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Ethological computational psychiatry: Challenges and opportunities

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Abstract

Studying the intricacies of individual subjects' moods and cognitive processing over extended periods of time presents a formidable challenge in medicine. While much of systems neuroscience appropriately focuses on the link between neural circuit functions and well-constrained behaviors over short timescales (e.g., trials, hours), many mental health conditions involve complex interactions of mood and cognition that are non-stationary across behavioral contexts and evolve over extended timescales. Here, we discuss opportunities, challenges, and possible future directions in computational psychiatry to quantify non-stationary continuously monitored behaviors. We suggest that this exploratory effort may contribute to a more precision-based approach to treating mental disorders and facilitate a more robust reverse translation across animal species. We conclude with ethical considerations for any field that aims to bridge artificial intelligence and patient monitoring.

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Introduction

Psychiatric conditions frequently involve complex interactions of mood and cognition that are non-stationary: they evolve across contexts and extended timescales [47]. Moreover, they are non-ergodic, indicating that individual behaviors and responses cannot always be reliably predicted from group averages [77]. To better understand their neural basis and develop novel precision-based (individualized) interventions (e.g., such as closed-loop neuromodulation, and wearable and/or phone-delivered "suggestions" for cognitive behavioral therapy), the field can further its efforts by studying behavior and neural circuitry over long time scales. This could help assess how neural dynamics become dysfunctional in disease, or how neural circuits malfunction over time, and help identify novel (behavioral or neural) biological markers.

For example, depression and bipolar disorder are characterized by fluctuations in emotional states that evolve over weeks, months, or even years, and are difficult to precisely phenotype with current approaches [13,30,35,42,109]. Similarly, cognitive and memory functions can vary significantly over time, posing a substantial obstacle to researchers seeking to understand their mechanisms and to reveal how these mechanisms break in disease, such as in post-traumatic stress disorder.

How can we be begin to quantitatively study the dynamics of mental disorders and the circuit malfunctions that underlie them? Designing behavioral research in humans and other animals contains the tension between "controlled or reductionist experiments" and less constrained approaches often referred to as "naturalistic" or "freely moving". While constrained experiments are essential for testing specific hypotheses and controlling for extraneous variables, being particularly useful for measuring economic preference and perception on a trial-by-trial basis, they can sometimes lack ecological validity, failing to mimic the complexity of real-world behavior. In contrast, studying behavior in unconstrained, naturalistic settings allows for a wide exploration of states and their dependencies, but presents challenges such as in data interpretation and causal inference. We argue that both approaches are necessary for the next generation of computational psychiatry and its linkage to research of neural circuits, and discuss how new technology can help us bridge this gap.

Conventional, trial-based experimental approaches, inspired by visual psychophysics and behavioral economics that are designed to measure behavioral preferences, attitudes, and biases [96], can be extended to capture long-term dynamics in behavior, neural circuitry, and in body physiology (for example by deploying these approaches in a repeated manner across extended periods of time in conjunction with other monitoring reviewed elsewhere in this article). This is particularly important for the perspective that we propose: that mental disorders are not simply breakpoints in stationary (stable) decision variables (e.g., risk attitude) but include disruptions in the broader ethological behavioral hierarchy — a concept we review further in this article. For example, in generalized anxiety disorders and other mental health disorders patients often have disruptions of sleep, and their behavior, decision making, and other activities may be particularly maladaptive within the context of a sleepless night [16].

The emerging effort to integrate genetics, neuroscience, behavioral science, and advanced data analytic with deep learning may shed light on the intricate relationships between mood, cognition, and behavior over extended timescales, and development [40,89,92]. Such research may not only enhance our understanding of mood disorders and related conditions but also could pave the way for a relatively more personalized and effective interventions in the realm of mental health that take time and context into consideration.

We believe that clinical research as well as non-human animal experiments that hope to reverse engineer the circuit basis of mental health disorders should carefully consider these issues. Ethological behavioral paradigms in conjunction with more classical econometric and psychological assessments could provide a more precise characterization of each individual's behavioral fingerprint (phenotype) and their behavioral breakpoints across time and context. These efforts will facilitate the reverse engineering of disease-relevant neural circuits in animal models and may shed light on the genetic underpinnings through Genome-Wide Association Studies (GWAS), by narrowing phenotype characterization and thus improving the ability of experimenters to establish gene-behavior relationships. Importantly, an expansion of ethological approaches, which we aim to outline here, will allow the field to further study how psychiatric traits interact with environmental and genetic mechanisms, which can profoundly affect patient outcomes [102].

