

## Research Article

# Genetic Testing and Neuroimaging: Trading off Benefit and Risk for Youth with Mental Illness

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Submitted: 21 January 2014

Accepted: 30 September 2014

Published: 14 October 2014

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## Keywords

- Mental health disorders
- Ethics
- Child psychiatry
- Neuroimaging
- Genetic testing

## Abstract

According to the World Health Organization, mental illness is one of the leading causes of disability worldwide. The first onset of mental illness usually occurs during childhood or adolescence. Neuroimaging and genetic testing have been invaluable in research on behavioral and intentional disorders, particularly with their potential to lead to improved diagnostic and predictive capabilities and to decrease the associated burdens of disease.

The present study focused specifically the perspectives of mental health providers on the role of neuroimaging and genetic testing in clinical practice with children and adolescents. We interviewed 38 psychiatrists, psychologists, and allied mental health professionals who work primarily with youth about their receptivity towards either the use of neuroimaging or genetic testing. Interviews probed the role they foresee for these modalities for prediction, diagnosis, and treatment planning, and the benefits and risks they anticipate.

Practitioners anticipated three major benefits associated with clinical introduction of imaging and genetic testing in the mental health care for youth: (1) improved understanding of illness, (2) more accurate diagnosis than available through conventional clinical examination, and (3) validation of treatment plans. They also perceived three major risks: (1) potential adverse impacts on employment and insurance as adolescents reach adulthood, (2) misuse or misinterpretation of the imaging or genetic data, and (3) infringements on self-esteem or self-motivation. Movement of brain imaging and genetic testing into clinical care will require a delicate balance of biology and respect for autonomy in the still-evolving cognitive and affective world of young individuals.

## ABBREVIATIONS

**PET:** Positron Emission Tomography; **SPECT:** Single Photon Emission Computed Tomography; **fMRI:** Functional Magnetic Resonance Imaging; **ARMS:** At-Risk Mental State; **ADHD:** Attention Deficit Hyperactivity Disorder; **OCD:** Obsessive-Compulsive Disorder

## INTRODUCTION

Mental illness encompasses a set of complex cognitive and affective disorders that represent a profound disease burden, and impact 10–20% of children and adolescents worldwide [1]. The World Health Organization identifies mental and behavior disorders as one of the leading causes of global disability and health-related burden in the first three decades of life (whqlibdoc.who.int). The onset and effects of mental illness

present challenges to individuals for functioning adequately during daily demands, and to societies for managing pervasive stigmatization [2] and rising health care costs [3]. Thus, efforts to improve mental health care through research using novel neurotechnologies have garnered tremendous interest and hope. While strategies for early intervention are important, of equal importance are discussions of ethical responsibility to children and adolescents who are most vulnerable to obstacles to their full developmental potential.

Research applications of neuroimaging and genetic testing have identified both neurobiological correlates and heritability of mental illness in adults. Various techniques such as positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic resonance imaging (fMRI) provide measures of the hemodynamic correlates

of neural processes in a non-invasive manner and have revealed neurocognitive correlates of mental health disorders and progressive changes associated with illness [4-6]. Genetics studies provide evidence for heritability and validated risk factors [7-9].

Studies in youth are more limited, however, even while interest in the role of neurotechnology for this population increases [10]. Attempts to demonstrate structural or functional abnormalities in at-risk youths are still complicated by the heterogeneity of changes occurring naturally and dynamically [11-13]. Several studies assessing parents' attitudes to pre-symptomatic genetic testing of their own children, for example, suggest a high hypothetical demand [14-18]. Growing interest has also been expressed in evidence-based predictive models to identify individuals in the At-Risk Mental State (ARMS) who are in the prodromal phase of psychosis [19,20]. While advances in psychiatric research have paved the way for testing and applying these neuroimaging technologies in youth, they thus far have been unsuccessful at finding consistently reliable and replicable predictors for the onset of mental illness [21].

