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Addiction-related gene GDNF and interaction network

Abstract

The glial cell line-derived neurotrophic factor (GDNF) is a produced protein. GDNF's role in the development of the central nervous systems and the remaining mature dopaminergic neurons is well known. Lately, lots of studies suggest that GDNF plays a key role in the actions of drug addiction. In this article, we used bioinformatic approaches these data and highlight the possibility that the GDNF pathway may be a promising target for the treatment of addiction. Our previous studies have demonstrated that among the putative targets of some miRNAs about the abuse of methamphetamine. According to our previously miRNA results, we showed that one of the important genes is GDNF about the addiction. This study is important to indicate the potential common target genes of addiction-related GDNF gene and help to figure out underlying molecular pathways of addiction in association with those common target genes.

Keywords: GDNF gene, target genes, drugs of abuse

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Introduction

Drugs of abuse are a serious worldwide health problem that is causing medical, social and economic trouble, for which pharmacotherapeutic approaches are highly limited.[1,2] Addictive drugs target the mesocorticolimbic dopamine (DA) system in the addiction center of the brain, including the ventral tegmental area (VTA), prefrontal cortex, and nucleus accumbens (NAc). The VTA, which contains the largest group of dopamine neurons, plays an important role in reward-related and goal-directed behaviors such as cognitive and emotional processes.[3] Infusion of GDNF into the ventral tegmental area (VTA), a dopaminergic brain region important for addiction, blocks specific adaptations to chronic cocaine or morphine as well as the rewarding effects of cocaine.[4] A possible factor that could play a key role in such protective mechanisms is glial cell line-derived neurotrophic factor (GDNF), a major growth factor for the development, remaining of midbrain dopamine (DA) neurons.[5] Recent studies have demonstrated that GDNF has been implicated as a negative regulator in some type of addiction.[6–8] Specifically, we previously found that some miRNAs key role in the abuse of methamfetamine in the ventral tegmental area (VTA) and nucleus accumbens. We showed that miRNAs upregulated the GDNF gene. In this study, we aimed to show GDNF target genes networks.

Materials and methods

In this article, we aimed to highlight the possibility that the GDNF pathway may be a promising target for the treatment of addiction. Predicted genes were enriched by using STRING We found the Protein-Protein Interaction Networks (PPI) of common GRM_4 targets (8).

Results and discussion

In this study, we researched the targets of the GDNF gene in bioinformatic approaches. We used bioinformatics tools to screen for GDNF gene and drug addiction related regulatory networks as shown in Figures 1&2. GDNF is a highly important neurotrophic factor that can assist in the survival of dopaminergic and motor neurons.[9] Some studies suggested that GDNF also regulates neuronal function and transmission.[10–13] Barak et al,[15] provide evidence that GDNF is an endogenous factor that gates the transition from moderate to excessive alcohol drinking and relapse in the mesolimbic system. Messer et al,[14] showed that GDNF from binding and activating brain reward receptors, resulted in increased sensitivity of mice to the rewarding effect of cocaine.[15] Thus the results suggest that GDNF is associated with the addiction, and it may be a potential target for novel treatments.

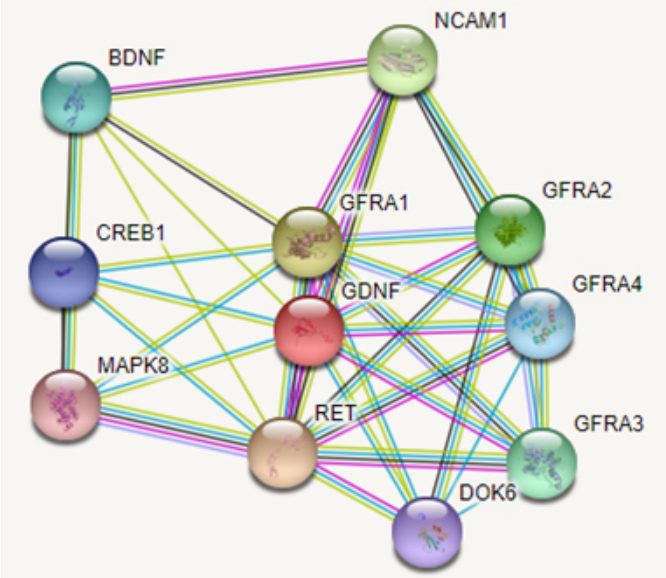

Figure 1 GDNF gene ınteraction networks (http://string-db.org/).

