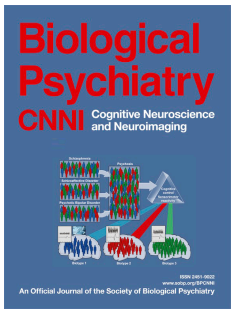
Journal Pre-proof



Threading the needle: Practical considerations for merging theory-driven computational psychiatry with data-driven analytics to enhance precision health at scale

Annie Cheng, Anna Konova, Albert Powers, Philip Corlett, Ifat Levy, Xiaosi Gu, Quentin Huys, Helen Pushkarskya, Sarah Fineberg, Tobias Hauser, Danilo Bzdok, Ilan Harpaz-Rotem, Theresa Babuscio, Lisa Nichols, Yize Zhao, Manu Sharma, Daniella Meeker, Hua Xu, Robb B. Rutledge, Godfrey D. Pearlson, Christopher Pittenger, Sarah W. Yip

PII: S2451-9022(26)00053-4

DOI: https://doi.org/10.1016/j.bpsc.2026.02.009

Reference: BPSC 1573

To appear in: *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*

Received Date: 22 October 2025

Revised Date: 27 January 2026

Accepted Date: 17 February 2026

Please cite this article as: Cheng A., Konova A., Powers A., Corlett P., Levy I., Gu X., Huys Q., Pushkarskya H., Fineberg S., Hauser T., Bzdok D., Harpaz-Rotem I., Babuscio T., Nichols L., Zhao Y., Sharma M., Meeker D., Xu H., Rutledge R.B., Pearlson G.D., Pittenger C. & Yip S.W., Threading the needle: Practical considerations for merging theory-driven computational psychiatry with data-driven analytics to enhance precision health at scale, *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2026), doi: https://doi.org/10.1016/j.bpsc.2026.02.009.

errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Threading the needle: Practical considerations for merging theory-driven computational psychiatry with data-driven analytics to enhance precision health at scale

Short title: Threading the needle

Annie Cheng[1], Anna Konova[2], Albert Powers[1,16], Philip Corlett[1,16,17], Ifat Levy[3,13,15,17], Xiaosi Gu[1,12,16], Quentin Huys[4], Helen Pushkarskya[1], Sarah Fineberg[1], Tobias Hauser[5,6,7,8], Danilo Bzdok[9,10], Ilan Harpaz-Rotem[1,13,16,17], Theresa Babuscio[1], Lisa Nichols[1], Yize Zhao[11], Manu Sharma[1], Daniella Meeker[12], Hua Xu[12], Robb B. Rutledge[1,13], Godfrey D. Pearlson[1,15,17,18], Christopher Pittenger[1,13-17], Sarah W. Yip[1,14,16,17]

Affiliations:

[1]Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA
[2]Department of Psychiatry, University Behavioral Health Care, & the Brain Health Institute, Rutgers University, New Brunswick, NJ
[3]Department of Comparative Medicine, Yale University School of Medicine, New Haven, CT, USA
[4]Applied Computational Psychiatry Laboratory, Mental Health Neuroscience Department, Division of Psychiatry and Max Planck University College London Centre for Computational Psychiatry and Ageing Research, Queen Square Institute of Neurology, University College London, London, United Kingdom
[5]Max Planck UCL Centre for Computational Psychiatry and Ageing Research
[6]Wellcome Centre for Human Neuroimaging, University College London
[7]Department of Psychiatry and Psychotherapy, Faculty of Medicine, University Tübingen, Tübingen, Germany
[8]German Center for Mental Health (DZPG), Tübingen, Germany
[9]McConnell Brain Imaging Centre, Montréal Neurological Institute, McGill University, Montréal, Canada
[10]Mila—Quebec Artificial Intelligence Institute, Montreal, Canada
[11]Department of Biostatistics, Yale School of Public Health, New Haven, Connecticut, USA
[12]Department of Biomedical Informatics and Data Science, Yale School of Medicine, New Haven, CT, USA
[13]Department of Psychology, Yale University, New Haven, CT, USA
[14]Child Study Center, Yale School of Medicine, New Haven, CT, USA
[15]Department of Neuroscience, Yale School of Medicine, New Haven, CT USA
[16]Center for Brain and Mind Health, Yale University, New Haven, CT, USA
[17]Wu-Tsai Institute, Yale University, New Haven, CT, USA
[18] Olin Neuropsychiatry Center, Hartford, CT, USA

Abstract

The rapidly evolving field of computational psychiatry enables quantification of specific cognitive processes, and their underlying mechanisms, in a translational and potentially scalable manner, using a combination of data collection via mechanistically informed behavioral tasks and theory-driven mathematical modeling. In parallel, transdiagnostic, dimensional approaches to psychiatric diagnostics, such as RDoC and HiTOP, seek to facilitate links between clinical research and real-world clinical reality, which rarely respects traditional diagnostic boundaries. These two approaches are seldom combined. In addition, while most psychiatric disorders are defined by their longitudinal course, our ability to predict symptom trajectories and tailor treatments to the individual remains limited, in part due to a dearth of longitudinal data collected using assessments sensitive to individual change over time. To address these gaps, the recently launched 'Individually Measured Phenotypes to Advance Computational Translation at Yale' (IMPACT-Y) study is collecting longitudinal data from a transdiagnostic cohort of 2400 individuals, using a combination of 'traditional' clinical research methods (e.g., health records, standardized assessments) and more novel computational approaches (e.g., behavioral tasks with demonstrated sensitivity to latent constructs and to within-person change, spoken narrative data). Here, we discuss unique challenges and opportunities in study design and analysis considerations of IMPACT-Y. Incorporating both theory- and data-driven analytics, we hope that IMPACT-Y will provide an unprecedented resource for characterizing longitudinal trajectories of core computational psychiatry constructs (e.g., reward learning) within and between individuals, for parsing heterogeneity beyond traditional diagnostic categories, and for linking inter- and intra-individual clinical variability to underlying mechanisms.

Introduction

Psychiatric disorders vary in both symptoms and longitudinal course [1]. Our ability to predict trajectories and tailor treatments at the individual level—often referred to as 'precision health'—remains limited [2-5]. Current clinical tools, including diagnostic categories, rating scales, and electronic health records, capture valuable information but fail to fully represent heterogeneity or predict outcomes [5]. Standard approaches to diagnosis and prognosis aggregate patients with diverse symptom expressions (and, conversely, with similar symptoms but presumed different underlying etiopathologies), lack mechanistic specificity, and rarely index underlying cognitive or neural processes that drive symptom trajectories. These challenges have been well documented, and some alternatives suggested, by initiatives such as the Research Domain Criteria (RDoC) [6, 7], the Hierarchical Taxonomy of Psychopathology (HiTOP) [8] and the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP)[9]. However, more mechanistically grounded approaches and corresponding data collection efforts are still needed.

Mechanism-focused research on mental illness typically relies on case-control designs, which emphasize group differences but offer limited prognostic utility [10, 11]. Group-level markers often do not align well with within-group measures and often have limited prognostic value at the individual level [12-14]. Recent mechanism-focused initiatives have moved toward more person-centered, longitudinal approaches. For example, repeated neuroimaging in the same individuals can link brain changes to clinical trajectories [3, 10, 11, 15, 16]. However, while mechanistically highly informative [17, 18], such densely sampled neuroimaging studies remain costly and are unlikely into translate at scale to routine clinical practice.

Computational psychiatry offers a complementary path by using behavioral tasks that are more affordable, mechanistically rich, and scalable [19-24]. The field combines theory-driven models of cognition and biology with data-driven machine learning [25, 26], increasingly blending the two to connect mechanistic insights with clinical prediction. Carefully designed, theory-based tasks can measure specific processes in an objective and reproducible manner that is well-suited for translational studies across preclinical, human experimental (e.g., drug challenge), and clinical work, and thus represent valuable tools both for probing behavior and for moving towards precision psychiatry. Mathematically modeling behavioral data can arbitrate between models of underlying processes, and latent parameters from these models can capture key sources of potentially informative variation (Figure 1A). The optimal model for a given task and individual

may provide information about *what* underlying computational process is being used by an individual (e.g., model-based vs. model-free learning), whereas individual differences in model-derived parameters (e.g., learning rate, inverse temperature) may provide information about *how* the individual implements that process (e.g., fast vs. slow learning rate, high vs low value sensitivity) [27-29].

Computational approaches have been applied to learning, decision making, and social and affective processes [30-40], and parameters from the resulting models have been used to tie behavior to underlying brain mechanisms [33, 34, 36, 41, 42]. Notably, some of these parameters have also been linked to prognosis, treatment response, and dimensional symptom measures, suggesting potential for clinical utility [26, 36, 38, 42-49]. To date, however, most studies have had modest sample sizes, often focusing on either single diagnostic groups or nonclinical community samples [32, 35-38, 42-45, 48, 50-62]. These limitations constrain scalability, clinical prediction, and generalizability. Moreover, while computational models applied to tasks targeting single (often disorder-specific) symptoms or processes assessed at a single timepoint have indisputably provided critical mechanistic insights [36, 63, 64], the ability of these approaches to capture the multidimensional interplay of processes shaping psychiatric outcomes longitudinally remains largely untested [23, 43, 65].

Recognizing these challenges, the NIH launched the IMPACT-MH consortium to harness big data for precision psychiatry (www.impact-mh.org). As the first of the articles in this Special Issue dedicated to IMPACT, we introduce one of its projects, the IMPACT study at Yale (IMPACT-Y), which employs repeated multitask computational assessments in a large transdiagnostic cohort (Figure 1B, Figure 2). By using IMPACT-Y as a touchstone, we aim to highlight foundational study design and analysis considerations that support precision psychiatry with an eye toward implementation in real-world clinical settings.

Figure 1

The IMPACT-Y study

Overview and goals

We briefly present the overall structure and goals of IMPACT-Y to provide a practical grounding for the discussions that follow (see Figure 2). Its aims are to: (1) characterize

longitudinal trajectories of computational processes across individuals and across traditional disorder boundaries; (2) enhance prediction of individual mental health outcomes; (3) identify biotypes, or data-driven subgroups with similar computational profiles – which may be transdiagnostic [66]. To do this, IMPACT-Y will collect naturalistic and task-based behavioral and clinical data from 1,800 individuals (Age 18-70) with a primary psychiatric diagnosis and 600 without one, across three waves of data collection, with longitudinal follow-up for two years (Figure 2D).