A multi-modal and multi-time scale view of behavior: from circuit dynamics to lifespan dynamics

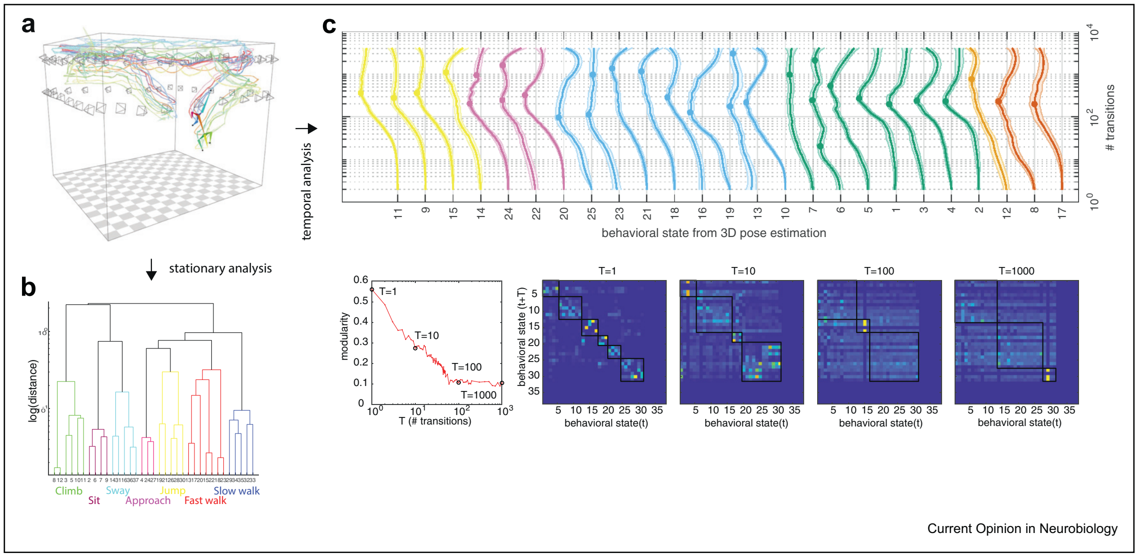
Recording behavior in unconstrained settings over long time scales may reveal richer information about the causes and adaptive or maladaptive features of many types of behaviors, because their dynamics (over time), their complexity, and variability are sensitive to statistics of a given environment, context, and physiological and mental state. More broadly, the behavioral lifespan of all organisms could be thought of as an intricate hierarchical organization of continuous (not purely discrete) states, each encompassing patterns of thoughts and behaviors that span various scales, from the microscale to the mesoscale to the macroscale. Therefore, the exploration of the organization and statistics of 'behavioral hierarchies' that are in part structured by timescales [68,73,117,118], will be an important future direction of computational psychiatry.

For example, on one level of such a hierarchy are behaviors such as sleep versus wakefulness, next, behaviors such as foraging, grooming or social interactions, and within each of these behavioral states, further compartmentalization into walking, climbing, standing or grasping (and they can be combinatorial). Longitudinal datasets can shed light on the conservation of such behavioral hierarchies across species and across development, and reveal the variability among individuals, relating their disorganization and psychiatric pathology.

There has been recent progress in the development of analyses to quantify such hierarchical organization and disorganization [22,72,116]. At the microscale, which includes timescales of milliseconds to seconds, technology can capture fleeting neural dynamics and behaviors. For instance, video recordings may detect facial micro expressions that could reflect momentary or short-time scale fluctuations in emotional states [5,24], while eye-tracking technology can identify rapid shifts in overt visual attention during decision-making processes [37,46]. Pose estimation software [6,70,73] such as that used by Bala et al. [6] can serve as an excellent dimensionality reduction step in order to then perform hierarchical clustering of behaviors (Figure 1a, b) in both healthy subjects and those with psychiatric conditions (Figure 1c).

Additionally, econometric tasks can readily measure the subject's attitudes to variables critical for adaptive behavior, such as risk attitude and uncertainty intolerance [39,43], and how they vary with endogenous and

Figure 1



Example approaches to study behavioral timescales in unconstrained behavior. a: Exemplary 3D pose trajectory of a monkey traversing the OpenMonkeyStudio system [6] **b:** Hierarchical clustering of 3D pose timeseries data used to identify the organization of macaque free-moving behavior. Timecourses of 3D pose data are normalized and embedded in a low dimensional space. Clustering is then performed to identify unique behavioral motifs or states. **c:** Top: Spectral decomposition identifying intrinsic timescales of behavior. For each behavior, a dummy vector is hanging tapered and spectrally decomposed via fast Fourier transform resulting in a behavioral spectrogram with unique peaks (dots). Colors indicate unique superclusters chosen by thresholding a dendrogram (as in **b**) of decomposed behaviors. Bottom: Modularity of behavior is temporally constrained. On shorter timescales (T = 1; T = 10), pose data clusters into many motifs while on longer timescales (T = 100; T = 1000) behavior is significantly less modular breaking down into simple motifs such as moving versus sitting or being awake versus asleep. Studying these behavioral timescale analytics could for example help identify if specific behavioral states undergo temporal alterations as is phenomenologically apparent in OCD [6,118].

