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‘Bioluminescence in Research: How the Discovery of Green Fluorescent Protein Revolutionized Biology’
- Sharanya Sriram

‘Epigenetic Mechanisms in the Pathology of Alzheimer’s Disease’
- Nikhil Dholaria
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Letter From the Editors

Sojas Wagle, Anita Singh, Anushka Sarda, and Sulekha Said

Dear Readers,

Welcome to the eighth and final issue of the second season of the IYNA Journal! We greatly appreciate your readership, continued or new. This year, we have worked hard at producing more high-quality articles for everyone to read and encouraging a growing number of high school students to submit their findings, research, and/or interviews to the journal.

We have been receiving many wonderful articles from you guys. It is clear how much the journal is improving as we progress into the new year. We would just like to thank everyone who have submitted articles to this issue and prior issues alike. Without your dedication and hardwork, we would not be able to spread the word about the amazing diversity in subject matter that neuroscience has to offer. With that being said, here are some previews of the articles in this release:

In the General Neuroscience section, Anjana Elapolu et al. describe the approach of human visual perception of physical world reality. In the Disease section, Annie Pan gives an overview on Attention Deficit Hyperactivity Disorder, Christine Shatrowsky reports on Hyperthymesia, and Nikhil Dholaria explores epigenetic mechanisms in the pathology of Alzheimer’s disease. In the Research section, Sharanya Sriram reports on bioluminescence in research and how the discovery of a green fluorescent protein revolutionized biology, Sachin Patel explores how effective Angiotensin-II is in stroke prevention, and Valencia Brown et al. research neuro-cortical coupling unravelling in the olfactory-visual saccadic pathway. In the Interview section, Chinmayi Balusu interviews Dr. Katherine Sharkey about sleep and circadian rhythms.

We would like to recognize all of our dedicated editors for helping us make this issue the success that it is. You can see all of their names and positions on our Contributors page. If you have any questions, comments, or suggestions for us, please feel free to contact us at info@youthneuro.org. We hope you enjoy reading this issue as much as we enjoyed editing it!

Best Regards,

Sojas Wagle - IYNA Journal Editor-In-Chief
Anita Singh - Managing Editor
Anushka Sarda, Sulekha Said - Senior Editors
Descriptive Approach of Human Visual Perception of Physical World Reality

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Abstract

The interpretation of what we view and how we see the physical world is referred to as visual perception. Our brain processes what our eyes congregate, creating a perception that sometimes is not parallel with reality. The brain has a peculiarity of acting in a bizarre way of perceiving the subjective physical reality of the objective state, even when there's no creation of illusion by the object. Even after multiple attempts of solving the theories behind such perceptions, our knowledge on them is still insubstantial. The mystery behind some perplexing aspects of human visual perceptions like color, luminance, motion, distance, and depth are attempted to be simplified. An amalgamation of various parameters of judgment leads to the perception of an object. This study focuses on parameters, such as psychological, physiological, interpretational, empirical, and neurological aspects. This analysis will evaluate the factors that help to convey outputs in a subjective manner under different conditions, will explain why our judgment is challenged by the moderate disparity in the framework of our field of vision, and demonstrates how much we rely on comparative analysis.

Keywords: visual perception, physical world perception, brain process, bizarre human visual perception

Introduction

The prediction of the physical reality through our sense of vision is termed visual perception. The human eye can view the world in a wider range of focus levels than any high-quality camera, yet in terms of visual perception, it often tends to get tricked into seeing things apart from reality. Sometimes our perception doesn’t quite match up with physical reality, but rather perceives an illusion that was never created by the object. Here, we attempt to illustrate some of these illusions in terms of color, luminance, motion, depth, and distance.

1. Color
Bezold Effect

The Bezold Effect was first described by Von Bezold in 1853. It occurs when the chromaticity (hue and saturation) of colors is altered due to the change in the intensity of light [1]. This effect shows the same red lines on a solid black background and a solid white background, yet the red hue appears to be lighter on the latter background. Though being the same color, both lines appear to be different to the human eye due to the corresponding backgrounds [2].

2. Luminance

Simultaneous Contrast Effect

The Simultaneous Contrast Effect was demonstrated by the German physiologist Ewald Hering. It is the visual perception of two colors as intensified or diminished when viewed simultaneously with greater or lesser exposure of light in the same direction [3].

Explanatory Strategies For Color & Luminance Perception

a. Psychological: “The color of an object or light is specified in terms of the additive mixture of three primary lights (red, blue and green).” Even though the stimulus has drastically different wavelengths of light, they are perceived as identical by the visual system [2].

b. Physiological: Mach bands are the consequence of a visual process that describes the image in terms of “edges” and “bars.” It was first demonstrated by Ernst Mach and was named after him [5].

When looking at the band along the dark edge, the color appears darker than the surrounding colors, and at the lighter edge, the color appears to be lighter than the adjacent colours, which is a direct consequence of a phenomenon known as lateral inhibition. This is important for visual perception and inhibition and enhances the representation of contrast, improving perception of edges by interneurons that pool signals over a neighborhood of presynaptic feed and send inhibitory signals back to them [6].
c. **Empirical:** The visual system evolved and formed the ability to transform small, biologically determined image patterns to useful perpetual responses that have the same frequency of occurrence [7].

*Figure 1(c) - Accumulated human experience with luminance patterns [7].*

Figure 1(c) has unique patterns that occur only once, and it is highly unlikely to have the same luminance patterns on the retina. A large catalog of such images are less effective, so a confined size of a sample can give the maximal frequency of occurrence, which corresponds to the way retinal images, roughly the size of the template shown in figure 1(c), are processed [7].

d. **Interpretational:** It can be explained by a phenomenon known as simultaneous contrast [8].

*Figure: 1(d) - shows a glare effect or luminous-mist effect [8].*

Though having the same luminance, the center white square surrounded by four dark rectangles gives an effect that light is emitted from the center [8].

e. **Neurological:** V1 transforms information received from the lateral geniculate nucleus (LGN) and distributes it to separate domains in V2 for transmission to higher visual areas. According to Hubel and Wiesel, retinal activation induced by bars of light led to the selective response of V1 neurons. In the second visual area of the primate (area V2), the segregation and compartmentalization of cells processing form, color, and depth information is evident [9].

