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The Neuroimaging Gap: Where do we go from Here?

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Abstract

This overview of the potential future clinical applications of neuroimaging outlines possible approaches to integrating different modes of imaging technology into neuropsychiatric practice. These include different types of structural and functional magnetic resonance imaging and newer technological approaches (specifically near infra-red spectroscopy, fNIRS). The former entail large costs in terms of finance and manpower, as well as significant burdens to clinical subjects, but they can also provide detailed information about developmentally based brain processes that otherwise will not be available. The latter techniques are in turn less costly and more "user friendly," but provide information for only selected brain regions and structures, mainly limited to the cerebral cortex. Given that the identification of reliable neuroimaging markers via the use of conventional neuroimaging (especially in combination with other reliable neuropsychological and neurophysiological indicators) may soon be able to predict the course of neuropsychiatric disease states and/or its response to interventions, we propose that such advances can be more effectively translatable to the clinic via the use of more cost-effective techniques such as fNIRS. The use of new technologies in this way will enhance the translation of brain imaging advances into clinical use, and thus begin to fulfill the as yet unrealized promises of neuroimaging for making significant contributions to the evidence-based foundations of neuropsychiatry.

Keywords: Neuroimaging; Development; Psychopathology; Clinical relevance; Infrared imaging

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Introduction

The field of neuroimaging, particularly Magnetic Resonance Imaging (MRI), has evolved to include a wide array of overlapping techniques that together comprise a set of dauntingly complex and potentially extremely powerful research tools. Indeed, the point has been reached where neuroimaging may perhaps best be conceptualized as a profoundly complex set of separate "specialties" that cannot be easily incorporated into the clinical training of those professionals who will deliver the vast majority of direct patient care in any given health care field. Even within the relatively rarefied confines of research-driven academia it remains the case that the vast majority of those attaining MD or clinical PhD credentials will not become truly expert in it. In turn, the community of experts who drive the methodological advances necessary for integrating technological progress in the diverse fields of neuroimaging with actual clinical applications consists of professionals with quite disparate sets of training, ability, and sometimes even competing interests (e.g., technology experts, statisticians, engineers, and research clinicians). This unavoidable complexity of neuroimaging has several serious drawbacks for the applicability of research advances to direct patient care in the clinic.

Despite great initial enthusiasm about its potential for creating paradigmatic shifts in approaches to clinical assessment and treatment selection, neuroimaging has not yet delivered anything close to this. Indeed, thus far its utility in clinical work has proven uncertain at best and irrelevant at worst. There are several issues that can be viewed as core problems in applying neuroimaging to patient care contexts. First, the procedural complexity of conducting imaging in a clinical setting is currently incompatible with standard approaches to care delivery. Second, the financial costs of obtaining and analyzing neuroimaging data surpasses all other laboratory measures utilized in psychiatry and cannot be justified in the face of the very limited clinical value of the data it provides. This issue of cost justification is intimately linked to another core problem of neuroimaging that remains

to be resolved, namely the critical issue of the replicability of findings in an ever growing, increasingly vast neuroimaging literature. This problem has become fodder for much discussion in lay media outlets, which in turn makes justifying the very significant financial outlays required to make neuroimaging more available to general medical settings much more difficult. In a word, neuroimaging has non-trivial credibility problems. So in addition to the problems of technical complexity and prohibitive cost we add the notion that we cannot be fully confident in what the results from neuroimaging are really telling us.

The key question thus becomes: How do we justify further large investments in neuroimaging? There is no single response. One methodological approach that could begin to address the critical replicability problem, and seems worthy of significant further effort, has been to create repositories of big data. Examples include the IMAGEN consortium [1], the Generation R project [2] and the ABCD study [3] among many others. These repositories could facilitate attempts by groups of affiliated researchers in wide ranging locations to replicate investigations in different samples, and compare groups of individuals that consist of far more than several dozens of subjects per cell that have become standard in the literature (a standard, of course, that is not always met).

A major objective for this concerted effort utilizing robust research samples would be to closely monitor and document changes in the anatomical structure and functional connectivity of the nervous system across the life span. Neuroimaging could potentially provide critical information in this regard that is not readily accessible by other means. For instance, in a recent review Pine and Fox [4] present a comprehensive overview for conceptualizing neuropsychiatric disorders that proposes a five-component model for differentiating neurodevelopmental, psychotic, and emotional disorders. One notable omission is the delineation of any criteria regarding anatomical structure and functional connectivity related to neurodevelopmental disorders. The reason is that the relevant data have not yet been well established. There is thus a pressing need for ongoing research focused on the objective of providing much needed information on the developmental changes in brain morphology, connectivity and function that can be reliably used to describe neurodevelopmental criteria for "normative development". These criteria could then be used as a template for intensive investigations aimed at validating a clinical neuroscience of neurodevelopmental disorders. Given the fact that MRI technologies are considered safe to use in very young individuals, they also provide unique opportunities for the systematic collection and analysis of the critical data necessary to such a large-scale endeavor.

