Maastricht University

From pieces to picture

Citation for published version (APA):

Reijnders, R. A. (2025). *From pieces to picture: systems biology, multi-omics and machine learning in complex brain disorders*. [Doctoral Thesis, Maastricht University]. Maastricht University. https://doi.org/10.26481/dis.20250129rr

Document status and date:
Published: 29/01/2025

DOI:
10.26481/dis.20250129rr

Document Version:
Publisher's PDF, also known as Version of record

Please check the document version of this publication:

• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

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Chapter 11

Impact

Scientific impact

Advancing the understanding of PTSD

This thesis identifies key genes that play crucial roles in immune response and neural adaptation to stress, thereby advancing our understanding of PTSD's molecular mechanisms. Historically, the understanding of biological markers for PTSD was limited, hindering the development of targeted treatments [1]. By shedding light on the genetic basis of PTSD, this research provides a more detailed picture of how these genes contribute to the disorder. For instance, the identification of genes involved in neural adaptation to stress helps explain why some individuals are more susceptible to PTSD than others. This knowledge can lead to more effective screening methods, enabling earlier and more accurate diagnosis of PTSD. Furthermore, understanding these genetic influences opens new avenues for developing targeted therapies that can address the specific molecular pathways involved in PTSD, offering hope for more effective and personalized treatment options.

Systems biology approach

Employing a systems biology approach, the research integrates transcriptomic, genetic, and epigenetic data to provide a comprehensive view of PTSD. This approach surpasses traditional methods by considering the dynamic interactions within biological systems. It offers deeper insights into how various factors contribute to PTSD development. For example, the research links trauma-related symptoms with specific DNA methylation changes, emphasizing the role of epigenetic modifications in how environmental stressors influence gene expression. This holistic view is crucial for developing more effective preventive and treatment strategies, as it allows for a better understanding of the complex interplay between genetic predispositions and environmental factors. The systems biology approach also facilitates the identification of potential biomarkers for PTSD, which can be used to develop more precise diagnostic tools and support targeted therapies.

Identifying biomarkers for PTSD and PD

The research identifies specific genes and CpG methylation sites associated with traumatic stress, enhancing the predictive modeling of PTSD susceptibility. These findings enable the development of biomarkers that can predict an individual's likelihood of developing PTSD, facilitating personalized interventions tailored to an individual's genetic and epigenetic profile. For PD, the study leverages machine learning techniques to predict long-term cognitive changes. By combining clinical assessments with biomarker data, the research creates highly accurate predictive models. These models help healthcare providers identify individuals at risk of rapid cognitive decline earlier than current methods, significantly enhancing early diagnosis and treatment planning. The identification of specific biomarkers and genetic factors opens new opportunities for targeted therapies, offering hope for more effective treatments for both PTSD and PD.

Impact on neurodegenerative disease research

The machine learning models developed are scalable and adaptable, continuously improving when more data becomes available. This approach sets a positive example for other neurodegenerative disease research by integrating clinical and biological data to advance disease management. The ability to predict cognitive decline in PD patients using machine learning techniques demonstrates the potential of these models to improve patient outcomes significantly. This approach can be applied to other neurodegenerative diseases, providing a framework for developing similar predictive models for conditions such as Alzheimer's disease. By leveraging machine learning and big data, researchers can uncover new insights into the progression of complex brain disorders and develop more effective preventive and treatment strategies.

Societal impact

Personalized treatment approaches

The shift towards personalized treatment approaches for conditions like PTSD and PD represents a major change in healthcare. For families and patients, the ability to receive treatments tailored to their specific genetic makeup offers hope for more effective and quicker solutions [2]. Traditional mental health treatments often involve a lengthy process of trial and error, which can be frustrating and time-consuming. With genetic screenings, doctors can identify who is at risk and choose treatments that are more likely to be effective for those individuals [3]. This means patients can avoid the cycle of trying multiple medications and therapies that might not be effective. Personalized treatments can also be adjusted as new genetic information becomes available, ensuring they remain effective, i.e. optimized, over time. This approach not only improves the quality of life for patients but also reduces the emotional and financial burden on families, leading to more stable and sustainable mental health outcomes.

Enhanced patient outcomes and healthcare savings

Healthcare professionals, including doctors and researchers, benefit greatly from integrating genetic and epigenetic data into their practice. Identifying specific biomarkers for PTSD and PD allows for the development of highly targeted preventive and treatment plans, which are more effective than general treatments. Understanding a patient's genetic predisposition and epigenetic profiles, which reflect environmental factors such as stress, smoking and diet, helps doctors manage their care more proactively, potentially preventing severe symptoms from developing. This proactive approach is particularly important for diseases like PD, where early intervention can slow disease progression and maintain cognitive function for longer [4]. The reduction in ineffective treatments may translate to significant cost savings for healthcare systems. By focusing resources on interventions that are likely to succeed, healthcare providers can optimize their budgets and improve patient care. The long-term economic benefits include fewer hospitalizations, reduced emergency interventions, and lower overall healthcare costs. As healthcare systems face increasing financial pressures, such innovations are crucial for maintaining high-quality care.