The future of psychiatric research will very likely integrate neuroimaging and genetic findings [22]. Advances in genetic research may lead to an improved understanding of mental health and disease, and support the development of pre-symptomatic and prenatal testing for a more informed diagnosis [23,24]. When combined, imaging and genetics have three key implications for clinical mental health care: prediction by imaging genetics for early intervention [25,26]; diagnosis using biologically-oriented classification [27,28]; and tailored interventions as a result of better understanding of mental disorders [25, 29]. These benefits may in turn help to foster supportive relationships between patients, providers, and society.

Despite the potential for functional neuroimaging and genetic testing to help shape clinical care, ethical questions challenge the benefit-risk equation. Prognostication is especially difficult in children and adolescents [30], and applications of neuroimaging or genetic tools for prediction oversimplify the complex experiences of living with mental illness [9,31]. Furthermore, a diagnosis based on aberrant imaging or genetic results is comparable to attaching a label that comes with irreversible social consequences [32,33]. Addressing these and other ethical challenges is essential to guide any translational aspirations for the fragile and ever-evolving world of youth.

## MATERIALS AND METHODS

Participants were recruited through announcements directed at the regional health authority of a Western Canadian metropolitan area as well as from North American professional associations, as previously described [34]. Inclusion criteria stipulated that respondents work as mental health care providers primarily for children and adolescents and that they be fluent in English.

Respondents participated in semi-structured telephone interviews about their receptivity towards either neuroimaging or genetic testing for the prediction, diagnosis, and treatment of mental illness in children and adolescents. Participants were randomly sorted into the neuroimaging or genetic testing groups

Interviews were audio recorded and transcribed verbatim and analyzed using NVivo 9 software. Two independent coders (G.L. and A.M.) reviewed and coded the interview transcripts using a constant comparative analytic approach to identify major emergent themes and to establish a consensus list of codes per modality [35,36]. This inductive process is iterative and interpretive, revealing new themes that would inform a final coding scheme applied to all interviews. Interviewing stopped when theoretical saturation was achieved with the brain imaging group, which drove the primary research question for the study.

We address themes for each modality separately in describing the results, and contrast but do not necessarily compare them to each other, as is appropriate for qualitative data analyses such as these [37]. Illustrative quotes highlight major points.

## RESULTS AND DISCUSSION

Thirty-eight health care providers representing psychiatry, psychology, mental health counseling, nursing, and social work participated in this study. Self-reported sub-specializations in order of increasing frequency were: depression, ADHD, bipolar disorders, autism spectrum disorders, OCD, and posttraumatic stress disorders.

Participants' ages ranged from 30 to 75 years, with a mean age of 49 years (Table 1). Sixteen participants were women and 22 of the 37 participants held medical degrees. A total of 21 hours of data were collected and analyzed from 28 interviews on brain imaging and 9 interviews on genetic testing.

**Table 1:** Sociodemographic details of participants.

Variables	N = 35 (%)
Gender	
Male	19 (54)
Female	16 (46)
Marital Status	
Married	24 (67)
Single	8 (23)
Common Law	1 (3)
Divorced	2 (6)
Widowed	1 (3)
Occupation	
Psychiatrist	22 (63)
Counselor	7 (20)
Registered Nurse	3 (9)
Social Worker	2 (6)
Psychologist	1 (3)
Mental health clinician	1 (3)
Specialty	
Depression	21 (60)
ADHD	20 (57)
Bipolar Disorder	14 (40)
Autism Spectrum	12 (34)
OCD	11 (34)
Highest level of education completed	

Overall, three interrelated themes represent the potential benefits that participants attach to neuroimaging and genetic testing. These themes underscore their optimism for eventually including neuroimaging and genetic testing into routine clinical care: (1) improved understanding of the brain and mental health conditions, (2) evidence-based diagnosis to facilitate accuracy and early detection, and (3) better informed treatment planning to facilitate patient management. Respondents also express concerns about risk in terms of: (1) misuse or misinterpretation of results, (2) societal impacts on employment and insurance, and (3) infringements on self-esteem or motivation.

