Urologist  Cardiologist  Gastroenterologist  Psychiatrist
Brainless discipline

Psychiatrist
I am depressed, 
sad, feel helpless, 
Despaired, 
what do I have doctor? 
Pleas 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 Appendecitis

I am depressed, what do I have doctor? Please tell me
You have depression

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

Why psychiatry can’t afford to be neurophobic

Ed Bullmore, Paul Fletcher and Peter B. Jones

Summary

The original vision of psychiatry was as a medicine – or physic – of the mind. If psychiatry aspires to be a progressive modern medicine of the mind, it should be fully engaged with the science of the brain. We summarise and rebut three countervailing or ‘neurophobic’ propositions and aim to show that not one provides a compelling argument for neurophobia. We suggest that there are several ways in which psychiatry could organise itself professionally to better advance and communicate the theoretical and therapeutic potential of a brain-based medicine of the mind.

Declaration of interest

E.B. is employed half-time by the University of Cambridge and half-time by GlaxoSmithKline (GSK), and he holds shares in GSK and the Brain Resource Company.
You have an altered small-world network in your brain, it is characterized by a reduced clustering coefficient and an increase of long-pathways.
Psychiatry = Descriptive Diagnosis

Medicine = Etiologic Diagnosis
BLEULER
1920
Mental disorganization
Affect
Associations
Ambivalence
Autism

4 A’s
Schizophrenia
Schizo - Prenus
1900
KRAEPLIN

Dementia praecox

Manic depressive psychosis

Paranoia (today delusional)

Based on prognosis medical model

*Based on prognosis*
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
‘On Being Sane in Insane Places’ 1973

• 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
Checklist
1. Depressed
2. Insomnia
3. Pessimism
4. Anorexia
5. Etc .....
### Table 1
*DSM Versions I–IV, 1952–1994*

<table>
<thead>
<tr>
<th>Version</th>
<th>Year</th>
<th>Total Number of Diagnoses</th>
<th>Total Number of Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1952</td>
<td>106</td>
<td>130</td>
</tr>
<tr>
<td>II</td>
<td>1968</td>
<td>182</td>
<td>134</td>
</tr>
<tr>
<td>III</td>
<td>1980</td>
<td>265</td>
<td>494</td>
</tr>
<tr>
<td>III-R</td>
<td>1987</td>
<td>292</td>
<td>567</td>
</tr>
<tr>
<td>IV</td>
<td>1994</td>
<td>297</td>
<td>886</td>
</tr>
</tbody>
</table>

Psychiatry has thus far failed to identify a single neurobiological phenotypic marker or gene that is useful in making a diagnosis of a major psychiatric disorder or for predicting response to psychopharmacologic treatment.

Reification of DSM-IV entities, to the point that they are considered equivalent to disease, is more likely to obscure than to elucidate research findings.

Epidemiological and clinical studies have shown extremely high rates of comorbidities among the disorders, undermining the hypothesis that the DSM syndromes represent distinct etiologies.

The efficacy of medications cut across the DSM-defined categories.
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.
<table>
<thead>
<tr>
<th>Domains/Constructs</th>
<th>Units of Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Genes</td>
</tr>
<tr>
<td><strong>Negative Valence Systems</strong></td>
<td></td>
</tr>
<tr>
<td>Acute threat (&quot;fear&quot;)</td>
<td></td>
</tr>
<tr>
<td>Potential threat (&quot;anxiety&quot;)</td>
<td></td>
</tr>
<tr>
<td><strong>Positive Valence Systems</strong></td>
<td></td>
</tr>
<tr>
<td>Reward valuation</td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive Systems</strong></td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td></td>
</tr>
<tr>
<td><strong>Systems for Social Processes</strong></td>
<td></td>
</tr>
<tr>
<td>Attachment formation and</td>
<td></td>
</tr>
<tr>
<td>maintenance</td>
<td></td>
</tr>
<tr>
<td><strong>Arousal and Regulatory Systems</strong></td>
<td></td>
</tr>
<tr>
<td>Arousal</td>
<td></td>
</tr>
</tbody>
</table>

RDoC
Prof. Klein
Prof. Klein
Neural Network modeling
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

