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FEATURED ARTICLES

‘The Blood-Brain Barrier and How to Cross It’
-Ryan Bose-Roy

‘A Personalized Approach to Parkinson’s Disease’
-William Blair and Shafiq Qaadri

‘Prosopagnosia: A Multifaceted Disorder’
-Angela Sun

‘Can Spinal Cord Injury Be Cured Through Neuroregeneration?’
-Lorna Bo

INTERNATIONAL YOUTH NEUROSCIENCE ASSOCIATION
**Contents**

**INTRODUCTION**
- Letter from the Editors  
  | IYNA Editorial Team  
  | pages

**GENERAL NEUROSCIENCE**
- The Neurobiology Behind the Placebo Effect  
  | Anushka Sarda  
  | pages

**DISEASE**
- Protopagnosia  
  | Angela Sun  
- Treating Alzheimer’s: Gamma Oscillations Entrainment  
  | Miruna-Elena Vlad  
  | pages
- The Genetic Correlations to Autism  
  | Ali Bauer  
- Can Spinal Cord Injury Be Cured Through Neuroregeneration?  
  | Lorna Bo  
- Glutamatergic Neurotransmission in Epilepsy  
  | Rachel Klick  
- A Personalized Approach to Parkinson’s Disease  
  | William Blair and Shafiq Qaadri  
  | pages

**RESEARCH**
- The Blood Brain Barrier and How to Cross It  
  | Ryan Bose-Roy  
  | pages

**NEUROTECHNOLOGY**
- Brain Computer Interfaces (BCI)  
  | Vishnu Kumar  
  | pages
Dear Readers,

Welcome to the third issue of the second season of the IYNA Journal! We greatly appreciate your readership, continued or new.

With this issue, we have redesigned our journal process so that authors get more direct feedback from our editing team. We hope that this will improve the experience for our contributors. That being said, here are some previews of articles in this release:

In the General Neuroscience section, Anushka Sarda discusses the placebo effect and its neurobiological causes.

In the Disease section, Angela Sun introduces us to the neurological disorder of prosopagnosia, which leaves those afflicted by it unable to recognize faces or other visual stimuli. Miruna-Elena Vlad explains the potential for treating Alzheimer’s disease with gamma oscillations. Ali Bauer evaluates the role of genetics in causing autism while also offering an overview of the symptoms and treatments for autism. Additionally, Lorna Bo considers the potential for treating spinal cord injury with neuroregeneration, Rachel Klick analyzes the role of glutamergic neurotransmission in causing epilepsy and treatments for epilepsy based on regulating glutamate transmission, and William Blair and Shafiq Qaadri discuss personalizing treatments for Parkinson’s disease.

In the Research section, Ryan Bose-Roy offers a historical overview of the discovery of the blood brain barrier in addition to explaining the restraints its existence places on neuropharmacology and its role in neurological disorders such as multiple sclerosis and brain tumors. Additionally, Vishnu Kumar discusses the ability of brain computer interfaces (BCIs) to treat neurological disorders in this section.

Finally, Chidiuso Ajaero interviews Allie Caldwell of the YouTube channel Neuro Transmissions, and Sharon Samuel explains the neuroscientific mechanisms involved in the formation and loss of memories.

We would like to recognize all of our dedicated editors and assemblers 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, Robert Morgan, Scott Massey - Senior Editors
The Neurology Behind The Placebo Effect

Anushka Sarda

Abstract

The power of mind over matter has fascinated scientists and doctors for decades. Naturally, we associate treating diseases with beneficial outcomes, allowing even placebos—nonfunctional treatments—to stimulate pain relief.

In the past, the placebo effect has been coined a sham, but studies have proved that placebos often have as much of an impact as actual medication. Placebos have been used for decades, commonly as a control to test the effectiveness of new medicine. Recently, researchers have been studying the exact cause and the neurology behind the placebo effect through a series of experiments brought to light by this article.

What is the Placebo Effect?

A placebo is a substance or treatment that has no actual therapeutic effect. When given to a patient who is told that the treatment is legitimate, a placebo can result in positive effects [1]. Placebos are used to test the effectiveness of a treatment or drug on a certain condition by comparing the effects of the treatment and the placebo on participants in a study [1]. The participants’ response to the placebo, positive or negative, is known as the placebo effect [1].

The placebo effect consists of a patient’s brain convincing their body that an innocuous treatment is real, in effect stimulating healing responses[2]. A placebo cannot cure a condition, but rather will alleviate one’s perception of symptoms. Historically, placebos have been effective in aiding pain management, stress-related insomnia, fatigue, and nausea [2]. Additionally, the use of a placebo can often result in negative, unanticipated side effects[3].
Further research of the placebo effect reveals that its effects are only prevalent when the patient thinks they are receiving a functional treatment, and expects a positive outcome. Placebos seem to be ineffective when patients in a study are given placebo medication without their knowledge [3].

**Neurology**

A recent study of Parkinson’s disease found that patients whose conditions improved due to a placebo displayed identical neurological changes as patients who received the actual medication, which increases dopamine levels. Although traditional expectations led many to believe that the placebo treatment should not have caused an increase in dopamine levels, it did, enabling the patients to feel relief [3].

Another study used a magnetic resonance imaging (MRI) machine to scan and observe the brains of patients with chronic pain suffering from knee osteoarthritis. Their neural activity was then scanned again after each patient was given a placebo. It was noted that the patients who felt relief from their knee pains had increased brain activity in the middle frontal gyrus region in the frontal lobe, implying the involvement of this region in the placebo effect [2].

Research shows that analgesia due to a placebo is caused by the activation of the endogenous opioid analgesia network, a congenital pain-relieving system consisting of scattered neurons that produce pain-relieving opioid neurotransmitters [3][5].

**Benefits to Medicine**

The expected benefits from medication, whether it be placebo or real, is what activates the neural pathways. Further study of these mechanisms and commercial use of them in clinics would allow patients to feel relief without experiencing the side effects of medications [3].

The discovery of the relationship of the placebo effect to endogenous systems of analgesia has birthed a new line of research dealing with the biochemical and neurophysiological mechanisms and their neuroanatomical localization. Until recently, the only study relating to the endogenous systems of analgesia was stress-induced analgesia. Further placebo research will provide us with a better understanding of the endogenous systems of analgesia [6].
References


Prosopagnosia: A Multifaceted Disorder

Angela Sun

Introduction

Prosopagnosia is a disorder colloquially referred to as face blindness. While cases of inability to recognize faces have been documented throughout history, the term prosopagnosia was first coined by the German neurologist Joachim Bodamer [2]. The disorder is classified into one of two types, acquired and developmental, based mainly on etiology and age at which symptoms appear. Prosopagnosia is caused by trauma or malformation of the occipitotemporal area of the brain, although affected areas and degree of impairment often differ from patient to patient, resulting in varied treatment and prognoses [8]. Most commonly, prosopagnosia is linked to damage in the right fusiform gyrus, an area of the brain heavily activated during both facial detection and identification [5]. For many years it was believed that there was no remedy for prosopagnosia, but recently, both facial recognition training and medical treatment have seen some successes. Prosopagnosia is a rather obscure yet surprisingly common disorder that will likely receive more attention in the coming years as it becomes better known in both the medical and scientific worlds.

History, Classification and Diagnostics

In 1947, a German neurologist named Joachim Bodamer published several accounts of a rather interesting deficit he had encountered amongst certain patients of his. In particular, Bodamer described a 24-year old man who had a bullet wound to the head, who he referred to as “Patient S”. The bullet had damaged the parts of Patient S’s brain that were responsible for visual processing causing him to experience difficulty with vision. Interestingly, even as his vision returned, Patient S had trouble assigning objects to their names, a symptom characteristic of general visual agnosia [2].

Bodamer noted that S had trouble recognizing faces; in particular, he could identify a face as a face, but struggled to differentiate between the faces of his close friends and those of strangers. In his published case study, Bodamer wrote that all faces appeared “sober” and “tasteless” to his patient. Bodamer called this disease Die Prosop-agnosie, combining the Greek root for face, próσπον, and lack of knowledge, agnòsia. Bodamer is widely credited with publishing the first clinical account of prosopagnosia and identifying it as a distinct disorder, separate from other types of visual impairments and agnosias.
Even now, prosopagnosia is often loosely defined, as patient cases often present varying degrees of severity [12]. Some sufferers report that they are unable to recognize previously encountered faces. Others may be unable to even identify a face as different from other objects; although, in these cases, prosopagnosia is often coupled with other visual agnosias, such as a difficulty in recognizing places, objects, and emotions [14]. In spite of these impairments, all prosopagnosics tend to retain normal intelligence and intact visual acuity [3].

Generally, prosopagnosia is classified into acquired and developmental types. Patients with acquired prosopagnosia exhibit normal facial recognition and then subsequently lose this ability after head trauma, stroke, or a degenerative disease. The onset of developmental prosopagnosia is typically much earlier, as patients suffer from face blindness prior to adolescence. The specific causes of developmental prosopagnosia are much more varied, as the term is broadly applied to prosopagnosia as a result of genetic, prenatal, or childhood brain damage, as well as to idiopathic cases [3].

Acquired prosopagnosia, such as in the case of Patient S, is much more commonly diagnosed because individuals who have experienced on-level facial recognition ability are more likely to notice and articulate such an issue. Since the disorder typically manifests itself through observable anatomical changes to the brain, fMRI imaging, CT scanning, and PET scanning are often used in case studies and diagnosis.

Several visually-based exams of facial recognition also exist. The Warrington Recognition Memory for Faces (RMF) test and the Benton Facial Recognition Test (BFRT) were commonly used by clinicians and cognitive neuropsychologists; however, studies have shown that they tend to be unreliable at identifying prosopagnosics because stimuli presented during the test contained an excess of non-internal facial information—hair, clothes, eyebrows—which could be used in identification [4]. As a result, they have been slowly phased out of clinical usage. Instead, the Cambridge Face Memory test has emerged as a relatively strongly assessor of facial recognition ability and an important diagnostic tool for prosopagnosics [4].

