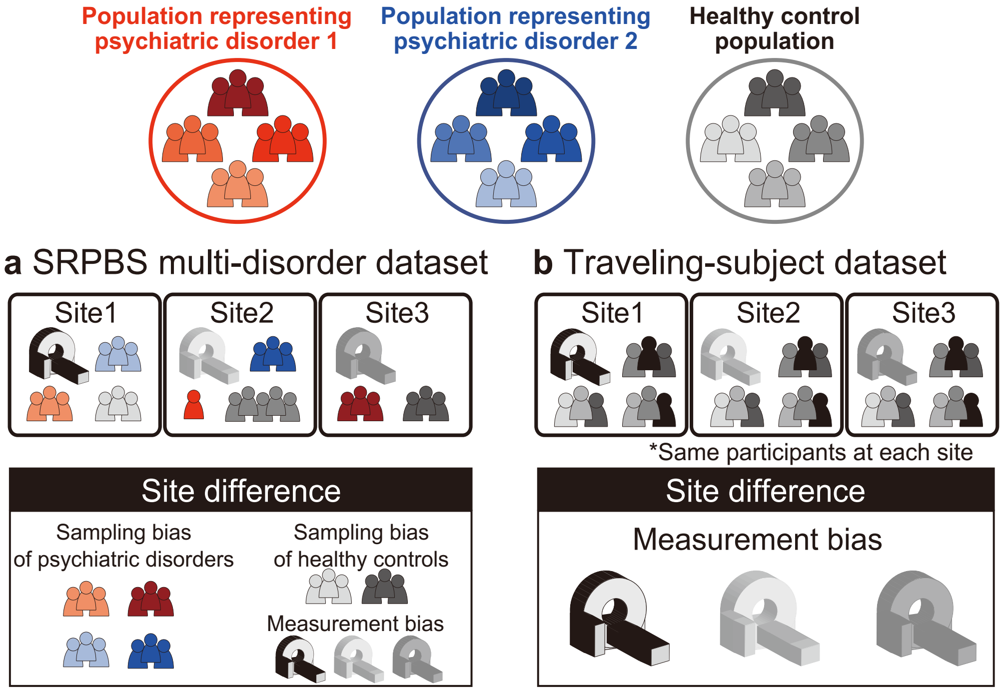
2,409 multi-disorder participants

+

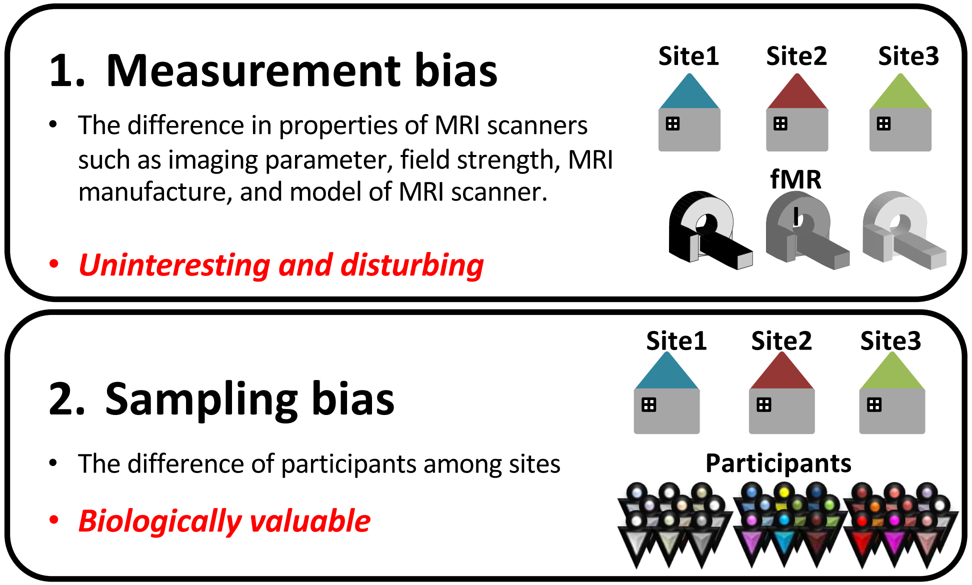
411 traveling subjects samples

# Traveling-subject harmonization

## 9 healthy subjects visited 12 scanning sites and 411 sessions were measured




Two types of bias in site difference




$$Connectivity = \mathbf{x}_{m}{}^{T}\boldsymbol{m} + \mathbf{x}_{s_{hc}}{}^{T}\boldsymbol{s}_{hc} + \mathbf{x}_{s_{mdd}}{}^{T}\boldsymbol{s}_{mdd} + \mathbf{x}_{s_{scz}}{}^{T}\boldsymbol{s}_{scz} + \mathbf{x}_{d}{}^{T}\boldsymbol{d} + \mathbf{x}_{p}{}^{T}\boldsymbol{p} + const + e$$

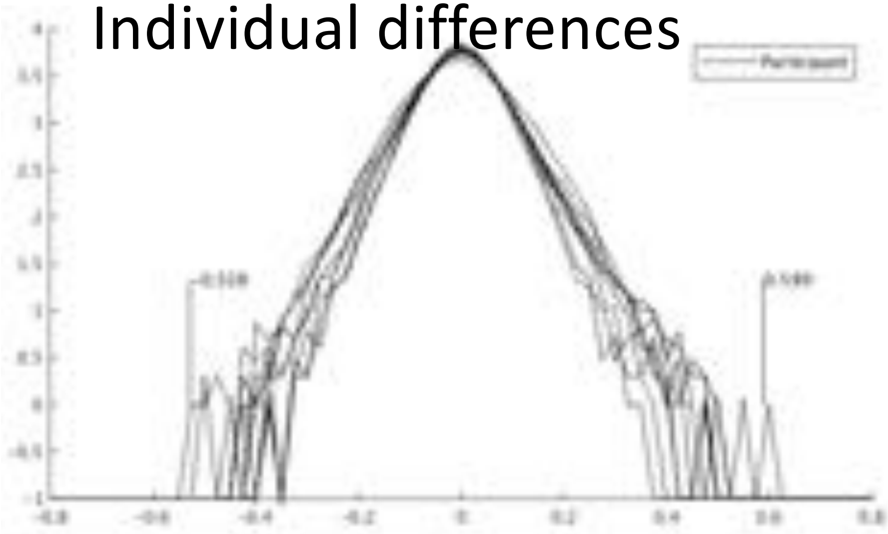
***Measurement bias**, **Sampling bias**, **Disorder factor**, **Participant factor***

$$Connectivity_{harmonized} = Connectivity - \mathbf{x}_{m}{}^{T}\boldsymbol{m}$$

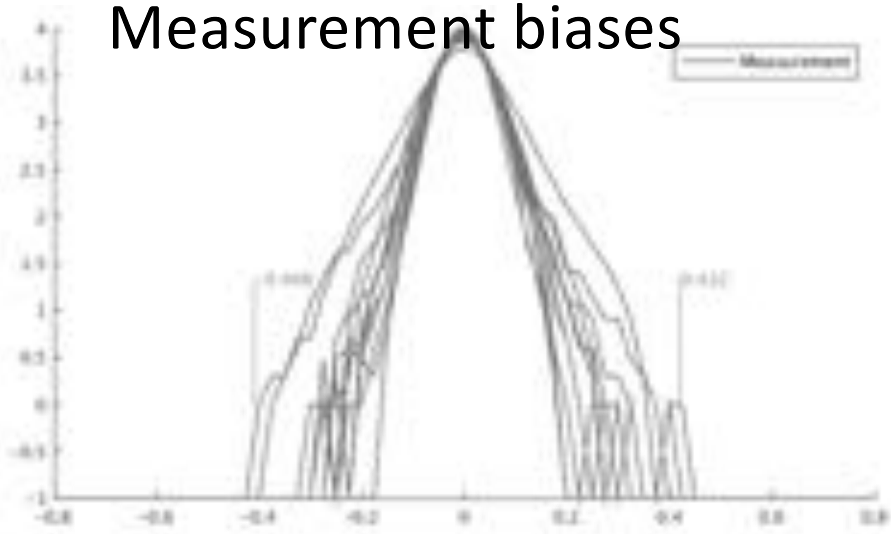
# Evaluation of measurement and sampling biases with 9 travelling subjects

