

The NeuroAnalyst: The Psychiatrist of the Future

Abraham Peled, M.D.

Sha'ar Menashe Mental Health Center, Hadera, Israel

Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel

Introduction / Abstract.

The NeuroAnalyst, the psychiatrist of the future will use NeuroAnalysis to diagnose and cure mental disorders. He will diagnose schizophrenia as a brain connectivity disorder (Jones 2010), mood disorders as a disorder of plasticity and optimization (El-Hage et al 2013; Peled 2013), and personality disorders as mal-developed resting-state network (Peled 2012). Thus the Neuroanalyst diagnoses mental disorders as disturbances, or breakdown, of the optimal (healthy) global brain organizations, as such the different phenomenological manifestations of mental disorders are distinct (but overlapping spectrum) Globalopathies (Peled 2013).

Schizophrenia a brain connectivity disorder.

More than in any other aspect of neuronal network literature of mental disorders, the disconnection syndrome is by far the most cited. The notion that psychosis, with its fragmented experience, correlates with some disintegrated brain organization, dates back to 1800 with the work of Meynert (1968) and Wernicke (1881). The modern version of schizophrenia as a disconnection syndrome was published in the eighties by Friston and Frith (1995). Thereafter a long series of publications report on similar disturbances detected by different types and methods of brain imaging technologies.

Over-connected systems tend to “freeze” become constrained to activate few repeated states. This simulates (Geva and Peled 2000) the constricted poverty of speech and preservative ideation characterizing negative signs schizophrenia (Andreasen 1983). Schizophrenia as a disorder alternating between psychosis and post-psychotic deficiency can be reconceptualized as a disease of brain connectivity alternating between disconnection and over-connection imbalances (Peled 1999).

Top down bottom up hierarchical brain balance is also afflicted by altered connectivity with reduced hierarchy resulting from destabilization, inflicting upon higher-level brain functions such as volition and motivation, markedly and continuously reduced in prolonged schizophrenia. Top-down biased control can distort incoming experiences resulting in systemized delusional ideations. Thus the spectrum of “schizophrenias” as traditionally known can be reconceptualized within the framework of connectivity and hierarchy imbalances (Peled 1999; 2009; 2010).

In modern network formulations, these changes can be attributed to Small World Network alterations (Bechtel

2013) as shifting the optimal normal balance between clustering coefficient and long pathways can undermined network stability producing both randomness disconnections as well as fixed constraint deficient stability.

Mood disorders; Disorder of plasticity and optimization

When things go well for us, or as planned, or if expectations are fulfilled, then satisfaction is experienced as elevated mood, while disappointment from things gone wrong, unplanned and unexpected are experienced as disappointing and depressing.

Our brains are Bayesian brains (Friston 2012) continually predicting occurrences and updating internal representations of those occurrences. When expectations are fulfilled this goes with good adaption where internal representations match the actual occurrences in our lives. Unexpected occurrences or failure of expectations are accompanied with depressed mood. Fulfillment of exceptions can be quantified as Free Energy (Schwartenbeck et al 2013) of a Bayesian Brain (Friston 2012). The brain acts to reduce free energy by fulfilling expectations (match between internal representations and actual occurrences) For this to be effective the brain must be changeable flexible and plastic. Plasticity is thus a key property for an effective adaptable brain that successfully reduced free energy adapting internal representations to actual occurrences and acting to adapt occurrences to the internal representations (expectations).

One can now relate mood to plasticity dynamics. Increased plasticity has antidepressant effect while reduction of plasticity has a depression-inducing effect. This is supported by psychiatric neuroscience as

synaptogenesis underlies the mechanism of action of antidepressant medication (Baudry et al 2011) and neuronal death and atrophy underlay depression (Duman and Aghajanian 2012).

