

Ethical translations of psychiatric genomics into mental health practice: Response to commentaries

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The rich array of commentaries generated out of our paper, ‘Psychiatric Genomics and Mental Health Treatment: Setting the Ethical Agenda’ (REF), illustrates the importance of devoting further inquiry into the ethics behind psychiatric genomics as well as the various levels of disagreement around the relationship between the translation of the scientific research and the promise of precision medicine. Below we set out a response to the commentaries of our target article, of which we divide into three thematic areas: (i) *additions to* our ethical agenda; (ii) the *realisation* of our ethical agenda; and finally, (iii) doubts that we have set out the *right* ethical agenda.

The first group of commentaries provides welcome additions to the ethical agenda that we laid out, drawing attention to the different pathways and contexts in which ethical considerations around psychiatric genomics could develop. These include de Vries et al’s (2017) closer examination of cultural and economic divergences between high income countries as opposed to lower and middle income countries, which may likewise require further exploration of culturally specific ethical recommendations in such contexts. Sabatello (2017) and Char (2017) also shed light onto the ethical implications of genetic findings in adolescent mental health and paediatric acute care decisions. Sabatello rightly suggests that adolescent genomic consumerism and agency presents additional issues about empowerment and protection, as well as the need to critically examine the socioeconomic and ethnic barriers to future access of benefits in genomic medicine. We find Char’s expansion of the agenda constructive, particularly as his research highlights additional areas of ethical concern, such as the ‘negative’ applications of psychiatric genetic findings in clinical decisions in paediatric acute care. Widdershoven et al (2017) also draw supportive observations about the importance of incorporating a relational, familial perspective in psychiatric genomics and mental health treatment more generally. These various commentaries provide valuable pathways on which the ethical agenda behind psychiatric genomics can develop further – we do not claim to speak for all contexts in our article and attentiveness to parallel pathways and emergent issues will be necessary. We treat these suggestions as refinements that are largely complementary to the broad ethical concerns articulated within our article.

The second thematic convergence of the commentaries revolves around the strategies of inquiry to realise the ethical agenda we have set out. Lázaro-Muñoz (2017) suggests bioethical research into this area should go beyond theoretical analyses and become embedded within different practice-based communities or research. This implies collaborating with neuroscientific

researchers, undertaking empirical work into stakeholders' perspectives, and examining current policy initiatives. We agree that bioethical analysis must begin with an understanding of the capacity and limits of genomic technology, that engagement with scientific researchers on the ground and various stakeholders is desirable, and an analysis of policy as it stands could help inform and shape the ethical issues in this area. We also strongly support calls for the embeddedness of ethics and ethics research into scientific practice. However, our focus in the paper is rather different. In it, our concern is with the ethical aspects of the *translation of research into practice* rather than the *scientific research agenda and its challenges as it stands* amongst neuroscientists. These translational issues may very well result from current policy, laws, and regulations, but analysis of these will not in itself be sufficient to shed light on the process by which socio-cultural contexts, popular narratives, and indeed, front-line clinical practices misinterpret the rather more modest claims and promises of scientists working in this area. The understanding of genomic evidence amongst researchers themselves is not our primary concern in this paper, but rather how such evidence and understanding becomes distorted, or misses its target, in the translational process. To embed the bioethical analysis within the areas suggested by Lázaro-Muñoz would be complementary but importantly different to the translational issues of psychiatric genomic research on which we seek to shed critical light. This is not to suggest that engagement with the research communities and stakeholders is exclusive to these concerns – indeed, bioethical engagement with these parties, and others from the mental health care professions, may well bring to the forefront the practical realities and limitations of translating genomic research to bedside clinical treatment.

This leads to the sceptical question as to whether we have in fact set out the correct ethical agenda. Appelbaum (2017) expresses doubts about our claim that psychiatric genomics per se requires an ethical agenda. In particular, Appelbaum argues that the issues we raise in our article are unlikely to become problematic, given that psychiatric genetics is likely to play a more supportive rather than primary role in our understanding and treatment of mental disorders. Appelbaum, and indeed, Mozosky et al. (2017), rightly point to the complex aetiology of mental disorders: biological mechanisms of mental disorder need not be genetic, and indeed, acknowledgement of biological causes of illness do not have to lead to fatalistic, essentialist attitudes towards disorders. Both Appelbaum and Mozosky et al. point out that the complex gene-environment interactions are crucial to keep in mind if interventions are appropriately targeted, and the fairly modest advances made in large-scale genome-wide association studies indicates many of our ethical worries may be premature. For example, Appelbaum suggests that the application of precision medicine to psychiatry and mental health treatment is unlikely to occur, making our analysis of personal responsibility in the context of psychiatric genomics 'far-fetched' (Appelbaum 2017). An ethical agenda focused on genomics may therefore be too narrowly

construed (Mozosky et al 2017), where a more appropriate target ought to be the broader issues related to neurobiological research programs and the neuroessentialism which creeps in as a result.