## Benefits

**Improved understanding of the brain and mental health conditions:** Interview respondents acknowledge the potential valuable contributions of neuroimaging for clarifying the patient's and family's understanding of mental illness. Participants regard an improved understanding as a prerequisite for an initial acceptance or admission of the psychiatric diagnosis.

I think there would be more compassion for what the patient is enduring. Because with many mental health diagnoses, let's just say depression as an example, I think there's a lack of compassion that people seem to feel you can snap out of it. But having a brain scan to indicate this is not the patient's fault it's something that is going on in the body. And, I think it would be helpful for all of us to have a clearer understanding, to help us appreciate that, you know, these changes are very real (Participant #006, Registered Nurse).

Overall, providers perceive the clinical benefits of neuroimaging as far outweighing the risks, by mitigating conflicts arising from the doctor-patient relationship or offering confidence measures in diagnosis.

Because the doctors will have some confidence about what they're showing, the modality that they're using is important and worth the time and the money that's involved (Participant #103, Psychiatrist).

[Brain imaging] would give a clinician a lot of information about the illness and the condition at hand and its response to the treatment. And it will be a very important addition to other kinds of clinical information gathered through other avenues or other techniques (Participant #107, Psychiatrist).

In parallel, providers feel that genetic testing would provide a reliable diagnosis for a young patient's symptoms. Participants' support for genetic testing in the context of improving the current understanding of mental illness relates to their values of having a definitive diagnostic option and mitigating anxieties around insufficient clinical information.

[Genetic testing] would clarify what they're experiencing. It would just reify it. The disorders in psychiatry and psychology are distorted; [they] are right now, currently, clusters of symptoms . . . So, this would make it more concrete, and that would, actually, really change the nature of the psychiatric diagnostic because it would all of a sudden have something concrete. That could be the defining thing about whether a disorder exists or not (Participant #048, Psychologist).

Sometimes just having a name to be able to put to what's going on, sometimes just that is a relief. I think it's also a relief because knowing what it is, whether this is true or not, but knowing what it is feels like (Participant #044, Counselor).

For some clients, having information about their genes may be—they may feel more normalized, they may understand their symptoms better, they might feel, you know, "okay, now I understand why things are the way they are." Versus other people [who] may not believe in that (Participant #055, Counselor).

**Evidence-based diagnosis to facilitate accuracy and early detection:** Under this general theme, three sub-themes touch on the potential for both modalities to have an impact on mental health diagnosis, diagnostic precision, evidence-based diagnosis, and early detection of mental illness. Diagnostic precision is attributed to the apparently objective nature of brain scans and their perceived ability to differentiate mental disorders with behaviorally indistinguishable phenotypes. In such circumstances, clinical utility of neuroimaging is widely described as a clarification of potentially disputable diagnoses by providing evidence of brain characteristics consistent to a particular disorder.

So, if there could be some definitive test that says, "Yes, this child really has the brain characteristics of what you see in bipolar disorder." If that were identified, it would be helpful, I think, in treatment for sure—choosing the appropriate medications and kind of overall treatment planning. So that would be terrific to have (Participant #111, Psychiatrist).

Well I think one of the biggest confounding factors is for us to have a more universal understanding of what diagnosis is. So maybe this would actually help us, by having imaging, because there's so much controversy of how to frame diagnosis . . . So perhaps neuroimaging would actually help resolve that (Participant #125, Psychiatrist).

Providers value early intervention for effective symptom management, and attribute the accomplishment of this goal to the diagnostic accuracy offered by neuroimaging.

I think it would have good impact in that there would be some public health benefit to early diagnosis, early case findings, and in terms of preventing worsening of disorders (Participant #120, Psychiatrist).

Similarly, participants postulate that genetic testing would improve diagnostic accuracy by providing a scientific basis for validation, and hence minimize the crucial time window between diagnosis and treatment.

Yeah, if it made the assessment process—like if you could diagnose something, it might make the assessment process go faster, which might mean we could get the treatment sooner (Participant #044, Registered Nurse).

