The Relationship Between Dopamine-Related Gene Methylation, Family Environment, and Creativity

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Abstract

The debate on “genetics and environment” has always been a core issue in creativity research, but currently no studies have addressed the molecular biological mechanisms through which environment and gene-environment interactions influence creativity. In recent years, with the rise of epigenetics, revealing the epigenetic mechanisms that affect psychological and behavioral processes has become a hotspot in psychological research. As a bridge between environment and genome, epigenetic research provides an opportunity to uncover the molecular biological mechanisms through which environment and gene-environment interactions affect creativity. This study takes dopamine-related genes, family environment, and their interactive effects on creativity as entry points to investigate the epigenetic mechanisms influencing creativity, and on this basis, explores the molecular biological mechanisms through which environment and gene-environment interactions impact creativity. The specific research contents are as follows: (1) Through systematic investigation of the relationship between methylation patterns of dopamine-related genes and creativity, to screen for genes whose methylation patterns are associated with creativity; (2) For the screened genes, to further examine the mediating role of their methylation patterns in the influence of family environment and its interaction with genetic polymorphisms on creativity. This study will help reveal the epigenetic mechanisms of creativity and deepen the understanding of the mechanisms of genetic and environmental influences on creativity.

Full Text

The Relationship Between Methylation of Dopamine-Related Genes, Family Environment, and Creativity

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Abstract: The "nature versus nurture" debate has long been a central focus in creativity research. However, the molecular biological mechanisms through which environmental factors and gene-environment interactions influence creativity remain unexplored. With the rise of epigenetics, identifying the epigenetic basis of psychological and behavioral traits has become a major frontier in psychological science. As a bridge between environment and genome, epigenetics offers a unique opportunity to uncover the molecular mechanisms underlying environmental and gene-environment effects on creativity. This study examines the epigenetic mechanisms of creativity by investigating the relationships among dopamine-related genes, family environment, and their interactive effects on creativity. Specifically, the research includes: (1) a systematic investigation of methylation patterns in dopamine-related genes to identify those associated with creativity; and (2) an examination of whether methylation patterns mediate the effects of family environment and gene-environment interactions on creativity. This work will advance our understanding of the epigenetic mechanisms of creativity and deepen our knowledge of how genetic and environmental factors jointly shape creative potential.

Keywords: creativity, gene, environment, epigenetics, DNA methylation
Classification: B845

1. Problem Statement

The "nature versus nurture" debate has been a persistent and fundamental issue in creativity research. Like other important psychological traits and behaviors, individual differences in creativity are not determined by genetic or environmental factors alone, but rather by their combined influence. Early quantitative behavioral genetics research, primarily using twin study paradigms, attempted to quantify the relative contributions of genetic and environmental factors to creativity. These studies revealed moderate heritability and non-shared environmental effects (Canter, 1973; Grigorenko et al., 1992; Nichols, 1978; Reznikoff et al., 1973), findings that have been corroborated by more recent research (Hur et al., 2014; Kandler et al., 2016; Piffer & Hur, 2014; Roeling et al., 2017). However, because quantitative behavioral genetics can only infer genetic and environmental effects by comparing correlations among individuals with varying degrees of genetic relatedness in shared and non-shared environments, it cannot directly identify specific genetic or environmental factors associated with creativity.

To identify the actual genetic and environmental factors influencing creativity, researchers have conducted numerous molecular genetics studies with fruitful results. For genetic factors, studies using candidate gene approaches have identified multiple polymorphisms in dopamine neurotransmitter pathway genes that may be associated with creativity, including those in the catechol-O-methyltransferase (COMT) gene, dopamine transporter (DAT) gene, dopamine D2 receptor (DRD2) gene, and dopamine D4 receptor (DRD4) gene. For environmental factors, research has demonstrated that early life experiences, particularly family environment, significantly impact creativity. Additionally, studies on gene-environment interactions have found significant interactive effects between dopamine-related genes and family environment on creativity. These findings collectively suggest that dopamine-related genes, family environment, and their interactions may be important sources of individual differences in creativity.