Research programs of this kind would be invaluable to clinicians insofar as these data could lead to the development of prognostic tools for recognizing structural and functional signs that indicate an individual is at higher risk to go on to develop a psychiatric disorder, as well as how individuals who develop such disorders demonstrate nervous system changes that differ from well-validated normal benchmarks. Still, there is an argument as to why the clinic will need neuroimaging measures that are difficult and costly to obtain if there are other markers to guide clinical decisions. The answer to such skepticism is that there is already emerging evidence on the unique predictive value of neuroimaging findings. A recent review on the clinical added value of imaging advances the notion that imaging findings can augment the predictive value of clinical and/or psychometric data in conditions like major depressive disorder, substance use, autism spectrum disorders, psychosis and dementia [5]. The authors also emphasize that clinically relevant markers may serve more than one purpose and don't need to be linked exclusively with psychopathology but can be used to identify possible targets to guide future research into disease mechanisms. Others have also pointed out that imaging markers are not simply additive to already known risk factors but can be used as independent tools to monitor treatment response [6,7]. This case might be best illustrated by the phenomenon of sensitization (i.e., rendering the brain reward system hyper-responsive to drugs of abuse after limited exposure to abusable substances early in development). As some have suggested, given the dearth of tools available to reliably assess "reward sensitivity" in humans, neuroimaging must be considered a potentially indispensable tool in the clinical assessment of the effects of sensitization [8].

This is not, however, an "all or nothing" scenario: It is not our premise that neuroimaging markers alone will guide clinical decisions. On the contrary, we believe a feasible goal would be to create constellations of markers, including neuroimaging, genetic and behavioral markers, that will constitute "risk profiles" or "treatment response profiles". For instance, the concept of "relapse risk phenotype" in addiction includes factors like smaller gray matter volumes in medial frontal and posterior regions, hypo-frontal brain response to stress and arousal with associated craving and relapse, increased stress and cue-induced cravings, increase serum levels of brain derived neurotrophic factor (BDNF, which has been shown to be predicative of cocaine relapse), altered Hypothalamic–Pituitary–Adrenal (HPA) axis responsiveness (which has been shown to be predictive of alcohol relapse), and high impulsivity measured by psychometric tests [9]. As is evident from this example, such an approach suggests that neuroimaging markers could be incorporated into an "at risk" profile alongside other behavioral and physiological measures. Furthermore, each individual measure would be assigned an empirically validated weighted "risk" value, so that a total "risk score" could be calculated for any given individual patient.

Yet there remain practical obstacles that need to be overcome if these important potential developments for the clinical relevance of neuroimaging are to be brought to fruition. The magnitude of the technical efforts that are necessary for conducting imaging procedures, analyzing the data, and putting the results to clinical use have associated costs (in both labor and money) that at the present time still make neuroimaging impractical in clinical practice.

One particularly vexing problem, especially with regard to children and adolescents, is the difficulty in reliably collecting

the kinds of high quality data critical to obtaining information about developmental windows relevant to the onset of illness. These kinds of data are necessary for intelligently applying the most effective types of early intervention. Moreover, such data must be obtained from both neuro-typical and youths with neuro-psychiatric disorders diagnosed early in life. The ability to exercise sufficient self-management to lie close to motionless in a scanner environment consisting of a cold confined space inundated with loud sounds, and to maintain stable performance while being personally isolated from the staff that provide the assistance and social support so helpful in tolerating such stressful situations, often outstrips the capacity of many neuro-typical children. This is, of course, even more acutely the case for children or adolescents with mental health problems. Not surprisingly especially vulnerable populations of children and adolescents with hyperactivity, anxiety, claustrophobia and the like are affected most strongly in a negative way. In other words the potentially decisive imaging data that would likely reflect the most pronounced deviations from "normality" are probably most prone to being unreliable due to movement artifacts and inadequate adherence to image acquisition protocols.

