OVERVIEW
Here we provide perspective on the past, present, and future of rapidly emerging technologies—digital devices and continuous telemetry—in the study and treatment of psychiatric illness from human patients to animal models. We focus on how commonly available technologies are helping to establish a robust data infrastructure in both clinical and research settings that has near-term potential to improve the precision in our ability to measure, monitor, and model behavior across a range of clinical, naturalistic, and basic research settings. We also forecast how these approaches and technical capabilities are likely to converge to the benefit of humans with neuropsychiatric conditions over the next five years.

The word “technology” comes from the Greek “technê” for art or skill, and “logia”, implying the systematic study or treatment, which together signifies the systematic study or application of an art or craft. Psychiatry derives from “psyche” or mind, but with a different Greek suffix (“iatría“), which means healing rather than study (as in “psychology” and “neurology”). If the essence of psychiatry is healing the mind, the goal of technology in psychiatry is to systematize the art of mind healing. From the mental status exam (MSE), the Diagnostic and Statistical Manual (DSM) and the International Classification of Disease (ICD) system, to manualized psychotherapies and treatment algorithms, the field has explored many approaches to systematizing the complex art of diagnosis, treatment, and prevention of neuropsychiatric conditions. Throughout this evolution, the tension between systems that work well at cohort and population scale by minimizing individual differences and those that work well for individuals has resulted in modest progress in care processes and outcomes. In this context, we focus on scaleable technologies intended to enhance the care experience and outcomes, providing platforms that can incorporate insights from prior traditions through a combination of measurement and systematic delivery of individualized therapy.

PAST
Ten years ago, smart phone usage and ownership among the general public, let alone patients with severe psychiatric illness, was limited. This gap in access—the so-called “digital divide”—meant that even though technology was available to remotely monitor individuals with complex conditions, many solutions relied on additional devices to support remote monitoring solutions. For instance, in 2007, the Bosch company introduced a telehealth service (Health Buddy), which used an internet-connected device with a simple 4-button interface to allow for patient prompts for conditions including depression. Despite the simplicity of the interface, this technology failed to create sustainable engagement. Also around this time, the global mental health crisis was driving considerable interest in solutions that incorporated technology to reach young people suffering from mental illness in both the developed and developing world [1].

Five years ago, the proliferation of smart phones and wearable devices led several software companies to form businesses around the smart phone itself as the remote monitoring platform. These companies leveraged increasing smart phone ownership with the needs of providers and healthcare system administrators to create dashboards that could capture patient acuity across a clinic or an entire system, while also providing therapeutic content and secure communications. In parallel, several groups developed internet-based cognitive behavioral therapy applications that showed promise in treating depression and anxiety [2]. While such systems continue to improve and gain traction in some clinical settings, platform engagement for both patients and providers has limited the uptake of these services and caused some of these companies to pivot their business models. For instance, one such company (Ginger.io) has re-focused on delivering coaching through their software platform with a direct-to-consumer focus, rather than being a product geared for providers.

In parallel, electronic health record (EHR) systems have gained increasing traction over the past decade; according to a CDC survey, >87% of physician practices use some form of EHR. The push for additional documentation and measurement afforded by EHR systems has both changed the landscape in terms of what devices and other software are needed to fill service gaps, but also in tempering enthusiasm among psychiatrists for whether technology in general is a help or hindrance to their practice. Psychiatry has the lowest EHR adoption of any specialty, with ~60% of psychiatrists using an EHR [3], even while the EHR data has been shown to provide predictive utility in risk stratifying psychiatric patients, such as identifying individuals who are more likely to make a suicide attempt following an evaluation [4, 5]. While substantial skepticism remains about the utility of EHRs in psychiatry, the American Psychiatric Association now devotes a webpage to the topic, including information about EHRs geared toward mental health providers (https://www.capterra.com/mental-health-software/). Moreover, we recently proposed several ways the federal government could improve adoption of EHRs in psychiatric care to meet the goals of the 21st Century Cures Act [6].

Citations for papers with the terms “digital technology” and “psychiatry” are ramping up in ways that resemble trends for
“fMRI” and “psychiatry” at the turn of the century (Fig. 1). Signs suggest that digital approaches will take the same exponential trajectory, if not potentially even more expansive given these approaches are more likely to gain traction in clinical practice in ways that neuroimaging was never well suited to realize, in part due to the lack of portability of the devices.

**CURRENT**

In 2018, psychiatrists and researchers now have many options for incorporating technology and digital devices into the management and study of psychiatric illnesses that go beyond what is provided by the EHR. Our culture has acclimated to the pervasiveness of personal computing devices, with >75% of US adults carrying smart phones and >90% using the internet; globally, the number of smart phone users will soon surpass 2.5 billion, with 48% able to access the internet. With this evolution has come increasing expectations for how technology should help us stay organized, communicate, stay mentally fit, and track our physical health. While today’s device landscape contains gadgets perched between being useful versus distracting, connecting vs. isolating, there is little doubt that in the right settings, and with appropriate guidance and support, technology can improve the quality of psychiatric care for a tremendous number of people in need [7].