Computational task battery

Details of the IMPACT-Y computational task battery are presented in Table 1A; additional details on the protocol (e.g., additional task details, natural language processing assessments, etc.) are in the Supplemental Materials. Task selection was guided by a workgroup of Co-Investigators with expertise in computational psychiatry, with the goal of probing mechanistic constructs that show robust relationships to psychiatric symptomatology, including reward processing, anhedonia, apathy, Pavlovian approach, risk and loss aversion, and social cognition. Although not explicitly organized around the RDoC structure, selected tasks map well onto major RDoC domains [6, 67] (see Table 1A for the domains probed by each task). Multiple reward-related tasks were intentionally included, given the centrality of reward processes in transdiagnostic models of psychopathology and evidence that distinct reward-related latent parameters map onto different symptom dimensions and exhibit different temporal dynamics [43]. Less well-covered domains (e.g., social-affective processes) are supplemented with more conventionally used measures, such as self-reports and assessments from the NIH Toolbox.

Outcome measures

To track disease course and treatment response, IMPACT-Y uses a combination of transdiagnostic outcome measures and clinically derived indicators (see Table 1B for the list of self-report, clinical and other measures collected). Primary outcomes come from the NIH Toolbox [68-72], which provides validated, continuous measures of functioning and distress. These are administered three times per year, with additional cognitive NIH Toolbox measures collected annually. Secondary outcomes are derived from self-report and the electronic health record (EHR), including changes in symptom severity, significant medical or psychiatric events, medication

adjustments, and major shifts in socioeconomic or other social-determinant-of-health variables. Together, these longitudinal data streams allow us to quantify treatment trajectories and relapse risk in a clinically meaningful, transdiagnostic manner.

Below, we highlight relevant literature that informed our study design, introduce the challenges and controversies it seeks to address, and discuss those it will not.

Figure 2

Transdiagnostic considerations

Determining model fit across subgroups

A core strength of computational psychiatry lies in its clear delineation of specific models to explain particular cognitive processes. It is common practice to test multiple models in a single dataset from a single task to study a single diagnosis. Here, identification of the optimal model itself provides elucidation of mechanism—for example, revealing that momentary shifts in happiness during a decision-making task depend on the history of expectations and reward prediction errors [42, 46, 47, 73], as in Figure 1. Critically, the optimal model may change as a function of participant characteristics, such as diagnosis or illness phase; differential model fit may provide insights into individual and group differences [59, 74-76]. As one example, a recent study revealed that while social learning task performance in healthy controls was best explained by a model incorporating generalization of information from self to others and from others to the self, task performance among individuals with borderline personality disorder was better explained by a model that did not involve generalization between self and others' information—despite both groups exhibiting equivalent behavioral accuracy during task performance [75].

This example highlights a key question: are variations between individuals or populations best reflected in variation in computational parameters within a shared model, or in differences in the models themselves? Answering this question is not straightforward. A first step is to determine whether the same model provides the best fit across groups. If not, parameter values cannot be meaningfully compared, even if we impose the same model structure; interpretation should instead focus on finding the best-fitting model within each group. That said, models may be nested, such that differences between groups reflect differential expression of lower-level processes within a supraordinate framework. Another approach is to use Bayesian model averaging, which allows

weighting across multiple plausible models rather than selecting a single "best" one; this, too, provides a way to characterize relevant sources of variation across groups. If the same model fits best across groups, life is simpler: parameter values can be compared and may provide insights into individual- or subgroup-level differences in transdiagnostic or otherwise heterogeneous populations. Importantly, evaluating these questions requires attention to both procedural factors that could bias our estimates (e.g., task order, digital literacy) and clinical/demographic factors that may meaningfully contribute to heterogeneity (e.g., medication status, comorbid substance use, sex, socioeconomic status). We will estimate their impact and report likely biases in parameter estimates, and conduct sensitivity analyses across subgroups (e.g., male versus female) in theory-driven models. For data-driven models, we will test for the effects of such variables as confounders, colliders or mediators and adjust predictive models accordingly [77]. Finally, IMPACT's longitudinal, repeated-measures design enables exploration of causal relationships, for example using path models, to identify key contributors, mediators, and moderators of outcomes.

Measuring transdiagnostic and dimensional constructs

Initiatives such as RDoC [6, 7] and HiTOP [8] have sought to formally address the limitations of categorical diagnoses by developing dimensional and hierarchical alternatives [6-8, 78]. Recognizing that multiple different constructs (e.g., reward learning) are often implicated in a single disorder and that a single construct is often implicated across different disorders, these taxonomies seek to provide a more tractable link between clinical research and real-world clinical reality in which the same psychiatric treatments and medications are often prescribed across diverse diagnoses [6-8, 78-80]. Indeed, recent work has argued for taxonomies of psychotropic medications that incorporate transdiagnostic symptom domains and underlying biological mechanisms beyond and across diagnostic categories [80]. Integrative computational models that link neural implementation (e.g., midbrain dopamine neurons and their projections to the striatum and prefrontal cortex), algorithmic frameworks (such as temporal difference learning), and computational manifestations (including delusional beliefs, hallucinations, or apathy) are well-suited to inform refinement of such pharmacological taxonomies [19, 81-86]. As an example, recent work has linked molecular abnormalities (e.g., NMDA receptor hypofunction and cortical hyperexcitability) and information processing abnormalities (i.e., aberrant prediction errors and

compensatory overweighting of priors) to describe the emergence of delusions and hallucinations in psychosis [86], offering both a mechanistic account that bridges levels of analysis and testable predictions about pharmacological interventions. Further transdiagnostic application of this approach could elucidate how proposed mechanisms fit within hierarchical, dimensional models of mental illness and drive symptom expression across diagnoses. Large, transdiagnostic datasets measuring dimensional constructs and computational mechanisms, such as IMPACT-Y, are poised to address this.

Dimensional computational psychiatry increasingly leverages large-scale data collection, often online, to probe mechanisms [87-89]. By recruiting thousands of unselected participants and combining self-report with task-based modeling, researchers have identified latent psychiatric dimensions (e.g., compulsivity, anxious-depression) and linked them to computational mechanisms such as altered model-based planning and metacognition [88]. A key issue is whether findings from unselected samples generalize to clinical populations. Sometimes results align—for instance, compulsivity relates to deficits in goal-directed control in both online samples [90] and in patients with OCD [91]. Other times they diverge: online samples with high self-reported autistic traits differ from clinically diagnosed individuals with autism in some symptom reports and social decision-making [92]. These patterns highlight limits to generalizability and the need to test whether computational parameters map onto dimensional traits in real-world clinical groups.

By recruiting a large, transdiagnostic clinical sample alongside a cohort of controls, IMPACT-Y will provide the data to begin to answer these and other outstanding questions. While some of the tasks included in our computational battery—such as those probing dimensional constructs (e.g., reward effort [35], risk and ambiguity tolerance [33] and random dot motion tasks [40])—are anticipated to have high relevance across multiple diagnoses (e.g., depression, substance-use disorder, schizophrenia), others (e.g., the conditioned hallucination task[36]) may only emerge as relevant to a single constellation of symptoms or participant subgroup. IMPACT-Y aims to characterize these relationships, assess critical interactions within and between constructs, identify contexts in which different measures map onto the same construct (i.e., global or local redundancy), and establish which computational parameters reflect enduring traits versus transient states.

Leveraging theory-driven modeling and data-driven analytics to assess core processes at scale

Considerations guiding theory-driven task selection and data-driven analysis

A central goal of IMPACT-Y is to inform the development of a practical, scalable, and clinically useful assessment battery appropriate for large-scale administration. IMPACT-Y is recruiting three consecutive large, transdiagnostic samples (Figure 1B, 2F), allowing for task validation and refinement, with modifications informed by analysis of earlier waves. Optimal tasks must meet several key practical requirements: At the level of data collection, tasks should balance statistical power with reasonable length, remain deployable across settings and platforms, while remaining accessible to individuals with varying cognitive abilities and robust to technical constraints such as hardware and connectivity differences. At the level of computational parameter inference, streamlined, automated pipelines, including the derivation of the target computational model parameters, would be ideal to lower technical barriers, with analytic strategies that minimize the number of trials required to yield robust estimates.

Data-driven analysis may enhance automation and facilitate integration with the existing framework of clinical information collection (e.g., clinical impressions, EHRs); but over-automation (e.g., invariant application of a single model) may cloud or obscure underlying mechanisms. Thus, the optimal approach will likely involve both data-driven approaches—such as deriving generative embeddings [93, 94] or using principal component analysis for dimension reduction—and theory-driven designs that provide mechanistic precision via mapping onto core, interpretable constructs in a tractable manner [23, 24], with algorithmic extraction of selected parameters (another form of data reduction) [21]. Finally, to have clinical utility, tasks must be sensitive to intra-person changes (e.g., track changes in reward sensitivity relevant to shifts from euthymia to mania) and/or track sensitivity to a given clinical intervention [15, 51, 95], and have good test-retest reliability (e.g., yield consistent reward sensitivity estimates when administered repeatedly during euthymia) [19, 23, 96].

These are not easy conditions to meet, and few (if any) existing computational tasks have been disseminated at the scale required to test them [23]. As summarized in Table 1, many of the tasks selected for IMPACT-Y's core computational battery meet some of these criteria, such as sensitivity to clinical change [43, 97] or transdiagnostic relevance [33, 36, 44, 60, 97]. Repeated task administration enhances detection of within-person change and improves the reliability of

283 computational parameters, which are often unstable in single sessions but more robust with
284 repeated sampling [98, 99].
285
286 *Relating computational insights to diverse clinical outcome measures*
287 Linking tasks to clinical trajectories requires equally robust symptom measures, scalable
288 across individuals. IMPACT-Y combines structured interviews, open-ended narratives, validated
289 self-reports, EHR, and NIH toolbox assessments. Each source has strengths and limitations: EHRs
290 provide integrated clinical data but often lack consistent symptom documentation; open-ended
291 narratives capture subjective experiences but may be difficult to quantify. By combining multiple
292 assessments, and by leveraging recent advances in AI and natural language processing (NLP) to
293 automate analysis of EHR and spoken narrative data [100-108], IMPACT-Y seeks to move
294 towards an integrated person-centered characterization of individual trajectories in both traditional
295 clinical and novel computational measures.
296 Critically, as with computationally derived task parameters, validation of resultant NLP-
297 derived features will also be required. Within the context of IMPACT-Y, this will include basic
298 validation of the NLP-pipeline itself, as well as conceptual validation across different patient
299 subgroups. For example, NLP models that have been optimized for use in healthy controls to
300 capture discourse coherence may fit well in individuals with affective disorders but fail in patients
301 with psychosis if linguistic disorganization manifests differently across these groups [109].
302
303 **Using 'computational snapshots' to characterize individual trajectories over time**
304 *The need for multidimensional assessment*
305 Most prior computational psychiatry studies have examined single psychological domains
306 and clinically homogenous samples. This 'limitation' has largely been by design: a key strength
307 of theory-driven work is its use of specific, testable hypotheses grounded in explicit theoretical
308 and mathematical frameworks [110], and these are best tested in 'pure' samples. Yet applying this
309 approach in clinical contexts, where presentations are heterogeneous and multiple processes
310 interact, requires a multidomain strategy that tracks multiple latent constructs across diverse
311 participants. This also enables identification of redundant constructs that appear prognostic in
312 isolation but overlap when considered together. As illustrated in Figure 3, such transdiagnostic,

multidomain approaches can provide finer-grained behavioral subtyping and allow testing of multiple theory-driven models within the same dataset.