Researchers have also developed a self-report tool, the 20-item prosopagnosia index (PI20), which targets developmental prosopagnosics who have yet to be diagnosed. The PI20 presents 20 statements that the subject is asked to rate on a five-point scale, with 5 indicating ‘strongly agree’. These statements include “When people change their hairstyle or wear hats, I have problems recognizing them.” The PI20 has been efficient at diagnosis, and its success indicates, to some extent, that even those with developmental prosopagnosia, whom have never experienced normal facial recognition, are generally aware of their deficit and how it affects them [5].
**Prevalence and Distribution**

Although diagnosis is much more likely to be obtained for those with acquired prosopagnosia, it is estimated that, in the general population, there is a much higher prevalence of those with the developmental type. In recent years, some research has been done with the purpose of determining a genetic basis of prosopagnosia. Congenital, inherited prosopagnosia was found to have a surprisingly high prevalence, especially among the German-Caucasian population, where it affects up to 2.5% of the population. Surprisingly, the majority of those with this form of prosopagnosia did not display the brain lesions that typically characterize prosopagnosics. The pattern of inheritance for this type of prosopagnosia appeared to be autosomal dominant, although the specific genes which are affected are not yet clear [6].

Overall, there is a scarcity of studies measuring prevalence of this disease. While media attention has made it better known, the clinical world is currently more focused on etiology rather than epidemiology with regards to prosopagnosia. One study conducted in Varanasi, India found that among 689 students of Banaras Hindu University, only one female student was afflicted with prosopagnosia. Some of her relatives reported symptoms similar to the ones that she had reported, suggesting that the hereditary form of prosopagnosia is not confined to those of Caucasian ancestry [6]. Nevertheless, more comprehensive studies are needed before conclusions about the prevalence of prosopagnosia in the general population can be made.

**The Role of the Fusiform Gyrus and Its Associated Areas**

Prosopagnosia is generally characterized by injury or malformation of the brain (save for the rare exceptions mentioned above). Clinicians and researchers have long associated the symptoms of this disease with damage to areas of the brain related to facial processing and recognition. By 1982, it was known that lesions of the central visual system were common in prosopagnosics [1].

Bilateral damage tends to be widespread among patients, but unilateral lesions of the right temporo-occipital region are also sufficient to engender impairments, a finding consistent with evidence that facial processing is heavily dependent on the right hemisphere [7, 8]. It is now believed that although regions of the left temporal and occipital lobes display activity during facial recognition, they are not critical such that in most patients unilateral left-hemispheric...
lesions would not result in prosopagnosia. Nevertheless, the degree of hemispheric dominance in facial processing tends to vary among individuals: in some left-handed individuals where hemispheric specialization is reversed, localized lesions in the left hemisphere have been known to cause prosopagnosia [13].

More recently, the advent of advanced neuroimaging techniques such as fMRI has allowed researchers to identify and isolate the areas of the brain that specifically respond to facial stimuli. Certain loci in the visual extrastriate cortex, regions of the occipital lobe bordering the primary visual cortex, are now hypothesized to constitute a core facial network (CFN). The CFN includes, primarily, the lateral middle fusiform gyrus, known as the fusiform face area (FFA), as well as the occipital face area (OFA) and the face-selective posterior superior temporal sulcus (pSTS) [9, 10].

The fusiform gyrus is the best known of this triad, likely because it displays the strongest response to faces and the largest difference in activity between perceptions of faces versus objects [11]. It was widely believed that the FFA was critical for facial processing and it was thus dubbed a “face module.” However, cases documenting patients of prosopagnosia who retain structurally intact FFA have recently arisen [11]. As such, it is likely that this area coordinates with other areas of the brain, such as the OFA, in the process of facial recognition.

Many hypotheses have been put forward with regards to the relationship between the FFA and other areas of the brain. It was originally suggested that the OFA was more involved in processing structural elements of faces, such as the individual features, information from which would then be transmitted in a feedforward system to the FFA for whole-face processing [11].

This hypothesis was countered by evidence demonstrating that processing of whole faces elicits a faster response than encountering isolated features, suggesting that facial processing happens first in the FFA then in the OFA. In particular, opponents cited the behavior of the N170 wave, a component of the event-related potential, a specific electrophysiological response to facial stimuli [15]. The N170 response is faster when viewing the face as a whole, essentially signifying that in facial processing, humans tend to process other human faces first as a whole, then subsequently by individual features [11]. The pSTS, while somewhat absent from extensive clinical review, is thought to play a role in transient aspects of facial recognition such as expression [10].

Accepted models of facial recognition generally include not only the core face network, but also an extended face network (EFN). The CFN includes the posterior areas highlighted above and is considered an “entry-point” for face processing. From there, information travels to the anterior temporal cortex, which contains areas of the EFN. Further identity processing occurs here, and loss of functional connectivity between these anterior regions and the CFN is also thought to play a role in prosopagnosia. Loss of connection to the amygdala, the area of the brain responsible for emotional response, has also been observed and may contribute to the failure of prosopagnosics to recognize emotional expressions and link a familiar face with a particular emotion (e.g. feeling affection when seeing your mother) [11].

While there is still debate surrounding which neural networks are responsible for the varying symptoms that prosopagnosics experience, the hope is that increasingly accurate models of
facial processing will pave the way for better and more accurate treatments for both acquired and developmental types of prosopagnosia.

Treatments and Ongoing Research

As far as we currently know, there is no fully effective cure for prosopagnosia. As recent as 2005, a renowned Australian cognitive scientist Max Coltheart articulated the belief that face processing could belong to a domain of cognition that, after severe impairment from brain injury, could not be restored [12]. While effective treatments have begun to emerge in the last half-century, there remains much room for improvement.

Treatment usually takes the form of cognitive training, in which facial processing deficits are addressed either through compensatory or remedial training. Compensatory treatment focuses on allowing patients to live a normal life despite their impairments rather than attempt to re-engage facial recognition skills which have been already lost. Remedial treatment attacks the problem directly and actually attempts to restore facial recognition to some extent. Unfortunately, this approach has been much less effective [12].

Clinicians employing the compensatory treatment approach often engage their patients in feature training, in which they are taught to work around their deficits by promoting recognition through specific facial features [12]. Patients are often asked to verbalize individual facial characteristics, such as “long thin face” or “blue eyes”. This approach has been particularly effective in young developmental prosopagnosics, although it has seen some success in patients with acquired prosopagnosia as well [12]. Remedial treatment is often an extension of feature training in which patients are eventually expected to reach a level wherein they can process multiple individual features almost simultaneously, thus leading to an almost normal holistic face response. Remedial approaches have seen more success in those with the developmental subset as well, but overall success rates are low [12].

Ultimately, prosopagnosia is an incredibly difficult disorder to treat. Whereas some may respond extremely well to training, others may show no signs of improvement. Most recently, researchers have seen some promise in the administration of intranasal oxytocin which has been shown to correlate with higher scores on the Cambridge Face Memory Test, at least in those with developmental prosopagnosia [16].

Moreover, variations in the oxytocin receptor gene, OXTR, were associated with performance on the Warrington Face Memory Test [12]. The exact physiological mechanism is unknown, but oxytocin is heavily involved in social cognition, bonding and trust, all of which requires sensitivity in visual processing. The same region also contains the main gyri responsible for facial recognition, which are damaged or dysfunctional in prosopagnosia [12].

While simple at a glance, prosopagnosia is a complex disorder which serves as a model from which neurologists have gleaned many insights on the facial processing mechanisms of our human
Prosopagnosia has not yet had its success story, but the ongoing and collaborative work of psychologists, biologists and the general community of those raising awareness for this possibly very prevalent disease have brought about some truly innovative solutions. As we learn more about the genetic and anatomical basis of facial processing in the brain, the path to finding a cure will sharpen into focus, the pieces of the prosopagnosic puzzle finally fitting together.

References


Treating Alzheimer’s: 
Gamma Oscillations Entrainment
Miruna-Elena Vlad

Abstract
Affecting more than 5.5 million US citizens and around 44 million people worldwide [1], Alzheimer’s disease (AD) involves the pathological formation and deposition of beta-amyloid plaques in the brain, which slowly disrupt neural connections. However, procedures aiming to reduce amyloid-β have failed to reverse cognitive symptoms, indicating that cognitive decline is a more complex process than previously thought [2]. Previous studies suggest that patients affected by the diseases exhibit not only abnormal brain function due to the plaques, but also an impairment in gamma oscillations — the brain waves that stand at the basis of elementary functions such as memory and attention. Studies related to gamma oscillations on mice models of Alzheimer’s disease elicited substantially reduced plaques in the visual cortices of the subjects even before the onset of plaque formation [3]. Determining how gamma oscillations affect molecular pathology in mice could have serious implications in possible treatment strategies.

Amyloid Beta

Amyloid-β (Aβ) is a fragment of the amyloid-β precursor protein (APP). In its natural state, amyloid is a common component and plays a number of beneficial roles in the human body, including antimicrobial defence [4].

At the beginning of its life, Aβ is a solitary molecule. Later it starts congregating into soluble mobile clusters of small dimensions [5] and eventually forms the pathological plaques characteristic of Alzheimer’s.
Gamma Oscillations in the Brain

Distinct regions of the brain communicate with each other through the coordination of neural activity in certain populations of neurons. When the firing of these neurons is synchronized, the brain starts producing ‘rhythms’— fast fluctuations in the activity of said groups— found in the extracellular electric fields, which can be detected by performing sets of noninvasive procedures on the scalp (electroencephalography, or EEG) or invasive intracranial recordings within the brain itself [6]. Alzheimer’s studies typically focus on the gamma oscillations, the component of these rhythms that corresponds to frequencies ranging from 30 Hz to 100 Hz. These neural vibrations play a central role in the normal evolution of cognitive processes like memory, consciousness, perception, and attention.

