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Hypothesis

Neuro analysis: a neuroscientifi c psychiatry. Why?, how? and when?

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Abstract

Introduction

Why do we need neuro-scientific psychiatry, how can we achieve it, and when will we know it has been achieved? Brain-related psychiatry is essential for us to know what exactly went wrong with our patients. Curative interventions are impossible before we understand about the etiopathology of our patients. How can we approach this daunting task? It has recently become apparent that global-distributed neuronal-network brain disturbances cause psychiatric disorders. Thus we need to find the correlated underlying neuronal-network disturbances of the various phenomenological manifestations of psychiatric disorders.

Hypothesis

Neuro Analysis is the proposed approach and Clinical Brain Profiling is a concrete plan by which mental disorders can be translated into their associated brain disturbances. A concise over-view explanation of NeuroAnalysis is presented in this hypothesis. Once we start eliminating mental disorders, we will understand that neuro-scientific psychiatry has been attained.

Conclusion

We can conclude the obvious questions of 'Why?', 'How?' and 'When?' associated with NeuroAnalysis from this hypothesis as follows:

1. Why?: Because we need to know what went wrong with our patients in order to cure them.
2. How?: We associate psychiatric phenomenology to neuronal-network disturbances in the brain.
3. When?: When we cure patients using the insights concisely described heretofore.

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Introduction

If one follows the general literature of neuroscience in psychiatry it is apparent that over the last decade, 'mental disorders' have been found to correlate with disturbances to global-distributed brain functions. If in the past, brain functions and disturbances were associated to localised-brain damage, in the recent times, it has become increasingly obvious that multiple parallel brain locations are involved in mental disorders; thus, disturbances to the global network in the brain account for mental illnesses.

Recent comprehensive formulations of this type of network approach to mental disorders are described by Menon[1] in his article 'Large-scale brain networks and psychopathology: a unifying triple network model' and by Joshua Buckholtz and Andreas Meyer-Lindenberg[2] in 'Psychopathology and the human connectome: toward a transdiagnostic model of risk for mental illness'. 'Connectome' is a new emerging concept that defines large-scale whole brain network organisation.

Global brain disturbances potentially help to conceptualise higher-level mental functions and disturbances, as emergent properties. Single neurons, genes or neurotransmitters, do not possess properties such as 'awareness', 'mood' or 'personality', but whole brain organisation emerges to support such phenomena. They are 'emergent properties', because they emerge from the brain functions as a whole.

Despite this, still there is a challenge of associating mental disorders to their causes at the level of brain disturbances, or in other words the creation of neuroscientific psychiatry. Today, the psychiatric diagnosis is descriptive, patients are classified and treated according to 'signs' and 'symptoms', and at the taxonomic level, the Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic nosology is not brain-related. Unlike other fields of medicine where the nosology reflects the aetiology, for example the diagnosis of 'appendicitis' refers to a location in the body, the 'appendix' and to the pathology, i.e., the infection; the diagnosis of 'depression' is not associated to brain systems or function.

Thus, rather than descriptive psychiatry, neuroscientific psychiatry is critical, because only neuroscientific psychiatry will lead us to effective treatments for mental disorders. The identification of the causes of mental disorders is crucial if we aim to cure them.

Being said that the first question of the title of this manuscript is answered, 'Why?' we need neuroscientific psychiatry, i.e., 'NeuroAnalysis?' to cure our patients[3].

As the title implies, we will explain 'How?' we can achieve 'NeuroAnalytic' neuroscientific psychiatry. Finally, 'When?'. When we shall achieve it, or in other words, what are the criteria by which we shall achieve NeuroAnalytic psychiatry.

Hypothesis

Capitalising on the vast literature of neuroscience combined with Physics

FOR CITATION PURPOSES: *Peled A.* Neuro analysis: a neuro scientific psychiatry. Why?, how? and when? OA Medical Hypothesis 2013 Apr 01;1(1):3.

Competing interests: none declared. Conflict of Interests: none declared.
All authors contributed to the conception, design, and preparation of the manuscript, as well as read and approved the final manuscript.
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of Complex Systems, new insights emerge, which are incomprehensible when each of these scientific bodies stands alone.

For the purpose of this manuscript, we shall concentrate on aspects of complex neural systems organisations consisting of both neuronal network connectivity and neuronal network dynamics.

Neuronal network connectivity will be subdivided into resting states, active networks and small-world networks, and neuronal network dynamics will be described in terms of entropy measurements, namely 'free energy' optimisation dynamics.

Evaluation of hypothesis

The author has referenced some of his own studies in this hypothesis. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees associated to the institutions in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in the studies.

In recent years, investigations of neuronal connectivity has found highly non-random network attributes, including high clustering and modularity combined with high efficiency and short-path length. The combination of these attributes simultaneously promotes high specialisation and high integration within modular small-world architecture. Small-world network organisation seems to be an optimal form of brain organisation offering functional optimisation; it characterises healthy mental functions. These networks are broad scale in nature, signifying the existence of pivotal connection hubs and resilience of the brain network to random and targeted attacks. The brain network seems to evolve progressively from a local, predominantly proximity-based connectivity pattern to a more distributed, predominantly functional-based connectivity pattern[4].

