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FEATURED ARTICLES

‘Finding a New Treatment to Relieve Symptoms of Depression’
- Amanda Azia

‘Neurological Manifestations of COVID-19’
- Saad Umar

INTERNATIONAL YOUTH NEUROSCIENCE ASSOCIATION
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Letter From the Editors
Sojas Wagle, Aayush Setty, Anita Singh, Kareena Thakur, Annie Pan, and Christine Zhou

Dear Readers,

Welcome to the fifth installment in the third season of the IYNA Journal! We greatly appreciate your readership, continued or new. We have worked hard at producing more high-quality articles for everyone to read and encouraging a growing number of high school students from around the world to submit their neuroscience findings, research, and/or interviews to the journal. We’ve hand-picked a special few to showcase in this month’s journal.

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

Muhammad Saqib Hussain discusses artificial intelligence and its applications, Varun Vasireddy gives an overview of dyslexia, Lori Saxena covers sudden unexpected deaths in epilepsy (SUDEP), Akhil Kumar sheds light on the intricacies of Alzheimer’s and how nanotechnology can be applied, Avikgna Lingenathan explains the pathology involved in hydrocephalus, Amanda Azia researches a new method — the Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) — to treat depression, Saad Umar shares how COVID-19 can affect the brain, and Vishruth Nagam interviews psychologist Dr. Leonard Abbeduto about COVID-19.

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

Best Regards,
Sojas Wagle - IYNA Journal Editor-In-Chief
Aayush Setty - Managing Editor
Anita Singh - Senior Editor
Kareena Thakur - Senior Editor
Annie Pan - Senior Editor
Christine Zhou - Head of Assembly
Artificial Intelligence to the Rescue
Muhammad Saqib Hussain

Abstract

Millions of people suffer from neurological diseases worldwide. Nearly 15 million people suffer a stroke each year, more than 65 million people have epilepsy, and 50 million have dementia [1][2][3]. The numbers are just astounding. This is why research has been conducted to develop faster and more accurate computer-aided diagnosis (CAD) systems for better and faster diagnosis. The ideology of CAD systems using large quantities of processed patient data and artificial intelligence/machine learning have long been advocated by neuroscientists [4]. These methods, when automated, have the potential to assist neurologists, neurosurgeons, and neuroradiologists to make better clinical decisions by helping them interpret and analyze images more effectively. This article presents an overview of neural networks and a review of research on the automated diagnosis of 5 incredibly common neurological disorders: epilepsy, Parkinson’s disease (PD), Alzheimer’s disease (AD), multiple sclerosis (MS), and ischemic brain stroke using physiological signals, images, and artificial intelligence.

Why Is CAD Important?

Diagnosis in the 21st century has become more complex than ever. Improved and sophisticated instruments provide more information and thus make diagnosis more accurate. On the other hand, diagnosis has become a more difficult process as stated by an article on TechRepublic: “The analysis, by neural networks, of thousands of scans can spot patterns that humans miss” [5]. For example, in Beijing, an artificially intelligent system beat elite physicians by 2-0 in two rounds of competition to diagnose brain tumors and predict the expansion of brain hematomas (rupture of a blood vessel) [6].

What Is the Difference Between ML and DLNN?

Machine learning involves coding features that a computer should know to make a prediction about an image. For example, if someone wanted to differentiate between images of cats and dogs, the programmer would tell the computer that a cat is furry, fluffy and is generally white and smaller in size, while a dog has short, brown, small hair. The lists of features could go on forever. DLNNs (deep learning neural networks), on the other hand, do not need to be told what to
look for. They can recognize all the features themselves, which is far more efficient and straight-forward.

DLNNs have significant advantages over ML (Machine Learning)-based CAD. First and foremost, DLNNs can handle large datasets using their multilayer technology. They can also handle imbalanced data samples without bias towards the majority class. For example, if the majority of MRI scans appear 40% gray and a few appear 65% gray, the lighter ones would still be classified as an anomaly. Also, researchers can expand or shrink these models by adding or removing hidden layers, which makes these models very adaptable to the requirements and complexity of the classifier [7].

ML-Based CAD Steps

Artificially intelligent systems require a lot of training data that first need to be processed to prove useful to the training algorithms [9]. The raw input (images, electroencephalogram (EEG) data, speech, etc.) is passed through filters where the redundant information is removed and features are extracted. Next, the extracted features must yield useful information on which the model can train. Gray-level co-occurrence matrix (a statistical method that examines texture) features are mostly used for image feature extraction [10]. For example, see Figure 3 (the useful feature is bounded by a blue stroke).

After this, dimensionality reduction is performed. This is because feature extraction results in a large amount of highly detailed images (or
electroencephalograms in the case of epilepsy). Dimensionality reduction allows quality and computational requirements to be reduced with a negligible effect on the accuracy of the NN. The 4th and 5th step is optimal feature extraction and ranking. They are exactly what they sound like. Most features contain redundant information that needs to be removed to obtain optimal classification performance. The analysis of variance on ranks (ANOVA on ranks) is the most common ranking technique. Essentially, the feature that is most useful is selected to be run on the images. The final step is classification. This is where the magic happens. It is composed of two steps: training and testing (definitions in the glossary). Once trained, they can be used for the classification of new cases that the model has not previously learned.

This was an overview of data processing. The next section deals with the selection of a suitable neural network for various neurological diseases.

Choice of AI Model
The following infographic provides the names of the most common neural networks used in artificial intelligence.
The list of artificially intelligent networks that can be chosen for a project is perpetually growing. This has obvious advantages. Researchers can choose the model that best fits their needs. Different types of models have different advantages (e.g. efficiency, memory usage, computation time etc.).

According to different researchers, different neural networks prove useful for different neurological diseases [12]. For example, the best classifier for Alzheimer’s disease is a probabilistic neural network, but it isn’t very effective for the diagnosis of Parkinson’s disease.

What’s Next?

Google’s Tensorflow, arguably the most popular Deep Learning framework today, is already being used for the diagnosis of diabetic retinopathy, which is the leading cause of blindness in the working-age population [13][14].

AI techniques have also been applied to stroke imaging in the following two respects: 1) automatic or accurate diagnosis and 2) prediction of prognosis [15].

One other area where CAD has been used is the accurate diagnosis of PD. The number of misdiagnoses is reduced with the help of CAD and diagnosis algorithms. Extracting features and selecting appropriate features yield good classification results [16].

CAD is a very promising area, but it currently has two limitations: training data and training time. Computer scientists are already working on improving these limitations. The next step is to design more efficient models that require less data and training time. Computers helping physicians in diagnosis and eventually in the treatment of diseases is the next big thing.

Glossary

- **Artificial Intelligence (AI)**: the simulation of human intelligence by computer systems
- **Machine Learning (ML)**: an application of artificial intelligence that provides systems with the ability to automatically learn and improve from experience without being explicitly programmed
- **Deep Learning Neural Networks (NN) or model**: a class of machine learning algorithms that uses multiple layers to progressively extract higher-level features from raw input
- **Training**: the feeding of inputs and desired outputs to an NN to facilitate learning in a model
- **Testing**: the feeding of a new set of data to a model to test its accuracy

References


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The Truth About Dyslexia: A Complete Overview
Varun Vasireddy

Introduction
As we mature from infancy to early childhood, we develop one of the most important skills known to our species, the ability to communicate, which begins with the capability to talk. Soon after, we begin to read and craft sentences. Oral communication has been present since the beginning of mankind. However, written language has only been present for roughly 5,000 years. Mastering the art of reading and writing is not an easy process, however some children, even with normal intelligence and motivation, find it unusually hard to read and write. Dyslexia is a common condition that affects as many as fifteen to twenty percent of all Americans [1]. This article discusses dyslexia in detail, its complications, and what a dyslexia diagnosis really means.

