Duquesne University

Duquesne Scholarship Collection

Graduate Student Research Symposium

2022-03-14

Gene Editing for Psychological Conditions: The Potential to Reduce Suffering Through Therapeutic Interventions

Gabriella Agostaro

Follow this and additional works at: https://dsc.duq.edu/gsrs

Gene Editing for Psychological Conditions: The Potential to Reduce Suffering Through Therapeutic Interventions. (2022). Retrieved from https://dsc.duq.edu/gsrs/2022/proceedings/5

This Paper is brought to you for free and open access by Duquesne Scholarship Collection. It has been accepted for inclusion in Graduate Student Research Symposium by an authorized administrator of Duquesne Scholarship Collection.

Gene Editing for Psychological Conditions: The Potential to Reduce Suffering Through Therapeutic Interventions

Introduction

Psychological well-being serves a crucial role in the health and productivity of humanbeings in our society.¹ Individuals with psychological conditions can experience symptoms which include the inability to distinguish fiction from reality, extreme thoughts of sadness, and intense anxiety.² When an individual's world becomes altered, their ability to thrive and flourish independently becomes tarnished. Individuals with psychological conditions experience extreme suffering as their symptoms can quickly become overwhelming and unmanageable. Individuals who experience difficulties mediating psychological symptoms can have difficulty obtaining traditional employment and can potentially experience higher rates of homelessness or incarceration.³

Patients with treatment-resistant psychological conditions continue to have difficulty with symptom mediation. This paper will analyze the potential to reduce suffering in patients with psychological conditions through therapeutic gene editing.

I. Genetics and Psychological Conditions

Many patients diagnosed with psychological conditions do not obtain symptom relief. This aspect comes as a result of psychological conditions that are treatment-resistant. Traditionally, when patients present with a diagnosed psychological condition, they fall into one of three categories:

- 1. The patient who has sought treatment and has no current symptoms
- 2. The patient who chooses not to receive medical interventions
- 3. The patient who has tried numerous medications and therapies but has obtained no relief

Patients who have been correctly diagnosed with a psychological condition or a psychiatric condition and have utilized two or more treatments for at least six weeks with no symptom improvement are classified as treatment-resistant.⁴

The three categories of diagnosis, treatment, and eradication can be utilized to distinguish genetic advancements in the field of psychology. When the diagnosis, treatment, and eradication categories for genetic advancements are applied to treatment-resistant psychological conditions, the potential to relieve suffering lies within the eradication phase.

a) Diagnosis

The diagnosis section utilized to categorize genetic advancements in psychological conditions assists clinicians in diagnosing and recognizing psychological conditions before symptoms present in the patient. Current research in genetics and psychological condition has allowed researchers to determine various genetic associations that contribute to the likelihood of developing a psychological condition.

Association studies have explored genetic associations present in individuals with schizophrenia disorder. Single nucleotide polymorphism (SNP) is a significant genetic factor that may increase an individual's susceptibility to schizophrenia disorder. Numerous SNP locations in a human leukocyte antigen (HLA) locus were explored in the Han Chinese population to determine the genes that contribute to an individual's susceptibility to schizophrenia disorder.⁵ This study indicates that the rs2021722 in the HLA locus could have a pathogenic relationship with schizophrenia disorder.⁶ This data contributes to foundational knowledge for this disorder, which builds a platform for future advancements for the etiology of schizophrenia disorder.

Researchers have similarly explored genetic risk loci associated with bipolar disorder. A genetic locus is the specific location of a gene or DNA sequence on a specific chromosome.

2

Genetic loci allow researchers to pinpoint the exact location of a gene to determine its nature and responsibility within the human body. For example, one study suggests that there is a linkage between the prevalence of bipolar disorder and the 4p16 and 16p13 genes.⁷ Similarly, a more recent study found that there is an association between the DGKH, CACNA1C, and ANK3 genes and bipolar disorder.⁸ While these genes have been independently linked to bipolar disorder, these association studies have further contributed to our understanding of the genetic make-up of this disorder and suggest a need for continued research in the field.