The push to integrate mental and behavioral health care into primary care has led to numerous advances in systematizing treatments. This is particularly important for people with dementia or severe mental illness, who may lose key mental faculties at times they are not around caretakers, or refuse a conventional Mental Status Exam (MSE). New metrics and approaches derived from digital devices have emerged in the past few years that should augment the conventional toolkit for human behavioral evaluation in naturalistic settings. Some of these metrics derive from smartphones and wearable fitness trackers, and allow researchers to ascertain key parameters of psychiatric health, including sleep patterns and overall activity levels, but also more nuanced metrics of mental state that could potentially recapitulate every aspect of the traditional MSE (Fig. 2). Another promising set of metrics derive from quantitative analysis of behavior during in-person evaluations, using video and computer vision to automatically code facial expressions, gaze, pose and postural dynamics that can inform clinical assessment for a range of conditions, including depression [8, 9], psychotic disorders [10], and autism [11]. These approaches have the advantage of retaining existing (and trusted) workflows. They emphasize the importance of face-to-face communication—a preferable form of interaction for many individuals—while bringing systematic evaluation through computer vision of behavior and acoustic analysis of speech in more conventional clinical settings.

Continuous data sets of these metrics may enable a better understanding of what people are doing before the signs and symptoms become evident—perhaps even before the patients themselves are aware—and thus help to avoid crises. For instance, application of continuous digital metrics have already been shown to have predictive value for estimating which individuals will develop worsening pathology, including conversion to psychosis [12, 13], re-attempt of suicide after a presentation to the emergency room with an initial attempt [14], or relapse during schizophrenia treatment requiring hospitalization [15]. These examples are among the first to show utility in what is likely to be a rapid expansion of predictive digital phenotyping. While exciting, the ability to anticipate and therefore prevent adverse outcomes is fraught with ethical challenges: questions include when and for whom it is appropriate to take preventative actions on the basis of these signals, and to what extent individual autonomy would be threatened or potentially preserved by increasingly accurate prevention technologies covering a range of mental health conditions and outcomes. By benchmarking against real-world events, including those selected by the individual seeking care, such approaches also have the potential to establish entirely new metrics with predictive value that do not necessarily map onto conventional assessments, but may be better suited to individual needs and definitions of what constitutes treatment success.

**FUTURE**

Much as occurred after the initial phase of neuroimaging, we anticipate that research groups without strong technical expertise to adopt these approaches to explore the full range of clinical prediction models in robust data-rich studies, such as those aimed to prevent suicide or relapse to drug seeking in at-risk individuals. We also expect some new technologies to surpass what is...
complementary studies in laboratory animals

The rapid evolution of technology has also affected another domain that influences mental health: basic neuroscience research. There has been a parallel evolution of molecular techniques (e.g., optogenetics, chemogenetics) that can be used to probe and dissect with great precision the neural circuitry underlying motivational and emotional behavior in laboratory animals. Unfortunately, technical and conceptual innovations in the behavioral end points themselves, as modeled in non-human species, have not advanced at similar pace. The literature is replete with examples of elegant new molecular neurocircuity techniques paired with behavioral end points such as time spent struggling during tail suspension, entries into the center of an open field, or latency to eat in a novel environment. Many of these tests are mischaracterized as disease “models” or are said to reflect depression or anxiety in mice or rats, whereas they are better characterized as assays that were developed and optimized to rapidly and inexpensively identify standard psychiatric medications (e.g., antidepressants, anxiolytics). These types of behavioral assays pose at least three major challenges. Foremost, they typically rely upon anthropomorphic inferences of how situations should affect the emotional state of the animal—often a mouse—which creates a degree of subjectivity that can make studies difficult to replicate, even among researchers working within the same lab. A second challenge is that behavioral tests performed in rodents are only rarely analogous to those that can be performed in humans, limiting translational value. Third, they are often brief tests that occur once at an arbitrary point in time; thus they are best considered “snapshots” that require fortuitous timing. The fact that these limitations represent major obstacles to developing therapeutics seems beyond debate, considering the obvious difficulties in developing mechanistically new drugs and the massive divestment by industry in CNS drug development. These factors have even led to questions about the utility of animal models in psychiatry research [16].