Support for high-stress professions

High stress-exposed professionals such as police officers, military personnel, and first responders can greatly benefit from this research. These jobs often involve frequent exposure to traumatic events, increasing the risk of developing PTSD and related conditions. Understanding the epigenetic changes that occur in response to stress can lead to the development of preventative mental health programs tailored specifically for these high-risk groups. Mental health screenings and early interventions can support individuals before they reach a critical point [5]. Customized resilience training programs, informed by genetic and epigenetic data, can enhance an individual's ability to cope with stress, reducing the incidence of PTSD. These insights can also guide workplace policies to promote a supportive environment that prioritizes mental health. Over time, these measures can lead to a cultural shift, normalizing mental health support and reducing the stigma associated with seeking help. The long-term impact includes a healthier, more resilient workforce capable of performing their duties effectively while maintaining their mental well-being.

Public health policy and early interventions

Integrating genetic and epigenetic screenings into public health protocols could revolutionize early detection and intervention strategies for PTSD and PD [6]. Early identification of at-risk individuals allows for timely and targeted interventions, potentially preventing these conditions from becoming severe. For example, those identified through genetic screenings can be monitored more closely and provided with preventative treatments or lifestyle recommendations to reduce their risk. This proactive approach can significantly decrease the number of severe PTSD and PD cases, leading to better health outcomes and a reduced societal burden. Public health policies that include these screenings can allocate resources more efficiently, ensuring that support is available for those who need it. The economic implications are substantial, as early intervention can reduce the need for extensive medical treatments and long-term care, resulting in significant cost savings. Public health campaigns can educate the population about the benefits of genetic and epigenetic screenings, fostering a more informed and proactive society. As these practices become standard, they have the potential to transform how mental health and neurodegenerative diseases are managed globally.

Educational and public awareness programs

Sharing the findings from this research through educational and public awareness programs can greatly improve understanding of PTSD and PD. By educating the public about the genetic and environmental factors that contribute to these conditions, we can create a more supportive and empathetic environment for those affected. Public awareness campaigns can demystify the biological causes of mental health disorders, reducing the stigma that often prevents people from seeking help [7]. Explaining how genetic predispositions and environmental stressors interact to influence mental health can help the public appreciate the complexity of these conditions. Educational initiatives can also provide practical information on recognizing early symptoms and accessing support services, empowering individuals to take proactive steps in managing their mental health. These programs can also highlight the importance of mental health research, encouraging public and private investment in further studies. As public understanding and acceptance grow, we can expect higher rates of help-seeking behavior, better adherence to treatment plans, and improved mental health outcomes across communities.

Commercial impact

Development of targeted therapies

Identifying specific biomarkers and genetic factors associated with PTSD and PD creates new opportunities for the pharmaceutical and biotechnology industries to develop targeted therapies. Traditional drug development often involves a lengthy and costly process, trying to find treatments that work for the majority of patients [8]. The insights from this research allow for a more precise approach. Pharmaceutical companies can now create drugs that specifically interact with identified biomarkers, leading to treatments that are more effective and have fewer side effects. For example, if a genetic variant is known to influence PD progression, drugs can be designed to target the specific pathway that it affects. Moreover, one path to development that is often suggested based on identified genetic contributors and biomarkers is drug repurposing. This method speeds up the process by using drugs developed for other conditions and already on the market for new conditions, based on the pathways affected. Systems biology and bioinformatics approaches are used to identify candidate drugs to repurpose, thus avoiding various steps related to safety, and reducing time and cost. This precision medicine approach reduces the need for broad-spectrum treatments, improving efficacy and patient outcomes. Tailoring therapies to individual genetic profiles can also speed up the drug approval process, as clinical trials can be more targeted and demonstrate clearer efficacy. This innovation in precision medicine sets a new standard for treating complex conditions, leading to a more personalized and effective healthcare system.

Advancements in diagnostic tools

The use of machine learning techniques to predict long-term cognitive changes in PD and susceptibility to PTSD represents a significant advancement in diagnostic capabilities. Traditional diagnostic methods often rely on clinical assessments that can be subjective. By integrating machine learning models with biomarker data, this research offers a more objective and accurate approach to diagnosis. These predictive models can continuously improve as more data is collected, ensuring that diagnostic tools remain at the cutting edge of accuracy. Companies specializing in diagnostic tools can adopt these models to enhance their products, providing clinicians with better resources for early diagnosis and treatment planning. For instance, a diagnostic tool incorporating genetic and biomarker data can offer real-time insights into a patient's condition, allowing for immediate and precise treatment adjustments [9]. This level of accuracy not only improves patient outcomes but also builds trust in diagnostic technologies, encouraging wider adoption in clinical settings. As these tools become more sophisticated, they have the potential to transform how we diagnose and manage a range of neurological and psychiatric conditions.