General Overview of Dyslexia

Dyslexia, commonly classified as a learning disability, affects the ability of people to read, write, and spell. The various symptoms of dyslexia include stuttered or slow speaking, difficulty naming objects, such as when shown a picture, problems with speed while reading, and articulating words while reading. Dyslexia is a chronic disability, which is most often diagnosed in the early schooling years. Although dyslexia cannot be cured, many dyslexics can improve their fluency, the speed at which they read, and their accuracy [1]. There is no comprehensive test or set of symptoms available to identify dyslexia, which often makes it go unnoticed. Dyslexia affects children in many different ways, which makes it common for parents and teachers to assume that a child’s difficulty with reading is just associated with slow development. A dyslexia diagnosis should be made by a licensed medical professional, usually a psychologist or a neurologist [2].

Dyslexia: Inside the Brain

The act of reading involves two main ideas, or processes: the orthography of the language and deriving the phonemic structure [3]. The orthography of the language refers to being able to recognize the language’s symbols in the right order while deciphering the respective symbols into accurate sounds, is the derivation of the phonemic structure. The English language has forty-four
phonemes or distinct sounds that differentiate words within a language [3]. Dyslexics have problems with these mechanisms, which is largely caused by issues with their visual processing. Magnocellular cells, meaning large cells, which are located throughout the visual system, are specialized to track moving stimuli and are key in concentrating on a target, such as while reading [3]. When the reader is distracted or loses concentration, the magnocellular cells send an error signal to the eyes which brings them back to focus. This feedback system is crucial to help maintain a steady focus while reading. However, this system is impaired in dyslexics, meaning that the reader cannot maintain a constant plane while reading. This is why patients will often complain that the letters are blurry, or even moving around.

**Anatomical Differences**

Brain imaging is now a common technique used to explore the human brain in a non-invasive manner. These various techniques include MRI, fMRI, CT scans, and many others. Functional magnetic resonance imaging, more commonly known as fMRI, takes place in a large magnetic tube with powerful magnets that are used to build a detailed three-dimensional picture of the brain, like a traditional MRI. However, an fMRI also tracks the oxygen flow throughout the brain which helps neurologists identify what parts of the brain are active during a certain task. Studies using brain imaging demonstrate that certain parts of the brain are less active in dyslexic readers than in fluent readers. One of these areas is the visual word-form area (VWFA), which is
located in the temporal lobe of the brain. The VWFA is responsible for recognizing letters and familiar words. This area also helps attach significance to a phrase or sentence with its connections throughout the brain [1]. Another area that shows considerably less activity in people with dyslexia is the left occipitotemporal cortex. The left occipitotemporal cortex is crucial in the recognition of letters and words by identifying their shapes. The left occipitotemporal cortex also works together with other parts of the brain to connect a number or symbol to a concept [1]. Overall, dyslexics have less brain activity in the left hemisphere of their brain, which is responsible for language processing and speech production. As a result, dyslexics often tend to rely more on their right hemisphere.

Potential Causes

There is no single cause of dyslexia. However, most studies agree that dyslexia is highly influenced by genetic factors. Some studies show that sixty to seventy percent of dyslexia cases are due to genetic factors and around thirty percent of cases are due to environmental factors [5]. Environmental factors include low birth weight, lead exposure during pregnancy, and premature birth among others. Twin studies have shown that when one twin is diagnosed with the disorder, the other twin also has dyslexia about fifty-five to seventy percent of the time [1]. There have been about 40 genes that have been shown to be connected to dyslexia in various studies [6]. Almost all of the chromosomes in our body have some linkage to dyslexia. However, no single gene has been identified as the major cause of genetically inherited dyslexia. There are various labs and studies going on around the world to find the main gene involved with genetic dyslexia.

Potential Drug Treatments

Dyslexia does not have a permanent cure. However, most patients are able to improve their skills of reading and writing to a certain extent. There are various treatment options for dyslexia and scientists do not agree on a so-called “best treatment”. Treatment is based on a patient to patient basis because dyslexia can affect people to various degrees. There are relatively few new treatments. These treatments have been experimental and have shown significant success. However, none of these treatments or drugs have been approved for commercial and pharmaceutical use. Many studies have shown that ADHD and dyslexia are linked disorders. ADHD, which stands for Attention Deficit Hyperactivity Disorder, is another common childhood psychiatric disorder. ADHD is characterized by being distracted easily, having trouble focusing on a set goal, acting on an impulse, and sometimes having trouble sitting still. Statistics show that anywhere from fifteen to forty percent of children with dyslexia also have ADHD [7]. A drug named atomoxetine, which is normally taken by children with ADHD, has shown success in a particular study. In this study, children were split into three groups. There were children with dyslexia only, children with ADHD and dyslexia, and children with only ADHD. These three groups were randomly assigned either atomoxetine or a placebo and instructed to take the pill daily for 16 weeks [8]. The children were given a baseline reading test before administering the pills. After the completion of the 16 weeks, another reading test was given. Researchers found that children with dyslexia or both dyslexia and ADHD showed significant progress with reading as opposed to children with only ADHD, who were not affected as much [8]. Atomoxetine is not yet a regularly
prescribed treatment for dyslexia. This is an exciting development in the trials of a drug for dyslexia. However, there are potential drawbacks of a drug including accessibility and affordability. There is no guarantee that a potential drug would be cost effective for all, or accessible to everyone around the world in large quantities.

**Potential Non-Drug Treatments**

There has also been a non-drug treatment that has shown success in a separate study. This particular study focuses on the fact that dyslexia is a problem with the lack of coordination [9]. Researchers assigned a series of exercises focused on the cerebellum and focusing on certain eye movements. These exercises are used by astronauts because they sometimes suffer a temporary form of dyslexia while in space [9]. The children were instructed to perform the exercises two times a day, one set in the morning and the other before bed [9]. The exercises included walking downstairs backward with their eyes closed, standing on a wobbly or uneven surface, and catching and throwing something from one hand to another [9]. The study was carried out for 3 years and during this period they were given reading checkpoints every 6 months and an SAT test yearly. The results of the study were astonishing. The dyslexic children caught up to the reading level of their peers in around a year and they scored better on the SATs than efficient readers. Another observation was that children who had more severe dyslexia showed the greatest improvement. This experiment proved the link of the cerebellum in processes such as reading and paying attention [9]. This non-drug treatment still has to be approved by medical professionals and tested on a more wide-scale basis before it is approved. This treatment would most likely be accessible for all. There would be no need to purchase drugs on a regular basis, which means there would be no worries of being able to afford a drug. Once a dyslexia diagnosis is made, these exercises can be performed virtually anywhere, with almost no equipment. The future of treatments for dyslexia is very bright as there are many labs, universities, and private studies trying to find a treatment for the most common learning disability in the world. There is hope that a dyslexia treatment will be found in the near future, improving the literacy rate all round the globe.