Measurement biases were larger than disorder effects

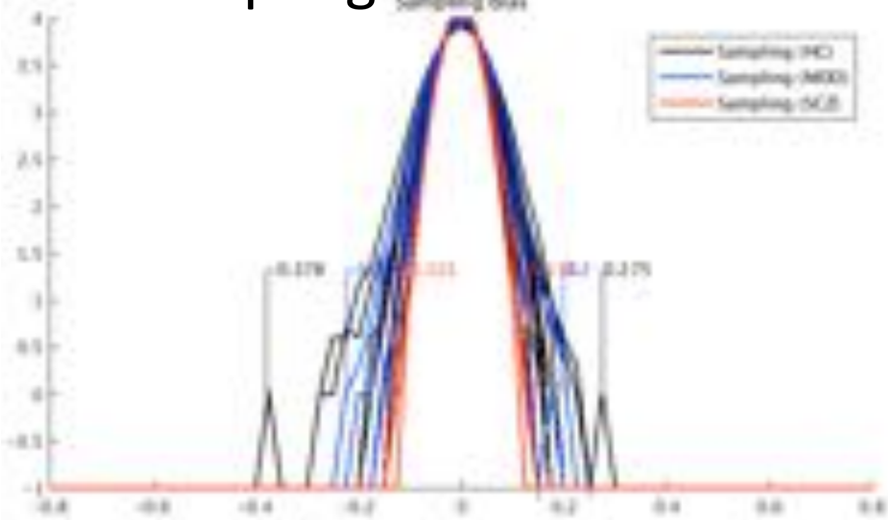
Individual differences



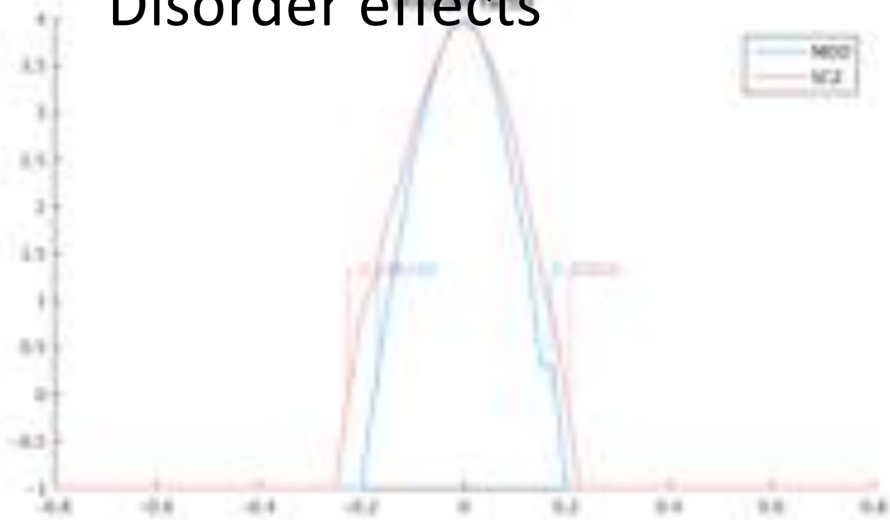
Measurement biases



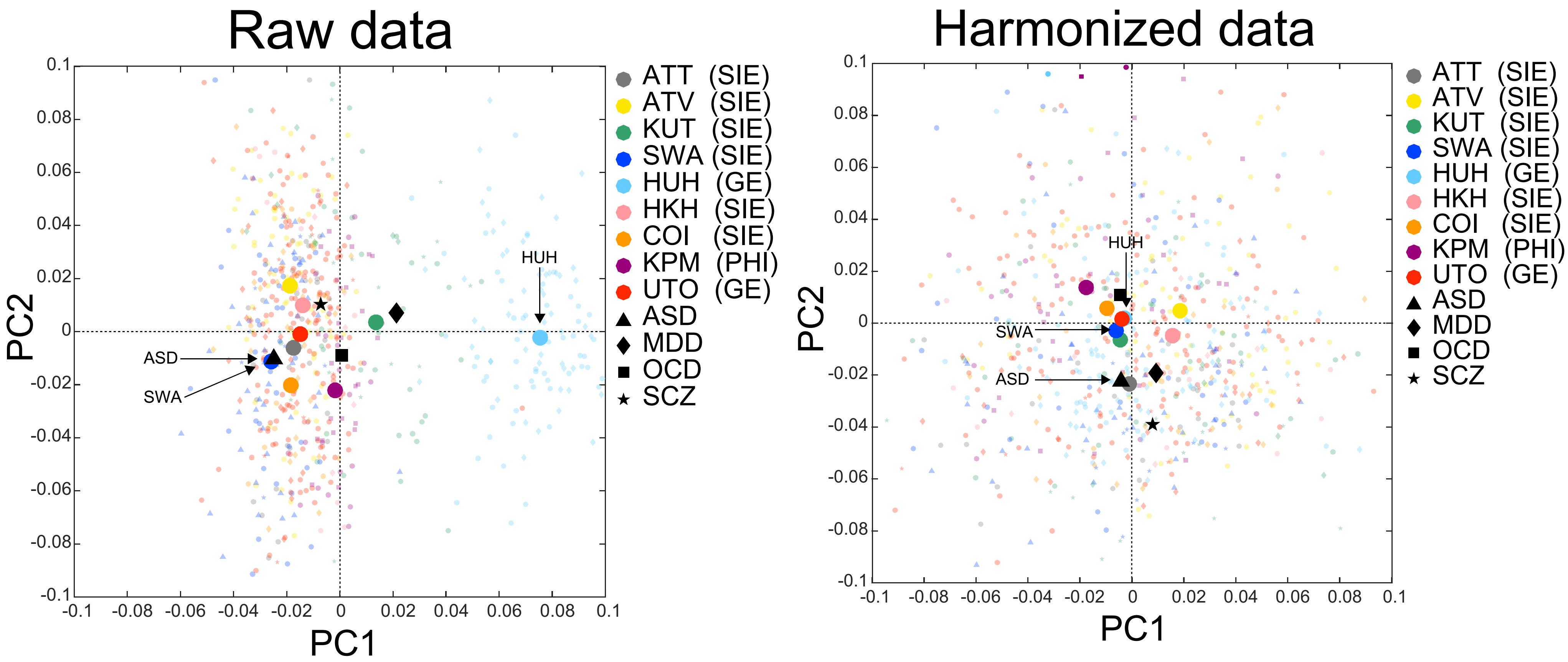
Sampling biases



Disorder effects

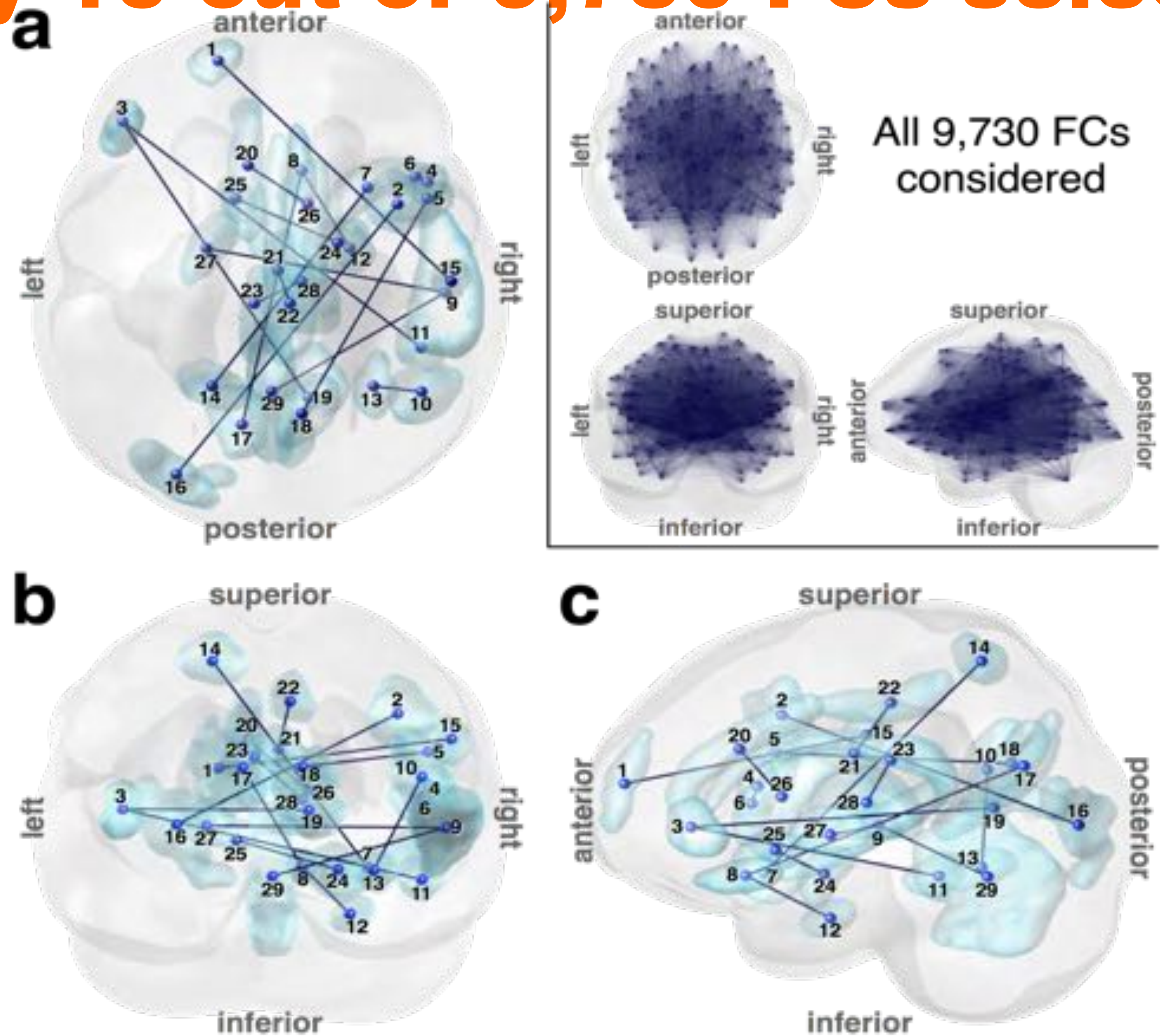


# PCA of multi-site multi-disorder data before/after harmonization



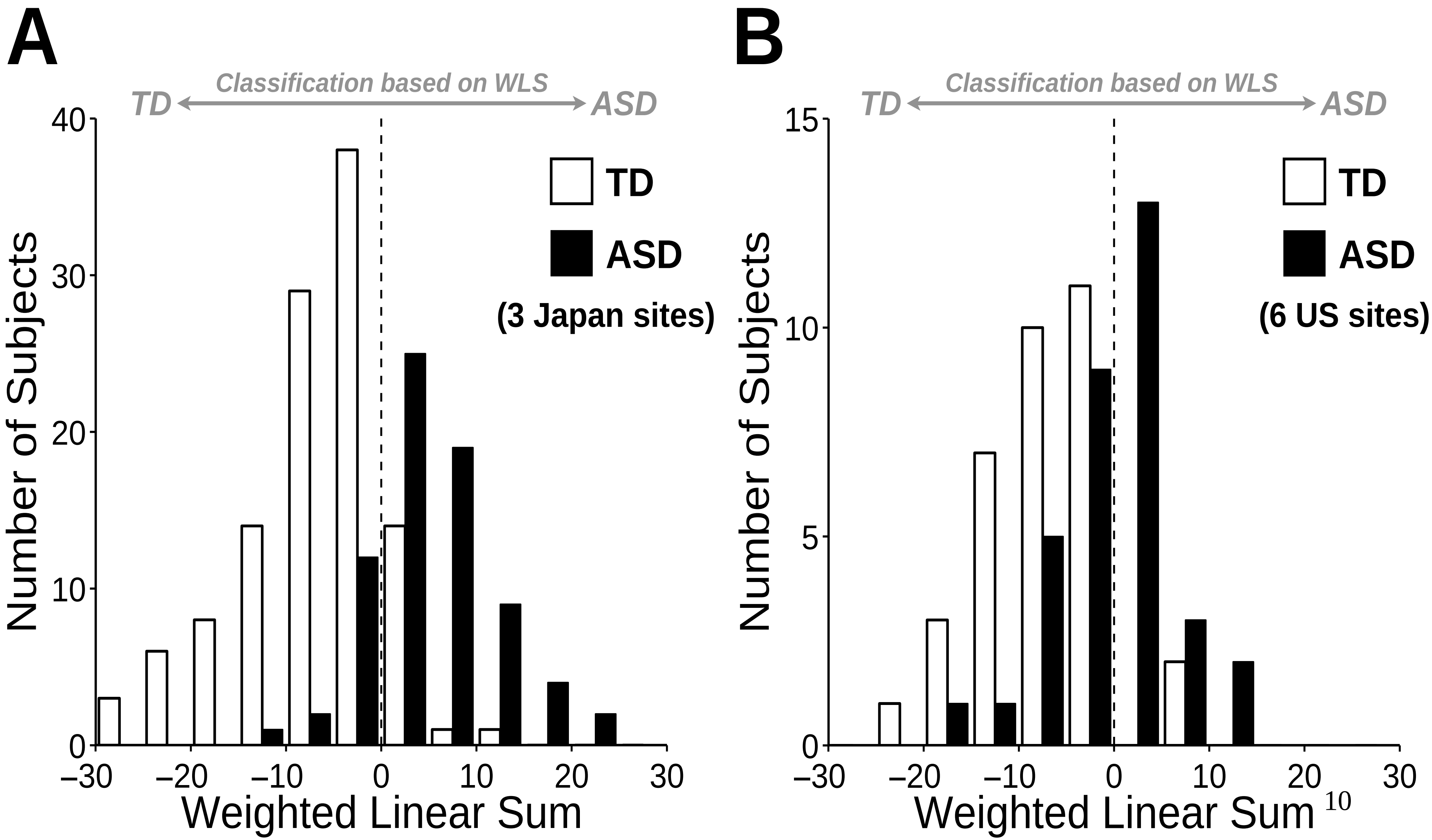

Yamashita A, Yahata N, Itahashi T, Lisi G, Yamada T, Ichikawa N, Takamura M, Yoshihara Y, Kunimatsu A, Okada N, Yamagata H, Matsuo K, Hashimoto R, Okada G, Sakai Y, Morimoto J, Narumoto J, Shimada Y, Kasai K, Kato N, Takahashi H, Okamoto Y, Tanaka SC, Kawato M, Yamashita O, Imamizu H: Harmonization of resting-state functional MRI data across multiple imaging sites via the separation of site differences into sampling bias and measurement bias, *PLoS Biology*, **17(4)**: e3000042. (2019)

# Only 16 out of 9,730 FCs selected

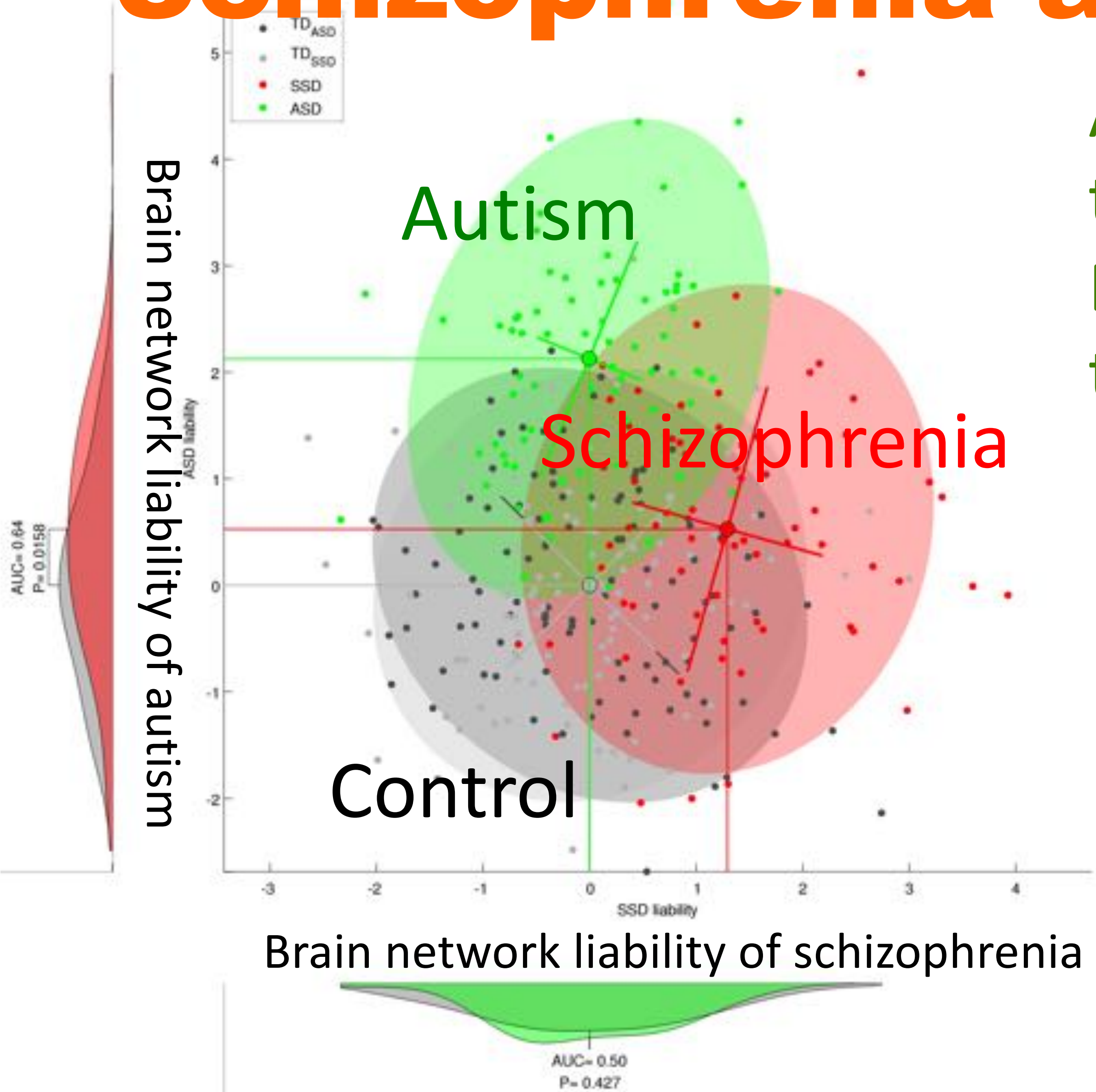



Yahata N, Morimoto J, Hashimoto R, Lisi G, Shibata K, Kawakubo Y, Kuwabara H, Kuroda M, Yamada T, Megumi F, Imamizu H, Nanez JE, Takahashi H, Okamoto Y, Kasai K, Kato N, Sasaki Y, Watanabe T, Kawato M : A small number of abnormal brain connections predicts adult autism spectrum disorder, *Nature Communications*, **7:11254**, (2016)

# Weighted linear summation of 16 fMRI functional connections classified ASD



# Schizophrenia and autism

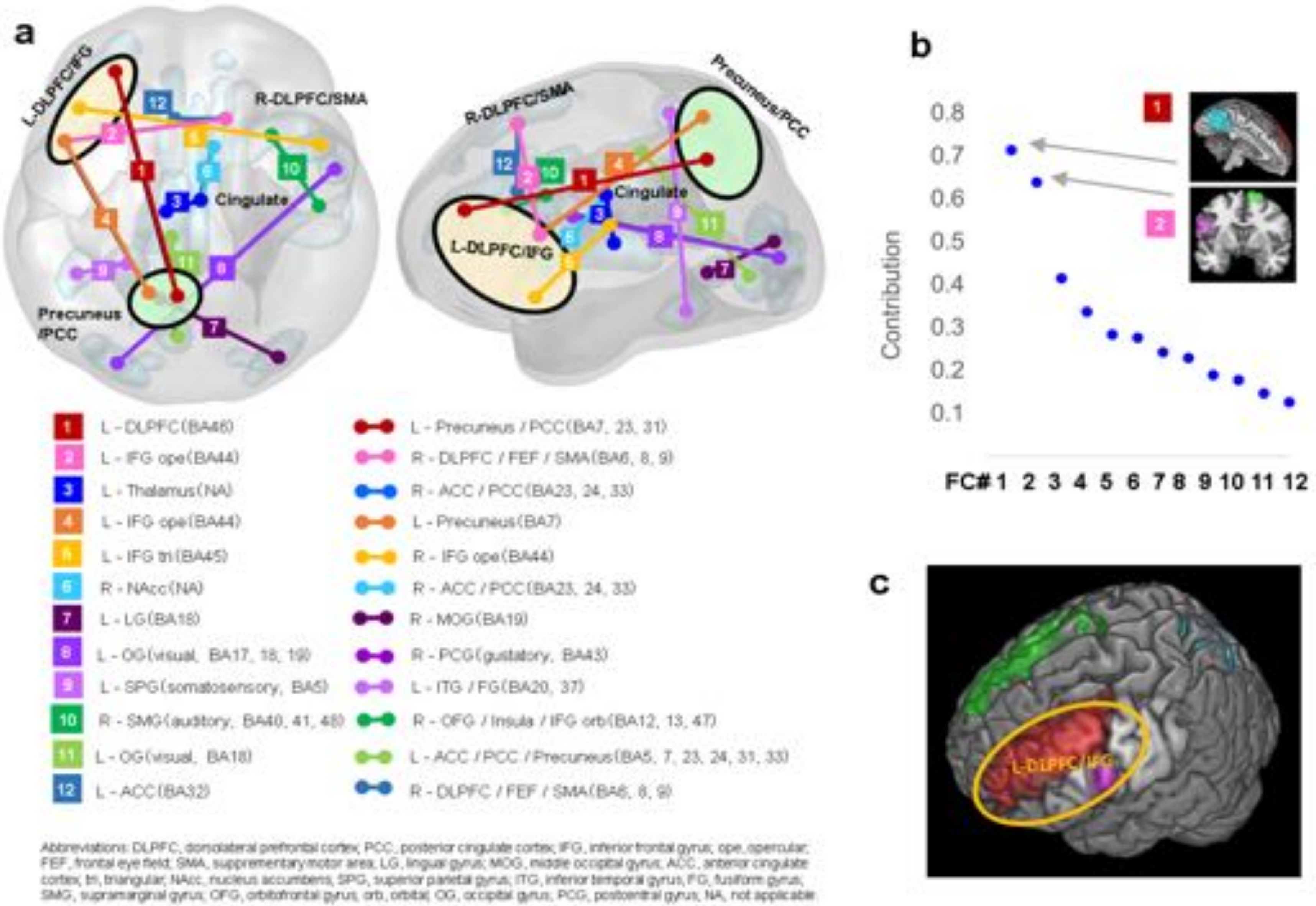



ASD and SSD regarded the same 80 years ago, DSM-III separated the two 40 years ago