IMPACT-Y adopts a 'computational snapshot' approach, indexing latent parameters from theory-driven models in a multidimensional space that can be mapped onto clinical or other individual difference factors [65] (Figure 3). This approach acknowledges that even conceptually related parameters—such as preference for known versus unknown risk—may map differentially onto the same outcome and/or may only explain limited variance alone and therefore should not be considered in isolation [19, 43, 65, 111-113]. By situating individuals in a multidimensional parameter space that captures latent information about multiple specific mechanisms, computational snapshots provide a way to link behavioral variation to underlying processes—something not possible with purely descriptive approaches. This and other multidimensional approaches allow researchers and clinicians to parse heterogeneity in ways that diagnostic classification systems cannot, in line with a dimensional approach to psychiatry [19].

The need for longitudinal, within-person sampling

Psychiatric illnesses rarely emerge fully formed but instead evolve dynamically over time (e.g., delusions often precede hallucinations in early psychosis [114], late-life depression is associated with an increased risk for dementia and Alzheimer's disease [115]), and an emerging account suggests that some temporal patterns may arise from interactions among parameters—for example, when changes in prediction error signaling alter the reliability of sensory evidence, this can in turn shift reliance on prior beliefs [86]. These dynamic interactions highlight how symptoms may not simply appear in isolation, but instead emerge as sequential outcomes of interacting mechanisms over time, further highlighting the need for multidimensional longitudinal data collection. By collecting multiple 'snapshots', IMPACT-Y enables longitudinal tracking of how a person's constellation of computational features shifts over time or in response to clinical interventions. Linking the trajectories of these snapshots to symptom changes over time using data-driven analytics (Figure 3, panel B-D) offers a window into the mechanisms of illness progression and recovery, with potential to identify periods when an individual's illness burden or treatment need is highest [116]. This approach complements traditional predictors from clinical assessments and electronic health records, which capture valuable information but have limited explanatory power [5, 117, 118]. In future work, longitudinal computational snapshots could also serve as a

core clinical interface—for example, by summarizing changes in mechanistic parameters over time and highlighting periods of elevated risk or treatment need—to support clinical decisions related to illness progression and treatment (see [19] for additional discussion). Complementary developments in digital phenotyping, which provide continuous and naturalistic behavioral measurement [119], and in NLP and machine learning methods for analyzing unstructured patient-reported outcomes in EHRs [120], highlight emerging directions for how computational approaches could eventually integrate into decision-support workflows. We expect that IMPACT-Y will provide practical experience in collecting and structuring longitudinal behavioral and clinical data at scale, informing best practices for how such outputs might be organized, visualized, and ultimately incorporated into clinician-facing dashboards or decision support tools in follow-up work.

Figure 3

Capturing computational snapshots across different timescales and contexts

Psychiatric processes unfold across multiple timescales, ranging from transitory moment-to-moment mood or symptom fluctuations to extended periods of illness or remission that can persist for weeks to years. However, computational psychiatry has tended to focus either on within-session fluctuations or on single-session aggregate parameters. Thus, for many tasks, whether computational parameters are better understood as reflecting transient states or enduring traits is unknown. Previous work has shed light on this issue for some, but not all, of the parameters measured in our tasks, but repeated longitudinal assessment over multiple timescales (e.g., days to months to years) is needed to more comprehensively address these questions.

It is not clear *a priori* what frequency of task administration will be the most informative for tracking clinical change. Thus, as an initial starting point, IMPACT-Y incorporates a mix of daily, monthly, tri-annual, and annual assessments, including randomization to daily vs. monthly collection of smartphone task data. This should provide an initial foundation for dynamic, adaptive sampling schemes that adjust to clinical state, increasing measurement frequency during periods of instability and reducing it during stability—much like blood tests are ordered more frequently when a patient is acutely ill and less often during remission. Importantly, different computational tasks may vary in their sensitivity to short-term fluctuations versus longer-term change (Figure 4),

so adaptive schemes will need to tailor sampling not only to the individual's clinical course but also to the temporal resolution of each task.

Collecting data across different timescales, with frequencies as high as daily, requires leveraging approaches that make such designs feasible at scale. Unlike biological measures such as brain imaging, which are difficult and expensive to deploy repeatedly, self-reports and behavior-based predictors provide measures that are closer to patient experience and are easier to deploy at scale, especially when almost every patient has a smartphone [121]. Data quality from decision tasks delivered on smartphone is comparable to lab data [122], with much lower costs associated with the longitudinal data collection needed to understand which patterns are stable risk factors and which follow or predict symptom change [123]. Moreover, smartphone-based data collection captures behavior as participants go about their daily lives, allowing the study of behavior in naturalistic settings [123].

Model parameters may not always generalize across contexts or cleanly capture unique and specific cognitive processes [124]. For example, some reinforcement learning parameters, such as learning rate, vary across contexts and are entangled with several other parameters (e.g., working memory) [29, 125]. Relatedly, caution is needed to avoid oversimplification when interpreting findings within particular theoretical frameworks. For example, although the model-free versus model-based reinforcement learning framework has been highly influential, a strict dichotomy can distort research questions and lead to an unnecessarily narrow perspective on learning and decision-making [89]. Ultimately, recognizing the limits of computational parameters and the complexity of underlying mechanisms will be critical for ensuring computational models capture the right constructs in the right contexts. We view IMPACT-Y's longitudinal design as essential for this purpose, as it enables data collection across multiple contexts and timepoints, serving as a platform to validate the robustness and clinical utility of models and parameters over time.

Figure 4

Data-driven considerations

The breadth of IMPACT-Y will ultimately require data-driven models to elucidate complex relationships within and between assessment domains (e.g., merging of computational and clinical 'snapshots'). These may include conventional machine learning approaches including canonical

correlation analysis (CCA) and CCA's longitudinal extension, LCCA, as well as more advanced deep learning-based methods including transformers and other pattern learning approaches [126-131]. These approaches have multiple advantages in handling complex and large-scale data. First, many high-dimensional datasets contain more variables than individuals (commonly known as the 'p>n' problem), a situation in which traditional linear regression models become infeasible. By enabling dimension reduction via penalization or low-dimensional latent embedding, data-driven approaches allow an end-to-end analysis for such datasets, where cross-validation (i.e., model generation in training data and testing in held-out testing data) is incorporated to avoid over-fitting and models further require validation in separate cohorts [5, 132, 133].

Reliance on hypothesis-driven univariate testing methods in well-powered datasets often yields highly statistically significant associations that nonetheless explain little variance. Such approaches may prevent detection of previously un-hypothesized relationships that are nonetheless robust and generalizable [111, 127, 134-136]. Data-driven analytics may also be used to identify critical sources of variance at the sub-group or individual-level, where such subgroups can be unspecified, and determined in a data-driven way based on similar profiles across multiple diverse measures, as in prior work in psychosis and depression [66, 137]. While the challenge of these approaches again lies in their replicability and stability [138], failing to test for such subgroups may lead to inaccurate statistical conclusions, as in Simpson's paradox: A classic statistical phenomenon in which an effect observed across different demographic or clinical subgroups is reversed or disappears when considered within each subgroup separately [128] (for example, the overall efficacy of antidepressants is reduced when considering individuals with both mild and severe symptoms relative to only those with severe symptoms [139]). As testing of such effects requires large amounts of data from heterogeneous samples, prior computational psychiatry work has not been powered to detect for such demographic—or potentially computationally derived (e.g., participants with high versus low sensitivity to reward)—subgroup effects.

Limitations

IMPACT-Y has several limitations. It does not include neuroimaging or electroencephalogram (EEG), which could enrich mechanistic interpretations of computational parameters. Due to practical time constraints, we are not measuring all possible domains (e.g., detailed family histories of psychiatric diagnoses) yet we will be revising the battery as we

continue the study when possible to address such gaps. The task battery emphasizes decision-making, with more limited coverage of interoception, perception, and social-affective domains. We note this as a current limitation but emphasize that these domains are nevertheless still assessed through existing tasks and standardized scales, and we may consider expanding these domains as the study continues to evolve. By design, the IMPACT-Y computational battery yields few parameters that map directly onto outputs from traditional, widely adopted tasks (e.g., delay discounting). While this arguably constrains comparability with existing datasets, our computational battery nonetheless measures core constructs that are tightly related to more widely studied processes (e.g., reward learning and sensitivity, both constructs related to delay discounting). Although the sample is large for computational psychiatry, it may be underpowered to detect subtle effects or rare subgroups, and relatively few participants are assessed at the earliest stages of illness, when changes may be most informative [86]. Relatedly, the sample includes only adults, limiting generalizability to adolescents—a critical developmental window for the emergence of many psychiatric disorders [140]. We note that other IMPACT sites, such as those described in other manuscripts of this special issue, are specifically focused on developmental cohorts. Finally, translational concerns remain, including how best to adapt these tasks for time-limited clinical settings and integrate them into routine care.

Conclusion

IMPACT-Y is an ambitious step toward clinical computational psychiatry. By collecting large-scale, transdiagnostic, longitudinal data, it aims to capture mechanistic processes underlying psychiatric disorders and track them over time, informing prognosis, treatment response, and relapse prediction. While gaps remain, IMPACT-Y lays the groundwork for computational psychiatry that bridges mechanistic insight with clinical application. An important consideration is the feasibility and validity of these tasks and models in real-world clinical contexts. As data collection is already ongoing (baseline assessments completed for ~350 individuals as of December 2025), IMPACT-Y is well-poised to begin to answer these initial questions.