3. **Motion**

The Barber Pole effect would best explain this attribute as its effect is “the orientation of the grating presented behind the rectangular aperture and the aspect ratio of the aperture, which in combination determine the relative contributions of local motion signals perpendicular to the gratings and parallel to the aperture borders, respectively.” [10]

**Explanatory Strategies for Motion Perception**
a. Psychological: Diagonally moving grating is perceived as moving vertically because of the narrow, vertical, rectangular shape of the aperture through which it is viewed. This shape–motion interaction endured through a wide range of parametric disparities in the shape of a window, the spatial and temporal frequencies of the moving grating, the contrast of the moving grating, complex variations in the composition of the grating and window shape, and the duration of viewing [11].

b. Interpretational: The perception of an image includes the brain’s interpretation of the image on the retina. Many 2D visual image features transpire where edges from two contrasting, yet overlapping, surfaces meet. Such compound features are “intrinsic” to neither surface and have been termed “extrinsic.” Human observers rationalize intrinsic and extrinsic aspects on the basis of depth-ordering cues that exist at occlusion periphery [12].

c. Empirical: Perceived motion can be determined by “linking retinal stimuli with moving objects according to the relative success of behaviour over evolutionary and individual time; however, by accurately modelling the relationships between moving objects and the perspective projection of their corresponding images, the simulated environment serves as a proxy for the relative success of visual behaviour instantiated in visual circuitry” [13].

d. Neurological: “In identifying an action, the perception of biological motions plays an enormous adaptive role. It may, therefore, be hypothesized that the perception of biological motions is subserved by a specific neural network” [14]. According to a functional MRI study on ‘motion areas’ involved in visual motion, processing occurred in the bilateral middle-temporal complex (V5+), the left SOG (lSOG; V3/V3A), the bilateral lingual and middle occipital gyri (V1/V2), and the ventral part of the occipito-temporal junction [15].

4. Depth

The perception of depth is substantially enhanced by the fact that we have binocular vision. This provides us with more precise and accurate estimates of depth and an improved qualitative appreciation of the three-dimensional (3D) shapes and positions of objects [16]. We took an example of inserting a pencil into a nut hole. With one eye, it was difficult to insert the pencil into the hole, whereas it was easy with two eyes. This is because with one eye, the human eye sees everything in 2D orientation, whereas with two eyes, the human eye can perceive everything in 3D orientation.

5. Distance

Ponzo Effect

This illusion is demonstrated by two lines. The line that is above appears to be longer than the line below, despite the fact that both lines are of the same length [17].

Explanatory Strategies For Depth And Distance Perceptions
a. Psychophysiological: Depth and distance are ascertained through both monocular (one eye) and binocular (two eyes) cues. The brain uses these cues to perceive depth and distance.

Monocular cue: We chose linear perspective to understand the monocular cue and how it influences the perception of depth and distance. Linear perspective occurs when two parallel lines converge as they travel away from the viewer into the distance. As we look at train tracks, for instance, the tracks appear to join together in the distance, even though they stay parallel.

Binocular cue: We chose retinal disparity to understand the binocular cue and how it influences the perception of depth and distance. One can see the difference in the images of the same object on the retina of two eyes. To demonstrate the example of retinal disparity, hold any object (pencil) close to your face, view it with just your left eye, then just your right eye, and you will see the image 'jump' back and forth.

b. Interpretational: Interpretation can be perceived by changing the distance of an object (pencil) in different angles from the observer. The retinal image appears to be different from different angles.

c. Empirical: We chose texture gradient as an example to explain the perception of depth and distance. One can see the clear texture of grass when it is right in front of one’s eyes, but as one goes further into the distance, grass appears to be blurred or isn’t clear in regard to texture.

d. Neurological: In humans, experiments using random dot stereograms have shown a stream of areas that respond to these three-dimensional cues: V1, V2, V3, VP, and V3A. V5 (hMT+). Nevertheless, all the regions activated by random dot stereograms show a correlation between the amplitude of the fMRI signal and disparity [8, 10].

Conclusion

This review on descriptive analysis is an attempt to simplify the complexities of the human visual perception of the physical world. It is a summary of how important our judgment is in situations where our comparative ability is challenged (what we perceive versus what exists in physical reality).

References


Attention Deficit Hyperactivity Disorder: An Overview

Annie Pan

Introduction

Attention deficit hyperactivity disorder (ADHD) is a chronic condition marked by persistent inattention, hyperactivity, and sometimes impulsivity [1]. To this day, between 5.29% - 7.1% of children and adolescents as well as 3.4% of adults suffer from ADHD worldwide [2]. There are over 3 million cases of ADHD each year, and ADHD has become an ongoing problem for kids and adults [3]. Throughout this article, we will look at the causes, symptoms, and solutions to ADHD.

Causes and Risk Factors

ADHD is one of the most prevalent disorders that appear during childhood. Research conducted at the National Institute of Mental Health (NIMH) and the National Institute of Health (NIH) has suggested that ADHD may be caused by interactions between genetic factors and environmental or non-genetic factors [1].

![Pre- and Perinatal Risk Factors for ADHD](image.png)

Figure 1. A chart of all risk factors associated with ADHD [7].
Like many other illnesses, a number of factors may contribute to ADHD, such as genetics, cigarette smoking and alcohol/drug use during childbirth, exposure to environmental toxins (e.g. lead) at a young age, and brain injuries [1]. Research suggests that there is a possible correlation between ADHD and pesticides. A 2010 study in *Pediatrics* found that children with higher urine levels of organophosphate, a pesticide used on produce, had higher ADHD rates [4]. Another 2010 study showed that women with higher urine levels of organophosphate were more likely to have a child with ADHD. Fetal exposure to alcohol has also demonstrated a strong correlation between ADHD and drug/alcohol abuse [4][5]. Children exposed to tobacco smoke prenatally are 2.4 times as likely to have ADHD as those who are not. But one of the biggest risk factors that lead to children developing ADHD is lead. A 2009 study found that children with ADHD tend to have higher blood lead levels than other kids. Because of lead’s toxicity, it can damage developing brain tissues and have effects on a child’s behavior [4]. Studies have shown that families with a history of ADHD are more prone to inherit the disorder. Thus, genes have been proven to play a huge role in inheriting ADHD.

There have been many suspicions over sugar being a risk factor for ADHD, but no reliable research has proven that there is a correlation between the two. Another popular belief is that allergies and sensitivities cause ADHD, but research has failed to prove the idea that diet plays a large role in the development of ADHD [4][5]. As more resources and money are being allocated towards research, researchers have the potential to gain more understanding about ADHD.

**Symptoms**

According to the Mayo Clinic, “The primary features of attention-deficit/hyperactivity disorder include inattention and hyperactive-impulsive behavior. ADHD symptoms start before age 12, and in some children, they’re noticeable as early as 3 years of age. ADHD symptoms can be mild, moderate or severe, and they may continue into adulthood.” Because of the varying effects of ADHD, afflicted individuals may need to seek varying treatments depending on the severity of their symptoms. ADHD occurs more often in males than in females, and behaviors can be different in boys and girls. For example, boys may be more hyperactive and girls may tend to be quietly inattentive. There are three subtypes of ADHD: predominantly inattentive, predominantly hyperactive-impulsive, and combined [3, 5]. The predominantly inattentive subtype occurs when the majority of the symptoms fall under being inattentive, while the predominantly hyperactive-impulsive subtype occurs when the majority of the symptoms fall under being hyperactive. The combined subtype is a mix between hyperactive and inattentive and is the most common in the US [5].

The most noticeable symptoms of ADHD is inattention, hyperactivity, and impulsivity. Children that have ADHD may be easily distracted, have trouble paying attention, fidget, and be very interruptive. They may struggle to complete activities quietly and appear to not listen even
when spoken directly to [1, 5]. Symptoms can cause children to be unable to express their feelings properly, learn subjects, and pay attention to people talking to them. These symptoms can negatively impact children in regard to their school, home, and social life [3, 5].

Figure 2. A chart of all the common symptoms associated with ADHD [8].