ASD pathological connections are a subset of SSD pathological connections

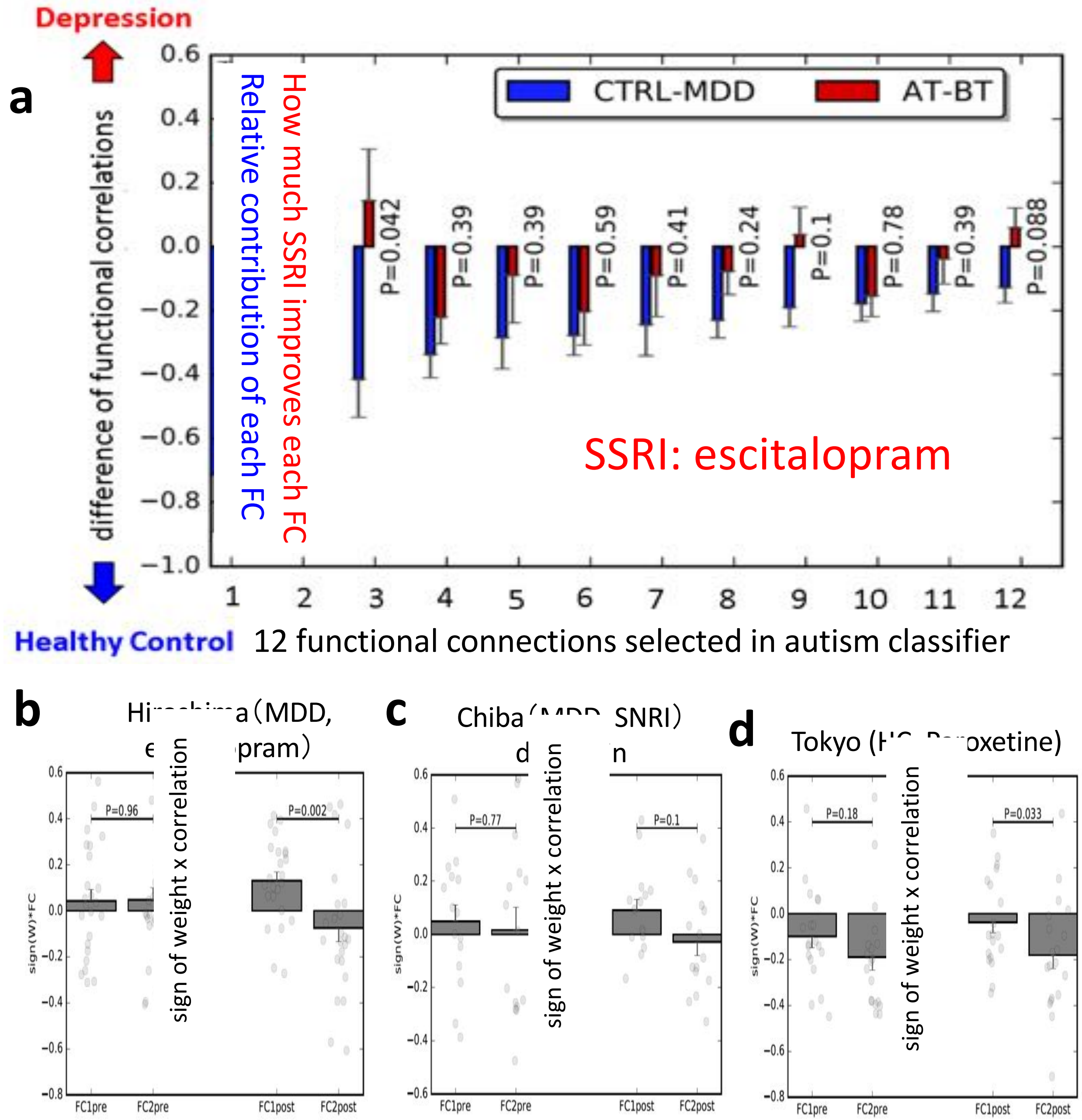
Yoshihara Y, Lisi G, Yahata N, Fujino J, Matsumoto Y, Miyata J, Sugihara G, Urayama S, Kubota M, Yamashita M, Hashimoto R, Ichikawa N, Cahn W, van Haren NEM, Mori S, Okamoto Y, Kasai K, Kato N, Imamizu H, Kahn RS, Sawa A, Kawato M, Murai T, Morimoto J & Takahashi H: Overlapping but asymmetrical relationships between schizophrenia and autism revealed by brain connectivity, *bioRxiv*, (2018)

# Circuit marker of melancholic depression



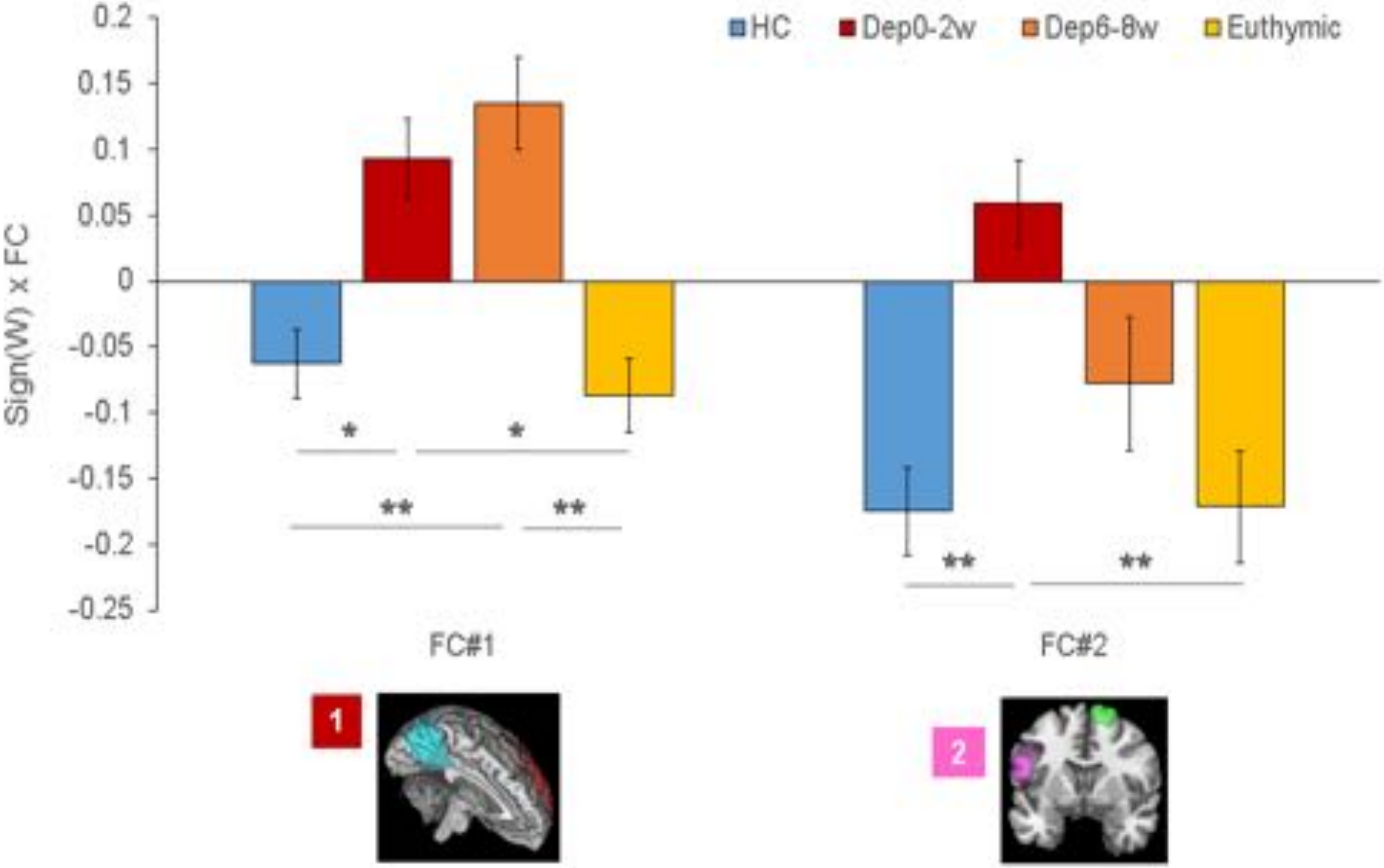

Ichikawa N, Lisi G, Yahata N, Okada G, Takamura M, Yamada M, Suhara T, Hashimoto R, Yamada T, Yoshihara Y, Takahashi H, Kasai K, Kato N, Yamawaki S, Kawato M, Morimoto J, Okamoto Y: Identifying melancholic depression biomarker using whole-brain functional connectivity, *arXiv.org*, **1704.01039** (2017)

# DLPFC-PDMN connection was worsened by anti-depressants treatments!!




SSRI or SNRI is not sufficient as a therapy for depression.
More specific treatment on DLPFC, such as r-TMS, neurofeedback or DBS, is suggested necessary.

# Functional connections of healthy participants and patients at 3 stages

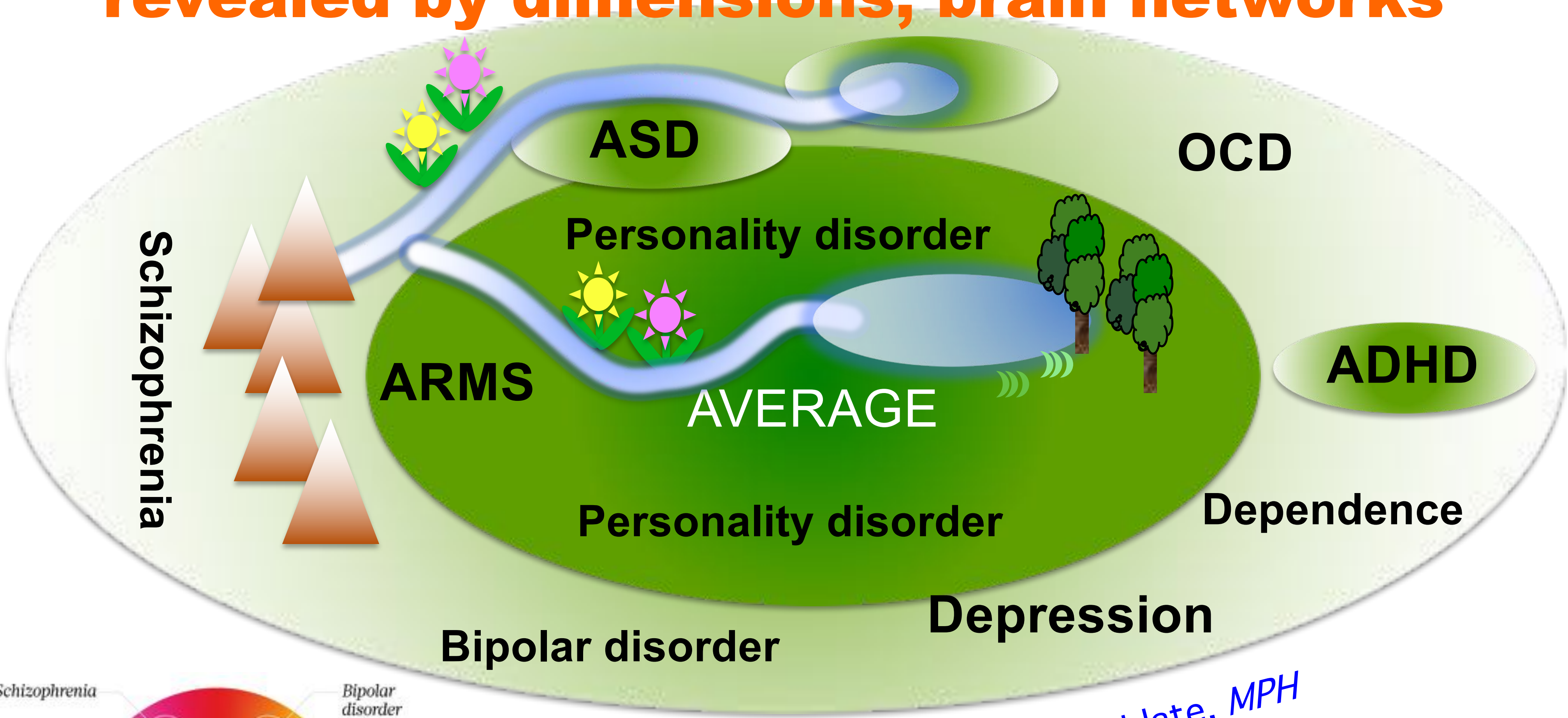



Ichikawa N, Lisi G, Yahata N, Okada G, Takamura M, Hashimoto R, Yamada T, Yamada M, Suhara T, Moriguchi S, Mimura M, Yoshihara Y, Takahashi H, Kasai K, Kato N, Yamawaki S, Seymour B, Kawato M, Morimoto J & Okamoto Y: Antidepressant modulation of the primary functional brain connections associated with melancholic major depressive disorder, *under second review* (2019)

# Starting from category and turning it into spectrum and subtyping

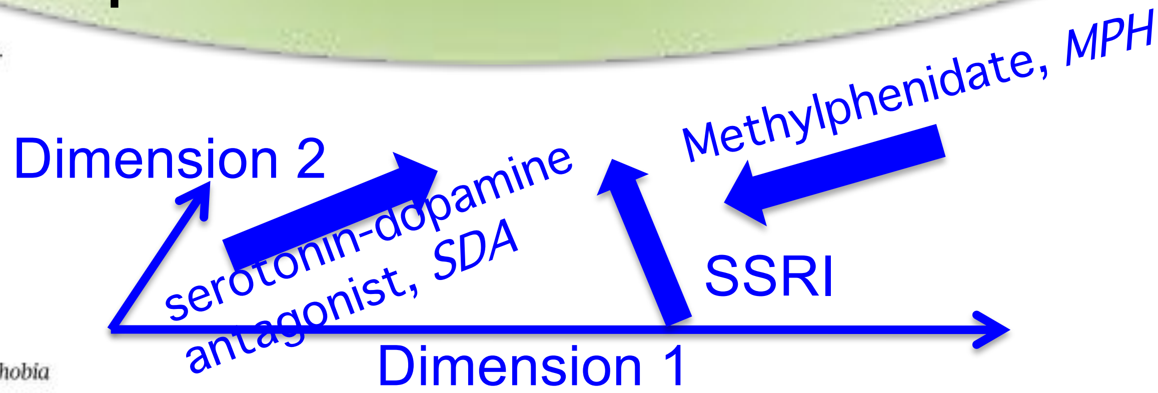
- Supervised machine learning with teaching signal provided as diagnosis by psychiatrists
- Sparseness to find a small number of functional connections (FCs) for classification
- Weighted linear summation of FCs define network liability and biological dimension useful for diagnosis, stratification, redefinition, drug evaluation, and selecting therapy target
- Precision medicine for each patient based on examination of many brain-network biomarkers

