Will there be a role for neuroimaging in clinical psychiatry?

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A consideration of the role of neuroimaging in clinical practice falls in the realm of discussions of personalized medicine. In reference to clinical psychiatry, personalized medicine can be simply conceptualized as falling into 3 domains: the study of genetic variation (including pharmacogenetics), the measurement of various molecular or biochemical indices of disease states (possibly including metabolomics or proteomics) and neuroimaging methods. Each of these approaches are being explored for their potential to improve the accuracy of diagnosis, but they may have a more immediate and prominent role in predicting outcomes or in matching patients with most appropriate treatment strategies. In fact, in a 2009 strategic plan for the National Institutes of Mental Health (NIMH), Insel[1] included personalized care based on individual responses as a priority area for research, identifying a need for basic science research to enable the development of effective care. For any of these approaches to be incorporated into clinical practice, however, there must be advances in science, clinical practice and policy.

The science of using neuroimaging techniques to diagnose psychiatric conditions is in a nascent stage. There are promising data from Fu and colleagues[2] that functional magnetic resonance imaging (MRI) methods combined with a support vector machine (SVM) pattern classification method can correctly sort depressed patients and controls into their appropriate categories with a sensitivity of 84% and a specificity of 89%. More recently the same group used a general probabilistic classification method to produce measures of confidence for MRI data.[3] Another group also used SVM applied to grey matter (structural) scans of patients with autism spectrum disorder and correctly classified affected participants with a specificity of 86.0% and a sensitivity of 88.0%.[4] There was a relation between symptom severity and the extent to which a participant differed from the test margin. Although these are compelling results, differentiating a depressed patient from a nondepressed patient is not usually as challenging as being able to ascertain whether a first depression represents the first episode of a major depressive disorder or a bipolar disorder, or whether psychotic symptoms represent the onset of schizophrenia or a drug-induced psychosis in a young substance-abusing patient. To date, there are a limited number of studies that have specifically used SVM to differentiate between patient groups. One group was able to show that SVM was superior to radiologists in both separating patients with sporadic Alzheimer disease from normal aging and in separating patients with sporadic Alzheimer disease from patients with frontotemporal lobar degeneration.[5] There is a need for large studies that include a range of patient populations to establish the specificity and sensitivity of these measures in distinguishing various illnesses not just from healthy brains but also from other illness states.

Relative to imaging studies focusing on the accurate diagnosis of psychiatric syndromes, there are more studies examining the utility of various imaging modalities for predicting treatment responses and clinical outcomes. Structural MRI studies have reported that small hippocampal volumes are associated with poor short- and long-term clinical outcomes in patients with major depressive disorder.[6–9] Reports of small hippocampal volumes being associated with poor clinical outcome are, so far, mostly confined to studies of patients with major depression, despite the fact that the hippocampus is known to be small in a variety of neuropsychiatric conditions.[10] Functional MRI studies and other imaging modalities have shown that activity in the anterior cingulate cortex is predictive of clinical response to antidepressant medication and to cognitive behaviour therapy for depression and anxiety.[11,12] Amygdala activation to emotional facial expressions among depressed patients also predicts symptom resolution.[13–16]

Neuroimaging methods are also being used to monitor and assess the effects of treatment. For example, cognitive enhancement therapy was recently compared against enriched supportive therapy in patients with schizophrenia. The main outcome measure was MRI-determined changes in grey matter over the course of 2 years.[17] The potential and pitfalls of

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using MRI-based methods as outcome measures in clinical trials has been reviewed,[18] as this approach is now routinely used in clinical trials of neurologic disorders.

If neuroimaging methods are ever to be used in routine psychiatric practice, there will need to be careful investigation of the feasibility and barriers of incorporating these modalities into routine clinical practice. From a practical clinical perspective, MRI investigations of the brain are noninvasive and safe; MRI methods such as resting state and structural imaging are not time-consuming or demanding on the patient. The optimal time for scanning patients will need to be determined because it might be early in the course of treatment when the use of early treatment changes in brain function could compliment baseline predictors of outcome. Early treatment changes in brain function may provide crucial information about whether the brain has the capacity to recover with treatment. In addition to routine clinical use, the use of imaging methods in clinical trials could reduce sample sizes in treatment studies by eliminating patients who are unlikely to respond to a specific treatment modality.