<table>
<thead>
<tr>
<th></th>
<th>Head</th>
<th>Hand</th>
<th>Leg</th>
<th>Italy</th>
<th>Body</th>
<th>Map</th>
<th>Bag</th>
<th>Hat</th>
<th>Rabbit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>2</td>
<td>0.3</td>
<td>0.3</td>
<td>-1</td>
<td>0.3</td>
<td>-1.5</td>
<td>1.3</td>
<td>1</td>
<td>-1</td>
</tr>
<tr>
<td>Hand</td>
<td>0.3</td>
<td>2</td>
<td>0.3</td>
<td>-1</td>
<td>0.3</td>
<td>-1</td>
<td>4.8</td>
<td>0.25</td>
<td>-0.25</td>
</tr>
<tr>
<td>Leg</td>
<td>0.3</td>
<td>0.3</td>
<td>2</td>
<td></td>
<td>0.3</td>
<td>-1.5</td>
<td>1.3</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td>0.25</td>
<td></td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>Body</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td></td>
<td>2</td>
<td></td>
<td>0.5</td>
<td>-0.5</td>
<td></td>
</tr>
<tr>
<td>Map</td>
<td></td>
<td></td>
<td></td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>Bag</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Rabbit</td>
<td>0.25</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Butterfly</td>
<td>0.25</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>Pelvis</td>
<td>0.25</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-9</td>
<td>0.25</td>
</tr>
<tr>
<td>Vase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-9</td>
<td></td>
</tr>
</tbody>
</table>
FIGURE 5  Results of neural network simulation.
Simulation of cognitive disturbances by a dynamic threshold semantic neural network

AMIR B. GEVA¹ AND AVI PELED²

¹Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer Sheva, Israel
²Department of Forensic Psychiatry, Sha'ar 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
Part One Clinical Neuroscience

http://www.brainprofiler.com/
In recent years we have learned a lot about the brain
For example we know that the brain is organized as a network.
Ego

Letters, the project
We also know that the brain is organized as a Small World network with Clusters and Hubs.
Stanley Milgram
1933-1984

Six degrees of separation

Albert-László Barabási

NETWORK SCIENCE
We know that **Small World** brain organization is optimal for modal-specific specialization and multimodal integration.
We also know that Small World brain organization supports Hierarchy with higher-level processing.
We know that such Small World brain organization is optimal for coherent integrated conscious experience.
The brain is **Plastic**; Neurons continually create (Synaptogenesis) and lose (Atrophy) connections.
The Plastic Brain interacts with the Environment.

Diagram:
- Environment → Brain
- Brain → Action
- Action → Brain
- Brain → sensation

Brain Profiler © All rights reserved August 2017
The Plastic Brain learns (Hebb) from the environment, Creating memories
The Plastic Brain uses memories to create an Internal-Representation of the environment, an internal model of the world.
A complexity measure for selective matching of signals by the brain.

When ‘Adaptive’ the internal model matches the environment, difference (free energy) between environment and internal representation is reduced.
$s = f_z(\psi, a) + \omega$

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

$\dot{\mu} = -\partial_\mu F(s, \mu)$

Action

Hidden states

Brain

Sensations

Internal states

Nature Reviews | Neuroscience
Once created the internal model determines how we view the world and react to it,

Experience-Dependent-Plasticity continually updates our internal model of the world
The internal model determines how we view the psychosocial world and react to it, this is our personality style.
Ego

Experience dependent plasticity, Hebbian dynamics, internal presentations storage and activation of memories, brain neural networks dynamics, default mode network individuality, personality

Ego is the default mode network resulting from experience dependent plasticity developmental process and embeds /represents the person’s individual personality, his set of conceptions and reactions to the world and psychosocial occurrences
Each of the organizational dynamics described so far can be disturbed in the brain of our patients.
Network connectivity and hierarchy can be disturbed
Plasticity and adaptability can be disturbed
Internal representations can be disturbed
Disturbed network connectivity and hierarchy lead to psychosis and negative signs

Disconnection and psychosis
Over-connection and poverty of thought
Bottom-up hierarchy insufficiency and
Avolition
Top-Down shift and delusions

Network organization
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**  \(\cong\) **Disconnection Syndrome**
Aberrant frontal and temporal complex network structure in schizophrenia: a graph theoretical analysis. 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


Psychosis ≡ Disconnection Syndrome
"Clinical brain profiling": A neuroscientific diagnostic approach for mental disorders

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

a Sheba Menorah Mental Health Center, Tel Aviv, Israel
b Rapaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel
c Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer-Sheva 84105, Israel
Disturbed plasticity and adaptability lead to mood disorders

Optimization and De-optimization, free energy changes, lead to Mania and Depression, respectively
Disturbed plasticity and adaptability lead also to altered unstable constraints between networks and anxiety disorders.