**Conclusion**

A dyslexia diagnosis does not mean the end of the world. There has also been some research that dyslexics might be better at perceptual thinking and making advanced connections. Dyslexics have proven to have great spatial awareness, being excellent puzzle solvers, and thinking outside of the box [10]. People with dyslexia have great imaginations which help them with critical and abstract thinking. Dyslexics go on to accomplish many things in various fields including art, music, and science. Leonardo da Vinci, Hans Christian Andersen, Thomas Edison, Albert Einstein, and other Nobel Laureates and artists were also dyslexic [3]. A cure of dyslexia may be in our near future, allowing many the ability to read and write, a skill which we often take for granted.

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References
Sudden Unexpected Death in Epilepsy (SUDEP): An Overview

Lori Saxena

Introduction

Epilepsy is a common neurological disorder associated with significant morbidity and a high mortality rate. The fourth most common neurological condition in the world, epilepsy, is characterized by abnormal neuronal activity resulting in seizures which have diverse clinical presentations, as well as widespread neuronal loss and pathological deficits in the brain. Despite the prevalence of epilepsy around the world, very few people are aware of the range of devastating impacts that epilepsy can potentially have on a patient, and sudden unexpected death in epilepsy (SUDEP) is one of the most important but least known of these possible worrying results. In 1997, SUDEP was defined as “sudden, unexpected, witnessed or unwitnessed, nontraumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which postmortem examination does not reveal a toxicologic or anatomic cause of death” [1], and although this formal definition has changed in recent years, it has remained relatively consistent.

What Is SUDEP?

Currently, SUDEP, or sudden unexpected death in epilepsy, is the leading cause of epilepsy-related death, and patients with epilepsy are 24 to 27 times more likely to experience sudden death, with drug-resistant patients having been proven to be even more likely to die from SUDEP [2]. However, despite the overall prevalence of SUDEP, its cases are currently considered to be highly unrecognized and underreported. This is because 90% of cases are unwitnessed, therefore critical information regarding the events leading to death are not known. This leaves the medical history and postmortem findings as the only source of information, and these often prove insufficient to accurately pinpoint the cause of death. Death certificates highly underestimate the SUDEP in epilepsy, attributing 1.5% of sudden deaths to seizure complications and seizures themselves [3]. When the patient undergoes autopsy, pathologists performing the autopsy tend to ignore SUDEP cases based on the rather vague pathological findings [4]. Another pitfall would be the existence of conditions such as a minor coronary artery disease in patients because death could be falsely attributed to these conditions instead of SUDEP. Therefore, better standardization of the
pathological criteria, raised SUDEP awareness and better documentation are essential in the pursuit to understand and prevent SUDEP.

**Understanding the Biological Mechanism Behind SUDEP**

Despite vigorous efforts, the pathophysiology of SUDEP remains obscure, however there have been numerous possible SUDEP mechanisms which have been proposed by a variety of different studies. For example, the 2013 MORTEMUS study, which studied 16 different SUDEP patients, was a milestone in SUDEP research. This study allowed scientists to better understand the mechanism underlying SUDEP and concluded that in the cases examined, a generalised epileptic seizure led to early alteration of respiratory and cardiac function. This led either to immediate death or to a period of restored cardiorespiratory function before cardiac arrest occurred [5]. Furthermore, a variety of SUDEP studies have observed that the majority of SUDEP cases occur at night [6]. This may suggest that circadian rhythm plays a role in SUDEP.

**Genetic Variants Contributing to SUDEP**

SUDEP has also been shown to potentially be linked to various genes. In a study, 61 people with SUDEP were genetically tested, and it was shown that four had mutations in the same four genes. A further nine had variants in candidate genes for cardiac arrhythmia, a disorder which is thought to accompany SUDEP [7]. Overall, various studies each propose different possible mechanisms for SUDEP, indicating that the condition could be attributed to a variety of possible factors in epileptic patients.

![Figure 1. A graphic showcasing basic facts and statistics regarding SUDEP](image.png)
Lack of Awareness

In addition to obscurity surrounding the specific biological mechanism behind SUDEP, there is little to no awareness about the condition. In fact, the concept of SUDEP only gained recognition in the 1990s. Until then, there was almost no public awareness of its potential impact on people with epilepsy and very little in the medical literature. In 1995, the charity Epilepsy Bereaved was founded by families who had been affected by SUDEP in order to raise awareness amongst the public and medical community. The first international conference was held in 1996 which led to the first international publication on SUDEP [7]. Following the landmark paper by Nashef which standardised the definition of SUDEP [1], research into SUDEP gained huge momentum.

Identifying SUDEP

Increased awareness of SUDEP amongst the medical community has been vital in ensuring that cases of possible SUDEP are referred to the coroner for investigation. All cases are now highly encouraged to receive a SUDEP autopsy in order to exclude other causes of death. There have been many reports of likely SUDEP cases being issued another cause of death, such as status epilepticus, or accidental death by medical professionals and coroners despite there being no evidence for this. SUDEP may therefore be underreported and the inaccurate classification of these deaths may skew studies aiming to identify relevant risk factors.

Patient Awareness

In addition to this overall misdiagnosis of SUDEP cases, the discussion of SUDEP with patients and their caregivers has always been a controversial topic. The National Institute for Health and Care Excellence updated their guidelines on epilepsy management in 2004 to include SUDEP [8]. They advise that giving patients tailored information about their risk of SUDEP should be done as part of a counselling checklist for patients with epilepsy and their families. The most common reasons given for not discussing SUDEP are that neurologists feel that their patients are at low risk and they fear a negative reaction. In fact, some doctors have even suggested that to disclose the risk of SUDEP when not sought by the patient may in fact be unethical as there is no proven intervention to minimise SUDEP and that knowledge of the condition may negatively impact quality of life. It was also reported that doctors are unlikely to be found negligent for not discussing SUDEP as there is no proven preventative measures or intervention [9]. On the flip side, the most common reasons given for discussing SUDEP were the patients inquiring about it themselves and the neurologist counselling someone with known SUDEP risk factors. However, there is mounting evidence that patients and their families wish to be informed of the risk of SUDEP [10]. Furthermore, despite not routinely being informed of the risk does not mean that patients are ignorant of SUDEP and they may resort to inaccurate and unreliable sources that do not take into account their personal risk of SUDEP, making it imperative that doctors address the issue.

Long Term Prevention
Partially due to a lack of understanding about SUDEP and a lack of overall awareness both by the public and medical community, there remains no effective evidence-based preventions against SUDEP. Strategies to try to prevent SUDEP include reducing the number of seizures a patient has (by considering epilepsy surgery or making lifestyle changes), examining for heart and breathing problems during and following seizures, and supervising patients at night or using safety pillows to prevent breathing difficulties. Furthermore, the use of a safety checklist has gained interest since it was first proposed and has subsequently been developed into a smart-phone app [1]. In addition, drugs that increase the brain chemical serotonin and reduce the brain chemicals adenosine and opioids have also been recently proposed as future targets for SUDEP prevention but there have been no trials examining the benefits of these in the prevention of SUDEP.