**Treatments**

Though there is no definite cure for ADHD, there are types of therapies and medications that can be taken to reduce symptoms. For many people, ADHD medications reduce hyperactivity and impulsivity, improving their ability to focus, work, and learn. Some medications offered to ADHD patients are stimulants. Although it may seem unusual to treat ADHD with a medication that is considered a stimulant, it is effective. Many researchers think that stimulants are effective because the medication increases the brain chemical dopamine, which plays an essential role in thinking and attention. Non-stimulants can also be offered. Doctors may prescribe a non-stimulant if a person had bothersome side effects from stimulants, if a stimulant was not effective, or in combination with a stimulant to increase effectiveness. Two examples of non-stimulant medications include atomoxetine and guanfacine. Although antidepressants are not approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of ADHD, antidepressants are sometimes used to treat adults with ADHD. Older antidepressants, which are called tricyclics, sometimes are used because they, like stimulants, affect the brain chemicals norepinephrine and...
dopamine [1, 3]. There are also different types of therapies to aid individuals afflicted with ADHD. Parents may want to take their children to behavioral therapy and social skills group if they have ADHD [6]. There are many treatments and medications available to those diagnosed with ADHD. Though there is still no cure for ADHD, over time, ADHD researchers may discover a cure and end the widespread threat of ADHD to both children and adults once and for all.

References


Epigenetic Mechanisms in the Pathology of Alzheimer’s Disease

Nikhil Dholaria

Abstract

The presence of early-onset, familial Alzheimer’s disease (AD) is rare (around 3% to 5% of cases) and may be accredited to disease-causing mutations. More prevalent, by contrast, is the late-onset, sporadic (non-Mendelian) form of AD, which reflects the interaction of both genetic and environmental risk factors as well as the disruption of epigenetic mechanisms regulating the expression levels of genes [1, 2]. Abnormal patterns of histone acetylation and methylation with anomalies in global and promoter-specific DNA methylation and a deregulation of non-coding RNA have been noted in AD patients as attenuating epigenetic shifts. Epigenetic dysfunction in AD has been linked to core pathophysiological features of the disease including excess production and accumulation of Aβ42, atypical post-translational modification of tau, axonal-synaptic dysfunction and neuritic dystrophy. Accordingly, DNA methylation, histone marks and the levels of multiple species of microRNA are moderated by oxidative stress, neuroinflammation, and Aβ42. Despite novel discoveries in transgenic mouse models and human brain tissue, further analysis and research of epigenetic shifts are of critical importance in elucidating the pathogenesis, biomarkers, and potential treatments for AD [2].

Genetic Risk Factors in Familial and Sporadic AD

Dominant, autosomal mutations in the gene encoding the Aβ42 precursor, amyloid precursor protein (APP), and in the genes encoding Presenilin (PS) 1 and Presenilin 2, the catalytic components of the γ-secretase complex that processes APP following β-secretase (BACE-1), induce a minority (approximately 5%) of familial AD cases [3,4]. APP is a single-pass transmembrane protein highly expressed in the brain, while also being metabolized in a rapid and highly complex mechanism by a series of sequential proteases, one being the intramembranous γ-secretase complex [5]. Mutations in the APP gene or the genes encoding the components of the γ-secretase complex alter the normal metabolism of the precursor protein, leading to an accumulation of neurotoxic peptides. APP processing (proteolysis) by γ-secretase generates β-amyloid (Aβ) peptides of various
lengths, including the two major isoforms: Aβ40 (about 90% of all amyloid peptides) and Aβ42 - the only difference being that Aβ42 has two extra C-terminal residues [6,7]. The result of these mutations generates extracellular senile plaques of aggregated Aβ42 (due to their hydrophobicity) and Aβ40 at times [7,8]. In addition, genome wide association studies (GWAS) and meta-analysis have tracked down other gene variants which are common in patients diagnosed with AD [8]. Further study, however, is necessary to ascertain how many and which genes in the human genome could be pathogenic.

Late-onset, sporadic (non-Mendelian) AD is considered to be multifactorial; however, it involves a strong genetic predisposition [9]. The apolipoprotein-E (APO-E) ε4 allele is the greatest genetic risk factor with more than 60% of patients being Apo-E4 carriers. Increased APP membrane insertion and processing decreased glial and blood-brain barrier Aβ42 clearance, and promotion of Aβ42 aggregation (though Aβ42-independent mechanisms are involved) are related to Apo-E4-accrued risk [2,10-12]. Nonetheless, an Apo-E4 phenotype is not sufficient enough on its own to provoke the disorder. And although additional risk genes have been identified by unbiased GWASs, genetic factors alone cannot explain late-onset AD [2,12]. It is also quite important to note that the APOE gene contains three major allelic variants at a single gene locus (ε2, ε3, and ε4), each encoding for different protein isoforms (ApoE2, ApoE3, and ApoE4) that only differ in two sites of the peptide sequence. ApoE is a polymorphic glycoprotein expressed in the liver, brain, macrophages, and monocytes. It participates in cholesterol and lipid transportation involved in neuronal growth, repair from injury, nerve regeneration, immunoregulation, and activation of lipolytic enzymes. The variant alleles pose rather contradictory functions, where the APOE ε2 allele is thought to have a protective effect, while the APOE ε4 allele increases risk in late-onset AD [8].

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**Figure 1:** The amyloid cascade hypothesis. This is the lead hypothesis in AD pathology. The figure summarizes the major pathways which leads to the common symptoms of AD patients [21].
Environmental Risk Factors in AD

It is important to not neglect environmental factors when discussing the mechanisms and pathology of AD. Research suggests that a host of factors beyond genetics may play a role in the development of AD. Risk factors include age, gender, cerebral trauma, stroke, hypertension, diabetes, chronic stress and depression. A strong deal of interest lies upon the relationship between cognitive decline and vascular conditions like heart disease, hypertension, and stroke. Also, metabolic conditions, such as diabetes and obesity, seem to play a role in the development of AD. Other findings also state that the climate and physical quality of the environment may have an effect on developing dementia, particularly AD. These environmental factors are superimposed on a genetic foundation and act via cellular mechanisms like inflammation, apoptotic cell loss, and oxidative stress. Ongoing research may help people understand how to reduce the risk factors of this disease and how one may also reduce the risk of AD. From previously compiled research, physical activity, nutritious diets, social engagement, and mental stimulation have been associated with keeping people healthy with age. As research continues, scientists and specialists may be able to propose specific models for people to follow to reduce the risk of AD pathology as well as the risk of other neurocognitive and neurodegenerative conditions [2, 13, 14, 15].

Regulating Gene Expression: Epigenetics

Epigenetics, in simple terms, refers to gene expression. The level at which a gene is expressed can have a significant large-scale impact, even potentially causing a change in phenotype. Upregulation and downregulation are direct products of epigenetics, and this change in protein products can increase the risk of AD. Upregulation of the amyloid precursor protein may result in increased plaque quantities, increasing the risk of AD. On the other hand, the downregulation of the protein products of neuroplasticity genes could result in cognitive decline, also increasing the risk of AD.

