Attachment G-8



DIGITAL PHENOTYPING – TECHNOLOGY FOR A NEW SCIENCE OF BEHAVIOR

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VIEWPOINT

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Digital Phenotyping Technology for a New Science of Behavior

Traditionally, psychiatry has offered clinical insights through keen behavioral observation and a deep study of emotion. With the subsequent biological revolution in psychiatry displacing psychoanalysis, some psychiatrists were concerned that the field shifted from "brainless" to "mindless."¹ Over the past 4 decades, behavioral expertise, once the strength of psychiatry, has diminished in importance as psychiatric research focused on pharmacology, genomics, and neuroscience, and much of psychiatric practice has become a series of brief clinical interactions focused on medication management. In research settings, assigning a diagnosis from the *Diagnostic and Statistical Manual of Mental Disorders* has become a surrogate for behavioral observation. In practice, few clinicians measure emotion, cognition, or behavior with any standard, validated tools.

Some recent changes in both research and practice are promising. The National Institute of Mental Health has led an effort to create a new diagnostic approach for researchers that is intended to combine biological, behavioral, and social factors to create "precision medicine for psychiatry."² Although this Research Domain Criteria project has been controversial, the ensuing debate has been

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a useful forum for highlighting the need for diverse data and dimensional approaches as fundamental principles for better diagnosis of mental disorders. The mental health policy world has been more concerned by the need to improve practice through "measurement-based care" rather than relying only on clinical judgment.³ According to one study,⁴ on the basis of clinical judgment alone, mental health practitioners (n = 14) detected deterioration for only 21.4% of 70 patients who experienced increased symptom severity. Lack of measurement, in this case, was not the absence of a biomarker but the failure to track changes in mood, cognition, and behavior.

Expecting mental health clinicians to complete rating forms may be a challenge for those with less than 15 minutes per patient encounter. Asking patients to complete rating forms might seem like an efficient alternative but it is unclear if patients with serious mental illness who are often nonadherent to their medication would be more compliant with self-ratings. What the field needs is an objective, passive, ubiquitous device to capture behavioral and cognitive information continuously. Ideally, this device would transmit actionable information to the patient and the clinician, improving the precision of diagnosis and enabling measurementbased care at scale.

The smartphone may be such a device (Figure). Would anyone have predicted a decade ago that 200 million individuals in the United States would be carrying powerful computers that were continuously and passively collecting data on activity, location, and social engagement? Who would have believed that patterns of typing and scrolling could reveal individual fingerprints of performance, capturing our neurocognitive function continuously in the real world? Could anyone have foreseen the revolution in natural language processing and artificial intelligence that is allowing voice and speech, collected on a smartphone, to become a possible early warning sign of serious mental illness?

Even though smartphone technology promises to transform many aspects of health care, no area of medicine is likely to be changed more by this technology than psychiatry. *Digital phenotyping* is the term now used for describing this new approach to measuring behavior from smartphone sensors, keyboard interaction, and various features of voice and speech.⁵ Already digital phenotyp-

ing is revealing new aspects of behavior that appear clinically relevant. In one study of 48 individuals, Saeb et al⁶ described behavioral entropy based on the variation in several sensor measures as a correlate of mood ratings. The study by Bedi et al⁷ proposed measures of semantic coherence from speech samples as a predictor of psychosis. Although most of

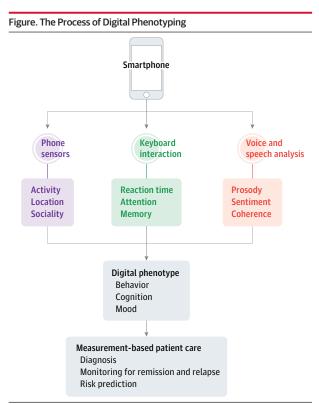
the early studies, seeking validation, have measured the correlation of digital phenotyping features with standard clinical ratings, it is not clear whether smartphone measures collected continuously in a patient's ecosystem will prove better at predicting clinical outcomes than episodic rating scales collected in a clinical setting. Even if digital phenotyping is more successful at predicting outcomes, the real question is whether this information can be used to monitor and improve patient outcomes.

Digital phenotyping is being tested in several areas where psychiatry needs better measurement of behavior. In clinical trials, smartphone data are being used as an outcome measure as well as a stratifying variable.⁸ In practice, digital phenotyping could become a potential path to measurement-based care, allowing care managers to monitor remission and relapse, potentially preempting emergency department visits or hospitalizations. For populations in which this approach has not yet been tried, there is potential for improving prediction of risk and identifying needs for services. In addition, mental disorders are global illnesses with high morbidity and mortality, but the workforce is limited in number. Smartphones are now common globally,

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Digital phenotyping involves collecting sensor, keyboard, and voice and speech data from smartphones to measure behavior, cognition, and mood.

even in communities without clean water or a well-developed power grid. Combining digital phenotyping with online psychosocial interventions could potentially transform global mental health.