# Spectral relationships of many disorders revealed by dimensions; brain networks



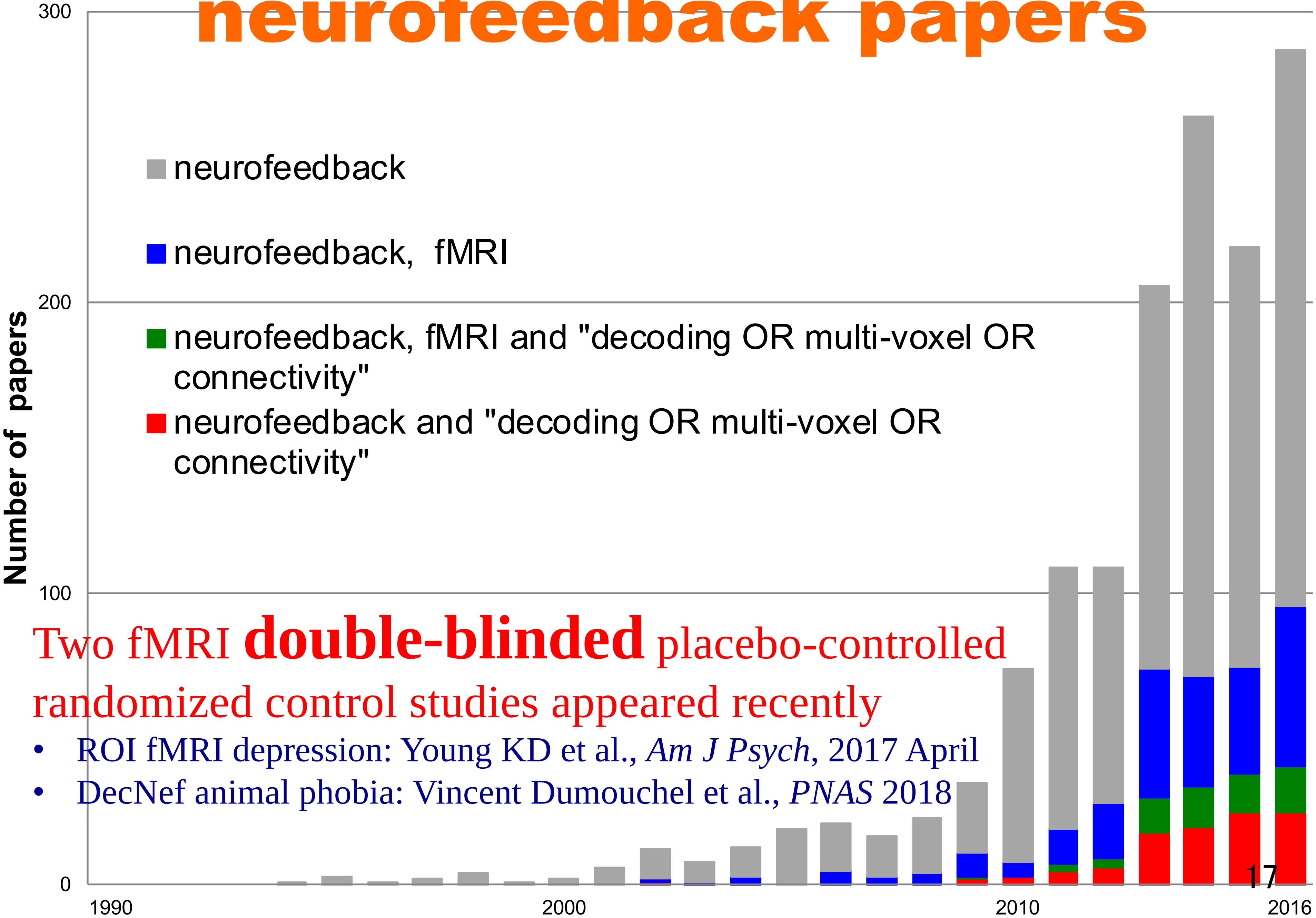


*Nature*, 24 April 2013




Estimated biological dimension as linear sum of the functional connectivity
Biological Dimension derived by Machine Learning from Big Data

# Rapid increase in numbers of neurofeedback papers

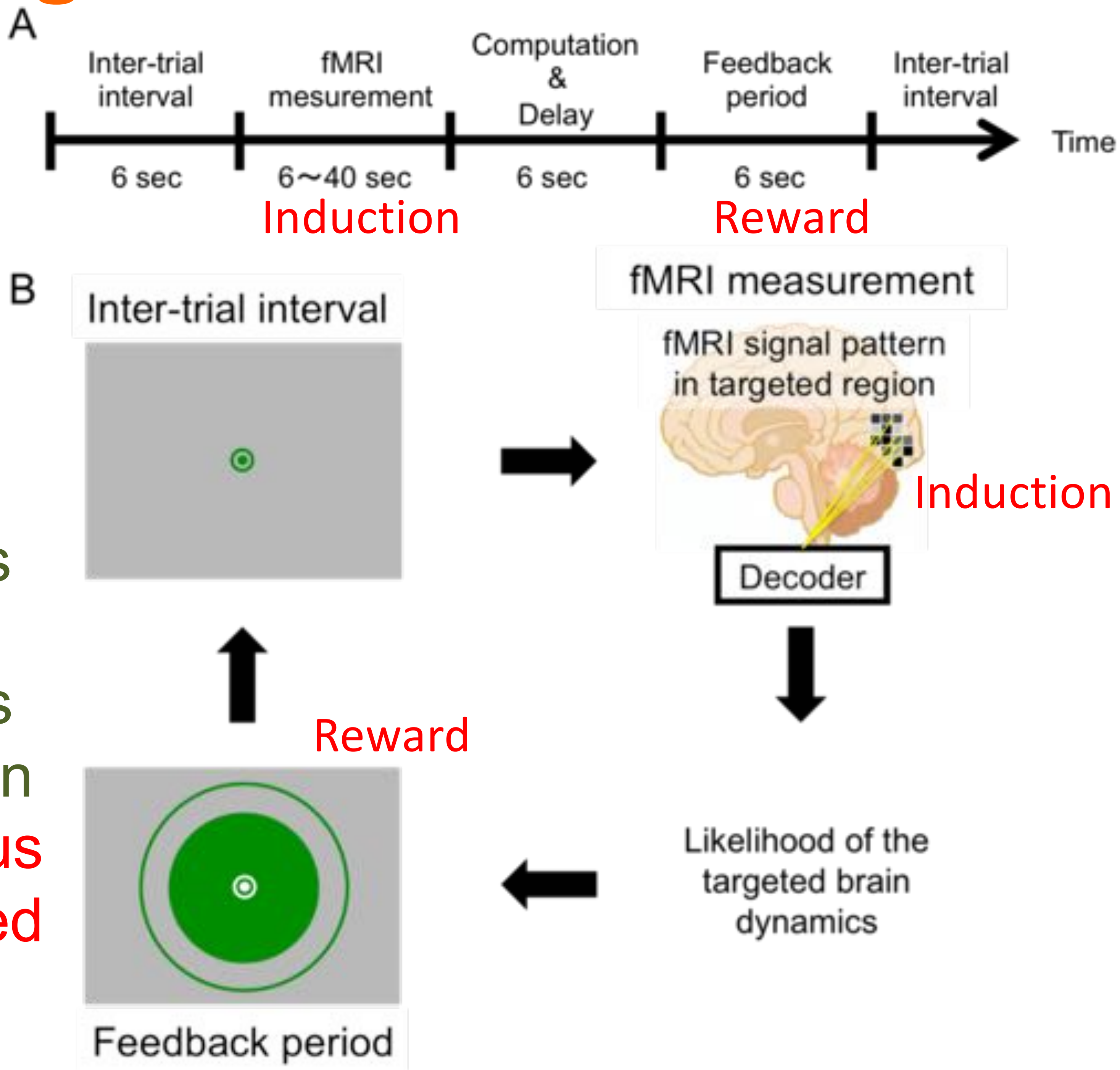



Two fMRI **double-blinded** placebo-controlled randomized control studies appeared recently

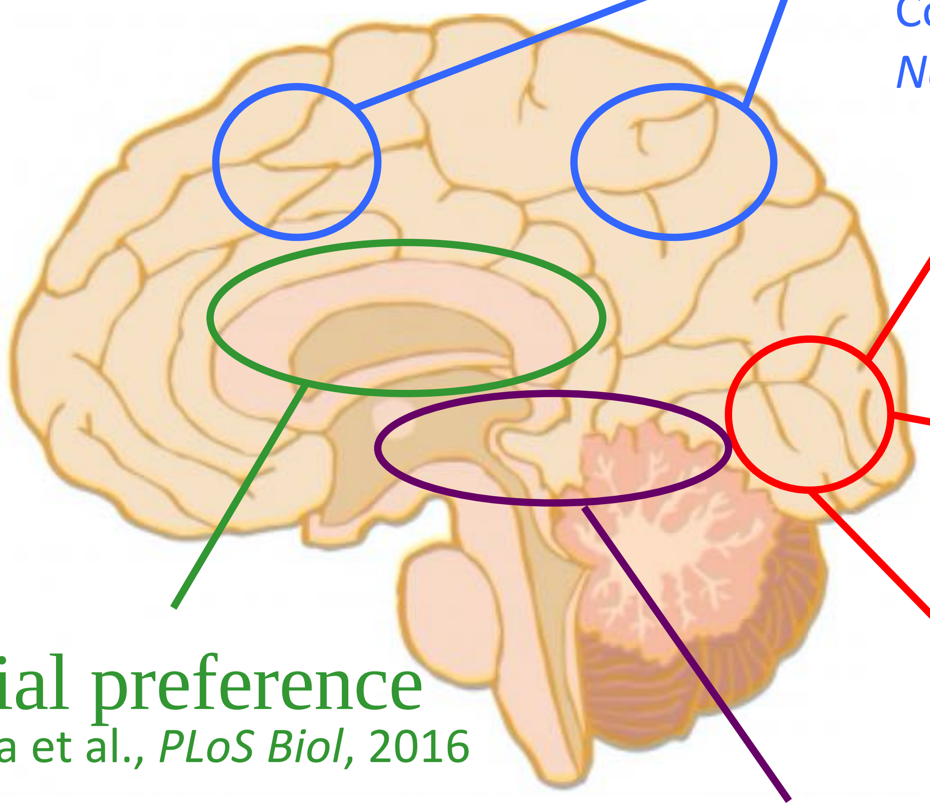
- ROI fMRI depression: Young KD et al., *Am J Psych*, 2017 April
- DecNef animal phobia: Vincent Dumouchel et al., *PNAS* 2018

# Trial design of DecNef and FCNef

- Decoding or functional connectivity
- Terminal monetary reward
- 50~200 trials per day
- Several days
- No instruction
- Not conscious about induced information



# Different information in different areas can be manipulated by DecNef



Metacognition(confidence)
Cortese et al., *Nat Commun*, 2016; *NeuroImage*, 2017

Visual perceptual learning
Shibata et al., *Science*, 2011

Association of color and orientation
Amano et al., *Current Biology*, 2016

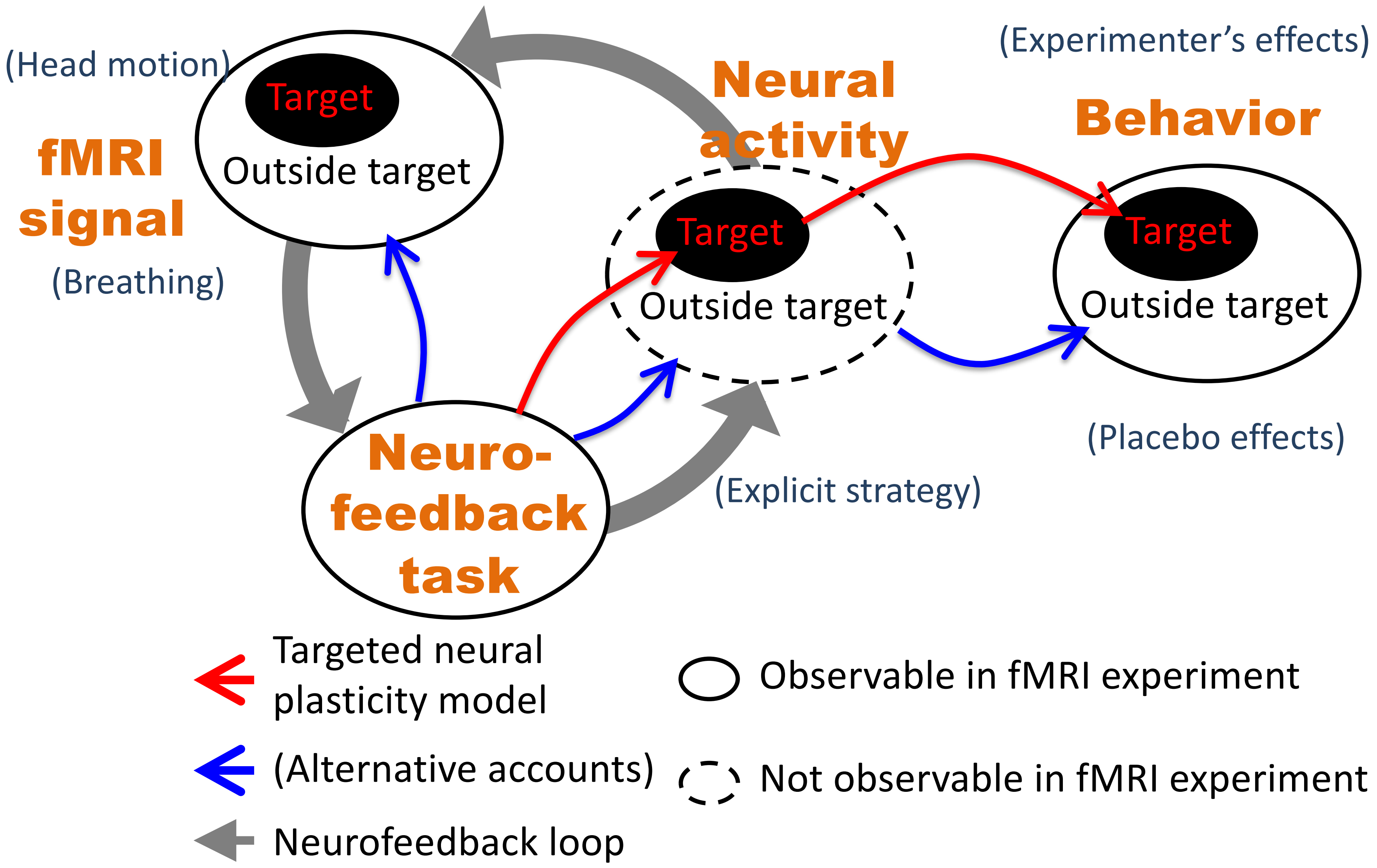
Fear memory extinction
Koizumi et al., *Nat Hum Behav*, 2016

Facial preference
Shibata et al., *PLoS Biol*, 2016

Intervention for animal phobia (double blind RCT)
Taschereau-Dumouchel et al., *PNAS*, 2018

