CHAPTER 11

Common Genetic Mutations In Psychiatric and Cardiovascular Diseases

İnci Tuğçe ÇÖLLÜOĞLU [1]
Melehat Hicran AKSU [2]

INTRODUCTION

Cardiovascular diseases (CVD) and psychiatric diseases are important causes of morbidity and mortality worldwide. In studies conducted over the years, it has been postulated that a bidirectional relationship exists whereby both conditions may mutually influence and precipitate each other (1). Moreover, psychiatric diseases and CVD seem to have common etiologies such as genetic mechanisms (1). There is an evidence of genetic overlap between CVD and psychiatric diseases (2). In addition, twin studies and molecular genetic studies have also revealed genetic correlations between cardio-metabolic abnormalities, CVD, and psychiatric disorders (3, 4). This chapter endeavors to provide a concise overview of the prevalent genetic mutations observed in CVD as well as phychiatric diseases.

Genetic Factors in the Relationship between Cardiovascular Diseases and Psychiatric Diseases

Genetic factors simultaneously exert an influence on both CVD and psychiatric disorders. These observations suggest potential pleiotropic effects originating from the same gene locus associated with psychiatric disorders and CVD (5, 6). The pleiotropic effects arising from the involvement of multiple genes associated with cardiovascular risk factors have been identified in patients diagnosed with schizophrenia (5). A total of seven pleiotropic genes (SLC39A8, MAML3,

[1] Asst. Prof., Karabük University, Faculty of Medicine, Cardiology Department, incitugcecolluoglu@karabuk.edu.tr, ORCID iD: 0000-0002-2227-6177
[2] Research Ass., Karabük University, Faculty of Medicine, Cardiology Department, melahathicranaksu@karabuk.edu.tr, ORCID iD: 0000-0002-4707-2939

such as transtuzumab have demonstrated replicated efficacy in the treatment of psychoses and other psychiatric diseases. These initial studies of immunological pathways and their interactions with pharmaceutical drugs can generate hypotheses for more research (26).

Conclusion

Psychiatric disorders and various cardiovascular diseases share important genetic variations. The presence of common genetic mutations in individuals with psychiatric disorders may lead to a notable comorbidity of cardiac diseases within this patient population. Given the common genetic mechanisms underlying cardiac and psychiatric diseases, future studies may shed light on the treatment of co-occurring diseases by focusing on the precise genetic factors in patients with both cardiovascular and psychiatric diseases.

REFERENCES

1. De Hert M, Detraux J, Vancampfort D. The intriguing relationship between coronary heart disease and mental disorders. *Dialogues in clinical neuroscience*. 2018;20(1):31-40. doi:10.31887/DCNS.2018.20.1/mdehert
2. Rødevand L, Bahrami S, Frei O, Lin A, Gani O, Shadrin A, et al. Polygenic overlap and shared genetic loci between loneliness, severe mental disorders, and cardiovascular disease risk factors suggest shared molecular mechanisms. *Translational psychiatry*. 2021;11(1):3. doi:10.1038/s41398-020-01142-4
3. Goldstein BI, Carnethon MR, Matthews KA, McIntyre RS, Miller GE, Raghuveer G, et al. Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2015;132(10):965-86. doi:10.1161/cir.0000000000000229
4. Adibfar A, Saleem M, Lanctot KL, Herrmann N. Potential Biomarkers for Depression Associated with Coronary Artery Disease: A Critical Review. *Current molecular medicine*. 2016;16(2):137-64. doi:10.2174/1566524016666160126144143
5. Andreassen OA, Djurovic S, Thompson WK, Schork AJ, Kendler KS, O'Donovan MC, et al. Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular-disease risk factors. *American journal of human genetics*. 2013;92(2):197-209. doi:10.1016/j.ajhg.2013.01.001
6. Zhang F, Cao H, Baranova A. Shared Genetic Liability and Causal Associations Between Major Depressive Disorder and Cardiovascular Diseases. *Frontiers in cardiovascular medicine*. 2021;8:735136. doi:10.3389/fcvm.2021.735136
7. Amare AT, Schubert KO, Klingler-Hoffmann M, Cohen-Woods S, Baune BT. The genetic overlap between mood disorders and cardiometabolic diseases: a systematic review of genome wide and candidate gene studies. *Translational psychiatry*. 2017;7(1):e1007. doi:10.1038/tp.2016.261

