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Mini Review

Behavioral Genetics and Predisposition to Aggressive Behavior

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Abstract

Aggressive behaviors can affect the quality of human relationships established throughout a person's life and thus the quality of life. Because successful social relationships have the potential to affect everything from the person's position in society to the support they receive in their old age or illness. Does the ability to direct our behavior, especially aggressive behavior, come from our DNA? To what extent are our aggressive behaviors inherited from our ancestors? This topic is discussed in this mini-review.

Introduction

Behavioral genetics is a science that aims to investigate the origin of behavioral tendencies with molecular biological methods. Neurogenetics, on the other hand, relies on both "neuroscience evidence" such as neuroimaging, and behavioral genetics that links a particular gene to an observable behavior or trait. Although genetic evidence suggests that behavioral patterns that makeup personality, such as delinquency, are facilitated by changes in one or more genes, it does not deny the contribution of environmental factors. Therefore, genetic disposition makes sense with the contribution of environmental factors such as education, culture, family, traumatic events, living environment, and conditions. Genetic and environmental factors, when combined, can increase the risk of developing aggressive/antisocial behavior exponentially, creating a synergy. The determinants of behavior are complex, and although certain genes may have an influence on behavior, they only constitute a "strong predisposition" should be written instead of "strong bias", at least according to current data. However, there is ample evidence that they should not be neglected. Evidence from twins and post-adoption follow-up reveals the importance of genetic factors in the formation of aggressive behaviors from childhood to adulthood [1]. In addition, it is known that the underlying biochemical mechanisms associated with aggression originate from certain genes [1].

Numerous studies have shown that both reactive and proactive aggressive behavior has the potential to be influenced by genetic factors. According to data from twin studies, genetic influences are more effective in adulthood and also play a larger role in men than in women [2,3]. In some studies, the effects of polymorphisms or mutations in the following genes (or gene-related regulatory regions) on behavioral genetics have been investigated and reported. Some of these genes are listed below.

a) MAO-A ("Monoamine oxidase A") [4],

b) 5-HTTLPR ("serotonin-transporter-linked polymorphic region") [5] is a functional polymorphism region in the promoter of the SLC6A4 ("Solute Carrier Family 6 Member 4") gene. These polymorphism occurs as repeating sequences (VNTR: "variable number of tandem-repeat") in the promoter region of the SLC6A4.

c) COMT ("Catechol-O-Methyltransferase") [6],

d) DRD4 ("Dopamine Receptor D4")[7],

e) DDR2 ("Dopamine Receptor D2") [8,9],

f) SLC6A3 / DAT1("Solute Carrier Family 6 Member 3" / "The dopamine transporter") [10] and

g) CDH13 ("Cadherin 13") [11].

MAO-A (Monoamine oxidase): is an enzyme that breaks down neurotransmitters such as noradrenaline, serotonin, adrenaline, and dopamine in the brain. It is known that drugs targeting the monoaminergic pathway in which this enzyme is found, cause mood changes in terms of side effects and/or desired effects. This shows that the monoaminergic pathway has an important effect on the determination of personality traits. The gene encoding this enzyme

is also known as the "warrior gene". The gene has a VNTR region 1200 bases behind its promoter. The number of repeats affects the expression level of the enzyme and the tendency for aggressive and impulsive behaviors [12]. The two-repeat allele (low enzyme expression) correlated with a tendency towards violence, while the 4-repeat allele (high enzyme activity) was associated with lower levels of impulsive aggression [13]. A rare mutation leading to a complete deficiency of MAOA has been observed to be associated with impulsive and aggressive behavior in a Dutch person [12]. It has been determined that carriers of the low-activity MAO-A variant, who were exposed to physical or psychological abuse in childhood, have a higher risk of impulsive, aggressive, and violent behavior in late adolescence and early adulthood [14]. Therefore, it is understood that those who have not been subjected to violence do not tend to violence even if they have MAO-A deficiency [13].