Respondents' views are generally convergent between neuroimaging and genetic testing in the context of diagnosing mental illness. Overall, youth providers describe the merits of both modalities as invaluable supplements to their current diagnostic tools. Providers also emphasize their preference to have access to these modalities for initial clinical assessment and for providing validity to their clinical diagnosis.

**Informed treatment plan to facilitate better patient management:** Providers underscore the desirable outcome of improved patient management through more informed and targeted treatment plans. This theme is often associated with the previous major theme of improving diagnosis.

Again we would now have some validity, some agreement. Everybody looking at the picture hopefully would see the same thing and would know the implications and treatment would be more streamlined and specific [...] a computer that would sort of use the data and have an ability to match that data and the diagnosis with available treatment. So there would be a greater validity to that as well, more evidence based treatment (Participant #103, Psychiatrist).

And also hopefully in the future I'll push another button on the computer and out will come a list of medications that are known to be effective and a list of therapies that are known to be effective. And perhaps also, a list for the parents of behavioral approaches to the child that are known to be effective... I certainly would love to be living in a world where that was happening (Participant #103, Psychiatrist).

Providers suggest that youth at risk would feel empowered by having this insight into their future well-being, and hence take a proactive approach in seeking treatment promptly or

making lifestyle changes to possibly prevent or delay symptom onset. In their expressed receptivity to neuroimaging in the context of patient management, participants extrapolate a role for neuroimaging in evaluating current clinical treatment protocols:

[...] it will also help more specific treatments to be found and explored and discovered for certain illnesses that have some neuroimaging-related findings. So it can have not only diagnostic classification but also developing specific treatment for conditions (Participant #107, Psychiatrist).

So, if I had a brain imaging scan where I could have someone come back in after they're on medicine, check the brain scan and see how much of that seems to have been corrected in terms of the biology, then I have a better sense that yes, we've got the right kind of medicine, it's doing what it should be doing biologically, and yet we're still having difficulties (Participant #116, Psychiatrist).

Providers affirm that parents would like to know whether their child will have a future without mental illness, especially because availability of a test that could give either a positive or negative predictive value would help establish an early informed treatment. A positive predictive value would empower health care providers to search for interventions directed towards changing the subsequent course of the disease. On the other hand, a negative predictive value would increase the family's awareness of the possibility of emerging symptoms and dispel any hesitation to seeking mental health care.

## Risks

**Misuse or misinterpretation of results:** Participants anticipate that disclosure of neuroimaging findings associated with mental illness might refocus the goal of care towards

routinely prescribing treatment for acute symptoms. The focus on prescribing treatment would result in replacement of thorough clinical assessment with neuroimaging to guide medication recommendations. Providers feel that this would be an unjustified use for neuroimaging results. Many providers feel that time may be better spent interviewing to understand the child's background and experiences rather than simply administering medical treatments.

Overall I think it's a positive move, but again it needs to be correlated with the clinical situation, discussed with the patient in an appropriate way and against one of the many tools that we use to evaluate patients. So the larger clinical context, it needs to be put into that context. If it's not, I think it could be misused—or people could come to the wrong conclusion on what a certain set of data may mean that's revealed from the image (Participant #134, Psychiatrist).

Participants also stress the importance of helping the family understand brain scan results in a manner that responsibly incorporates privacy and cultural considerations. Providers urge for better correlation of neuroimaging results with the clinical condition, and for more appropriate discussion of the results in the larger clinical context of brain imaging as one of the many tools used to evaluate patients. They express concerns that misinterpretation of results may cause young individuals to be passive about moral responsibility:

People may then use that information to try to absolve themselves of some responsibility for their actions and say, "Well, you know, I can't help it. It's just the way my brain is wired" (Participant #133, Psychiatrist).

Providers express concerns about the careful handling of genetics information given its probabilistic nature, and stress the importance of education and support for both the family and the individual.

I guess I would be more concerned about what's done with that information afterwards as long as there's education and support for the family or the individual, even though there are say genetic factors that are put into place (Participant #036, Psychiatrist).