Scalable and adaptable solutions

The machine learning models developed in this research are designed to be both scalable and adaptable, offering significant benefits for the healthcare industry. Scalability ensures that as more data becomes available, these models can be updated to improve their predictive power and accuracy. This continuous improvement is crucial for maintaining the relevance and effectiveness of diagnostic and treatment tools. Adaptability means that these models can be applied to various conditions beyond PTSD and PD, providing a versatile framework for understanding and managing other complex diseases. Healthcare companies can use these scalable and adaptable solutions to enhance their product offerings, staying ahead in a competitive market. For example, a company developing a diagnostic tool for PD could redevelop or expand its application to other neurodegenerative diseases by incorporating additional biomarkers and genetic data. This flexibility allows companies to address a broader range of healthcare challenges, driving innovation and improving patient care across multiple domains. The vision for the future includes a healthcare landscape where scalable and adaptable models are integral to personalized medicine, ensuring that patients receive the most accurate and effective care possible.

Influence on mental health services

The implementation of advanced healthcare solutions can greatly benefit the healthcare services industry. These innovations can make operations more efficient, reduce costs, and improve patient care. By using technologies like AI and machine learning, healthcare providers can better manage resources, make more accurate diagnoses, and create personalized treatment plans. This not only improves the quality of care but also supports a more sustainable healthcare system by reducing waste and using medical resources more effectively. Better data management and system interoperability can also lead to improved coordination of care, ensuring patients receive timely and appropriate treatments. These advancements enhance the overall patient experience and make healthcare organizations more competitive and commercially viable.

In conclusion, the scientific, societal and industrial impacts of this research are significant and promising. By advancing our understanding of the genetic and epigenetic underpinnings of PTSD and PD, this thesis not only supports enhanced and more precise patient care but also helps drive innovation in the healthcare industry. The potential to improve patient outcomes, reduce healthcare costs, and transform mental health strategies and mental health services represent a significant step forward in creating a healthier and more resilient society.

References

[1] R. A. Bryant, “Post-traumatic stress disorder: a state-of-the-art review of evidence and challenges,” World Psychiatry, vol. 18, no. 3, pp. 259–269, Oct. 2019, doi: 10.1002/wps.20656.

[2] R. C. Wang and Z. Wang, “Precision Medicine: Disease Subtyping and Tailored Treatment,” Cancers (Basel), vol. 15, no. 15, p. 3837, Jul. 2023, doi: 10.3390/cancers15153837.

[3] J. Pinzón-Espinosa et al., “Barriers to genetic testing in clinical psychiatry and ways to overcome them: from clinicians’ attitudes to sociocultural differences between patients across the globe,” Transl Psychiatry, vol. 12, p. 442, Oct. 2022, doi: 10.1038/s41398-022-02203-6.

[4] K. S. Bhalsing, M. M. Abbas, and L. C. S. Tan, “Role of Physical Activity in Parkinson’s Disease,” Ann Indian Acad Neurol, vol. 21, no. 4, pp. 242–249, 2018, doi: 10.4103/aian.AIAN_169_18.

[5] M. Colizzi, A. Lasalvia, and M. Ruggeri, “Prevention and early intervention in youth mental health: is it time for a multidisciplinary and trans-diagnostic model for care?,” Int J Ment Health Syst, vol. 14, p. 23, Mar. 2020, doi: 10.1186/s13033-020-00356-9.

[6] G. I. Al Jowf, Z. T. Ahmed, R. A. Reijnders, L. de Nijs, and L. M. T. Eijssen, “To Predict, Prevent, and Manage Post-Traumatic Stress Disorder (PTSD): A Review of Pathophysiology, Treatment, and Biomarkers,” Int J Mol Sci, vol. 24, no. 6, p. 5238, Mar. 2023, doi: 10.3390/ijms24065238.

[7] H. Stuart, “Reducing the stigma of mental illness,” Glob Ment Health (Camb), vol. 3, p. e17, May 2016, doi: 10.1017/gmh.2016.11.

[8] S. Kraljevic, P. J. Stambrook, and K. Pavelic, “Accelerating drug discovery,” EMBO Rep, vol. 5, no. 9, pp. 837–842, Sep. 2004, doi: 10.1038/sj.embor.7400236.

[9] S. A. Alowais et al., “Revolutionizing healthcare: the role of artificial intelligence in clinical practice,” BMC Med Educ, vol. 23, p. 689, Sep. 2023, doi: 10.1186/s12909-023-04698-z.