IMPACT-ING the practice of computational psychiatry

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Word count
Total: 1483
Figures & Tables: 0
References: 5

IMPACT-MH stands for Individually Measured Phenotypes to Advance Computational Translation in Mental Health (IMPACT-MH). It is a major funding initiative by the NIMH which aims to "change the game for precision medicine in psychiatry". The initiative reflects a wider acceptance within the psychiatric research community about the importance of computational methods. While a decade ago seminars involving computational methods were still few and far between, all of today's major psychiatric conferences and journals have regular and substantial contributions by researchers with computational backgrounds. This acceptance reflects two broad trends: First, an understanding that the functions the brain affected by psychiatric diseases are quintessentially computational and thus, perhaps best discerned through computational means. Second, it reflects the increase in analytic proficiency researchers faced with a deluge of increasingly rich and complex data have had to acquire. As such, the IMPACT initiative is clearly timely.

Here, we comment on one component of this major initiative, namely the project on Clinical and behavioral fingerprints of psychopathology led by Yale University. Briefly, the project focuses primarily on the longitudinal and behavioral assessment of computational processes in psychiatric populations. It will see 600 healthy controls and 1800 individuals with mental illness and currently in psychiatric care undergo repeated assessments with extensive task batteries over two years. Critically, the study will recruit patients from a wide variety of treatment settings, covering psychosis, mood disorders, trauma, substance use, impulse control, neurodevelopmental and personality disorders. The stated aims of the project are threefold. First, it aims to compare the predictive value of traditional, computational and natural language processing measures. Second, it aims to characterize the longitudinal trajectories of these measures, intending to establish normative models to track the clinical course of patients. Its third aim is to use the rich characterization to identify subgroups which differ in longitudinal course.

From the outset, then, several features prominently distinguish this project from previous research. First, it is aimed at generating valuable datasets more than testing any specific hypotheses. As such, it is more in keeping with the ethos of cohort studies and will provide much-needed information on the longitudinal characteristics of computational processes in a clinical setting. It will provide important clues as to whether computational processing impairments do cohere in a syndromic form suggestive of shared underlying mechanisms.

Second, it has an explicitly broad, transdiagnostic scope, rather than a focus on specific diagnostic category or intervention. This is a bold step, removing traditional siloes and mirroring aspects of established care, where, for instance, pharmacological interventions are used effectively across diagnostic boundaries.

Third, it is squarely focused on behavioral data, including verbal data, which augurs well for clinical translation – a computerized battery of tasks, surveys, and brief verbal prompts that requires little specialist equipment is likely to be broadly adopted more readily than a protocol that demands costly equipment or trained interviewers, which often limit potential beneficiaries to those in the immediate geographical

vicinity.

How, then, will this project change the game for precision psychiatry?

We see both challenges, and opportunities. One critical challenge is power – especially given the heterogeneity of participants (drawn from numerous research clinics) and treatments to which they will be exposed during the longitudinal study). This will make drawing conclusions about particular groups or interventions rather challenging – except in so far as it is possible to ignore group membership and focus on transdiagnostic symptoms and treatments (since, presumably, pharmacotherapies will transcend diagnostic and research clinic boundaries).

Next, computational psychiatry is in its infancy still – particularly with regards to practical implementation. We wonder whether it is premature to examine task behaviors longitudinally when task psychometrics remain poorly understood. We note that behavioral tasks often have poor test-re-test reliability and so too do model fits. These will be crucial challenges to the longitudinal approach[4]. More fundamentally, we must acknowledge a toothbrush problem; it has often been quipped that a computational psychiatrist wants to use another's task or model about as readily as they would use that person's toothbrush. We each have our favored approaches and would want to see them represented (similarly to the construction of matrices in the RDoC initiative). This speaks to a certain fractionation of what remains a young field. Projects such as IMPACT might just catalyze an emerging consensus; its lack, however, is a risk, signifying a dearth of broadly validated approaches.