**Short-Term Prevention**

Within the hospital setting, several interventions are also recommended to reduce the duration of seizures, respiratory dysfunction and EEG suppression, which are all thought to contribute to SUDEP. These include repositioning of the patient during a seizure, oral suctioning and oxygen administration. The MORTEMUS study also showed that in near-SUDEP cases, where patients almost died from SUDEP but ended up surviving, resuscitation was prompt whereas in the SUDEP cases it was delayed suggesting that close monitoring of patients in hospitals with the use of direct supervision, ECG, EEG and oxygen may reduce the risk of SUDEP significantly [5].

**Conclusion**

Despite all these efforts, there remains no consistently proven preventative strategy for SUDEP, although several of those described show promise and deserve further research to determine their effectiveness. Furthermore, many neurologists fail to mention the risk of SUDEP to epilepsy patients, reminiscent of when doctors and families would not tell people they had cancer. But today, patients learn not just about cancer but about many other potentially fatal conditions. So the quiet about the epilepsy death risk appears to be an anomaly. This is due to a variety of different factors including an overall lack of awareness, lack of understanding, and lack of diagnosis or recognition of SUDEP cases. Overall, more attention needs to be brought to the prevalence of SUDEP among epileptic patients in order to more effectively diagnose, research, and understand SUDEP, and ultimately mitigate the risks of the condition.

**References**


Alzheimer’s and Nanotechnology: The Missing Puzzle Piece

Akhil Kumar

Introduction

Alzheimer’s is a disease that affects over 44 million people worldwide. To many families, when a loved one receives a diagnosis of Alzheimer’s, it may seem like the end of the world. They have to endure their loved ones losing precious memories and forgetting who they actually are. Recently, scientists and researchers have discovered a new way to tackle this problem. Nanotechnology is a new kind of science that allows researchers to study extremely small particles which can help them develop a cure or can lead them to make an early diagnosis. This entry will talk about the new therapies being developed and how it all fits into the bigger picture.

The Formation of Alzheimer’s Disease

In healthy aging, the brain shrinks but does not lose a lot of neurons. In Alzheimer’s disease, many neurons stop functioning, lose connections with other neurons, and eventually die. The disease disrupts vital processes to neurons and their networks which results in the loss of memory, communication, logical reasoning, and social behavior. A person with Alzheimer’s gradually loses their ability to function independently and ultimately dies from the disease.

A lot of the molecular and cellular changes that happen in a person who has Alzheimer’s occur long before the first sign of memory loss (about 7-10 years). There are five main causes of this disease, and they are all interconnected in many different ways.

1. Amyloid Plaques
The protein, beta-amyloid, is formed from the breakdown of a larger protein called the amyloid precursor. Beta-amyloid may come in different molecular forms and one such form, beta-amyloid 42, is known to be extremely toxic. The protein is naturally found in the brains of humans but abnormal levels of this protein can lead to them clumping together to form plaques that form between neurons that disrupt cell function.

2. Neurofibrillary Tangles

Neurofibrillary tangles occur when abnormal amounts of a protein called tau accumulate inside of healthy neurons. In the brain of a person who does not have Alzheimer’s, neurons are supported by structures called microtubules, whose main job is to guide nutrients and molecules from the cell body to the axon and dendrites of the neuron. It does this by binding to microtubules and stabilizing them. However, in a person who has Alzheimer’s, abnormal chemical changes cause tau to detach from the microtubules and attach to other tau molecules that form threads that eventually lead to tangles inside neurons. These tangles effectively block the neuron’s transport system which in return harm’s the synaptic communication between neurons.

3. Chronic Inflammation

Chronic inflammation is caused by the buildup of glial cells which are normally meant to help keep the brain free of any debris. In a healthy brain, microglia and astrocytes (types of glial cells) engulf and destroy waste and toxins. In Alzheimer’s, microglia fails to clear away the waste, debris, and the protein collections which include beta-amyloid plaques. A study found the TREM2 gene to be the culprit of the abnormal function of microglial cells. TREM2 usually tells the cells to clear the beta-amyloid plaques from the brain and it is supposed to help fight inflammation. In the people where this gene does not function normally, plaques build up between neurons and they collect around the neurons but fail to perform their tasks. When this happens, they also release chemicals that cause chronic inflammation and further damage the neurons which they are meant to protect.

4. Vascular Contributions

The majority of people who have Alzheimer’s also have a lot of vascular issues such as beta-amyloid buildup in brain arteries, atherosclerosis (hardening of the arteries), and mini-strokes. These vascular problems lead to reduced blood flow and oxygen to the brain and to the breakdown of the blood-brain barrier which protects the brain from harmful agents and only allows necessary agents to enter, such as glucose. A faulty blood-brain barrier prevents glucose from reaching the brain and prevents it from clearing away the toxic beta-amyloid and tau proteins. This results
in inflammation which further adds to the vascular problems in the brain. 
Alzheimer’s is the cause and the consequence of most of the vascular problems that occur in the brain.

5. Loss of Neuronal Connections and Cell Death

➢ As neurons are injured and die off, the connections between networks of neurons break down and many brain regions begin to shrink. This process is known as brain atrophy and by the final stages of Alzheimer’s this process is widespread which causes significant loss of brain volume and eventually results in death.

All of the causes of the disease are linked together, but the main cause of the disease in most people is the buildup of plaque in the brain. Some of the causes may or may not happen depending on the type of person and the severity of the disease. Alzheimer’s may also be caused by a variety of other reasons such as genetic mutations, age, gender, lifestyle, cognitive impairment, etc. [1][2].

Nanotechnology and Nanoparticles Overview

Nanotechnology is the study of extremely small things and is used in all fields such as chemistry, biology, engineering, and many more. Nanotechnology involves the ability to see and control individual atoms and molecules [3]. Nanomaterials have a relatively large surface area when compared to a material that has the same mass but in a larger form. This is because as objects get smaller their surface area to volume ratio increases, which means that the rate at which the volume increases is not the same as the rate of decrease in the object’s surface area. When objects are this small, they exhibit more quantum effects and don’t follow normal physics laws. For example, Vantablack 2.0, is the most black paint in the world and absorbs almost all of the light that reaches it [4].

Nanoparticles are microscopic particles between the size of 1 nanometer to 100 nanometers, as defined by the International Organization for Standardization (ISO). Gold nanoparticles are a type of nanoparticle that has the ability to get extremely small, and usually have a diameter of 5nm or less. They can be used in many applications but are mainly used as a catalyst (a substance that increases the rate at which another substance goes through a chemical change without undergoing any permanent chemical change itself) to help reactions occur. Gold nanoparticles also have the capability to convert certain wavelengths of light into heat. This occurs because gold contains electrons that are free to move throughout the metal and these electrons help conduct a current through the gold when a voltage is applied to it. Depending on the size and shape of the nanoparticles, these free electrons absorb energy from particular wavelengths of light. If it absorbs the right wavelength, a cloud of free electrons will form on the surface of the gold nanoparticles thus generating heat [5].

Nanoparticles and Alzheimer’s
To develop a treatment, researchers and scientists have to properly visualize the protein build up inside and around neurons. If we get to know more about their structure it could lead to the detection of weak spots that could be targeted for treatment. On March 11, 2020, scientists from EPFL published a solution. The research showed that gold nanoparticles with a diameter of about 3nm have the unique ability to label amyloid proteins in a hydrated state. It was done using a specialized form of TEM called cryogenic transmission electron microscopy (cryo-EM), in which they first rapidly freeze the proteins to a very low temperature and they then can be visualized in their original state without having to be stained or modified beforehand thus making the visualization of the amyloids a lot easier [6].