Theoretically it will be optimal if the information (or at least part of the information) that is currently obtained in neuroimaging studies could be obtained in environments that more closely resemble a traditional clinical laboratory. So it is a very positive development that the collection of data in clinical settings is becoming increasingly feasible and efficient. For example, psychometric tests are becoming available on iPhone apps, genotyping is becoming more affordable especially for selected sets of genes, and skin conductance devices are becoming readily available to collect continuous data. Similarly, near-infrared spectroscopy (fNIRS) holds the potential to detect brain activation in non-specialized environments and it will make become possible to more thoroughly and more routinely assess and characterize populations of patients or individuals at risk in general clinical settings. The potential for fNIRS to be used as a substitution for the much more expensive functional MRI is potentially a very important development, but one requiring a significant amount of further research. Substituting an expensive and technologically complex imaging method with a more "user friendly" analog might be possible, but only after we have established that each method can reliably distinguish between normal and abnormal development and can detect change over time (i.e., pre and post-treatment). Moreover, there would be a pressing need to establish cross reliability–to rigorously demonstrate that imaging with fNIRS in the clinic will yield results that are compatible with those obtained in conventional imaging labs. A recent report [10] seems to support this possibility since the authors provide evidence suggesting that knowledge extracted from functional imaging studies can be used to conduct experiments with fNIRS that produce results similar to the ones obtained with functional magnetic resonance (fMRI). As a proof of principal this is a potentially major step forward.

Summary for Applications of Neuroimaging Technology

To summarize, a basic overview for a plausible path to achieving more clinically relevant applications of neuroimaging technology is as follows: Initially, established neuroimaging methods such as MRI would continue to provide reliable and reproducible data for both structural and functional brain changes related to normal and abnormal development, associated with clinically relevant behavioral and psychological indicators. In the process of these on-going investigations, and potentially even more importantly, cerebral changes that may remain "silent" (i.e., without behavioral manifestations) during any particular developmental period, but still may influence future phenotypic expression, may be uncovered and elucidated. Findings such as these would have clear and profound clinical relevance. Advancing trends in big data approaches will very likely expedite discoveries of this type.

Subsequent to such high level (and very costly) research advances, we may be at the threshold of being able to actually utilize the knowledge obtained from them, by implementing their clinically relevant applications via the use of much less expensive technologies such as fNIR. This can potentially provide what would essentially be clinical tests for specific and already identified reliable markers in a cost-effective and scientifically valid manner.

Conclusion

In conclusion we believe that if and when this approach to translational applications of brain imaging comes to fruition, the skepticism of psychiatric clinicians and therapists who see the field of neuroimaging as an intellectual exercise detached from the real world they inhabit may be meaningfully addressed and ameliorated. Through gaining understanding about the advantages and limitations of existing neuroimaging techniques, and with the advances of new technologies, neuroimaging, and functional neuroimaging in particular, can potentially make very meaningful contributions to the process of clinical decision-making in relation to risk assessment and potential treatment outcomes.

References

1 Schumann G, Loth E, Banaschewski T, Barbot A, Barker G, et al (2010) The IMAGEN study: reinforcement-related behaviour in normal brain function and psychopathology. Mol Psychiatry 15: 1128-1139.

2 Jaddoe VW, van Duijn CM, van der Heijden AJ, Mackenbach JP, Moll HA, et al. (2010) The generation R study: design and cohort update 2010. Eur J Epidemiol 25: 823-841.

3 https://addictionresearch.nih.gov/abcd-study

4 Pine DS, Fox NA (2015) Childhood antecedents and risk for adult mental disorders. Annu Rev Psychol 66: 459-485.

5 Jollans L, Whelan R (2016) The clinical added value of imaging: a perspective from outcome prediction. Biological Psychiatry, Cognitive Science and Neuroimaging 1: 423-432.

6 Whitfield-Gabrieli S, Ghosh SS, Nieto-Castanon A, Saygin Z, Doehrmann O, et al. (2016) Brain connectomics predict response to treatment in social anxiety disorder. Mol Psychiatry 21: 680-685.

7 Doehrmann O, Ghosh SS, Polli FE, Reynolds GO, Horn F, et al. (2013) Predicting treatment response in social anxiety disorder from functional magnetic resonance imaging. JAMA Psychiatry 70: 87-97.

8 Robinson TE, Berridge KC (2001) Mechanisms of action of addictive stimuli; incentive-sensitization and addiction. Addiction 96: 103-114.

9 Sinha R (2011) New findings of biological factors predicting addiction relapse vulnerability. Curr Psychiatry Rep 13: 398-405.

10 Liu Y, Piazza EA, Simony E, Shewokis PA, Onaral B, et al. (2017) Measuring speaker-listener neural coupling with functional near infrared spectroscopy. Sci Rep 7: 43293.