Funding and acknowledgements: This work was supported by NIMH grant (U01MH136497, MPIs: Pittenger, Pearlson and Yip). AK is supported by NIMH grant (P50MH136296) and NIDA grant (R01DA053282 and R01DA054201). XG is supported by National Institute on Drug Abuse

(R01DA060220) and National Institute of Mental Health (R01MH123069, R01MH133625). TUH has received funding from the Wellcome Trust (316955/Z/24/Z), the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 946055), and the Carl-Zeiss-Stiftung. TUH was supported by the Alexander von Humboldt foundation, (more) precisely the Alexander-von-Humboldt-Professorship award to Peter Dayan. QJMH has received research grant funding from Carigest S.A., Koa Health, NIHR and Wellcome Trust. QJMH acknowledges support by the NIHR UCLH BRC and NIHR MH-TRC MHM. RBR is supported by the National Institute of Mental Health (R01MH124110)

Disclosures: PC is a cofounder, board member, and holds equity in Tetricus Labs, a computational Psychiatry company who did not fund this work. XG is a Scientific Advisor to Soihtu DTx and Co-Editor-in-Chief for the journal Computational Psychiatry (CPSY). Dr Harpaz-Rotem receives funding via an Investigator Initiated Research Grant (IIR) - Precision Psychiatry -from Boehringer Ingelheim (BI) International GmbH. TUH consults for limbic ltd and holds shares in the company, which is unrelated to the current project. QJMH was employed by University College London during this work. QJMH has obtained fees and options for consultancies for Aya Technologies and Alto Neuroscience, and consultancy fees from IMPACT-MH. CP is a consultant for Biohaven Pharmaceuticals, Freedom Biosciences, Mind Therapeutics, and lucid/care, has received research funding from Freedom and Biohaven, and holds equity in Mind, lucid/care, and Alco Therapeutics. He is an inventor on several patents unrelated to the work discussed here. RBR holds equity in Maia, an AI tool for relationship communication. All other authors report no biomedical financial interests or potential conflicts of interest.

ChatGPT was used to revise portions of this manuscript for concision and clarity. The authors take full responsibility for the content of this work.

Supplement Description:

Tables S1-S2

References

1. Caspi, A., et al., *Longitudinal Assessment of Mental Health Disorders and Comorbidities Across 4 Decades Among Participants in the Dunedin Birth Cohort Study.* JAMA Netw Open, 2020. **3**(4): p. e203221.
2. Collins, F.S. and H. Varmus, *A new initiative on precision medicine.* N Engl J Med, 2015. **372**(9): p. 793-5.
3. Lynch, C.J., et al., *Frontostriatal salience network expansion in individuals in depression.* Nature, 2024. **633**(8030): p. 624-633.
4. Siontis, G.C., et al., *External validation of new risk prediction models is infrequent and reveals worse prognostic discrimination.* J Clin Epidemiol, 2015. **68**(1): p. 25-34.
5. Chekroud, A.M., et al., *Illusory generalizability of clinical prediction models.* Science, 2024. **383**(6679): p. 164-167.
6. Insel, T., et al., *Research domain criteria (RDoC): toward a new classification framework for research on mental disorders.* Am J Psychiatry, 2010. **167**(7): p. 748-51.
7. Insel, T.R., *The NIMH Research Domain Criteria (RDoC) Project: precision medicine for psychiatry.* Am J Psychiatry, 2014. **171**(4): p. 395-7.
8. Kotov, R., et al., *The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies.* J Abnorm Psychol, 2017. **126**(4): p. 454-477.
9. Clementz, B.A., et al., *Psychosis biotypes: replication and validation from the B-SNIP consortium.* Schizophrenia bulletin, 2022. **48**(1): p. 56-68.
10. Yip, S.W. and A.B. Konova, *Densely sampled neuroimaging for maximizing clinical insight in psychiatric and addiction disorders.* Neuropsychopharmacology, 2021: p. 395–396.
11. Kraus, B., et al., *Insights from Personalized Models of Brain and Behavior for Identifying Biomarkers in Psychiatry.* doi:10.31234/osf.io/48u5r, 2023.
12. Whitfield-Gabrieli, S., et al., *Brain connectomics predict response to treatment in social anxiety disorder.* Mol Psychiatry, 2016. **21**(5): p. 680-5.
13. Yip, S.W., B. Kiluk, and D. Scheinost, *Toward Addiction Prediction: An Overview of Cross-Validated Predictive Modeling Findings and Considerations for Future Neuroimaging Research.* Biol Psychiatry Cogn Neurosci Neuroimaging, 2020. **5**(8): p. 748-758.
14. Lichenstein, S.D., et al., *Dissociable neural substrates of opioid and cocaine use identified via connectome-based modelling.* Mol Psychiatry, 2021. **26**: p. 4383–4393.
15. Hafeman, D.M., et al., *Longitudinal stability of mood-related resting-state networks in youth with symptomatic bipolar-I/II disorder.* Transl Psychiatry, 2025. **15**(1): p. 187.
16. Yip, S.W., et al., *Intra-individual changes in Stroop-related activations linked to cigarette abstinence in adolescent tobacco smokers: Preliminary findings.* Drug Alcohol Depend, 2016. **167**: p. 182-9.
17. Newbold, D.J. and N.U.F. Dosenbach, *Tracking plasticity of individual human brains.* Current Opinion in Behavioral Sciences, 2021. **40**: p. 161-168.

18. Newbold, D.J., et al., *Plasticity and Spontaneous Activity Pulses in Disused Human Brain Circuits.* Neuron, 2020. **107**(3): p. 580-589.e6.
19. Yip, S.W., et al., *From Computation to Clinic.* Biological Psychiatry Global Open Science, 2022.
20. Karamanakos, P.N., et al., *Differentiation of disulfiram effects on central catecholamines and hepatic ethanol metabolism.* Pharmacol Toxicol, 2001. **88**(2): p. 106-10.
21. Huys, Q.J., T.V. Maia, and M.J. Frank, *Computational psychiatry as a bridge from neuroscience to clinical applications.* Nat Neurosci, 2016. **19**(3): p. 404-13.
22. Browning, M., M. Paulus, and Q.J.M. Huys, *What is Computational Psychiatry Good For?* Biol Psychiatry, 2023. **93**(8): p. 658-660.
23. Karvelis, P., M.P. Paulus, and A.O. Diaconescu, *Individual differences in computational psychiatry: A review of current challenges.* Neurosci Biobehav Rev, 2023. **148**: p. 105137.
24. Hauser, T.U., et al., *The promise of a model-based psychiatry: building computational models of mental ill health.* Lancet Digit Health, 2022. **4**(11): p. e816-e828.
25. Bennett, D., S.M. Silverstein, and Y. Niv, *The Two Cultures of Computational Psychiatry.* JAMA Psychiatry, 2019. **76**(6): p. 563-564.
26. Huys, Q.J.M., T.V. Maia, and M.J. Frank, *Computational psychiatry as a bridge from neuroscience to clinical applications.* Nature Neuroscience, 2016. **19**(3): p. 404-413.
27. Palminteri, S., V. Wyart, and E. Koechlin, *The Importance of Falsification in Computational Cognitive Modeling.* Trends Cogn Sci, 2017. **21**(6): p. 425-433.
28. Daw, N.D., *Trial-by-trial data analysis using computational models.* Decision making, affect, and learning: Attention and performance XXIII, 2011. **23**(1): p. 3-38.
29. Collins, A.G. and M.J. Frank, *How much of reinforcement learning is working memory, not reinforcement learning? A behavioral, computational, and neurogenetic analysis.* Eur J Neurosci, 2012. **35**(7): p. 1024-35.
30. Behrens, T.E., et al., *Associative learning of social value.* Nature, 2008. **456**(7219): p. 245-9.
31. Forbes, E.E., D.S. Shaw, and R.E. Dahl, *Alterations in reward-related decision making in boys with recent and future depression.* Biol Psychiatry, 2007. **61**(5): p. 633-9.
32. Huys, Q.J., et al., *Mapping anhedonia onto reinforcement learning: a behavioural meta-analysis.* Biol Mood Anxiety Disord, 2013. **3**(1): p. 12.
33. Levy, I., et al., *Neural representation of subjective value under risk and ambiguity.* J Neurophysiol, 2010. **103**(2): p. 1036-47.
34. Na, S., et al., *Humans use forward thinking to exploit social controllability.* Elife, 2021. **10**.
35. Nair, A., et al., *Opportunity cost determines free-operant action initiation latency and predicts apathy.* Psychol Med, 2023. **53**(5): p. 1850-1859.

36. Powers, A.R., C. Mathys, and P.R. Corlett, *Pavlovian conditioning-induced hallucinations result from overweighting of perceptual priors.* Science, 2017. **357**(6351): p. 596-600.
37. Reed, E.J., et al., *Paranoia as a deficit in non-social belief updating.* Elife, 2020. **9**.
38. Sheffield, J.M., et al., *Belief Updating and Paranoia in Individuals With Schizophrenia.* Biol Psychiatry Cogn Neurosci Neuroimaging, 2022. **7**(11): p. 1149-1157.
39. Smoski, M.J., et al., *Decision-making and risk aversion among depressive adults.* J Behav Ther Exp Psychiatry, 2008. **39**(4): p. 567-76.
40. Banca, P., et al., *Evidence accumulation in obsessive-compulsive disorder: the role of uncertainty and monetary reward on perceptual decision-making thresholds.* Neuropsychopharmacology, 2015. **40**(5): p. 1192-202.
41. Keren, H., et al., *Reward Processing in Depression: A Conceptual and Meta-Analytic Review Across fMRI and EEG Studies.* Am J Psychiatry, 2018. **175**(11): p. 1111-1120.
42. Rutledge, R.B., et al., *Association of Neural and Emotional Impacts of Reward Prediction Errors With Major Depression.* JAMA Psychiatry, 2017. **74**(8): p. 790-797.
43. Konova, A.B., et al., *Computational Markers of Risky Decision-making for Identification of Temporal Windows of Vulnerability to Opioid Use in a Real-world Clinical Setting.* JAMA Psychiatry, 2020. **77**(4): p. 368-377.
44. Pushkarskaya, H., et al., *Contrasting contributions of anhedonia to obsessive-compulsive, hoarding, and post-traumatic stress disorders.* J Psychiatr Res, 2019. **109**: p. 202-213.
45. Pushkarskaya, H., et al., *Value-based decision making under uncertainty in hoarding and obsessive- compulsive disorders.* Psychiatry Res, 2017. **258**: p. 305-315.
46. Rutledge, R.B., et al., *The social contingency of momentary subjective well-being.* Nat Commun, 2016. **7**: p. 11825.
47. Rutledge, R.B., et al., *Dopaminergic Modulation of Decision Making and Subjective Well-Being.* J Neurosci, 2015. **35**(27): p. 9811-22.
48. Suthaharan, P., et al., *Paranoia and belief updating during the COVID-19 crisis.* Nat Hum Behav, 2021. **5**(9): p. 1190-1202.
49. Berwian, I.M., et al., *Computational Mechanisms of Effort and Reward Decisions in Patients With Depression and Their Association With Relapse After Antidepressant Discontinuation.* JAMA Psychiatry, 2020. **77**(5): p. 513-522.
50. Brazil, I.A., et al., *Psychopathy-related traits and the use of reward and social information: a computational approach.* Front Psychol, 2013. **4**: p. 952.
51. Brown, V.M., et al., *Reinforcement Learning Disruptions in Individuals With Depression and Sensitivity to Symptom Change Following Cognitive Behavioral Therapy.* JAMA Psychiatry, 2021. **78**(10): p. 1113-1122.
52. Charpentier, C.J., et al., *Enhanced risk aversion, but not loss aversion, in unmedicated pathological anxiety.* Biological Psychiatry, 2017. **81**(12): p. 1014-1022.
53. Chung, D., et al., *Valuation in major depression is intact and stable in a non-learning environment.* Sci Rep, 2017. **7**: p. 44374.
54. Fineberg, S.K., et al., *Differential Valuation and Learning From Social and Nonsocial Cues in Borderline Personality Disorder.* Biol Psychiatry, 2018. **84**(11): p. 838-845.