To conclude mood is an emergent property (Peled and Geva 1999) from plasticity dynamics and brain adaptability, adaptability between internal representations and the actual manifestations of these representations (Peled 2013). If the brain adaptability is reduced due to curtailed plasticity, (as is typical in dementia and widespread brain atrophy) than depression arises. Also if environmental occurrences shift abruptly as is typical in stressful events than, reality departs (is removed) from regular expectations (internal representations), free energy increases because plasticity cannot compensate for the changes rapidly enough, consequently reactive depression ensues.

Personality disorders a mal-developed resting-state network

A resting-state-network was already anticipated by Theodor Meynert when he predicted that experience organizes the developing brain by associative pathway structure (Meynert 1868). He actually foreseen what would later be known as Experience-Dependent-Plasticity (Hebb 1949; Whitt et al 2013). He stated that every one of us develops a unique individual connectivity brain organization, determined by our experiences and thoughts, and he named such organization "Ego." His student Sigmund Freud and his followers have shown the relevance of the Ego to personality (even-though theoretically unrelated to neuroscience Freud, 1938). Coming full-circle around, recently initial findings show altered resting-state networks in personality disorders especially Borderline personality disorders (Wolf et al 2011).

Experience-Dependent-Plasticity was further described by Donald Hebb (1948) and entails strengthening of connections among neuronal ensembles (Whitt et al 2013) based on experience (Input). This has been found to occur at many levels of neuronal networks, from neurotransmitter calcium-related processes (Cooke and Bear 2013) to structural dendritic spine formation.

Mathematical models using Hebbian algorithms, of strengthening connections "embed" information in the form of "attractors" shaping the state-space landscape of the network physical dynamics (Geva and Peled 2000). These attractor formations are memories created internally within the network organization (Yan et al 2013). It is likely that the brain uses similar

mechanisms of memory-formations when creating the internal representations we hold in our brains, and use to govern our reactions and behaviors while interacting with the environment and others (Fairbairn 1944).

Internally represented models of the psychosocial world are termed "Object Relationships" by object relationships psychologists which elegantly show how personality styles are determined and explained by such internal representations of objects. They are internal maps that both determine our perception of the psychosocial world and are constantly shaped by our interacting experience of the same psychosocial occurrences (Fairbairn 1944).

To conclude, one can begin integrating the above knowledge in order to start and formulate personality disorders as undeveloped, or biased, resting-state network organizations, resulting from unstable biased past experiences (Peled 2012). In fact, from clinical experience we know that those suffering from personality disorders typically have disturbed and unstable personal histories dating back to infancy and childhood.

A new diagnostic framework

Each patient can now be characterized by an etiopathological brain-related neuroscientific diagnosis, a revolution in terms of psychiatric diagnosis which currently involves only descriptive phenomenological classification (i.e., signs and symptoms only). It must be emphasized that a descriptive diagnostic system cannot be validated, and in psychiatry the current diagnosis has reached only some increase in reliability but not validity. Devising effective cures to mental disorders will definitely require a valid brain-related diagnosis for mental disorders.

Translating the signs and symptoms of mental disorders to their related brain disturbances generates for each patient a "profile" of disturbances, sometime mixtures of several disturbances. The psychotic patient will suffer from disconnection dynamics and fragmentation of global brain organizations, the deficient schizophrenia patient will suffer from over-connected and impaired hierarchical organization of the brain. The patients with schizophrenia alternating between these phenomenological manifestations (or suffering from mixtures of positive and negative symptoms *) will demonstrate certain degrees of fragmented as well as over-connected damaged hierarchical brain organization.

The depressed patient will suffer from increased free energy due to mismatch between internal-representations and actual environmental occurrences, either due to reduced impaired plasticity, or due to stressful radical changes of environmental occurrences, or both. If internal representations are biased, non-adaptive in respect to environmental situations than personality disorder is the diagnosis and distress (typical to personality disorders) is the depression resulting from continuous mismatches and increases of free energy.