Researchers have not identified a specific genetic marker determining if a psychological condition will be treatment-resistant. While researchers are unable to associate treatment-resistance with a particular gene, enhanced diagnostic abilities allow for early education for individuals that may suffer from psychological conditions in the future.⁹ Early diagnosis can assist an individual in determining the likelihood of transferring a genetically linked psychological condition to their future children.¹⁰ For example, an individual may want to receive genetic testing to determine if their child will have an extreme psychological condition. In the future, genetic markers and genetic testing can assist in the early diagnosis of psychological conditions and encourage mediation before symptoms become too problematic.

b) Treatment

Through genetic sequencing techniques, treatment methods and therapeutic interventions can be targeted more efficiently and effectively in patients suffering with psychological disorders. For example, pharmacogenetic techniques can be utilized to assist clinicians in determining which medication will be most effective in patients with schizophrenia or bipolar disorder. Through genetic sequencing of the patient, clinicians can utilize this technology to individualize a treatment plan for each patient presenting with a psychological disorder. Additionally, pharmacogenetics can be utilized to determine which medications will have the most negligible side-effects.¹¹ Since medication compliance is challenging to attain for patients suffering from psychological conditions, pharmacogenetics can predict which side effects will be prevalent depending on the medication prescribed and the genetic make-up of the patient.

The pharmacogenetics of serotonin reuptake inhibitors (SSRIs) and the presence of sexual dysfunction in patients was examined. Sexual disfunction as a result of SSRI use is present in 20-70% of patients being treated for long-term depression.¹² As a result of this symptom, the patients willingness to comply with long-term medication protocols have been influenced. As a result of this study, an association was found between serotonin and glutamate system genes and the symptom of sexual disfunction.¹³ Side effect and symptom management are crucial to consider when determining the most beneficial medication to treat a patient. Through this type of pharmacogenetics clinicians are able to recognize potential side effects in an attempt to limit their disturbances amongst the body.

In contrast, pharmacogenetics does not account for patients who experience treatmentresistant psychological conditions. Patients suffering from treatment-resistant psychological conditions will not get any relief from the genetic advancements resulting from pharmacogenetic research.¹⁴ Patients who were nonresponsive to pharmaceutical therapy will still not find relief through pharmacogenetics. Pharmacogenetic solutions will not serve as a one-time cure for psychological disorders. Each patient will require multiple drug administrations, and drug adherence will still be crucial for patient recovery.

c) Eradication

The eradication category for psychological conditions is crucial to patients diagnosed with treatment-resistant conditions. This conceptual model serves as an approach that allows patients

with treatment-resistant psychological conditions to receive a source of mediation for their suffering. The eradication phase for physical conditions involves therapeutic gene editing, allowing patients to receive a one-time genetic correction for their illness or condition. Therapeutic gene editing allows the patient to be cured of their condition and eliminates the likelihood of the patient passing a genetic disease to their child.¹⁵ Therapeutic gene editing can be utilized to eradicate psychological conditions entirely.

Therapeutic gene editing for eradicating genetically linked psychological conditions has become increasingly researched in psychology. While researchers are not currently at a point where psychological conditions can be pinpointed to one specific genetic risk loci, continued research will advance clinicians' understanding of the disorders and will contribute to future eradication methods. Although researchers cannot conduct therapeutic gene editing for psychological conditions at this time, this method serves as the only real promise to mediate the suffering experienced by patients with these treatment-resistant psychological disorders.

II. Ethical Considerations

As researchers explore new niche aspects of therapeutic gene editing and new data is obtained and published, the ever-changing discipline must continue to be examined. When assessing the ethical principles in conjunction with therapeutic gene editing, the traditional principles of beneficence, nonmaleficence and patient suffering are relevant for examination.¹⁶

a) Beneficence

The physician's primary goal is to work to treat and improve the quality of life of their patients. While the aim is to improve quality of life, the physician must weigh the probability of risk and success with new and obscure clinical interventions. Advancements in medical technology are currently produced by assessing various experiments' risks and benefits. Beneficence explores the clinician's duty to improve psychological health or physical health.¹⁷ Clinicians practice beneficence by diagnosing and treating a patient for their ailment. For example, in genetics, beneficence would be practiced through a physician genetically testing a woman for the BRCA1 and BRCA2 genes. If a positive test is obtained, the physician can offer a double mastectomy to prevent future cancer development.¹⁸

In patients with psychological conditions, clinicians do aim to bring about improvements in physical and mental health. While this is achievable for patients with traditional psychological conditions, this is not attainable for treatment-resistant psychological conditions. Therefore, resilient treatment options must be explored and implemented in patients with treatment-resistant disorders. These options will work in the best interests of the patients being served and will bring about the most significant improvements to the health of patients suffering from treatmentresistant disorders.

b) Nonmaleficence

Nonmaleficence aims to improve a patient's physical and psychological health in a way that reduces risk and prevents further harm.¹⁹ This ethical principle is similar to the portion of the physician's Hippocratic oath, which directs physicians to "do no harm". Physicians can do no harm by analyzing the side effects associated with a procedure or ensuring medical indications are in place to suggest a procedure is necessary to improve the patient's health.

