DYNAMIC APPROACH to the PATHOLOGICAL BRAIN

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Michael, János Szentágothai and Luigi Ricciardi
Capri, Italy, September, 1992
Center for Complex Systems Studies

Budapest CNS Group
study abroad program for undergraduates
• Dynamic approach to neurological and psychiatric diseases: general remarks

• Schizophrenia and associative learning: combined behavioral, imaging and computational approach
Dynamic approach to neurological and psychiatric diseases: general remarks

Theoretical framework: dynamical diseases

The theory of dynamical diseases emerged from chaos theory.

Dynamical disease occurs due to the impairment of the control system: associated to 'abnormal' dynamics.

- Develop realistic mathematical models and study effects of parameter changes.
- Neurobiological interpretation.
- Integration of molecular, cellular and system neuroscience.
- Therapeutic strategies.
Theoretical framework: dynamical diseases

Alzheimer–disease
Changes in attractor structure pathological attractors

Migraine
Dynamical diseases

Schizophrenia
Storage and recall of memory traces

Parkinson–disease
Fixed point attractor

Anxiety

Epilepsy

ADHD
Schizophrenia and associative learning: combined behavioral, imaging and computational approach

- The Schizophrenic Brain: A Broken Hermeneutic Circle
- Experimental paradigm
- Basic behavioral data
- Basic fMRI data
- A functional neural model of an associative learning task
- Dynamical Causal Modeling
- Broken hermeneutic circle
Hermeneutics and its relationship to science

Hermeneutics: branch of continental philosophy which treats the understanding and interpretation of texts.

"A physicist friend of mine once said that in facing death, he drew some consolation from the reflection that he would never again have to look up the word "hermeneutic" in the dictionary." (Steve Weinberg)

Hermeneutic circle: definition or understanding of something employs attributes which already presuppose a definition or understanding of that thing. The method is in strong opposition of the classical methods of science, which does not allow such kinds of circular explanations.
Understanding situations: needs hermeneutic interpretation

- logic, rule-based algorithms, and similar computational methods are too rigid to interpret ill-defined situations,

- hermeneutics, "the art of interpretation" can do it.

- hermeneutics: emphasize the necessity of self-reflexive interpretation and adopts circular causality

Mental models: fundamental role in thinking and reasoning

Kenneth Craik (1914 - 1945): people rely on mental models: the mind constructs "small-scale models" of reality that it uses to predict events

Analogical thinking an effective method of cognitive science to understand other minds, i.e. to show empathy is to simulate other minds.

The neural basis of theory of mind related to mirror neurons, which is the key structure of imitation, and possibly language evolution (Michael Arbib)
A failure in interpreting self-generated action generated by the patient himself: lack of ability to close the hermeneutic circle) can be characteristic for schizophrenic patients (Chris Firth). -> Neural basis: disconnection syndrome
Experimental paradigm

Associative Learning

ENC
RET
ENC
RET
ENC
Experimental paradigm

Associative Learning

[Diagram showing a sequence of ENC and RET blocks with grid elements indicated]
Basic Behavioral Data
fMRI data - brain areas involved

- Superior Parietal Cortex (SP)
- Dorsolateral Prefrontal Cortex (PFC)
- Visual Cortex (VC)
- Inferior Temporal Cortex (IT)
- Hippocampus (HIPP)
Basic fMRI data

Encoding

Visual cortex

Inferior temporal cortex

Right hippocampus

Figure legend

black: HC
red: patients

Percent signal change

Point number in trial

learning baseline recall baseline
Basic fMRI data - Adaptation

Dentate gyrus

% signal change

Early  Late

CA region

% signal change

Early  Late

Right Hippocampus

Black: Healthy control

Red: Patients
Brain Area Function

- VC: visual signal processing (receptive fields)
- IT: object recognition
- SP: location recognition
- HIPP: associative memory
- PFC: motivation, attention, context, **cognitive control**
A functional neural model of an associative learning task
Michael:

Péter, you should cut back the stuff in your lectures with 30%. Less is more!
Visual system

retina → visual cortex → inferior temporal cortex

OBJECT

superior parietal cortex

LOCATION
Competitive network in the Dentate Gyrus, to make unique, orthogonal representation for each object-location pair. Cortical signals (from SP and IT) arrive to the hippocampus through the entorhinal cortex.

