Annals of Depression and Anxiety

Austin Publishing Group

Open Access Full Text Article

Editorial

Exploring the Genetic Landscape of Depression

Andreas Menke*

Max Planck Institute of Psychiatry, Germany

***Corresponding author:** Andreas Menke, Max Planck Institute of Psychiatry, Kraepelinstr, 10, D-80804 Munich, Germany, Tel: 4989306221; Fax: 498930622605; Email: menke@mpipsykl.mpg.de

Received: August 31, 2014; **Accepted:** August 31, 2014; **Published:** September 01, 2014

Editorial

Stress-related disorders like major depression are predicted to become a leading cause of mortality and morbidity world-wide [1]. They impair patient's mood, cognition, functioning and social relations and may result in suicidal behavior. With a prevalence of 15-20% in the general population major depression is the most commonly observed psychiatric disorder [2]. Despite this tremendous impact, the pathogenesis of major depression remains poorly understood. Even with the advent of DSM-5, no diagnostic parameters derived from peripheral blood, brain imaging, or genomics have been established for diagnosing affective disorders [3]. Additionally, the development of antidepressant drugs was put on hold by many pharmaceutical companies [4] and the efficacy of treatment with novel antidepressants in daily practice is questioned once in a while [5]. Since antidepressant drugs were introduced into the clinic in the 1950s there has been little improvement in efficacy, only side effects were significantly reduced. Hence, there is still great need to further intensify efforts to expand the understanding of the pathophysiology and treatment of major depression. Obviously, these efforts require a suitable platform to spread and share new insights giving rise to this new journal.

Current studies analyzing genetic markers associated with affective disorders provided only modest results, even in a mega-analysis of several GWAS no gene reached genome-wide significance [6]. Likewise no gene was robustly associated with antidepressant treatment response in a meta-analysis of the three large pharmacogenetic samples STAR*D, GENDEP and MARS [7]. The discrepancy between the consistently observed substantial heritability of major depression and the failure to successfully replicate detected genes has been attributed to several factors [8,9] and gave rise to investigate the interplay of genes and environmental factors [10], epigenetic modifications [11] and alterations in gene [12] and protein expression [13]. Additionally, next to the genetic driven approaches brain imaging, neuroendocrinology and metabolomics provide substantial pieces to characterize subtypes of depressed patients. A combination of these approaches already lead to a better understanding of systems implicated with the development of major depression, such as the monoaminergic system [14], the hypothalamic-pituitary-adrenal axis [15], inflammatory pathways [16], neuroplasticity [17] and several other brain circuits [18]. Interestingly, alterations in these systems not only predispose for the development of affective disorders, but also may underlie neural mechanisms responsible for resilience [19]. Most recently, the advent of somatic cell reprogramming technologies allowed with patient-specific, induced pluripotent stem cells new insight into molecular mechanisms of psychiatric disorders [20]. Somatic cell reprogramming enabled the direct conversion of no neuronal somatic cells, such as skin fibroblasts, to neuronal phenotypes [21]. This approach facilitates the in vitro modeling of human neuropsychiatric diseases without having to rely on brain biopsies.

Despite of these sophisticated approaches there are still no reliable biomarkers as diagnostic tools to allow the early identification of subjects at risk to develop a depressive episode. Biomarkers for the identification of severe side effects or successful response following therapy with antidepressants or psychotherapy would enable a tailor-made treatment of depressed patients, but are still not available. The complexity of the regulation of gene transcription and its interactions with environmental factors makes a direct translation of individual genetic information into tailored treatment unlikely [22]. However, the advent of somatic cell reprogramming may uncover mechanisms involved in neuropsychiatric disorders caused by multiple interacting genetic and nongenetic factors, thus support previous approaches with new targets and foster the development of personalized medicine strategies [21].

This new open access peer-reviewed journal publishes innovative clinical, translational and basic research that advances our understanding in the biology of emotions and related disorders. Additionally, new treatment algorithms targeting specific affective symptoms are presented. The open access mode will provide a fast and reliable method for publication and visibility.

Disclosures

Inventor: Means and methods for diagnosing predisposition for Treatment Emergent Suicidal Ideation (TESI). European patent number: 2166112. International application number: PCT/EP2009/061575.