exogenous influences (for example on neuromodulatory systems [52]). Stepping up to the mesoscale, spanning days to weeks, digital platforms and communication tools provide valuable insights. Social media posts and messaging content can reveal evolving thought patterns and behaviors, such as changing sentiment or communication style during significant life events, like starting a new job or experiencing personal milestones [62,107]. Importantly, behaviors measured at the microscale (e.g., economic preferences) may fluctuate with these mesoscale patterns causing changes in health and behavior [21,49,75,93,115].

On the macroscale, which spans months to years or even a lifetime, long-term data collected through personal devices, electronic health records, and online archives enable the identification of enduring behavioral states. Examples include tracking shifts in physical activity and sleep patterns over years, monitoring the progression of chronic health conditions, or observing long-term changes in cognitive functioning and emotional well-being [2,97]. For animal behavior, continuous tracking of autonomic and body functions as well as continuous life-time video tracking could further offer insights into developmental and emotional fluctuations over time, as has been done in worms and flies [74,103]. We propose that within these measures, precise psychophysics and econometrics can be implemented to assess the relationship of microscale and mesoscale dynamics. Such work will further the effort to use behavioral paradigms to reverse engineer mental health disorders in humans and animal models, highlighting a critical need for converging “interactionist” work across species and levels of analysis [4].

Detection and analyses of these patterns at different scales may deepen our understanding of individual and collective behavior and could aid in the development of novel applications in mental health and social sciences. For example, psychiatric disorders often are first detectable during distinct phases of a person’s life and could be quantitatively associated with unique developmental changes and divergences [8,15,27,48,54,60,91,132] including disorganization of behavioral hierarchies,—which could further be assessed in animal studies. Understanding this at a population level with the help of data collected in unconstrained settings and linking such an understanding to both neurobiology and precise econometrics along with traditional psychological assessment ought to be a critical effort in future studies in computational psychiatry.

From this perspective, in the following sections we discuss some emerging opportunities to further assess behavior, behavioral organization, and their breakpoints in psychiatry to improve mental health interventions, and then turn to the critical aspect of linking these studies to animal work through emerging technology and algorithms aiming to shed light on neural mechanisms of mental health disorders.

Towards long timescale studies of unconstrained behavior for psychiatry

Traditional approaches in human ethology, psychiatry and psychology have relied heavily on qualitative methods such as interviews, participant observation, and fieldwork to understand population level human behavior (i.e., culture). Ethology (and anthropology) researchers typically immerse themselves in the studied communities, often aiming to conduct in-depth interviews and making detailed observations to uncover patterns and nuances in behavior. These traditional methods may sometimes lack the ability to observe patterns in behavioral phenotype over time that are fine-grained enough to link behavior, genetic data, and circuit or cellular function.

