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Behavioral Genomics

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Synonyms

Gene; Genetics; Omics

Definition

The influence of gene expression on behavior.

Introduction

The diversity of behavior across the animal kingdom, including both invertebrate and vertebrate classes, is vast, complex, and is not always predictable or easily explained by physiological makeup (Harris and Hofmann 2014). Nature versus nurture debates have been long standing; however, since the development of genomic analysis, it has become apparent that there is a relationship of environmental impact on physiological and behavioral phenotypes, inextricably linking nature and nurture together in the phenotypic expression of diverse behaviors (Hofmann 2003).

The primary constituents of deoxyribonucleic acid (DNA) are four nucleic acids: adenine (A), guanine (G), thymine (T), and cytosine (C) arranged in a double helix. Sections of DNA of a specific order, called genes, are hereditary and some encode for proteins that form and maintain cellular components and processes throughout an organism. Genes are either active or silent, and vary depending on hereditary succession. Gene regulatory expression can be modified, however, especially during developmental periods, by events such as toxin exposure, malnutrition, or hypoxia (Khurana et al. 2019; Lalonde et al. 2020; Murray et al. 2020). These events lead to changes in offspring that can often be heritable – known as epigenetic modification. Other behavioral differences can occur through chromosomal or gene mutations and deletions that lead to permanent changes in the DNA sequence. The advance of molecular technology used to study modifications, mutations, and heritable status of the genome has expanded scientific understanding and exploration of different aspects of animal behavior, such as cognition, social interactions, and pathologies.

Cognition

Often defined as the ability to acquire and process new knowledge, cognition involves experiential

learning, perception, short- and long-term memory, evaluation, and decision making. Cognition in animals with neural complexity comprises multiple brain regions and neural pathways. Normal cognitive function is important in an animal's success, which, on a basic level, is survival and reproduction.

Epigenetic regulation of parental alleles, variants of a gene, can lead to monoallelic expression or co-expression providing a refined modulatory effect on neural networks (Ho-Shing and Dulac 2019). Use of novel high throughput molecular technology such as Next Generation Sequencing (NGS) can reveal DNA sequences including abnormalities and variations such as copy number variants, deletions, and insertions. Investigation of brain regions at various stages of development using NGS implicates stage-specific and region-specific sensitivity of gene regulation in the brain (Ho-Shing and Dulac 2019).

The functionality of synaptic transmission and plasticity – fundamental processes to multiple aspects of cognition – relies on proper cellular operation and maintenance. Deletion of maternally expressed genes can change neuronal firing patterns, vesicle turnover rates, as well as long-term depression and potentiation (Ho-Shing and Dulac 2019; Jiao and Li 2011; Sun et al. 2015; Wallace et al. 2017). Expression changes in the genes involved in these processes have been linked to memory deficits and interrupted sleep patterns in mice and is directly associated to Birk-Barel Intellectual Disability Syndrome as evidenced by the rescue of the phenotype with paternal alleles of the gene (Cooper et al. 2020; Gotter et al. 2011; Ho-Shing and Dulac 2019).

With chromosomal microarray analysis, a process that detects deletions and additions by comparing genomic data to a normal control, behavioral phenotypes with impaired cognition show copy number variants present in a specific gene, CHRNA7 (Gillentine et al. 2017). Duplication of CHRNA7, a gene that encodes for a subunit of a neuronal nicotinic acetylcholine receptor, is related to intellectual deficits, autism spectrum disorder, and attention deficit hyperactivity disorder (Gillentine et al. 2017).

Normal cognitive variation is also heavily attributed to genetic expression, which is influenced by the environment (Tucker-Drob et al. 2013). Enriched environments promote increased learning and memory function in rodents, as well as increased genetic expression in genes responsible for synaptic transmission and plasticity (Rampon et al. 2000). Environmental enrichment alters cognitive abilities sufficiently such that substantial research is focused on ameliorating disorders by using it as a treatment, such as in Alzheimer's disease, which presents with cognitive decline and memory loss (Griñán-Ferré et al. 2018; Jake Rogers et al. 2019).

Developmental plasticity through environmental exposure can lead to a variety of adaptive and maladaptive cognitive phenotypes (Lafuente and Beldade 2019). Behavioral modifications through context-dependent genetic expression, induced by the environment, may be heritable and occur through a myriad of multifaceted processes such as histone acetylation, methylation of CpG islands on gene promotor regions, and microRNA regulation. The end results are a change in differential expression and a downstream effect on cellular functioning and neural networks. The changes in cognitive abilities can vary depending on the species and the stage of development. Further to cognitive function, social behavior is an important aspect of animal behavior and is subject to genetic influence.

Social Interactions

Social interaction is not a significant component of all animal classes, but it is pertinent for many, especially in nonhuman primates (Sueur and Mery 2017). Social interactions influence group hierarchy, learning, and mating success (Kurvers et al. 2014; Senior et al. 2016; Silk et al. 2003; Sueur and Mery 2017).