Several studies on neurodegenerative diseases have found disrupted gamma oscillations but have not yet determined the exact coaction between the hippocampal circuit property and the pathology [7]. In the case of Alzheimer’s, the molecular pathology can be altered by any changes in the synaptic activity of the brain [8].

The Brain Wave Stimulation

Mice can be genetically programmed to develop AD and examined in the early developmental stages of the disorder as well as after amyloid starts accumulating and characteristic symptoms like memory deficits develop. Scientists observed impaired gamma rhythms during the essential learning processes generated when running a maze and then studied the correlation between the quantity of amyloid in the brain and the performance of the gamma oscillations level [3].

A first step included stimulating the hippocampal area—which is responsible for forming and retrieving memories—with gamma oscillations at a frequency of 40 Hz for an hour. This stimulation technique, co-pioneered by Edward Boyden and also known as optogenetics, is a precise, noninvasive way to control activity in populations of neurons by directing light beams...
towards them [9]. The procedure resulted in a 40%–50% decrease in the levels of amyloid-β proteins in the affected areas.

Even though the stimulation at other frequencies did not lead to the same favorable results, these preliminary experiments opened the way towards looking for alternatives to produce the same outcomes through less invasive techniques. One of the first such devices consisted of a strip of LED lights set to flicker at distinct frequencies and to drive oscillations to the brain [3].

**Results**

In the case of Alzheimer’s, amyloid is produced more abundantly, while the microglia—immune (glial) cells of the central nervous system, with roles against certain infections, and meant to clear out the excess protein in the brain [10]—inflame and drop in efficiency. Researchers found that gamma entrainment produces results both by lowering the amyloid-β generation rate and by enhancing the abilities of the microglia.

**Subjects were treated as follows [3]:**

a) Those suffering from early-stage AD underwent therapy for an hour. The procedure managed to halve amyloid levels in their visual cortices, and the effect lasted for around 24 hours before returning to the initial state.

b) The mice found in more advanced phases of the disease were subjected to longer-term treatments—an hour a day for the duration of a week. This lead to decreases in the quantity of both amyloid plaques and free-floating protein in the brain.

The same steps were repeated on multiple models of mice, leading to similar outcomes [3].

![Figure 2. A-β levels in the visual cortex—progress in the first 24 hours from the one-hour treatment [3]](image-url)
Conclusion

Studies conducted on gamma entrainment demonstrate that inducing non-invasive light flickers to the visual cortex at 40 Hz result in substantial declines in the amount of amyloid-β peptides.

By extrapolation, the ability to replicate the experiment on various types of mice could mean that these improvements are not particular for one specific category of vertebrates, encouraging further research in this direction.

However, because gamma oscillation stimulation is unlike any other medical approach in the domain, it is yet to be determined whether it can be used as a therapeutic means in human Alzheimer’s disease cases.

Reference


The Genetic Correlations to Autism

Ali Bauer

Introduction

Ranging from almost unnoticeable issues to severe disabilities, autism is a spectrum of disorders. An awkward child capable of solving advanced math problems in his head might receive the same diagnosis of autism as another child who cannot speak. In the last twenty years, autism has been more frequently diagnosed [3]. Nearly one in every eighty-eight children are autistic, and the boy to girl ratio is four to one [3]. The cause for this disorder is somewhat unknown, but research suggests that genetics plays a greater role than previously thought [3]. In fact, genetics is thought to have a greater impact on this disorder than almost any other.

DNA Configuration Effects and Autism

The genome contains all the DNA in an organism. Many cases of autism are linked to mutations that occur in the genome. The exome, a portion of the genome that codes for proteins, is the site for most of the most influential mutations [3]. Most mutations occur naturally and are non-threatening, but some can be harmful. In damaging mutations, the structure of a protein is changed, and if that protein is key in brain development, it may lead to neurological disorders such as autism. These mutations can occur either by modifying a single DNA base or by changing the whole strand. DNA sequencing is very specific, so the slightest change can cause severe alterations to the organism [2].

People commonly assume that a genetic disorder is always one that has been inherited but this is not always the case. With autism, some mutations can be formed by combining multiple harmful genes from the parents. However, others may develop autism spontaneously without ever having inherited the mutation [3].

In total, there are about sixty-five genes that contribute to autism [3]. These genes may be altered in many ways, often differing between individuals [2]. More than one gene variation yields the condition. If an individual has a less important DNA base affected, highly functioning forms of autism might not be as obvious to identify as cases that are much more extreme, in which a more important or larger section of DNA is affected and symptoms will likely be more pronounced. Generally, the more DNA that is altered, the more extreme the condition becomes. Some genes that may be altered in an autistic child are those that help neurons send signals to the brain, and those that keep DNA neatly packaged in the cell nucleus [2].
To corroborate genetics’ impact on autism, if one identical twin has autism, the other twin has an eighty-eight percent chance of also having the disorder [3]. In fraternal twins, chances of autism are the same as in normal siblings; they have a one in eighty-eight chance each. The reason that the risk is so high in identical twins is because they share almost all of their genes. Even though identical twins do not have the exact same DNA sequence, they do have many similarities that average siblings do not [2].

**Health of the Parents is a Pivotal Factor in Developing Autism**

While many links to autism development come from genetic variations, studies show that environmental factors can play a role as well. The health of the parents, both mentally and physically, is also linked to developing autism. If a child’s mother is not well nourished and healthy, the child is at a much higher risk of being autistic [2]. Medicines taken by the mother also have correlations to autism development [1]. In addition, parental age can also affect the health of the baby [2]. If the parents are over a certain age, their child is more likely to develop autism than a child produced from parents of average ages [2]. The paternal age is particularly influential in the manifestation of autism in young children [2].

**Common Effects of Autism On an Individual**

Common symptoms of autism include communication challenges, abnormal sensitivity, and uncontrollable repetitive actions [1]. In extreme cases, an autistic individual may not be able to speak or only be able to communicate minimally [3]. On the higher functioning side of the spectrum, individuals may have unusually high IQ scores. These individuals are very intelligent, but often struggle with social situations [4].

This diagram shows a normal brain compared to one affected by autism. As the diagram portrays, the typical brain contains only three main locations in which neurons are sent, while there are three extra locations in the autistic brain. These extra locations make it slower and harder for an autistic child to think and act appropriately [5].
Treatments and Specialized Learning Systems

Treatments such as therapies and meeting with a special multidisciplinary team (physician, speech-language pathologist, and an occupational therapist) are encouraged for children with autism [2]. Good qualities in a program are structured activities, well-defined learning objectives, progress evaluations, focus placed on social skills, speech, imagination, and daily living skills [2]. Such a program gives the individual opportunities to interact with autistic peers and includes parent and family involvement [3].

Drawing Conclusions

From what is known about autism, finding a cure for the condition might prove difficult to accomplish. However, activities to lessen symptoms and awkwardness are as close to a solution as it seems possible in the near future. Studies are still being done, so more therapeutic activities will likely be identified as the causes and effects of autism are explored.

References


Can Spinal Cord Injury Be Cured Through Neuroregeneration?

Lorna Bo

Abstract

The origins of spinal cord injury can be traced back more than 4500 years, to the oldest known trauma text: the ancient Egyptian Edwin Smith Papyrus. It was here that spinal cord injury was first described by clinicians, who, even then, described it as an injury 'not to be treated' - an attitude that was to last for millennia. Only after breakthroughs in imaging, medicine, and rehabilitation in the 20th century did we begin to develop a greater understanding of the mechanisms behind the debilitating, often paralysing injury, which affects between 250,000 to 500,000 people worldwide each year. We now understand that although the peripheral nervous system (PNS) can regenerate fully after damage, the central nervous system (CNS) cannot, and this is why CNS trauma carries such a poor prognosis. It is only by picking apart the reasons for this dichotomy that researchers are now able to develop therapies incorporating the rapidly expanding fields of gene therapy and stem cell research to stimulate regeneration, finally offering hope of treatment to an injury historically thought to be untreatable.

In order to better understand the inability of the CNS to heal, it is important to first consider the mechanisms behind successful regeneration in the PNS, as illustrated in Fig. 1. If a PNS neuron’s axon is damaged, it will regrow at a rate of around 1 mm a day in small neurons and 5 mm a day in larger ones[i] (note that if the cell body is damaged, regeneration is impossible). Immediately after axotomy (the severing of the axon), supporting glial cells such as Schwann cells recruit macrophages by releasing cytokines, and accompany them to the site of the injury to clear away debris - for example, by the phagocytosis of myelin. The distal stump (the end of the neuron not attached to the cell body) then undergoes Wallerian degeneration, a process that takes around 24 hours and results in the complete fragmentation of the axon. The endoplasmic reticulum degrades, mitochondria disintegrate and microtubules are depolymerised. The endoneurium (layer of tissue around the myelin sheath) remains intact, however, to provide a conduit to guide growing axons in a later stage of regeneration. This

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[i] Note: This rate of regeneration is effective in small neurons and larger ones, as mentioned in the text. Reference should be provided for this. [citation needed]
involves the proximal end (the end of the neuron attached to the cell body) sprouting axons with growth cones on their ends, which produce a protease that further digests debris on its journey to reinnervation through the endoneurial, or basal laminar tube, along which Schwann cells assemble in ordered longitudinal columns called ‘bands of Büngner’ to preserve the channel and help guide the axon to its target. Schwann cells and macrophages also upregulate neurotrophic factors such as nerve growth factor (NGF), while the PNS neuron itself upregulates regeneration-associated genes (RAGs). This intracellular encouragement, structural guidance, and expression of growth factors all create a favorable environment for regeneration and eventual reinnervation [2,3].