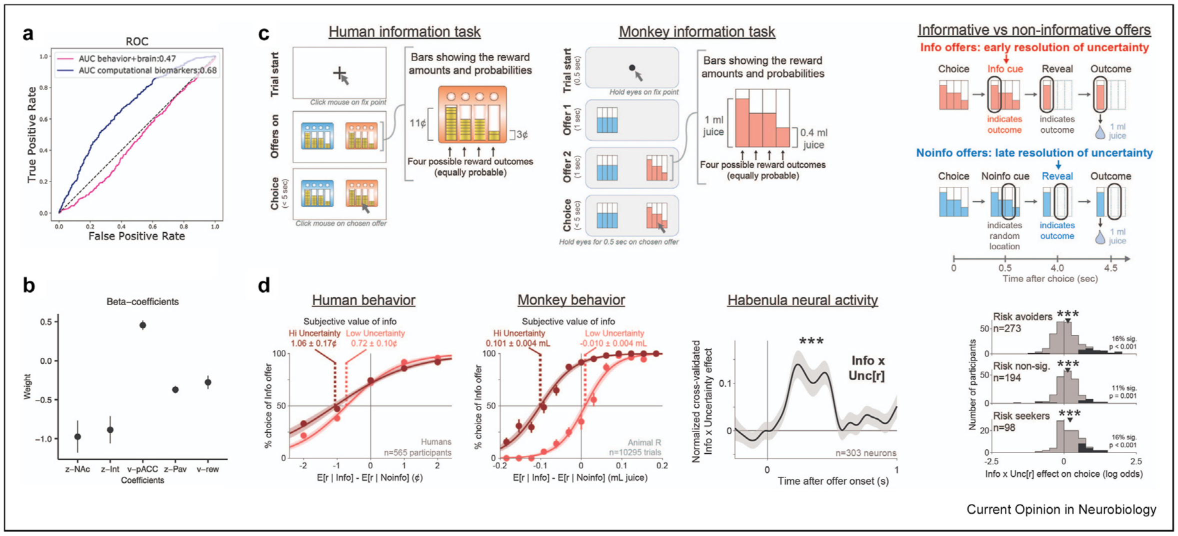
Age and development are critical factors that influence mood, cognition, and behavior. Across the lifespan, individuals undergo significant changes in their neural function, hormonal profiles, social environments, and even subjective preference [56,58,92,101]. Such changes impact mood regulation, cognitive processing, and behavioral tendencies. Additionally, cyclic patterns, such as daily circadian rhythms and monthly hormonal fluctuations, and their associated changes in neuromodulatory tone, can profoundly affect mood and some cognitive operations [25,33,34]. Understanding how these cycles interact with long-term trends is essential for a comprehensive understanding of human behavior. For example, human mood fluctuations may have a relationship to accumulating effects of momentum on processing reward prediction errors [10,29] which may explain at least some aspects of bipolar disorder, and could be manipulable with pharmacological interventions of serotonin [78]. Similarly, in rodent models, striatal dopamine depletion or blockade can mimic the impact of negative reward prediction errors that accumulate over time in striatal indirect pathway neurons to induce aberrant learning and progressive motoric symptoms [7,19] relevant for both Parkinson's disease and motor impacts of antipsychotics in schizophrenia.

Studying the effects of drugs or substance, both prescribed and recreational, on disorders of mood and cognition, presents challenges in disentangling their impacts from other factors and in assessing the long-term consequences of their use on complex sequences of behaviors and internal states [67,105,122]. For example, while stimulants are used as cognitive enhancers, recent studies suggest that their impact is not necessarily in improving cognition *per se*, rather they may act by altering the motivational incentives to perform cognitive work—particularly in those subjects with low striatal dopaminergic tone [121]. Such findings are consistent with broader computational frameworks showing how striatal dopaminergic signaling alters the impact of benefits vs costs of candidate actions at multiple levels of abstraction, including physical and cognitive effort [83,119]. Moreover, dopamine signaling varies with the reward richness or sparseness of the environmental context and dictates distinct optimal choice policies, providing a lens into psychiatric mechanisms that vary with context and dopamine [52].

Ideally, behavioral measures in humans and other animals ought to quantitatively identify and model breakpoints in an individual subject's behavior, such as in their decision strategy over time. This can be done with psychophysics and econometrics allowing the experimenter to map precisely the perceptual capacities, behavioral biases, and preferences of each subject. This approach could be extended such that these measures of individual attitudes and behavioral biases can be sampled along with continuous measures of behavior allowing for the detailed exploration of the effects of arousal, mood, sleep, physical activity, and other factors on individual decisions.

Recent work identified conserved economic subjective value computations in humans and monkeys as they made choices that incorporated trade-offs among their curiosity to resolve uncertainty and physical reward [11] (Figure 2a–d). Bromberg-Martin and Feng et al. showed that valuation of an abstract cognitive reward—the value of information—is computed through a conserved computation in monkeys and humans, and therefore could be supported by a conserved neurobiological substrate. The investigators then showed that an ancient structure—the lateral habenula—integrates the subjective value of information and the value of physical reward to guide decision making. The field now has opportunities to develop precise modulation approaches for clinical disorders associated with aberrant trade off among the curiosity to reduce uncertainty and physical reward, such as observed in some patients with obsessive-compulsive disorder (OCD). Some OCD patients display context-dependent checking behavior aiming to reduce uncertainty and gather information, even when they know the uncertainty may not be reducible or behaviorally relevant. To get a deeper understanding of how and when curiosity becomes maladaptive and when to intervene, the field needs to combine repeated fine-scale behavioral econometric mapping [11] with continuous behavioral measures in naturalistic settings to understand how information seeking changes across time and context.