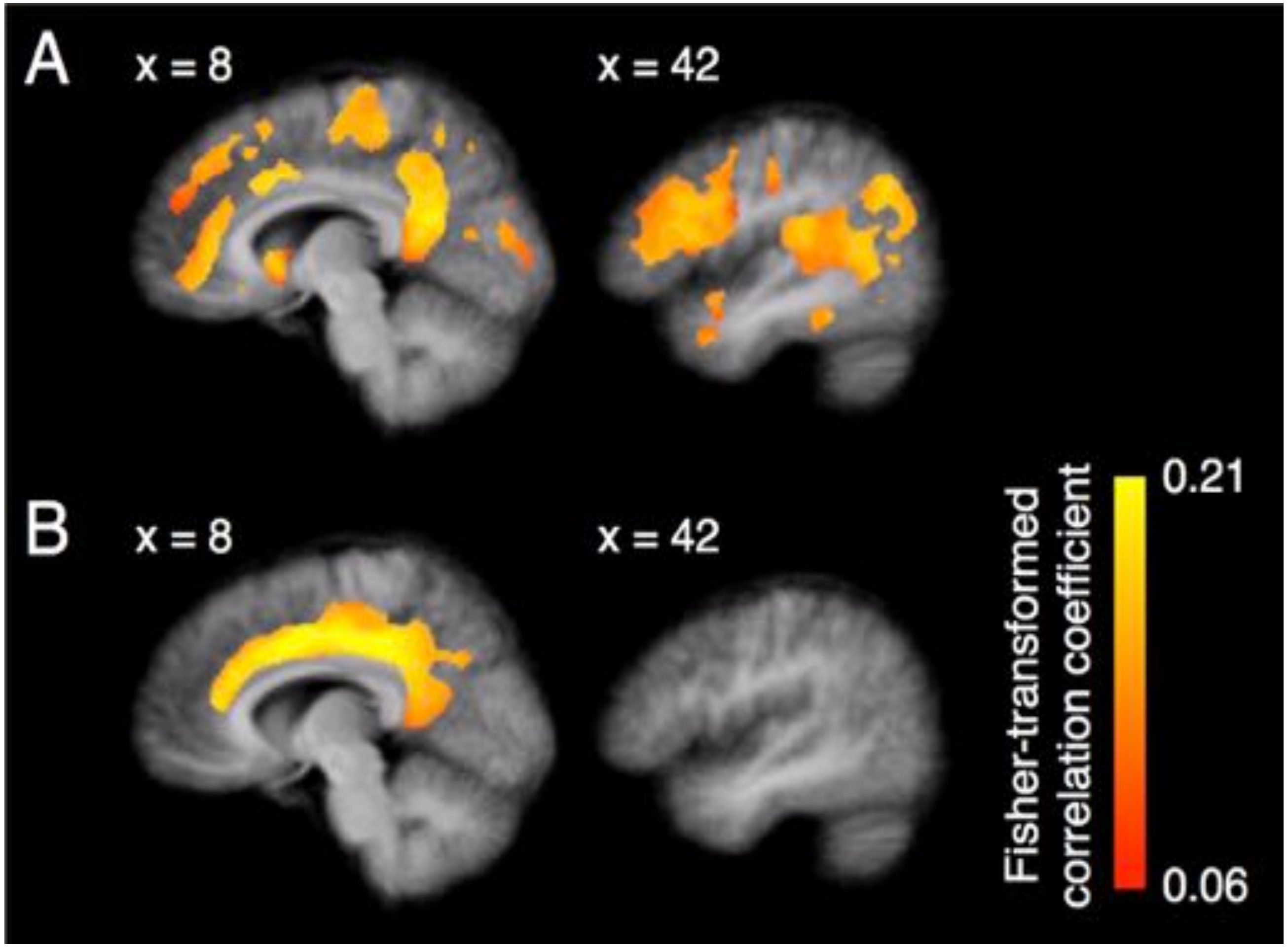
Watanabe T, Sasaki Y, Shibata K, Kawato M: Advances in fMRI real-time neurofeedback, *Trends in Cognitive Sciences*, **21(12)**, 997-1010 (2017)

# Targeted neural plasticity model




Shibata K, Lisi G, Cortese A, Watanabe T, Sasaki Y, Kawato M: [Toward a comprehensive understanding of neural mechanisms of decoded neurofeedback](), *NeuroImage*, **188**, 539–556 (2018)

# Little information leak of facial preference from CC to other regions




A: decoder construction, B: DecNef induction

Shibata K, Watanabe T, Kawato M, Sasaki Y: Differential activation patterns in the same brain region led to opposite emotional states, *PLoS Biology*, **14(9)**: e1002546 (2016)

# Human causal systems neuroscience with DecNef

- DecNef is versatile and efficient in manipulating different cognitive functions of various brain regions with good effect sizes
- DecNef is a neural operant conditioning combined with decoding technique
- fMRI-MVP PCA and ring-attractor network simulation suggest that spontaneous and target neural activity is reinforced
- DecNef is better than optogenetics for several aspects including human usage, spatiotemporal control, derived from hundreds of brain activity patterns, information specified by decoding.

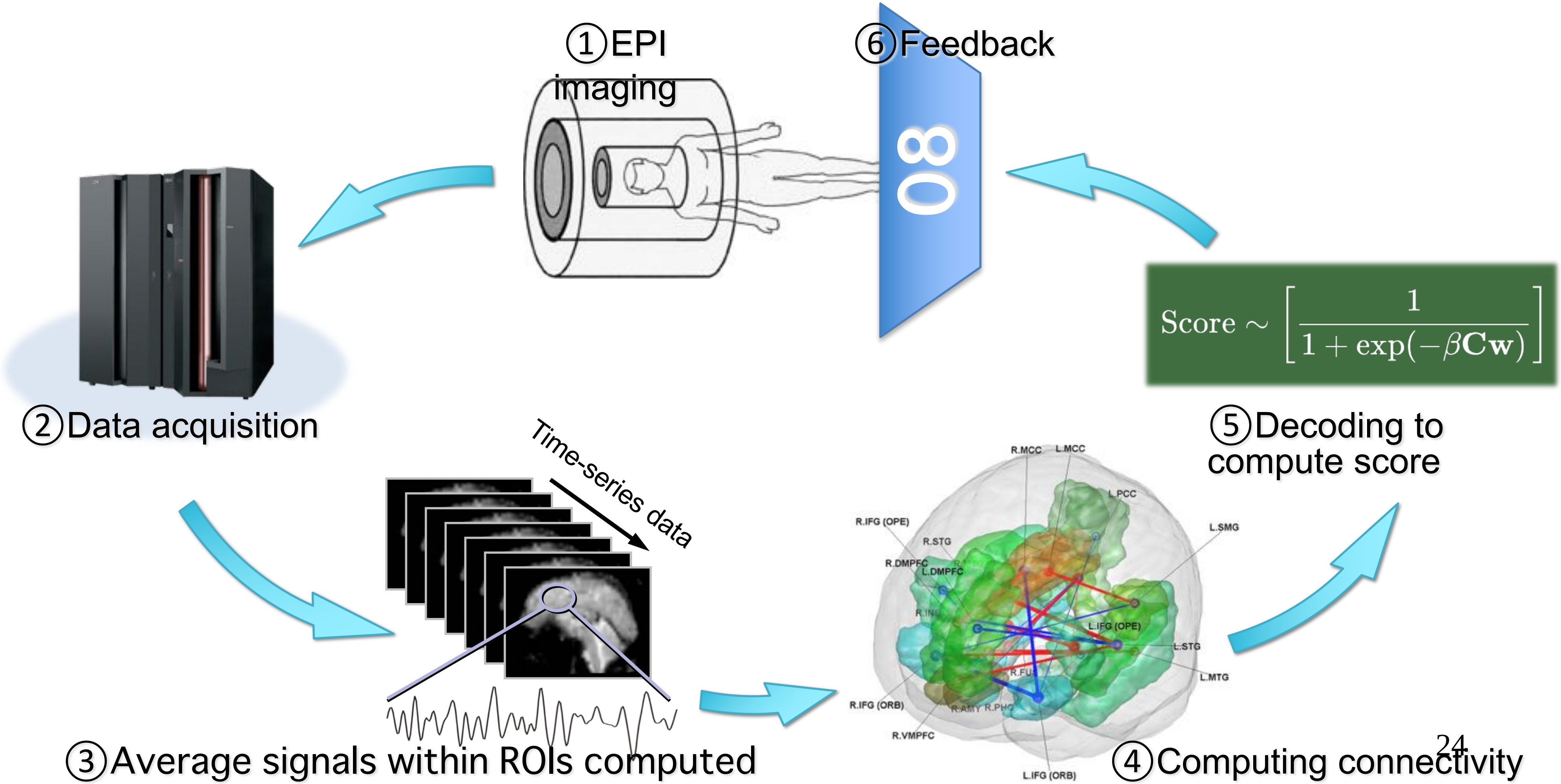
# Medium, large even huge effect sizes (Cohen's $D_z$) on brain and behavior changes

| Year | Reference | Population | Method | Target brain area/connectivity | Purpose of neurofeedback training | Change in neurofeedback scores? (effect size of major results) | Behavioral change? (effect size of major results) | Correlation between neural and behavioral changes? |
|---|---|---|---|---|---|---|---|---|
| 2011 | Shibata et al. [1] | Normal | DecNef | Early visual cortex | To test if inductions of activations in the early visual cortex lead to visual perceptual learning of an orientation | Yes (1.06) | Perceptual learning of an orientation occurred (1.77) | Significant (r = 0.87) |
| 2015 | Megumi et al. [2] | Normal | FCNef | Parietal and motor cortices | To test if FCNef is capable of inducing long-term increase in a target connectivity | Yes (0.69) | Behavioral measurements were not conducted in this study | N/A |
| 2016 | Amano et al. [3] | Normal | DecNef | Early visual cortex | To test if the early visual cortex is capable of associative learning of an orientation and color | Yes (2.14) | Associative learning of an orientation and red color occurred (1.07) | N/A |
| 2016 | Shibata et al. [4] | Normal | DecNef | Cingulate cortex | To test if inductions of activations in the cingulate cortex increase and decrease preferences to faces | Yes for increase (1.17) and decrease (0.70) groups | Preferences to faces increased (1.38) and decreased (0.96) | Significant (r = 0.78) |
| 2016 | Koizumi et al. [5] | Normal | DecNef | Early visual cortex | To test if pairings of monetary reward and activations of the early visual cortex lead to counter-conditioning of fear memory | Yes (0.53) | Skin conductance response to a fear-associated stimuli decreased (0.64) | N/A |
| 2016 | Cortese et al.[b] [6] | Normal | DecNef | Parietal and frontal cortices | To test if inductions of activations in the parietal and frontal cortices increase and decrease perceptual confidence | Yes for increase (1.50) and decrease (1.34) groups | Confidence in a visual task increased (1.15) and decreased (0.47) | Significant (r = 0.68) |
| 2017 | Yamada et al. [7] | Major depression | FCNef | Middle frontal gyrus and precuneus | To test if FCNef on abnormal connectivity for patients with major depression ameliorates severity of depression | Yes (2.22) | Hamilton depression rating scale improved (1.52) | Significant (r = 0.87) |
| 2017 | Yamashita et al. [8] | Normal | FCNef | Parietal and motor cortices | To test if changes in a target connectivity lead to changes in reaction times in a visual task | Yes (0.22) | Changes in reaction times in a color-word stroop task were different between increase and decrease groups (0.37) | Significant (adjusted $R^2$ = 0.22) |
| 2018 | Taschereau-Dumouchel et al. [9] | Phobia | DecNef | Ventrotemporal cortex | To test if pairings of monetary reward and activations of the ventrotemporal cortex reduce fear to a specific object category | Yes (0.60) | Skin conductance response to a fearful category decreased (0.56) | N/A |

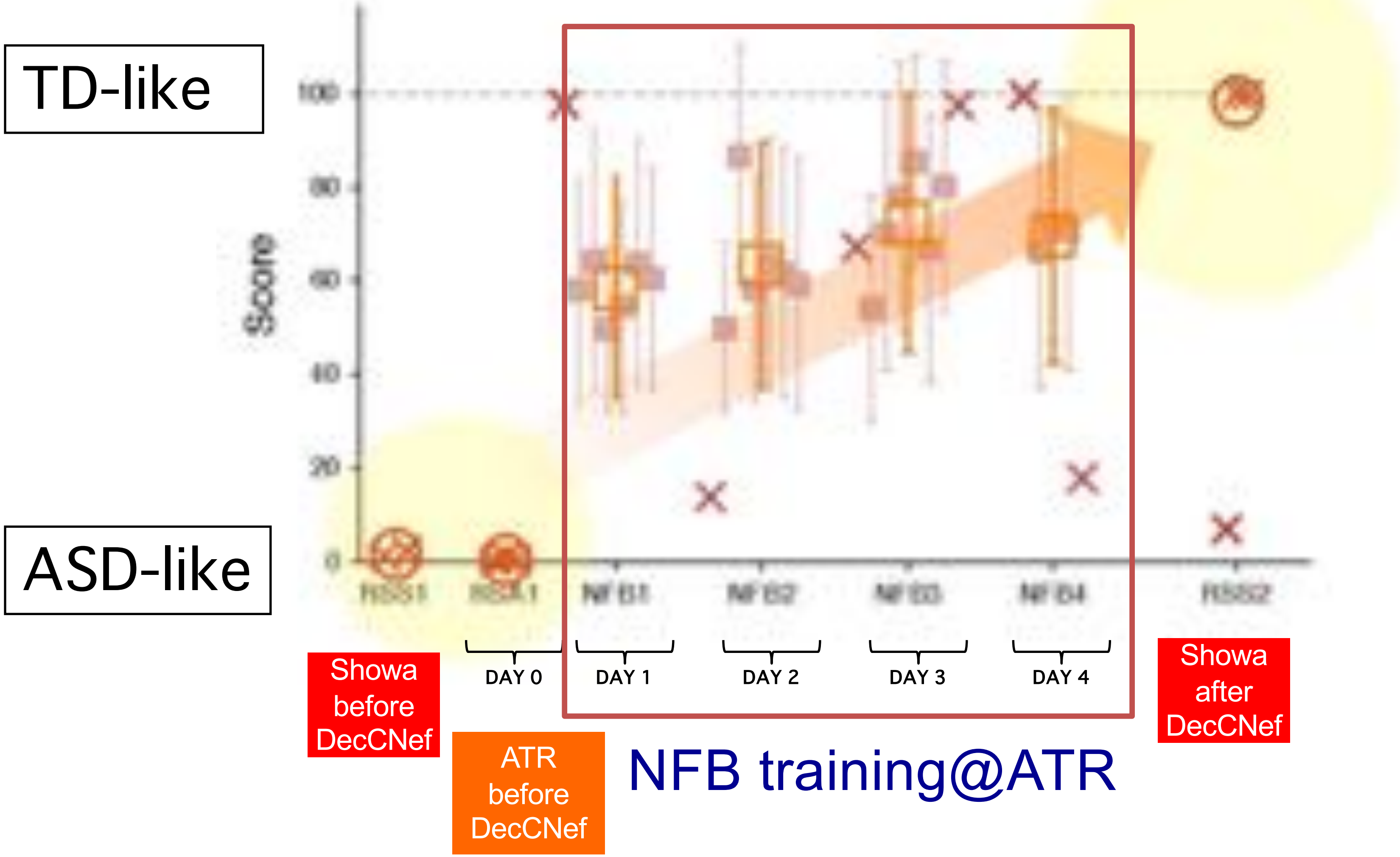
Watanabe T, Sasaki Y, Shibata K, Kawato M:Advances in fMRI real-time neurofeedback. *Trends in Cognitive Sciences*, **21(12)**, 997-1010 (2017) & https://bicr.atr.jp/decnefpro/