8. Howard DM, Adams MJ, Clarke TK, Hafferty JD, Gibson J, Shirali M, et al. Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *Nature neuroscience*. 2019;22(3):343-52. doi:10.1038/s41593-018-0326-7
9. van der Harst P, Verweij N. Identification of 64 Novel Genetic Loci Provides an Expanded View on the Genetic Architecture of Coronary Artery Disease. *Circulation research*. 2018;122(3):433-43. doi:10.1161/circresaha.117.312086
10. Imbrici P, Camerino DC, Tricarico D. Major channels involved in neuropsychiatric disorders and therapeutic perspectives. *Frontiers in genetics*. 2013;4:76. doi:10.3389/fgene.2013.00076
11. Espregueira Themudo G, Leerschool AR, Rodriguez-Proano C, Christiansen SL, Andersen JD, Busch JR, et al. Targeted exon sequencing in deceased schizophrenia patients in Denmark. *International journal of legal medicine*. 2020;134(1):135-47. doi:10.1007/s00414-019-02212-z
12. Berne P, Brugada J. Brugada syndrome 2012. *Circulation journal : official journal of the Japanese Circulation Society*. 2012;76(7):1563-71. doi:10.1253/circj.cj-12-0717
13. Jiang H, Qiao F, Li Z, Zhang Y, Cheng Y, Xu X, et al. Evaluating the association between CACNA1C rs1006737 and schizophrenia risk: A meta-analysis. *Asia-Pacific psychiatry : official journal of the Pacific Rim College of Psychiatrists*. 2015;7(3):260-7. doi:10.1111/appy.12173
14. Dedic N, Pöhlmann ML, Richter JS, Mehta D, Czamara D, Metzger MW, et al. Cross-disorder risk gene CACNA1C differentially modulates susceptibility to psychiatric disorders during development and adulthood. *Molecular psychiatry*. 2018;23(3):533-43. doi:10.1038/mp.2017.133
15. Ripke S, O'Dushlaine C, Chambert K, Moran JL, Kähler AK, Akterin S, et al. Genome-wide association analysis identifies 13 new risk loci for schizophrenia. *Nature genetics*. 2013;45(10):1150-9. doi:10.1038/ng.2742
16. Zhu D, Yin J, Liang C, Luo X, Lv D, Dai Z, et al. CACNA1C (rs1006737) may be a susceptibility gene for schizophrenia: An updated meta-analysis. *Brain and behavior*. 2019;9(6):e01292. doi:10.1002/brb3.1292
17. Ferreira MA, O'Donovan MC, Meng YA, Jones IR, Ruderfer DM, Jones L, et al. Collaborative genome-wide association analysis supports a role for ANK3 and CACNA1C in bipolar disorder. *Nature genetics*. 2008;40(9):1056-8. doi:10.1038/ng.209
18. Napolitano C, Bloise R, Monteforte N, Priori SG. Sudden cardiac death and genetic ion channelopathies: long QT, Brugada, short QT, catecholaminergic polymorphic ventricular tachycardia, and idiopathic ventricular fibrillation. *Circulation*. 2012;125(16):2027-34. doi:10.1161/circulationaha.111.055947
19. Judy JT, Seifuddin F, Pirooznia M, Mahon PB, Jancic D, Goes FS, et al. Converging Evidence for Epistasis between ANK3 and Potassium Channel Gene KCNQ2 in Bipolar Disorder. *Frontiers in genetics*. 2013;4:87. doi:10.3389/fgene.2013.00087
20. Chen CJ, Liao WY, Chattopadhyay A, Lu TP. Exploring the genetic correlation of cardiovascular diseases and mood disorders in the UK Biobank. *Epidemiology and psychiatric sciences*. 2023;32:e31. doi:10.1017/s2045796023000252
21. Wang L, Ding C. Major depression disorder may causally associate with the increased atrial fibrillation risk: evidence from two-sample mendelian randomization analyses. *BMC medical genomics*. 2023;16(1):144. doi:10.1186/s12920-023-01565-0
22. Kalstø SM, Siland JE, Rienstra M, Christophersen IE. Atrial Fibrillation Genetics Update: Toward Clinical Implementation. *Frontiers in cardiovascular medicine*. 2019;6:127. doi:10.3389/fcvm.2019.00127

23. Garg PK, O'Neal WT, Diez-Roux AV, Alonso A, Soliman EZ, Heckbert S. Negative Affect and Risk of Atrial Fibrillation: MESA. *Journal of the American Heart Association*. 2019;8(1):e010603. doi:10.1161/jaha.118.010603
24. Liu H, Sun Y, Zhang X, Li S, Hu D, Xiao L, et al. Integrated Analysis of Summary Statistics to Identify Pleiotropic Genes and Pathways for the Comorbidity of Schizophrenia and Cardiometabolic Disease. *Frontiers in psychiatry*. 2020;11:256. doi:10.3389/fpsyt.2020.00256
25. So HC, Chau KL, Ao FK, Mo CH, Sham PC. Exploring shared genetic bases and causal relationships of schizophrenia and bipolar disorder with 28 cardiovascular and metabolic traits. *Psychological medicine*. 2019;49(8):1286-98. doi:10.1017/s0033291718001812
26. Zhang L, Lizano P, Guo B, Xu Y, Rubin LH, Hill SK, et al. Inflammation subtypes in psychosis and their relationships with genetic risk for psychiatric and cardiometabolic disorders. *Brain, behavior, & immunity - health*. 2022;22:100459. doi:10.1016/j.bbih.2022.100459