Exciting Times

Computational Psychiatry

Digital Mental Health
Psychiatric diagnosis
I am depressed, sad, feel helpless, despaired, what do I have doctor? Please tell me.
You have depression
Gee – isn’t that what I just told you
Can’t you give me any added value
My stomach hurts, what do I have doctor?

You have Appendicitis

Place in the body
What happened to it
It is infected
How to treat it
Antibiotics

You have depression

I am depressed, what do I have doctor? Please tell me
Urologist  Cardiologist  Gastroenterologist  Psychiatrist
‘On Being Sane in Insane Places’

- Rosenhan undertakes groundbreaking study: *will sane people ('pseudo-patients') be recognized as sane by hospital staff in a psychiatric ward?*

- **Experiment**
  - 8 sane people admitted into 12 hospitals; 3 women, 5 men
  - Initially complained of 'hearing voices' of an 'existential nature':
  - Symptoms chosen because there were zero reports of 'existential psychoses in the literature'
  - After being admitted, pseudo-patients behaved normally
  - Length of stay ranges from 7 to 52 days, average of 19 days

D. L. Rosenhan
STUDY: COOPER ET AL. (1972)  
THE US-UK DIAGNOSTIC PROJECT

- The aim of the study was to investigate reliability of diagnosis of depression and schizophrenia.
- The British psychiatrists diagnosed the patients in the interview to be clinically depressed twice as often.
- The American psychiatrists diagnosed the same patients to be suffering from schizophrenia twice as often.
- The results indicated that the same cases did not result in similar diagnosis in the two countries.
- Problems of reliability.
- Cultural differences in interpretation of symptoms and making a diagnosis.
Checklist

1. Depressed
2. Insomnia
3. Pessimism
4. Anorexia
5. Etc. ....

Inter-rater Reliability
### Table 1
**DSM Versions I–IV, 1952–1994**

<table>
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<th>Total Number of Pages</th>
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<td>265</td>
<td>494</td>
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<td>III-R</td>
<td>1987</td>
<td>292</td>
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<td>IV</td>
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<td>886</td>
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Currently

No Etiology (not brain related)

No Category & Not Personalized

No Pharmacology (no med’ efficacy)

Hampered Research (no advance)
This is what Tom Insel had to say about the DSM

The goal of this new manual, as with all previous editions, is to provide a common language for describing psychopathology.

While DSM has been described as a “Bible” for the field, it is, at best, a dictionary, creating a set of labels and defining each.

The strength of each of the editions of DSM has been “reliability” – each edition has ensured that clinicians use the same terms in the same ways.

The weakness is its lack of validity ... Patients with mental disorders deserve better.

Tom Insel
Previous head of NIMH

- Moller HJ et al. DSM 5 reviewed Eur Arch Psychiatry Clin Neurosci. 2015
- Cuthbert BN, & Insel TR Toward the future of psychiatric diagnosis BMC Med. 2013
- Tomason T 2014 file:///C:/Users/Peled/Downloads/fulltext_stampe.pdf
Translate
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<td>Acute threat (“fear”)</td>
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<td>Potential threat (“anxiety”)</td>
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<td><strong>Positive Valence Systems</strong></td>
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<td>Attachment formation and maintenance</td>
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RDoC
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<tr>
<td>Potential threat (“anxiety”)</td>
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</table>

- P: PHYSICAL
  - EXHAUSTED
  - CONFUSED
  - ERECT
  - Quilty
  - SUSPICIOUS
- C: Cognition
  - ANGRY
  - INTERESTED
  - FRUSTRATED
  - CONFUSE
- S: Self
  - ASHAMED
  - HAPPY
  - MIGHTY
  - DISAPPOINTED
  - GUILT
- A: Arousal
  - OVERWHELMED
  - PLACID
  - JEALOUS
  - MOODY

**RDoC**
Example for Computational psychiatry
Hallucinations
Loosening
Delusions
restlessness

Positive
symptoms

Poverty thought
Perseverations
Avolition

Negative
symptoms

Function

Age 18

BLEULER
1920
Mental disorganization
Affect Associations
Ambivalence Autism
4 A’s
Schizophrenia
Schizo - Prenus

1900
KRAEPLIN
Dementia praecox
Based on prognosis

Kraepelin

Positive symptoms

Loosening
Delusions
restlessness

4 A’s

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Positive symptoms

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Schizophrenia

Kraepelin

Dementia praecox
Based on prognosis

Kraepelin
THE PERCEPTION OF RORSCHACH INKBLOTS IN SCHIZOPHRENIA: A NEURAL NETWORK MODEL

AVI PELED and AMIR B. GEVA

*Technion-Israel Institute of Technology, Haifa, Israel;
Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer Sheva, Israel