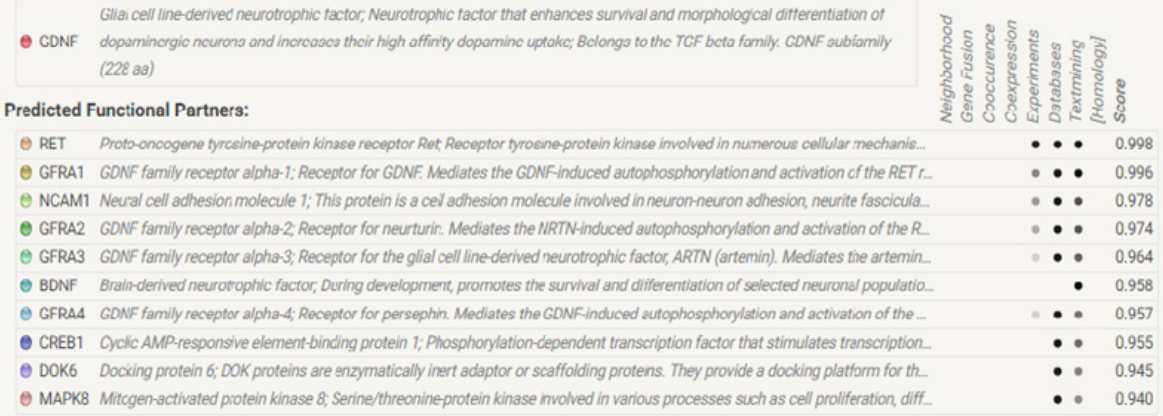

Figure 2 Predicted functional partners (http://string-db.org/).

Conclusion

As a result, we found eleven target genes of the GDNF gene have an important role in the mesocorticolimbic system. String database results showed that target genes of GDNF involved in several biological processes which are drug-induced neuroplasticity and gene regulatory.

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Conflicts of interest

The authors declare that there is no conflict of interest.

References

1. World Health Organization. WHO Global status report on alcohol Geneva. *World Health Organization.* 2004.
2. Spanagel R, Holter SM. Long-term alcohol self-administration with repeated alcohol deprivation phases an animal model of alcoholism. *Alcohol Alcohol.* 1999;34:231–243.
3. Demirel G, Guzel E, Creighton C. MDMA Abuse in relation to microrna variation in human brain ventral segmental area and nucleus accumbens . *Iranian Journal of Pharmaceutical Research*. 2019;18(4):1989–1999.
4. Airaksinen MS, Saarma M. The GDNF family signalling, biological functions and therapeutic value. *Nat Rev Neurosci*. 2002;3(5):383–394.
5. Pascual A, HidalgoFigueroa M, Piruat JI, et al. Absolute requirement of GDNF for adult catecholaminergic neuron survival. *Nat Neurosci*. 2008;11(7):755–761.
6. Carnicella S, Ron D. GDNF a potential target to treat addiction. *Pharmacol Ther*. 2009;122(1):9–18.
7. Ghitza UE, Zhai H, Wu P. Role of BDNF and GDNF in drug reward and relapse: a review. *Neurosci Biobehav Rev*. 2010; 35(2):157–171.
8. Davies DL, Bortolato M, Finn DA, et al. Recent advances in the discovery and preclinical testing of novel compounds for the prevention and/or treatment of alcohol use disorders. *Alcohol Clin Exp Res*. 2013;37(1):8–15.
9. Lindholm P, Voutilainen MH, Lauren J, Peranen J, et al. Novel neurotrophic factor CDNF protects and rescues midbrain dopamine neurons in vivo. *Nature*. 2007;448(7149):73–77.
10. Wang CY, Yang F, He X, Chow A, Du J, et al. Ca(2+) binding protein frequenin mediates GDNF-induced potentiation of Ca(2+) channels and transmitter release. *Neuron*. 2001;32(1):99–112.
11. Yang F, Feng L, Zheng F, et al. GDNF acutely modulates excitability and A-type K(+) channels in midbrain dopaminergic neurons. *Nat Neurosci*. 2001;4(11):1071–1078.
12. Wang HJ, Cao JP, Yu JK, et al. Calbindin-D28K expression induced by glial cell line-derived neurotrophic factor in substantia nigra neurons dependent on PI_3K/Akt/NF-kappaB signaling pathway. *Eur J Pharmacol*. 2008;595(1-3):7–12.
13. Kobori N,Waymire JC, et al. Enhancement of tyrosine hydroxylase phosphorylation and activity by glial cell line-derived neurotrophic factor. *J Biol Chem*. 2004;279:2182–2191.
14. Messer CJ, Eisch AJ, Carlezon WA, et al. Role for GDNF in biochemical and behavioral adaptations to drugs of abuse. *Neuron*. 2000;26(1):247–257.
15. Barak S, Wang J, Ahmadiantehrani S, et al. Glial cell line-derived neurotrophic factor (GDNF) is an endogenous protector in the mesolimbic system against excessive alcohol consumption and relapse. *Addiction Biology*. 2014;20(4):629–642.