Visualizing and Manipulating Brain Dynamics

ATR Computational Neuroscience Labs
Mitsuo Kawato
List of Topics

• Robots and Brain Machine Interface
• Brain Decoding and Neurorehabilitation
• Spontaneous Brain Activity and Neurofeedback
• Biomarker of Psychiatric Disorder
• Ubiquitous Brain Visualization and Control
Humanoid “CB-i”:
Computational Brain Interface

- Human-size robot
  - Height 155cm, Weight 85kg
- 51 joints
- Human-like movement range

- Human comparable power
  - Hydraulic actuation
- Mechanically compliant
  - Force position control

- Various sensors
  - Vision, audition, vestibular, proprioception
- Computers
  - Sensorymotor control; PC×2
  - Perception and learning; PC-cluster with wireless
Humanoid Posture Control on Unstable Terrain - Sang-Ho Hyon

Brain-like control without vision or force feedback from foot

Adaptation to unknown incline

Unpredictable Incline
Base for Christian Ott

One-foot balance on unknown and unstable object
Compensate, cure and enhance sensory, central and motor functions of the brain by artificial electrical circuits

Artificial sensory BMI
- Artificial cochlear; Cochlear™
- Artificial retina
- Artificial vision; Dobelle Institute
Brain Machine Interface

Compensate, cure and enhance sensory, central and motor functions of the brain by artificial electrical circuits

Central intervention BMI
Deep brain stimulation; Medtronic™
Brain Machine Interface

Compensate, cure and enhance sensory, central and motor functions of the brain by artificial electrical circuits

BMI for motor control compensation
- Silicon electrodes; Cyberkinetics™
- ECoG
- EEG
- NIRS
- Noninvasive combined (HONDA-ATR-Shimadzu)
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Decoding of Brain/Mind

Encoding

Stimulus → Brain activity

Decoding

Brain activity → Stimulus prediction

V1 activity

Yukiyasu Kamitani @ATR CNS

Scientific American 50 (2004-2005) Award!!
Dream Reading

Imagine to extend fingers

The cursor moves up and down according to the degree of success of motor imagery.

The position of the cursor reflects the mu rhythm amplitude during motor imagery.

Upon successful motor imagery, fingers are extended by an electrically powered orthosis triggered as a result of the EEG classification.

Training protocol

- Patients imagine to extend their paretic fingers for 5 seconds in every 10 seconds
- 50–100 trials/day, 1-2 weeks
- More than 100 patients treated
- Clinical trials started in 2012
- More than 80% curing effect for severest patients without EMG
- 66 y.o lady with left hemiparetic stroke (right MCA infarction)
- 5 years post onset, no voluntary finger extension
- Anodal t-DCS (10 min, 1mA) + BMI neurofeedback (60 min/d, 5 d/wk for 2wks)

Improvement of BMI classification

More apparent μ-ERD and EMG activities observed

Initial

Final

Hybrid actuators composed of air muscles and electric motors are employed.

Noda, Hyon, Matsubara, Morimoto
Decoded Neurofeedback Paradigm with XoR and Human in a Loop

Brain

Exoskeleton Humanoid Robot; XoR

Decoder

Decoded information

Audio-visual stimuli

Rewards

Force and position feedback

Tactile stimulation

Body

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Spontaneous Brain Activity and Intrinsic Functional Connectivity

• Brain is not a mere input-output transformation system, but a dynamical system generating inherent spatiotemporal patterns even at rest.

• Correlations of slow fMRI BOLD oscillation (~0.03Hz) between brain regions define intrinsic functional connectivity

• Spontaneous brain activity contains evoked brain activities, and the latter constructs the former.
Spontaneous activity in visual cortex wanders over activities induced by different orientation stimuli

- Anesthetized cats, voltage sensitive dye, BA18, 4x2 mm
Spontaneous activity in the visual cortex represents internal model of visual world and prior provability for Bayesian estimation

- Wake ferrets, primary visual cortex, 16 multi-electrodes, 4 young-old stages
- Natural scene movie, KL-Div
- Bayes theory, prior $P(N)$, Posterior $P(N|V)$, visual stimulus $V$

\[
P(N \mid V) = \frac{P(V \mid N)P(N)}{P(V)}
\]
Independent Component Analysis of Big Data (30,000 sub., 10,000 exp., and 2,000 papers)


16 components out of 18 correspond well to those obtained from resting states
Meta Analysis of Big fMRI Data

BrainMap ICA

Laird et al., 2011, J Cogn Neurosci
ICA from resting state activity of 306 subjects; rs-fcMRI

PDMN

Biswal BB et al. (2010) PNAS, 1734
Orthodox and ROI-based fMRI Real-time Neurofeedback; Pain, Parkinson’s Disease, Anxiety

Siemens Sonata 1.5T: EPI, 16 slices, TR = 1.5s

Turbo-BrainVoyager: Functional analysis

Samba connection

Scanner console

Image reconstruction


ACC for Pain; De Charms RC et al. (2005) PNAS 102, 18626
SMA for Parkinson; Subramanian L. et al. (2011) J Neurosci. 31, 16309
Contrast Detection

(Adini et al., 2002; Fiorentini & Berardi, 1980; Furmanski et al., 2004; Rainer et al., 2004; and others . . .)
Are V1/V2 plastic enough to accommodate visual perceptual learning?