However, the general mechanism detailed above does not occur for a damaged CNS neuron. This is not entirely due to the CNS neurons’ inherent inability to regenerate – on the contrary, when placed into a permissive environment of a peripheral nerve graft, they are able to grow long distances [4], thus indicating that the explanation lies in the CNS environment. Indeed, research has shown that the difference between PNS-CNS regeneration is likely to be due to their different glial cell populations and their reactions to injury. The CNS’ glial cells are not Schwann cells, but oligodendrocytes and astrocytes. Oligodendrocytes require axon signals to survive [5], and therefore undergo apoptosis (cell death) and fail to recruit macrophages to clear debris after injury, as Schwann cells do in the PNS. Instead, the CNS must rely on the action of microglia (the CNS analogue of macrophages in the peripheral immune system), which are slower than macrophages and may also fail to function. This causes the distal stump to degenerate slower than in a PNS neuron, resulting in the accumulation of inhibitory myelin debris. This is exacerbated by the formation of a glial scar (see Fig. 2), which axons cannot cross. It consists mainly of reactive astrocytes, which undergo heavy proliferation after CNS injury and form a dense network of gap junctions which act as a physical barrier to regrowth. Compelling proof of this inhibitory environment hypothesis comes from studies in which axotomy of the dorsal root ganglion neurons is followed by regeneration within its peripheral environment, but further growth is arrested at the PNS-CNS interface, also known as the dorsal root entry zone (DREZ). This is a phenomenon which has been known since the early twentieth century, and for which ultrastructural analysis has shown astrocytes in the glial scar to be responsible [3].

Although this barrier serves the beneficial purpose of preventing cytokine release from the injury site, causing further damage to surrounding tissue, it is the main physical inhibitor of CNS regeneration. Furthermore, the CNS glia do not produce neurotrophic factors, and instead produce factors that inhibit remyelination. Oligodendrocytes express myelin-associated inhibitors (MAI) such as Nogo-A, ephrin-B3 and Semaphorin-4D, and the astrocytes in the astrogial scar produce chondroitin sulfate proteoglycans (CSPGs), such as neurocan [2] (as well as providing a physical barrier in the form of the glial scar) (Fig. 3). CNS neurons themselves are also at fault, as it has been found that they upregulate RAGs less than do PNS neurons. Therefore, a mixture of a poor
intracellular regenerative response and a hostile extracellular environment serve to inhibit axonal regrowth and restoration of function in the CNS.

It is by targeting these factors that combine to prevent regeneration that researchers have begun to make headway in developing treatments to promote it. For example, neurotrophin (NT) treatment showed some success in a study in which rats were injured on dorsal roots, and osmotic mini-pumps were immediately implanted to infuse neurotrophic factors such as NGF, GDNF and NT3 over the next week [6]. This allowed the dorsal roots to overcome the transitional zone between the PNS and CNS that had previously been shown to be insurmountable, restoring some function. Yet delivery by a mini-pump is inconvenient for long-term treatment and does not stimulate the production of NTs in the spinal cord itself and can cause more parenchymal damage than other treatments such as viral-vector based gene therapy [7].

This type of therapy involves injecting gene-edited viruses which express NTs along the DREZ, leading to near-normal recovery of function [8]. However, this also causes the sprouting of non-injured neurons, which, although it can enhance recovery, may cause chronic pain [9]. Nonetheless, research has demonstrated strategically using a gradient of both neurotrophic factors and growth inhibitory factors can prevent hyperinnervation. Alongside using NGF to encourage growth across the DREZ, the use of increasing concentrations of the inhibitory Semaphorin-3A can prevent the growth of the neuron into unwanted areas, allowing for directed growth. NT treatment, either through protein delivery or gene therapy, has therefore been shown to have potential therapeutic applications.


Besides manipulating the extracellular environment, the intracellular hindrances to regeneration can also be manipulated. For example, induced RAG over-expression in CNS neurons has been shown to promote sensory axon regeneration [12]. Inhibitory intracellular signaling pathways can also be manipulated to promote regeneration. A key example is the RhoA/Rho-kinase pathway. When activated, the protein RhoA activates the protein kinase 2, which, in turn, regulates the dynamics of the cytoskeleton and results in the cessation of neurite growth. C3 transferase, an enzyme that deactivates RhoA, has been shown to promote axonal
sprouting and motor function in mouse models [13], and kinase 2 knockout mice (mice in which the
gene to produce kinase 2 is deleted) also showed functional recovery after spinal cord injury [2].

Perhaps the answer may not lie in changing the extrinsic or intrinsic, but rather replacing the
damaged neuron altogether. Stem cell transplants have received much attention from the media and
general population, and they do show some promise for morphologically replacing neurons or glial
cells in the damaged CNS, sometimes even altered with therapeutic genes (for example, to
over-produce neurotrophins [14]). This is due to their multipotency, meaning they can differentiate
into the appropriate neuronal or glial subpopulation. When oligodendrocytes were replaced by
embryonic stem cells in a rat with spinal cord injury, the rat’s locomotion improved [15]. Yet this
study is one of very few studies that have shown a functional use for stem cells in spinal cord injury,
and it is unclear whether the stem cells actually differentiated into functional cells that contributed
to structural reorganisation, or whether they simply secreted factors that aided the pre-existing cells
to recover. In any case, despite the need for more rigorous studies as this new field develops, its
preliminary success does show that future therapies may not need to be derived from the nervous
system itself.

Thanks to our newly found understanding of multifactorial causes that facilitate PNS
regeneration and hinder CNS regeneration, the latter, once an unachievable goal, is now a viable
possibility. Targeting the glia that create physical barricades and inhibitory cues, as well as boosting
the intrinsic regenerative capacity of the neuron itself, and even perhaps replacing them altogether
with stem cells are all therapies that have shown promise in in vivo experimentation. Yet
extrapolating these results to the inherently complex adult human CNS would be naive, and for
each successful experiment, one must question its implications carefully. What role does neural
plasticity – the compensation of undamaged systems for the function of damaged systems – play? To
what extent does recovery of function correlate with anatomical and structural recovery? Perhaps
most importantly – how applicable is the therapy for clinical use? The answers to these questions
will only be found with a more rigorous evaluation of all these different therapies, facilitated by
ongoing technological advances. In the future, we may finally be able to bring new life not only to
the damaged spinal cord, but also to the lives that have been irrevocably impaired by it.
References


DISEASE

Glutamatergic Neurotransmission In Epilepsy

Rachel Klick

Abstract

Epilepsy is a neurological condition identified by recurrent seizures. Glutamate, an excitatory neurotransmitter in the brain, has a correlation to epilepsy symptoms and epileptogenesis, the process by which epilepsy develops in a patient. With this knowledge, experts are conducting research to develop anticonvulsant drugs that use glutamate antagonists to target seizures and eliminate the difficulties that epilepsy causes in the daily lives of patients. In addition, new advances in neurosurgery have been particularly useful when treating seizures in pediatric patients.

The Nature of Epilepsy and Epileptogenesis

In the brain, high levels of neuronal excitability cause recurrent involuntary seizures [1, 2]. In half of all epileptic patients to date, the epileptogenic causes, or the causes of an otherwise healthy brain developing epileptic seizures, have been unidentifiable. Without a certain etiology, the diagnosis of the patient is defined as cryptogenic [3].

Epilepsy is typically diagnosed through an electroencephalogram (EEG). Electrodes are attached to the scalp to monitor neurological levels of electrical activity. Blood tests, magnetic resonance imaging (MRI), computed tomography (CAT) scans, and lumbar punctures are procedures used to assist and corroborate the diagnosis [4]. A patient must have had at least two seizures to be formally diagnosed [1]. Although no cure has been discovered, current treatments...
include medication, ablative surgery, and vagus nerve stimulation (VNS) with 70% of treatments resulting in successful management [4][5].

A seizure occurs when a burst of unusually strong electrical signals in the brain interrupts regular brain function. There are multiple causes of seizures including, but not limited to high fever, progressive brain disease, brain tumors, low blood sugar, concussions, and withdrawal from alcohol and drugs.

Seizures fall into two general categories, either focal or generalized, with each further divided into subtypes. Focal seizures, otherwise known as partial seizures, occur when an irregular burst of electrical activity takes place at one or more locations on one side of the cerebrum. Specific examples of focal seizures include simple focal seizures and complex focal seizures. Generalized seizures result from abnormal electrical activity on both sides of the brain. Specific examples of generalized seizures are absence seizures (“petit mal” seizures), atonic (drop attacks), generalized tonic-clonic seizures (GTC or “grand mal” seizures), myoclonic seizures, infantile spasms, and febrile seizures [5].

**Glutamatergic Neurotransmission**

Glutamate is an excitatory neurotransmitter in the mammalian brain, and in any animal with a rudimentary nervous system, strongly associated with epilepsy and other central nervous system disorders [7, 8, 9]. Glutamate was initially believed to be simply a factor in metabolic function in the central nervous system due to its ubiquitous nature and presence in intracellular compartments. This includes involvement in the mitochondria and cytosol of all central nervous system cell types [9, 10, 11].

Glutamate was first identified in 1984 as a neurotransmitter after research corroborated the existence of intense regulation of glutamate by the CNS [6]. Glutamate, an amino acid, is synthesized via glucose outside of the CNS through the Krebs Cycle, producing pyruvate. Joint activity of the enzymes pyruvate dehydrogenase and pyruvate carboxylase
have an essential influence. Via α-ketoglutarate, the citrate is converted to glutamate. Glutamine synthetase then converts the glutamate to glutamine which enters the glutamine–glutamate (GABA) cycle [1,11].