Despite these advances, critical questions remain regarding the underlying molecular biological mechanisms through which dopamine-related genes, family environment, and their interactions influence creativity. Most importantly, the lack of knowledge about the molecular biological mechanisms by which family environment affects creativity has prevented researchers from effectively linking genetic and environmental factors and from elucidating the molecular mechanisms underlying gene-environment interactions.

Recent developments in epigenetics offer a promising solution to this problem. Epigenetics complements classical genetics by examining how environmental factors induce epigenetic modifications that regulate gene transcription and expression without altering the DNA sequence itself (Bird, 2007; Jaenisch & Bird, 2003; Petronis, 2010). This perspective reveals that environmental factors can influence gene expression and function through epigenetic regulation of the genome, thereby affecting physiology, psychology, and behavior (Bagot & Meaney, 2010; Meaney, 2010; Roth, 2012; Szyf & Bick, 2013; Zhang & Meaney, 2010).

Research on the epigenetics of psychological traits has shown that DNA methylation, a primary form of epigenetic modification, is closely associated with individual differences in behavior and may serve as a "bridge" between environment and genome, mediating the effects of environmental and gene-environment interactions on psychological outcomes (Barker et al., 2018; Mulder et al., 2017; Zhang & Meaney, 2010). These findings redefine our understanding of how environment and gene-environment interactions influence behavior and provide important insights into the potential molecular mechanisms underlying environmental and interactive effects on creativity. Based on this evidence, we hypothesize that methylation of dopamine-related genes may be an important factor influencing individual differences in creativity and may serve as a key molecular mechanism mediating the effects of family environment and gene-environment interactions on creative potential.

Therefore, this study aims to investigate the relationship between methylation of dopamine-related genes and creativity, and to explore the mediating role of gene methylation in the effects of family environment and gene-environment interactions on creativity. This research will deepen our understanding of the molecular biological mechanisms through which environment and gene-environment interactions influence creativity and contribute to a more integrated understanding of how genetic and environmental factors shape creative ability.

2.1 Dopamine-Related Genes and Creativity

Since Reuter et al. (2006) published the first molecular genetics study on creativity, numerous investigations have examined candidate genes in the dopamine neurotransmitter pathway (Ren et al., 2019; Li et al., 2016; Yi et al., 2013). Given the well-established links between dopamine function and creativity-related cognitive processes (Boot et al., 2017; Chermahini & Hommel, 2010; Cools & d' Esposito, 2009; Flaherty, 2005), genes in the dopamine pathway have been considered prime candidates for creativity research. Using candidate gene approaches, researchers have identified multiple polymorphisms associated with creativity in the COMT, DAT, DRD2, and DRD4 genes (Han et al., 2018; Jiang et al., 2015; Lu & Shi, 2010; Mayseless et al., 2013; Runco et al., 2011; Takeuchi et al., 2015; Zhang & Zhang, 2016; Zhang et al., 2014a). Additionally, based on polygenic contribution theories, researchers have examined interactions among different dopamine pathway genes and identified potential multivariate gene-gene interactions (Murphy et al., 2013; Zabelina et al., 2016; Zhang et al., 2014b).

2.2 Family Environment and Creativity

Research on family environmental influences on creativity has systematically examined factors including family socioeconomic status, family atmosphere, and parenting styles. Studies on socioeconomic status and family atmosphere have found that higher socioeconomic status and positive family environments promote creativity (e.g., Dai et al., 2012; Zhang et al., 2018; Li et al., 2004; Shi & Shen, 2007; Wang et al., 2009). Research on parenting styles has shown that positive approaches (e.g., autonomy support, democratic parenting) enhance creativity, while negative approaches (e.g., psychological control, authoritarian parenting) inhibit it (e.g., Fearon et al., 2013; Mehrinejad et al., 2015; Miller et al., 2012; Moltafet et al., 2018; Zhang et al., 2014). However, despite identifying these potential environmental influences, current research remains at the psychological and behavioral level, with no studies investigating the molecular biological mechanisms through which family environment affects creativity.

2.3 Dopamine-Related Gene × Family Environment Interactions and Creativity

Because individual development results from the interaction of genetic and environmental factors, creativity and its individual differences are shaped by both rather than by either alone (Bouchard Jr et al., 1993). Individuals with different genetic backgrounds may show differential sensitivity to the same environment, and identical genotypes may respond differently to different environments. Therefore, to accurately identify the causes of individual differences in creativity, it is essential to examine gene-environment interactions.