Perceptual learning

Conventional way: Correlation

Our goal: Causality

Behavioral pre- and post-test

Behavioral pre-test

FMRI Decoder construction

Decoded fMRI neurofeedback

Behavioral Post-test

Stimulus presentation

Report orientation

Time

Orientation

10 deg
70 deg
130 deg

Noise level

Hard
Easy
fMRI decoder construction

1. Behavioral pre-test
2. FMRI Decoder construction
3. Decoded fMRI neurofeedback
4. Behavioral Post-test

Decoder

Multinomial Sparse Logistic Regression

Likelihoods

21%
61%
18%
10-day Decoded fMRI neurofeedback

Behavioral pre-test

FMRI Decoder construction

Decoded fMRI neurofeedback

Behavioral Post-test

Visual stimulus to subjects

Induction Period

Reward feedback

Target Orientation

Time

61%

Neurofeedback system
10-day time-course of NFB performance (N=10)

Mean likelihood for each orientation [%]

Training day

-60 deg  Target  +60 deg

Chance level
Accuracies only in target orientation improved in post-tests compared with pre-tests

3-way ANOVA: Day * Orientation * S/N ratio, P = 0.02
Brain Dynamics causes Consciousness

- Hypothesis fundamental, long-standing, and popular for theorists but not yet examined
  
  • Brain is not a mere input-output transformation system but could function as an autonomous dynamical system.
  
  • Without sensory stimulus, movement, or cognitive tasks, spontaneous brain activity is generated as spatiotemporal patterns.
  
  • Spatiotemporal brain activity patterns cause behaviors, learning and consciousness.
DecNef Success Story

- Learning orientation of gratings in V1/V2
- Phenomenal consciousness of color in V1/V2
- Facial preference in the cingulate cortex
- Fear memory extinction in V1/V2 and amygdala
- Stroke patients rehabilitation therapy in M1
- Confidence of perceptual discrimination without performance change in DLPFC and IPL
- Treatment of chronic (phantom) pain patients for phantom limb in M1 (MEG) Yanagisawa et al.
- OCD therapy in frontal areas and basal ganglia

Other labs: deBettencourt et al. Nature Neuroscience, 2015
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Dynamical Disease


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)


Dynamical Disease

- Dynamics could become pathological even without substance abnormality.
- The dynamical system might possess multiple stable and possibly chaotic attractors.
- Transition from a normal attractor to a pathological attractor initiates a disorder.
- Prolonged stay in the pathological attractor would lead to changes in substances, that is, organic diseases.
Psychiatric Disorder as Dynamical Disease

- A small number of genes or transmitters, or limited brain regions cannot account for psychiatric disorders.
- Abnormal functional connections found specific to psychiatric disorders.
- Normalization of connections found correlated with improvements.
- Effective biomarkers and neurofeedback therapies based on brain dynamics.
Understanding of Psychiatric Disorders by Brain Connectivity Dynamics

(A) Normal Dynamics

Fluctuation of brain state

Normal depression

Schizophrenia

(B) Onset of Disorder

State Transition

Schizophrenia depression

Normal

Genes, development, environment
Field F
Hiroshima Univ. (Yamawaki)
OIST (Doya)
fMRI-based biomarker for Depression

Hiroshima Univ. (Okamoto)
Depression
fNIRS DecNeF

(Yamada, Hayasaka, Nakamura)
Depression
rTMS+fMRI FCNef

Kyoto Univ. (Takahashi)
Depression and Schizophrenia
rTMS+ fMRI FCNef

Tokyo Univ. (Yahata)
Depression, Autism
fMRI FCNef

Tokyo Univ. (Ikegaya)
DecNef technical development

Tamagawa Univ.
DecNef mechanism understanding monkey

Showa Univ. (Hashimoto, Kato)
Autism
fMRI FCNef

(ATR)
Machine learning algorithms for biomarkers of multiple disorders
(Saori Tanaka)
Database of multiple disorders

(Sakai, Tanaka, Narumoto)
OCD
fMRI DecNeF

(Seymour, Yoshida)
Lower back pain
fMRI DecNeF

Osaka Univ. (Saitoh)
Central chronic pain
rTMS+ MEG DecNeF

(Sakai, Tanaka, Narumoto)
OCD
fMRI DecNeF

(Yamada, Hayasaka, Nakamura)
Depression
rTMS+fMRI FCNef

(Imamizu)
Cognitive function
FCNef

(Sakai, Tanaka, Narumoto)
OCD
fMRI DecNeF

(Watanabe, Sasaki, Shibata)
DecNef technical development

OIST
DecNef mechanism understanding mouse

Hiroshima Univ.
OIST (Doya)
fMRI-based biomarker for Depression

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(Watanabe, Sasaki, Shibata)
DecNef technical development
Functional connections for FCNef
- Developments of biomakers
- Clinical indices and modeling

(1) Functional connections for FCNef
- Developments of biomakers
- Clinical indices and modeling