It is generally accepted that epigenetics works through two mechanisms: modification of histones, the proteins that package DNA, and direct methylation of DNA. These two mechanisms can lead to changes in gene expression, either greatly increasing or greatly reducing the availability of mRNA, and down the line, peptides and proteins. Understanding these mechanisms may go a long way in elucidating possible treatments for AD, including the possible allosteric or competitive blocking of deacetylases and demethylases or even the hyperactivation of these enzymes. Generally, these alterations on epigenetic modifications may provide novel therapies for treating AD, and they may be added to existing therapies to construct a patient-specific therapy. Other epigenetic mechanism, though not considered pure mechanisms under epigenetics, are chromatin remodelers and non-coding RNAs (ncRNAs) [16, 17, 18].
Histone Modification

**Histone Acetylation:** Based on the identity, histone modifications performed post-translationally have varying effects on gene expression. Generally speaking, increased gene activity is associated with histone acetylation [19]. This marked gene activation is the result from the diminished basic charges of histones following acetylation, reducing the electrostatic interaction it has with the negatively charged DNA backbone. Nucleosome compaction is, therefore, relaxed, allowing transcriptional machinery to do its work [20]. The enzymes responsible for this are classified as histone acetyltransferases (HATs), and in AD, they can upregulate the proteic products of inflammatory genes, contributing to the major symptoms that are involved in the pathology of the disorder. Neuroinflammation and gliosis can, therefore, be exacerbated.

Antagonistic to HATs are histone deacetylases (HDACs), and their actions could cause a downregulation in the products of neuroplasticity genes, leading to neuronal apoptosis and neuritic dystrophy [16]. On a larger scale, the interplay between HATs and HDACs at various locations on the genome can lead to cognitive decline and personality changes, which are commonly seen in AD or pathologically similar disorders.

**Histone Methylation:** Unlike acetylation, histone methylation depends on both the form of modification and the residue of the specific amino acid in which it occurs. Facilitated by histone methyltransferases (HMTs), methylation is similar to the activity of acetylation, where the genome can vary in terms of expression. Similar to those enzymes under HDACs, histones can be demethylated via histone demethylases.

**DNA Methylation**

DNA methylation is the most studied epigenetic modification. It includes the introduction of a methyl group at cytosines preceding guanines, coined CpG dinucleotides [22]. DNA methylation is considered an epigenetic mark of repression. This, alongside the enzymes under the HDAC category, can repress the expression of neuroplasticity genes, ultimately leading to AD symptoms. The enzymes that carry this function of methylation are known as DNA methyltransferases (DNMTs) [23].
Neuroepigenetics

The nervous system is a highly specialized system in which millions of neurons and supporting glia are organized into varying structures with characteristic epigenetic and expression profiles that are associated with particular functions [24]. The importance of epigenetic mechanisms in the functioning of the nervous system is underscored by the idea that mutations in epigenetic genes cause severe mental disorders [25]. The treatment of these disorders can be interconnected with the epigenetic mechanism commonly seen in somatic cells, including histone acetylation and DNA methylation. Altering these mechanisms may play a role in symptomatic relief or even a cure. Research in AD has been focused on explaining the genesis of these epigenetic mechanisms and how they can be altered to prevent the progression of the disease. While HDAC inhibitors, such as valproic acid, sodium butyrate and others, potentiate learning and memory formation in animal models and have been useful in treating different neurological disorders, including AD, further research is required to truly elucidate the mechanism of these epigenetic enzymes [26,27]. Future research is directed towards answering these mechanisms, and in doing so, neurological research can get one step closer to treating neurological disorders.

References


The Real Life Perfect Memory: Hyperthymesia
Christine Shatrowsky

Abstract
Hyperthymesia is a neurological syndrome in which those affected remember nearly every event of their lives in perfect detail. It is extremely rare, affecting only a handful of people alive today. Although many people desire the idea of having a "perfect memory", the reality of living with hyperthymesia is often less-than-stellar.

Figure 1. Electrical Activity in the Brain [10].
Have you ever wondered what it would be like to remember all that you’ve ever experienced, in almost perfect detail? Wouldn’t it be amazing to be able to remember everything your teacher went over during class, or what it was like being an infant?

This is the astonishing reality for those living with hyperthymesia, but it’s not always as “bright and sunny” as it may seem.

What is Hyperthymesia?

Hyperthymesia, also known as Highly Superior Autobiographical Memory (HSAM), is a neurological syndrome that is characterized by a person’s ability to recall every event in their life in almost impeccable detail. It is extremely rare, as only 61 people in the world are known to have it [1].

Individuals who have this extraordinary memory are identified through two criteria: 1) they spend an inordinate amount of their time thinking about and even living through their past, and 2) they have a phenomenal ability to recall previous events with exceptional precision. What truly makes a hyperthymesiac special is their uncanny ability to remember even the most mundane circumstances and events. When asked about a specific date 10 years ago, these people with HSAM can tell you what day of the week it was, what they were wearing, what the weather was like, and any significant events that happened in the news with 97% accuracy [2].

Those with hyperthymesia are different from others who have advanced memories. People who win memory competitions, for example, have to put effort into remembering. They often utilize memory techniques such as mnemonics to successfully encode and recall information. Those with hyperthymesia, on the other hand, have a memory that works automatically and does not require conscious effort to form their highly-specific memories. Interestingly, traditional memory testing was performed on hyperthymesiacs and found that their performance was comparable to that of a control group [3]. This further supports the idea that hyperthymesiacs possess a truly unique and inborn episodic memory.

When Was it Discovered?

Hyperthymesia was discovered in 2006 by a team of researchers from the University of California, Irvine. These researchers were presented with the case of a woman called AJ, later identified as Jill Price, who demonstrated the ability to recall a seemingly-impossible number of personal events [4]. By studying Jill Price and other individuals who were later identified to have hyperthymesia, researchers were able to learn more about the syndrome.

Do Hyperthymesiacs Have Special Brains?

Researchers from the University of California Irvine found that those with hyperthymesia had differing brain and mental processing from average people. Their study found that hyperthymesiacs had variations in nine different structures of their brains, most of which were in areas known to be linked to autobiographical memory [3]. These regions include the uncinate
fasciculus, which may be involved in facial naming and recognition, and the parahippocampal gyrus, which is essential for memory formation and retrieval [5,6].

What's it Really Like to Live With Hyperthymesia?

According to HK, a hyperthymesiac interviewed by the National Institute of Health, dates and events just “come into” his mind. “I remember everything that happens during my day. All of it is easy to remember. I feel like I am a walking computer sometimes. The information just gets stored in my brain. It can get distracting but I can let it go too.”

When asked about whether he thinks about his memories a lot, HK responded with, “Well, I think about them quite a bit. Especially if it is something that affects me. A lot of times, when someone mentions something to me, it triggers a memory. I like telling my grandmother what certain anniversaries are. Like I’ll think about what we did 5 years ago. You know, she also takes me to appointments so that I can help her remember stuff too [7].”

