Editorial

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A Futuristic Approach to Psychiatric Diagnosis

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INTRODUCTION

Earlier diagnosis and intervention have value in virtually every illness. Concentrating on early treatment even before the clinical syndrome emerges is a futuristic goal in neuropsychiatric disorders. But psychiatric diagnosis relies exclusively on subjective considerations, not on objective laboratory tests and biological markers.

Nevertheless, at some point in the future, a new way of diagnosing psychiatric disorders will overtake conventional diagnostic procedures that are depending on symptom checklists. Developing a new set of diagnostic criteria based on genomics and neurocircuitry of psychiatric disorders will not only lead to a more precise diagnosis but will also help us develop more specific, biotechnological, and disease-modifying pharmacologic agents.

It is truly thought-provoking to consider that online search systems, or other commonly used social network systems may be used to detect those who may be at very high risk of developing psychosis. Recently, long-time director of the National Institutes of Mental Health (NIMH) Dr. Thomas R. Insel joined Google Life Sciences. In an interview Insel acknowledged that he believed that technology companies are going to play an increasingly important role in understanding the complexities of brain function and improve our understanding of conditions such as Alzheimer's disease and autism[1].

In this editorial, we briefly review the candidate diagnostic tests in psychiatry and make recommendations on the future development.

Automated Speech Analysis Programs

The speech provides important clues about thought and feeling. A recent study demonstrated that automated speech analysis program demonstrated 100% accuracy in identifying whether at-risk young people went on to develop psychosis over the next two years[2]. This study involved a small sample of 34 participants age 14 to 27 at clinical risk for psychosis. Participants were asked to describe a subjective experience in an interview, and the computer program analyzed their narrative; focusing on semantics, structure, coherence, phrase length and determiner words to link phrases. After 2.5 years, 5 participants developed psychosis and 29 did not. The computer program correctly differentiated these patients.

This speech analysis computer program may increase predictive power beyond expert clinical opinion. The program identified that breaks in the flow of meaning, shorter phrases, and less elaboration were key determinate features. Clinicians do assess disorganized speech on the basis of clinical observation, but this objective tool may be able to identify thought disorder in its earliest, most subtle form, years before the onset of psychosis. Nevertheless, it must be recognized that these results need to be replicated in larger samples.

For the field of psychiatric research, this opens the possibility that new technology can aid in prognosis and diagnosis of severe mental disorders. We could potentially track speech abnormalities by using computer analysis techniques, to diagnose not only psychiatric but

also neurological and medical conditions. An Automated speech analysis program could detect speech abnormalities associated with delirium, alcohol intoxication, and dangerous hypoglycemia in individuals with diabetes. Since verbal fluency declines over time in neurocognitive disorders, using automated speech analytic techniques may increase the chance of early diagnosis. As being an inexpensive, portable, fast, and non-invasive, automated speech analysis has the potential to be a clinical tool that can complement clinical interviews and ratings.

Nanopsychiatry

Nanomedicine is a branch of medicine that concerns treating a disease with nanotechnology. Examples of ways in which nanomedicine could be used in psychiatry include: developing nanoelectronic biosensors (improve diagnostic accuracy and track neurophysiological changes), nanocarriers (for superior drug delivery), and nanorobots (to modulate neurophysiological conditions). Nanotechnology may help to follow the response to the treatment as well as providing biological data to make more accurate diagnoses[3]. The nano-size materials have several advantages that make their use as drug delivery systems, and imaging agent. One of the very important aspects is that these materials can transfer across the blood-brain barrier.

Among the potential applications of nanotechnology in neurosciences include nerve nano-repair. Carbon nanomaterials, due to their unique physical, chemical and biological properties, are currently considered as promising candidates for applications in regenerative medicine[4].

Nanotechnology is also used to develop artificial neural networks based on biological networks. Researchers has already achieved success in modeling inorganic synapses[5]. With the advancement of nanotechnology, it is hypothesized that the artificial networks will be able to model human brain, helping us determine pathological neural activity among those with psychiatric disorders.

Psychiatric Genetic Testing

The researchers demonstrated that many of the genetic variants that have already been shown to increase the lifetime risk of developing a mental illness by producing an effect on immunity, brain signaling, and genome function. Recently genes associated with serious psychiatric disorders have been identified. Neuregulin 1, Dysbindin, DISC1, PRODH, COMT and so on[6]. In the long run, these genetic discoveries will provide signs to the pathophysiology of mental disorders. Results from large genome-wide association studies (GWAS), point that over 20 haplotypes are profoundly correlated with the mental disorders in general[7]. Although none is associated with a specific syndromic category, cumulative associations remain to be examined. Psychiatric genetic research may eventually lead to the utilization of genetic testing in routine clinical practice. However, all genetic tests raise ethical, legal, and social issues; psychiatric genetic knowledge adds further controversial issues.

Endophenotypes

Endophenotypes are the subsets of biological markers that are correlated with an illness, related to shared underlying genetic influences. They can be neurophysiological, biochemical, endocrinological, neuroanatomical, cognitive, or neuropsychological. The strength of an endophenotype is its ability to differentiate between potential diagnoses that present with similar symptoms[8]. The endophenotype notion has developed as a strategic tool in neuropsychiatric research. Researchers currently are trying to identify candidate endophenotypes that are less genetically complex and potentially closer to the level of gene actions.