Even though the potential for this new technology is evident, with any new technology, the risks need to be considered. Two major hurdles must be overcome if digital phenotyping is to move from the current stage of hype to the hoped-for stage of public health effect. First, the technology must demonstrate its value, not in economic terms but in terms of clinical effectiveness. Will digital phenotyping confer better outcomes in the real world of clinical practice? Will better measurement reduce morbidity and mortality? Currently, there are no studies with which to answer these questions, but there are few areas of medicine in which better measurement alone confers better outcomes. Data that improve decisions or improve efficiency will be helpful, but bridging the "last mile" from better data to better care is a major challenge. This bridge needs to be built before digital phenotyping can prove its full value. Fortunately, the smartphone can provide the efferent limb of intervention as well as the afferent limb of assessment. Ideally, these will be combined to create a learning mental health system in which the continuous feedback from digital phenotyping allows optimal titration of the intervention.

As important as demonstrating value is the issue of ensuring trust. Digital phenotyping research has been limited to consenting research participants who are essentially collaborators. Questions of privacy and agency need to be addressed in the research environment, but these questions become even more acute in clinical practice or when digital data are part of population surveillance for disease risk. Proponents may point out that digital data of each person are being collected all the time without that person's awareness, and that everyone must adjust to a world without privacy protection for actions and information on phones. But will people feel the same way about their behavioral data being collected for health purposes? Who will own these data? Will the data be used to empower patients and families to make better decisions about health issues or, like online data collected today, used to identify consumers and link to potential markets?

Currently, no group or agency, public or private, is setting standards for value or ensuring trust. Some of the products being developed by academics are subjected to rigorous testing but have not benefitted from creative design or user experience testing. Conversely, many of the products developed in the private sector have engaging design but have not been tested in rigorous trials. The field of digital health needs a set of standards for quality that will include measures of efficacy, engagement, and privacy, such as with development of a consumer's guide for digital mental health, complete with user reviews. Without these standards, a few bad actors or a few adverse events can quickly erode trust and preclude value.

After 40 years of psychiatry becoming more mindless than brainless, perhaps digital phenotyping will help the pendulum swing back toward a fresh look at behavior, cognition, and mood. It has been said that new directions in science are launched by new tools much more often than new concepts. In this case, a tool that is inexpensive and ubiquitous may change the direction of the field. But even if psychiatry may be the source for developing this new approach to phenotyping, it will not be the only benefactor. Behavior, cognition, and emotion are critical factors for much of human disease. A passive, objective, continuous approach to measuring these factors may transform the way we assess risk and resilience for diabetes, dementia, and a range of chronic diseases. Over the next decade, as the revolution in genomics continues to play out, digital phenotyping is likely to yield new insights at scale, based on a technology that is already used by billions of people.

ARTICLE INFORMATION

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REFERENCES

1. Eisenberg L. Mindlessness and brainlessness in psychiatry. *Br J Psychiatry*. 1986;148:497-508.

2. Insel TR. The NIMH Research Domain Criteria (RDoC) project. *Am J Psychiatry*. 2014;171(4):395-397.

3. Fortney JC, Unützer J, Wrenn G, et al. A tipping point for measurement-based care. *Psychiatr Serv*. 2017;68(2):179-188.

4. Hatfield D, McCullough L, Frantz SHB, Krieger K. Do we know when our clients get worse? *Clin Psychol Psychother*. 2010;17(1):25-32.

5. Jain SH, Powers BW, Hawkins JB, Brownstein JS. The digital phenotype. *Nat Biotechnol*. 2015;33(5): 462-463.

6. Saeb S, Lattie EG, Schueller SM, Kording KP, Mohr DC. The relationship between mobile phone location sensor data and depressive symptom severity. *PeerJ*. 2016;4:e2537.

7. Bedi G, Carrillo F, Cecchi GA et al. Automated analysis of free speech predicts psychosis onset in high-risk youths [published online August 26, 2015]. NPJ Schizophr. doi:10.1038/npjschz.2015.30

8. Bidargaddi N, Musiat P, Makinen VP, Ermes M, Schrader G, Licinio J. Digital footprints. *Mol Psychiatry*. 2017;22(2):164-169.

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