As incredible as it may seem, hyperthymesia has its downsides. It is linked with Obsessive-Compulsive Disorder (OCD) behaviors, and has been known to consume the individuals who have it [8]. Jill Price suffers major disruption in her daily life. She states, “As I grew up and more and more memories were stored in my brain, more and more of them flashed through my mind in this endless barrage, and I became a prisoner to my memory… Learning how to manage a life in the present with so much of the past continually replaying itself in my mind has been quite a challenge, often a debilitating one. I have struggled through many difficult episodes of being emotionally overwhelmed by my memory through the course of my life.”

Price hopes that her brain will help solve the “riddles of the tragic disorders of memory loss” and that her story will inspire others. “For now, I hope that my story is illuminating and thought provoking for readers; and helps explain the role of memory in all of our lives — as well as that of forgetting — and how our memories to such a significant degree make us who we are [9].”

What’s Next For Research on Hyperthymesia?

At this point, the structural brain differences in hyperthymesiacs are not entirely understood. Further research on how each difference affects development of the condition may be beneficial to the current understanding of memory. Moreover, some researchers believe that the brains of hyperthymesiacs hold the key to finding a cure for Alzheimer’s disease [4]. These extraordinary brains may be the next gold mine in neurocognitive research.

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Bioluminescence in Research: How the Discovery of Green Fluorescent Protein Revolutionized Biology

Sharanya Sriram

Abstract

Across all major classes of taxa, the ability to bioluminesce has remained largely untraceable throughout evolution as it does not appear to follow any specific phylogenetic path. This fascinating natural phenomenon allows for the emission of light in living creatures through chemical reactions in the body, and for centuries, people have often pondered the potential applications of bioluminescence in the human world. This vision, however, was only made a reality upon the isolation of the green fluorescent protein (GFP) from the jellyfish species Aequorea victoria by scientist Osamu Shimomura, which would go on to completely revolutionize cell tracking and imaging as we know it today.

Bioluminescence Throughout Evolution

Convergent evolution of bioluminescence in a diverse variety of phyla suggests an importance of the trait to each organism as well as the ease at which bioluminescence is able to evolve. At the molecular level, the oxidation of luciferin allows for the emission of light with the reaction rate controlled by a catalyzing enzyme (typically luciferase or a photoprotein). While the evolution of luciferins has remained largely conserved, the array of luciferases and photoproteins is rather diverse and unique [8]. When a photoprotein binds to another ion (e.g. Ca2+ or Mg2+), it prompts a structural change in the protein, and light is emitted [2]. The claim that the evolution of bioluminescence is relatively simple is further supported by the fact that predators must only develop luciferase in order to prompt light emission from a bioluminescent prey. Bioluminescence is especially remarkable in its vast distribution across the ocean, acting as the primary visual stimulant for many organisms as sunlight grows increasingly scarce [8].
GFP Discovery and Isolation

An especially groundbreaking discovery in modern science is that of the green fluorescent protein, responsible for bioluminescence in the marine cnidarian hydrozoan *Aequorea victoria*. Isolated by Nobel laureate Osamu Shimomura, green fluorescent protein (GFP) plays a vital role in the transduction of blue chemiluminescent light into a green fluorescent light. The protein was first harvested as a by-product of a luminous photoprotein aequorin from the jellyfish *Aequorea victoria* [1]. Isolation of GFP was made possible through a performance of polymerase chain reaction on the DNA fragment coding for GFP taken from *Aequorea victoria* DNA [4]. Upon stimulation by Ca²⁺ ions, *Aequorea victoria*’s catalyzing photoprotein aequorin releases blue light, which is then absorbed by GFP and re-emitted as green light [3]. In 1992, the full green fluorescent protein gene was cloned by microbiologist Douglas Prasher, though Prasher himself was unable to see through the expression of GFP in microbes due to lack of funding. His work was continued by biologist Martin Chalfie, who successfully achieved GFP expression in E. coli and C. elegans and thus extinguished doubt that jellyfish-specific cellular conditions are necessary for fluorescence [6].

**Figure 1. Aequorea victoria**

Applications

Specific to neuroscience, GFP is especially useful in its ability to illuminate and allow for the visualization of neural networks. In a broader sense, GFP is most often fused with other proteins in order to observe the distinct protein in action. The protein of interest now expresses green fluorescent properties without losing its original function. Another application of GFP lies in bacterial pathogenesis, specifically in the study of the host-pathogen interaction wherein GFP is used as a biological marker. Insertion into the pathogen prior to replication

**Figure 2. Mouse hippocampal neurons, labeled with GFP**
enables a thorough visualization of the colonization and spread of bacteria \textit{in vivo}. GFP is successful in this role due to its low toxicity and ability to continuously replicate [5].

Roger Tsien, an American cell biologist, first utilized the fundamental principle of mutation to reap the full benefits of GFP. By altering wild GFP (with two excitation maxima) to have only a single excitation maximum at 484 nm, a single point mutant (S65T) of GFP was introduced, bearing a higher intensity and stability than naturally occurring GFP. S65T came to be known as enhanced GFP or EGFP [6]. Many colored mutants of GFP have been designed by scientists shifting the emission spectra, allowing different proteins in a system or process to fluoresce in different colors and thus making large-scale visualization plausible. Tsien and colleagues were able to create multiple fluorescent variants upon further research, such as T203Y or YFP (yellow), CFP (cyan) and BFP (blue) [6].

\textbf{Fluorescence in Research}

The institution of GFP in the bioscientific world paved the way for the discoveries of a plethora of light-emitting molecules that would go on to stake their own claims in bioluminescence imaging. One such discovery was made in 2003 by Russian biochemist Sergey Lukyanov, who stumbled upon red fluorescence in Discosoma (a coral) and was able to trace this property to a red fluorescing protein he dubbed DsRed [6]. Furthermore, FLuc (firefly luciferase), cloned from the North American firefly \textit{Photinus pyralis}, has become a standard reporter gene for \textit{in vivo} cell observation due to its prolonged light emission. A codon-optimized variant has been modified specifically for cell tracking in mammalian cells. RLuc, isolated from the sea pansy \textit{Renilla reniformis}, calls upon the catalysis of coelenterate luciferin oxidation to exhibit a bluish-green bioluminescence. Although RLuc is unable to sustain luminescence for extended periods of time, dual imaging in the same subject using both FLuc and RLuc is applicable in tracing two molecular events or two cell populations simultaneously [7].

\textbf{Conclusion}

The discovery, isolation, and application of green fluorescent protein have had a revolutionary impact on the field of biomedical and neuroscientific research. Luminescence has given way to the most stable and clear cellular and biochemical imaging achievable thus far. In a field developing at such a rapid pace, the utilization of fluorescent proteins and luciferases in visualizing neural networks is vital to understanding the connections between individual neurons. Ultimately, the most fascinating verity in this study is that the tools for progressing the global database of scientific knowledge often lie within nature itself.
References


Stroke Prevention: A Review of the Effectiveness of Angiotensin-II

Sachin Patel

Introduction

Stroke affects around 750,000 people each year and 144,000 die from it [1]. These alarming statistics make this condition the fifth leading cause of death in the world [2]. One of the most detrimental risk factors of stroke is high blood pressure [3]. Many classes of antihypertensives (AH) have been created in order to lower blood pressure, which take different paths to curtail this condition. The approaches mostly differ in their use of angiotensin-II (AII), a hormone in the body that is known to constrict blood vessels [4]. Two main classes of AH drugs have taken lead: Angiotensin II suppressors such as Angiotensin-II Converting Enzyme Inhibitors (ACEIs) and Angiotensin II promoters such as Angiotensin Receptor Blockers (ARBs). ACEIs have generally been accepted by researchers as a viable blood pressure medication. On the other hand, ARBs have been criticized more due to the counterintuitive nature of the drug [5].

