N e u r o – H a t

Patent Proposal for Brain-Profiling Synchronization of Phenomenology and Brain-Imaging in psychiatry

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ABSTRACT

The Neuro-Hat device is proposed to integrate theory and technology to help discover the causes of mental disorders and provide for future therapeutic brain-pacing technology. “Neuro” signifies NeuroAnalysis Clinical Brain Profiling, and the “Hat” refers to a head-mounted sensors platform that captures psychiatric phenomenology (i.e., mental status examination) and EEG brain activity. Thus the Neuro-Hat integrates clinical phenomenology and brain imaging using NeuroAnalysis conceptualizations and aspires to provide for therapeutic pace-making interventions.

Current neuroscientific knowledge allows for preliminary formulation of brain-related diagnoses for mental disorders. When translating clinical phenomenology to brain disturbances we assign the diagnosis of schizophrenia and psychosis to connectivity perturbations of the brain. We assign mood and anxiety disorders to disturbances of brain plasticity resulting in disturbed optimization dynamics. Finally we assign the phenomenology of personality disorders to immature, biased unstable resting state networks.

In recent years deployed sensor technology has seen substantial development; video cameras, vocal recordings, motion sensors and dry EEG electrodes have been miniaturized and have become cost-effective to the extent that they can easily be deployed on portable wearable devices. Sensors technology can be converged onto a head-mounted hat device; the “Neuro-Hat.” It is the first conceived platform that combines real-time online estimation of psychiatric phenomenology coupled with simultaneous synchronized EEG brain imaging.

Various signal processing methods for a sensing Neuro-Hat device are described and its utility for construction of a future brain pacing therapeutic technology is presented.

INTRODUCTION

Neuro-Hat is a device that will be used to integrate theory and technology to help discover the causes of mental disorders and provide for future therapeutic brain-pacing technology. "Neuro" signifies NeuroAnalysis theory of Clinical Brain Profiling, and the "Hat" refers to head-mounted sensors that use technology to captures psychiatric phenomenology (i.e., mental status examination) and EEG brain activity. Thus the Neuro-Hat integrates clinical phenomenology and brain imaging using NeuroAnalysis conceptualizations and aspires to provide for therapeutic pace-making interventions.

NeuroAnalysis is an attempt to reformulate mental disorders as brain disorders (1-8). NeuroAnalysis formulates mental disorders as disturbances to the neuronal network organization of the brain (7) recently also termed as disturbances to the "Connectom" of the brain (9). Disturbances to the connectom can be structural or functional. NeuroAnalysis reformulates mental disorders as disturbances to the functional dynamics, i.e., plasticity organization of the connectom. Clinical Brain Profiling (CBP) is the term chosen for the translation algorithm which classifies clinical phenomenology to plasticity connectome disturbances. The translation matrix incorporates recent advances in computational psychiatry (8)

NeuroAnalyisis validation of CBP requires combination of ongoing phenomenology of mental disorders with constant brain-imaging dynamics such as that of Holter EEG sampling. CBP predicts the relationships between patient's phenomenology and the brain disturbances identified in ongoing EEG brain imaging. A device that combines sampling of psychiatric phenomenology (i.e., mental status examination) and continuous EEG brain imaging can create the platform to validate CBP. Once validated, such a device can become an effective diagnostic tool for psychiatric illnesses. This same device can further constitute a guiding device for therapeutic intervention technologies.

In this paper: ***i***) brief description of CBP will be presented, for in-depth details of CBP the reader is referred to (1-8). ***ii***) A Hat-device titled "Neuro-Hat" for sampling ongoing psychiatric phenomenology and EEG brain-imaging is conceived. ***iii***) Some requirements for CBP-related EEG analysis are proposed and ***iv***) prospects of future intervention technologies are discussed.

Brief description of CBP

Current neuroscientific knowledge allows for preliminary formulation of brain-related diagnoses for mental disorders. The brain develops from infancy to adulthood, and beyond, by a process of "experience dependent plasticity". This process enables synapses to form connections among neurons (i.e., plasticity) based on their activations by the experience of incoming stimuli. Such activity enables experience to shape neuronal network organizations in the brain and encoding life experiences in the form of memories which are actually patterns of synaptic connection strengths. Thus each brain develops an internal model (or representation) of the outer world, or internal "Object Relationships" as psychologists term them, to explain personality traits, behaviors and reactions.

