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Investigating the Formation of Consciousness Through Transcriptomic Analysis

Yutong Zhu[1,a,*]

[1]*The Chinese University of Hong Kong, Hong Kong, China*
a. 1155211238@link.cuhk.edu.hk
**corresponding author*

Abstract: Consciousness research is one of the most important research in the development of science. People have always been exploring the formation of consciousness and the mechanism of human brain. With the development of consciousness formation research, the complexity of the brain and the elusive nature of consciousness make it challenging to identify the exact neural mechanisms and lead to the limitation and stagnation of research. Transcriptomics has become a powerful tool in the field, providing advanced insights into the molecular mechanisms behind consciousness through comprehensive analysis of the transcriptome. Transcriptomics in the field of consciousness formation research also has some challenges and difficulties that researchers should pay more attention to. This review analyzes the current applications of transcriptomics in consciousness research, and discusses the challenges and future directions. While summarizing the progress of transcriptomics in consciousness research, it also puts forward the prospect and domain of future development, aiming to provide theoretical basis and possible development direction for the application of transcriptomics in consciousness formation research in the future.

Keywords: Consciousness, transcriptomic analysis, gene expression.

1. Introduction

The study of consciousness is a profound and complex endeavor that has long captivated the minds of philosophers, psychologists, neuroscientists, and cognitive scientists. The study of the origin of consciousness can be traced back to the philosophical thinking of ancient Greece. Plato believed in the immortality of the soul, while Aristotle focused on the rational capacity of the soul, linking it closely to the body [1]. These early philosophical inquiries set the stage for later scientific explorations into the nature of consciousness.

With the advent of neuroscience, researchers have sought to identify the neural correlates of consciousness (NCC), aiming to understand how specific brain activities give rise to conscious experiences [2]. To get closer to the truth, theories including the Higher-order Theory (HOT), the Integrated Information Theory (IIT) and the Global Workspace Theory (GWT) have emerged to explain the nature of consciousness.

Although there are significant theoretical advancements, the complexity of the brain and the elusive nature of consciousness still make it challenging to pinpoint exact neural mechanisms. Many methods have been applied to explain this complex neural activity in the brain and gain insights into the molecular underpinnings of consciousness, among which transcriptomics is one of the most

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important methods. Transcriptomics involves the comprehensive analysis of the transcriptome, which is the entire collection of RNA molecules in a cell or tissue at a specific time and environment. Researchers can learn more about the molecular processes that control brain circuits and have a role in conscious perception by focusing on patterns of gene expression [3,4].

A variety of transcriptomic methods have been used to study the emergence of consciousness, including gene expression profiling, single-cell transcriptomics, and spatial transcriptomics, whose applications have resulted to remarkable results and developments. Gene expression profiling gives researchers a picture of a cell or tissue's transcriptional activity at a certain time by measuring thousands of genes' expression levels at once. Single-cell transcriptomics enables high-resolution analysis of gene expression in individual cells, allowing for the exploration of rare cell populations and different cell lineage tracks. Spatial transcriptomics, one of the most advanced technique in transcriptomics, can combine spatial information of tissue sections with gene expression data. While detailed pictures of brain gene expression patterns can be displayed, neurons and the spatial context in which they are connected can also be preserved. Through high-resolution spatial and single-cell transcriptomic analysis, the study [5] revealed the synergistic effect of neurons and astrocytes, which has a positive impact on the study of memory formation. At the same time, transcriptomics has also made a lot of progress in the changes of consciousness states, such as anesthesia and sleep, showing different regular changes in gene expression patterns in the brain [6,7]. Studies [7] on neurological diseases such as Alzheimer's disease have also discovered more sites and potential molecular mechanisms through transcriptomics methods, providing new directions for the treatment of neurological diseases.

Despite these promising developments, transcriptomics in consciousness research also faces several challenges. The brain's complexity, with its a large number of various cell types and complicated neural circuits, makes it difficult to interpret the plenty of data generated by transcriptomics. Also, current techniques have limitations in terms of spatial resolution, and more advanced techniques are needed to capture gene expression patterns at a high spatial resolution at the single-cell level. Moreover, the computational analysis of the data also requires sophisticated statistical and computational methods to handle the large and complex datasets. But overall, although there are still many limitations and challenges that urgent to be figured out, it is undeniable that transcriptomics holds great promise in the research of consciousness formation.