New approaches are emerging that reflect attempts to overcome these limitations. Some are generating digital phenotyping-like data sets that are directly analogous to those that can be collected in humans using wearable tracking devices or smart phones; end points such as locomotor activity, body temperature, sleep/wakefulness states, and vocalizations can now all be measured across phylogeny. Those with the greatest promise share three important qualities: they are objective (enabling identical conclusions across independent observers), continuous (obtaining large data sets over long periods of time), and translational (reflecting end points that are similar if not identical in humans and the model species). One example is the development of large-scale behavior-based systems [17] that use continuous tracking to measure locomotion, trajectory complexity, and simple behavioral sequences, collecting large numbers of data points (on the scale of hundreds of thousands) for each subject over long periods of time (on the scale of hours). These systems use machine learning to generate specific behavioral signatures of different classes and subclasses of drugs such as those with known anxiolytic or anxiogenic effects in humans, or compare known drug signatures to the effects of genetic manipulations. Other versions incorporate RDoC-relevant behavioral domains including social behavior, cognitive behavior, and circadian rhythms, and can provide insight on the probability of transitioning from one behavioral event to another. Such systems may be able to uncover complex behavioral patterns that would be impossible for human observers to detect, but represent fundamental “syllables” of rodent behavior [17]. Under the right

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circumstances, it may also be possible to identify antecedents that reliably predict at meaningful timescales the future occurrence of patterns (e.g., impulsivity) that represent risk factors for harmful behaviors (e.g., relapse to drug-seeking, suicide) (Fig. 3).

A second example of an end point with high translational relevance is sleep (or sleep quality), which is altered across various psychiatric illnesses. In humans, mood and anxiety disorders are associated with increased sleep latency and sleep disruption. It is currently unknown if sleep dysregulation precedes (or is a risk factor for) the development of these conditions, but it is clear that disrupted sleep exacerbates their pre-existing symptoms. In rodents, immobilization stress, footshock, and social defeat stress all affect sleep architecture, with numerous similarities to the human conditions [18, 19]. In addition, inflammatory processes—which have been broadly implicated in psychiatric illness [20]—can affect sleep end points [21]. Inflammation can also cause persistent effects on vocalization patterns in mice that are detectable with specialized microphones tuned to ultrasonic frequencies [22]. The fact that numerous types of stress produce alterations in sleep that are similar to those found in psychiatric illness suggests that examining sleep architecture represents a currently underappreciated approach to identifying physiological biomarkers with translational relevance.

Sleep can now be studied in great detail, under ethological (untethered) conditions, using wireless transmitters that are implanted subcutaneously and collect an uninterrupted stream of data for months, enabling longitudinal, within-subjects experimental designs that can provide detailed insight on the onset, recovery, and persistence of changes in sleep. These same systems also offer the ability to examine rhythms (diurnal, circadian) in locomotor activity and/or body temperature, as well as EEG spectral power, which may have potential as biomarkers for psychiatric conditions.

In humans, wearable devices and smart phones can collect data on locomotor activity body temperature, biological rhythms, sleep, speech patterns and cadences, and response control. As described above (Fig. 2), these end points represent key elements of the MSE: activity, speech, cognition. If homologous end points can be collected in rodents—activity, vocalizations, EEG spectra—and can be shown to be reliably sensitive to manipulations (e.g., stress) that cause or exacerbate psychiatric illness in humans, their use represents an innovative opportunity to better align basic and clinical research. Although insight on sleep in humans is often unavailable except via self-report, the easy availability of objective sleep metrics via devices may offer an added dimension to a modernized version of the digital MSE, and homologous data can be derived in laboratory animals via data sets that include EEG and EMG (electromyography). While more validation in laboratory animals is needed, use of a common set of end points (i.e., a cross-species MSE: Fig. 4) and endophenotypes can more fully exploit the myriad advantages of basic research, including the ability to perform carefully controlled manipulations, study mechanism in exquisite detail, and establish cause–effect relationships. Effective use of common end points would represent the basis for screening methods that better predict effects that will be seen humans.

**CAVEATS**

While there is tremendous potential in this digital landscape to improve our science and healing abilities, there are also

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**Digital MSE for rodents**

**Fig. 3** Use of continuous data to predict behavior. In the example depicted, with behavior B serving as the reference (“Seed”) Event, machine learning algorithms may be able to identify antecedents (i.e., Event A, which could be a behavior, an EEG signature, a temperature fluctuation, etc) that would have been predictive of Event B, and future behaviors (i.e., Event C) that are predictable on the basis of Event B (or the combination of Events A and B). Maximizing the timeframe between events within which predictions are reliable is critical and could be life-saving in neuropsychiatric conditions such as suicide or substance abuse.

**Fig. 4** Digital MSE for rodents, using end points that are objective, continuous, and translational. Research in laboratory animals is increasingly employing temporally dense behavioral recordings alongside neural data in ways that could translate to the human MSE. Sleep, diurnal and circadian rhythms, locomotor activity, and vocalizations can routinely be studied as a function of targeted interventions to expose new relationships among genes, circuits, systems, and complex behavior. Vocalizations courtesy of Galen Missig; VV: vehicle control; PL: perinatal immune-activated.
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ADDITIONAL INFORMATION

Competing interests: JTB serves as a consultant for Pear Therapeutics and Niraxx Therapeutics, LTG serves as a consultant for 23andme, and KJR is on the Scientific Advisory Board for Resilience Therapeutics and serves as a consultant for Biogen. The other authors declare no competing interests.

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