The internal representations serve as guiding maps of our experiences and predictions of actual occurrences. "Optimization" is when internal predictions match real occurrences (reduction of free energy, i.e., predictive errors (10). Inversely, in "De-Optimization" there is a mismatch between internal expectation and actual occurrences. Optimization dynamics is considered a characteristic of global plasticity. Any reduction in plasticity will hamper optimization dynamics and cause depression (4-5). This link to plasticity is evident from antidepressant medications that are known to have plasticity inducing effects (11). Plasticity also stabilizes the brain system, thus producing a calm tranquil sensation as opposed to anxious sensations that emerge from perturbed unstable neuronal networks (1). Mood, either anxiety or depression, is an "Emergent Property" from whole brain optimization dynamics (3).

Finally the brain needs to function and maintain optimization in the face of continued perturbations and instabilities generated by the computational load. The optimal (healthy) brain archives small-world network organization which balances connectivity and hierarchy. When connectivity is perturbed it can cause disconnection and over-connection disturbances (7), these are clinically expressed as disorganization psychosis, or perseverative stereotype deficiency syndromes, respectively. When hierarchy is perturbed it can collapse leaving the brain deprived of higher level functions (deficiency symptoms), or alternatively top-down biases can create delusions that may even become systemic (7).

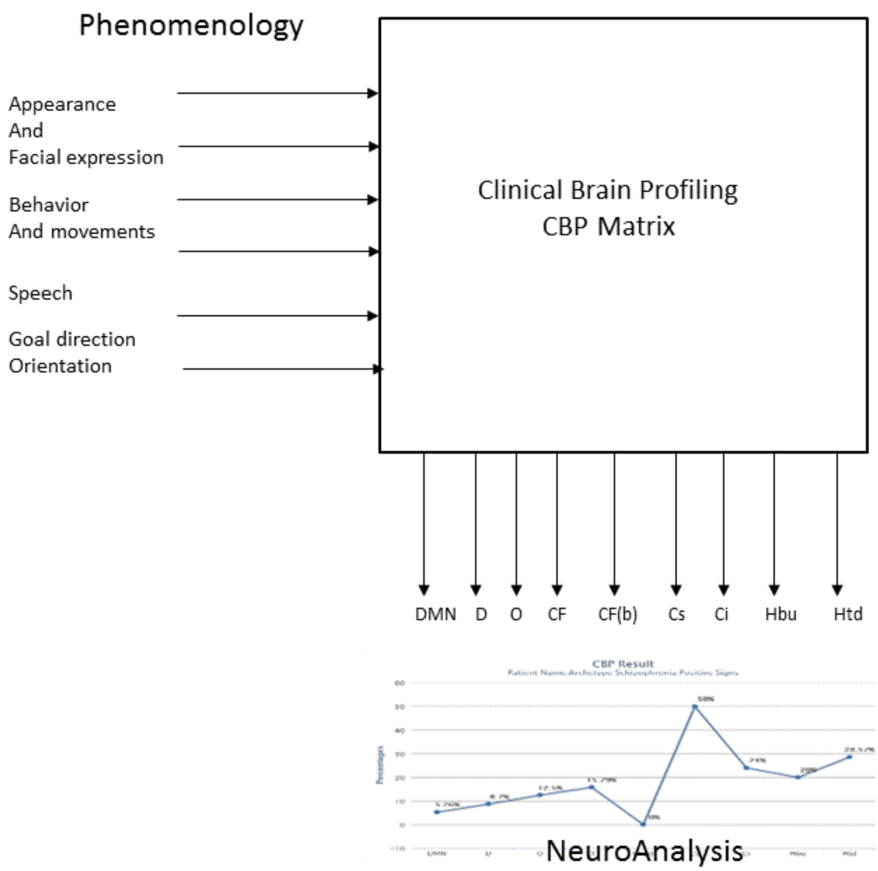
When translating clinical phenomenology to brain disturbances we assign the diagnosis of schizophrenia and psychosis to connectivity perturbations of the brain. We assign mood and anxiety disorders to disturbances of brain plasticity resulting in disturbed optimization dynamics. Finally we assign the phenomenology of personality disorders to immature, biased unstable resting state networks Table 1 summarizes the CBP parameters