Our previous work has demonstrated interactive effects between dopamine pathway genes and parenting styles on creativity. For example, studies on DRD2 and COMT genes found that authoritarian, authoritative, and permissive parenting, as well as maternal overprotection, influenced creativity only in individuals carrying specific alleles or allele combinations (Si, Su et al., 2020; Si et al., 2018; Si, Zhang et al., 2020). Although these studies confirm the importance of gene-environment interactions, the lack of knowledge about the specific molecular biological mechanisms of environmental effects prevents further elucidation of the mechanisms underlying these interactions.

2.4 Family Environment and Methylation of Dopamine-Related Genes

DNA methylation, one of the earliest discovered epigenetic modifications, is widespread in higher organisms. It occurs primarily at CpG islands (regions rich in CpG dinucleotides) through the action of DNA methyltransferases, which convert cytosine to methylcytosine at the 5’ end of CpG dinucleotides. DNA methylation can suppress gene expression by altering chromatin structure, DNA conformation, and DNA-protein interactions. Generally, increased methylation in gene promoter regions inhibits expression, while decreased methylation enhances it (Bagot et al., 2014).

Environmental factors can regulate gene expression and function through methylation modifications, thereby influencing development and psychological traits (Bagot & Meaney, 2010; Meaney, 2010; Roth, 2012; Szyf & Bick, 2013; Zhang & Meaney, 2010). Moreover, research suggests that although DNA methylation does not involve changes to the DNA sequence itself, individual differences in DNA sequence may moderate the effects of environmental factors on methylation. For a given gene, the same environmental factor may produce different methylation effects depending on an individual’ s alleles, leading to different psychological and behavioral outcomes (Barker et al., 2018; Mulder et al., 2017).

Studies have shown that environmental factors significantly influence methylation of dopamine-related genes. For example, COMT gene methylation has been linked to stress-related environmental factors (Moriam & Sobhani, 2013; Robinson et al., 2013; Ursini et al., 2011; Vaessen et al., 2015). While most epigenetic research on family environment has focused on stress-related genes (e.g., HPA axis genes, glucocorticoid receptor genes), a few studies have examined dopamine genes. One study found significant interactions between adolescents' DAT genotype and paternal/maternal externalizing problems on DAT methylation (Cimino et al., 2019). Another study reported similar findings regarding maternal psychological traits and DAT methylation in adolescents with eating disorders (Cimino et al., 2021). These findings provide preliminary support for the influence of family environment and gene-environment interactions on dopamine gene methylation.

2.5 Methylation of Dopamine-Related Genes and Creativity

Although theoretical models such as Feist' s (2010) "Functional Model of Personality and Creativity" have emphasized the importance of epigenetic phenomena for creativity, epigenetic research on creativity remains limited. In one of the few review articles, researchers theoretically analyzed epigenetic factors influencing artistic creativity, proposing that methylation of neurotransmitter-related genes (e.g., dopamine-related genes) may be an important epigenetic mechanism (Karlic & Baurek, 2011).

Recent studies have demonstrated that methylation of dopamine-related genes significantly affects creativity-related cognitive functions. For instance, COMT methylation is associated with working memory, executive function, and prefrontal activation during tasks (Alelu-Paz et al., 2015; Ibrahim et al., 2018; Ursini et al., 2011; Walton et al., 2014). DRD2 methylation has been linked to executive control network connectivity in individuals with addictive behaviors (Hagerty et al., 2018). A twin study found that differences in methylation of multiple dopamine genes (COMT, DAT, DRD2, DRD4) between monozygotic twins predicted their performance on executive function tasks (Lewis et al., 2019). Additionally, methylation of COMT, DRD2, and DRD4 genes has been implicated in the pathogenesis of creativity-related psychiatric disorders such as schizophrenia and ADHD (Abdolmaleky et al., 2006; Kordi-Tamandani et al., 2013; van Mil et al., 2014; Yoshino et al., 2016). Based on this evidence, we hypothesize that methylation of dopamine-related genes represents an important epigenetic mechanism influencing creativity, and this study will examine this hypothesis as a central focus.