# Biomarker and data-driven FCNef application to mental disorder therapy

- NF score computed by rs-fcMRI based biomarker
- Larger reward for healthier network dynamics



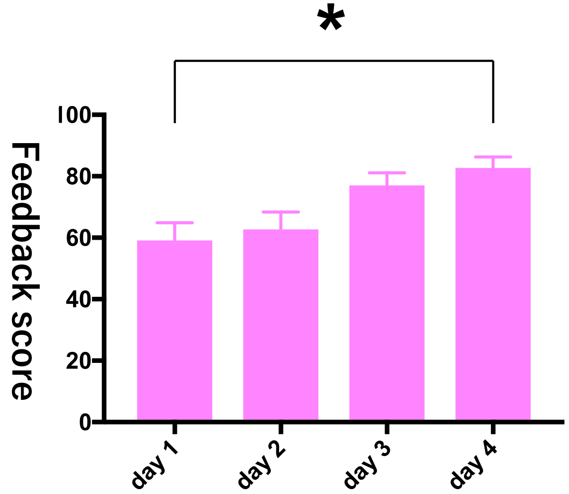
# Improvement of ASD liability estimated by rs-fcMRI biomaker after FCNef



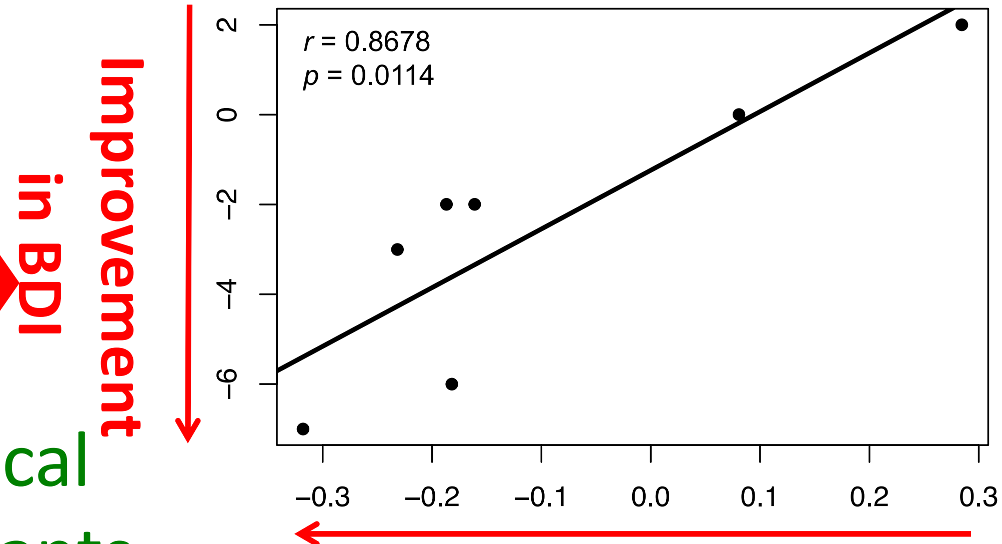

Yamada T, Hashimoto R, Yahata N, Ichikawa N, Yoshihara Y, Okamoto Y, Kato N, Takahashi H, Kawato M: Resting-state functional connectivity-based biomarkers and functional MRI-based neurofeedback for psychiatric disorders: a challenge for developing theranostic biomarkers. *Int J Neuropsychopharm*, **20,** 769-781. (2017)

# FCNef normalized abnormal positive functional connection between left dorsolateral prefrontal cortex and left precuneus in major depression

## Success in NF training



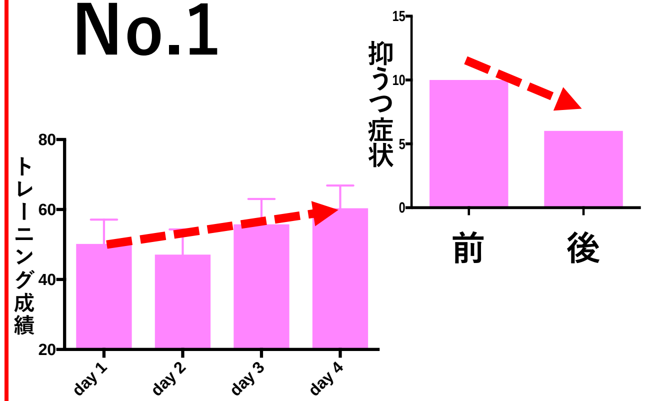

Subclinical participants



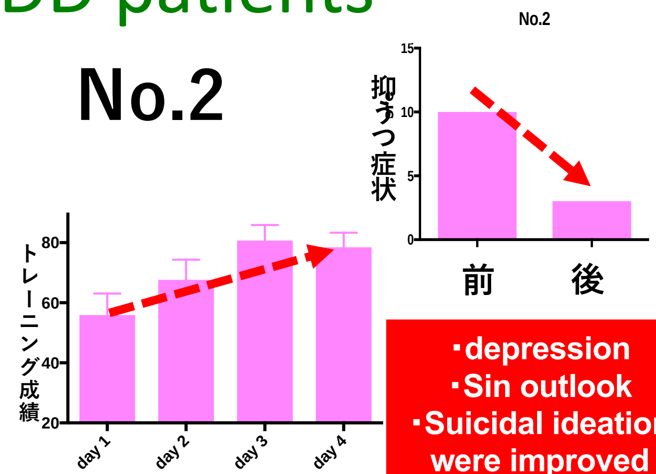

Improvement in FC

## Therapy resistant MDD patients

### No.1



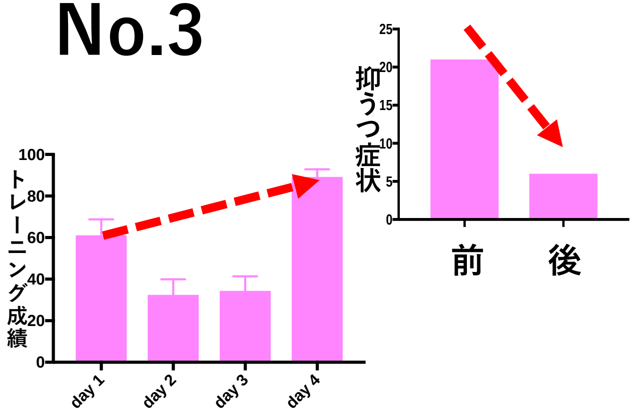

### No.2




- depression
- Sin outlook
- Suicidal ideation

were improved

### No.3



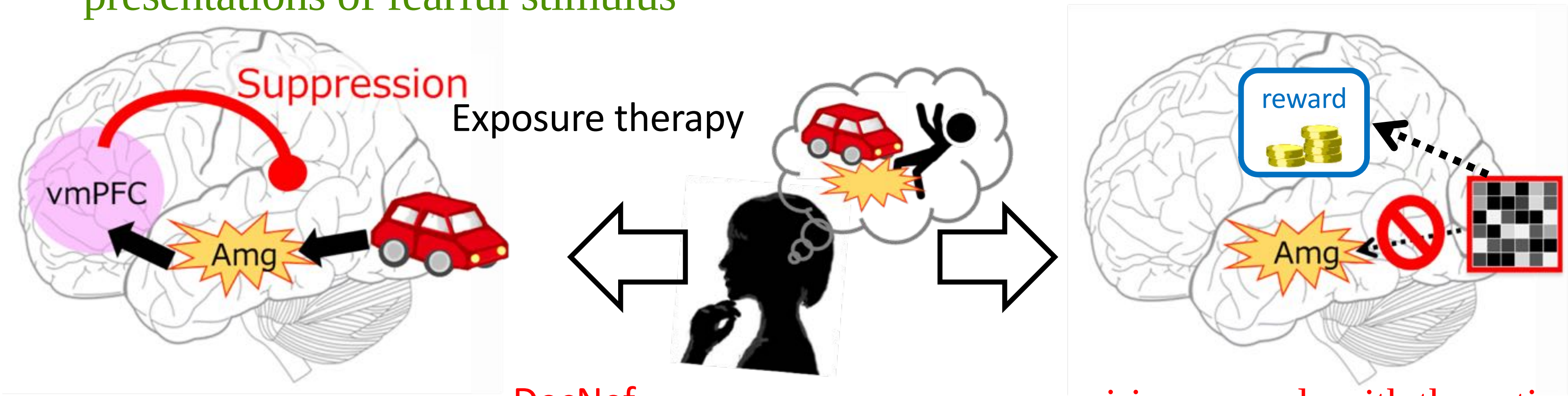



Yamada T, Hashimoto R, Yahata N, Ichikawa N, Yoshihara Y, Okamoto Y, Kato N, Takahashi H, Kawato M: Resting-state functional connectivity-based biomarkers and functional MRI-based neurofeedback for psychiatric disorders: a challenge for developing theranostic biomarkers. *Int J Neuropsychopharm*, **20**, 769-781. (2017)

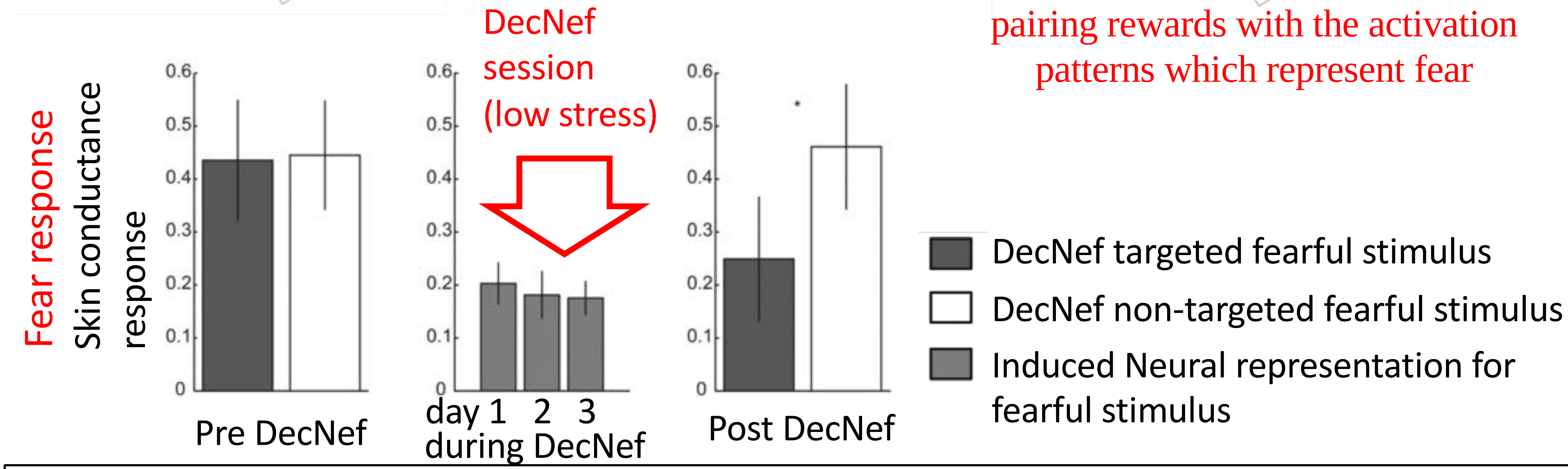
# DecNef reduced responses to fear-conditioned stimulus without conscious exposure

Conventional fear reduction by explicit presentations of fearful stimulus

Fear reduction using DecNef



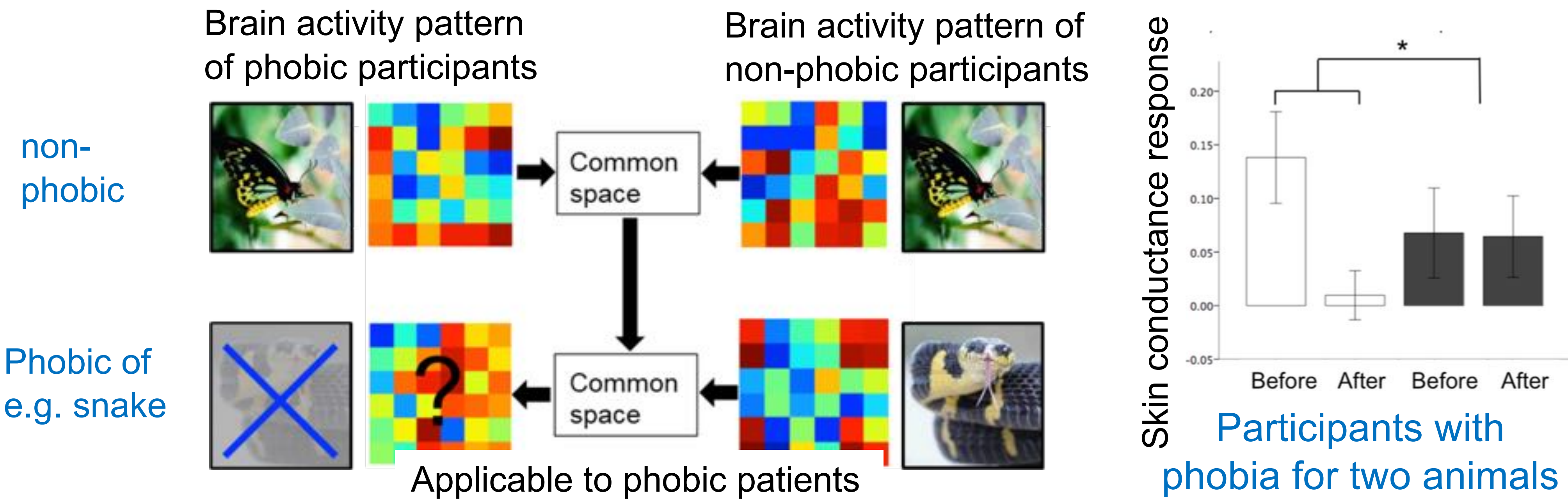

pairing rewards with the activation patterns which represent fear




Koizumi A, Amano K, Cortese A, Shibata K, Yoshida W, Seymour B, Kawato M, Lau H. Fear reduction without fear through reinforcement of neural activity that bypasses conscious exposure. *Nature Human Behaviour*, **1, e0006** (2016)