Biased non-adaptive mal-developed resting-state networks can disintegrate and fragment resulting in psychotic phenomenology thus one can understand how spectrum symptoms can arise involving psychosis, depression and personality disorders all at once.

Correspondingly each patient can show higher degrees of certain disturbances and lower for others, or a combination of elevated/reduce levels of the different disturbances ranging from global integration and stability to altered plasticity matching-dynamics and free energy, and resting state mal-developed neuronal networks.

A translation program titled "Clinical Brain Profiling (Peled 2006; 2013)" is available on the web at: http://neuroanalysis.org.il/?page_id=114 by entering the signs symptoms and history of the patient, the web-based CBP-computer-program generates a personalized-specific brain-related profile predicting the patterns of brain-disturbances of that specific patient.

NeuroAnalysis Therapy

From the insights above it becomes clear that to cure psychosis and schizophrenia connectivity balances and hierarchal organizations should be restored and optimized. The means for such therapy should be based on technologies that can monitor and correct (using feedback loops) such disturbances. Recently promising technologies ranging from DBS (Harati and Müller 2013), and Optogenetics (Peled 2011; Williams and Deisseroth 2013) to focused ultrasound (Jolesz and McDannold 2014) are emerging, with some promising perspectives.

From the above insights it is clear that by controlling and enhancing plasticity as is achieved with SSRI's, depression can be treated, however better control over plasticity will improve control over mood alterations and disturbances even further. We can also begin to understand how psychotherapy, being an experience-dependent process, can "correct" biased

internal resting-state-network formations, thus helping to reduce distortions and increase adaptability thus alleviating depression of personality disorders (by reducing free energy). Experience enhancing technology such as virtual reality (Sorkin et al 2006) can assist in certain therapeutic interventions. In the future it is also conceivable how plasticity enhancement, using specially designed medications, can boost both the specific psychotherapeutic like experience dependent therapy as well as control mood alterations in general.

Reference

- Andreasen N.C., The Scale for the Assessment of Negative Symptoms (SANS). Iowa City, University of Iowa, 1983.
- Bechtel W. Network organization in health and disease: on being a reductionist and a systems biologist too. *Pharmacopsychiatry*. 2013 May;46 Suppl 1:S10-21. doi: 10.1055/s-0033-1337922. Epub 2013 Apr 18.
- Baudry A, Mouillet-Richard S, Launay JM, Kellermann O. New views on antidepressant action. *Curr Opin Neurobiol*. 2011 Dec;21(6):858-65. doi: 10.1016/j.conb.2011.03.005. Epub 2011 Apr 27.
- Cooke SF, Bear MF. How the mechanisms of long-term synaptic potentiation and depression serve experience-dependent plasticity in primary visual cortex. *Philos Trans R Soc Lond B Biol Sci*. 2013 Dec 2;369(1633):20130284. doi: 10.1098/rstb.2013.0284. Print 2014.
- Duman RS, Aghajanian GK. Synaptic dysfunction in depression: potential therapeutic targets. *Science*. 2012 Oct 5;338(6103):68-72. doi: 10.1126/science.1222939.
- El-Hage W, Leman S, Camus V, Belzung C. Mechanisms of antidepressant resistance. *Front Pharmacol*. 2013 Nov 22;4:146.
- Fairbairn, R.D. 'Endopsychic structure considered in terms of object relationships' In: *An Object-Relationships Theory of the Personality* New York, Basic Books 1944, 82-136.
- Freud, S. (1938) 'Splitting of the ego in the process of defense' standard edition 23: 275-278
- Friston K.J., and Frith C.D. (1995) Schizophrenia a disconnection syndrome? *Clinical Neuroscience* 3, 89-97.
- Friston K. The history of the future of the Bayesian brain *Neuroimage*. 2012 Aug 15;62(2):1230-3. doi: 10.1016/j.neuroimage.2011.10.004. Epub 2011 Oct 17.
- Geva AB and Peled A. Simulation of Cognitive Disturbances by a Dynamic Threshold Neural Network Model. *Journal of International Neuropsychology*, 2000 Jul; 6(5);608-19.
- Harati A¹, Müller T². Neuropsychological effects of deep brain stimulation for Parkinson's disease. *Surg Neurol Int*. 2013 Nov 20;4(Suppl 6):S443-7. doi: 10.4103/2152-7806.121637.