Hierarchy in some social groups leads to increased mating success and preference as well as preferred resource allocation. Inherited phenotypes can lead to offspring dominance succession; however, candidate genes for social dominance have not been replicable in other studies (van der

Kooij and Sandi 2015). Relatable traits for aggression and reward behavior, however, have been associated with social rank in offspring (van der Kooij and Sandi 2015).

When presented with a novel conspecific, vervet monkey reactions to the strangers were recorded and analyzed, showing variability in aggression that was associated with genetic differences (Jeffrey Rogers 2018). Analysis of grooming behavior in chimpanzees has shown variations in the arginine vasopressin receptor gene, AVPR1A (Jeffrey Rogers 2018). Increasingly, multiple studies are producing similar results, providing further evidence of a genetic component to social behavior in animals.

Adaptive cognition and social interaction have implications for survival and fitness; however, genetics can also influence deleterious diseases and disorders.

Pathology

Predominantly, animal research into behavioral pathology focuses on human-comparative animal models and are often not wild, free range expressed behaviors; however, some researchers have begun implementing tasks devised to enhance animal participation rather than forced manipulation (Spanagel 2017). Early research in the 2000s began to link genetics as a putative factor in psychiatric disorders (Inoue and Lupski 2003). Technology quickly advanced over the next two decades and led to sincere developments in genetic predispositions and foundations for a number of disorders such as schizophrenia, bipolar disorder, major depressive disorder, and addictions (Maldonado et al. 2021; O'Donovan and Owen 2016).

Increased expression in regulatory genes in the ventral tegmental area and a decrease in DNA methylation within the prefrontal cortex of rodent animal models have been associated with food addictive behaviors (Maldonado et al. 2021). Substance abuse addictive behaviors are also explored using animal models, including transgenic mutant models, whereby researchers utilize gene editing,

such as CRISPR/Cas9, to modify a gene of interest by insertion or silencing (Spanagel 2017).

Contextually-inappropriate aggression has been linked to attention deficit hyperactivity disorder, schizophrenia, and bipolar disorders and is another focus of human-comparative animal studies (Zhang-James et al. 2019). Excessive aggression and violence are maladaptive behaviors modeled in feral animal studies that have illuminated serotonin signal malfunction through receptors (de Boer 2018). A large, integrated analysis of the human genome; animal transcriptomes from mice, rats, zebrafish, and *Drosophila*; and genetic knock-out studies has linked aggression to functional gene pathways common to both humans and animals, leading to putative targets for further research in psychiatric disorders (Zhang-James et al. 2019).

Anxiety can lead to inhibition, indecisiveness, and retreat of social interactions. For some animals, inhibition and reluctance to explore can be a protective mechanism and increase chances of survival; however, it could also lead to loss of opportunity for food and potential mates. Anxiety disorders in humans are common and research on animal models is abundant (Purves et al. 2020; Schiele and Domschke 2018). Serotonergic and methyltransferase genes are among the list of putative targets for treatment of anxiety disorders (Gottschalk and Domschke 2017). Some evidence has also linked single nucleotide polymorphisms (SNP), which is a gene with a substituted nucleotide, to anxiety; however, the combined efforts of genetic research currently does not account for the heritability of anxiety disorders, leading researchers to turn to epigenetic modifications (Schiele and Domschke 2018).

Relevance to Understanding Human Behavior

Often, animal models aim to glean information that might ultimately be relevant to human phenotypes. The study of behavioral genomics is longstanding in human models as well, beginning with Sir Francis Galton, who studied twins who varied in reported similarity to ascertain the extent

to which individual differences in some traits, such as intelligence, appear heritable. He suggested that similar twins remained similar as they aged, even if they were raised in different environments. This approach led Galton to conclude that genetics is a major determinant of human behavior (Galton 1875). Today, research has highlighted the role of genetics in accounting for upward of 20–50% of variance in human intelligence (Plomin and Von Stumm 2018). Researchers now recognize the role of gene x environment interactions in shaping psychology and behavior. For example, Caspi et al. (2002) showed that adverse effects of childhood maltreatment in terms of manifestation of conduct disorder were strongest among children who also exhibited low monoamine oxidase (MAOA) activity via a functional polymorphism in the gene encoding for MAOA. Other research has demonstrated that individuals exposed to stressful life circumstances are more likely to experience depression and suicidality if they also have a short allele in the promoter region of the serotonin transporter (5-HT T) gene relative to those who were homozygous for the long allele (Caspi et al. 2003). Today, the diminishing cost of genomic sequencing has made the field more accessible, leading some to describe behavioral genetics as a postgraduate growth area in the field of psychology (Willyard 2010).

Conclusion

Animal behavior is complex and variable across species, sexes, and stages of development. Within each of those categories, there is significant variability in many behavior phenotypes including but not limited to cognition, social interaction, aggression, and anxiety which appear to be best predicted by consideration of both genetic and environmental factors. Modification of gene expression can occur via different intricate processes influenced by the environment and by parental inheritance that can be linked to variability in animal psychology and behavior.

Cross-References

- ▶ Alleles
- ▶ Candidate Gene
- ▶ Copy Number Variant
- ▶ Genotype
- ▶ Heritability of Behavior
- ▶ Methylation
- ▶ Nature Versus Nurture

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