References

1. Ustün TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJ. Global burden of depressive disorders in the year 2000. Br J Psychiatry. 2004; 184: 386-392.
2. Fava M, Kendler KS. Major depressive disorder. Neuron. 2000; 28: 335-341.
3. Nemeroff CB, Weinberger D, Rutter M, MacMillan HL, Bryant RA, Wessely S, et al. DSM-5: a collection of psychiatrist views on the changes, controversies, and future directions. BMC Med. 2013; 11: 202.
4. Holsboer F. Redesigning antidepressant drug discovery. Dialogues Clin Neurosci. 2014; 16: 5-7.
5. Nierenberg AA, Leon A, Price LH, Shelton RC, Trivedi MH. The current crisis of confidence in antidepressants. J Clin Psychiatry. 2011; 72: 27-33.
6. Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium, Ripke S, Wray NR, Lewis CM, Hamilton SP, Weissman MM, Breen G, et al. A mega-analysis of genome-wide association studies for major depressive disorder. Mol Psychiatry. 2013; 18: 497-511.

Citation: Menke A. Exploring the Genetic Landscape of Depression. Ann Depress Anxiety. 2014;1(2): 1009.

7. GENDEP Investigators1; MARS Investigators; STAR*D Investigators. Common genetic variation and antidepressant efficacy in major depressive disorder: a meta-analysis of three genome-wide pharmacogenetic studies. Am J Psychiatry. 2013; 170: 207-217.

8. Keller MC, Miller G. Resolving the paradox of common, harmful, heritable mental disorders: which evolutionary genetic models work best? Behav Brain Sci. 2006; 29: 385-404.

9. Uher R. The role of genetic variation in the causation of mental illness: an evolution-informed framework. Mol Psychiatry. 2009; 14: 1072-1082.

10. Klengel T, Binder EB. Gene-environment interactions in major depressive disorder. Can J Psychiatry. 2013; 58: 76-83.

11. Menke A, Klengel T, Binder EB. Epigenetics, depression and antidepressant treatment. Curr Pharm Des. 2012; 18: 5879-5889.

12. Menke A. Gene expression: biomarker of antidepressant therapy? Int Rev Psychiatry. 2013; 25: 579-591.

13. Patel S. Role of proteomics in biomarker discovery: prognosis and diagnosis of neuropsychiatric disorders. Adv Protein Chem Struct Biol. 2014; 94: 39-75.

14. Morilak DA, Frazer A. Antidepressants and brain monoaminergic systems: a dimensional approach to understanding their behavioural effects in depression and anxiety disorders. Int J Neuropsychopharmacol. 2004; 7: 193-218.

15. Holsboer F. Stress, hypercortisolism and corticosteroid receptors in depression: implications for therapy. J Affect Disord. 2001; 62: 77-91.

16. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. Nat Rev Neurosci. 2008; 9: 46-56.

17. Castrén E, Rantamäki T. The role of BDNF and its receptors in depression and antidepressant drug action: Reactivation of developmental plasticity. Dev Neurobiol. 2010; 70: 289-297.

18. Sibille E, French B. Biological substrates underpinning diagnosis of major depression. Int J Neuropsychopharmacol. 2013; 16: 1893-1909.

19. Feder A, Nestler EJ, Charney DS. Psychobiology and molecular genetics of resilience. Nat Rev Neurosci. 2009; 10: 446-457.

20. Haggarty SJ, Perlis RH. Translation: screening for novel therapeutics with disease-relevant cell types derived from human stem cell models. Biol Psychiatry. 2014; 75: 952-960.

21. Qiang L, Inoue K, Abeliovich A. Instant neurons: directed somatic cell reprogramming models of central nervous system disorders. Biol Psychiatry. 2014; 75: 945-951.

22. Holsboer F. How can we realize the promise of personalized antidepressant medicines? Nat Rev Neurosci. 2008; 9: 638-646.

Ann Depress Anxiety - Volume 1 Issue 2 - 2014
ISSN : 2381-8883 | www.austinpublishinggroup.com

Citation: Menke A. Exploring the Genetic Landscape of Depression. Ann Depress Anxiety. 2014;1(2): 1009.