Hebb D.O., The Organization of Behavior. New York, John Wiley & Sons, 1949.

Jolesz FA, McDannold NJ, Magnetic resonance-guided focused ultrasound: a new technology for clinical neurosciences. *Neurol Clin.* 2014 Feb;32(1):253-69. doi: 10.1016/j.ncl.2013.07.008. Epub 2013 Nov 8.

Jones MW. Errant ensembles: dysfunctional neuronal network dynamics in schizophrenia. *Biochem Soc Trans.* 2010 Apr;38(2):516-21. doi: 10.1042/BST0380516.

Meynert, T. *Psychiatry.* New York, Hafner 1885 (1968).

Peled A. Brain "Globalopathies" Cause Mental Disorders. *Med Hypotheses* 2013 Oct 5.

Peled A. Personality disorders disturbances of the physical brain. *Med Hypotheses* 2012 July 23

Peled A. Multiple Constraint Organization in the Brain: A Theory for Serious Mental Disorders. *Brain Research Bulletin* 1999 49: 245-250.

Peled A. Neuroscientific psychiatric diagnoses. *Medical hypothesis* 73, 220-229 2009.

Peled A. The neurophysics of psychiatric diagnosis: Clinical brain profiling. *Med Hypotheses.* 2010 Sep 7.

Peled A and Geva AB. Brain Organization and Psychodynamics. *J Psychotherapy Practice and Research* 1999 Winter; 8(1):24-39

Peled A. Brain profiling and clinical neuroscience. *Medical hypothesis* 67, 941-946 2006.

Peled A. Optogenetic neuronal control in schizophrenia. *Med Hypotheses.* 2011 Apr 9.

Schwartenbeck P, Fitzgerald T, Dolan RJ, Friston K. Exploration, novelty, surprise, and free energy minimization. *Front Psychol.* 2013 Oct 7;4:710. doi: 10.3389/fpsyg.2013.00710.

Sorkin A, Weinsahl D, Modai I, Peled A. Improving the accuracy of the diagnosis of schizophrenia by means of virtual reality. *American Journal of Psychiatry.* 163:3, March 2006

Wernicke, K. (1881) *Text Book of Cerebral Diseases.* Berlin, Karger, ed.

Whitt JL, Petrus E, Lee HK. Experience-dependent homeostatic synaptic plasticity in neocortex. *Neuropharmacology.* 2013 Mar 4. pii: S0028-3908(13)00073-7. doi: 10.1016/j.neuropharm.2013.02.016.

Williams SC, Deisseroth K Optogenetics. *Proc Natl Acad Sci U S A.* 2013 Oct 8;110(41):16287. doi: 10.1073/pnas.1317033110.

Wolf RC, Sambataro F, Vasic N, Schmid M, Thomann PA, Bientreau SD, Wolf ND.

Aberrant connectivity of resting-state networks in borderline personality disorder. *J Psychiatry Neurosci.* 2011 Nov;36(6):402-11. doi: 10.1503/jpn.100150.

Yan H, Zhao L, Hu L, Wang X, Wang E, Wang J. Nonequilibrium landscape theory of neural networks. *Proc Natl Acad Sci U S A.* 2013 Nov 5;110(45):E4185-94. doi: 10.1073/pnas.1310692110. Epub 2013 Oct 21.

Correspondence;

Avi Peled MD

Sha'ar Menashe Mental Health Center

Mobile Post Hefer, 37806, Israel

Tel: 972-522844050

Email: neuroanalysis@gmail.com