After crossing the blood-brain barrier to arrive at the neuronal astrocytes, intracellular glutamate is transaminated to accept an amino group from a branched chain amino acid donor such as leucine and valine, γ-aminobutyric acid (GABA), and alanine. Glutamate release refers to the process by which cytosolic glutamate uses vesicular glutamate transporters to cross the vesicular membrane.

Glutamate clearing and cycling are essential to the prevention of excitotoxic damage due to high concentrations of extracellular glutamate and extrasynaptic glutamate that form due to dysregulated excitatory neurotransmission. The clearance of extracellular glutamate must transpire within the boundaries of a millisecond timescale to prevent excitotoxic damage and protect neuronal health. The central nervous system tightly regulates glutamate in order to account for glutamate metabolism, release, transport, and clearance [11].

Glutamatergic synapses provide communications between postsynaptic dendritic spikes (axodendritic synapses) or adjacent nerve endings (axon-axonal synapses) and presynaptic nerve terminals. Glutamate receptors are divided into two categories: metabotropic and ionotropic:

(i) Ionotropic receptors are categorized into N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), and kainate (KA) [11, 12]. To generalize, these receptors are ligand-gated ion channels that function to flux cations (Ca²⁺, Na⁺).

(ii) Metabotropic glutamate receptors initialize or restrain second messenger systems through the use of cognate G-proteins. Metabotropic receptors are divided into three groups. Group I consists of mGluR1 and mGluR5, group II involves mGluR2 and mGluR3 and group III is composed of mGluR4-8. Both general categories of receptors use their intracellular C-termini to establish an interaction with postsynaptic proteins [8, 11].

The process by which glutamate receptors, glutamate transporters, and glutamate interact with the cerebral environment is referred to as glutamatergic neurotransmission [6, 11, 12].

The Pathology Between Glutamate and Epilepsy

Pathology between glutamate and epilepsy has been proven to contribute to epileptogenesis. Through microdialysis studies, it has been identified that extracellular concentrations of glutamate and aspartame increase before and/or during seizures [7]. Therefore, it can be concluded that seizures induce elevations of extracellular glutamate, leading to issues with the clearance of extracellular glutamate, the excitotoxic damage of neurons in the brain, and further epileptogenesis.

In addition, a 1974 study revealed that an antihelminthic called kainic acid caused seizure-like convulsions in small mammals [7]. Kainate is a potent agonist towards AMPA and
kainate receptors [7]. It elicits the assumption that there is an association between seizures and biological processes, and structures directly or indirectly related to glutamate.

**Anticonvulsant Drugs**

In an effort to develop anticonvulsant drugs and further treatments for epilepsy, research has been conducted on the mammalian brains of rats through the use of glutamate antagonists [7, 8]. Antagonists for N-methyl-D-aspartate (NMDA) and non-NMDA receptors have been used as models of anticonvulsant drugs and have been found to have limited efficacy when treating seizures in small mammals, in addition to human patients with drug-refractory complex seizures.

Negative cognitive effects from competitive and non-competitive NMDA antagonists have been found to exist. However, anticonvulsant compounds of the lamotrigine variety were found to be free of any side effects associated with NMDA antagonists.

Lamotrigine anticonvulsant compounds use channels of sodium and diminish glutamate release caused by ischemia, a condition in which the blood supply to tissues is reduced. Glutamate receptor antagonists were discovered to be cerebroprotective from forms of brain damage following acute brain trauma or global or focal cerebral ischemia [7].
The Future of Epilepsy Research and Treatments

In order for new anticonvulsant drugs to be produced and distributed by the pharmaceutical industry, it is essential that there be further research into the properties of glutamate, glutamate antagonists, and the association between glutamatergic neurotransmission and epileptogenesis. It is necessary to discover and comprehend the relevance between NMDA antagonists and the cognitive dispositions that develop as a result of biologically targeting NMDA receptors. It is of critical importance that there be an understanding of the pathology between the numerous factors of epilepsy, not limited to the human genome, and this disease that affects over 50 million individuals every day.

According to the National Institutes of Health, approximately 60% of all patients with epilepsy suffer from focal epilepsy syndromes. For approximately 15% of these patients (an estimated 4.5 million patients), the seizures are not adequately controlled with antiepileptic drugs. The majority of this group are pediatric patients (18 years old or less), potential candidates for surgical ablation of the epileptic foci in the brain [15].

Surgery in carefully selected epileptic children with intractable seizures has been demonstrated in approximately two-thirds of children to either eliminate or significantly reduce (>90%) the frequency of seizures. While further research is necessary, current advances in structural and functional neuroimaging, neurosurgery, and neuroanaesthesia seem to have improved the outcomes of surgery for children with intractable epilepsy [15].

Early surgery can improve the quality of life and cognitive and developmental outcomes. These remarkable breakthroughs, and more which can come of future research and treatments, can finally allow many of children to lead more normal lives free from these debilitating seizure patterns.

References


A Personalized Approach to Parkinson’s Disease
William Blair and Shafiq Qaadri

Parkinson’s Disease

Parkinson’s Disease (PD) is the second most common neurodegenerative disorder in the world. The cause of the disease is unknown. Parkinson’s defining symptoms are motor impairments, which manifest due to damage of neurons in the substantia nigra, a structure of the basal ganglia located in the midbrain. The damage of its neurons causes a reduction in the release of dopamine, resulting in a biochemical imbalance causing poor balance and motor coordination.

The treatment of Parkinson’s Disease (PD) has long consisted of imprecise medications and therapies with low degrees of efficacy [1]. Neurologists consider Parkinson’s to be a highly variable disease, resulting in starkly different clinical profiles and with symptomology progressing at vastly different rates for different patients. Indeed, patients with Parkinson’s report differing responses to the traditional mode of dopamine replacement therapy (DRT) and Levodopa medication. They also vary widely in their susceptibility to medication-related side effects such as dystonia, dyskinesia or hallucinations.

As the average age of the global population continues to increase, the frequency of PD is estimated to grow by four times by 2040 [2]. With the proliferation in incidence and onset of the disease, it is necessary to consider novel methods to treat Parkinson’s Disease. Personalized medicine offers the greatest potential in improving patient outcomes and health as well as supporting considerable advances within the field [3].

Treatment

Neurologists automatically categorize PD patients into a handful of clinical subtypes. Patients presenting with a tremor, for example, tend to have a more benign treatment course than patients presenting with gait and posture symptoms. Patients with an older age of disease onset tend to develop more aggressive symptomology sooner than patients with a much younger age of diagnosis.

Bas Bloem, professor of neurological movement disorders at Radboud University Medical Center and founder of ParkinsonNet, argues that it is high time we solved this puzzle [4].
“So now we have...five or six Parkinson’s Disease phenotypes, whereas in reality there are 5 million Parkinson Disease phenotypes: corresponding to the 5 million people worldwide with Parkinson’s, each with their own individual profile.”

While they are inefficient and unrealistic to develop 5 million phenotypes, the goals of Bloem and his colleagues may lead to a much more precise granular profiling and effective treatment strategies [5]. Currently, the most common form of treatment for Parkinson’s Disease is levodopa (3,4-dihydroxy-l-phenylalanine), a naturally occurring intermediate in the pathway of dopamine synthesis (Figure 1).

Following the oral ingestion of the drug, levodopa is transported from the upper small intestine into the circulation. As a result of ongoing metabolism and distribution throughout the body, only a small portion of levodopa reaches the brain where it takes effect. Once levodopa reaches the brain, it is rapidly formed from aromatic L-amino acid decarboxylase (AAAD), a naturally occurring enzyme. The conversion to dopamine accounts for most of the pharmacologic effect of the drug by improving diminished motor function.

**Clinical Evidence and Use**

Over several decades of investigation, levodopa has become the preferred treatment for Parkinson’s Disease with its ability to relieve motor symptoms and provide confirmation of the disease’s diagnosis. Despite levodopa therapy being the gold standard of Parkinson’s treatment, tremors sometimes persists and also retropulsive imbalance rarely improves. As well, intake of the drug over time leads to lower efficiency of the drug, causing patients to discontinue its usage as soon as two years after initial treatment [6]. There is also a litany of adverse effects, including nausea, vomiting, postural hypotension and cardiac arrhythmia. Thus, the effects of levodopa remain uncertain. While levodopa has been proven to improve motor impairments in Parkinson’s patients, there has been evidence to suggest that the drug may promote the progression of the disease, yet by no means is this conclusive as scientific literature largely varies in the interpretation of this effect.
Personalized Medicine

The consideration of personal needs and the specific clinical phenotype of patients before prescribing is the basis of personalized medicine (PM). The National Human Genome Research Institute (NHGRI) maintains that a personalized medicine is an approach to medicine using “an individual’s genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease [8].” Personalized medicine is an important consideration for multifactorial conditions such as PD and should be prescribed based on the susceptibility of specific subtypes of PD to side effects with consideration of lifestyle, age, nutrition, health status, environmental exposure and epigenetic factors [9].

The Personalized Parkinson Project (PPP), an international collaboration involving Radboud University, ParkinsonNet and Verily Life Sciences, aims to track 650 patients with early onset Parkinson’s disease diagnosis (5 years or less), for a period of two years. Researchers plan to periodically measure a plethora of biological and performance metrics through brain imaging, spinal fluids, blood serum, plasma, DNA, and stool. Trained assessors will annually conduct detailed clinical exams. And, thanks to the Verily Study Watch, participants will be followed 24/7 outside the clinic as well. The PPP hopes to gather high quality physiological and environmental data, combining it to ascertain to what extent the known Parkinson’s disease genes account for the variation in symptoms and individual rates of progression. [5]

PD is now recognized as a multi system, multi neurotransmitter, heterogeneous, dysfunction-related disorder. Biomarker-driven evidence suggests that PD is a complex disease that could also present with non dopaminergic syndromes. Therefore, in a growing number of cases, the generic prescribing of DRT and Levodopa may not be sufficient in restoring motor function and health. There is a growing awareness of the “one size does not fit all” concept regarding mass treatment of PD. Scientists, however, are still unaware as to how the disease works or the extent to which genetics plays a role in the disease. Unlike other genetic diseases such as Huntington’s, there is no single genetic signal for PD [10].