Table 1

Table 1: Clinical Brain Profiling - Diagnoses

Symbol	Brain dynamic disturbance	Assumed clinical correlate
DMN	Undeveloped disturbed DMN organization	Personality disorders
Cs	Disconnectivity dynamics	Psychosis and positive signs schizophrenia
Ci	Overconnectivity dynamics	Repetitive poverty ideation perseverations
Hbu	Hierarchical bottom-up insufficiency	Avolition and negative signs schizophrenia
Htd	Hierarchical top-down shift	Systemized organized delusions
D	Deoptimization dynamic shift	Symptoms and signs of depression
O	Hyper-optimization dynamic shift	Symptoms and signs of mania
CF	Constrain frustration	Symptoms and signs of anxiety
CFb	Stimulus bound Constrain frustration	Symptoms and signs of phobias

Figure 1 schematizes the input-output relationships of CBP, entries (inputs) constitute parameters from the mental status examination involving appearance facial expression behavior, and speech. CBP outputs are predictions about distances to the dynamic neuronal network organization of the brain.



To estimate these CBP-generated predictions about brain disturbances, a continuous brain-imaging sampling is required. A portable continuous sampling of brain network activity can be estimated using EEG activity. Modern technology offers such EEG estimations as will be explained in the next section.

Neuro-Hat

In recent years deployed sensor technology has seen substantial development, video cameras, vocal recordings, and motion sensors have been miniaturized and became cost-effective to the extent that they can easily be deployed on portable devices such as smartphones and wearable devices (e.g., google-glass). Wireless signal-transmission offers effective effortless data collection-storage from these sensors, which in turn opens up possible signal processing for sensing of various real-life events and occurrences.

Glenn and Monteith (12) claim that in the future, new medical measures will assist with the screening, diagnosis, and monitoring of psychiatric disorders. They describe that new technologies and algorithms will be used to estimate new measures of mental state and behavior based on digital data. The algorithms will analyze data collected from sensors in smartphones and wearable technology, and data collected from internet and smartphone usage and activities. They indicate that there are societal and ethical implications related to the use of these measures of mental state and behavior for both medical and non-medical purposes. Markowetz et al (13) emphasize that for the first time in history, it is possible to study human behavior on a great scale and in fine detail simultaneously. Online services and ubiquitous computational devices, such as smartphones record our everyday activity. The resulting Big Data offers unprecedented opportunities for tracking and analyzing behavior. They claim that these sensing and monitoring technologies induce the single biggest methodological shift since the beginning of psychology or psychiatry. The resulting range of applications will dramatically shape the daily routines of researchers and medical practitioners alike. Transferring techniques from computer science to psychiatry and psychology is about to establish Psycho-Informatics, an entire research direction of its own.

Mimura and colleagues (14) searched for simple behaviors using smartphone sensors with three axes for measuring acceleration, angular speed and direction. They used quantitative analytic methodology of pattern recognition for work contexts, individual workers and seasonal effects in their own longitudinally recorded data. Behavioral characteristics such as speed, acceleration and azimuth, pitch, and roll angles were monitored. Afterwards, participants noted subjective scores of warmth sensation and work efficiency. The multivariate time series behavioral data were characterized by the subjective scores and environmental factors, using the linear mixed model. Daily behaviors allowed them to quantify the effects of the psychological states and environmental factors on behavioral traits.