Some distinct genes that could underlie certain endophenotypic traits in schizophrenia include RELN, FABP7, and CHRNA7; coding reelin protein, fatty acid-binding protein 7 and neuronal nicotinic acetylcholine receptor alpha7 subunit, respectively[9-11].

In bipolar disorder, one commonly identified endophenotype is "face emotion labeling" deficit. This endophenotype has been associated with dysfunction in the dorsolateral and ventrolateral prefrontal cortex, anterior cingulate cortex, striatum, and amygdala[12]. A polymorphism in the CACNA1C gene coding for the voltage-dependent calcium channel has been found to be linked to deficits in facial emotion recognition[13].

Another promising test related to neurophysiological endophenotypes in schizophrenia is prepulse inhibition (PPI) of startle. Reduced or abnormal PPI in schizophrenia is among the most consistent markers of brain-based inhibitory deficits in this disorder; however, studies vary in their findings. Research results indicated that patients with schizophrenia, their relatives, and subjects with schizotypal personality disorder all had abnormal PPI relative to the healthy subjects[14]. It is hoped that further research will clarify these issues and that the clinical utility of measuring PPI in screening or treatment will be found.

EEG

Based on EEG technology, the Neuropsychiatric EEG-Based Assessment Aid (NEBA) System (NEBA Health, Augusta, GA) was developed and recently received Food and Drug Administration (FDA), in July 2013, to help assess ADHD in children and adolescents 6-17 years of age. It is not to be used as a stand-alone diagnostic test, but as a conjunctive tool for diagnosing ADHD. NEBA is a non-invasive test that calculates the ratio of theta and beta waves frequencies in 15-20 minutes (FDA and NEBA websites accessed September 28, 2015). This is just the first brain scan to be used in the diagnosis of mental illness.

Another encouraging utilization of EEG in differential diagnosis relates to the biological underpinnings of unipolar (UD) and bipolar depression (BD). Results of EEG studies demonstrate that EEG cordance and coherence values have a potential to discriminate between UD and BD. The loss of temporal synchronization in the frontal interhemispheric and right sided fronto-limbic neuronal networks may be a unique feature that distinguishes between BD and UD[15].

One well-replicated finding in UD is that, compared to healthy subjects, an interhemispheric frontal alpha asymmetry has been found due to an increased left frontal alpha power as it is well-known indicator of idling activity on that side[16]. Partly as a result of these findings, frontal alpha asymmetry has consequently been suggested to be a trait marker for depression in many studies[17], though some controversy still exists.

Eye Tracking Test

The link between schizophrenia and abnormal eye movements is well established. Eye tracking dysfunction is a phenomenon that includes both the smooth pursuit and saccade systems. Studies have shown that patients with schizophrenia and their family members have eye tracking dysfunction.

Until recent years, eye tracking dysfunction has never been used to diagnose schizophrenia. In a recent study, researchers gave the visual tests of steadily holding a gaze and viewing an image to a group of people with a confirmed diagnosis of schizophrenia, and to a healthy control group[18].

The researchers found that performance on the smooth pursuit, fixation, and free-viewing tasks were all abnormal in the schizophrenia group compared to the healthy control group. Results suggest that people who had significant difficulties with both of the tests were far more likely to be from the schizophrenia group than the control group – the results of the testing allowed them to build a diagnostic model that they claimed was 98.3% accurate. The researchers conclude that the tests may be a useful adjunct to current schizophrenia diagnostic practices that are based on the presence of symptoms.

Single Photon Emission Computed Tomography

Numerous research findings revealed by neuroimaging methods exist on the biological correlates of psychiatric illness. However, the diagnostic criteria of the psychiatric illnesses described by the Diagnostic and Statistical Manual of Mental Disorders (DSM) do not include any of these findings from the brain imaging.

Many of the clinicians guess that brain imaging will play a role in psychiatric diagnosis soon. This may happen first for differential diagnosis, particularly for diagnostic distinctions that are challenging to perform on the basis of behavioral observations alone. In such cases, potentially distinctive patterns of brain activation identified through imaging will be valuable.

Single photon emission computed tomography (SPECT), measures regional cerebral blood flow by detecting a gamma-emitting tracer in the blood. Today some clinics use a system of diagnosis depending on SPECT analysis instead of the standard diagnostic categories defined by the American Psychiatric Association's DSM[19]. The use of diagnostic SPECT in psychiatry is in its infancy and unproven yet.

A significant limitation of imaging studies is that the imaging is not highly sensitive to the diversity between disordered and healthy brain. Indeed, there is a noteworthy similarity in the abnormalities noted in functional brain imaging results across different diagnoses, like limbic hyperactivity or prefrontal hypoactivity. More advanced methods of image analysis may reassure us for distinguishing the differences between the disorders that emphasize similar regional abnormalities.

CONCLUSIONS

We have enough clues for being optimistic about the future of hi-tech tools to help us accurately diagnose mental disorders. Today, by correlating the various biological markers, clinicians may strengthen the ability to predict risk for some mental disorders. A new technology, called "social sensing", use continuous sensor data from our mobile phones. The collected data are used for analyzing subtle signals of behavior change to better understand users' social, physical and mental health status. Social sensing is a bright idea for considering changes in behavior and showing the possibility on inexpensive personal health monitoring. But it will be a long time before these studies result in reliable techniques and applications to predict illness based on collected data.

Utilization of technology promises to improve diagnostic processes, rather than conclusively rule in or rule out a diagnosis. Clinical judgment must invariably be used in the interpretation of these results.

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