55. Forbes, E.E., D.S. Shaw, and R.E. Dahl, *Alterations in reward-related decision making in boys with recent and future depression*. Biological Psychiatry, 2007. **61**(5): p. 633-639.
56. Henco, L., et al., *Aberrant computational mechanisms of social learning and decision-making in schizophrenia and borderline personality disorder.* PLoS Comput Biol, 2020. **16**(9): p. e1008162.
57. Jia, R., et al., *Neural valuation of rewards and punishments in posttraumatic stress disorder: a computational approach*. Transl Psychiatry, 2023. **13**(1): p. 101.
58. Kafadar, E., et al., *Modeling perception and behavior in individuals at clinical high risk for psychosis: Support for the predictive processing framework*. Schizophr Res, 2020. **226**: p. 167-175.
59. Pushkarskaya, H., et al., *Decision-making under uncertainty in obsessive-compulsive disorder.* J Psychiatr Res, 2015. **69**: p. 166-73.
60. Raio, C.M., et al., *Cumulative lifetime stressor exposure assessed by the STRAIN predicts economic ambiguity aversion*. Nat Commun, 2022. **13**(1): p. 1686.
61. Shapiro-Thompson, R., et al., *Modulation of trust in borderline personality disorder by script-baed imaginal exposure to betrayal*. PsyArXiv, 2021.
62. Smoski, M.J., et al., *Decision-making and risk aversion among depressive adults*. Journal of Behavior Therapy and Experimental Psychiatry, 2008. **39**(4): p. 567-576.
63. Ashinoff, B.K., et al., *Rethinking delusions: A selective review of delusion research through a computational lens*. Schizophr Res, 2022. **245**: p. 23-41.
64. Baker, S.C., et al., *Prior overweighting relates to delusional ideation in individuals at clinical high-risk for psychosis*. Schizophr Res, 2024. **266**: p. 153-155.
65. Gueguen, M.C.M., E.M. Schweitzer, and A.B. Konova, *Computational theory-driven studies of reinforcement learning and decision-making in addiction: What have we learned?* Curr Opin Behav Sci, 2021. **38**: p. 40-48.
66. Clementz, B.A., et al., *Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers*. Am J Psychiatry, 2016. **173**(4): p. 373-84.
67. Cuthbert, B.N., *Research Domain Criteria (RDoC): Progress and Potential*. Curr Dir Psychol Sci, 2022. **31**(2): p. 107-114.
68. Cook, K.F., et al., *Pain assessment using the NIH Toolbox*. Neurology, 2013. **80**(11 Suppl 3): p. S49-53.
69. Cyranowski, J.M., et al., *Assessing social support, companionship, and distress: National Institute of Health (NIH) Toolbox Adult Social Relationship Scales*. Health Psychol, 2013. **32**(3): p. 293-301.
70. Fox, R.S., et al., *Uses of the NIH Toolbox(R) in Clinical Samples: A Scoping Review*. Neurol Clin Pract, 2022. **12**(4): p. 307-319.
71. Salsman, J.M., et al., *Emotion assessment using the NIH Toolbox*. Neurology, 2013. **80**(11 Suppl 3): p. S76-86.
72. Salsman, J.M., et al., *Assessing psychological well-being: self-report instruments for the NIH Toolbox*. Qual Life Res, 2014. **23**(1): p. 205-15.
73. Rutledge, R.B., et al., *Risk Taking for Potential Reward Decreases across the Lifespan*. Curr Biol, 2016. **26**(12): p. 1634-1639.

74. Gold, J.M., et al., *Negative symptoms and the failure to represent the expected reward value of actions: behavioral and computational modeling evidence.* Arch Gen Psychiatry, 2012. **69**(2): p. 129-38.
75. Barnby, J.M., et al., *Self-other generalisation shapes social interaction and is disrupted in borderline personality disorder.* Elife, 2025. **14**.
76. Hauke, D.J., et al., *Altered Perception of Environmental Volatility During Social Learning in Emerging Psychosis.* Comput Psychiatr, 2024. **8**(1): p. 1-22.
77. Komeyer, V., et al., *Overview of Challenges in Brain-Based Predictive Modeling: Toward Meaningful Predictive Insights.* Biol Psychiatry, 2025.
78. Balling, C.E., et al., *Clinician perception of the clinical utility of the Hierarchical Taxonomy of Psychopathology (HiTOP) system.* Clinical Psychological Science, 2023. **11**(6): p. 1108-1121.
79. Yip, S.W. and M.N. Potenza, *Application of Research Domain Criteria to childhood and adolescent impulsive and addictive disorders: Implications for treatment.* Clin Psychol Rev, 2018. **64**: p. 41-56.
80. McCutcheon, R.A., et al., *Psychotropic Taxonomies: Constructing a Therapeutic Framework for Psychiatry.* Biological Psychiatry, 2025. **98**(6): p. 446-454.
81. Braver, T.S., D.M. Barch, and J.D. Cohen, *Cognition and control in schizophrenia: a computational model of dopamine and prefrontal function.* Biol Psychiatry, 1999. **46**(3): p. 312-28.
82. Maia, T.V. and M.J. Frank, *An Integrative Perspective on the Role of Dopamine in Schizophrenia.* Biol Psychiatry, 2017. **81**(1): p. 52-66.
83. Smith, A.J., et al., *Linking animal models of psychosis to computational models of dopamine function.* Neuropsychopharmacology, 2007. **32**(1): p. 54-66.
84. Heinz, A., et al., *Towards a Unifying Cognitive, Neurophysiological, and Computational Neuroscience Account of Schizophrenia.* Schizophr Bull, 2019. **45**(5): p. 1092-1100.
85. Adams, R.A., et al., *The computational anatomy of psychosis.* Front Psychiatry, 2013. **4**: p. 47.
86. Powers, A., et al., *A Computational Account of the Development and Evolution of Psychotic Symptoms.* Biological Psychiatry, 2025. **97**(2): p. 117-127.
87. Gillan, C.M., et al., *Characterizing a psychiatric symptom dimension related to deficits in goal-directed control.* Elife, 2016. **5**.
88. Wise, T., O.J. Robinson, and C.M. Gillan, *Identifying Transdiagnostic Mechanisms in Mental Health Using Computational Factor Modeling.* Biological Psychiatry, 2023. **93**(8): p. 690-703.
89. Brown, H.R., et al., *Crowdsourcing for cognitive science – the utility of smartphones.* PLOS ONE, 2014. **9**(7): p. e100662.
90. Gillan, C.M., et al., *Characterizing a psychiatric symptom dimension related to deficits in goal-directed control.* eLife, 2016. **5**: p. e11305.
91. Gillan, C.M., et al., *Comparison of the Association Between Goal-Directed Planning and Self-reported Compulsivity vs Obsessive-Compulsive Disorder Diagnosis.* JAMA Psychiatry, 2020. **77**(1): p. 77-85.

92. Banker, S.M., et al., *Phenotypic divergence between individuals with self-reported autistic traits and clinically ascertained autism.* Nature Mental Health, 2025. **3**(3): p. 286-297.
93. Brodersen, K.H., et al., *Dissecting psychiatric spectrum disorders by generative embedding.* Neuroimage Clin, 2014. **4**: p. 98-111.
94. Friston, K., *Computational psychiatry: from synapses to sentience.* Mol Psychiatry, 2023. **28**(1): p. 256-268.
95. Kwan, J.W., et al., *Reward sensitivity and the course of bipolar disorder: A survival analysis in a treatment seeking sample.* J Affect Disord, 2020. **261**: p. 126-130.
96. Gourlay, C., et al., *Psychometric assessment of social cognitive tasks.* Appl Neuropsychol Adult, 2022. **29**(4): p. 731-749.
97. Kafadar, E., et al., *Conditioned Hallucinations and Prior Overweighting Are State-Sensitive Markers of Hallucination Susceptibility.* Biological Psychiatry, 2022. **92**(10): p. 772-780.
98. Brown, V.M., et al., *Improving the Reliability of Computational Analyses: Model-Based Planning and Its Relationship With Compulsivity.* Biol Psychiatry Cogn Neurosci Neuroimaging, 2020. **5**(6): p. 601-609.
99. Karvelis, P., M.P. Paulus, and A.O. Diaconescu, *Individual differences in computational psychiatry: A review of current challenges.* Neuroscience & Biobehavioral Reviews, 2023. **148**: p. 105137.
100. Spiller, T., et al., *Efficient and Accurate Transcription in Mental Health Research - A Tutorial on Using Whisper AI for Sound File Transcription.* 2023. **https://doi.org/10.31219/osf.io/9fue8**.
101. Ballentine, G., S.F. Friedman, and D. Bzdok, *Trips and neurotransmitters: Discovering principled patterns across 6850 hallucinogenic experiences.* Sci Adv, 2022. **8**(11): p. eabl6989.
102. Perl, O., et al., *Neural patterns differentiate traumatic from sad autobiographical memories in PTSD.* Nat Neurosci, 2023. **26**(12): p. 2226-2236.
103. Hur, J.K., et al., *Language sentiment predicts changes in depressive symptoms.* Proc Natl Acad Sci U S A, 2024. **121**(39): p. e2321321121.
104. Kingsbury, P., et al., *SEnDAE: A resource for expanding research into social and environmental determinants of health.* Comput Methods Programs Biomed, 2023. **238**: p. 107542.
105. Phuong, J., et al., *Extracting Patient-level Social Determinants of Health into the OMOP Common Data Model.* AMIA Annu Symp Proc, 2021. **2021**: p. 989-998.
106. Chen, Z., et al., *Assess the documentation of cognitive tests and biomarkers in electronic health records via natural language processing for Alzheimer's disease and related dementias.* Int J Med Inform, 2023. **170**: p. 104973.
107. Keloth, V.K., et al., *Representing and utilizing clinical textual data for real world studies: An OHDSI approach.* J Biomed Inform, 2023. **142**: p. 104343.
108. Rasmy, L., et al., *Recurrent neural network models (CovRNN) for predicting outcomes of patients with COVID-19 on admission to hospital: model development and validation using electronic health record data.* Lancet Digit Health, 2022. **4**(6): p. e415-e425.