Pharmacogenetics

Personalized medicine relies on the inherent genetics of PD to determine susceptibility on an individual basis. Identifying at-risk individuals by widely known genetic markers in the prodromal stage of PD could aid precision medicine’s ability to delay or stop the its progression. This is especially important as neurologists often remark that Parkinson’s is a highly variable disease, with tremendous divergence in clinical profiles, age, lifestyle and response to dopamine replacement therapies (DRT). Genome-wide
association studies have identified PD loci, but still do not explain the bulk of the heritability issues with PD [11].

PD is rarely monogenic. However, autosomal dominant presentations can identify specific genes and gene products. Of specific interest is alpha-synuclein, a protein whose function is unknown, but forms a major constituent of Lewy bodies, abnormal aggregates of protein that develop inside nerve cells and which form the pathological hallmark of PD. Another area of interest is the increased frequency of PD in carriers of the mutated Glucocerebrosidase gene (GBA), which approximately 5% to 10% of PD patients possess [12]. The GBA mutation is currently the single most important known factor in predicting PD. The enzyme that gene codes for, glucocerebrosidase, has a reciprocal relationship between its regular activity and alpha-synuclein function [15]. Gaucher’s Disease, a genetic disorder in which the sphingolipid glucocerebroside accumulate in cells, has been investigated as sharing similar mutations to PD [16].

Steps Towards Personalized Medicine

The treatment of Parkinson’s Disease remains largely monopolized by the use of levodopa, as discussed above, along with other dopamine replacement therapies. Although these treatments have the ability to improve motor functionality of PD patients, they are also shown to have a number of unwanted adverse effects and inefficiencies [17]. Nevertheless, the treatment offers unlimited potential due to the individual, rather than collective, nature of personalized medicine. The field has continued to make significant progress in identifying the neuropathological and genetic risk and causal factors that may underlie PD. The personal genomics company 23andMe sifted through DNA samples from more than 2 million customers, identifying more than a dozen new mutations [18]. Technological advances in molecular profiling and neuroimaging will allow us to better dissect disease subtypes and target therapies to those most likely to benefit. Still, truly transforming PD treatment into a precision approach will require tackling key research and regulatory challenges and the effort of the entire PD community. To reach this stage, a comprehensive strategy is needed. Firstly, biosamples must be more accessible for scientists, as 23andMe have done. We must also partner with patients and their families to create a diverse and representative picture of Parkinson’s Disease to better understand its plethora of genetic variants. It is also necessary to continue to generate intensive molecular profiling from a number of cellular pathways, including neuroinflammation and oxidative stress, to attempt to create a clearer picture of PD and its causes. Finally, we must drive biomarker validation towards a personalized medicine approach, rather than one championed by traditional medicine. In this way, we can create well defined biomarkers to identify patients and prescribe drugs appropriate for their condition, genetics lifestyle, and many other factors [19].
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The Blood-Brain Barrier and How to Cross It

Ryan Bose-Roy

Introduction

A series of thick, tight membranes separating blood vessels from the brain is responsible forsinglehandedly ensuring the safety of the body’s most vital organ. This so-called blood-brain barrier (BBB) is critically important in the study of disease and treatment. Our susceptibility to a vast variety of neurological problems is often a result of the ability of harmful substances to bypass this protective layer and cause damage to cerebral tissue. Additionally, the ability of scientists to design drugs for neurological disorders is largely hampered by the blood-brain barrier, which often prevents these otherwise useful substances from passing through to the target area. Elucidating the mechanisms of how the blood-brain barrier allows substances to cross into the brain, as well as how to replicate this process in drug treatments, could allow us a much greater ability to combat brain tumors, addiction, and a wide variety of other debilitating neurological problems.

What is the Blood Brain Barrier?

More than 100 years ago, scientist Paul Ehrlich observed that when he injected colored dyes into the bloodstream, he was able to change the color of nearly every organ in the body except for the brain and spinal cord \[1\]. Ehrlich’s technique to “stain” tissues was useful because it allowed researchers to study specific biological structures (that would otherwise be impossible to see) in fine detail. However, his experiment also presented a problem: how were scientists supposed to study the nervous system if they could not see it?

The answer to this question was determined separately by two researchers. Edwin Goldman, an associate of Ehrlich, found that when the same colored dyes were injected into the cerebrospinal fluid that surrounded
the central nervous system (CNS), they stained the brain and spinal cord, but did not stain any other organ [2]. German neurologist Max Lewandowsky found that neurotoxic substances did not affect the brain when injected into the bloodstream, but altered function only when directly injected into the brain [3]. These two experiments implied the existence of a blockade between the blood vessels and the brain preventing certain substances in the vascular system – such as colorful dyes or toxic chemicals – from entering the central nervous system. Lewandowsky creatively called this blockade the “Blood-Brain Barrier” [3].

Simply discovering the existence of the structure, however, was not enough. For years, scientists were unable to stain and visualize this blood-brain barrier, mostly due to the lack of a microscope powerful enough to define structures surrounding blood vessels [4]. It took another 70 years until researchers, aided by the development of the electron-microscope, were finally able to understand of what this barrier was made [5].

In 1967, scientists Thomas Reese and Morris Karnovsky at Harvard Medical School injected the enzyme horseradish peroxidase into the bloodstream of mice, and used an electron microscope to visually show that this enzyme could not pass through the endothelial cells surrounding the mice’s cerebral blood vessels [5]. Perhaps, they thought, this conglomeration of endothelial cells separating blood vessels from cerebral tissue made up the blood-brain barrier they were trying to find.

By examining the differences between endothelial cells in the brain in comparison to endothelial cells elsewhere in the body, Reese and Karnovsky elucidated two unique features of this “cerebral endothelium” that served as a barrier to horseradish peroxidase entering the brain. The first feature was the relatively low frequency of transport structures in the cerebral endothelium [6]. The sparse transport vesicles took in only minimal amounts of horseradish peroxidase, only doing so to serve some nutritional or other need of the endothelial cell [7]. The second feature was the existence of so-called “tight junctions,” connections between endothelial cells that were pressed so tightly against each other that there existed virtually no space between the two [8]. This structure, the researchers believed, formed a continuous “unbroken belt” of endothelial cells around the cerebral blood vessels, that prevented molecules from diffusing into the brain at any point in the capillaries [9].

This groundbreaking experiment raised two crucial issues. The first issue was that the brain, like any other organ, requires glucose from the blood to sustain its demand for energy. So how could the brain get its glucose if glucose couldn’t enter the brain through the blood? The second issue was the already determined existence of a constantly maintained “hydrogen-ion gradient” between blood and brain that could only exist if ions were constantly being pumped in and out of the central
nervous system [10]. How could that be possible, if molecules couldn’t pass through the blood-brain barrier? Clearly, the structure could not be completely impermeable. But then how were substances able to pass through it?

From their experiments, Reese and Karnovsky hypothesized three possible answers. One potential explanation was that special transport structures and mechanisms in endothelial cells allowed certain molecules (like glucose) to pass through [11]. A second potential explanation was that the tight junctions between endothelial cells were not completely foolproof – rather, they allowed for exceedingly small molecules to permeate into the brain [12]. Their final potential explanation was the existence of certain structures within these tight junctions that served as “metabolic pumps,” taking in certain molecules from vascular tissue and “pumping” them into the brain, maintaining the hydrogen-ion concentration gradient [13]. These pumps could also exist along the endothelium, which would provide a continuous surface along which these pumps could act [14].

**Crossing the Blood-Brain Barrier**

All three of these explanations appear to be correct. In the late 20th Century, it was found that the transport protein GLUT-1 was highly enriched in brain capillary endothelial cells, and carried glucose molecules through the blood-brain barrier, thus supporting Reese’s and Karnovsky’s first hypothesis [15]. Patients with genetic defects in this transport protein can have severe learning difficulties and can be diagnosed with low glucose levels in cerebrospinal fluid, but not in the blood [16]. Researchers identified various other transport proteins existing in endothelial and surrounding astrocyte cells that allow for the transport of glucose and certain amino acids into the brain [17]. In addition, amino acids that cannot be synthesized by the brain, such as phenylalanine, leucine, tyrosine, isoleucine, valine, tryptophan, methionine, histidine, and L-DOPA, are transported into the brain by “L-type transport proteins” [18]. Certain non-essential amino acids already manufactured in the brain, such as alanine, glycine, proline, and gamma-aminobutyric acid are transported in by “A-type transport proteins” [19]. Drugs that target areas in the brain, such as levodopa, must often display strong affinity to these transport proteins.

A number of other ways in which substances pass through the endothelial membrane also exist. Substances that are highly soluble in lipids can often pass through the barrier by simple diffusion [20]. This is because chemicals that have a high degree of lipid solubility can easily pass through the lipid bilayer of the endothelial cells and cross over to the other side. Many psychoactive drugs such as cocaine, MDMA (ecstasy), ethanol (the active ingredient in alcohol), and ephedrine utilize this mechanism of “transmembrane diffusion” to cross the BBB and effect regions inside the brain [21]. Despite its disadvantages, this weakness in the BBB could potentially be useful in the design of therapeutics to enter the brain. Current research is focused on tackling two drawbacks to this idea. Drugs affecting the brain must be able to work in the aqueous interstitial fluid surrounding the organ, and substances that have too high of a lipid solubility might not enter this watery environment [22]. In addition, lipid soluble substances are often taken up by peripheral tissues,
lowering the concentration of the drug in the blood [23]. Thus, although the drug is able to pass from blood to brain, it may prove difficult for the substance to actually reach the brain in the first place.