Beneficence and nonmaleficence are best analyzed and assessed through benefit-risk ratios. Benefit-risk ratios allow the physician to analyze the intended benefit of a medical intervention and the perceived risks associated with a procedure. Physicians can then calculate if the risk factors associated with an intervention are ethically justified.²⁰ The benefit-risk ratios can give physicians direction when assessing possible treatment plans for patients and allow for

patient involvement in medical decision-making. Additionally, these analyses can ensure that physicians continue to do no harm and act in the patients' best interests while assessing treatment plans.

Physicians frequently encounter medical disorders that do not respond to conventional treatment or require therapies that create tremendous side effects for the patient. In an attempt to create the most beneficial treatment plan for the patient that incorporates the least amount of harm, innovative treatment methods and procedures are necessary. Therapeutic gene editing offers clinicians the ability to edit out genetic discrepancies before an illness ever occurs.²¹ This methodology reduces or potentially eliminates pain and suffering due to psychological conditions associated with a type of genetic origin. This treatment method ensures that patients with treatment-resistant psychological conditions get mediation for the pain and suffering and are not inflicted with additional treatment measures that are not medically indicated.

c) Potential to Reduce Suffering

The suffering in patients dealing with physical conditions and the suffering in patients dealing with psychological conditions can be comparable in numerous aspects. To illustrate this, consider treatment-resistant psychological conditions and terminal physical conditions. Patients with terminal physical conditions experience extreme physical symptoms that can also bring about psychological symptoms such as extreme depression or anxiety.²² As a result of these symptoms, patients with terminal conditions, such as cystic fibrosis or cancer, have an increased likelihood of experiencing job loss²³ or strained relationships²⁴ due to these unbearable symptoms.

Patients with treatment-resistant psychological conditions have unbearable psychological symptoms that frequently lead to the development of physical symptoms.²⁵ For example,

common physical symptoms that may develop as a result of psychological conditions are increased heart rate or difficulty breathing.²⁶ As a result of these symptoms, these patients may also experience strained relationships or job loss.

Where terminal physical conditions and treatment-resistant psychological conditions differ is the mediation of the suffering resulting from the symptoms experienced by these patients. Palliative care is a discipline that focuses primarily on comfort and supportive care.²⁷ The palliative care service is traditionally utilized for any patient needing pain mediation for a physical condition. Patients who have received a terminal diagnosis are typically referred to either palliative or hospice care to receive symptom mediation and to make them comfortable through a painful illness, whether it be terminal, a chronic condition, or just a severe recoverable injury.

Patients dealing with treatment-resistant psychological conditions do not receive palliative care services to assist with the extreme suffering they endure due to their disorder. While the physical symptoms that the patient endures will be mediated, the psychological symptoms will not be resolved. The patients dealing with treatment-resistant psychiatric episodes receive basic therapeutic services without the long-term opportunity for symptom mediation.

Conclusion

As developments continue to be made in genetics, researchers become closer to determining the definitive genetic sequences of psychological conditions. While significant progress has been made in genetics, continued research is essential to understand the vast contributions that genetics can make to the field of psychology.

While genetic sequencing aims to assist patients suffering from debilitating psychological conditions, there is still a lack of mediation for patients dealing with these conditions. Given the

suffering associated with treatment-resistant psychological conditions and the current lack of mediation for these disorders, therapeutic gene editing should be considered to assist patients with these conditions. Therapeutic gene editing offers patients with treatment-resistant psychological conditions an opportunity to mediate their suffering and offers significant improvements for future generations that have genetically linked psychological conditions in their family history.

Endnotes

¹ MaryBeth Gallagher, Orla T. Muldoon, and Judith Pettigrew, "An Integrative Review of Social and Occupational Factors Influencing Health and Wellbeing," *Frontiers in Psychology* 6 (2015).