The battery as constructed is rather heavy with tasks that have been related to psychotic symptoms and studies in patients with schizophrenia; and to reinforcement learning. This likely reflects representation in the field (and locally at Yale). However, the risk is that tasks are included in the battery that relate to symptoms that simply do not occur in other diagnoses (like hallucinations, for example). This seems like an inefficient use of experimenter and participant time. However, it will furnish important tests of the precision of behavioral deficits; for example, if non-hallucinating participants behave like hallucinators in some contexts, then the validity of some computational explanations of hallucinations will be challenged and those accounts will need to be updated.

Furthermore, the tasks in a battery represent commitments to particular ontologies. There are phenomenologists of psychopathology who will criticize the overarching assumptions of the computational psychiatry approach[1]. They argue that psychiatric symptoms cannot be understood as vitiations of cognition and perception (in the tradition of cognitive neuropsychiatry; Feyaerts et al. 3). Rather, they claim that many psychiatric symptoms (particularly psychotic ones) must be understood as different ways of being in the world – that psychosis entails a change in the sense of reality and of living in numerous different realities. By and large, the task-model approaches in the Yale IMPACT project are committed to an observing the observer approach. Phenomenologists argue that psychiatric illnesses impact the observer and their relationship to the world (e.g. their sense that the world is real), and they have suggested that this cannot be modelled computationally. We disagree and have presented data to the effect that reality sense can be the purview of computational psychiatry [2]. Indeed, some of the tasks do examine subjective experience parametrically, and start to bridge such gaps.

Ultimately, we want the science we do to be representative of the key concerns of the stakeholders (academic, clinical, patient) with whom we are collaborating. A broader aspect of the phenomenologists' point is hence a good one: Are we answering questions about psychiatric symptoms that address the features of those symptoms that are of most import to patients? Answering this question necessitates bringing in the perspectives of people with lived experience of mental illness. This is beginning to happen in computational psychiatry [5], but the technical complexity of much of the work is an important barrier; as are the differing educational backgrounds of practitioners. Fruitfully combining these facets to improve face, construct and indeed psychometric validity of tasks and methods is a challenging task, the methodology of which is still in development itself. Maybe computational methods could themselves foster this. Or maybe a Delphi approach could bring together experts by training and people with lived experience. The speed of the Yale IMPACT data acquisition start prevented much of this work, raising some risks that we may not ask the questions that most matter to patients.

What are the other risks of this work? One concern, spanning the points above, is that this effort is premature. If large amounts of effort are expended, at great expense, without clinical benefit, there will almost certainly be a cooling effect on the field. We think that the broad portfolio of impact projects mitigates this risk, though it does remain a concern, particularly if the projects are committed to trans-diagnostic symptom approaches and clinical practice remains syndromic. This approach is likely to miss 'epistatic-like' interactions. For example, people with two different illnesses may behave similarly on a cognitive task, but for different underlying computational reasons.

One important resource will be to open data analysis to a competition wherein laboratories inside and outside Yale could compete to answer these questions with novel analytic pipelines and approaches. This sort of community building is essential for the field. The Yale project proffers numerous opportunities in this regard. It will facilitate the training of new academic and clinical members of our community. It may bring therapeutic processes into the explanatory fold with its focus on longitudinal change, but it will be as important to train a new generation of clinicians who are facile with computational cognitive neuroscience to ensure that these ideas are adopted and leveraged for therapeutic benefit. It will be particularly informative to learn from the Yale project about the experiences of patients completing the tasks. If successful, the project may furnish new tools for screening into clinical trials or tracking clinical endpoints for treatment in the clinic and in new clinical trials. There are of course risks with any scientific endeavor. But we believe that fortune favors the bold, especially when that boldness is shared by the community.

Disclosures

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. 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. PRC is supported by the NIMH, the Templeton Foundation, and by the Yale University Department of Psychiatry, the Connecticut Mental Health Center (CMHC) and Connecticut State Department of Mental Health and Addiction Services (DMHAS). The funders had no role in the decision to publish or preparation of the manuscript.

PRC is a cofounder, and Board Member of Tetricus Labs, a precision-psychiatry company, in whom he also holds equity. They did not fund this work.

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