(Received 15 October 1999; In final form 14 November 1999)
**TABLE I** Symmetric half (R and L) weight connection array

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<th>Leg</th>
<th>Italy</th>
<th>Body</th>
<th>Map</th>
<th>Bag</th>
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FIGURE 5  Results of neural network simulation.
Simulation of cognitive disturbances by a dynamic threshold semantic neural network

AMIR B. GEVA\(^1\) AND AVI PELED\(^2\)

\(^1\)Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer Sheva, Israel
\(^2\)Department of Forensic Psychiatry, Shaar Menashe Mental Health Center, Israel; Technion-Israel Institute of Technology, Haifa, Israel

(Received May 15, 1999; Revised October 1, 1999; Accepted October 8, 1999)
Formulate brain dynamics as a physical state-space dynamic system
Clinical Brain Profiling
What do we know about brain organization

Disorders = Perturbation
Connectivity

- Connectivity segregation (Cs)
  - Psychosis

- Connectivity integration (Ci)
  - Negative signs

Hierarchical top-down shift (Htd)
- Delusions
- Hallucinations

Hierarchical bottom-up insufficiency (Hbu)
- Avolition

Psychosis

Connectivity

- Segregation (Cs)

Plasticity

- De-Optimization (D)
  - Depression

- Optimization (O)
  - Mania

- Constraint frustration (CF)
  - Anxiety
  - Phobia

Negative signs

Optimization (O)

Depression

Constraint frustration (CF)

Mania

Anxiety

Phobia

Stimulus bound CF(b)

DNM

Constraint frustration (CF)
Psychosis and schizophrenia disorders
Connectivity

Hierarchical top-down shift (Htd)
Delusions
Hallucinations

Connectivity segregation (Cs)
Psychosis

Connectivity integration (Ci)
Negative signs

Hierarchical bottom-up insufficiency (Hbu)
Avolition

Plasticity

DNM
Hallucinations
Loosening
Delusions
restlessness

Positive symptoms

BLEULER
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KRAEPLIN
*Dementia praecox*
*Based on prognosis*

Poverty thought
Perseverations
Avolition

Negative symptoms

Function

Age 18

Function
The associations of an *adult* ego could be temporarily or permanently weakened, with a similar result of random or confused thought processes. ... resulting in psychotic states.

**Psychosis** ≡ **Disconnection Syndrome**

van den Heuvel MP, Mandl RC, Stam CJ, Kahn RS, Hulshoff Pol HE. Our findings suggest that schizophrenia patients have a less strongly globally integrated structural brain network with a reduced central role for key frontal hubs, resulting in a limited structural capacity to integrate information across brain regions. Biochem Soc Trans. 2010 Apr;38(2):516-21.


Psychosis = Disconnection Syndrome
Order
Randomness
Complexity

Giulio Tononi

Disconnection dynamics

Over-connection dynamics

Neural Complexity

Human Brain

Degree Distribution
Heterogeneity

Regular Lattice
Homogeneity

Order

Small-worldness

Positive symptoms

Negative symptoms

Bassett DS. 2011.

Randomness
Order
Disconnection dynamics

Random
Disorder
“Clinical brain profiling”: A neuroscientific diagnostic approach for mental disorders

Abraham Peled a,b,*, Amir B. Geva c

a, b Sheba Medical Center, Tel-Hashomer, Israel
b Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel
c Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer-Sheva 84190, Israel
Positive symptoms

Negative symptoms
Delusions

Joaquin Fuster

Positive symptoms

Negative symptoms

Avolition

Delusions

Joaquin Fuster
Bernard Baars

Stanislav Dehene

Giulio Tononi

Marcel Mesulam
Connectivity

* Connectivity segregation (Cs)
  * Psychosis

* Connectivity integration (Ci)
  * Negative signs

* Hierarchical bottom-up insufficiency (Hbu)
  * Avolition

* Hierarchical top-down shift (Htd)
  * Delusions
  * Hallucinations

* Connectivity

* Plasticity

* DNM

Clinical Brain Profiling (CBP)
Mood disorders
Connectivity

Hierarchical top-down shift (Htd)

Delusions
Hallucinations

Hierarchical bottom-up insufficiency (Hbu)

Avolition

Connectivity segregation (Cs)