# DecNef reduced animal-phobic responses without exposure to feared animals

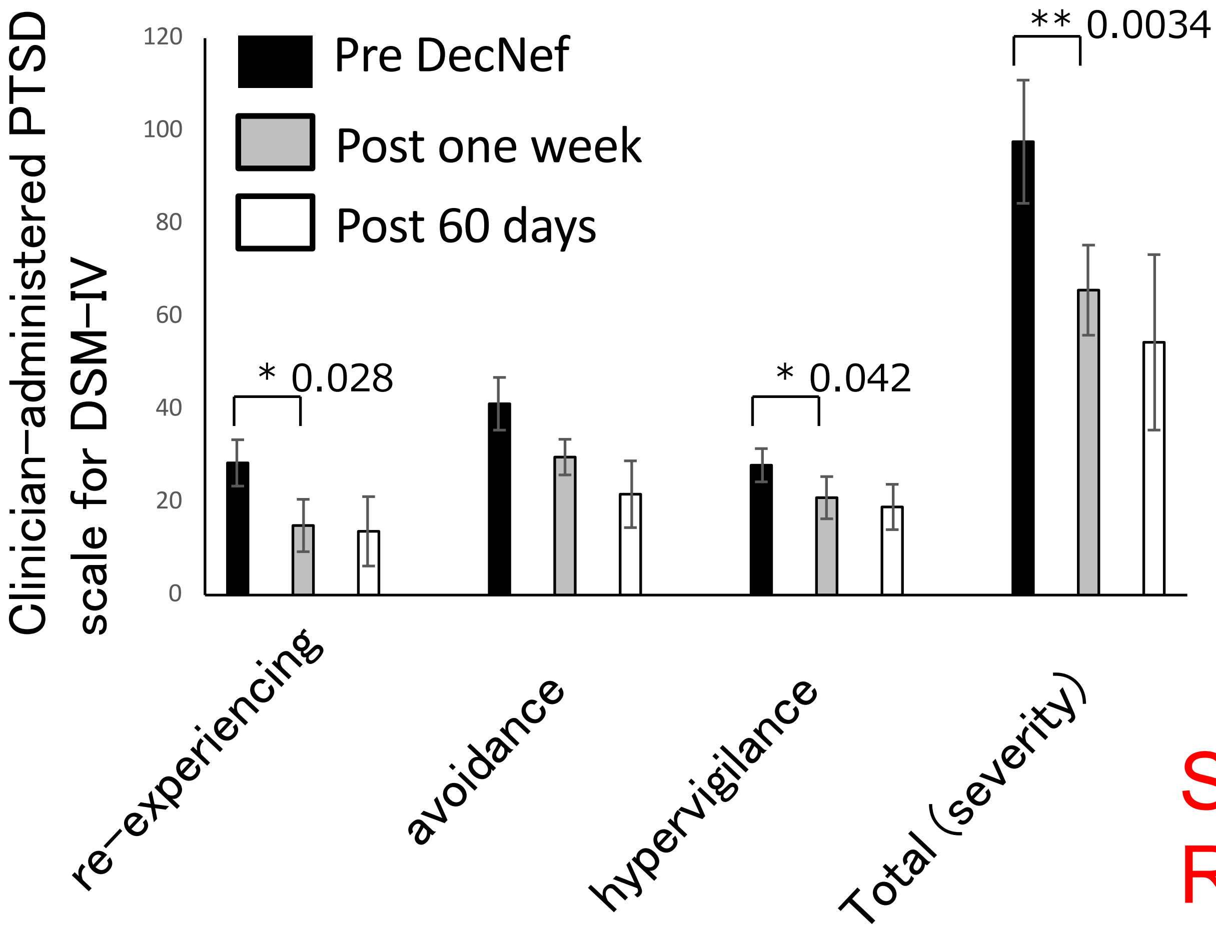
- Translation of DecNef to anxiety disorders including PTSD
- Decoder construction based on brain activities of non-phobic participants by hyperalignment while avoiding presentation of fearful stimuli to phobic participants
- Success of double-blinded RCT (target animal was known to neither participant or experimenter) disproves any placebo effect




Taschereau-Dumouchel V, Cortese A, Chiba T, Knotts JD, Kawato M, Lau H. Towards an unconscious neural reinforcement intervention for common fears. *Proc Natl Acad Sci U S A.* **115(13),** 3470-3475 (2018)

# DecNef intervention for PTSD patients

PTSD severity scales significantly decreased one week, as well as 60 days, after DecNef intervention.

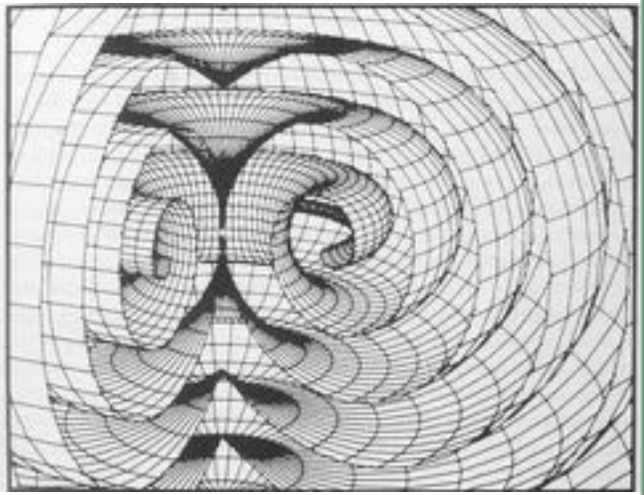


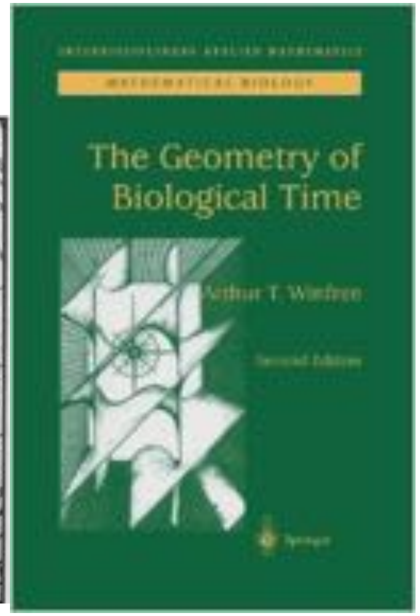

Single blinded RCT is on going

Chiba T, Kanazawa T, Koizumi A, Ide K, Taschereau-Dumouchel V, Boku S, Hishimoto A, Shirakawa M, Sora I, Lau HC, Yoneda H, and Kawato M. Current status of neurofeedback for Post-traumatic stress disorder: a systematic review and the possibility of decoded neurofeedback, *Frontiers in Human Neuroscience*, **13(233)**, https://doi.org/10.3389/fnhum.2019.00233 (2019)

# Dynamical disease

*Nature*. 1984 Oct 18-24;**311(5987)**:611-5.
Organizing centres for three-dimensional chemical waves.
Winfree AT, Strogatz SH.






## Arthur Winfree (1942-2002)

**Heart, Sudden death, Chaos**

*Sci Am* 1983 **248**: 144-9
Sudden cardia death: a problem in topology

## Leon Glass

~1992 Dynamical diseases
*Chaos* (1995)
*Chaos* (2015)

Kawato M, Fujita K, Suzuki R, Winfree AT: *Journal of Theoretical Biology*, **98,** 369-392 (1982).

Kawato M, Suzuki R: Biological oscillators can be stopped -topological study of a phase response curve. *Biological Cybernetics,* **30,** 241-248 (1978).

# Proposal of topics

- Reproducible, causal and computational psychiatry based on multi-disorder and multi-site "big" data, as well as multi-scale modeling
- Functional connectivity is just a convenient and tentative tool, thus next, multi-scale data assimilation and computational modeling for quantifying abnormal dynamics should come
- Redefining causality in neuroscience by DecNef; certain brain dynamical attractors cause specific cognitive processes and/or mental disorders
- Neuroscience understanding of learning from a small sample; future AI such as conscious robots based on revealed neural mechanisms

# Brain Modeling Strategies

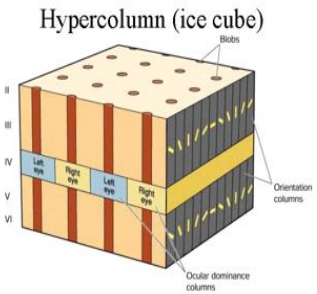
| Models | Single Neuron | Local Circuit | Brain Part | Whole Mouse/Marmoset Brain | Whole Human Brain | Aims |
|---|---|---|---|---|---|---|
| Functional | | | TD Learning | | AI<br>CogSci | Computation Principles |
| Rate Coding | | | basal ganglia model | | Deep Learning<br>*What We Need!* | Brain-like Algorithms |
| Spiking | | K | Post-K | Fugaku | Nengo | Dynamics Flexibility Low energy |
| Biophysical | HH<br>Neurc<br>MOOSE | Blue Brain | | | | Genetic mechanisms Molecular targets |
| | dendrites, spines | retina, column, pattern generator, spinal controller | cortex, thalamus basal ganglia cerebellum | perception, control, navigation, communication | dexterity, mental simulation, language | |

by Kenji Doya

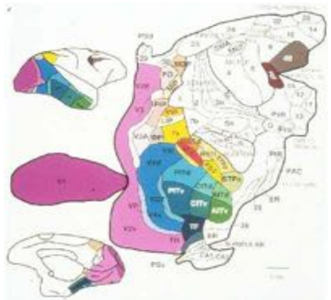
# マルチスケールにまたがる脳の統合的理解

ニューロン

カラム

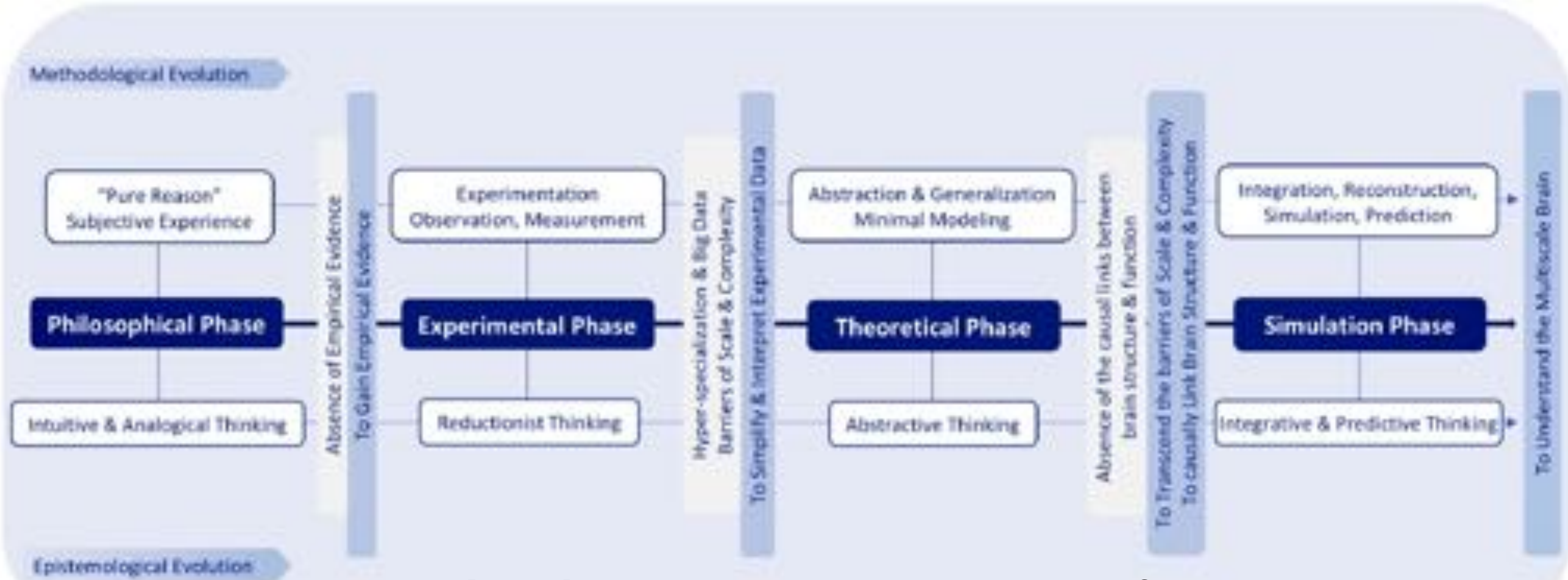



領野



全脳

10μm　100μm　1 cm　10cm



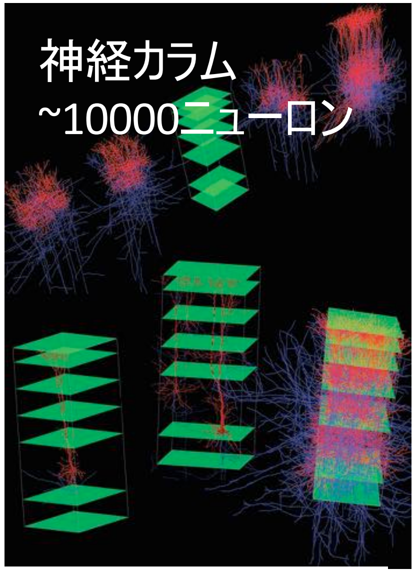

Fan and Markram 2019, *Frontiers in neuroinfomatics*

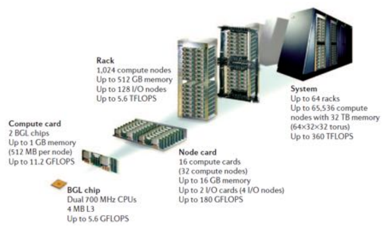
by Okito Yamashita

# 神経細胞レベルのシミュレーション

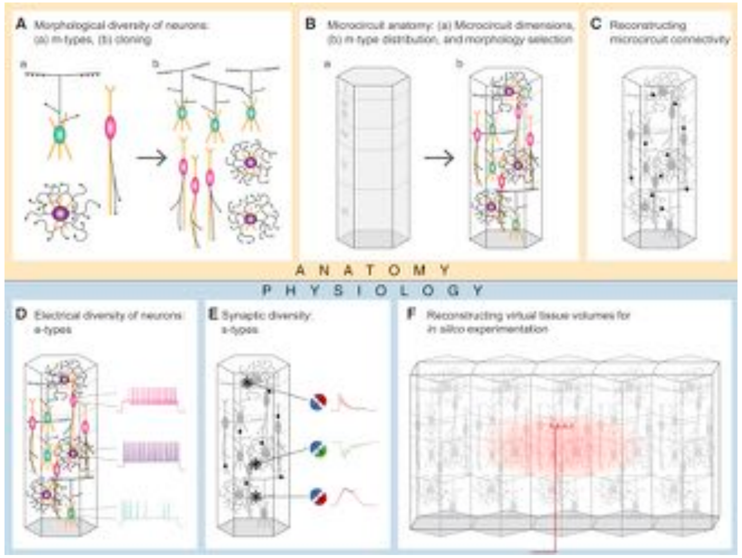
神経細胞1個1個の形、結合、配置を実験データを元に忠実にデジタル再現し、スパコンを用いたダイナミクスのシミュレーション