Brown and Brown were the first to propose the hypothesis that this increase of AII has cerebroprotective benefits. His study showed that when patients used diuretic benzouoride (an angiotensin increases), the likelihood of stroke decreased 70 percent compared to a 27 percent when administered propranolol (an angiotensin II suppressor) [6]. A deeper look at the mechanisms behind the production of AII along with several studies reinforce Brown and Brown's initial hypothesis.

What is Blood Pressure?

The pressure blood exerts on vessel walls is referred to as blood pressure. Using a sphygmomanometer, one is able to get their own blood pressure by looking at the systolic and diastolic blood pressure (SBP and DBP respectively) [7]. The SBP is found on top representing the pressure exerted on vessel walls when the heart is contracting, and the DBP is on the bottom representing the blood pressure when the heart is at rest. When one's blood pressure becomes too high, it can cause abnormal stretching of vessel walls possibly to the point of being ripped apart. In order to placate the situation, the body sends platelets to the damaged area to repair it. However, this can easily trap in unhealthy cells which may cause weakened vessels and blockages [7].
Treatment for Hypertension

A recent study using the stroke registry at the Chang Gung Healthcare system shows that the severity of stroke correlates with high blood pressure [8]. This relationship makes controlling blood pressure the best way to prevent stroke. In order to do this, researchers first identified how blood pressure increases and decreases (see figure 1). As mentioned earlier, AII is responsible for the regulation of blood pressure. AII follows a specific process before binding to a receptor.

Angiotensinogen is a protein in the liver that is broken down via the process of a renin enzyme becoming angiotensin-I (AI) [9]. Next, AI continues its path by going through the angiotensin converting enzyme in order to become AII. This is where one group of AH drugs takes effect. Angiotensin suppressors essentially block the ACE enzyme from converting AI to AII. By blocking this transformation, it also prevents AII from binding to Type 1 (AT₁) receptors which prevents vasoconstriction, increased sodium absorption, and decreased endothelial function (see table 1). Another way to lower blood pressure in possible stroke patients has been to block AII from binding to the AT₁ receptor while allowing it to bind to Type 2 (AT₂) receptors using ARBs. This allows the body to gain the benefits of AT₂, such as vasodilation, less sodium absorption, and increased endothelial function (see table 1). It also protects the body from the dangers of AT₁ receptor [9].

ACEIs vs ARBs

Although it is apparent now that Angiotensin-II Receptor Blockers (ARBs) are more effective, it was not as effective 30 years ago—when Brown and Brown (1986) proposed their hypothesis. The scientific community widely discredited their hypothesis due to the counterintuitive nature of their claim [5]. In an effort to support Brown and Brown's hypothesis, Fournier conducted a study looking at the outcomes of major trials that tested their idea. Fournier studied the results of a Medical Research Council study conducted in 1992 [5]. Patients were either given atenolol (AII suppressor) or hydrochlorothiazide/amiloride (AII promoter) [10]. This resulted
in a stroke reduction of 17% and 33%, respectively, when tested against a placebo group, further showing the benefits of AII promoters [10]. Fournier also looked at the results of Professor Dahlöf’s trial where losartan (AII promoter) or atenolol (AII suppressor) was administered to a patient [11]. The results showed similar decreases in blood pressure (30.2/16.6 mmHg and 29.1/16.8 mmHg for AII promoter and AII suppressor respectively). However, when patients were given losartan, there were only 232 stroke outcomes compared to 306 when administered atenolol [11].

Conclusion

Overall, the benefits of ARBs drugs show to be overwhelmingly more positive than those of ACEIs. However, the problem with definitively stating that ARBs are better than ACEIs is that not enough trials have accounted for other covariates that arise from the different ages of patients. For example, patients in Professor Dahlöf’s trial were between the ages of 55 and 80 [11]. As we age, our body starts to lose more heart muscle making us more susceptible to hypotension which is another source of stroke [12]. On the other hand, patients of younger ages have healthy hearts meaning that their stroke probably spurred from hypertension [12]. It is very possible that there would be skewed data from using these two vastly different ages groups in one trial. In conclusion, in order to further the science of stroke prevention medicine, studies should focus on specific age cohorts in order to best eliminate any potential deviations that could skew the data.

References


Novel Neuro-Cortical Coupling Unravelled
In Olfactory-Visual Saccadic Pathway


Abstract

This confirmatory study aims to unravel the neural structural connectivity of “Olfactory-Saccadic pathways” extending between “Piriform and Entorhinal Cortices to Frontal Eye Field (FEF),” and to correlate its functional importance with possible clinical implications, using “Diffusion Imaging fibre Tractography”.

The confirmatory observational analysis used thirty-two healthy adults’ ultra-high b-value, diffusion imaging datasets from an Open access platform in Human Connectome Project (HCP) [17]. In all the datasets from both the sexes, fibres were traced and the neural structural connectivity was confirmed. The hemispheric differences between male and female subjects were analysed using independent sample t-test. Thus, the study confirmed the structural existences of Olfactory-saccadic pathways that may be involved in influencing the movements of the neck and eyeball gaze (saccadic eye movement), towards the spatial orientation of olfactory stimulus.

Introduction

Saccadic eye movement can be described as a visual process that can be achieved by orienting the eyes towards an object due to influence from a particular stimulus, a process controlled by CNS [16]. The olfactory-visual saccadic pathway is a new structural finding observed by our “Team Neuron”. On an attempt to trace the neural structural connectivity of Olfactory- motor pathways, we identified new structural connections between the “Piriform and Entorhinal Cortex (Brodmann’s area 27, 28 and 34) to Frontal Eye Field (FEF)” (Brodmann’s area 8). Previous evidences on these hypothetical streams remain unclear, hence we pursued these connections to confirm their structural existence, to identify their possible functional and clinical correlations [2, 3, 4].
FEF participates in the transformation of visual signals into saccades in conjunction with the supplementary eye fields, insula, and median part of the cingulate gyrus. Both the superior colliculus and the frontal eye field (Brodmann’s area 8) are the gaze centres, important for the initiation and accurate targeting of saccadic eye movements [12]. There has been evidence to suggest that vision drives olfactory perception, but there has been little indication that olfaction could modulate visual perception [3]. Shenbing Kuang & Tao Zhang performed a test to extend their understanding on vision-olfaction couplings and suggested that a functional interaction between the visual dorsal pathway and the olfactory system exists [4].

