Objective markers for psychiatric decision-making: How to move imaging into clinical practice

Psychiatric disorders result from abnormal brain functioning. However, despite significant advances in our understanding of their neural underpinnings with the help of neuroimaging, clinical decision-making (diagnosis, treatment selection and risk stratification) still relies largely on subjective impression rather than objective tests. A growing body of work shows the potential of brain imaging to help in single-subject prediction; however, these results are not yet being translated to clinical practice (Arbabshirani et al., 2017). For a biomarker to have clinical utility, it needs to be valid, reliable, accurate, accessible, affordable, useful, valuable, easy to interpret, and improve clinical outcomes (Milham et al., 2017). We propose key steps that are needed to develop neuroimaging as a pragmatic tool for use in the clinical setting, including potential implementation strategies.

First, large quantities of real-world samples will need to be examined in order to address challenges in diagnostic criteria and nosology (e.g. individuals with multiple overlapping diagnoses), moving away from traditional "patient-control" contrasts (Milham et al., 2017). Relatedly, longitudinal outcomes data will be necessary in order to understand how imaging data can inform treatment selection and risk stratification. Existing consortiums and the growth of open-science will aid greatly in this process (Milham et al., 2017). Patient heterogeneity in psychiatry has limited progress, but large samples will allow for linking imaging findings with dimensional measurements of disorders in line with approaches like RDoC.

Second, focusing on magnetic resonance imaging (MRI) sequences (structural, diffusion weighted, functional MRI during resting state) that can be combined across sites, and are standardized (Wilcox & Claus, 2017) (as is done in the human connectome project), relatively easy to obtain, non-invasive, and affordable will facilitate implementation. Supplementing these data with genetic, environmental, neuropsychological and demographic information, and possibly other brain imaging modalities could increase biomarker accuracy.

Third, most existing imaging studies use analysis methods that limit replicability and generalizability of results. First of all, analysis approaches are often not equivalent, making comparison and aggregation across studies difficult (Wilcox & Claus, 2017). Furthermore, state-of-the-art prediction methods need to be the norm rather than the exception, and the use of out-of-sample cross validation is essential to avoid overfitting of the data. Simply using standard regression or correlation analyses to measure relationships between baseline imaging signals and treatment outcomes are likely overly optimistic about how a finding in a given data set will generalize to a new data set (Arbabshirani et al., 2017; Steele et al., 2017). As is true for any diagnostic test, once algorithms are identified, simple sensitivity and specificity analyses will need to be performed and useful cutoffs will need to be determined.

Fourth, we will need to ask clinically relevant questions of our available data. In psychiatry, neuroimaging will need to inform decision-making in such a way that improves treatment outcomes and is more efficient and discerning than available assessment tools. Example areas where imaging could be useful are to facilitate distinguishing bipolar from major depressive disorder, as differentiating these disorders can be difficult with clinical history alone and diagnosis could influence treatment (Jie et al., 2015), or to identify which medication an individual with alcohol use disorder is more likely to respond to (one blocking cue reactivity, like naltrexone, or one that acts via another mechanism) (Mann et al., 2014) thereby avoiding multiple sequential trials of medications.

To achieve these goals, and identify useful biomarkers, we will need developments in clinical, research, and information technology infrastructure that can support a clinical/research iterative cycle. In neurosurgery and neurology, imaging is often a part of an initial assessment; in fact resting state functional MRI data is already being utilized clinically to map the brain prior to surgical interventions (Lee et al., 2016). However, in psychiatry, imaging is not a part of standard clinical practice. Consequently, in psychiatry, we do not have large imaging databases which are linked with the clinical record, containing a variety of clinical psychiatric longitudinal data to draw from for research necessary to establish the utility of clinical imaging. One solution would be to link large local or national research databases containing MRI data (human connectome project, UK Biobank, ABCD, Mind Research Network) with patient clinical data in collaboration with existing health information exchanges (HIE). HIEs pull information from various medical record databases and standardize them into a common system and language. A "hub and spoke" structure could be employed to standardize clinical documentation across sites, perhaps disseminating templates to clinicians, and having medical informaticists facilitate standardized clinical record-keeping (Brooklyn & Sigmon, 2017). Clinicians and researchers would both be involved in developing such a system, with needs from both parties being elicited and addressed in bidirectional exchanges, fostering interdisciplinarity and ongoing learning for both parties. As data comes online, and biological predictors identified, providers would be given feedback about individual patients to help them risk stratify and select treatments using unbiased analysis approaches (Arbabshirani et al., 2017).

Funding of such cross-disciplinary efforts will be essential for success. Funding may initially need to come from federal research grants, but once even a single biomarker is identified that helps improve the rates of treatment success and overall healthcare costs, reimbursement for scans by health care systems and insurance companies will likely follow for scans. With more data, more biomarkers can be identified. Cost effectiveness studies should be performed (perhaps also harnessing SAMHSA funding) during piloting to investigate effects on overall healthcare costs.

To some this may seem like a "pie in the sky" approach. Functional imaging has now been around for decades and still has not been widely deployed into psychiatric clinical practice. Some key reasons for this, including heterogeneity within patient populations, and lack of replication of results (either due to replication studies not being funded or when done, findings not replicating) are within our power to address as we mention above. Effect sizes of neuroimaging measures have been modest thus far but, again, using state of the art prediction approaches such as machine learning with cross validation, many studies are now achieving clinically useful prediction accuracies (Arbabshirani et al., 2017; Steele et al., 2017). Finally, having an infrastructure linking the clinical with the research world will aid in development of answering clinically relevant questions.

In summary, in order to move imaging forward, we will need to engage the clinical community to inform clinically-relevant research questions, obtain large samples of imaging data, and follow patients longitudinally.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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