

# The Neuroscientific Psychiatric Clinician: Is that possible?

Avi Peled M.D.

## Summary

Psychiatrists will soon be able to diagnose their patients' neuroscientifically. Using "Brain Profiling" neuroscientific conceptualizations, psychiatrists can diagnose ' brain disturbances, and thus take a critical step toward finding effective cures for mental disorders. This editorial outlines how this can be achieved.

## Editorial

Can psychiatrists diagnose their patients neuroscientifically? And if so, how? In this editorial I will offer answers to these questions, and discuss their implications for treatment.

Today when a psychiatrist diagnoses patients with depression, anxiety or schizophrenia, the diagnoses are not related to neuroscience. Typically the diagnosis will involve descriptions, of the patient's complaints (symptoms). If the patient complains of depressed mood, helplessness, reduced motivation, reduced appetite and insomnia, he will be diagnosed with "depression". This diagnosis has no added value to the patient or the clinician. This situation differs from that of the internist who diagnoses appendicitis when the patient complains of stomach pains. Upon diagnosing appendicitis the physician gains added values - he knows what organs are involved and what needs to be done to facilitate a cure. The psychiatrist that has diagnosed depression or schizophrenia does not know what part of the brain is involved or where to focus treatment to promote recovery.

Diagnosing mental disorders neuroscientifically is based on the assumption that mental disorders arise from alterations in brain organization. The normal brain optimizes connectivity and hierarchical organizations to achieve integrated information processing and high-level coherent stable conscious experience (1). This is achieved via active synaptic plasticity, offering adaptive dynamic connectivity necessary for brain organization and computation. Small world organization has been found to be an optimal organization for brain networks (2). The healthy brain generates predictions about its environment, creating prophetic internal models of the world around it (3) and uses them as guidance for adaptive efficient behaviors and decision making. These internal models determine how we perceive ourselves and react to others and to a large extent, configure our personality styles. These internal representative predictive models are embedded in basic

network connectivity structures recently called default-mode networks (4).

Following is an attempt to relate different major types of mental disorders to disturbances of different aspects of normal brain organization; *(i)* schizophrenia to connectivity imbalance, *(ii)* mood disorders to hampered plasticity dynamics and *(iii)* personality disorders to altered default-mode networks.

*i* For many years it has been noted that altered dopaminergic activity is related to schizophrenia, additionally hypofrontality has been repeatedly revealed in schizophrenia patients. Over the last decade psychotic symptoms of schizophrenia have been correlated with many findings pointing toward disconnection dynamics that afflict the brains of such patients (5). The frontal brain systems have decisive roles in balancing widespread connectivity in the brain and the dopaminergic innervations act upon prefrontal pyramidal cells probably by regulating input-output relationships of these neurons. Such regulation is in a position to "disconnect" or "over-connect" wide spread cortical systems. Thus these findings together point to the assumption that schizophrenia symptoms relate to connectivity imbalances in the brain (6). When global brain organizations collapse, fragmentation of integrated experience ensues with resulting psychotic symptoms. The range of schizophrenia symptoms and their heterogeneity can be explained by the various degrees and wide range of patterns of connectivity imbalances that afflict the brains of schizophrenia patients (6).

*ii* Accumulating implications of neuronal plasticity in depression has been documented in the recent literature (7). Neuronal death is correlated with depression, and antidepressant medications act by inducing neurogenesis and synapto-genesis. A synapto-plasticity etiology of depression can begin to take shape based on neuronal plasticity and adaptability. Whole brain adaptability is directly related to plasticity of connections, making plasticity

relevant to the formation of stable internal models within default-mode networks (relevant to personality) as well as fast plasticity of connectivity balances (relevant to conscious experiences). It can be presumed that effective plasticity and good adaptability of network connectivity correlates with elevation of mood. The opposite is associated with depression, i.e., reduced plasticity, adaptability and optimization dynamics in the brain (8).

*iii* The idea that personality relates to internal representations upon which we perceive and react to psychosocial occurrences is centuries old wisdom (9). The ability of neuronal network ensembles to incorporate and activate memories is also well known (10). Thus neuronal network organization of the brain can account for internal representations and the recently discovered Default-Mode-Network can offer a reasonable basic, whole-brain, network construction for internal representations that determine personality styles and traits. These advances in neuroscientific understanding allow for a "default-mode-network-

disturbance" hypothesis underlying the causes of personality disorders.