Figure 2



Precision and mechanism: classifying and deconstructing. a: Computational biomarkers, extracted by fitting computational models to behavior and neural data, can improve classification of major depressive disorder (MDD), compared to classification based on traditional measures of behavioral and neural data. Adapted from the study by Pedersen et al. [84]. **b:** Classifier coefficients determine which parameters, and their covariation with activity in neural regions of interest, are most predictive of mental health disturbances. These provide potential targets for treatment manipulation for those individuals. Adapted from the study by Pedersen et al. [84]. **c, d:** Discovering the algorithms of decision making across species that assign value to the cognitive reward of gaining information about the future. Choice procedure during the multi-attribute information decision tasks for humans and monkeys. Choosing informative offers granted access to early information about the upcoming uncertain reward outcome, while non-informative offers did not. Psychometric curves measuring the subjective value of information based on the choice of informative vs. non-informative offers (y-axis) as a function of the difference in their expected reward (x-axis), separately for trials where both offers had high or low reward uncertainty (dark or light red) for human and monkey species. The value of information was regulated by the uncertainty about future outcomes in either species–the more uncertain they are the more they were willing to pay for information. This conserved mechanism was reflected in the neural activity of the habenula–a conserved neural structure involved in processing negative value across species. Moreover, across large sample of humans aided by online behavioral mapping, we found that risk attitude (preference for uncertainty) did not predict their preference for information (information attitude) suggesting that risk attitude and information attitude may be regulated through different mechanisms; adapted from the study by Bromberg-Martin, Feng et al. [11].

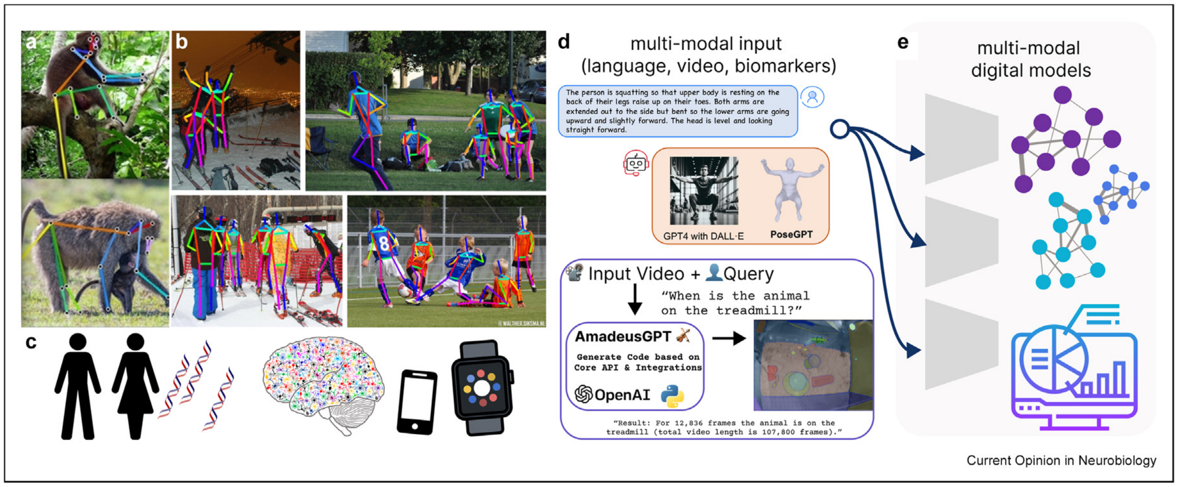
Another example can be seen in studies of neural circuits involved in approach—avoidance decision making and their utilization to motivate the characterization of how value-based decisions are altered in major depressive disorder (MDD) [50]. Computational models can be used to dissect the specific facets of decision making dynamics altered in MDD, increasing the predictive power beyond that which was possible with raw behavioral or brain data (Figure 2a—b) [84]; similar improvements have been drawn in several other computational psychiatry investigations). Moreover, this study showed that the same neural signal—nucleus accumbens activity—was predictive of dynamic decision biases toward approach in healthy control subjects but to avoidance in MDD. Because MDD is non-stationary, these findings reciprocally motivate further basic science research to more rigorously characterize the mechanisms of such opposing influences at the neural circuit level across long or extended time epochs.

Moreover, not all MDD patients show alterations in approach/avoidance decision making (and indeed, classification still remains far from perfect) just as not all OCD patients display persistent checking behaviors to reduce uncertainty. These complex mental illnesses are heterogeneous and likely involve changes in and interactions of many potential mechanisms. Thus, deploying decision-making tasks and obtaining repeated measures, in conjunction with long-term continuous behavioral measures over large populations of humans, will be critical for identifying MDD and OCD sub types and their mechanisms (that can be further studied in animal models and in genetic data).

Technological advances, challenges, and opportunities in studying behaviors and circuits over long timescales

Observing, documenting, and categorizing animal and human behavior over time has been a long-standing goal in science [3,9,59,72,108,111]. The contributions of Nobel laureate ethologist Tinbergen over many decades in the middle of the last century marked a significant milestone in this field, sparking a growing interest in bringing the “natural,” spontaneous, and continuous behaviors of animals into controlled laboratory environments.