5-HTTLPR (the polymorphic region associated with the serotonin transporter) is a polymorphic region in SLC6A4, the gene encoding the serotonin transporter. This region is a VNTR region. The polymorphisms here are functional insertions/deletions in the promoter of the gene and its connection with neuropsychiatric diseases has been shown [5]. The protein that results from the polymorphism, namely the serotonin transporter called SERT (also called 5-HTT), has two variants: a long (L) version containing 16 repeats and a short (S) version containing 14 repeats. The short SERT allele has a lower transcriptional activity compared to its long variant [15]. Thus, the long variant produces more SERT mRNA. SERT is a transmembrane protein that affects the transport of serotonin to neurons. Serotonin is a hormone that gives happiness, vitality, and enthusiasm. Its deficiency results in aggression, malaise, depression. It has been shown that the aforementioned polymorphism affects the serotonin uptake rate and may play a role in sudden infant death syndrome, aggressive development of Alzheimer's disease, post-traumatic stress disorder, and susceptibility to depression. The long allele (L) is associated with personality traits such as shyness in primary school children [16]. In another study published in 2009, it was stated that individuals homozygously carrying the long variant compared to heterozygous and short allele-homozygotes paid more attention to positive emotional pictures on average, while selectively avoiding negative emotional pictures presented alongside positive pictures, and may therefore tend to be more optimistic [17]. It has been reported that the presence of the short SERT variant (S) may be associated with neuroticism, depression, and suicidality [18,19]. In addition, the homozygously coded short variant was found to be significantly associated with aggression and impulsivity [20].

COMT (Cathethol Methyl Transferase) [6] gene encodes the Catechol-O-methyltransferase (commonly referred to as COMT) enzyme. This enzyme limits the activities of dopamine, epinephrine, and norepinephrine. Therefore, different variants of COMT cause the balance of these neurotransmitters and brain biochemistry to be altered and may have serious consequences. For example, changes in COMT activity have been associated with schizophrenia [21]. There are two variants of COMT. One is S-COMT ("Soluble" form and cannot bind to the cell membrane), which consists of 221 amino acids, and the other is the MB-COMT ("Membrane-Bound"- able to bind to the membrane) isoform, which contains an additional 50 amino acids and can bind to the membrane. Both isoforms are found in body tissues such as glial cells, liver, kidneys, and blood. However, there are polymorphisms (changes in codon 108 of S-COMT and codon 158 of MB-COMT) that affect both isoforms, and these affect functional activity. In a study reported in 2012, a significant relationship was found between polymorphisms in the COMT gene (rs6269 and rs4818) and aggressive behavior in children [22].

DRD4 is the dopamine D4 receptor gene, also known as the "adventure gene". This gene also has a VNTR polymorphism, as in the above. There are 48 base pair sequences with repeat ranges of 2-11, which manifest themselves as the "short" variant (five repeats or less - DRD4S) or the "long" variant (six or more repeats - DRD4L). Two, four, and seven repeats are considered the most common genotypes. The length of the variant has functional effects on the dopamine receptor. DRD4L with seven or more repeats is less sensitive to dopamine [23]. Dopamine is a neurotransmitter, also known as the happiness hormone. As it affects the reward center of the brain, it affects many behaviors such as attention, memory, learning, mood, sleep, movement. Another dopamine-related gene is the dopamine receptor D2 (DRD2) gene. The DRD2 receptor is one of the most important targets of antipsychotic drugs. Both genes are thought to be potentially associated with antisocial behavior. In a study, it was revealed that there is a significant interaction between small variants of the DRD2 gene and the 7-repeat allele of DRD4 in novelty-seeking propensity [9]. It has also been shown that three polymorphisms in DRD2 are associated with childhood aggression [24].

The dopamine transporter (DAT1), encoded by the SLC6A3 gene, is a master regulator of dopaminergic neurotransmission. DAT1 limits the level and duration of dopamine receptor activation, thereby controlling the synaptic dopamine level. Guo et al. showed that the DAT1*10R variant contributes to serious criminal behavior in 2,500 adolescent boys [8].

CDH13 (Cadherin-13), is a calcium-dependent adhesion protein that regulates neural cell growth. In a GWAS (Genome-Wide Association Study) study, the genomes of 1889 Finnish prisoners and controls were examined, as a result, single point polymorphism (rs11649622) in the CDH13 gene was associated with people convicted of 10 or more aggravated violent crimes. CDH13 is encoded at the 16q23.3 locus and the single point polymorphism mentioned is the A/G change in the intron region. In the same study, a significant relationship was found between inmates who committed the same violent crime and MAOA, which encodes low enzyme activity [11].

Conclusion

Among the genes examined above, especially low monoamine metabolism (MAOA) and neural membrane dysfunction (CDH13)

can be considered as plausible factors in the etiology of aggressive behavior. Indeed, Tiihonen et al. Implied that at least about 5-10% of all violent crimes in Finland can be attributed to the MAOA and CDH13 genotypes [11]. Again, a study using the Swedish Adoption Database, which has a long and stringent follow-up system, found convincing evidence that criminal records of biological parents predicted both violent and nonviolent crimes among their adopted children [11]. As a result, genetic factors may form the basis for the emergence of aggressive behaviors. However, attributing the responsibility for the emergence of aggressive behavior to genetic factors alone does not seem like a realistic point of view. Therefore, further studies are needed with candidate genes that influence aggressive behavior and personality.