By combining these preliminary insights, explanation can be provided for many psychiatric manifestations that we encounter in the clinic. For example, a major complaint of patients suffering from personality disorders is depressed mood. Non adaptive internal models hamper optimization dynamics (i.e., mismatch with actual occurrences) resulting in depression. Another example is schizoaffective manifestations where it is conceivable that connectivity imbalance alters plasticity, inducing de-optimization dynamics and depression.

Equipped with these preliminary insights, a neuroscientific approach to psychiatric complaints can be generated. Clinical brain profiling (CBP) translates clinical manifestations of patients to their presumed set of brain alterations or disturbances Table 1).

Table 1: CBP (Clinical Brain Profiling)

<i>Brain dynamic disturbance</i>	<i>Assumed clinical correlate</i>
Undeveloped disturbed Default-mode network	Personality disorders
De-optimization (plasticity) dynamic shift	Symptoms and signs of depression
Hyper-optimization (plasticity) dynamic shift	Symptoms and signs of mania
Disconnectivity dynamics	Psychosis and positive signs schizophrenia
Over-connectivity dynamics	Repetitive poverty ideation perseverations

What is achieved by introducing CBP? First it achieves a novel introduction of neuroscience into psychiatric clinical work. Second, it offers new perspectives for more effective future therapeutic strategies.

Regarding introduction of neuroscience into psychiatry, for example the psychiatrist on the night shift, presenting a patient to his colleague who will replace him on the ward for the morning shift, will describe patient phenomenology in neuroscientific terms. He may say "this patient complains of depression and has a long history of non-adaptive personality traits; it seems he is suffering from de-optimization dynamics related to immature biased default-mode-network organizations." Another patient suffering from disintegrated conscious experience (psychosis), will be presented as having "connectivity imbalance" of a "disconnection type." This language engages the clinician with the relevant neuroscience of his patient. Next, it opens up directions for therapeutic interventions.

Regarding novel perspectives for more effective future therapeutic strategies, these neuroscientific conceptualizations immediately entail what needs to be achieved to cure the patients. For example the first patient requires induction of plasticity dynamics that will, both optimize brain dynamics (antidepressant effect), and lay the ground for improving upon the default-mode-network organization. This can be done by applying relevant experience-dependent corrective protocols (more targeted psychotherapy-like strategies). The second patient, who suffers from psychotic manifestations, may be scheduled for connectivity rebalancing protocols using brain stimulation, magnetically/electrically driven, or optogenetically engineered.

In summary it seems we are fast approaching the time when psychiatrists will diagnose their patients' neuroscientifically using CBP-like formulations. Such achievement is a critical step toward effective cures for mental disorders.

## References

1. Tononi G. Information integration: its relevance to brain function and consciousness. *Arch Ital Biol.* 2010; **148**(3): 299-322.
2. Yan C, He Y. Driving and driven architectures of directed small-world human brain functional networks. *PLoS One.* 2011; 6(8):e23460. Epub 2011 Aug 12
3. Carhart-Harris RL, Friston KJ. The default-mode, ego-functions and free-energy: a neurobiological account of Freudian ideas. *Brain.* 2010;133(Pt 4):1265-83.
4. Otti A, Gündel H, Wohlschläger A, Zimmer C, Sorg C, Noll-Hussong M. [Default mode network of the brain : Neurobiology and clinical significance.] *Nervenarzt.* 2011 May 18. [Epub ahead of print] [German]
5. Jones MW Errant ensembles: dysfunctional neuronal network dynamics in schizophrenia. *Biochem Soc Trans.* 2010; 38(2): 516-521.
6. Peled A. Multiple constraint organization in the brain: a theory for schizophrenia. *Brain Res Bull* 1999 1;49(4):245-250.
7. Baudry A, Mouillet-Richard S, Launay JM, Kellermann O. New views on antidepressant action. *Curr Opin Neurobiol.* 2011 Apr 27. [Epub ahead of print]
8. Peled A. The neurophysics of psychiatric diagnosis: clinical brain profiling. *Med Hypotheses.* 2011; 76(1):34-49.
9. McCarthy JB. Adolescent character formation and psychoanalytic theory. *Am J Psychoanal.* 1995; 55(3):245-267
10. Rumelhart DE, McClelland JL. Parallel Distributed Processing: Exploration in the Microstructure of Cognition, PDP Research group ed., Vol. 1 and 2. MIT Press, Cambridge, 1986.