Another application for nanoparticles is that they could break up the beta-amyloid plaques in the brain. A research study published from the University of Michigan at Ann Arbor and South Korea’s Kyungpook National University showed that when a short chain of amyloid peptides wraps around a tetrahedron-shaped nanoparticle, the nanoparticles’ edges destroy the peptides which prevent the additional peptides from attaching to the chain. The scientists used CdTe nanoparticles for their particularly sharp-faced structures. The researchers think this work offers a blueprint for the nanoscale engineering of nanoparticles from a variety of materials with properties similar to the CdTe nanoparticles. The problem with CdTe nanoparticles is that they are toxic and can’t be used in vivo, which means they can’t be used in a living organism. This research is an excellent proof-of-concept that demonstrates that nanoparticles can be devolved to break up protein bonds in the brain which can lead to the eventual cure for Alzheimer’s [7].

**Conclusion**

To summarize, Alzheimer’s is caused by a variety of reasons, some of which many researchers still do not understand to this day. Nanoparticles give researchers hope that they can finally solve what seemed like an impossible puzzle. Even though it seems like a never-ending puzzle, we just have to find the right pieces to put together. Nanoparticles are just one piece of that puzzle and I hope that in the future we could uncover more pieces of this puzzle that could someday lead to the cure to this incurable disease.

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An Endoscopic Nightmare: Hydrocephalus
Avikgna Linganathan

Abstract

Hydrocephalus often arises due to a number of causes including genetic abnormalities, trauma or injury and often affects patients at infancy or over the age of 60. The disease involves a dilation of the cerebral ventricular system with a following compression of the brain’s parenchyma thus leading to increased intracranial pressure. It can be both communicative and obstructive and the current forefront of treatment is the insertion of a shunt. Recently, endoscopic third ventriculostomy has gained popularity as an alternative form of treatment. Recent studies show that the disease has an estimated incidence of 1 in 1500 births [1]. Have modern research studies come far enough to accurately explain the pathology and treatment of such a disease?

Overview and Etiology

The disease hydrocephalus is described to be caused by an accumulation of cerebrospinal fluid (CSF) in the ventricles of the brain which are located within the brain’s parenchyma. The parenchyma consists of several ventricles, two lateral ventricles and the Sylvius aqueduct. The disease affects a wide age range, however it is most prevalent after fetal development and in the infancy stage as well as in people above 60 years of age. The accumulation of CSF is the main contributing factor towards hydrocephalus, and its accumulation causes a blockage in its circulation pathway which begins in the lateral ventricles and passes through the subarachnoid space before finally being absorbed in the bloodstream [2], causing the ventricles to expand and to exert intracranial pressure, thus causing hydrocephalus.

There are multiple types of hydrocephalus including, normal pressure hydrocephalus (NPH), obstructive hydrocephalus, congenital hydrocephalus, and hydrocephalus ex-vacuo. The first and possibly the most common is communicating hydrocephalus. It occurs when the blockage or restriction in flow occurs
once the CSF exits the ventricle; the term ‘communicating’ essentially means that it will still be able to flow between open ventricles. Normal pressure Hydrocephalus is a form of hydrocephalus where CSF abnormally builds up in the ventricle, as opposed to outside the ventricle due to complications following surgery, head trauma, or some form of injury. Obstructive hydrocephalus arises when the flow of CSF is blocked before it can enter the ventricle. This is often linked to aqueductal stenosis, in particular, the stenosis of the aqueduct Sylvius (the aqueduct leading to the third and fourth ventricle) which narrows and obstructs the flow of CSF into the ventricle [4]. Congenital hydrocephalus often develops in the fetal stages of development due to genetic abnormalities. Congenital hydrocephalus has been specifically linked to genes regulating brain growth and development [5]. Although we don’t fully understand the origins of congenital hydrocephalus, it is believed to develop during a specific embryonic time period of neural stem cell proliferation and brain differentiation [6]. Finally, hydrocephalus ex-vacuo emerges when neurodegenerative diseases, such as dementia, cause a reduction in brain tissue rather than a buildup in CSF, thus increasing intracranial pressure and causing hydrocephalus.

Pathology

The development of hydrocephalus in an individual is often credited to genetic abnormalities, trauma, injury, or diseases such as meningitis. Congenital hydrocephalus in particular occurs in the fetal development stage and is caused by a genetic abnormality that contributes towards brain growth and development [5]. A genetic abnormality contributing towards the narrowing of the aqueduct Sylvius or towards the narrowing of the brain’s ventricles is likely to cause hydrocephalus as it allows pressure to more easily build up in the brain due to CSF accumulation. Trauma and injury often also contribute towards a CSF accumulation by causing a subarachnoid hemorrhage. This form of stroke or hemorrhage causes the blood to block the exit of CSF from the ventricles to the cisterns or to block the passageway for CSF within the cisterns. Furthermore, the hemorrhage can block arachnoid granulations via scarring. Arachnoid granulations act as one-way valves that allow CSF to exit the subarachnoid space and enter the bloodstream by allowing CSF to diffuse across the granulations and into the superior sagittal sinus and enter venous circulation [7]. This essentially means that subarachnoid hemorrhage further contributes to CSF accumulation by damaging the arachnoid granulations. Additionally, meningitis has often been linked to increased intracranial pressure (ICP) and hydrocephalus. Pathogens linked to meningitis often reach the subarachnoid space through the bloodstream and are able to penetrate the blood-brain barrier (BBB). As it enters the subarachnoid space, it influences and imbalances the water content of the brain parenchyma, CSF volume, and cerebral blood flow, thus increasing ICP and contributing towards hydrocephalus [8].

Extra-cranial processes within the neck, heart, and mediastinum are primary CSF disturbances which are exacerbated by an increased venous pressure, reduce the rate of CSF absorption and therefore contribute towards increased ICP and hydrocephalus. Studies regarding

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Figure 2. Image displaying the periventricular white matter [9]
hydrocephalus and its effects often link the majority of its damage to the periventricular white matter as well as the area surrounding the subarachnoid space in terms of neuropathological changes. The cerebral blood vessels are distorted and the capillaries often collapse while the myelin and axons suffer damage within the periventricular white matter [10]. This damage is attributed to continuous increased ICP and an overall distortion of the brain’s structure.

**Treatment and Diagnosis**

Increased ICP and hydrocephalus often exhibit a specific triad of symptoms. Hydrocephalus often induces a gait disturbance in which the patient has difficulty walking, some form of mild dementia along with impaired control of the bladder. NPH in particular exhibits potentially reversible dementia, frequent falls as a result of gait disturbance, and recurrent urinary tract infections in the elderly [11]. It is this triad of symptoms that is often viewed as a major indicator for Hydrocephalus. Gait disturbance is often the first observed symptom as the expansion of the lateral ventricles affects the corticospinal tract motor fibres which disturbs motor function and gait. Bladder incontinence arises as hydrocephalus causes absent central brain inhibition which leads to a hyperactive detrusor muscle thus releasing an increased amount of urine with decreased control.