When an odour approaches from an unknown distance and from an unknown direction, it can still be perceived without looking, hence one can perceive, detect, discriminate and identify a given olfactory stimulus, then our eyes engage in rapid movement (saccadic eye movement) towards the localized stimulus for fixation [3, 4]. So, according to our hypothesis, we are suggesting that there exists some structural connectivity between the primary olfactory cortex to the frontal eye field and in case of any damage to this connectivity, it may lead to olfactory attention deficit. Olfactory impairments, as described in various neurodegenerative and psychiatric disorder, lead to deficits in the detection, discrimination, and identification of odours; therefore, they are likely to share affected brain anatomical substrates with Alzheimer’s disease, Parkinson’s disease, Obsessive-compulsive disorder (OCD), Schizophrenia, Huntington’s Disease and multiple sclerosis among others [1, 5].

Materials and Methods

The study used open access datasets of ultra-high b-value and various diffusion sensitizing direction diffusion imaging software with the in-plane resolution and slice thickness of 1.5 mm. The datasets are originally developed and reposted by Massachusetts General Hospital – US Consortium Human Connectome Project (MGH-USC HCP). The study involves Thirty-two healthy adult datasets (16 male and 16 female, between the ages of 20–59 years old, mean age = 30.4). Given de-identification considerations, age information is provided in 5-year age bins (Table-1). All participants gave written informed consent, and the experiments were carried out with approval from the Institutional Review Board of Partners Healthcare of MGH-USC HCP project [17].
Table 1 shows age information of male and female subjects

| TOTAL | 16 | 16 |

Fig. 1 Shows Coronal sections of right side of female and male brain fibres respectively in olfactory-saccadic pathway

Results

Fibre tracking datasets were collected from 32 subjects, data which confirmed the existence of a structural connectivity between the Piriform and Entorhinal cortices and the frontal eye field. The datasets were analysed within the following parameters:

(A)-Number of tracts,

(B)-Tract volume (mm³)

(C)-Tract length mean (mm)

(D)-Tract length standard deviation (mm)

Variances within the parameters observed were also evaluated among male and female subjects. According to our secondary hypothesis, we theorized that similarities would be observed in the connectivity that exist within the hemispheres with respect to each sex and also when compared between both sexes which was observed, overall, statistically significant findings were seen.

Discussion

Saccades can be initiated by peripheral stimuli through uni-modal sensory interaction but are most times influenced by the interaction of multisensory signals where the potential target exudes signals from sensory modality interaction based on visual, auditory and even tactile inputs [8, 12]. The influence of these associations on the production of saccades individually have been widely explored, predominantly establishing neural connectivity between auditory and visual pathways anatomically and
functionally but such studies pertaining to olfactory-visual associations had yet to discover anatomical and functional links between both pathways [7]. Auditory and visual sensory stimulations recorded by electroencephalogram (EEG) in an experiment conducted by Kirchner, H. et al (2009) provided evidence that the FEF is not limited to eliciting saccades purely based on visual stimulations but found evidence that the FEF responded to auditory and visual stimulation within a similar scope suggesting that the FEF processes multimodal signals [2, 6]. In light of this finding, we hypothesized and explored a possible structural connection between the FEF and the olfactory cortices.

Based on studies carried out by Judauji, J. et al (2012) and Morrot, G. et al (2001), which investigated to what extent visual cues could affect olfactory processing through visual-olfactory associations, we deduced that visual cues directly influences odor identification, perception and also attention [10]. Alternatively, studies conducted by Kuang, S. and Zhang, T. (2014) and Harvey, C. (2018) examined cross-modal integration in olfactory-visual coupling and found that olfactory cues influence gaze shifts and visual attention finding a functional pathway with which odor stimuli can initiate and guide eye movements [6]. These studies made implications of a functional association between odor and visual pathways, but the structural associations remained undiscovered [14, 15].

Our data demonstrates a new finding that structural connectivity exists between the ventral and dorsal Entorhinal cortex (Brodmann area 28 (V) & 34 (D), Piriform cortex (Brodmann area 27) and the Frontal eye field (Brodmann area 8), hence supporting previous documentation that suggested that olfactory cues could modulate visual attention, prompting saccades leading to spatial perception through neck and eye movements towards the stimuli [3, 4]. These new findings were discovered through non-invasive imaging methods where brain fibres were traced using diffusion tensor imaging from magnetic resonance imaging (MRI) data collected from both male and female subjects. The results suggest that the findings of this study are mainly significant within the population and supported our initial conjecture. The data collected within the population generally showed consistent results in the parameters observed which were number of tracts, tract volume, tract length mean and tract length standard deviation in male and female subjects on both left and right brain hemispheres. For the most part the difference in the data collected for males and females deemed insignificant. However, slight variance was observed among some variables deviating from our subsidiary hypothesis where we suggested that general hemispheric similarities would be maintain when comparing between the parameters observed. It was observed among male subjects that on average, the right side had a greater number of tracts than the left side and it was also seen that female subjects had a greater number of tracts than male subjects on the left side. These results have now unravelled a novel neuro-cortical pathway anatomically that fortifies studies that have previously indicated olfactory-visual coupling through cross-modal interaction between the senses [2, 3, 10, 11].

In converging the data of this study, the findings were deemed significant; however, we were minimally limited in the sample size and diversity in randomness of collection of data within the population. In future research, a larger sample size could be explored with additional parameters and variables such as imaging of the neuropathology of the structural pathway discovered. Also, since our
topic of study is rather contemporary, literature to directly support the scope of our study was sparse and this report should then serve as a window to explore this topic further.

In light of these findings, additional functional and clinical correlations can be deduced as a potential bio-marker for evaluating and assessing certain neurodegenerative and psychiatric disorders where olfactory attention deficits are manifested as early onset of such disorders [1, 5]. Oftentimes, olfaction is referred to as the vestigial sense and as one study showed, it can be observed that olfactory function is given little evaluation in routine clinical examination, hence minimal importance is placed on the fact that olfaction can provide conclusive assessments for cognitive function [1, 9, 13]. A decline in olfactory function has been found to be an initial symptom of numerous neurodegenerative disorders such as Alzheimer’s, and Parkinson’s disease. Hence, early identification of olfactory functional deficit can serve as an initial symptom for differential diagnostic purposes with the ability to assess and evaluate strategies and therapies that can provide neuroprotective properties. This new structural connectivity found between the olfactory and visual pathway can be used in advancing neuroimaging technique for diagnostic purposes in evaluating cognitive decline and progression of disease [1, 9].

Further research could focus on identifying and evaluating alterations in the structural integrity of the olfactory-visual pathway in patients that suffer from certain neurodegenerative diseases, as such diseases makes them susceptible to olfactory attention deficits and also the exact causes and pathological actions that lead to olfactory dysfunction in these diseases since the concept remains unclear [1, 9]. These findings should draw more attention toward how critical olfactory function assessment is in the clinical setting. We publish this in hopes that these findings are further supported since olfactory function evaluation could possibly predict neuro-aging deficit predisposition and assess cognitive decline.