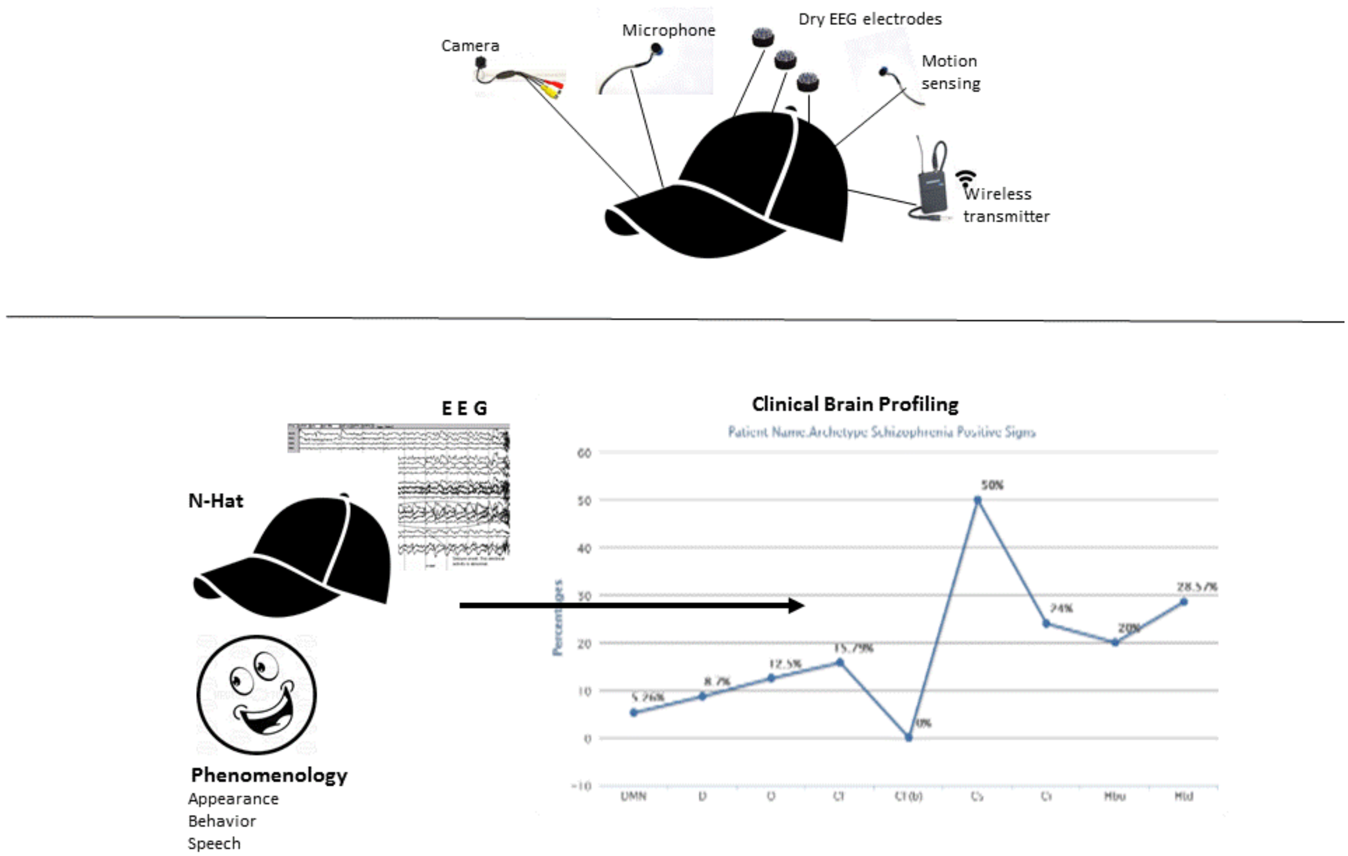
Another recent study (15) discusses a personalized wearable monitoring system, which provides information and communication technologies to patients with mental disorders and physicians managing such diseases. The system, called the PSYCHE system, is mainly comprised of a comfortable t-shirt with embedded sensors, such as textile electrodes, to monitor electrocardiogram-heart rate variability piezo resistive sensors for respiration activity, and triaxial accelerometers for activity recognition. The smartphone collects the physiological and behavioral data and sends the information out to a centralized server for further processing. They present experimental results gathered from ten bipolar patients, wearing the system. Their results provide promising and viable support to clinical decisions in order to improve the diagnosis and management of psychiatric disorders.

Companies such as “Cognionics” and (Holst Center” are developing dry EEG sensors that can be attached to wearable devices such as head-bands (17) other companies such as “LifGraph” and “Mont4t” (17) are developing smartphone deployed sensing of behavioral and mental activity.