Figure 3



Technological Advances in measuring human and other animal behaviors over timescales. Multi-modal data such as smart devices, genetic profiling, histology, neural and video-based behavior can be leveraged to build complex models. **a, b:** Video-based pose estimation can be used to measure posture and then for downstream behavioral analysis; examples from state-of-the-art algorithms for monkeys [6] and humans [131]. **c:** Examples of biological input data from patients. **d:** Top: Language and 3D human models can be used to reason about behaviors (ChatPose [32]), and Bottom: LLM-systems such as AmadeusGPT can be used for analysis [127]. **e:** These data can be combined to build foundation-like models that can be used for diagnostic evaluation. Icons adapted from scidraw.io and flaticon.

While current computational analyses remain challenged by “naturalistic” or less constrained settings, the emergence of software−hardware solutions offers promising prospects for advancing computational psychiatry in studying “real-world” behavior (Figure 3). Emerging approaches include the use of video technology, wearable sensors, and smartphone apps to collect continuous, real-time data on mood and behavior [45,92,97], large scale behavioral economics studies on the Internet [11,38,51], as well as developing advanced machine learning algorithms to analyze these large high dimensional datasets.

In short, with modern computational tools that automate analysis there has been a resurgence in the study of natural behavior. This automation ranges from the availability of commercial instruments for common tasks such as open field assays and rotarod tests to the development of novel machine learning techniques for capturing movement in diverse contexts [12,22,71]. In a recent review of the field of deep learning for video analysis, Mathis et al. [72] discussed the application of machine learning in behavior measurement, highlighting advancements in 2D and 3D tracking and suggesting the potential for dense reconstruction of animals’ behaviors on multiple timescales. Also recent work has discussed how computer vision is impacting ecology [44] and can be combined with hardware based sensors [110]. Yet, automating tracking the posture, location, and specific actions of animals over very long timescales is still hard and can be separated into several sub-goals and challenges. Furthermore, understanding the relationship of these measures and neural internal state(s) is a formidable theoretical and computational bottleneck.

Let us discuss what is currently possible. First, detecting where an animal or person is in the environment, computing posture in 2D or 3D along with other environmental or contextual features (such as detecting objects), is possible [71] but often requires the deployment of multiple cameras and other tools to collect the necessary data. Algorithmically, computer vision research is exploding with advances in transformers, large language models, multimodal models, computer vision, and beyond [17,32,55,98,104,113,127,129]. For example, just in the last year, we have seen large advances and gains on benchmarks for computing the posture of humans and animals in crowded scenes [131], for segmenting objects nearly everywhere [63], and in animal research the development of methods and critical benchmarks to build models that can capture the pose of multiple animals across species [14,125,126,128].

There are customized laboratory-based assays for mice that allow hardware−software solutions for tracking identity (with RFID chips, for example) such as LiveMouseTracker [23], and RFIDPose [124], and for primates (including humans) there are several non-invasive computer vision pose estimation solutions [6,65,69,125,131] (Figure 3a, b). These specific yet robust models for capturing detailed behavior in both nature-inspired lab and “in-the-wild” settings are yielding exciting new advances in both computer vision and are beginning to expand our understanding of complex neural circuits [6,118].

Humans can voluntarily wear wearable devices and sensors to provide detailed data that may be required for an individualized behavioral characterization and/or treatment (Figure 3c). The evolving cultural norms surrounding personal device and general technology usage, including smartphones, wearables like smartwatches, and routine audio—visual recordings, have opened up opportunities for researchers to study human behavior and health over extended timescales in a variety of settings. These devices can also track heart rate, sleep quality, physical activity, location and more [26,95,97], providing researchers with a continuous stream of data that could be correlated with various aspects of mood, cognition, and overall health.

It is also possible that in the future, we may have detailed enough GPS data to attempt less-invasive tracking, and combined with new light-weight sensors that not only could capture position, but could help discern individual actions [32,66]. Namely, it may be possible to use paired data to train models to directly predict actions from GPS, accelerometer, and other data loggers (like those sensors found in cell phones). Our projection is that multimodal data that collects across timescales, i.e., from sub-second RGB and accelerometer data, to GPS snapshots on the order of minutes or hours, plus natural language descriptions of behavior may become useful to train digital twin models that can make predictions about human behavior and its malfunctions (Figure 3a—e). We also pause to note here the obvious ethical concerns that we currently face and will only accelerate in the future with advances in technology.