⁴ Koen Demyttenaere, "What Is Treatment Resistance in Psychiatry? A 'Difficult to Treat' Concept," *World Psychiatry* 18, no. 3 (October 2019): 354–55.

⁵ Gangqin Li et al., "Association Study between Genetic Variants and the Risk of Schizophrenia in the Chinese Population Based on GWAS-Implicated 6p21.3–23.1 Human Genome Region: A Case-Control Study," *BMC Psychiatry* 21, no. 1 (October 1, 2021): 1–9.

⁷ Nick Craddock and Ian Jones, "Genetics of Bipolar Disorder," *Journal of Medical Genetics* 36, no. 8 (August 1, 1999): 585–94.

⁸ Barnett and Smoller, "The Genetics of Bipolar Disorder."

⁹ Chia-Hsiang Chen et al., "Chromosomal Microarray Analysis as First-Tier Genetic Test for Schizophrenia," *Frontiers in Genetics* 12 (October 1, 2021).

¹⁰ Chia-Hsiang Chen et al.

¹¹ Liana Osis and Jeffrey R. Bishop, "Pharmacogenetics of SSRIs and Sexual Dysfunction," *Pharmaceuticals* 3, no. 12 (December 2010): 3614–28.

¹² Osis and Bishop.

¹³ Osis and Bishop.

¹⁴ Demyttenaere, "What Is Treatment Resistance in Psychiatry?"

¹⁵ Versha Prakash, Marc Moore, and Rafael J Yáñez-Muñoz, "Current Progress in Therapeutic Gene Editing for Monogenic Diseases," *Molecular Therapy* 24, no. 3 (March 2016): 465–74.

¹⁶ Albert Jonsen, Mark Siegler, and William Winslade, *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*, 8th ed. (McGraw-Hill Education, n.d.).

¹⁷ Jonsen, Siegler, and Winslade.

¹⁸ Glenn Cohen et al., *Consumer Genetic Technologies: Ethical and Legal Considerations* (New York, NY: Cambridge University Press, 2021).

¹⁹ Jonsen, Siegler, and Winslade, Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine.

²⁰ Jonsen, Siegler, and Winslade.

²¹ Deepthi Alapati and Edward E. Morrisey, "Gene Editing and Genetic Lung Disease. Basic Research Meets Therapeutic Application," *American Journal of Respiratory Cell and Molecular Biology* 56, no. 3 (March 2017): 283– 90.

²² Chafi et al., "Prevalence and Correlates of Job Loss among Schizophrenia Outpatients at St. AmanuelMental Specialized Hospital, Addis Ababa, Ethiopia; Cross Sectional Study."

²³ Victoria S. Blinder and Francesca M. Gany, "Impact of Cancer on Employment," *Journal of Clinical Oncology* 38, no. 4 (February 1, 2020): 302–9.

²⁴ Eve Wittenberg, Adrianna Saada, and Lisa A. Prosser, "How Illness Affects Family Members: A Qualitative Interview Survey," *The Patient* 6, no. 4 (December 2013): 10.1007/s40271-013-0030–0033.

²⁵ Javier I. Escobar et al., "Idiopathic Physical Symptoms: A Common Manifestation of Psychiatric Disorders in Primary Care," *CNS Spectrums* 11, no. 3 (March 2006): 201–10.

²⁶ Escobar et al.

²⁷ Max Watson et al., *Oxford Handbook of Palliative Care* (Oxford University Press, 2019).

² J. H. Barnett and J. W. Smoller, "The Genetics of Bipolar Disorder," *Neuroscience*, Linking Genes to Brain Function in Health and Disease, 164, no. 1 (November 24, 2009): 331–43.

³³ Yohannes Kifle Chafi et al., "Prevalence and Correlates of Job Loss among Schizophrenia Outpatients at St. AmanuelMental Specialized Hospital, Addis Ababa, Ethiopia; Cross Sectional Study," *PLoS ONE* 15, no. 12 (December 28, 2020): 1–11.

⁶ Gangqin Li et al.