The diagnosis for hydrocephalus is often performed for two reasons: to identify if the patient is indeed suffering from hydrocephalus, and to identify the patient’s candidacy for shunt treatment (Shunt treatment is the insertion of a hollow tube into the brain via a surgical procedure which drains and redirects cerebrospinal fluid). A doctor will often begin with a physical and neurological exam, and a short interview to assess the severity of symptoms and agony. To assess the severity of the ventricle enlargement and the location of the CSF accumulation, a doctor may conduct either an MRI (Magnetic Resonance Imaging) or a CT scan (Computed Tomography). Finally, before treatment may commence, the patient’s candidacy for shunt treatment must be assessed. Therefore, a doctor may perform a lumbar spinal tap, external lumbar drainage or measure CSF outflow resistance in order to help predict shunt pressure and responsiveness.

A patient that is a likely candidate for shunt treatment often displays the following characteristics:

- A known cause for the increased ICP and hydrocephalus
- Temporary solutions such as the lumbar spinal tap display a dramatic relief in symptoms over a temporary period
- Candidates where gait disturbance is the most prominent symptom.

The foremost treatment for a neurological disorder such as hydrocephalus is the insertion of a shunt to perform shunt treatment. Symptomatic hydrocephalus patients are likely to improve due to shunt treatment, especially patients suffering from post-traumatic hydrocephalus (PTH). [12]. The main function of a shunt is to drain the excess CSF into another part of the body where it can be easily drained. The first part of a shunt is the collection catheter which is placed within the enlarged ventricle. In the case of an enlarged ventricle with multiple septations, a neuroendoscopy
can be specifically used to place a collection catheter in a location where it may be connected to an Ommaya reservoir to drain the CSF or to administer medicinal drugs [13]. There is also a valve mechanism which ensures the rate of CSF flow is controlled. Finally, a shunt is latched to an exit catheter which may be linked to an Ommaya reservoir to drain the CSF away.

A rare form of treatment for obstructive hydrocephalus is an endoscopic third ventriculostomy. This form of treatment is often performed on patients who have a CSF accumulation in the third ventricle of the brain’s parenchyma. The neuroendoscopy allows the doctor to view the ventricular system and make a small hole on the base of the third ventricle, thus allowing the CSF to bypass the obstruction and flow on its normal path around the brain surface. This technique is viewed as a valid treatment for obstructive hydrocephalus, and is an alternative to cerebrofluid shunt application [15]. Complicated cases of hydrocephalus have now improved management, and advances in technology have improved our opportunities for minimally invasive techniques [16]. Alternatively, in the case of congenital hydrocephalus, where the baby suffers from increased ICP, cephalocentesis (hollow needle inserted for drainage) without ultrasound may be performed in conjunction with fetal delivery with a baby that has massive cranial enlargement. This process has a high risk of foetal morbidity and is often only selected when cranial dimensions preclude uncomplicated vaginal delivery [17].

Conclusion

Modern medicine has been observed to have an ever-evolving nature that has pivoted over the years. With the study of medicine, our understanding of anatomy and disease has developed rapidly where we have manufactured classifications and treatments for a number of diseases that once served an undeniable threat to humanity. Although our knowledge of the pathology, origin and treatment of Hydrocephalus has evolved through a number of sources, it is apparent that a clearer, more apparent method for classifying this condition in particular should be developed due to its complex etiology. Developing a medicinal unanimity on the classification and treatment of the disease will create a manner of structure in the medical community in terms of pursuing medical trials for the disease and the development of further technologies to decrease the invasiveness of surgical procedures to treat Hydrocephalus.

References


Finding a New Treatment to Relieve Symptoms of Depression

Amanda Azia

Abstract
Depression, also called major depressive disorder or clinical depression, is a mood disorder in which a patient has a persistent feeling of sadness. Depression may lead to numerous problems, both emotional and physical. The following essay includes a general overview of depression, such as its symptoms, causes, and treatments. This article is intended to provide further awareness on depression and explain a new treatment, which helped relieve its symptoms.

Overview of Depression

Depression is characterized as a mood disorder that involves continuously feeling sad and having a loss of interest in activities that were once enjoyed [1]. Depression leads to individuals’ daily lives being negatively affected. This includes how they think and handle daily activities, such as eating or working. Symptoms of depression must be present for at least two weeks before an individual can be diagnosed with depression [2]. Depression is a complex disorder in that there are many different forms, and depression affects people in different ways [3]. For example, women with depression usually experience symptoms of guilt and sadness, while men experiencing depression are typically tired and irritable [3]. Depression symptoms can range from being mild to severe. Some include trouble sleeping or excessive sleeping, feeling valueless, guilty, sad, or having thoughts of death or suicide [4]. In any given year, depression affects around 6.7% of adults, and 16.6% of people experience depression sometime during their life [4]. Scientists have concluded that there are numerous causes for why individuals experience depression; this includes individuals’ biochemistry, genetics, personality, and exposure to environmental factors [4].

Depression can be treated with medication and/or psychotherapy. However, if those treatments do not reduce
symptoms, brain stimulation therapy is another treatment option for mental health professionals and patients to explore [3]. Medications, referred to as antidepressants, can work to treat depression [3]. The patient’s brain chemistry may contribute to an individual’s experience with depression, which may factor into their treatment. Therefore, antidepressants might be prescribed to assist in modifying their brain chemistry [4]. Antidepressants can lead to many side effects, such as headaches, weight loss or gain, or drowsiness [6]. Psychotherapy, or “talk therapy”, may be used alone for treating patients with mild depression, but patients with moderate to severe depression usually use psychotherapy along with antidepressants [4]. There are many brain stimulations, such as electroconvulsive therapy (ECT), that may be an option for people with severe depression who do not notice their symptoms improving with antidepressants or psychotherapy [3]. ECT is a procedure performed under general anesthesia where small electric currents pass through the brain [7]. The goal of ECT is to cause a change in brain chemistry and reverse symptoms of severe depression [7].

**Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT)**

A small study directed by researchers at the Stanford University School of Medicine used a new form of transcranial magnetic stimulation (TMS) called SAINT [8]. TMS is a noninvasive procedure to improve symptoms of depression that utilizes magnetic fields to stimulate nerve cells in the brain [9]. SAINT was approved by the Food and Drug Administration (FDA) for treating depression [8]. The researchers reported that by increasing the number of magnetic pulses, speeding up the pace of the treatment, and targeting the pulses according to the individual's neurocircuitry, SAINT surpasses current FDA-approved protocols [8]. Researchers used magnetic resonance imaging to locate the dorsolateral prefrontal cortex, especially a specific subregion within it [8]. Researchers located the subregion in every participant that has a relationship with the part of the brain that is overactive in people who experience depression, called the subgenual cingulate [8]. The relationship between the two regions is weak in people who have depression, and this leads to the subgenual cingulate becoming overactive [8]. By stimulating the subregion of the dorsolateral prefrontal cortex, this reduces the activity in the subgenual cingulate [8].

According to numerous diagnostic tests for depression, all 21 participants were seriously depressed before undergoing SAINT and had suicidal thoughts before therapy [10]. However,
medications, FDA-approved TMS, or ECT did not improve symptoms for any of the 21 participants [8]. With SAINT, the participants of the study undertook 10 sessions daily of 10-minute treatments, along with 50-minute breaks in between [8].