3.1 Research Content

This study will first investigate the relationship between methylation patterns of dopamine-related genes and creativity, and then explore the relationships among family environment, genetic polymorphisms, methylation patterns, and creativity. The specific research contents include:

1. **Relationship between methylation patterns of dopamine-related genes and creativity:** Identifying dopamine-related genes whose methy-

lation patterns are associated with creativity is the foundational work of this study. Using a cross-sectional design, we will systematically examine the relationship between methylation patterns of dopamine-related genes and creativity to screen for relevant genes, providing a basis for subsequent investigations of mediating mechanisms.

2. **Relationships among family environment, dopamine-related gene polymorphisms, methylation patterns, and creativity:** For the identified genes, we will employ a cross-lagged longitudinal design to examine whether their methylation patterns mediate the effects of family environment and gene-environment interactions on creativity.

3.2 Research Protocol

To provide comprehensive information for future research, this study will simultaneously examine methylation patterns of multiple genes in the dopamine neurotransmitter pathway (COMT, DAT, DRD2, and DRD4). Given that our participants will be primarily college students and adolescents, we will use saliva samples for methylation detection to facilitate recruitment and minimize participant burden. Although methylation patterns in saliva cells may differ from those in brain tissue, previous research has demonstrated high correlations between the two (Braun et al., 2019; Smith et al., 2014).

The research protocol will be implemented in two stages:

Stage 1: In a college student sample, we will comprehensively detect methylation patterns in the promoter regions of COMT, DAT, DRD2, and DRD4 genes. Using both single-site and gene-level methylation analyses, we will systematically examine their relationships with creativity to identify genes whose methylation is associated with creative potential.

Stage 2: Based on Stage 1 results, we will select genes for further methylation analysis and genotyping. In a primary and secondary school student sample, we will conduct methylation analysis and genotyping of the selected genes. Using longitudinal tracking data and a cross-lagged design, we will examine whether later methylation patterns mediate the effects of early family environment (including socioeconomic status, family atmosphere, and parenting styles) and early gene-environment interactions on later creativity.

[Figure 1: see original paper]

4. Theoretical Framework

Research on the genetic basis of psychological traits has advanced to the molecular biological level. However, as research has progressed, scientists have recognized that in addition to classical genetic factors (e.g., DNA sequence variation), epigenetic factors (e.g., DNA methylation) can regulate gene expression and function without altering the DNA sequence itself. This suggests that epigenetic factors are equally important as genetic factors for gene expression and function, and that a comprehensive understanding of molecular mechanisms must consider both (Bird, 2007; Petronis, 2010).

Creativity is closely linked to dopamine neurotransmitter function, and recent evidence indicates that methylation of dopamine-related genes significantly influences creativity-related cognitive functions. We therefore hypothesize that methylation of dopamine-related genes represents a potentially important epigenetic mechanism underlying creativity. This study will examine the relationship between dopamine gene methylation and creativity from an epigenetic perspective, aiming to reveal the epigenetic mechanisms of creativity and deepen our understanding of its molecular biological basis.

Furthermore, as a "bridge" between environment and genome, epigenetics provides a new perspective for understanding the relationships among genetics, environment, and creativity. Previous research, lacking knowledge of molecular mechanisms through which environmental factors influence creativity, could only examine environmental and gene-environment effects at the psychological and behavioral levels. This prevented an integrated understanding of how genetic and environmental factors jointly shape creativity. Epigenetics examines individual differences from a gene-environment interaction perspective, proposing that environmental and gene-environment effects on behavior are mediated by epigenetic factors such as DNA methylation (Barker et al., 2018; Zhang & Meaney, 2010). This provides crucial insights for revealing the molecular mechanisms underlying environmental and interactive effects on creativity.

Family environment and its interaction with dopamine-related genes have been shown to significantly influence creativity. Since environment-induced DNA methylation plays an important role in regulating dopamine gene expression and function, we hypothesize that methylation of dopamine-related genes may be the molecular mechanism through which family environment and gene-environment interactions affect creativity. This study will examine the role of DNA methylation in mediating environmental and gene-environment effects on creativity, aiming to reveal these molecular mechanisms and provide a new level of understanding of the relationships among genetics, environment, and creativity.

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Note: Figure translations are in progress. See original paper for figures.

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