Bibliography

- Alapati, Deepthi, and Edward E. Morrisey. "Gene Editing and Genetic Lung Disease. Basic Research Meets Therapeutic Application." *American Journal of Respiratory Cell and Molecular Biology* 56, no. 3 (March 2017): 283–90. https://doi.org/10.1165/rcmb.2016-0301PS.
- Barnett, J. H., and J. W. Smoller. "The Genetics of Bipolar Disorder." *Neuroscience*, Linking Genes to Brain Function in Health and Disease, 164, no. 1 (November 24, 2009): 331–43. https://doi.org/10.1016/j.neuroscience.2009.03.080.
- Blinder, Victoria S., and Francesca M. Gany. "Impact of Cancer on Employment." *Journal of Clinical Oncology* 38, no. 4 (February 1, 2020): 302–9. https://doi.org/10.1200/JCO.19.01856.
- Chafi, Yohannes Kifle, Tadele Amare, Kelemua Haile, Woynabeba Damene, Getaneh Tesfaye, and Woredaw Minichil. "Prevalence and Correlates of Job Loss among Schizophrenia Outpatients at St. AmanuelMental Specialized Hospital, Addis Ababa, Ethiopia; Cross Sectional Study." *PLoS ONE* 15, no. 12 (December 28, 2020): 1–11. https://doi.org/10.1371/journal.pone.0242352.
- Chia-Hsiang Chen, Min-Chih Cheng, Tsung-Ming Hu, and Lieh-Yung Ping. "Chromosomal Microarray Analysis as First-Tier Genetic Test for Schizophrenia." *Frontiers in Genetics* 12 (October 1, 2021). https://doi.org/10.3389/fgene.2021.620496.

Cohen, Glenn, Nita Farahany, Henry Greely, and Carmel Shachar. *Consumer Genetic Technologies: Ethical and Legal Considerations*. New York, NY: Cambridge University Press, 2021.

- Craddock, Nick, and Ian Jones. "Genetics of Bipolar Disorder." *Journal of Medical Genetics* 36, no. 8 (August 1, 1999): 585–94. https://doi.org/10.1136/jmg.36.8.585.
- Demyttenaere, Koen. "What Is Treatment Resistance in Psychiatry? A 'Difficult to Treat' Concept." *World Psychiatry* 18, no. 3 (October 2019): 354–55. https://doi.org/10.1002/wps.20677.

Escobar, Javier I., Alejandro Interian, Angelica Díaz-Martínez, and Michael Gara. "Idiopathic Physical Symptoms: A Common Manifestation of Psychiatric Disorders in Primary Care." *CNS Spectrums* 11, no. 3 (March 2006): 201–10.

https://doi.org/10.1017/s1092852900014371.

- Gallagher, MaryBeth, Orla T. Muldoon, and Judith Pettigrew. "An Integrative Review of Social and Occupational Factors Influencing Health and Wellbeing." *Frontiers in Psychology* 6 (2015). https://www.frontiersin.org/article/10.3389/fpsyg.2015.01281.
- Gangqin Li, Jie Dai, Hao Liu, Yushan Lin, Qiaoni Liu, Kaiyuan Zheng, Suyu Li, Siyu Chen, and Yi Ye. "Association Study between Genetic Variants and the Risk of Schizophrenia in the Chinese Population Based on GWAS-Implicated 6p21.3–23.1 Human Genome Region: A Case-Control Study." *BMC Psychiatry* 21, no. 1 (October 1, 2021): 1–9. https://doi.org/10.1186/s12888-021-03496-5.
- Jonsen, Albert, Mark Siegler, and William Winslade. *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*. 8th ed. McGraw-Hill Education, n.d.

Osis, Liana, and Jeffrey R. Bishop. "Pharmacogenetics of SSRIs and Sexual Dysfunction." *Pharmaceuticals* 3, no. 12 (December 2010): 3614–28. https://doi.org/10.3390/ph3123614.

- Prakash, Versha, Marc Moore, and Rafael J Yáñez-Muñoz. "Current Progress in Therapeutic Gene Editing for Monogenic Diseases." *Molecular Therapy* 24, no. 3 (March 2016): 465–74. https://doi.org/10.1038/mt.2016.5.
- Watson, Max, Rachel Campbell, Nandini Vallath, Stephen Ward, and Jo Wells. Oxford Handbook of Palliative Care. Oxford University Press, 2019.
- Wittenberg, Eve, Adrianna Saada, and Lisa A. Prosser. "How Illness Affects Family Members: A Qualitative Interview Survey." *The Patient* 6, no. 4 (December 2013): 10.1007/s40271-013-0030–0033. https://doi.org/10.1007/s40271-013-0030-3.