**Disease and Treatments**

The dysfunction of the blood-brain barrier is often the cause of a variety of brain dysfunctions [23]. Afflictions such as encephalitis, multiple sclerosis, stroke, and brain tumors often involve substances passing through the endothelial layer that would not typically do so [24]. Researchers have yet to completely understand why the blood-brain barrier allows these substances to pass through; however, we have been able to elucidate a great deal of information. For example, these conditions decrease the production of claudin, a protein found in tight junctions [25]. Brain tumors can also lead to the breakdown of the blood-brain barrier, causing swelling around the tumor [26]. In addition, tumor cells can also secrete growth factors that cause the formation of leaky and somewhat dysfunctional blood vessels [10].

Designing treatments for these diseases often requires the design of novel mechanisms to cross the blood-brain barrier. One rapidly growing area of research is in nanotechnology-based deliverance methods. These systems consist of binding drugs to small particles capable of crossing the barrier. While the potential health risks of this method of drug delivery have to be considered, a promising nanoparticle compound is human serum albumin, which is seemingly non toxic and has been shown to traverse the blood-brain barrier carrying host drugs [29].

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Brain Computer Interface (BCI)

Vishnu Kumar

Abstract

Originally an idea from science fiction, Brain Computer Interfaces (BCIs) are now devices of serious scientific inquiry. These devices have much potential in the medical field and in industry. However, if BCI technology is used recklessly, consequences can be extremely dangerous. Thus, society must understand BCI's effects in order to use it without jeopardizing the health and safety of its users.

Background

A Brain Computer Interface (BCI) is a device which relays information between computers and the human brain. A BCI works by interpreting neural function, translating it to electrical data, and sending the electrical data to a computer or the internet. A BCI can also work by recording visual or auditory information from the outside world, and then stimulating specific areas of the brain with electrical signals. There are numerous types of BCIs. For example, Magnetic Resonance Imaging (MRI) and functional Magnetic Resonance Imaging (fMRI) are forms of BCI since both of these devices use magnetic fields to capture brain activity (neural function). Electroencephalography (EEG) is another type of BCI. EEG uses electrodes on the scalp of the head to detect electrical activity, which indicate brain waves. An example of this is an Emotiv Insight Headset. Another example of a BCI is electrocorticography (ECoG), which is similar to EEG except that ECoG uses electrodes located within the skull. Finally, other examples of BCI include prosthetics connected to electrodes or neural chips.

As many BCIs measure neural activity, this technology can play a critical role in detecting and treating neurological disorders.
Medical Uses

One example of BCI’s potential in medicine is its ability to improve the conditions of people with strokes. In one study, scientists used a home-designed prosthetic controlled by a BCI for motor function improvement in patients that previously had a stroke. The BCI did this by using the “contralesional hemisphere”, or the unharmed side of the brain, to control the limb on the same side. During a stroke, one side of the brain is impaired and loses many functions. Since each hemisphere in the brain controls its opposite limbs, stroke patients often suffer from motor dysfunction in the limbs opposite of the damaged brain hemisphere. BCI enables them to use the healthy half of their brain to control their whole body. Thus, BCI is helpful to stroke patients since it provides a tool with which these people can better recover.

BCI has also helped people suffering from Amyotrophic Lateral Sclerosis (ALS). In the scientific paper “Interface–Based Communication in the Completely Locked-In State”, a type of BCI called functional Near Infrared Spectroscopy (fNIRS), was used to provide a way for ALS patients to interact with their muscles. fNIRS is able to detect the changes in oxygen in the brains of ALS patients, allowing it to determine ALS patients’ responses to simple questions. This ability is incredibly valuable for ALS patients because they often lose full motor function and their ability to speak. With this technology, ALS patients can cope with their condition and communicate with loved ones and the external environment.

BCI has been extremely valuable for paralyzed patients. One brand called “BrainGate” has been used to give Matthew Nagle, a quadriplegic, the ability to play ping pong and draw a circle. This is a major step towards giving quadriplegics the ability to function normally again. BCI was able to partially restore motor function in his hands, allowing Matthew to play ping pong when there were no other options for him to gain motor function. In Matthew’s case, BCI detects neural signals from his brain, and sends it to a computer, which then relays signals to his hands in order to partially restore his motor skills.

BCI has great potential for treating drug addictions. (EEG) was able to help one patient with addictions to multiple drugs overcome his addictions by undergoing neurofeedback. EEG data was used to help patients see the effect of addiction on their brain, thus allowing them to self-regulate themselves. This is beneficial to addiction patients since this reduces their dependency. In addition, this allows many drug addiction patients to control themselves emotionally and physically.

Figure 2: Argus II Retinal Prosthesis System [6]
thus allowing them to attain a higher quality of life.

Finally, BCI has also been helpful to people with sensory disabilities. The Argus II, a type of BCI, can help people with retinitis pigmentosa by improving their vision. The Argus II assumes the function of “light sensing cells” that have been damaged due to retinitis pigmentosa[5]. This prosthesis first gathers visual information from the outside world and translates that information into electrical data. Then, the prosthesis transfers that information into the patient’s eyes. Thus the patient can see despite the damage to some of their photoreceptors. Thus, BCI is able to significantly improve the patient’s quality of life.

Consumer Uses

BCI is also used for commercial purposes. For example, BCI is used to play games that measure focus [7]. It is able to do this by detecting brain waves to determine focus levels. By providing people’s potential thoughts to games, BCI has been able to make games more fun by using brain activity to tailor games to the player. In addition, BCI has been used to play music that correlates to one’s unconscious thoughts [8]. In this way, BCI could present a novel way for discovering new music, and eventually, films and other media.

Potential Consequences

Although BCI can offer enormous benefits, it also can have negative consequences. For example, BCI is able to record brain activity of patients without properly securing the data. Hence, it could provide unauthorized access to people’s medical records, which would pose a great threat in the wrong hands [9]. For instance, BCI captures a wealth of private information from people. If this data were to be improperly secured, hackers could obtain the brain activity, and use it for fraudulent purposes. In addition, advertisers could use the information captured by a BCI to show advertisements that are tailored to patients’ thoughts.

Another disadvantage of BCI is how it could be abused to give people unfair advantages. For example, athletes with a BCI could potentially perform better than athletes without a BCI due to BCI’s ability to improve motor function. In addition, BCI could allow people to gain unnatural physical strengths to circumvent law and order. For example, one could gain access to a restricted area by climbing over physical fences that are considered protective barriers. These capabilities could lead to people with supernatural abilities.

Finally, one must consider the various health issues BCI could cause. For example, ECoG has been known to cause infection and hemorrhages [11]. ECoG requires patients to undergo surgery in which surgeons must penetrate the skull and place the ECoG on top of their brain, which can cause side effects like infection and hemorrhages. The blood-brain barrier makes it difficult to
successfully treat infections in the brain since the blood-brain barrier prevents many drugs from entering the brain.

**The Future**

In the near future, BCI could have many applications. For instance, BCI could be used for brain to brain communication [12]. This would allow humans to interact with each other in new and more profound ways than ever before. In addition, effective brain to brain communication will allow for humans to not rely on language, and thus allow for faster communication between humans. For example, people with severe brain injuries could communicate with their family and friends through their thoughts.

BCI could also lead to more privacy issues in the future. For example, BCI could lead to controversy since there could be legal issues about who owns the data gathered from the BCI.

For example, medical institutions may want to use BCI data for research whereas individuals and their families may want to have ownership of their data. In addition, people accused of crimes could blame BCIs for their actions.

Figure 3: Diagram of Direct Brain to Brain Communication [13]

**Conclusion**

After thoroughly examining potential uses of BCI, a understanding of both BCI’s advantages and its disadvantages become apparent. Therefore, it is essential for society as a whole to better understand the benefits and adverse effects of BCI in order determine how BCI should be used as to help as many people as possible without infringing the rights, freedoms, and the health of patients.
References


To Forget or Not Forget?
Why and How Memories are Lost
By Sharon Samuel

Abstract
Forgetting a piece of information now and then is a very ordinary part of life; in fact, it is part of what makes us human. But why do we forget some things and remember others? Information is forgotten when our brain fails to retrieve a memory or an interference occurs. Failure to retrieve a memory is usually caused by the absence of stimuli or cues that were formed when the memory was encoded. An interference can occur when information gets confused with other information. Our memory can be interfered either proactively or retroactively. When a memory has been interfered proactively, an old memory makes it more difficult to remember new information. On the other hand, a retroactive interference makes it harder to remember previously learned information. There is an advantage to losing memories: it makes room for the incorporation of new memories. Our brain gets rid of information by first sorting it out into two categories: information that is impactful and important and information that is not. Pieces of information that fall into the former category become long-term memories, and the rest become short-term memories.

How Memories are Formed
Every day, our brains receive information from our environment. From perceiving the color of someone’s socks to knowing how to solve a math equation to even learning about cellular respiration in Biology, any and every small bit of information perceived is processed in the brain, or the limbic system to be exact [1].

Before discussing why and how we lose memories, we must first review how they are formed in the first place. Memory is not an entity; it is a concept that refers to the
process of remembering. Most people talk about their memory as if it were something like bad eyesight, when really, it does not exist in a physical sense like a body part [3].

Nonetheless, memories do have a physical origin. Memories are formed when neurons communicate with each other through synaptic connections when certain neurotransmitters are present. A neurotransmitter can be thought of as a text message on a phone. A person may not notice one or two messages, but once hundreds of messages are received, one is more likely to notice and respond. This can be related to the idea that the strength of the connections between neurons is what determines how a memory is formed [4].