(2) Intervention experiment for patients by NF
- Neurofeedback experiments
- Clinical test

(3) Elucidation of neural mechanisms of NF and safety in animals
- mice for FCNef
- monkeys for DecNef

(4) Clinical rTMS
- rTMS Research

DecNef Safety Commission
Chair: Saitoh (Osaka Univ.) Vice Chair: Nakamura, Kawato (ATR)

Multi-disease Data-Base
Tanaka, Yoshioka (ATR)

Tokyo U ATR Showa U
Hiroshima U (Tokyo U, Kyoto U, ATR)
Kyoto U Hidehiko Takahashi

Showa U ATR

Kyoto U Hiroshima U ATR

ATR

ATR (Kyoto Pref U Med)

Osaka U ATR

ATR (Kyoto Pref U Med)

Osaka U ATR

Pain rTMS Preparations and application of clinical trial

Tamawaga U (Sakagami and Tanaka) mokeys for DecNef

Tokyo U (Yuji Ikegaya) mice for FCNef

Depression rTMS Planning to apply advanced medical care Type B

ATR (Kyoto Pref U Med)
Biomarker for ASD from rs-fcMRI using L1-CCA & SLR

- Connectivity matrix data from resting-state functional connectivity fMRI (rs-fcMRI) were obtained from the three sites; different scanners and protocols.
- Machine learning classifier selects only 16 (0.2%) relevant connections from 9,730=140*139/2 (BAL) connections through L1-regularized CCA and SLR.
ASD Biomarker Generalization across the Pacific Ocean

Training data
- ATR
- Showa Univ.
- Tokyo Univ

Test data
- 6 sites in USA

Learning of ASD/NC classifier by L1-regularized CCA and SLR 82%

Application to the Second Cohort

Percent Correct 75%
Spectrum of 3 Psychiatric Disorders and 1 Developmental Disorder in Connectivity

55 functional connectivity chosen by biomarkers for the four disorders based on CCA and SLR, 630 samples collected at dozen scanners

Hierarchical clustering

Disorders label

Right percentage shows the followings

- Percentage of each disorder data that were contained in each corresponding self-organized cluster
- Percentage of healthy control participants data contained in the self-organized control cluster

- ASD: cluster/ASD = 76%
- DEP: cluster/DEP = 75%
- SCZ: cluster/SCZ = 89%
- OCD: cluster/OCD = 80%
- HS: HS/cluster=84%

× : HS
× : ASD
× : DEP
× : SCZ
× : OCD
Biological Dimensions of the Functional Connectivity for Many Psychiatric Disorders

Estimated canonical variable 1, as linear sum of the functional Connectivity Biological Dimension derived by Machine Learning from Big Data

- Schizophrenia
- Bipolar disorder
- Personality disorder
- Depression
- Personality disorder
- ADHD
- ASD
- OCD
- Dependence

Nature, 24 April 2013

Goodkind et al., 2015, JAMA Psychiatry
DecNef: OCD, Pain

needs a decoder for each patient and its application is currently limited to OCD and pain. In cases of high decoding performance, the success rate is 10/10. The long-term effect depends on the situation; from three to five months in 2/3 studies.

Connectivity Neurofeedback: FCNef

ASD, Depression, Schizophrenia

Ready-made treatment based on an across-patient functional-connectivity biomarker. NF training for four days has long-term effect at least two months.

Possible DecCNeF Application to Therapy of Psychiatric Disorders

- Score computed by DecCNeF-decoder is fed back to patients in real time from resting state fMRI.
Improvement of rs-fcMRI based Biomarker after DecCNef

- Biomarker score computed from 5 minutes: X

TD-like

ASD-like

![Graph showing improvement of biomarker scores](chart.png)
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Non-continuous Innovation for Portable BMI; ImPACT 2014~8 Yamakawa Y PM

Achieve low-cost but high-accuracy measurements through physiological modeling and machine learning

Reduce brain information acquisition cost to 1/10

Supported by Cabinet

Simplicity and low cost
Purpose
- Support elderly people and those who need nursing care
- Improvement of Quality of Life

Properties
- Available in the house or the hospital
- Long-term brain recording with low-constrained
- Accurately decode with network cloud
- Low system delay
- Run the process in safe with Robots

Supported by
Japanese MIC

ATR
NTT
Shimazu
Sekisui House
Keio Univ.
Ishii, Suyama, Kawanabe, Ogawa, et al.

- Entrance (mini-elevator)
- Bath room & toilet
- Washstand
- Automatic doors
- Bedroom (light, air-con, BGM)
- Kitchen
- Automatic sash
- Horizontal transfer (bedr=bath)

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Summary

- Decoded neurofeedback and functional connectivity neurofeedback are noninvasive causal methods to alter human brain dynamics, and resultingly behavior and consciousness.
- Biomarkers for ASD, depression, schizophrenia, and OCD exhibit their spectrum relationships in resting-state functional connectivity MRI.
- DecNef are effective for phantom pain (15 patients, VAS) and OCD (1 patient, Y-BOCS), and FCNef are effective for ASD (10 patients) and depression (60 healthy, BDI).