109. Ehlen, F., et al., *Linguistic findings in persons with schizophrenia—a review of the current literature.* Frontiers in psychology, 2023. **14**: p. 1287706.
110. Marr, D. and T. Poggio, *From understanding computation to undestanding neural circuitry.* Artificial Intelligence Laboratory. A.I. Memo, 1976. **Massachusetts Institute of Technology**(hdl:1721.1/5782).
111. Kohler, R., et al., *Identification of a composite latent dimension of reward and impulsivity across clinical, behavioral and neurobiological domains among youth.* Biol Psychiatry Cogn Neurosci Neuroimaging, 2023.
112. Nichols, E., et al., *Measurement Error and Methodologic Issues in Analyses of the Proportion of Variance Explained in Cognition.* Neuropsychol Rev, 2024.
113. Fillingim, M., et al., *Biological markers and psychosocial factors predict chronic pain conditions.* Nat Hum Behav, 2025. **9**(8): p. 1710-1725.
114. Mourgues-Codern, C., et al., *Emergence and Dynamics of Delusions and Hallucinations Across Stages in Early Psychosis.* Biological Psychiatry.
115. Diniz, B.S., et al., *Late-life depression and risk of vascular dementia and Alzheimer's disease: systematic review and meta-analysis of community-based cohort studies.* Br J Psychiatry, 2013. **202**(5): p. 329-35.
116. Gueguen, M.C.M., E.M. Schweitzer, and A.B. Konova, *Computational theory-driven studies of reinforcement learning and decision-making in addiction: what have we learned?* Current Opinion in Behavioral Sciences, 2021. **38**: p. 40-48.
117. Meehan, A.J., et al., *Clinical prediction models in psychiatry: a systematic review of two decades of progress and challenges.* Mol Psychiatry, 2022. **27**(6): p. 2700-2708.
118. Koning, N.R., et al., *The Usefulness of Electronic Health Records From Preventive Youth Healthcare in the Recognition of Child Mental Health Problems.* Front Public Health, 2021. **9**: p. 658240.
119. Baker, J.T., et al., *Digital devices and continuous telemetry: opportunities for aligning psychiatry and neuroscience.* Neuropsychopharmacology, 2018. **43**(13): p. 2499-2503.
120. Sim, J.-a., et al., *Natural language processing with machine learning methods to analyze unstructured patient-reported outcomes derived from electronic health records: A systematic review.* Artificial Intelligence in Medicine, 2023. **146**: p. 102701.
121. Gillan, C.M. and R.B. Rutledge, *Smartphones and the Neuroscience of Mental Health.* Annu Rev Neurosci, 2021. **44**: p. 129-151.
122. Brown, H.R., et al., *Crowdsourcing for cognitive science–the utility of smartphones.* PloS one, 2014. **9**(7): p. e100662.
123. Gillan, C.M. and R.B. Rutledge, *Smartphones and the neuroscience of mental health.* Annual review of neuroscience, 2021. **44**(1): p. 129-151.
124. Eckstein, M.K., L. Wilbrecht, and A.G.E. Collins, *What do Reinforcement Learning Models Measure? Interpreting Model Parameters in Cognition and Neuroscience.* Curr Opin Behav Sci, 2021. **41**: p. 128-137.
125. Eckstein, M.K., et al., *The interpretation of computational model parameters depends on the context.* Elife, 2022. **11**.

126. Lee, S., et al., *Longitudinal canonical correlation analysis.* Journal of the Royal Statistical Society Series C: Applied Statistics, 2023. **72**(3): p. 587-607.
127. Wang, H.T., et al., *Finding the needle in a high-dimensional haystack: Canonical correlation analysis for neuroscientists.* Neuroimage, 2020. **216**: p. 116745.
128. Kopal, J., L.Q. Uddin, and D. Bzdok, *The end game: respecting major sources of population diversity.* Nat Methods, 2023. **20**(8): p. 1122-1128.
129. Vaswani, A., et al., *Attention is all you need*, in *Advances in Neural Information Processing Systems 30* I. Guyon, et al., Editors. 2017, NIPS 2017: Long Beach, CA.
130. Jin, Y., et al., *The Applications of Large Language Models in Mental Health: Scoping Review.* J Med Internet Res, 2025. **27**: p. e69284.
131. Hua, Y., et al., *A scoping review of large language models for generative tasks in mental health care.* npj Digital Medicine, 2025. **8**(1): p. 230.
132. Wang, Y., et al., *From big to small: Emerging methods for enhancing precision psychiatry through transfer learning.* Biological Psychiatry, 2025. **Minor Revision**.
133. Whelan, R. and H. Garavan, *When Optimism Hurts: Inflated Predictions in Psychiatric Neuroimaging.* Biological Psychiatry, 2014. **75**(9): p. 746-748.
134. Subramanian, J. and R. Simon, *Overfitting in prediction models - is it a problem only in high dimensions?* Contemp Clin Trials, 2013. **36**(2): p. 636-41.
135. Yip, S.W., et al., *Multivariate, Transgenerational Associations of the COVID-19 Pandemic Across Minoritized and Marginalized Communities.* JAMA Psychiatry, 2022. **79**(4): p. 350-358.
136. Smith, S.M., et al., *A positive-negative mode of population covariation links brain connectivity, demographics and behavior.* Nat Neurosci, 2015. **18**(11): p. 1565-1567.
137. Drysdale, A.T., et al., *Resting-state connectivity biomarkers define neurophysiological subtypes of depression.* Nat Med, 2017. **23**(1): p. 28-38.
138. Dinga, R., et al., *Evaluating the evidence for biotypes of depression: Methodological replication and extension of Drysdale et al. (2017).* NeuroImage: Clinical, 2019. **22**: p. 101796.
139. Fournier, J.C., et al., *Antidepressant drug effects and depression severity: a patient-level meta-analysis.* Jama, 2010. **303**(1): p. 47-53.
140. Paus, T., M. Keshavan, and J.N. Giedd, *Why do many psychiatric disorders emerge during adolescence?* Nature Reviews Neuroscience, 2008. **9**(12): p. 947-957.
141. Marr, D., *Vision: A computational investigation into the human representation and processing of visual information*. 2010: MIT press.
142. Rutledge, R.B., et al., *A computational and neural model of momentary subjective well-being.* Proceedings of the National Academy of Sciences, 2014. **111**(33): p. 12252-12257.

Figure titles and legends

Figure 1 – Schematic depicting traditional computational psychiatry research approach and IMPACT-Y's multi-task, longitudinal approach. A. Schematic diagram based on Marr's three-levels of analysis: the computational 'goal' level (process or behavior), the algorithmic modeling level (model and parameters), the implementation level (underlying brain or other systems) (see [141]). To enhance clinical translation and scalability, neuroimaging is not part of IMPACT-Y but is included in the above schematic to reflect the centrality of the implementation level to computational psychiatry. Many of the processes elicited by the tasks in the IMPACT-Y battery (Table 1A) already have established brain mechanisms. **B.** Key elements of IMPACT-Y's computational approach, including the use of multiple tasks in a longitudinal manner, collection of data from a large transdiagnostic sample, and data collection across three separate waves of 800 individuals, including 600 individuals with a psychiatric diagnosis and 200 controls in each wave, for a total sample of N=2400.

Figure 2 – Individually Measured Phenotypes to Advance Computational Translation at Yale (IMPACT-Y). This two-year longitudinal study of 2400 individuals leverages recent advancements in theory-driven computational models, natural language processing, clinical assessments and data-driven analytics using a multi-wave transdiagnostic approach. Additional details on computational tasks are provided in Table 1A and the Supplemental Materials. **A. Theory-driven** algorithmic models are used to extract computational parameters mapping onto core latent constructs such as reward learning. **B.** Open-ended narrative prompts are used to collect spoken language data for analysis using natural language processing (NLP) algorithms, as in [102]. **C.** Clinical data are collected via a combination of structured interviews, validated self-report scales, NIH Toolbox assessments and electronic health records (EHR). **D.** We will recruit a large transdiagnostic cohort of 1800 individuals and 600 healthy controls (*controls not shown in graph). Colors represent theoretical broad subgroups of participants, such as individuals with chronic schizophrenia or at clinical high-risk for psychosis (red), recruited from 16 different research clinics. **E.** Participants are assessed longitudinally for two years using a combination of computational, clinical, NLP and cognitive assessments. **F.** We utilize a multi-wave design such that three cohorts of 800 individuals are followed in each wave. This allows for both replication of findings across independent cohorts as well as continued refinement of the battery in later waves (e.g., a measure with very low clinical predictive utility in Wave 1 may be replaced in Wave 2). **G.** Our overarching Specific Aims (predictors, trajectories and biotypes) are support by **data-driven** analytics. *SZ=schizophrenia; SZ*=high-risk for schizophrenia [first-episode psychosis (n=90), clinical high-risk for psychosis (n=90)]; BD=bipolar disorder; MD=major depressive disorder, PTSD=posttraumatic stress disorder; CS=chronic stress disorders; MOUD=medications for opioid use disorder (i.e., individuals with opioid use disorder who are in treatment); SUD=substance-use disorders (non-MOUD); ADHD=attention deficit hyperactivity disorder; BPD=borderline personality disorder; ICD=impulse control disorder; OCD=obsessive compulsive disorder; ASD=autism spectrum disorder.*

Figure 3 – Using computational and clinical 'snapshots' to track trajectories in model-based parameters. A-C adapted from [65]. **A.** Latent parameters extracted using **theory-driven** algorithmic models, such as those in Table 1A, are summarized in a multidimensional radar plot representing an individual's 'computational snapshot'.
B. Multiple snapshots are collected over time and at varying intervals. In this example, snapshots are theorized to vary somewhat within-individuals over time in the absence of clinical change (e.g., healthy controls, biotypes 1 and 2 that are chronic) but to be relatively stable on average and may differ between meaningful subgroups (e.g., healthy controls, biotypes 1 and 2). During clinical change, as in 'Person 2, Biotype 1 in remission', the evolution of snapshots is theorized to be more variable and to track with changes in symptom presentation.