Psychosis

Connectivity integration (Ci)

Negative signs

Plasticity

De-Optimization (D)
Depression

Optimization (O)
Mania

Constraint frustration (CF)
Anxiety

Stimulus bound CF(b)
Phobia
Plasticity

Mood
Depression
Anxiety

Environment

Optimization
Adaptability
Free energy

\[ \dot{\psi} = f_\psi(\psi, a) + \omega \]

\[ s = f_z(\psi, a) + \omega \]

\[ \dot{\mu} = -\nabla_\mu F(s, \mu) \]

\[ \dot{a} = -\nabla_\sigma F(s, \mu) \]
Plasticity

Optimization (O)

Mania

De-Optimization (D)

Depression

Constraint frustration (CF)

Anxiety

Stimulus bound CF(b)

Phobia

Clinical Brain Profiling (CBP)
Personality disorders
Connectivity

- Connectivity segregation (Cs)
- Connectivity integration (Ci)
- Hierarchical top-down shift (Htd)
- Hierarchical bottom-up insufficiency (Hbu)
- Delusions
- Hallucinations

Psychosis

Plasticity

- De- Optimization (D)
- Optimization (O)
- Constraint frustration (CF)
- Stimulus bound CF(b)

Depression
Mania
Anxiety
Phobia

DNM
Default Mode Network

\[ s = f_z(\psi, \alpha) + \omega \]

\[ \psi = f_\psi(\psi, \alpha) + \omega \]

\[ \mu = -\partial_a F(s, \mu) \]

Environment

Personality

Hebbian Dynamics
Clinical Brain Profiling (CBP)

DNM
Brain Profiler
Brain Related Psychiatric Diagnosis
All of the various brain disturbances are mapped onto a 9 axis profile “the Clinical Brain Profile (CBP)"
The Clinical Brain Profile (CBP) of the patient looks like this:

Millisecond range activity

Connectivity

Plasticity over weeks and months

Optimization

De-Optimization

Constraint frustration

Stimulus bound

Lifetime Developmental

DMN

Clinical Brain Profiling

Hierarchical top-down shift

Hierarchical bottom-up insufficiency

Connectivity integration

Connectivity segregation

Optimization

De-Optimization

Constraint frustration

Stimulus bound

Default Mode Network

Delusions

Hallucinations

Avalition

Negative signs

Psychosis

Mania

Depression

Anxiety

Phobia

Personality disorder
Unsupervised fuzzy clustering of CBP into two categories classifies patients based on clinical severity validating CBP sensitivity to clinically meaningful phenomenology.
The Brain Profiler Site

The Clinical Brain Profiling Software

Available now on an interactive web platform. Just register or login and start working seamlessly.
Brain Profiler is a Computer and an App platform
EEG

- EEG
- Objective digital
- Subjective Condition
- Powerful Statistics
- Psychiatrist Assessment

BrainProfiler
Clinician → Scale pheno CBP
Patient → Symptoms CBP
Cyber Mob sensors → Obj’ digital CBP
Brain Imaging → VALID CBP

Clinical Brain Profiling (CBP)

Unique

COMPUTATIONAL PSYCHIATRY

Big Data

EMR, Personalized, Tele-medicine, Alerts & Notifications, Queuing and Management, Treatment-Response
Signal Processing & Validation
EEG Attractor signals can be informative about chaotic and periodic dynamics of disconnection and over-connection activity respectively. They can also inform about general stability of the brain systems.
Calculating correlation matrices can inform us about brain connectivity by constructing Graphs of connectivity patterns. These can be evaluated over different and extended time-scales.
Graphs can help estimate Small-World optimal brain networks as well as fixed overly connected or randomly disconnected networks.
Node attacks (random versus degree-related) can measure network reliance and vulnerability to functional perturbations.
**Path length** = inversely related to global efficacy of parallel information transfer

**Clustering Coefficient** = Measure of density of connections between nearest neighbors

**Small-worldness** = high clustering small path length comparable to random graph

**Hierarchy** = Hubs with many long distance connections and few local connections

**Mean connection distance** = Euclidean distance between centers in stereotactic space

**Assortativity** = measures the preference of a node to connect to other nodes of similar degree

**Rent exponent** = topo-physical embedment in physical space of the network, scaling relationships
Dynamic Causal Modeling (DCM) can be specifically relevant to estimating error predictions in hierarchical systems, and matching dynamics with free energy reduction within hierarchies.
Contact information
neuroanalysis@gmail.com