

Digital phenotyping: hype or hope?

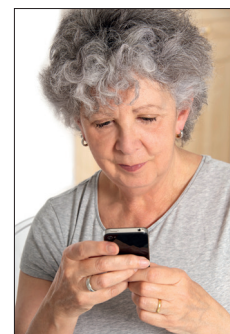


In September, 2018, Thomas Insel speculated that, in 2050, psychiatrists will have realised that “the revolution in technology and information science will prove more consequential for global mental health,” compared with the developments in genomics and neuroscience.¹ This is an astounding statement in itself, especially from somebody who advocated genomics and neuroscience² in his former position as head of The National Institute of Mental Health. However, what exactly is meant by information science and why should it outpace neuroscience and genetics?

Digital phenotyping refers to the moment-to-moment quantification of human behaviour in everyday life using data from personal digital devices.^{3,4} This process will, according to Insel, overcome challenges in mental health by providing objective assessments of symptomatology in the context of patients’ daily lives with continuous measurements. Indeed, subjective reports, specifically those assessed retrospectively, are known to be biased.⁵ As a prime example, Prince and colleagues⁶ showed in a meta-analysis of 147 studies that subjective assessments and objective assessments of the same construct, namely physical activity, are only weakly related ($r=0.37$), which indicates that these two measures capture different phenomena. Similarly, focusing on patients’ everyday lives when assessing symptomatology has proven valuable, such as when measuring blood pressure. Office hypertension, the well-documented phenomenon of heightened blood pressure only evident in the physician’s office, results in thousands of patients unnecessarily receiving medication.⁷ The most promising feature of digital phenotyping is the possibility of continuous measurements. Use of apps, phone calls, typing speed, and voice features can be monitored unobtrusively every second over a lifetime, with real-time algorithms checking for alarming transformations. A data stream of continuous measurements can be used to detect transitions and predict relapse. Tracing in real-time that somebody either loses control over drinking alcohol and thereby switches from a high-risk individual into a patient needing care, or crosses the line drifting into a depressive or manic episode, would indeed revolutionise psychiatry.

However, is there any empirical evidence for an upcoming revolution besides the attention-grabbing

commentaries in highly ranked journals^{1,3,4} and the theoretical promises of continuous objective assessments in patients’ everyday lives? In our opinion, predicting upcoming episodes in bipolar disorder should be the most promising application for digital phenotyping, as symptomatology (eg, activity, sleep, communication) and smartphone behaviour match uniquely. The prime example is the MONARCA II trial,⁸ a randomised controlled trial using continuous measurements of smartphone behaviour (eg, phone usage and social activity), subjective e-diary ratings, and automated real-time prediction to trigger interventions before patients experience a full-blown episode. Although this trial is impressive in terms of the technology used, and the authors well published in this field, the findings are disappointing, showing no effects on the primary outcome. This result is in stark contrast to the high expectations regarding digital phenotyping. Two reasons might explain the meager results. First, digital phenotyping studies are highly dependent on naturally occurring variance. By contrast to laboratory studies, where conditions are experimentally manipulated to ensure differences in the independent variable, in digital phenotyping changes in symptomatology have to occur naturally. In the MONARCA II trial, the assessment period was 9 months. Given a mean age of 43 years in the intervention group, an estimated onset of the disorder of below 20 years, and a clinical history of, on average, four depressive and three manic episodes in the intervention group, the estimated chance to experience an actual illness episode in the 9-month monitoring period was about 20% per patient. Thus, the assessment period seems too short for ensuring enough variability in symptomatology (ie, episodes of illness) to leverage the promises of digital phenotyping. Second, variation in symptomatology is not all that is needed. This variation must also be captured. In the MONARCA II trial, five outcome assessments were implemented over time for each participant (occurring at baseline, 4 weeks, 3 months, 6 months, 9 months). Accordingly, there might have been much more variation and more episodes during the 9-months trial, which were not assessed because of infrequent clinical assessments. Therefore, even technologically cutting-edge studies, such as the



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MONARCA II trial, will fail if they are underpowered regarding detectable upcoming episodes and will undermine the true potential of digital phenotyping. Fortunately, there are now registered trials using digital phenotyping that have implemented much more extended assessment periods (ie, 21 and 24 months)^{9,10} in combination with closer monitoring of the outcome. An extended assessment period may result in not only positive findings in secondary and exploratory outcomes⁸ but also significant primary outcomes.

Even though the methods underlying digital phenotyping have been used for a long time before the term was coined,⁵ we are confident that digital phenotyping is more than a buzzword because its core features, namely objective and continuous assessments in patients' daily lives, can address the current challenges in psychiatry. To fully leverage the promises of digital phenotyping, psychiatric expertise is now needed to do well-powered studies that carefully diagnose the clinical states repeatedly over time. Thus, we have more hope than hype.

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