Vertes and Duke[5] found that small-world networks perform an order of magnitude better than random ones, enabling reliable discrimination between inputs even when prompted by increasingly incomplete recall cues. They show that small-world architectures operate at significantly reduced energetic costs and that their memory capacity scales favourably with network size.

Because small-world networks explain hierarchy in the brain, it is known that the brain organises hierarchically with bottom-up processes of unimodal, multimodal and transmodal integration[6] in which our conscious experience is integrated into coherent experiences from the integration of basic precepts i.e., auditory, visual, somatosensory and olfactory.

In recent years, resting-state brain networks (RSNs) have been described, as opposed to activated cognition-related networks, these are typically called 'default-mode networks' (DMN). Ding and colleagues[7] investigated the topological properties of the default-mode, dorsal attention, central-executive, somato-motor, visual and auditory networks derived from resting-state functional magnetic resonance imaging (fMRI). They found small-world topology in each RSN.

Over the years, accumulated research work has shown that disturbances to neuronal network connectivity have been associated to psychosis[8], thus it can be shown that the phenomenology of the schizophrenia spectrum can be explained by different disturbances to connectivity and hierarchy of brain neuronal networks.

Hebbian plasticity[9] teaches us that connectivity can embed information, i.e., memories and internal representations, by strengthening sets of connections spread in the brain to facilitate activations (i.e., recall) of neuronal ensembles that likewise spread in the brain. Thus, Hebbian plasticity can explain formations of internal representations emerging from experience during the lifetime, i.e., experience dependent plasticity can account for who we are in terms of personality development and psychological identity[3].

Neuronal network activity changes over time as a continuous flux of dynamic change; this is naturally explained in the random versus deterministic characteristics of brain organisation and also in the plasticity and adaptability of the brain during neuronal computations and information processing. 'Free energy'[10] is a quantifiable statistical entropy measurement that is kept low when differences between environmental occurrences and internal brain organisations are reduced. However, free energy increases whenever biases, or mismatch between environmental occurrences and internal representational models in the brain occur.

Intuitively, plasticity and changeability of neuronal networks directly associate to free energy. If a network is more plastic and changeable, it will adapt better to incoming stimuli from the environment, thus reducing the free energy more effectively. If plasticity is hampered, adaptability is reduced and free energy may even increase. Because altered plasticity is dominant in depression, plasticity-dependent free energy alterations can be tied to mood disorders in psychiatry[3].

Consequences of hypothesis

Psychiatrists have always desired to achieve an objective of a direct linear 'cause-and-effect' correlation between the cause of a disease and its outcome. This is not possible when non-linear complex systems are involved. Thus, a first result from this study of the scientific literature is that the task of associating each mental disturbance to a specific phenomenological clinical entity is impossible, which is against the nature of brain organisation. Rather, the psychiatric phenomenologies are emergent

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properties from whole-brain disturbances in terms of connectivity (of active networks and RSNs, as well as small-world alterations), Hebbian experience-dependent plasticity and finally, altered dynamics of plasticity in relationship to reduction of free energy.

Nevertheless, a rough approximate correlate can be described for personality disorders with small-world alterations of RSNs, mood disorders with plasticity disturbances and free energy alterations and finally, schizophrenia spectrum and psychosis with altered connectivity balances within active and resting-state neuronal networks.

Psychologists teach us that personality is associated to the way we perceive ourselves and others, the way we react and behave in complex psychosocial situations, and all that is a result of our past experiences learned and accumulated across time from infancy to adulthood. In the early 1850, Theodor Meynert[11] argued that in the process of development experiences, thoughts create individual network brain organisations representing individual experiences and thoughts are responsible for our conduct in the world. The existence of Meynert's individual network structure has been recently established under the term DMN. It is a basic at-rest (non-task) associated brain organisation. Information in DMNs is embedded into neuronal connections using Hebb plasticity[9], in other words it is embedded by adjusting (strengthening) connections among neuronal ensembles. This is similar to experience-dependent plasticity[12], a process of synaptic changes and connections shaped by experience. Taken together, these insights make it possible to begin and reconceptualise personality disorders as disorders of the DMN. Such reconceptualisation will replace the descriptive (non-brain-related) term of 'personality disorder' with the brain-related neuroscientific term of 'disordered DMN'. This is not merely a semantic change. The DMN obeys small-world organisations and disturbances to the small-world of the DMN detected by signal processing of future imaging data can offer an objective brain-related neuroscientific diagnosis for personality disorders.