Here the described Neuro-Hat which is actually a head-mounted set of sensors for extracting information about mental-status (i.e., psychiatric phenomenology) and also EEG sensors for extracting electrical brain activity, one that will be used to estimate the ongoing neuronal network dynamics of the brain. Thus the Neuro-Hat is the first conceived platform that combines real-time online estimation of psychiatric phenomenology coupled with simultaneous synchronized EEG brain imaging.
It is proposed that the existing technologies described above will converge on a head-mounted (wearable) device that is similar to a baseball hat. Psychiatric phenomenology as well as EEG can be simultaneously extracted using a microphone, camera, motion detector, navigation indicator and dry EEG electrodes

Behavior and activity such as restlessness or slowness can be detected by motion and navigation assessments; speech-intensity and modulation as well as speech content can be extracted from speech analysis recorded by the microphone; facial expression and change-ability can be detected by facial analysis captured by the video-camera. This extracted phenomenology is recorded simultaneously and in synchrony (synchronized) with brain activity as sampled by the EEG recordings.
The uniqueness and advantage of the Neuro-Hat over regular sensing technologies described so far, is the coupling of sensing from the environment and the brain simultaneously, and the introduction of the CBP context applied to give a theory-driven meaning to the phenomenology-brain data-analysis. In sum, one device 1) extracts ongoing psychiatric phenomenology, 2) monitors brain-related imaging EEG activity synchronized specifically with that phenomenology and 3) and combines their analysis within the meaningful theory-driven context of CBP. This analysis is detailed in the next section.

Figure 2 upper part shows microphone (voice sensing), video-camera (appearance), motion sensing and EEG electrodes that are all deployed on a regular hat. The lower part of figure 2 shows how simultaneous phenomenology and EEG extraction can be used to validate CBP.



CBP-related EEG analysis

To detect all of the various CBP predictions connectivity dynamics at multiple network scales spanning large (years) to small (millisecond-range) time delays, will be needed. Thus a "toolbox" of many types of signal processing acting in parallel will be needed to search for the different CBP predictions. It seems that one single type of signal processing cannot be equally sensitive to all of the CBP predictions.

The general logical and most common analysis for whole brain signal analysis involves generating functional correlation matrices where connectivity is assumed to show as increased correlations among different sensors (in this case EEG electrodes). From the functional matrices graphs representing connectivity organization can be extracted and studied. For example one common investigation of network can be that of Small-World organization which maximizes information transfer reducing connection cost, this is typically achieved at certain balance between clustering coefficient and long track pathways (18).

Constructing correlation matrices can involve simple regular correlations, but in highly non-linear systems such as the brain more sophisticated nonlinear estimations are probably required, e.g., Granger causality, estimating entropy, Mutual information, "Dimension estimation (20), dynamic causal modeling (DCM 21). When going up to levels that require analysis of vast cortical connectivity and even whole brain connectom organizations, analysis such as Neural Complexity (22) measures is warranted. Graphs are probably the most powerful visualization and estimation of brain organization at the network level (23). K-Shell decomposition (24) divides the network in layers (the cores) thus providing a centrality measure for nodes.

In summary, graph theory gives us a language for networks. It allows us to define networks exactly and to quantify network properties at all different levels. Such characterizations can become measurements of well-organized optimal networks of healthy brains and can also become the basic language identifying and specifying altered insufficient and damaged brain networks. In other words graphs dynamics can become the language of "brain arrhythmias" similar to ECG alterations for cardiac arrhythmias. Specifically for CBP, both connectivity and hierarchy alterations are predicted and thus assessments of graphs extracted from the EEG measurements are in position to validate these predictions. In addition "exposing" the resulting graphs to node attacks of various patterns (random versus degree-related 25) can further give rise to their reliance and robustness adding additional estimation to their vulnerability to breakdown and disease-generation according to CBP predictions. Table 2 proposes CBP-sensitive signal-processing parameters likely to be a good starting point for validating NeuroAnlysis assumptions.