C. Evolution of the resultant snapshots may be tracked over time within individuals. Resultant trajectories are summarized in a shared parameter space. Different colors correspond to different individuals.
D. Individual's computational (left) and clinical (right) trajectories are represented as an individual points. **Data-driven** analytics (e.g., longitudinal canonical correlation analysis, LCCA [126]) can then be used to identify modes of covariation that most closely link computational and clinical trajectories across individuals. Once identified, canonical modes (essentially equivalent to components in PCA) can be mapped back to individual features enabling elucidation of factors driving associations (i.e., elucidation of mechanism).

Figure 4 – Schematic examples of different timescales of within-person variability that may be tested with IMPACT-Y. Different timescales of within-person variability are presented. At the most fine-grained level, computational tasks capture moment-to-moment fluctuations in behaviors that may be tied to momentary mood fluctuations, as in [142]. Between-session fluctuations (e.g., 'day-to-day') may also occur, and these first two timescales have traditionally been the focus of trait-based computational psychiatry research. By extending our data collection longitudinally and collecting complementary clinical data, IMPACT-Y aims to capture state-based fluctuations in computational model parameters, enabling explicit testing of which parameters are more trait- (i.e., stable within individuals over months to years) versus state- (e.g., changing as a function of mood or symptom change) in a large transdiagnostic sample.

Table 1A – Overview of primary computational tasks included in IMPACT-Y (additional details in Table S1; references in SI)

Task (length; domain assessed) and description	Transdiagnostic and clinical relevance	Test-retest reliability and sensitivity to change
Risk and Ambiguity Task (10min; uncertainty attitudes): Participants choose between a sure reward and a risky or ambiguous lottery; models estimate risk and ambiguity tolerance. [1]	Widely used in healthy and clinical populations[1-10]; greater early-life stress is associated with heightened ambiguity aversion[7]; ambiguity tolerance prospectively predicts opioid-use[4]. PTSD symptoms linked to altered neural encoding of value and greater ambiguity aversion in loss decisions [11, 12].	Risk tolerance is stable in healthy controls longitudinally[4, 13]; Ambiguity tolerance is predictive of opioid use[4] and smoking[13] longitudinally during treatment.
Risky Decision-Making Task with Feedback (10min; reward valuation, anhedonia): Participants choose between safe and risky options in the context of potential gains and losses[14-17]. Models estimate mood as a weighted combination of recent expected values and reward prediction errors; decision parameters include risk and loss aversion and Pavlovian biases.	Affective dynamics are fit equally well in depressed individuals; baseline mood parameters are correlated with depressive symptoms[18]; parameters for Pavlovian approach are linked to phasic dopamine release[19]; risk aversion are related to anxiety in some[20, 21] but not all studies[22].	Replicated in a large group of unpaid participants on smartphone app, and individuals with depression[18]; shows parameter stability across sessions within individuals[23].
Reinforcement Learning Task (10min; reward learning, depression): Participants learn which stimulus is more rewarding and report their happiness after every few trials[24, 25]. Models estimate mood as a function of baseline mood and recent reward prediction errors; decision parameters include reward sensitivity and learning rate; parameters estimated separately for gain and punishment versions.	Anhedonia is associated with greater reward sensitivity and reduced learning rates[24].	Parameters are stable (in the absence of symptom change) over weeks to months.
Reward-Effort Task (10 min; reward valuation, apathy): Participants tap to catch fish; fish value changes periodically. [26]. Models quantify the relationship between reward history and both effort and mood.	Participants with higher apathy are more sensitive to changes in rewards rates, which can be quantified in relation to effort[26].	Reward sensitivity is correlated with apathy [26]; parameters are stable (in the absence of symptom change) over weeks to months.
Social Controllability Task (10 min; social, understanding of others): Participants play a repeated ultimatum game where choices can influence partner's future offers (controllable) or not (uncontrollable). They rate perceived control and affect. A forward-thinking framework is applied to capture social influence and norm sensitivity. [27]	Computation of social controllability involves ventromedial prefrontal cortex (vmPFC) [27]; individuals with nicotine dependence[28] and ASD [29] showed alterations in neurocomputations of social controllability; delusional ideation[30], misophonia and obsessive-compulsive traits[31] are also associated with aberrant neurocomputation of social controllability.	The forward thinking model of social controllability were replicated in an independent, large online sample (n=1342)[27].
Social Craving Task (10 min; social): Participants choose between options differing in the likelihood of leading to social-cue-rich environments and rate their current social craving. Models link craving to cue-reactivity and expectations, influencing future choices.	Social isolation/loneliness is a key transdiagnostic symptom and a risk factor for many poor mental health outcomes, including depression and anxiety[32].	Simulation experiments revealed robust parameter recovery; preliminary data from an online sample (N=93) indicates experimental paradigm successfully elicit higher social cravings[33].
3-Option Probabilistic Reversal Learning Task (10 min; cognition; prediction error): Participants form and revise associations between stimuli and outcomes under unknown, changing reward contingencies[34-36]. A hierarchical Gaussian filter (HGF) model is used to compare belief updating across individuals and groups.	Used in online[36] and clinical samples (high/low paranoia, patients with paranoid delusions, schizophrenia) [34, 37-39]. Computational parammeters robustly track paranoia and cognitive mechanisms.	High test-retest reliability between visits in healthy controls; intra-individual changes in alignment with changing delusion severity[40].
Conditioned Hallucinations Task (10 minutes; prediction error): Participants are first conditioned to associate an auditory tone with a visual stimulus, then later tested for conditioned hallucinations (i.e., hearing tones that were not actually presented)[41]. A hierarchical Gaussian filter (HGF) model is used to extract belief updating, prior weighting, and prediction errors across trials.	Effectively induce conditioned hallucinations (CH) among individuals with and without psychiatric diagnoses; rates of CH vary by prior experiences of auditory hallucinations (e.g., 'hearing voices'), treatment-seeking status among individuals with schizophrenia [41, 42], and clinical risk for developing psychosis. [43]	Individuals with more non-task-evoked auditory hallucinations over time also exhibit higher rates of task-induced CH; individuals without a change in frequency demonstrated no change in task-induced rates of CH[42].
Moving Dots Task (5 minutes; perception): Participants judge the direction of moving dots with varying coherence levels; responses are modeled using a drift diffusion model [44]. Data are analyzed with a drift diffusion model (DDM) using reaction times and choices.	Drift diffusion parameters, particularly drift rate, have been shown to be reduced across a range of psychopathologies, including schizophrenia, OCD, depression, and anxiety[45].	Good test-retest reliability over 1-3 weeks (ICC = 0.64 [46, 47]), when symptoms are stable. Relation of drift rate to a range of psychiatric symptoms is consistent across conditions[48-50]:

Table 1B – List of self-report, clinical and other measures collected for IMPACT-Y (references in SI)

Measure	Construct(s)	Duration	Frequency	Reference
Clinical Assessment				
DIAMOND Diagnostic Interview	DSM diagnosis	45-60 min	baseline	[51]
DIPD Diagnostic Interview	DSM personality disorders	30 min	screening	
Self-Reports				
Depression, Anxiety, and Stress Scale (DASS)	depression, anxiety, stress	42 items	yearly	[52]
Brief Irritability Test (BITe)	irritability	5 items	yearly	[53]
Dimensional Obsessive-Compulsive Scale (DOCS)	obsessions and compulsions	20 items	yearly	[54]
WHO Adult AHD Self-Report Scale (ASRS)	attention	20 items	yearly	[55]
Prodromal Questionnaire-Brief (PQ-B)	psychotic-like experiences	21 items	yearly	[56]
Peters Delusions Inventory (PDI)	delusional thinking	21 items	yearly	[57]
Launay-Slade Hallucination Scale-Revised (LSHS-R)	perceptual experiences	12 items	yearly	[58]
Social Adjustment Scale (SAS)	socio-occupational problems	24 items	yearly	[59]
Fagerstrom Test for Nicotine Dependence (FTND)	nicotine use	6 items	yearly	[60]
Alcohol Use Disorders Identification Test (AUDIT)	alcohol use	10 items	yearly	[61, 62]
Drug Use Disorders Identification Test	substance use	11 items	yearly	[63]
Positive Valence Systems Scale (PVSS)	reward/depression/anxiety	21 items	yearly	[64]
WHO Disability Assessment Schedule 2.0 (WHODAS 2.0)	Health/disability	13 items	yearly	[65]
DSM-5 Cross-cutting Symptom Measure	Mental Health	23 items	yearly	[66]
Patient Health Questionnaire (PHQ-9)	depression	10 items	yearly	[67]
Generalized Anxiety Disorder (GAD-7)	anxiety	7 items	yearly	[68]
Altman Self-Rating Mania Scale	mania	5 items	yearly	[69]
Affect Intensity Measure (AIM)	affect	20 items	yearly	[70]
Behavioral Activation for Depression Scale (BADS)	depression	25 items	yearly	[71]
Childhood Trauma Questionnaire (CTQ)	trauma	28 items	yearly	[72]
Positive and Negative Affect(PANAS)	affect	15 items	yearly	[73]
Mood and Anxiety Symptom Questionnaire (MASQ)	anxiety	10 items	yearly	[74]
Behavioral Subscale of Apathy Motivation Index (bAMI)	apathy	6 items	yearly	[75]
Auditory Hallucinations Rating Scale (AHRS)	psychosis	7 items	yearly	[76]
Green Paranoid Thoughts Scale (GPTS)	psychosis	18 items	yearly	[77]
Massachusetts Adult Gambling Scale (MAGS)	gambling	15 items	yearly	[78]
UPPS-P Impulsive Behavior Scale	impulsivity	59 items	yearly	[79]
PTSD Checklist for DSM-5 (PCL-5)	PTSD	20 items	yearly	[80]
NEO Personality Inventory (NEO)	personality	60 items	yearly	[81]
Delaney Spirituality Scale	spirituality	23 items	yearly	[82]
Domain-Specific Risk-Taking Scale (DOSPERT)	risk taking	30 items	yearly	[83]
Menstrual Bleeding Questionnaire (MBQ)	menstruation	4 items	yearly	[84]
Social Needs Screening Tool	social determinants of health	18 items	yearly	