If neuroimaging studies eventually provide compelling evidence that imaging modalities have an ability to impact clinical care, there will still remain many policy issues, perhaps barriers, that will determine whether there is clinical uptake of neuroimaging techniques. A policy framework supporting the dissemination of basic science information into clinical environments can facilitate the transfer of necessary information between disciplines. Indeed, Insel[1] noted that NIMH would have a focus on dissemination science in order to strengthen the public health impact of NIMH-supported research.

Adequate policies about the management of large amounts of personal data are generally recognized to be a necessary condition for the uptake of personalized approaches to treatment.[19] Although such information management is often associated with genomic data, imaging data also has the potential to be viewed as containing highly sensitive information, particularly if functional or structural markers of disease states are established. Of course, information about the economic costs and benefits of using such technologies for patients with psychiatric illnesses will be needed; this kind of work would be facilitated by policies that enable interdisciplinary work. The fact that some psychiatric illnesses are common may actually be a deterrent to policy makers supporting the integration of imaging data into clinical practice because the demands for such investigations could be significant. Psychiatric disorders are also extremely costly, however, and it may therefore be possible to overcome barriers to access if there is a convincing case that such investigations can lower the direct or indirect costs of these illnesses. The cost-effectiveness of having patients undergo neuroimaging will need to be established if there is any likelihood of integrating imaging into routine use.

Beyond the scientific, clinical and policy changes that may be necessary if neuroimaging and other elements of personalized medicine are to be incorporated into clinical practice, a cultural shift may also be necessary. Psychiatry may be both optimally and poorly placed to be receptive to the integration of elements of personalized medicine into clinical practice. As psychiatrists, we still teach and advocate for holistic and comprehensive assessments of our patients. We work to balance the information provided by randomized clinical trials with specific patient features as we select treatments. This occurs in part because we have so few comparative effectiveness trials that we often have no other way to select among the many first- and second-line treatments other than by trying to match patients' symptoms with the effect and side-effect profiles of treatments. Clinicians are already cognizant that individual tailoring of treatments to patients is optimal. Notably, early uses of the term "personalized medicine" referred to personalized behavioural plans for patients or to acknowledge the psychologic and sociologic elements of illness — notions that are extremely familiar to psychiatrists.

In contrast, psychiatrists have not had many opportunities to date to use laboratory measures or other tests to improve diagnosis, prognosis or response prediction. Early studies of the utility of biomarkers in diagnosis, such as the use of the dexamethasone suppression test in patients with major depression, did not translate into clinical use despite initial enthusiasm and considerable investment. The marketing in some jurisdictions of "genetic tests" and "brain scans" claiming to diagnose psychiatric disorders, makes clinicians and patients alike wary of technology that promises more than can be delivered at this time. Clinicians may also be resistant to the introduction of technologies that appear to threaten the dominance of clinical acumen and the importance of the information that comes with observing a patient longitudinally and understanding each patient's unique experience with an illness.

Insel[1] recently outlined a strategic vision for research at NIMH that included personalized medicine based on basic science informing clinical practice. In the United Kingdom, Bullmore and colleagues[20] recently outlined a proposal for strategic actions to reduce neurophobia among psychiatrists. The proposal included revamping the curriculum for the specialty examination and influencing the evolution of the psychiatric curriculum at the level of undergraduate medical education, more effective communication to the public about the scientific basis of psychiatric illness and considering ways to integrate psychiatry with other cognate disciplines. Whether these approaches will prepare the next generation of clinicians and patients to accept, and perhaps even demand, an integration of neuroimaging methods into routine clinical psychiatric practice remains to be seen.

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2. **Are SAMe and 5-HTP safe and effective treatments for depression?**
   Young
   J Psychiatry Neurosci 2003;28(6):471
3. **Treatment plans and interventions for depression and anxiety disorders**
   Antony
   J Psychiatry Neurosci 2001;26(5):422–3
4. **Stressed or stressed out: What is the difference?**
   McEwen
   J Psychiatry Neurosci 2005;30(5):315–8
5. **Functional atlas of emotional faces processing: a voxel-based meta-analysis of 105 functional magnetic resonance imaging studies**
   Fusar-Poli et al.
   J Psychiatry Neurosci 2009;34(6):418–32
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   Marcotte et al.
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   Young
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   MacQueen et al.
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    Ananth et al.
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