Related concerns for medical privacy are raised in the context of access to medical records containing diagnostic and treatment information following a genetic test. There is an emphasis on the need for establishing safeguards to prevent misuse of genetic testing results that could impose limitations on access and cost of health care.

**Societal impacts on employment and insurance:** Under this theme, respondents address the societal impact of neuroimaging or genetic testing on individuals and their support pillars. Participants expect both increased demands for neuroimaging and genetic testing as well as the subsequent societal consequences of inappropriate sanctions on individuals who receive an indication of mental illness.

[...] someone who is labeled as potentially developing a certain mental illness. There might be employment opportunities, schooling opportunities that would be closed to you if people knew that you were at risk for those conditions (Participant #103, Psychiatrist).



There is a lot of concern about any kind of prediction of a mental health or a physical health problem that could impact a person's eligibility for insurance coverage and medical care (Participant #109, Psychiatrist).

And here you have we're again labeling someone as inevitably developing a condition that would perhaps interfere with their job perspective, or relationships. So [brain imaging] would open up, that person for further risk, other sorts of difficulties. It's like any screening tool, now that you know you have it what can you do about it? (Participant #103, Psychiatrist)

Are people, are employers in the future going to be able to access some kind of [genetic testing] database that says, "You've got the depression gene, I don't want to hire you because you might get depressed in five years and miss work." I mean there's all these room for abuses later on (Participant #128, Counselor).

Participants recount how the knowledge of being at risk for mental illness may affect parent hopes and dreams for the child and cause emotional changes to family dynamics.

For some families, knowing that means they are going to change the way they feel about that child. They're going to change their expectations, in a negative way, and perhaps distance themselves. Or more or less reject the child (Participant #127, Psychiatrist).

Participants further express concerns about possible detrimental effects of neuroimaging and genetic testing on parents and in turn how they relate to the child.

[...] knowing that means they are going to change the way they feel about that child. They're going to change their expectations, in a negative way, you know, and perhaps distance themselves. Or, you know, more or less reject the child (Participant #127, Psychiatrist).

I would hate for a parent to either lose hope in their child, you know, because they're thinking, "Oh, this is where we're going to end up anyway. So, what's the point of doing any of these interventions right now, or getting the help that my child needs?" (Participant #036, Registered Nurse).

**Infringements on self-esteem and motivation:** Interview participants also anticipate a possible negative impact on self-esteem and motivation as a risk of positive predictive testing for mental illness. Participants describe a double-edged scenario where brain imaging has the potential to provide clarity on one hand, while condemning individuals into misery associated with morbidity or even mortality in some instances. Several providers express concerns that neuroimaging would have adverse influences on an individual's attitude or outlook in their private thoughts and outward expressions despite having an informed treatment plan.

[Brain imaging] is also very limiting and may impact client's motivation levels. And kind of may set them up for a doomed kind of scenario as opposed to a resilient hopeful scenario (Participant #023, Counselor).

I think no matter what the news is about genetic testing, it would definitely impact an individual's perception of themselves and their, their behavior, their environment, their development; their life, really (Participant #058, Registered Nurse).

To the extent that a predictive diagnosis may impact an individual's behavioral development, practitioners consider the vulnerability to develop affective characteristics such as apathy, depression, and apprehensiveness.

So you'd worry about suicide, you'd worry about people falling short of their expectations, not pushing themselves (Participant #125, Psychiatrist).

There may be the sense of, "Hey, this is the way the brain is, and nothing can change." There can be a sense of feeling defeated or feeling that their opportunities in the future are limited (Participant #133, Psychiatrist).

## CONCLUSION

In this study, we identified perceived benefits and risks of neuroimaging and genetic testing for youth at risk for mental illness, and values and perspectives from providers who work with children and adolescents in clinical practice. Three major themes emerged about benefits of neuroimaging and genetic testing as diagnostic or predictive tools for mental illness in youth: an improvement in understanding the brain with mental illness and clarity in an emotionally charged time of life; the confirmatory nature of brain scans and acceptance of a diagnosis; and legitimization of treatment recommendations from members of the health care team. The present findings are consistent with other studies suggesting that perceptions of objectivity arising from biological evidence of mental illness through brain imaging replace subjective feelings of "being crazy" [32,38,39]. Our findings of stakeholder receptivity to neuroimaging as a diagnostic tool for clinical evaluation also parallel other interview studies [40,41] and surveys studies [42] focused on adults.