2. Background of Consciousness

The term "consciousness" in psychology describes a person's awareness of their own internal and external stimuli. It involves being conscious of one's thoughts, emotions, sensations, and surroundings. Issues related to consciousness, such as understanding the relationship between consciousness and the brain and judging the states of consciousness in different individuals and systems, have always been key to human development. Plato believed in ancient Greece that the soul was immortal, while Aristotle believed that the mind (or "nous") was the rational capacity of the soul, closely linked to the body [8]. Descartes summarized the ideas of his predecessors and proposed a dualist theory and put forth a dualist thesis, contending that the body and mind are distinct substances: the body is a material, extending reality, while the mind is an immaterial, thinking entity. The rise of neuroscience has brought a biological perspective to consciousness, and the discoveries in Broca's and Wernicke's areas have confirmed the strong connections between specific areas of the brain and conscious-related functions. Since then, people have aimed to find "neural correlations of consciousness". NCC theory has prioritized finding correlations between brain activity and consciousness, while theoretical approaches have focused on identifying explanatory connections between neural mechanisms and various aspects of consciousness [9,10].

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Nowadays, due to the complexity of the brain, the development of NCC is limited, and various theories have emerged to try to explain the nature of consciousness. NCC theory prioritizes finding correlations between brain activity and consciousness, while theoretical approaches focus on identifying explanatory connections between neural mechanisms and various aspects of consciousness. Higher-order theory(HOT) holds that consciousness arises when the brain monitors its own activity, resulting in higher-order awareness of experience [10]. Giulio Tononi proposed five axioms and five assumptions in Integrated Information Theory (IIT) and posits that consciousness corresponds to the level of integration and information processing in a system [10,11]. According to IIT, the more interrelated systems, the stronger the consciousness [11]. On the other hand, Bernard Barth's Global Workspace Theory (GWT) gives the point that consciousness arises from a global workspace in the brain in which information from specialized modules is integrated and accessible on a global scale [12].

3. Transcriptomic Analysis in Consciousness Research

3.1. Introduction to Transcriptomics

Transcriptomics is a research field that utilizes microarray technology to study the relative abundance of RNA [9], and a comprehensive analysis of a complete set of transcripts from a specific cell, tissue, organ, or entire organism at a specific time and environment. It involves the comprehensive study of the transcriptome, which is the complete collection of RNA molecules in a cell or tissue, aiming to provide functional annotation of the genome, insights into the transcriptional structure of genes, and the ability to decipher transcriptional start sites, splicing, and post-translational modifications [4,13]. Researchers analyze the transcriptome to explore gene expression patterns in neural circuits necessary to regulate conscious perception.

3.2. Applications of Transcriptomics in Consciousness Formation Research

3.2.1. Gene Expression Profiling

Gene expression profiling, an effective bioinformatics tool, is used for understanding the molecular basis of complex biological processes, including the formation of consciousness in situ. This technique can measure thousands of gene expression levels and states at the same time, which allows cells to reveal their transcriptional activity at a specific time. This can help identify genes that exhibit differential expression in various states of consciousness, providing insights into the molecular mechanisms behind consciousness. For example, researchers can use gene expression profiling to identify genes involved in neural circuits active during conscious or unconscious periods. At the same time, gene expression profiling can also help identify molecular markers associated with consciousness. Among them, certain genes, including Arc (Activity-regulated cytoskeletal-associated protein), BDNF (Brain-derived neurotrophic factor), c-fos (FBJ murine osteosarcoma viral oncogene homolog), and Npas4 (Neuronal PAS domain protein 4), associated with synaptic plasticity and neurotransmitter signaling have been identified as playing a key role in the formation and maintenance of consciousness [14-17].

3.2.2. Single-cell Transcriptomics

Single-cell transcriptomics is a technique that enables high-resolution analysis of gene expression in individual cells, which can help explore rare cell populations and different cell lineage tracks. This technique allows for specific studies of cell types, which is considered to be a crucial aspect of consciousness formation research [18.19]. For instance, a study [20] that successfully constructed

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high-resolution single-cell transcriptome maps of the hippocampus of mice with temporal lobe epilepsy (TLE) using single-cell RNA sequencing (ScRNA-seq) and single-cell RNA sequencing (SnRNA-seq). The fundamental processes of TLE associated inflammation activation and changed cell contacts were further confirmed through the mapping, which also indicated changes in gene expression of TLE associated inflammation [20]. These results offer important new information for the investigation of HS development and epileptogenesis.

