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Perspectives of psychiatric investigators and IRB chairs regarding benefits of psychiatric genetics research

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ABSTRACT

There is hope that psychiatric genetics inquiry will provide important insights into the origins and treatment of mental illness given the burden of these conditions. We sought to examine perspectives of psychiatric genetic investigators regarding the potential benefits of genetic research *in general* and the potential benefits of genetic research for the diagnosis and treatment of mental illnesses *specifically*. We compared investigator attitudes with those of chairs of Institutional Review Boards (IRBs) entrusted with evaluating the benefits and risks of human research studies. Two groups directly engaged with the conduct and oversight of psychiatric genetic research were examined (psychiatric investigators, n = 203; IRB Chairs, n = 183). Participants rated 15 survey items regarding current and future benefits of general genetic research, possible benefits of psychiatric genetic research, and the importance to society of *genetic vs. non-genetic* research examining causes and treatments of illnesses. Investigators and IRB Chairs strongly endorsed the *future* benefits of general genetic research for society and for the health of individuals; compared to IRB Chairs, investigators were more positive about these benefits. Even after adjusting for demographic variables, psychiatric genetic investigators were significantly more optimistic about genetic research compared with IRB Chairs. Both groups were moderately optimistic about the possible benefits of genetic research related to mental illness. Greater optimism was seen regarding new or personalized medications for mental illnesses, as well as genetic predictive testing of mental illnesses. Greater precision and circumspection about the potential benefits of psychiatric genetic research are needed.

1. Introduction

The ultimate promise of precision psychiatry rests substantially on the insights that genetics inquiry can offer. As noted by Gandal et al., the strong heritability of neuropsychiatric disorders (over 46% as a class) "is a tantalizing clue that genetics will finally provide a rigorous neurobiological framework for comprehending conditions that have evaded biological understanding for decades" (Gandal et al., 2016). Large-scale genome-wide studies in the form of exome sequencing and genome sequencing have yielded robust results identifying genetic loci underlying certain neuropsychiatric disorders. Investigations of the genetic underpinnings of neuropsychiatric disorders have proliferated in recent years, in hopes that such inquiry will aid and accelerate the development of novel therapeutics that are so desperately needed, given the global burden associated with diseases of the brain.

Immense challenges to fulfilling the promise of psychiatric genetics nevertheless remain. The effects of common and rare genetic variants on cellular, molecular and circuit level processes influencing brain function and dysfunction are not yet well understood (Gandal et al., 2016; Lesch, 2016). Moreover, scientists continue to grapple with the complexity of characterizing genetic and environmental contributions and interactions in the development and expression of brain-based illnesses (Abbott et al., 2018; Hall et al., 2015; O'Donovan and Owen, 2016). Thus, while numerous benefits of genetic research are now being realized across many fields of medicine (e.g., oncology), hoped-for improvements in the prevention, diagnosis, monitoring, and treatment of mental illnesses have been much slower to emerge (Biesecker and Peay, 2013; Salm et al., 2014).

As they persevere in this challenging but important work, psychiatric genetics investigators have much at stake in earning and keeping the trust of research participants and the public (Candilis, 2003; Hoge and Appelbaum, 2012). Tragically, the history of psychiatry provides too many examples of the immense consequences of ethical failures (Biesecker and Peay, 2003; Hoop, 2008; Schulze et al., 2004). While the few studies that have been conducted suggest that the general public, as well as psychiatrists, hold generally favorable views regarding potential uses of psychiatric genetics and genomics research (Hoop et al., 2008a, 2008b; Meiser et al., 2008; Milner et al., 1999), the public's trust, once lost, is not easily regained.

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The ethical conduct of research substantially depends on the ethical integrity of investigators. Investigators must carefully anticipate, appraise, describe, and manage study risks; accurately describe the potential benefits to participants and society; and, importantly, weigh and explain how the study's risks are justified by the potential benefits. Institutional Review Boards (IRBs) have a distinct yet equally critical role in fostering ethical conduct of research and upholding public trust in research, namely, by ensuring that the rights and welfare of human volunteers are protected and that applicable regulatory requirements are met. IRBs are charged with evaluating the balance of benefits and risks associated with different research studies and ensuring that appropriately rigorous safeguards are in place to protect volunteers.

In recruiting human research participants, researchers must temper their scientific enthusiasm and optimism with appropriate skepticism in order to minimize the chances of inadvertently overselling or "hyping" the positives of their research, or, alternatively, downplaying the potential risks. Although this issue may be particularly salient in more cutting-edge research, few studies have examined such "therapeutic optimism" in the context of genetic research (Kimmelman and Palmour, 2005). The literature on perspectives of psychiatric genetics researchers, in particular, is thin (DeLisi and Bertisch, 2006).