Table 2: Clinical Brain Profiling validation

Symbol	Brain dynamic disturbance	Detecting signal processing
DMN	Undeveloped disturbed DMN organization	Life-long assessment of small-world parameters, hierarchy and hub formation, attempt attractor space-state assessments
Cs	Disconnectivity dynamics	Connectivity matrices and small-world graphs will show disconnection dynamics and tendency to randomness.
Ci	Overconnectivity dynamics	Connectivity matrices and small-world graphs will show over-disconnection dynamics and tendency to reduced dynamics anf fixations .
Hbu	Hierarchical bottom-up insufficiency	Reduced hierarchy demonstrated by reduction of hub degrees and numbers and by K-shell decomposition. Susceptibility to node attack
Htd	Hierarchical top-down shift	Demonstrated by increas of hub degrees and by K-shell decomposition. Resilience to node attack
D	Deoptimization dynamic shift	Reduced plasticity detected by time-related tardiness of connectivity dynamics, and by slow rest-to-task transitions
O	Hyper-optimization dynamic shift	Increased plasticity detected by time-related increase of connectivity dynamics, and by fast rest-to-task transitions
CF	Constrain frustration	Destabilized millisecond-range connectivity dynamics susceptibility to node attack
CFb	Stimulus bound Constrain frustration	Specific stimulus-bound destabilized millisecond-range connectivity dynamics susceptibility to node attack

N-Hat future intervention technologies

In the future therapy will need to become personalized and specific; personalized to the condition of the individual patient which is unique and different than other patients, and specific because it will need to react to specific pathological disturbances of the brain of that patient. In order to tailor specific interventions monitoring is a must, the brain disturbance will need close monitoring to guide the therapy. Monitoring of patients’ conditions is increased multifold using the Neuro-Hat. Instead of periodic visits at the clinic where history-taking is the standard monitoring method, an online continuous objective accurate history can be extracted (13). State-of-the-art advanced therapeutic monitoring is a direct feedback-loop where the intervention is coupled in real-time synchronization with the monitoring. This feature needs more direct brain-monitoring such as EEG signals and the signal processing detecting the specific disturbance occurring in real-time. The loop idea is critical since the disturbances of the brain are a highly dynamic changing from instant to instant. In affect we are dealing with a dynamic system that can be metaphorically compared to cardiac pacemakers to cure arrhythmias. The future therapeutic intervention in psychiatry might require some "brain-pacing" device that will depend on continuous online constant monitoring and re-monitoring occurring for the entire time of the therapeutic brain-pacing activity. Neuro-Hat can become the platform upon which the future brain-pacemaker is constructed.

A variety of brain stimulation devices are currently being developed, each constituting a preliminary potential for the future brain-pacemaker device. The growing field of brain stimulation is beyond the scope of this paper, thus only the relevance of the Neuro-Hat to some of the brain stimulating technologies is mentioned.

The most naturally adapted to a Hat-Device are the Direct and Alternating transcranial current stimulations (tDCS and tACS respectively). These are applicable using electrodes adhered to the scalp which act as Anode and Cathode for injecting small electrical current to the brain (26). The advantages of such technology, being non-invasive, are its simplicity and safety. The disadvantages are low effectiveness and accuracy owing to difficulty of controlling and focusing the interventions. Another non-invasive intervention is that of Transcranial Magnetic Stimulation (TMS 27), however using magnetic coils technology is not compatible with head-mounted devices such as the hat.at least until the magnetic field can be delivered with miniaturized apparatuses. TMS shares the disadvantages characterizing tACS and tDCS. Recently focused ultrasound is being developed for non-invasive brain stimulation, but such technology will encounter the miniaturization problem similar to TMS, as the ultrasound transducers require large-size equipment.

The Neuro-Hat can become the monitoring-arm in the feedback-loop of invasive brain-pacing devices; these are typically Deep Brain Stimulation (DBS 28) and Optogentics (29). The disadvantage of invasiveness is countered by the advantage of focus and specificity of stimulation. In such dedicated devices the monitoring turns critical and inseparable from the pace-maker, accurate guidance must accompany the stimulation itself. While DBS injects electrical current which is not cell-specific, thus activating or inhibiting both neuronal and interneurons, in a fairly large neuronal ensemble, Optogenetics is cell-targeted only to the neurons engineered genetically to react to light stimulus. This light stimulus is injected invasively (requires brain in-plant) with fiber-optics. In sum it is obvious that any brain-stimulating technology will require a monitoring-stimulating feedback-loop in order to become a real brain-pacer and the Neuro-Hat will be required to transform brain-stimulating to brain-pacing.

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