The parallel benefits of genetic testing arise from the compassion that participants suggested would accrue to afflicted individuals from others, and a higher personal level of acceptance of a diagnosis [43]. Our findings also parallel several studies reporting positive attitudes from family members, parents, and clinicians and a high hypothetical demand from individuals for genetic testing for mental illness [15–18, 44]. On the other hand, critics have cautioned that genetic testing for mental illness will increase stigma and discrimination, even creating prognostic pessimism, general hopelessness, and self-fulfilling prophecies that hamper recovery [45–47]. In this regard, it has been argued that in the absence of medical benefit, offering genetic testing to children and adolescents could compromise the child's autonomy as an adult when deciding whether or not to obtain their genetic information [48].

Findings for the benefits of the potential clinical uses for neuroimaging are counterbalanced by weighty potential risks. In particular, providers anticipated that an emphasis on neurobiology might divert attention from patient history or support networks that are part in parcel of providing comprehensive mental health care. These findings stand apart from other studies that have suggested that neural markers for mental illness would augment clinical decision making rather than replace symptom and behavioral clinical assessments [49]. Further research is necessary to understand these conflicting phenomena, alongside the refinement of neuroimaging techniques to be seamlessly integrated in the therapeutic process once they are resolved [50,51].

Providers cautioned that receiving a positive neuroimaging test result for mental illness might also raise the risk of guilt, shame, and stigma that could compromise patient motivation and emotional quality of life. These findings are consistent with previous work reporting public concerns about stigma [2] and individuals ceding self-determination or hope to predictive brain imaging [40]. Perceived stigma by providers and family members was reported to have a major influence on whether individuals were willing to pursue treatment for mental illness [52,54].

The participant sample comprised providers from a range of educational and occupational backgrounds. This heterogeneity is both a benefit and a limitation of the study: it yields wide a range of interdisciplinary views, but limits the transferability of the data to other groups not included in this study, such as community mental health workers, primary educators, or affected youth themselves [55]. Another limitation of the study is the hypothetical nature of the interviews and responses that are based on projections rather than actual experience.

In summary, the results of this study identify the positive potential benefits of neurotechnology, specifically imaging and genetics, for mental health in the youth population and highlight the risk factors of such modalities as key challenges to psychiatric health care. Data collection preceded the release of DSM-V, which is aimed at providing more thoroughly delineated classifications of mental disorders than prior versions. Among professionals who disapprove of DSM-V, the most common criticism is that it proliferates diseases by placing a medical disease nomenclature to previously described behaviors, which provides more reasons to administer medications [56-58].

Critiques of DSM-V argue that medical classifications are valuable if they are grounded in biological findings, a view that underscores the importance of neurotechnology as studied here. For many, the future application of functional neuroimaging, genetic testing, or both combined, may be key to reaching the goal of understanding disease origin, beneficially responding to its trajectory, and helping to achieve better intersections of young sufferers with society.

## ACKNOWLEDGEMENTS

We thank the interview participants for their time and contribution to this study.

## Funding

This study was supported by the NIH/NIMH RO1 #9R01MH084282. The funder had no further role in the study design, data collection, or analysis. Judy Illes is Canada Research Chair in Neuroethics. Grant support from CIHR CN #85117, the Canadian Foundation for Innovation, the British Columbia Development Fund, and Vancouver Coastal Health Research Institute also enabled this research.

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**Cite this article**

Lee G, Mizgalewicz A, Borgelt E, Illes J (2014) Genetic Testing and Neuroimaging: Trading off Benefit and Risk for Youth with Mental Illness. *Ann Psychiatry Ment Health* 2(2): 1010.