**Blue brain project**



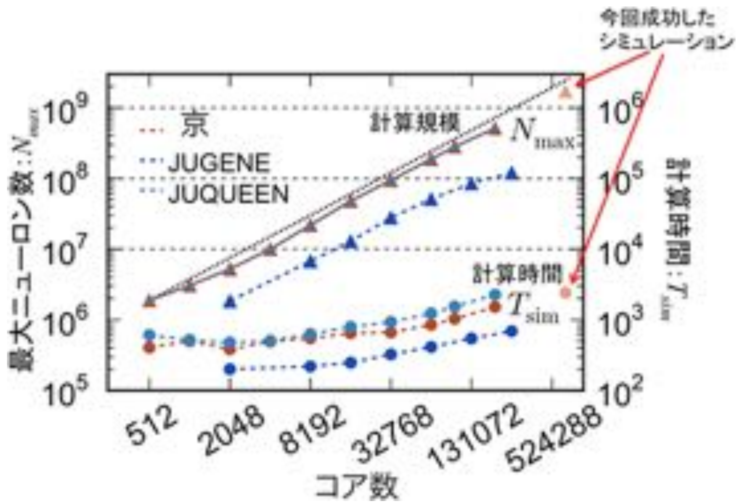



マウス体性感覚野
31000ニューロン、800万結合




Markram 2005, *Nature reviews neuroscience*,
Markram 2015, *Cell*

**理研京コンピュータ**



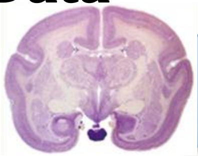

17億ニューロン
10兆結合

Kunkel et al. 2014,
*Frontiers in Neuroinfomatics*

by Okito Yamashita

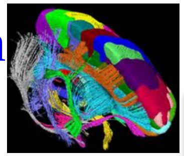
# Multiscale Brain Data Assimilation

## Anat./Phys. Data



structural MRI
diffusion MRI
resting/task fMRI

NIRS/EEG/MEG
ECoG

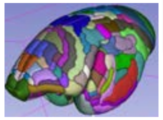


transparent brain
neural tracers
LFP
electrode arrays
$Ca^{2+}$ imaging

molecular imaging
serial section EM

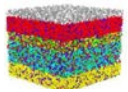
## Multiscale Models

**Functional Models**
<u>Behavior/Cognition</u>

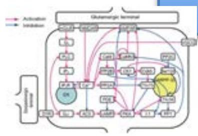


**Rate Coding Models**
<u>Representation/Algorithm</u>

*constraint* *prior*



**Spiking Models**
<u>Dynamic computation</u>



**Biophysical Models**
<u>Cellular mechanisms</u>

## Discovery/Impact

Principle of computation
Prediction of failures

Scalable algorithms
Diagnosis/prognosis

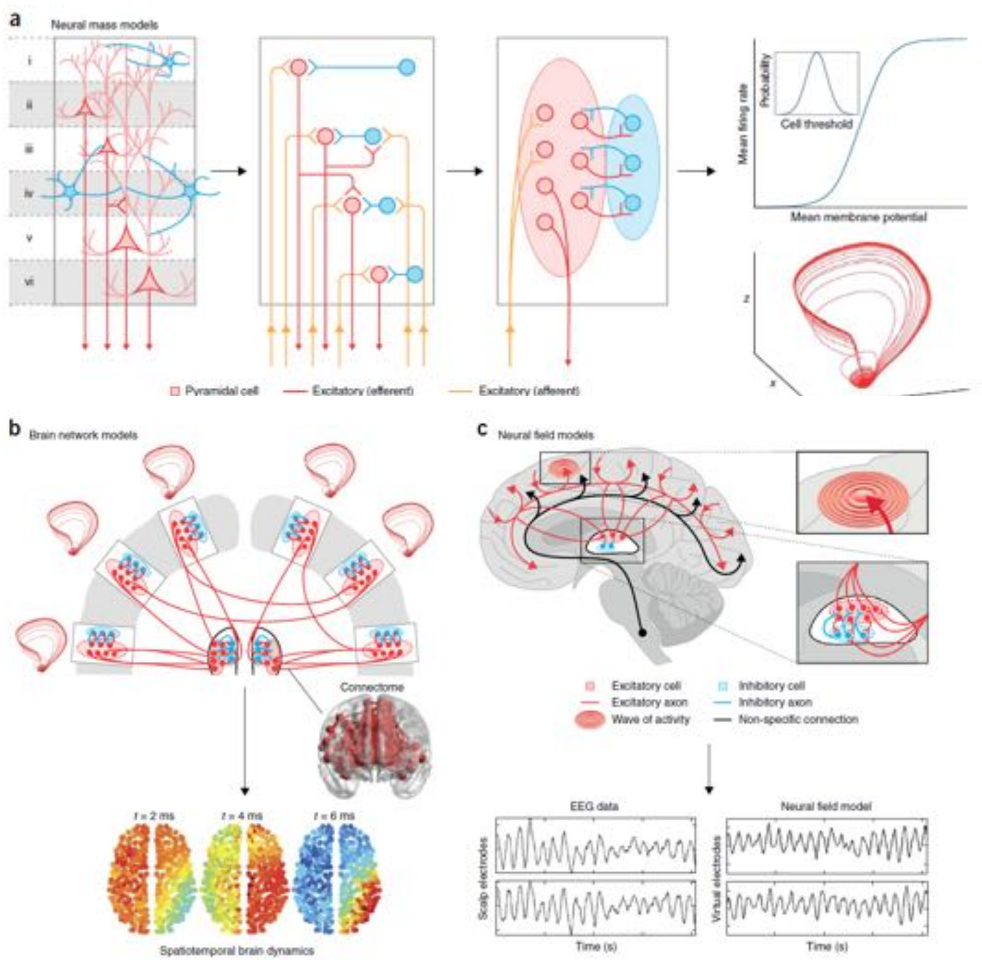
Flexibility/robustness
Low-energy computation

Physical computing
Genetic mechanisms
Therapeutic targets

by Kenji Doya

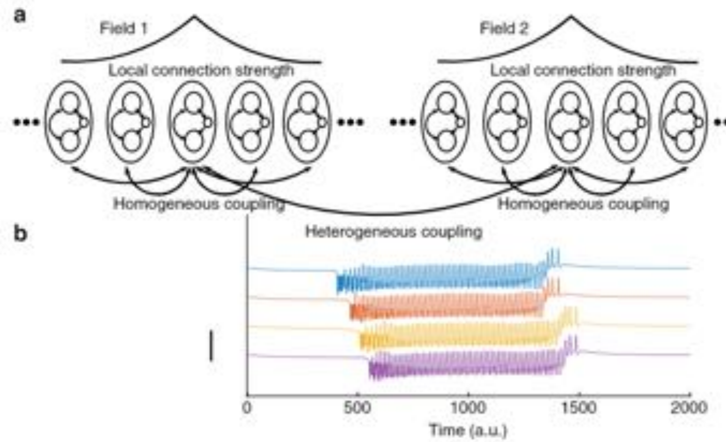
# 領野レベルのシミュレーション

平均場近似により得られる神経集団モデルと全脳解剖結合を用いたシミュレーションによる、マクロスケールな脳活動データ再現




Breakspear 2017, *Nature Neuroscience*

てんかん発作の多様な伝播波の
統一的なメカニズムを提唱



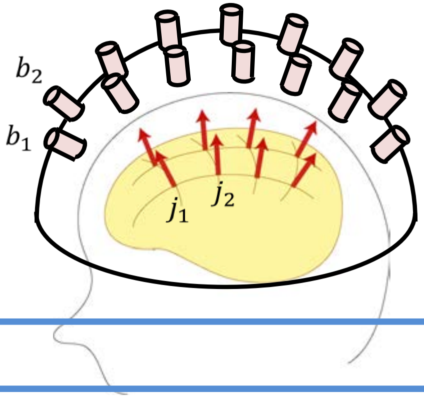

Proix et al. 2018, *Nature Commun*.

安静時脳ネットワーク・α波
麻酔・睡眠のメカニズム解明など

by Okito Yamashita

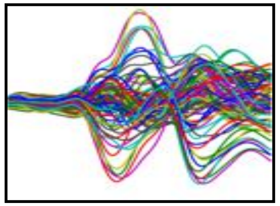
# データ同化と脳ネットワークダイナミクスモデリングの融合による意識生成メカニズムの解明

**観測モデル**　電磁気の法則



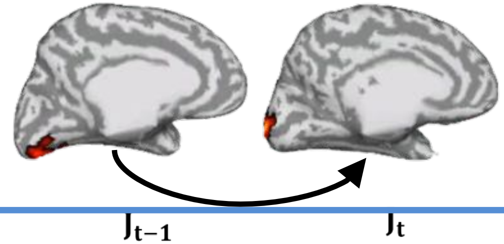

$$\mathbf{B_t} = G\mathbf{J_t} + \boldsymbol{\epsilon}_\mathbf{t}$$

"脳磁図/脳波"



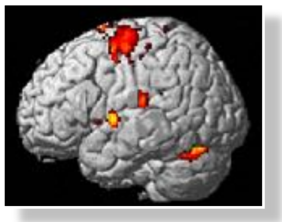
**ダイナミクスモデル**　神経活動の時間発展

時刻t-1　時刻t

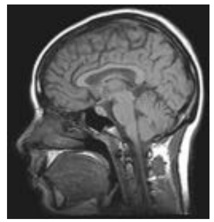



$$\mathbf{J_t} = f(\mathbf{J_{t-1}}) + \boldsymbol{\eta}_\mathbf{t}$$

"fMRI"



"T1-MRI"



"拡散MRI"

脳構造に基づく脳ネットワークダイナミクスモデリング

複数データと"データ同化による" 脳ネットワークダイナミクスモデルのデータ適応

ミクロとマクロスケールのシミュレーションギャップ解消のための解析技術

by Okito Yamashita

# Brain Data Assimilation Project

- Aim: Integrate varieties of brain data into coherent models to show how the brain works.
- Organization: *Center for Brain Data Fusion*
  - Theory team: Okito Yamashita (ATR)
    - multiscale data assimilation methods
  - Data fusion team: Ken Nakae (Kyoto U)
    - data-driven model building
  - Computation team: Jun Igarashi (RIKEN)
    - brain-scale simulation
- Impact: Understand robust, flexible, low-energy computation of the brain, and predict how that can fail and be restored/improved.

by Kenji Doya

# 研究課題

1. 脳ネットワークダイナミクスモデリング
ヒト脳イメージングに適したネットワークモデルの探索。
fMRI : 遅いダイナミクスと 脳波/脳磁図 : 速いダイナミクスを同時に再現するモデルに関する研究を行う(Roberts et al, 2019, *Nature Commun*)。

2. データ同化による神経活動推定と脳ダイナミクスパラメータ同定
高次元の状態推定の問題を効率的に解くアルゴリズムの開発。
ダイナミクスパラメータ決定法を考案。

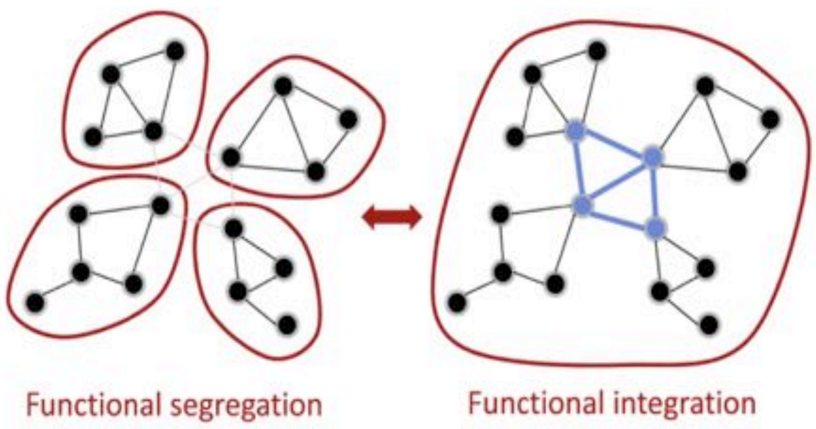
3. 実験データによる検証
レスト時の脳活動や構造情報を計測し、開発した手法の精度検証を行う。
可能であればマーモセットなどの動物データを用いた検証を行う。

4. シミュレートした複雑な脳活動を理解するための方法
アトラクタステートなど非線形ダイナミクスの理論に基づいた手法、または、ダイナミックモード分解などデータドリブンな次元圧縮の方法を用いる。

5. ミクロとマクロスケールのシミュレーションを繋ぐ技術の開発
深層学習でミクロスケールの入出力関係を模倣するなどのアプローチにより、ミクロとマクロを繋げる。

by Okito Yamashita

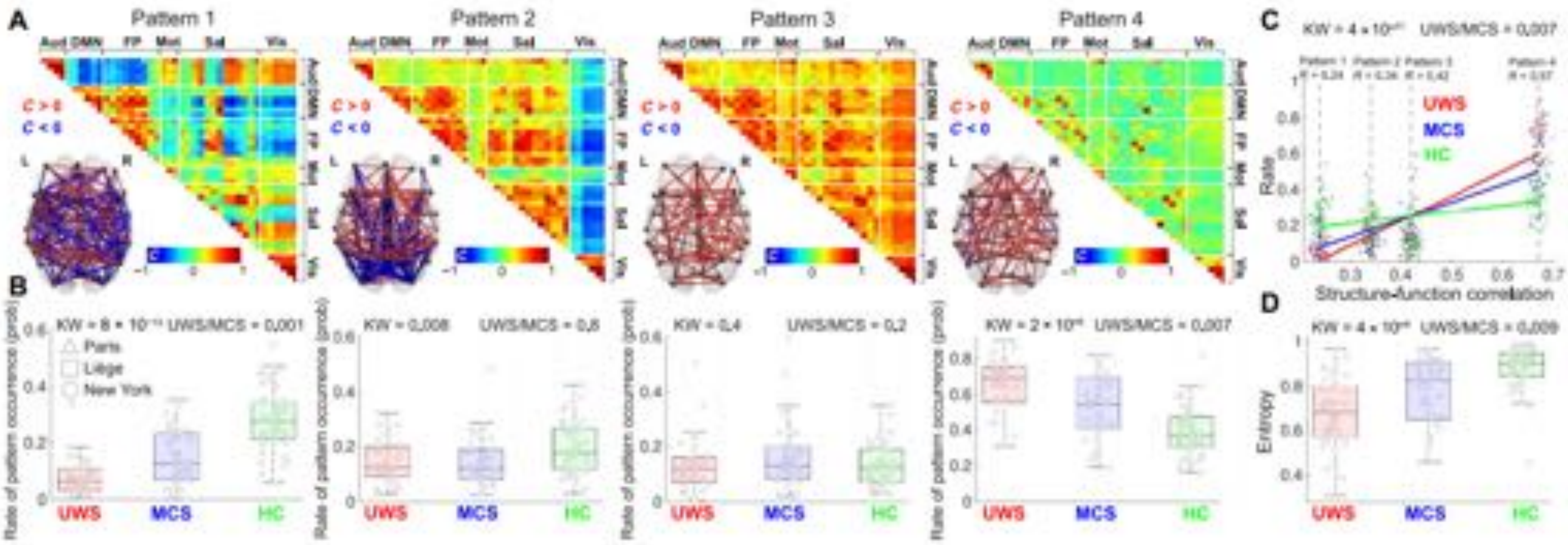
# 脳状態は常に遷移しており意識レベルと関係している




Shine 2019, *TICS*

脳はSegregationとintegrationの状態を遷移している。

構造との関係性
意識レベルとの関係性
疾患との関係性




Demertzi et al. 2019, *Science Advances*

by Okito Yamashita

# International Networking

- Partner Organizations
  - International Brain Initiatives
  - INCF
  - Allen Institute
  - Jülich Center
  - Blue Brain Project
  - Kavli Foundation
  - Neurodata Without Borders
  - International Brain Laboratories
- Advisory Board
  - Karl Friston (UCL)
  - Tomoyuki Higuchi (Chuo U)
  - Christoph Koch (Allen Institute)
  - Henry Markrum (Blue Brain)
  - Terrence Sejnowski (Salk)

by Kenji Doya

# Timeline

– 2020–2025: Foundation
  - multiscale data assimilation framework
  - data pipeline for mouse/marmoset brain
  - data assimilation of resting brain on Fugaku

– 2025–2030: Extension
  - model translation to human brain
  - data pipeline for human brain
  - data assimilation for behavioral/cognitive tasks

– 2030–: Application
  - neuromorphic chip and OS development
  - personalized assimilation for diagnosis/therapy

by Kenji Doya