**Results of SAINT**

Researchers of the study did not find many side effects of the new therapy as fatigue and minimal discomfort during treatment were the only side effects reported [8]. Researchers discovered an improvement in that participants could switch between mental tasks and solving problems, which is the usual outcome for people who are no longer depressed [8]. After therapy, 19 out of the 21 participants scored within the nondepressed range, and none of the participants reported having suicidal thoughts after undergoing treatment [10]. A month after therapy, 60% of participants remained in remission from depression meanwhile 90% of patients noticed that their symptoms of depression were quickly relieved [10].

The researchers are conducting a bigger, double-blinded trial where half of the participants receive treatments that are fake [8]. The researchers are confident that the second trial will be just as effective in being able to treat people whose condition was not improved with medication, psychotherapy, or electromagnetic stimulation [8]. Also, the researchers plan to study the effectiveness of SAINT on numerous other conditions including obsessive-compulsive disorder (OCD), addiction, and autism spectrum disorders. [8].

**Conclusion**

As much as we know about depression, there are still many unknowns regarding how one’s brain chemistry impacts the effectiveness of different treatments. It is important for scientists to continue to study the side effects of these new treatments on patients as well. Also, it is crucial for us as a society to see depression as a medical condition rather than an individual’s decision. Overall, our society should learn to equally value mental and physical health, as well as removing the stigma of seeking help with mental illnesses.

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**References**


Neurological Manifestations of COVID-19

Saad Umar

Abstract

The coronavirus disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It typically presents with cough, fever, and difficulty in breathing, but can affect the central and peripheral nervous system. The neurological manifestations can include minor symptoms such as headache, altered mental status, confusion, loss of smell, and taste sensations. However, some patients can have serious complications due to life-threatening neurological emergencies such as ischemic and hemorrhagic strokes, cerebritis and encephalitis, seizure disorder, and acute inflammatory demyelinating polyneuropathy resulting in paralysis. Therefore, it is important to watch for any neurological signs and symptoms in these patients to prevent long term disability and mortality.

Introduction

The coronavirus, SARS-CoV-2, was first reported in December 2019 in Wuhan, China [1]. It has very rapidly spread around the world resulting in a pandemic [1]. The spread of COVID-19 to the nervous system occurs via the hematogenous route or by retrograde axonal transport (RAT). The RAT of COVID-19 may be possible through some of the cranial nerves, such as the olfactory nerve or the trigeminal nerve. This virus can affect both the central nervous system (CNS) and the peripheral nervous system (PNS) due to its directly toxic effect on nerve cells or because of a neuroinflammatory response. Some resulting neurological manifestations can be from the effects of the virus on other body systems and related complications such as sepsis and disseminated intravascular coagulation (DIC) [2-6]. However, the exact mode of entry to the nervous system and the mechanism of CNS toxicity is not clear.

The mild neurological manifestations of the disorder include headache, nausea, altered mental status, confusion, anosmia (loss of smell) and ageusia (loss of taste sensation). The impairment or loss of smell, or taste sensation, could be a marker for identifying infected COVID-19 patients, who do not yet exhibit any other symptoms. The most serious effects of the virus are on the brain and peripheral nerves, resulting in life-threatening complications such as
stroke, seizures, and acute inflammatory demyelinating polyneuropathy (AIDP), requiring intensive care unit (ICU) care. The time before developing serious neurological complications in COVID-19 patients varies, but the average time from infection to onset of cerebrovascular manifestations is about 12 days [2-6]. This article will mainly focus on ischemic and hemorrhagic strokes, seizure disorder, and AIDP related with COVID-19 infection (Figure 1).

**Ischemic Stroke**

Ischemic stroke results from a blockage in the cerebral blood vessels. There are two main types of ischemic strokes: (i) large vessel strokes and (ii) small vessel strokes. Large vessel strokes result from an occlusion of cerebral vessels, such as the internal carotid and middle cerebral arteries. Small vessel stroke results from a blockage in the lenticulostriate blood vessels in the brain. COVID-19 can potentially result in both small and large vessel strokes, but one of the most dramatic manifestations of the virus are large vessel occlusions in young adults. The exact mechanism by which COVID-19 causes blockage of these blood vessels is unknown. The currently proposed mechanisms include vasculitis, arteriopathy, and hypercoagulable condition, as the virus can cause inflammation and impair coagulation mechanisms. The inflammation of blood vessels may result in blood clot formation, causing the blockage of blood vessels and blood supply cut-off to the brain. COVID-19 infection can result in cardiomyopathy, leading to the formation of blood clots in the heart and cardioembolic strokes. It has been reported that COVID-19 patients with stroke have an elevated white blood count, C reactive protein, and D-dimer levels, indicating enhanced immune response and inflammation. [3, 4]. These stroke patients can have an involvement of the bilateral thalami and the temporal lobes. However, some of these patients also develop associated hemorrhage, as discussed in the next section. The cases of cerebral venous sinus
thrombosis, resulting in venous infarcts, have also been reported in a single-center retrospective observational study [3, 4].

Patients with ischemic stroke are treated with tissue plasminogen activator (t-PA) if indicated or with other blood thinners such as aspirin. However, in some cases of large vessel strokes and elevated D-dimer levels, stronger blood thinners such as heparin and Factor Xa inhibitors may be indicated. [3, 4]. The healthcare professionals will likely need to individualize treatment for each case, to document the reasons for selecting a particular approach for the patient and be sure to have the patient/care-giver assent to such an approach knowing there is clinical equipoise.

Hemorrhagic Strokes

Hemorrhagic Strokes result from the rupture of blood vessels. COVID-19 seems to cause damage and necrosis of blood vessels resulting in acute necrotizing encephalopathy (ANE). This is a rare complication of some viral infections and is thought to be related to severe immune response and cytokine storm in the brain. The blood vessel wall becomes very leaky, risking brain bleed, or intracerebral hemorrhage. The cases of ANE have also been reported with COVID-19. The commonly affected areas in these patients include the bilateral thalami, brain stem, cerebral white matter, and cerebellum [3, 4].

Computerized tomography (CT) scan of the brain and magnetic resonance imaging (MRI) brain can help determine if a patient has an ischemic or hemorrhagic stroke. Some of these patients also need special imaging studies of cerebral blood vessels, including a CT angiogram or MR angiogram. Blood thinners are not used in hemorrhagic stroke patients, with some exceptions. This discussion is beyond the scope of this article.

Seizure Disorder

Patients with CNS involvement are prone to develop abnormal brain activity and seizure spells. This can result in altered mental status and unresponsiveness. If there are concerns about abnormal brain activity in COVID-19 patients, electroencephalography (EEG) should be considered. This can help to determine if a patient has any ongoing subclinical seizure activity, also known as subclinical status epilepticus. This might require aggrieve management and treatment with anti-epileptic drugs to prevent any ongoing seizure activity and potential brain damage [4].

Acute Inflammatory Demyelinating Polyneuropathy

Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is a post-viral immune-mediated complication also known as Guillain-Barré syndrome (GBS). This results in the demyelination of peripheral nerves and ultimately causes muscle weakness of upper and lower extremities. This may also involve the diaphragm, causing difficulty breathing, which might require
intubation and mechanical ventilation. Intubation can prolong patients’ critical care unit stay and can increase the risk of other complications like ICU myopathy [5-6].