Constraint frustration, unstable networks lead to Anxiety sensations.
Disturbed internal representations lead to personality disorders

Default mode network development biased to the extent that internal representations are either rudimental or unstable (borderline personality disorders) or biased internal representations dominate the network (i.e., other personality disorders).
The brain can be disturbed to various extents in all network parameters leading to mixed clinical phenomenology.
Each patient may suffer from a specific personalized profile of brain disturbance.
In other words, the optimally organized brain can be perturbed and disturbed thus generate mixtures of clinical psychiatric phenomenology.
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:

**Connectivity**
- Htd: Hierarchical top-down shift
- Hbu: Hierarchical bottom-up insufficiency
- Ci: Connectivity integration
- Cs: Connectivity segregation

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

**DNM**
- DMN: Default Mode Network

Clinical Brain Profiling
It is important to remember that different disturbances inflict different time-scales of organization and activity.
“Clinical brain profiling”: A neuroscientific diagnostic approach for mental disorders

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

a Sheba Medical Mental Health Center, Hadera, Israel
b Rapaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel
c Electrical and Computer Engineering Department, Ben-Gurion University of the Negev, Beer-Sheva 84105, Israel


HFC 2 groups

Cluster 1 = 97% schizophrenia
Cluster 2 = 80% others
Personality disorders Anxiety

Axis Y: Percentages
Axis X:
1 = DMN Default Mode Network
2 = D De-optimization
3 = O Optimization
4 = CF Constraint Frustration
5 = CF Constraint Frustration bound
6 = G Connectivity segregation
7 = CI Connectivity integration
8 = H1u Hierarchical bottom-up
9 = Htd Hierarchical top-down

Fig. 3. Clustering of data into two groups.
Fig. 1. CBP of archetypes.

Fig. 2. Comparison of results to archetypes.
Part two Brain Profiler
Signal Processing and Brain Pacing

http://www.brainprofiler.com/
Brain Profiler is a Computer and an App platform
The clinician evaluates the patient’s clinical condition using an easy sliding cursor of the Brain Profiler.
The patient makes timely reports about his condition also using an easy sliding cursor.
Brain Profiler combines the assessment of the clinician with the reported complaints of the patient.
Brain Profiler also offers a passive and objective assessment of the patient using digital signatures collected from his mobile and cyber activity.
The predicted phenomenology-dependent brain disturbance is VALIDATED by collecting brain imaging from the client’s EEG using the Clinical Brain Profiling translation of Brain Profiler.
Brain Profiler offers follow-up over time, monitors treatment responses and prognosis; Alerts prevent deterioration and improve treatment outcomes.
With statistics of big-data, Brain Profiler will predict prognosis, treatment responses and medication outcome and response.
Big-data relating psychiatric phenomenology to brain imaging will reveal the causal relationships between brain disorders and clinical phenomenology thus validating clinical brain profiling and discovering the causes of mental disorders.
Here is the prediction table made by Clinical Brain Profiler to findings that will be revealed by Big-data

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Impact Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychosis and schizophrenia</td>
<td>Disturbances to connectivity and hierarchy in millisecond range inflicting whole brain connectivity</td>
</tr>
<tr>
<td>Mood and Anxiety disorders</td>
<td>Disturbances adaptability of brain states over weeks months inflicting whole brain state dynamics</td>
</tr>
<tr>
<td>Personality disorders</td>
<td>Disturbances to life-time developmental changes whole brain network configurations</td>
</tr>
</tbody>
</table>
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.
EEG signals can be synchronized with stimulus as in Evoked Potentials; however, in Brain Profiler, they can be synchronized with phenomenological disturbances.
Calculating segregation versus integration of neural complexity (Tononi) can measure connectivity and hierarchy disturbances.
Calculating Correlation matrices can inform about brain connectivity by constructing Graphs of connectivity patterns, these can be evaluated over different and extended time-scales.
Purely data-driven clustering mechanisms can evaluate higher-level connectivity and relatedness processes in the brain.
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

Node = cortical region or neuron

Edge = statistical measure of association

Degree = the number of edges connecting a node
Dynamic Causal Modeling (DCM) can be specifically relevant to estimating error predictions hierarchical systems, and matching dynamics with free energy reduction within hierarchies.
A battery of all types of signal processing will be required for big data analysis, synch with phenomenology CBP predictions

<table>
<thead>
<tr>
<th>Disturbances to <strong>connectivity</strong> Disturbances to <strong>hierarchy</strong> in millisecond range inflicting whole brain connectivity</th>
<th>Attractor assessment random versus periodic Segregation integration Correlation analysis Small world and node attacks analysis Dynamic causal model for hierarchy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disturbances adaptability of brain states over weeks months inflicting whole brain state dynamics</td>
<td>Timescale weeks for attractor assessment dynamics brain states Dynamic causal model for adaptability Free energy</td>
</tr>
<tr>
<td>Disturbances to life-time developmental changes whole brain network configurations</td>
<td>All of the above over lifetime</td>
</tr>
</tbody>
</table>

Brain Profiler © All rights reserved August 2017
Brain pacing devices that will cure mental disorders in the future will all need the online feedback loop information collected by Brain Profiler, thus Brain Profiler is the functional platform for any future brain pacer device.
Miniaturized to a sensing-acting sticker the EEG will be monitored and intelligent feedback energy will be delivered to relevant neural circuitry acting on pre-inserted neural-nanoparticles.
Contact information

neuroanalysis@gmail.com