These criticisms have an either-or structure: the suggestion is that attending to ethical issues around psychiatric genomics would divert attention away from critically examining the wider issues around a neurobiological research program for mental disorders. However, it is unclear why these two need to be seen as contrary rather than complementary agendas. It is not our claim that the scientific research conflates genetic and neurobiological causes of mental illness, nor that genetic explanation means genetic determinism. Nor is it our claim that the development of precise and personalised treatments for mental disorders – to the extent that genomics may play a role as part of an appropriately multidimensional care plan – means that the treatment of such disorders is ever likely to be entirely ‘genomic’. Our claim is, rather, that regardless of agreement in the scientific community and academic specialists that the genetic factors behind mental disorders are not coextensive with a neurobiological cause, the translational trends of such research have been and are likely to continue to be prone to distortion. Likewise, Viaña’s (2017) discussion of Bipolar Disorder mistakenly suggests that we portray a clear distinction between biogenetic and psychosocial explanation, but we make clear in our discussion of epigenetics that genetic explanations do in fact accommodate psychosocial causes of mental disorder. Empirical studies we cite in our article nonetheless cast doubts as to whether this scientific view of the complex interaction between environment and genes makes its way to the popular understanding. It is therefore worthwhile examining ways in which the translation of genomic research into lay and health professional understandings of serious mental illness can *perpetuate, strengthen, and build upon* biogenetic essentialist views which have already been shown to accompany overly reductive neurobiological explanations of mental disorder.

Second, in our article we do not claim that genomics will necessarily fulfil promises of precision medicine in mental health as is purported in other areas of physical health care, nor would we want to suggest that the realities of psychiatric genetics and mental health therapies makes such promises: indeed, we mention explicitly that researchers are properly cautious since identification of risk alleles have been slow to emerge. Both Hyman (2017) and Appelbaum are nonetheless sceptical that our article’s attendance to ethical issues concerning precision medicine in mental health are likely to require extensive examination, with Appelbaum suggesting that we overstate the dangers of genomic responsibility and its impact on the clinical treatment of mental disorder. Yet these commentators may be too optimistic that *translational marketing* of genomic and genetic research has not already embarked on this path. The more cautious conclusions drawn by clinical and scientific researchers have not stopped health care providers from making ambitious claims about the promise of pharmacogenomics for mental health treatment. Redinger’s (2017) commentary article in fact vindicates our concerns, particularly as a worrying illustration of how direct-to-consumer [DTC] campaigns have tended to perpetuate contested claims about the

precision medicine potential of genetic testing in determining appropriate psychotropic medication for patients. For example, Redinger points to GeneSight Psychotropic laboratory claims that they can test ‘how your genes affect the way your body may respond to FDA-approved medicines commonly prescribed to treat depression, anxiety, bipolar disease, schizophrenia or other behavioral health conditions’ (GeneSight). GeneSight further asserts that their tests ‘can help your healthcare provider select the medicine(s) and dose(s) that are best suited to your condition and your genetic makeup. Medicines that align well with your genes may work better with fewer side effects’ (GeneSight).

Despite the absence of scientific evidence to support the reliability of such tests, this trend is deeply worrying because it not only perpetuates contested claims about genetics (thus raising possible concerns about essentialism and stigma), but also reduces the required intervention for mental illness to one of pharmaceutical treatment. Whilst regulatory interventions might be seen as the necessary mechanism to rein in this trend (Lander, 2015), the likely effects of regulation (or indeed any broad legal or ethical framework) on the broad attitudes and behaviours of patients or practitioners involved in mental health care delivery would need to be examined carefully. Indeed, we believe it is important not to *underestimate* the role that psychiatric genomics plays currently, and could continue to play in the future, in its emerging mistranslation of evidence into practice – through DTC campaigns, the promises of health providers, to the attitudes and practices of clinicians on the ground (Lawrence and Appelbaum, 2011; Abbate et al., 2014), including those who are marketing genetic testing towards patients who have, or are parents of children with, mental disorders such as ADHD (See Genomind).¹ Hyman may be right to attribute this push towards genetics as a response to the seeming research and clinical stasis with regards to medical and psychosocial understanding of mental disorder. Nonetheless, whether its fairly modest gains thus far justify the resource allocation imbalance that continues to favour biological rather than psychosocial research and interventions should be questioned – a concern that Appelbaum likewise echoes in his commentary.

These issues therefore lead us to the pressing question of how and why the mistranslation of psychiatric genomics occurs. Steve Hyman makes the valuable suggestion that some further work on clarifying the essentialising mechanisms in operation is needed. Mental disorder, even before the genomic revolution, remains prone to misconceptions and stigmatising beliefs. Hyman is right that part of the ethical agenda should incorporate future research into what these essentialising mechanisms are and how they can be resisted and challenged. In addition to Hyman’s mention of automatic cognitive mechanisms, we would recommend that further substantive analysis on the *content* and *ethical justifiability* of beliefs and values about agency and culpability must accompany this examination. Understanding the mechanisms behind such beliefs

¹ Numerous blogs feature parents questioning whether their child with ADHD should be undergo pharmacogenetic testing to determine the most appropriate drug.

and values is important, but we likewise need to be equipped with the necessary normative language and tools if our critique of essentialist beliefs and moral valuations about illness are to be ethically grounded.

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