Cognitive Measures (NIH Toolbox)				[85]
Face-Name Associative Memory Test	visual memory	7 min	yearly	[86]
Picture Sequence Memory Test	episodic memory	3 min	yearly	[86]
Dimensional Change Card Sort	executive function	4 min	yearly	[86]
Visual Reasoning Test	executive function	7 min	yearly	[86]
Computational Cognitive/Behavioral Battery				
Social Craving Task	craving, motivation	20 min	yearly	[87]
Social Controllability Task	perceived control over others' behaviors	10 min	yearly	
Probabilistic Reversal Learning Task	cognition, prediction error	20 min	yearly	[34, 37]
Moving Dots Task	perceptual decision making and motion	5 min	yearly	
Adaptive matrices Task	intelligence and abstract reasoning	5 min	baseline	
Conditioned Hallucinations Task	perception, prediction error	20 min	yearly	[41]
Aversive Learning Task	learning and avoidance	20 min		
Reinforcement Learning, Risky Decision-Making, Reward-Effort, and Risk & Ambiguity Tasks, and Free Text Prompt	reward learning, depression, reward valuation, anhedonia, apathy, uncertainty attitudes	50 min	yearly	
Natural Language Processing Battery				
Open-ended/Free Text Prompts		10 min	3x/year	
Reading and Recall		4 min	baseline/yearly	
Picture Description		4 min	baseline/yearly	
Procedural Task		2 min	baseline/yearly	
High-Density Behavioral Testing				
Reinforcement Learning, Risky Decision-Making, Reward-Effort, and Risk & Ambiguity Tasks, and Free Text Prompt	reward learning, depression, reward valuation, anhedonia, apathy, uncertainty attitudes	10 min **OR** 50 min	daily x 4 weeks **OR** monthly x 4 months	
Outcome Measures (NIH Toolbox)				[85]
Anger/Hostility	negative affect	2 min	3x/year	[88]
Fear/Somatic Arousal	negative affect	2 min	3x/year	[88]
Fear/Anxiety	negative affect	2 min	3x/year	[88]
Apathy	negative affect	2 min	3x/year	[88]
Sadness/Depression	negative affect	2 min	3x/year	[88]
General Life Satisfaction	psychological well-being	2 min	3x/year	[89]
Meaning and Purpose	psychological well-being	2 min	3x/year	[89]
Positive Affect	psychological well-being	2 min	3x/year	[89]
Self-Efficacy	stress & self-efficacy	2 min	3x/year	[88]
Perceived Stress	stress & self-efficacy	2 min	3x/year	[88]
Companionship	social relationships	2 min	3x/year	[90]
Loneliness	social relationships	1 min	3x/year	[90]
Instrumental Support	social relationships	2 min	3x/year	[90]
Perceived Hostility	social relationships	2 min	3x/year	[90]
Perceived Rejection	social relationships	2 min	3x/year	[90]
Pain Interference Test	sensation	1 min	3x/year	[91]
PROMIS-Sleep Disturbance	sleep disturbance & impairment	8 items	3x/year	[92]
Genetic Sample				

Blood or saliva sample		<5 mins	1x	
Smartphone Data				
Smartphone app download	digital phenotyping data	<5 mins	baseline	

A. Traditional computational psychiatry approach

Computational level:
Tasks designed to measure specific behaviors / processes

Data from homogenous cohort

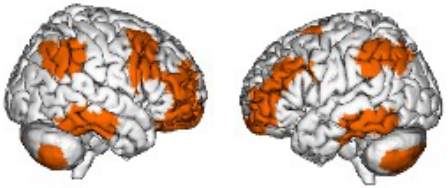
Single timepoint assessment

Algorithmic level:
Mathematical modeling of *how* the behavior/process occurs (e.g., how input is transformed into output)

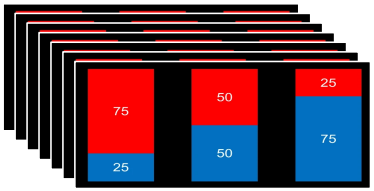
$$Happiness\ (t) \ = \ w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} CR_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} EV_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} RPE_j$$

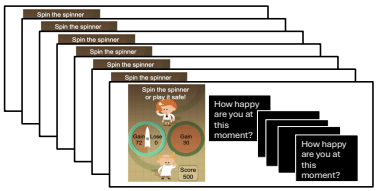
Marr's Levels of Analysis

Implementation level:
How the neural process occurs (e.g., network connections supporting process)



B. IMPACT-Y's longitudinal computational psychiatry approach





+

Heterogenous transdiagnostic cohort (N=2400) collected in 3 separate waves of 800 individuals.

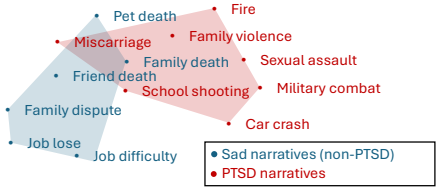
Repeated behavioral testing over two years using multiple tasks

A. Theory-driven computational models

$$Happiness\ (t) \ = \ w_0 + w_1 \sum_{j=1}^{t} \gamma^{t-j} CR_j + w_2 \sum_{j=1}^{t} \gamma^{t-j} EV_j + w_3 \sum_{j=1}^{t} \gamma^{t-j} RPE_j$$

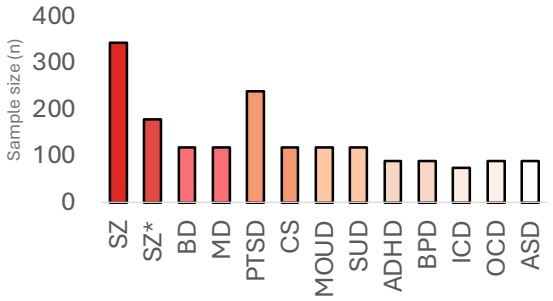
$$v\Big|_{a_i} = U\,(r_i, f_i) + \sum_{j=1}^{n} \gamma^j \times U\left(\hat{E}\left(r_{i+j} \middle| a_i, a_{i+1}, \ldots, a_{i+j}\right), f_i\right)$$

B. Natural language processing

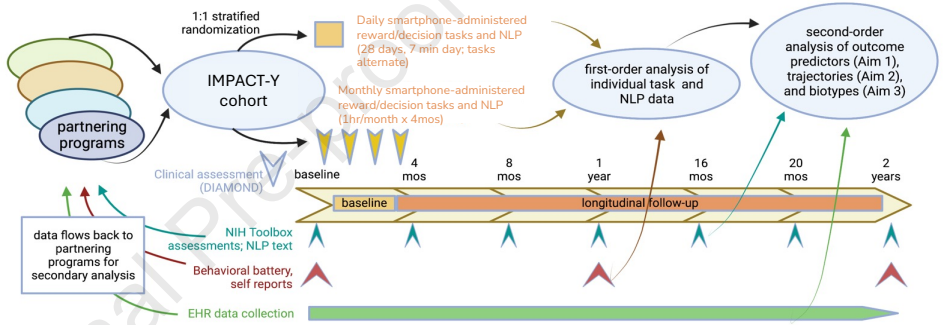


C. Clinical and cognitive task data

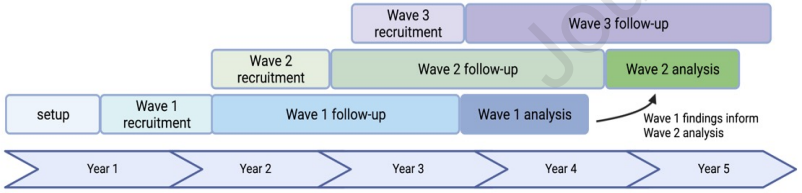
D. Primary diagnosis (expected N=1800)*



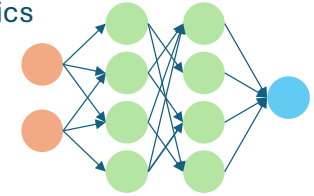
E. Longitudinal assessment over two years



F. Multi-wave design

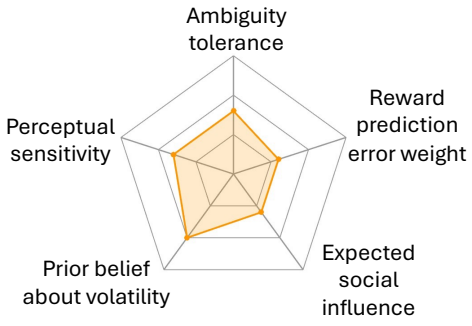


G. Data-driven analytics

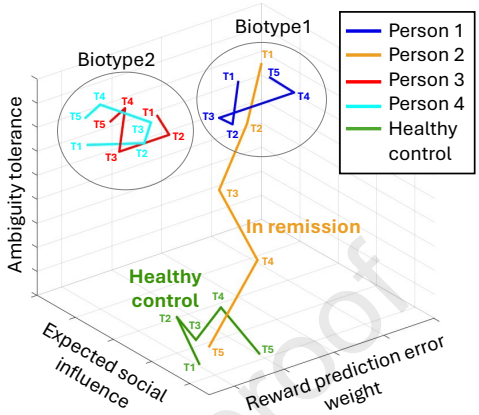


Input layer Hidden layer Output layer

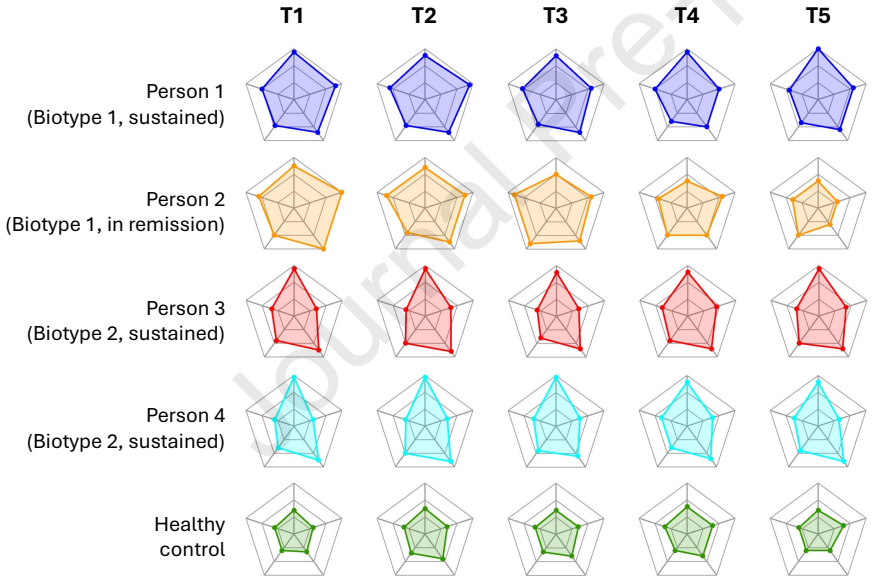
A. Computational snapshot at one timepoint



B. Computational snapshots as trajectories in multidimensional space



C. Computational snapshots over time



D. Clinical versus computational trajectories