Nonetheless, there are recent advances in machine learning that point to this promise of multi-modal, multi-timescale models. For example, we can jointly train multi-modal time-series models with auxiliary variables [94], and there is an explosion of work at the intersection of large language models (LLMs) combined with machine vision [32,98,104,127]. There are already efforts underway to merge pose estimation, segmentation, and advanced machine learning models with large-language systems for laboratory behavior [127] (Figure 3d). While this is far from solved, it gives us a glimpse into a multi-modal, highly interactive data world that certainly will open new directions in the measurement of behavior across increasingly long timescales and may contribute to the current limitations in understanding the relationship of external behaviors (actions) and internal states across time and context.

Additionally, LLMs (and other natural language processing methods (NLP)) could enable the analysis of textual and social media data to gain insights into individuals' mental states and behaviors [18,36,86,112,127]. The collection and analysis of behavioral data on a larger scale may uncover subtle behavioral patterns and social dynamics that might be challenging to discern through traditional methods alone, ultimately advancing our understanding of human behavior in an increasingly digital and interconnected world. This is important for psychiatry for example because in the "age of information" aberrant psychological thought patterns or behaviors could be triggered or related to particular contexts or interactions with social media or other digital platforms that otherwise would be hard to discern because they evolve over long timescales as an aggregate.

Modern geocoding approaches utilizing technology offer a robust lens to characterize the naturalistic human macroenvironment across various dimensions at the level of zip codes or neighborhoods. This innovative methodology enables the assessment of enrichment, impoverishment, and adverse conditions across socioeconomic, environmental, and infrastructural realms. Such analyses prove pivotal in shedding light on disparities in access to resources, healthcare, and educational opportunities [106]. Moreover, this approach holds particular relevance in understanding the etiology and pathogenesis of social determinants of health, thereby facilitating the development of targeted public health-oriented prevention strategies aimed at addressing systemic inequities and fostering holistic well-being within communities.

However, to date, continuous long-term studies of the details of behavior and neural data in animal models are scant [85], and are very rare in human patients [88]. Though emerging efforts are clearly aiming at this goal, for example using clinical assessment of depression symptoms along with analyses of facial expression and electrophysiological bio-markers overtime in the study of MDD intervention at the level of ventral medial prefrontal cortex (vmPFC) stimulation in Area 25 [1].

From the neural perspective, we are just starting to obtain an understanding of the mechanistic underpinnings of specific behavioral states and their execution. Initial research shows promise in the ability to establish connections between mechanisms investigated in laboratory settings and their impact on real-world behavior. For example, individual differences in striatal dopaminergic release during reinforcement learning tasks are related to reward-oriented behavior in daily life (e.g., the tendency for people to pursue activities that they had enjoyed when first trying them) [57] and also correlates with everyday smartphone use [120]. Similarly, Eldar et al. [28] used smartphones in combination with electrophysiological sensors to dissociate people who exhibited different reinforcement learning profiles. Those whose brains learned more quickly from reward prediction errors, as decoded from their electrophysiological signatures, reported increased mood hours later, whereas those with slower neural learning systems exhibited a change in mood the following day. Because previous work showed that not all prediction errors impact mood on a short time scale [10,29], this finding further highlights the need to monitor behavior and subjective experience continuously over time to refine our understanding of the causes our fluctuations of mood and internal state.

Ideally, we can now start to leverage neural population activity with behavioral variables and in particular take into consideration the behavioral hierarchies that emerge in naturalistic settings over short and long timescales. Recent developments in machine learning such as CEBRA that allow for the discovery of latent features in time series data such as neural recordings with behavior over time [94] across subjects. Using self supervised learning, a non-linear encoder learns a mapping of behavioral actions to neural activity, and can be combined across patients for building generalizable encoding—decoding models [76]. In the future, this could be highly useful for merging datasets across studies to compare joint behavioral—neural latent embeddings in health vs. disease states.

Over which timescales do we need to measure behavior to build such models? While many neural circuits operate over short time scales, for example processing incoming sensory information, other neural circuits operate over multiple or even over relatively long timescales (e.g., minutes, hours), integrating over a long history of events and internal states [20,61,64,68,100,130].

Brain regions that are particularly linked to the control of affect and mood, and their disorders, such as the vmPFC and cingulate cortex, track the valence of states over long timescales, likely integrating information about state value and physiological and autonomic states [1,79,80,87,90,100]. Interestingly, an important modulator of the medial prefrontal cortical areas —serotonin—also plays a prominent role in psychiatric disorders and is currently at the center of drug development efforts. Like vmPFC neurons, serotonin-releasing neurons in the dorsal raphe nucleus seem to be sensitive to changes in state value over both long and short timescales, and are sensitive to physiological and autonomic states [31,41,81,82,114,123]. As technology for continuous tracking and analyses emerges, one important future target for research must therefore be the raphe→vmPFC circuitry and its functions across short and long timescales in guiding behavior and animals and humans.