3.2.3. Spatial Transcriptomics

Spatial transcriptomics is a powerful technique that combines the spatial information of tissue sections with the gene expression data. By combining histological techniques with high - throughput sequencing, spatial transcriptomics can generate detailed maps of gene expression patterns across the brain. It not only reveals gene expression profiles, but also preserves their spatial context in tissue samples. This is particularly useful in the studies of brain, where the spatial arrangement of neurons and their connections is crucial for understanding consciousness. For example, a study [21] using spatial transcriptomics on the human dorsolateral prefrontal cortex (DLPFC) demonstrated the transcriptome-wide gene expression topography across cortical laminae. The 10× Genomics Visium platform was used in this study to map patterns of gene expression and find new lamina-enriched genes [21]. The findings provided insights into the spatial organization of the brain and its implications for neurological disorders such as schizophrenia and autism spectrum disorder [21].

Moreover, spatial transcriptomics technology can map cell type and location simultaneously, which is an advantage of this technology over single-cell RNA sequencing. Because the brain is an extremely complex body, spatial transcriptomics avoids the delicate and complex operation of single-cell RNA sequencing, which requires isolating entire neurons. The development of this technology has made it more adaptable to complex neuroscience problems, including mapping various neural pathways and discovering differences in cell types in neuro-related diseases.

4. Challenges

Despite progressive achievements, transcriptomics in consciousness formation research faces several challenges. The complexity of the brain is one of the main challenges. A vast number of cell types and complex neural pathways in the brain make it difficult to interpret the large amounts of data generated by transcriptomics. Another challenge is the computational analysis of the data. The large and complex datasets of brain requires advanced statistical and computational methods to handle. Additionally, the spatial resolution of current techniques is limited, and there is a need for more advanced technologies to capture gene expression patterns at the single-cell level and with high spatial resolution. Technical limitations make it difficult to generate, process and analyze spatial transcriptomic data efficiently. In view of this, when selecting transcriptomic methods, researchers need to carefully weigh the pros and cons of various methods, and select the most suitable method according to their own biological problems and experimental conditions. For example, in the study of Alzheimer's disease, for the research on the impact of changes in gene expression in the brain on cognitive function, gene expression profiling should be the first choice [22]. To investigate the abnormal differentiation of neural stem cells in the course of disease, single-cell transcriptomics is needed. If the aim is changes in gene expression caused by the interaction of nerve cells with surrounding cells in a specific region of the brain, spatial transcriptomics is the key. Moreover, the high experimental cost of some data formation remains a significant obstacle, especially for laboratories with limited budgets.

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5. Future Directions

Future directions in transcriptomics for consciousness research include the development of new technologies and computational methods to improve spatial resolution and data analysis. Meanwhile, there is also a need for more interdisciplinary approaches, combining transcriptomics with other omics technologies, including genomics, epigenomics and proteomics, to comprehensively analyze the molecular mechanism behind consciousness. Additionally, combining transcriptomic data with other types of data, like imaging data, can provide insight into the spatial organization of gene expression in the brain. For example, single-cell transcriptomics and proteomics have already been effectively combined for analysis with transformer, which further demonstrates that the multi-omics approach at the single-cell level is the mainstream trend of future research in consciousness and even biology field [23]. CITE-Seq (Cellular Indexing of Transcriptomes and Epitopes by Sequencing), as one of the most advanced examples, is a method for simultaneous mRNA sequencing and surface proteins profiling using available antibodies at the single-cell level. This technique is supported by both proteomics and transcriptomics and provide abundant data of single-cell in different aspects, offering a comprehensive view of cellular functions.

6. Conclusion

This review has explored the pivotal role of transcriptomics in advancing our understanding of consciousness formation. The application of transcriptomic techniques, such as gene expression profiling, single-cell transcriptomics, and spatial transcriptomics, has provided unprecedented insights into the molecular mechanisms Among them, the underpin conscious experiences. the synergistic effects of neurons and astrocytes in memory formation, the differential gene expression patterns associated with various states of consciousness, and the potential molecular markers involved in the regulation of neural circuits have been mentioned in this review, showing the significant achievement of transcriptomics in consciousness research.

This review also outlines the future directions of transcriptomics in consciousness research and provide the thought that the development of new technologies to improve spatial resolution is a key breakthrough in the future development of transcriptomics in consciousness research. In summary, although transcriptomics has made significant contributions to the understanding of consciousness, there are still many problems that need to be worked out. The challenges and limitations identified in this review strengthen the need for continued innovation and interdisciplinary collaboration. Also, as researchers continue to improve the effectiveness and efficiency of these methods, transcriptomics will enhance our theoretical understanding of consciousness, and also provide information for the development of new therapeutic strategies for neurological diseases. The future of transcriptomic consciousness research is promising, and the continued advances in this field will lead to a more comprehensive understanding and breakthrough of this fundamental human experience about consciousness.

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