A number of prior studies have evaluated the attitudes of investigators and IRB members toward ethical aspects of innovative research in general (Stryjewski et al., 2015), or genetic research specifically (Edwards et al., 2011, 2012; Lemke et al., 2010; Williams et al., 2012). Several of these studies have reported divergent views regarding genetic research (Edwards et al., 2011; Lemke et al., 2010; Stryjewski et al., 2015). However, these studies did not examine investigators' or IRB members' views of psychiatric genetic research either in isolation or in comparison to genetic research in general. Little is known about these important groups' attitudes toward genetic research, and in particular, toward the potential benefits of genetic research related to mental illnesses.

The purpose of this study was thus to describe and compare the attitudes of psychiatric investigators and IRB Chairs regarding the potential benefits of genetic research *in general*, as well as regarding the potential benefits of genetic research for the diagnosis and treatment of mental illnesses *specifically*. Given the exploratory nature of this analysis, we did not specify *a priori* hypotheses regarding group differences, although we did expect to find overall positive attitudes regarding the potential benefits of genetic research.

2. Method

2.1. Study design

This study is part of a larger project, jointly funded by the National Institute of Mental Health (NIMH) and the National Human Genome Research Institute (NHGRI), that was designed to assess the perspectives of key stakeholders regarding psychiatric genetic research (Roberts et al., Submitted). For the present study, the perspectives of two groups directly engaged with the conduct and oversight of psychiatric genetic research were examined: (1) psychiatric genetic researchers ("Investigators"), and (2) Institutional Review Board Chairs ("IRB Chairs").

2.2. Participants

Investigators were identified for potential participation through a search of the RePORTER database of the National Institutes of Health (NIH); Principal Investigators conducting research related to psychiatric genetics were invited to participate. To further enrich the sample, we also invited corresponding authors of published manuscripts on psychiatric genetic studies from the previous five years in five major journals identified from PUBMED searches.

IRB Chairs were identified for potential participation using a full database of IRB Chairs from the Office of Human Research Protections (OHRP) that contained > 3600 IRB Chairs. After deleting > 2000 international chairs, we screened this list, deriving a sample of about 300 IRB Chairs serving at institutions that had experience with psychiatric genetic grants. We selected IRB Chairs from institutions matching those of our investigators in our investigator sample, as well as IRB Chairs for all U.S. medical schools and major research institutions listed in the OHRP IRB database. Our goal was to survey only those IRBs that had some history of psychiatric genetic research so that the IRB Chair survey responses would have meaning based on relevant protocol experiences.

Investigators and IRB Chairs received personally addressed, hand-signed survey announcement letters indicating that a follow-up email with a link to the survey would arrive within a few days. Electronic invitations to an online survey were then sent, with monthly reminders from the automated survey system. Investigators also received two postcard reminders to complete the survey and one paper copy of the survey with consent form. Non-responders also received one reminder phone call.

Overall, 353 IRB Chairs and 332 Investigators were contacted, excluding those with returned undeliverable mail. From this group, 203 IRB Chairs (58% response rate) and 183 Investigators (55% response rate) completed the surveys. Investigators and IRB Chairs who completed the surveys received a $50 certificate from an online retailer via e-mail.

2.3. Survey instrument

Parallel surveys were developed for the two stakeholder groups. The complete survey consisted of 222 original items, which were derived from extensive review of the published scientific and ethics literature related to psychiatric genetic research, as well as content generated through qualitative analyses of interviews with 10 key informants (i.e., experts with various backgrounds concerning genetics, psychiatric genetics, and research ethics). The survey items were designed to assess 13 different aspects of ethical, legal, and social issues related to psychiatric genetic research. A number of sociodemographic characteristics (age, gender, race/ethnicity, religious values, and spirituality) were also collected. The survey instruments were extensively pilot-tested with researchers and IRB members from the New Mexico study site.

We analyzed 15 items in total for this analysis. Participants rated four items regarding the current and future benefits of general genetic research on a 10-point Likert scale (0 = "no benefit at all"; 5 = "somewhat benefit"; 10 = "greatly benefit"). Participants also rated ten items regarding the likelihood of a number of possible benefits of psychiatric genetic research on a 10-point Likert scale (0 = "no chance"; 5 = "moderate chance"; 10 = "certain to occur"). Finally, participants rated the importance to society of *genetic vs. non-genetic* research examining causes and treatments of illnesses on a 10-point Likert scale (0 = "non-genetic research is much more important"; 5 = "genetic and non-genetic research are equally important"; 10 = "genetic research is much more important").

2.4. Ethics safeguards

The study protocol was approved by the IRBs at the University of New Mexico, Medical College of Wisconsin, and Stanford University. As part of the survey procedure, all participants were provided with background information about the project. The online survey website included an initial informed consent page for this minimal risk survey, which respondents were asked to read carefully. Respondents were then asked to click one of two boxes, i.e., either "I agree to complete this survey" or "I prefer not to complete this survey." Data were encoded and analyzed with identifiers removed.

2.5. Data analysis

Descriptive statistics were generated for sociodemographic characteristics. Independent sample t-tests and Chi-square tests were used to