“The persistent strengthening of these activated synapses (connections) between neurons is called long-term potentiation,” states William Griffith, Ph.D., a cellular neuroscientist and chair of the Department of Neuroscience and Experimental Therapeutics at the Texas A&M Health Science Center College of Medicine. “Long-term potentiation (LTP), is the most recognized cellular mechanism to explain memory because it can alter the strength between brain cell connections. If this strength is maintained, a memory can be formed.” LTP acts as an Ethernet cable, allowing one’s brain to “upload or download” and process information at a higher rate, which may explain why some memories are more vivid than others. The pathway on which the brain connects them performs at a faster pace [4].

Figure 2: Electrical signals move from the cell (above right) along the axon to the synapse (detail at left), where they are relayed across the synaptic cleft to neighboring cells in the form of chemicals called neurotransmitters [5].

Failure to Retrieve Memory

Not being able to retrieve a stored memory is one of the most common causes of forgetfulness. Retrieval failure is the inability to recall a memory due to missing stimuli or cues that were present at the time the memory was encoded. This theory claims that a memory is temporarily forgotten simply because it cannot be retrieved, but with the proper cue, that information can again be brought to mind [6]. This is also a strategy that is widely used in memorization competitions.

Interference with Retrieval

Interference occurs when information gets confused with other information in our long-term memory [6]. Basically, if cues are too similar, they are more likely to get confused with each other,
causing an interference and the wrong memory to be retrieved. There are two types of interferences that can happen when trying to retrieve a memory: proactive and retroactive.

Proactive interference is when an old memory makes it more difficult to remember new information. Current information is lost because it is mixed up with previously learned information that may be similar.

Retroactive interference occurs when new information interferes with the brain’s ability to remember previously learned information [6]. It works backward in the sense that it is interfering with previously gained information. The old information is lost due to it being mixed up with new or similar information.

The Purpose of Forgetting Information

Forgetting actually has its fair share of advantages. For example, learning a new locker combination would be accomplished by gradually forgetting the old locker combination. This step is necessary in order to enable space to be made for the new memory. When we acquire new information, like a new locker combination, the brain automatically tries to incorporate it within existing information. This is done by forming associations, and, when we retrieve information, both the desired and associated information are recalled [7].

Key Terms and Points Recap

1. **Limbic System** - the portion of the brain that deals with emotions, arousal, and memories

2. Memories are formed when neurons communicate with each other through synaptic connections when certain neurotransmitters are present.

3. **Long-term potentiation** - the most recognized cellular mechanism to explain memory because it can alter the strength between brain cell connections.

4. **Retrieval failure** - the failure to recall a memory due to missing stimuli or cues that were present at the time the memory was encoded.

5. **Interference** - occurs when information gets confused with other information in our long-term memory.

6. **Proactive interference** - occurs when an old memory makes it more difficult to remember new information.

7. **Retroactive interference** - occurs when new information interferes with the brain’s ability to remember previously learned information.
8. When we acquire new information, the brain automatically tries to incorporate it within existing information by forming associations.

9. The information retained is what we call long-term memory, and the information that was lost is called short-term memory.

10. **Long-Term Memory** - the type of memory stored for an extended period of time.

11. **Short-Term Memory** - the type of memory stored for a short period of time.

12. When new information comes along, we have to give up some space in our brains to incorporate it.

References


An Interview with Alie Caldwell of Neuro Transmissions

Chidüssọ Ajaero

Introduction

Alie Caldwell, better known as Alie Astrocyte, is the neuroscience-half of the two-person team of the increasingly popular YouTube channel, Neuro Transmissions. Launched in 2015, Neuro Transmissions brings information about neuroscience to a wide audience through social media [1]. The channel now has over 10,000 subscribers and teaches psychology in addition to neuroscience through Alie’s husband and co-presenter, Micah, also known as Micah Psych [1, 2]. Alie is a graduate of Brain and Cognitive Sciences at MIT and PhD-candidate in Neuroscience at the University of San Diego, and she has written over forty episodes for SciShow, one of the most popular scientific channels on YouTube. Through Neuro Transmissions, Alie and Micah use humour and elements of popular culture to make neuroscience more engaging for the average viewer. As their slogan puts it, “It’s not rocket surgery, it’s brain science” [3]. I was lucky enough to be able to ask Alie some questions about neuroscience.

Chidüssọ Ajaero (CA): “What inspired you to begin your channel?”

Alie Caldwell (AC): “Before I started graduate school, my partner did videos as a hobby, running his own YouTube channel. When I got to UCSD (University of California, San Diego), I discovered that the students here have a tradition of making a parody music video to advertise for their social event during the SfN (Society for Neuroscience) meeting in San Diego. My partner, Micah, offered to help with that year’s video, which lead to the creation of Get Data. We had so much fun, we decided to enter the Brain Awareness Video Contest the following year, and then, started talking about doing more. At the time, when you searched “Introduction to Neuroscience” on YouTube, all you got were recordings of college lectures. I started wondering if we could take those same concepts from an introductory college course and break
them down into 5-7 minute long videos, using animations to help clarify the message. In 2015, I wrote the Neuro 101 series and started releasing them in September. Since then, we’ve tried to put out a new video every two weeks.”

**CA: “What are the goals of your channel?”**

AC: “We always say that our goal is to ‘make the brain accessible for everyone.’ Neuroscience isn’t really part of the public school curriculum (at least in the U.S.), but everyone has a brain, so the brain is a really great place to get people engaged with science. We’re trying to bridge the gap between things people are familiar with - like pop culture and common disorders - and things they might not know much about, like neurotransmitters and fMRI. Our hope is that viewers can get enough information to answer a question they had, but also leave them interested in knowing more. We also want our work to reflect the fact that science is a human enterprise, done by human beings; we’re not geniuses up in an ivory tower, but just people trying to do the best job we can do at answering the questions we see in the world around us.”

**CA: “What is the role of neuroscientists in society?”**

AC: “That’s a good question. I would argue that the role of a neuroscientist in society is sort of up to the person. All scientists are trying to learn more about our world, so we can understand it and ourselves a little bit better. Neuroscientists can - and should - think not only about the positive implications of their work, like life-saving, new drug therapies, but also the negative, like the possibility of marginalizing already struggling members of society by "curing" conditions that aren’t always seen as a disease. We are chipping away at the doorway of the human mind, and our work will have enormous repercussions in the future. To me, that means our role is to work on these questions as objectively and thoughtfully as we can while working to break down the barriers between our work and the public and carefully considering the ethical dilemmas our work might bring up.”

**CA: “How did you become a neuroscientist?”**

AC: “I’ve always wanted to be a scientist in some capacity, but for a long long time, I wanted to be an astronaut (I still do, really). It was when I got to college and took my first physics class that I realised I didn’t really want to study engineering. At the same time, I was taking an introduction to psychology course with Dr. John Gabrieli as a humanities elective. I really love the stories of different famous patients, like H.M. and Patient Tan, and what psychologists and scientists have learned from them. The next semester I took an introduction to neuroscience class, and I just couldn’t get enough. I’ve always loved biology and studying neurobiology means I get to study the biology of the mind.”
CA: “What are efficient ways that you believe can be used to increase public understanding of neuroscience?”

AC: “I think that digital media platforms offer incredible new opportunities to reach new audiences in really unique ways. I know a lot of neuroscientists who do outreach, but for many, it’s limited to volunteering in classrooms, giving the occasional public lecture, and maybe writing some blog posts. That kind of outreach is important, and it’s wonderful that scientists do it. But there are other options, too. For scientists who want to reach the people who think they’re not interested in science, social media platforms like Instagram and YouTube offer a chance to showcase science and the scientist. You can use hashtags and tags to help people find your video and hopefully reach a few people who weren’t looking for it but enjoy it anyway. So I encourage scientists to get familiar with social media, and try their hand at something new - like taking a picture of interesting pieces of lab equipment, explaining what it is on Instagram, or filming how they use an everyday object like nail polish in the lab and sharing the video on YouTube.”

CA: “How do neuroscientists interact with other scientists, neurologists and neurosurgeons?”

AC: “It sort of depends on the neuroscientist. I study basic science, which means I’m answering basic questions about neurobiology - I’m not working on clinical trials with human patients, but with mice and cells in a dish. That means that I interact with a lot of neuroscientists. I talk to them about protocols and techniques and ask for advice when I’m trying something new or when I’m looking for a new reagent [a substance used because of its chemical or biological activity]. Sometimes they train me, or I train them. We often travel to present our research at conferences, like SfN in November, and sometimes attend courses or symposia on specific topics related to our research. A lot of this also includes networking, which is meeting and getting to know others in the field, with the hopes that they might be a good resource for a job or a collaboration later on. People who work on more clinical stuff will often end up interacting more with neurologists and neurosurgeons. Some doctors have both an M.D. and a PhD., so they’re a neurologist and neuroscientist. They might work together if the doctor’s patients are part of a clinical trial; for example, if they are sharing tissue or data. But I personally rarely interact directly with M.D. - except for the ones who are my friends in real life, and then we’re not talking about their patients!”

CA: “Your biography notes that your research focuses on astrocytes and neurodegenerative diseases. What is your most interesting finding?”

AC: “I’m trying to understand how the proteins made by astrocytes are different in mice that have particular kinds of genetic mutations. In humans, these mutations cause serious neurodevelopmental disorders, including severe intellectual disability. So I isolate these mutant
astrocytes in a dish, collect the proteins they spit out, and compare them to normal astrocytes. My work hasn’t been published yet, so I can’t say very much about it, but I can say that we have found some very interesting changes in mutant astrocytes, and I am working on figuring out whether or not those changes have a direct effect on neurons.”

References


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