\[
\begin{align*}
    a_{dg}^i &= \sum_j w_{sp2dg}^{ji} r_{sp}^j + \sum_k w_{it2dg}^{ki} r_{it}^k \\
    r_{dg}^i &= F(a_{dg}, s_{pdg}) \\
    \Delta w_{sp2dg}^{ij} &= \alpha r_{dg}^j (r_{sp}^i - w_{sp2dg}^{ij}) \\
    \Delta w_{it2dg}^{ij} &= \alpha r_{dg}^j (r_{it}^i - w_{it2dg}^{ij})
\end{align*}
\]
The strong mossy fiber synapses act as teacher signal for CA3 pyramidal neurons. Perforant path synapses are modified via Hebbian learning.

\[
\begin{align*}
\alpha^{i} = \sum_{j} w_{dj2ca}^{ij} r_{dg}^{j} \\
\alpha_{ca}^{i} = F(a_{ca}, s_{pca}) \\
\Delta w_{sp2ca}^{ij} = \alpha r_{ca}^{j} (r_{sp}^{i} - w_{sp2ca}^{ij})
\end{align*}
\]
Cortex - heteroassociative stage

$$\Delta w_{ca2it}^{ij} = \alpha r^j_{it} (r^i_{ca} - w_{ca2it}^{ij})$$

The hippocampal representations are associated to the representation of the original object in the IT.
During the recall connections are not modified. The attractor network in the IT help the recall by converging to one of the learned objects.
Prefrontal control:
(i) background input: don’t do anything!
(ii) two inputs (i.e. ‘object’ and ‘location’): bind them and store!
(iii) one input (i.e. location cue): recall the associated object!
Modeling fronto-hippocampal interactions

\[ a_{ca}^i = L \sum_j w_{dg2ca}^j r_{dg}^j \]
\[ + R \sum_j w_{sp2ca}^j r_{sp}^j \]
\[ \Delta w_{sp2ca}^{ij} = (1 - R) \alpha r_{ca}^j (r_{sp}^i - w_{sp2ca}^{ij}) \]

Learning: red line shows the activation of DG and CA3
blue: plastic synapses

Recall: chain of activation SP->CA3->IT
No plastic synapses
By slight impairment in the prefrontal control the performance decreases to the schizophrenic level.
Dynamics in the model

Model

Hippocampal activation

BOLD data

Right Hippocampus

Black: Healthy control

Red: Patients
Dynamical causal Modeling

Karl Friston and Klaas Stephan

A

state changes  fixed connectivity  modulation of connectivity  input parameters

\[ \dot{x} = (A + \sum_{j=1}^{m} u_j B^j)x + Cu \]

General bilinear state equation

B

\[ \dot{x}_1 = a_{11} x_1 + a_{12} x_2 + c_{11} u_1 \]

\[ \dot{x}_2 = a_{21} x_1 + a_{22} x_2 + b_{21}^{(2)} u_2 x_1 \]
black arrows: (functional) connections
grey arrows: external inputs
dotted arrows: transformation of neural activities to hemodynamic responses
specific example: the propagation of visual stimuli
Dynamical causal Modeling

- Comparative study of schizophrenia patients (SCZ) and healthy controls (HC)

- Model comparison results: solid arrow - connection present in SCZ and HC, dashed arrow - present only in HC

- Impairment of prefrontal-hippocampal causal interaction and of the effects of Retrieval in SCZ (supports the disconnection syndrome hypothesis)

- Estimated parameters of the model containing all indicated connections. Black: HC, red:SCZ
the role of prefrontal cortex: interpretation of the incoming signal: associative learning vs. recall

less accurate interpretation/control $\rightarrow$ poorer performance:

if the PFC does not tell to the hippocampus when to learn and when to recall; $\rightarrow$ poorer performance

disconnection syndrome hypothesis is supported

the hermeneutic circle is broken

therapeutic strategy: broke loops should be healed:

towards a computational psycho-pharmacology: another story