**Glossary**

Brodmann area- a region of the cerebral cortex, defined by its histological structure and organization of cells.
Cortical- relating to, associated with, or depending on the cerebral cortex.
Entorhinal cortex- is an area of the brain located in the medial temporal lobe, functioning as a hub in a widespread network for memory, navigation and the perception of time.
Neuro- relating to nerves or the nervous system.
Piriform cortex- relating to the part of the cerebral cortex that receives primary input from the olfactory bulb.
Saccade- a small rapid jerky movement of the eye especially as it jumps from fixation on one point to another.
Team Neuron- organized exclusively for neuroscience and related neuroscientific research guiding purpose, mainly focusing on guiding the Basic and Clinical Neuroscience research activities among the young research scholars.
References


Sleep and Circadian Rhythms: An Interview with Dr. Katherine Sharkey

Chinmayi Balusu

Introduction
I had the honor of interviewing Dr. Katherine Sharkey, MD, Ph.D., Associate Professor of Medicine and Psychiatry & Human Behavior at the Alpert Medical School of Brown University and Assistant Dean for Women in Medicine and Science. Dr. Sharkey also serves as the Associate Director of the Sleep for Science Research Laboratory. Her research focuses on sleep and circadian rhythms, especially as they relate to mood regulation and women’s health. In this interview, Dr. Sharkey talks about her research, her path to researching sleep and circadian rhythms, and the importance of sleep medicine [1].

According to the National Sleep Foundation, a circadian rhythm is “a 24-hour internal clock that runs in the background of your brain and cycles between sleepiness and alertness at regular intervals.” Circadian rhythms, also known as the sleep/wake cycle, are controlled by the suprachiasmatic nucleus of the hypothalamus and greatly affected by light and dark [2]. Circadian rhythms function the best when people have regular sleep habits, but in times such as pregnancy and the postpartum period, they can change. Studying pregnancy and the postpartum period is an interesting model for Dr. Sharkey’s research, which focuses on mood regulation and sleep, because circadian rhythms can drastically change.

Dr. Sharkey currently conducts research for about a third of her time, where she sees people that are in the study and writes reports about the data that they’ve collected. The other portion of her time is spent on seeing patients. Dr. Sharkey is “boarded in internal medicine, sleep medicine, and psychiatry but [she] practices sleep medicine exclusively, [and she sees] patients two half-days a week.” Finally, Dr. Sharkey serves as the Assistant Dean for Women in Medicine and Science, where
she “fosters professional development for women in the department of biomedicine or the division of biomedicine at the medical school.”

Dr. Sharkey also spoke about her background. She majored in psychology at the College of Arts and Sciences at the University of Pennsylvania and completed her pre-med requirements. Dr. Sharkey began working in a sleep lab after college. At that point, she was interested in mood research but didn’t know about circadian rhythms, but she was able to work with a mentor named Mary Carskadon. It was there that she realized that sleep was “an interesting lens to look at circadian rhythms.” After working at the sleep lab for three years, Dr. Sharkey entered an MD/Ph.D. program at Rush University in Chicago. After the first two years of medical school, she studied melatonin in shift work during the four years of her neuroscience Ph.D. She did a “randomized control trial where [she] studied how melatonin can help night-shift workers adapt their circadian rhythms.” There, she learned “techniques about studying sleep and circadian rhythms that [she] didn’t know before.” After finishing medical school, she completed a residency in internal medicine and psychiatry, where she looked at the “mind-body” connection.

One study that Dr. Sharkey conducted “enrolled women and followed their sleep from pregnancy to postpartum. One of the things [they] looked at was [the women’s] circadian rhythms, and they found that the circadian rhythms did not stay stable.”

Chinmayi Balusu (CB): “Can you tell me more about your research with circadian rhythms?”

Dr. Katherine Sharkey (KS): “If I measured your circadian rhythm at a normal time, melatonin levels increase during the night and lower during the morning. If you and I were to be studied now, tonight, and three weeks from now, the circadian rhythm would be stable because most of the time people are in a regular habitat. In the pregnancy and postpartum period, there are big changes across that time period suggesting that circadian rhythms don’t stay stable because of this massive life change people have when they have a baby. And, it’s partly because of how that life change affects sleep. The most important thing for keeping our circadian rhythm in sync is the light-dark cycle. Imagine you’re a pregnant lady getting up five times a night or you’re a postpartum lady with a baby and you turn the lights on in the middle of the night to go and feed the baby.

The light-dark cycle was getting so messed up because women were getting up so much at night and also getting sleep during the day. And, one of the common things that people say in western society is ‘sleep when the baby sleeps,’ which isn’t the greatest advice because a lot of times women can’t sleep in the middle of the day when the baby is sleeping because their circadian clock is programming them to sleep at night and stay awake during the day. This can be a very frustrating experience.

In our research, we found, when looking at the magnitude of light exposure, that pregnant women got more light during the day than postpartum women. Light levels in the morning or evening were
lower during the postpartum period than they were during pregnancy. In the postpartum period, there wasn’t a robust difference between daytime and nighttime; overall, the amplitude from the lowest amount to the highest amount was decreased in the postpartum period.”

CB: “What is your current research work focused on?”

KS: “My current work involves taking women who are experiencing depression and anxiety during the postpartum period and treating them with light. With manipulation of their sleep schedule, we can stabilize those circadian rhythms as much as possible during the postpartum. We are measuring the women’s circadian rhythms throughout the course of the study and track their mood.”

As Dr. Sharkey says, “people care about postpartum depression. It affects a lot of women, and if the mother doesn’t feel well, then things may not be so great for the baby.”

CB: “Have you faced any obstacles in your research?”

KS: “One was when we did a study where we tested the breast milk of women with narcolepsy. People with narcolepsy have the intrusion of sleep into wakefulness, and they can have hallucinations or paralysis. The medications for narcolepsy are very helpful, but if you are pregnant, should you breastfeed a baby while taking those medications? We don’t know. In the study, we tested the breast milk of women who had narcolepsy and were taking medication. When we submitted the paper to a journal, it was rejected because there was too small a sample size. But how many ladies with narcolepsy who are breastfeeding can you find? So there’s difficulty in finding participants for studies, and papers are often rejected from journals or people criticize the research because there’s too small a sample size or because it seems like the conclusions are going beyond the results.”

Dr. Sharkey also spoke about the importance of circadian rhythms and sleep research:

KS: “I believe that circadian rhythms are what help us regulate and organize all of our behaviors and all of our physiology to live on this planet. It’s one of the major adaptations for living on this planet ... The sleep and circadian fields are pretty new! And, compared to other fields, the brain is a much newer frontier. We call it sleep medicine but a lot of times it’s also wake medicine. It’s not just what happens at night but also to what extent that translates into what you do in the day and how you perform your best ... There’s less known about what makes a normal circadian rhythm and what it’s important for. It’s pretty complicated to measure circadian rhythms, which is why we don’t measure it clinically very often, which is why I think there is a gap. When I talk about the pregnant women I’m studying, the women have to collect twelve samples of their saliva across the night and they have to wear dark glasses while doing it because melatonin is suppressed by bright light. It’s pretty complicated.”
CB: “Do you have any advice for students who are interested in neuroscience and psychology?”

KS: “If you want to do science, the brain is a great thing to study. With science, it has to be something that interests you! It’s important to be a good writer and communicator and learn how to work well in diverse teams; science is now about networks of people. It’s important to have leadership skills, learn to read scientific papers critically, and be able to translate scientific work to the public. We have solved the easy parts of science. What’s coming up next are the hard parts.”

References


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