References

1. Cadoret RJ, Leve LD, Devor E (1997) Genetics of aggressive and violent behavior. Psychiatr Clin North Am 20(2): 301-322.
2. Tuvblad C, Raine A, Zheng M, Baker LA (2009) Genetic and environmental stability differs in reactive and proactive aggression. Aggress Behav 35(6): 437-452.
3. Bezdjian S, Tuvblad C, Raine A, Baker LA (2011) The genetic and environmental covariation among psychopathic personality traits, and reactive and proactive aggression in childhood. Child Dev 82(4): 1267-1281.
4. Sabol SZ, Hu S, Hamer DA (1998) Functional polymorphism in the monoamine oxidase A gene promoter. Hum Genet 103(3): 273-279.
5. Heils A, Teufel A, Petri S , Stober G, Riederer P, et al. (1996) Allelic variation of human serotonin transporter gene expression. J Neuro chem 66(6): 2621-26214.
6. Lichtenberg P, Bachner Melman R, Gritsenko I, Ebstein RP (2000) Exploratory association study between catechol-O-methyltransferase (COMT) high/low enzyme activity polymorphism and hypnotizability. Am J Med Genet 96(6): 771-774.
7. Lichter JB, Barr CL, Kennedy JL (1993) A hypervariable segment in the human dopamine receptor D4 (DRD4) gene. Hum Mol Genet 2(6): 767-773.
8. Guo G, Roettger ME, Shih JC (2007) Contributions of the DAT1 and DRD2 genes to serious and violent delinquency among adolescents and young adults. Hum Genet 121(1): 125-136.
9. Lee HJ, Lee HS, Kim YK (2003) D2 and D4 dopamine receptor gene polymorphisms and personality traits in a young Korean population. Am J Med Genet B Neuro psychiatr Genet 121B(1): 44-49.
10. Persico AM, Vandenbergh DJ, Smith SS, Uhl GR (1993) Dopamine transporter gene polymorphisms are not associated with polysubstance abuse. Biol Psychiatry 34(4): 265-267.
11. Tiihonen J, Rautiainen MR, Ollila HM (2015) Genetic background of extreme violent behavior. Mol Psychiatry 20(6): 786-792.
12. Brunner HG, Nelen M, Breakefield XO, Ropers HH, van Oost BA (1993) Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A. Science 262(5133): 578-580.
13. Caspi A, McClay J, Moffitt TE (2002) Role of genotype in the cycle of violence in maltreated children. Science 297(5582): 851-854.
14. Fergusson DM, Boden JM, Horwood LJ, Miller A, Kennedy MA (2012) Moderating role of the MAOA genotype in antisocial behavior. Br J Psychiatry 200(2): 116-123.
15. Lesch KP, Bengel D, Heils A (1996) Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. Science 274(5292): 1527-1531.
16. Arbelle S, Benjamin J, Golin M (2003) Relation of shyness in grade school children to the genotype for the long form of the serotonin transporter promoter region polymorphism. Am J Psychiatry 160(4): 671-676.
17. Fox E, Ridgewell A, Ashwin C (2009) Looking on the bright side: biased attention and the human serotonin transporter gene. Proc Biol Sci 276(1663): 1747-1751.
18. Benjamin J, Li L, Patterson C (1996) Population and familial association between the D4 dopamine receptor gene and measures of Novelty Seeking. Nat Genet 12(1): 81-84.
19. Caspi A, Sugden K, Moffitt TE (2003) Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 301(5631): 386-389.
20. Patkar AA, Berrettini WH, Hoehe M (2002) Serotonin transporter polymorphisms and measures of impulsivity, aggression, and sensation seeking among African-American cocaine-dependent individuals. Psychiatry Res 110(2): 103-115.
21. Zammit S, Spurlock G, Williams H (2007) Genotype effects of CHRNA7, CNR1 and COMT in schizophrenia: interactions with tobacco and cannabis use. Br J Psychiatry 191: 402-407.
22. Hirata Y, Zai, CC, Nowrouzi B, Beitchman JH, Kennedy JL (2013) Study of the catechol-o-methyltransferase (COMT) gene with high aggression in children. Aggress Behav 39(1): 45-51.
23. Ray LA, Bryan A, Mackillop J (2009) The dopamine D Receptor (DRD4) gene exon III polymorphism, problematic alcohol use and novelty seeking: direct and mediated genetic effects. Addict Biol 14(2): 238-244.
24. Zai CC, Ehtesham S, Choi E (2012) Dopaminergic system genes in childhood aggression: possible role for DRD2. World J Biol Psychiatry 13(1): 65-74.

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