Depression is associated with reduced neuronal plasticity in the form of cell death, reduced dendrite arborisation and reduced number of spines on dendrites[13–18]. Antidepressant effects correlate with synaptogenesis and neurogenesis, which are the late effects of selective serotonin re-uptake inhibitors (SSRIs) and electroconvulsive therapy (ECT)[19]. The changes in plasticity associated to mood seem to be spread over vast cortical regions, as SSRIs are known to effect large percentages of cortical neurons. Thus, mood regulation seems to involve whole brain dynamics. Increased plasticity and changeability has an antidepressant effect while reduced plasticity is correlated with depressed mood[20]. We can conceptualise mood alteration in conjunction with free energy reduction. It is conceivable that the plastic malleable brain will adapt better to its environment, thus reducing free energy more effectively. As explained above, increased plasticity has an antidepressant effect, and also offers better free energy reductions, thus reduction of free energy is associated to antidepressant effect. The opposite assumption argues that increase in free energy has a mood depressing effect. Reduced brain plasticity causes the brain to be less adaptive, this creates mismatch and biases between internal constructs and environmental occurrences—mismatch, which is measured as the increase of free energy. Stress always involves a substantial change in the environment, losing a dear one, losing a home, a job and so on, significantly changing every-day experiences. Changes, abrupt and large, immediately create a difference and mismatch with the internal representations of the habitual world represented in the brain. This results in the immediate increase of free energy and results in the depressed mood. The advanced formulations so far can explain endogenic depression as reduced neuronal plasticity and brain adaptability unrelated to external stress. Reactive depression is an increase of free energy due to changes in the environment. In summary, the descriptive terminology of mania and depression can now be substituted with brain-related reduction and increase of free energy within brain-environment interactions.

In his article, 'Errant ensembles: dysfunctional neuronal network dynamics in schizophrenia', Jones[8] summarises mounting empirical evidence for connectivity disturbances of neural network in the brains of schizophrenia and psychotic patients. Disconnectivity has also been shown to afflict hierarchical brain organisation[21] interfering with top-down cognitive control and bottom-up hierarchical dynamics.

Neural network models that simulate thought processes[22] and perception[22] demonstrate that by disconnecting the processors (simulated neurons) of the network, the activity of the network models' clinical phenomenology such as loosening of associations, fragmentation of perception hallucinations and delusions encounter the clinical manifestations of psychosis. Connectivity imbalances in the bottom-up top-down dynamics can result in systemised delusions when top-down shifts result in overly controlling schemata that bias the actual experiences. Bottom-up insufficiencies result in impaired higher-level organisation, curtailing higher-level phenomena such as motivation and volition[6]. Taken together, these insights can associate phenomenology of schizophrenia to brain connectivity disturbances and offer to begin and reconceptualise descriptive phenomenology such as positive and negative

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signs of schizophrenia in term of 'disconnection', 'over-connection', 'bottom-up insufficiency' and 'top-down shift'[3].

Discussion

'How?' How can we achieve neuroscientific diagnosis from the insights accumulated so far? and 'When?' when will we know that we have achieved neuroscientific psychiatry?

Clinical Brain Profiling (CBP) involves translating clinical phenomenology into different neuronal-network disturbances as described so far. An old Chinese adage states that 'wisdom begins by calling things by their correct names', thus we must start calling mental disorders based on their underlying brain disturbances. Hence, CBP can offer a starting point for brain-related psychiatry.

CBP is available on the internet[23] and assigns signs, symptoms and history, each to the presumed brain disturbance that is associated with it. In general, the phenomenology associated to personality disorders is linked to altered-small-world of RSNs. The one linked to mood disorders predicts plasticity disturbances and free energy alterations and finally, signs and symptoms of psychosis and schizophrenia are assumed to originate from connectivity imbalances within active and resting-state neuronal networks.

Neuroscientific psychiatry can be achieved by developing a CBP approach that associated phenomenology to the brain. It has the advantage of making the clinical discussion about personal patients on the ward relevant to neuroscience by describing maladies using brain-related neuroscientific terminologies. This process can be conceptualised as NeuroAnalysis; brain-related neuroscientific psychiatry is defined by the term 'Neuro', and the analytic development of CBP by the term 'Analysis'.

The ultimate goal of NeuroAnalysis is to validate the CBP approach. When will we know that NeuroAnalytic psychiatry has been achieved? The answer to this is when we will be able to find the cure for the most severe non-responsive illnesses in psychiatry, such as severe forms of schizophrenia.

Optogenetics[24] is an emerging technology that can control neurons, specifically activating and inhibiting targeted neurons in the brain[25]. This technology has the potential to correct altered erroneous neuronal network activity just as a cardiac pacemaker corrects arrhythmias in the heart. Similarly, an optogenetic brain-pacemaker will one day be able to correct brain disturbances, optimise the brain organisation to eliminate the signs, symptoms and course of severe mental disorders. That day we will know that we have triumphed over mental disorders, and the question of 'When?' will be answered.

Conclusion

NeuroAnalysis: Why? How? and When? 'Why?': Because we need to know what went wrong with our patients in order to cure them. 'How?': We will associate psychiatric phenomenology to neuronal-network disturbances in the brain. 'When?': When we cure patients using the insights concisely described heretofore.

Abbreviations list

CBP, Clinical Brain Profiling; DMN, default-mode –network; RSN, resting-state brain network; SSRI, selective serotonin re-uptake inhibitors.

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