Concluding remarks

We provide a perspective that mental disorders evolve over extended timescales and include breakpoints in mechanisms that organize behaviors into broader behavioral hierarchies, and point out that whether adaptive or maladaptive, this process of organizing and maintaining behavioral hierarchies is by definition highly time and context dependent. We therefore also review key technological innovations that we believe will be critical for understanding the underlying mechanisms of mental disorders and their extended timescales.

Three key innovations: (i) progress in machine learning, (ii) extended, multimodal technology for behavioral monitoring, and (iii) the yet premature, but rapidly expanding, knowledge of the neural circuit basis for cognition and emotion are critical to the exploratory journey proposed in this review. Yet because these innovations are undergoing rapid development, we must now carefully consider how we want to organize, facilitate, and regulate our relationship with technology and medicine [53,99]. These questions are deeply ethical, philosophical and complex in nature, and span personal and societal levels of consideration. Examples include, when does psychological suffering need intervention? When ought the intervention be as simple as a reminder to meditate, exercise, or seek psychotherapy versus when to suggest exploring other options (e.g., pharmacology or closed-loop circuit-specific neuromodulation)?

We underscore the emerging pivotal role that continuous, long timescale behavioral and neural research in constrained and less-constrained (naturalistic) environments will have within the field of computational psychiatry. While traditional approaches have provided valuable insights into psychiatric disorders, the dynamic and complex nature of these conditions necessitates research that spans months, years, and even lifetimes, all while capturing individuals in their real-world contexts [47]. By tracking individuals over extended periods, researchers can uncover temporal trends, transitions between different mental health states, and the profound influence of life events on psychiatric symptoms. Such insights are essential for developing interventions and treatment strategies that are not only effective but also adaptable to the dynamic nature of these disorders. By mirroring this approach in basic neurobiological experiments in animals [4] and designing new analytic approaches and frameworks for analysis of continuous data, neuroscience can create better approaches to modeling the causes of and breakpoints in behavior and mental health.

Now, and in the future, ethics, consent, and human alignment with models will need front and center in any discussion around large-scale data collection. Willful, responsible, and consented participation in critical, and such studies also promote the concept of “citizen science” or participatory research, where individuals actively contribute data about themselves. This collaborative approach fosters a more comprehensive understanding of mood, cognition, and behavior across diverse populations and contexts. The opportunity is that the vast amount of data collected from personal devices will be harnessed through advanced machine learning and data analytics, allowing for the detection of subtle patterns and correlations that were previously challenging to uncover. Yet, society must setup proper infrastructure, ethical frameworks, and legal policies to facilitate the use of technology for individual-level advancement with regards to each person’s mental health goals and greater personal freedom.[b]

Thus, while efforts for continuous long timescale research in naturalistic settings will allow for the observation of mental health and behavior as they continuously unfold, they must align with the evolving ethical principles of society. In general, development of precision-driven approaches would represent a significant leap forward in mental health care, where one-size-fits-all treatments often fall short. Crucially, computational psychiatry must make further strides in linking human and animal behavior in order to study circuit functions, and assess these insights using both traditional and less constrained approaches, where time becomes an ally in our quest for insights, more effective reverse-translation strategies, and treatment development. In this, the narrowing of phenotypic characterization of mental disorders and their heterogeneity across individuals must be critically considered.

Another important issue to consider as we ponder these questions is that the definitions of what is a mental disorder, and what is not, are deeply contextual and even cultural, strongly influenced by whether a given behavioral or “thought” pattern is adapted to the current context. Characterizations of psychopathology using transdiagnostic, rather than disorder-specific, assessment strategies is crucial for capturing nuanced patterns, contextual dependencies, and underlying mechanisms that transcend traditional diagnostic boundaries, enabling more comprehensive and personalized approaches to mental health assessment and intervention. For example, population level species attitudes towards unpredictability or uncertainty that may have evolved over thousands of years may not be adapted to the information age with more and more people displaying signs of general anxiety and OCD, possibly in certain contexts triggered by digital platforms. The right path forward to address this issue remains unclear.

In short, the relationship of rapidly evolving artificial intelligence and neurobiology, neuromodulation in particular, must be carefully considered much in the same way we are currently considering how the relationship of artificial intelligence with privacy, military decisions and technologies, and with our own biases ought to be shaped by our broader goals and desires.

[b] https://www.whitehouse.gov/ostp/ai-bill-of-rights/& https://gdpr.eu/what-is-gdpr/.

Declaration of competing interest
Authors have no competing interests to declare.

Data availability
No data was used for the research described in the article.

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