**At-Risk Patients**

The neurological manifestations of COVID-19 are relatively rare or under-reported at this time but should be considered when taking care of these patients to avoid any potential complications and poor outcomes. Older patients with multiple comorbidities such as hypertension, diabetes, and immunocompromised status are more prone to have cerebrovascular complications of COVID-19. The potential mechanism of poor outcome in some of these patients may be related to angiotensin-converting enzyme-2 (ACE2) activation as it helps the virus easily enter the cells by attaching to ACE2. Therefore, special attention should be paid to older patients with vascular disorders and other risk factors as mentioned above [4,7].

**Treatment**

There is no definite treatment of COVID-19 at this time. However, different drugs such as antimalarials, antivirals, and immunotherapies are currently being considered and tried currently. Researchers are also working on a vaccine against COVID-19 but it is not conclusive as to when it will be available for public use [1].

**Conclusion**

COVID-19 patients with severe infection are more likely to develop neurological manifestations such as ischemic and hemorrhagic strokes. This is especially the case if they have other comorbidities, including cardiovascular risk factors. COVID-19 may enter the CNS through the hematogenous or retrograde neuronal route. The damage to the nervous system may be from the direct toxic effects of the virus, a neuroinflammatory response, and/or a cytokine storm. The key neurological manifestations involve CNS, PNS, and skeletal muscles. The mainstay of clinical treatment consists of symptomatic management and oxygen therapy. Several antiviral, antimalarial, and immunotherapy drugs are being tested, but none have been specifically approved for COVID-19. The safety and efficacy of new vaccines is further being assessed via clinical trials. Developing a working vaccine is now the most important matter for addressing the pandemic.

References


COVID-19 From a Psychologist’s Perspective: An Interview with Dr. Leonard Abbeduto

Vishruth Nagam

Abstract
I had the honor of interviewing Dr. Leonard Abbeduto, Ph.D., Director of the MIND Institute and Tsakopoulos-Vismara Endowed Chair of Psychiatry and Behavioral Sciences at the University of California, Davis. Dr. Abbeduto also serves as an editor for the American Journal on Intellectual and Developmental Disabilities and directs the Interdisciplinary Training Conference on Developmental Disabilities. His research focuses on the behavioral patterns of people with intellectual disabilities, especially as they relate to development and use of language. In this interview, Dr. Abbeduto talks about the recent COVID-19 pandemic, the resulting neurological and psychological complications, and the importance of addressing future crises as a society. Specifically, he recommends that everyone, including recovering COVID-19 patients, should regularly exercise, have strong support systems, and refrain from being too engrossed in COVID-19-related news to maintain good mental health. He also advises health professionals and patients to proceed cautiously with politically sponsored therapeutics, especially in the United States with highly divisive partisan politics. Healthcare systems, educational institutions, governmental agencies, and our society at large, he emphasizes, must be better prepared for dealing with similar situations in the future.

Vishruth Nagam (VN): “How are neurologists and psychiatrists handling telemedicine during the pandemic?”

Dr. Leonard Abbeduto (LA): “For the most part, we’re trying to do as much we can through Zoom, Webex, and other video conferencing platforms for face-to-face interaction. I think we’re going to
have a big influx of patients and things to work on when the pandemic is over, but I think we have
done a lot of good work through telehealth. I think we also now maybe recognize that we can do
even more through telehealth; when you’re pushed, sometimes you’re forced to innovate or find
new strategies to overcome issues.”

VN: “I feel that it might go for us too. We can use this as a learning experience and try to grow
ourselves on how we can deal with situations like this, where we don’t always have access to direct
face-to-face interaction.”

LA: “Right, and I think that’s a really good point. The MIND Institute has been doing research on
different types of technologies to deliver therapies, and what we need to also make sure of is that
going forward, we develop our technologies, we understand our limits, [and] we have evidence for
what can be done effectively through technology and what can’t so that we don’t assume
technology can do everything for us. I really do think this pandemic will push us to think about a lot
of things. For example, one of the limitations for physicians, in terms of telehealth, is that they
traditionally can’t practice across state lines because you’re licensed in a particular state. But that’s a
geographical boundary that doesn’t make any sense. Other systems, such as reimbursements and
insurance, will really need to be looked at, as we are being pushed to now recognize the potential of
new telehealth technologies.”

VN: “Do you have any advice for people who are stressed during this time?”

LA: “I think that recognizing that this is not permanent is really important. I do think that trying to
also not be so deep into it [may help]. For example, you could pretty much watch COVID-related
news on CNN twenty-four hours a day. There’s a balance, however, between being informed and
[being engrossed] in it, so trying to get yourself away from the news at times, I think, is important.
Also, having social contact shouldn’t be underestimated. I have a group I’m involved in, and we
have all-day meetings once a month. We do a Zoom meeting every Wednesday afternoon, and
whoever can join it can join it. There’s something very comforting about connecting and seeing
people’s faces, which is really important to get a sense of how you’re interacting with them and that
they really are okay. I think that physical activity shouldn’t be underestimated as well. Getting
outside, especially now that the weather is really nice, and running in the morning makes me feel
better. Also, we tell our families that have children with developmental challenges to engage in
self-care and that they can’t just devote themselves to their kids, who are now home all the time.
Parents should take the time to do things for themselves that they want so that they feel less
stressed and be more confident in their interactions with their own children. I also think it’s
interesting that, in my neighborhood at least, families are out riding bikes or taking walks together,
and parents aren’t going to work, so people are finding ways to connect and do things, and I think
those are good things. And also, [considering] how air pollution is decreasing in major cities, as
people are not driving [as much as before], I guess that if we’re looking for silver linings, we can
definitely find a few.”
VN: “In the future, though vaccines may be developed, people may still live in fear, believing that the virus will mutate at rapid rates. What are some possible ways to reduce or even eliminate such paranoia?”

LA: “I think that’s a good question. One of the realities is that this can happen again. We had [the] SARS pandemic, which was a scare. We had the ebola outbreak, which was a scare. Th[e] [COVID-19] pandemic is certainly on a larger scale in terms of cross-global impacts, so I think the best way to address it is by being honest with people, [as well as] really engaging in the science that needs to be done so that we understand this more. There are a lot of things we have found, just in the United States, that we didn’t do very well, right? I don’t think we tracked this early enough. I don’t think we had enough tests ready, so I think if we can, as a society, make inroads in creating better systems, it will help us all feel better for the next time [something like this happens]. The tragic thing would be if we did nothing different as a society in terms of preparation for this. We need much better tracking systems, and we need to recognize that we need to respond earlier. We need to have better cooperation between private businesses that are making relevant products and the government and the universities so [that] we’re all working together. On the scientific front, people are talking about different approaches to the development of vaccines. I think maybe we need to look for vaccines that have the potential to treat a number of different viruses rather than being specific to each different type of virus. I think that there will be a lot of changes that will result, and so I think that it will be these changes that will be the most important. People are going to be nervous, and rightfully so, if we don’t do anything to change our ability to deal with the next pandemic. We need to
understand this particular virus, and we need to make sure that we are trying to create systems of care, systems of response, and government agencies that can be more nimble than they were this time. It’s on the medicine, the science, the government, and the social service systems to figure out how to do this better than we did. We need to convince people that we’ll be overall better prepared the next time this happens.”

**VN:** “How will neurologists and psychologists play a larger role in future pandemics? What’s your advice to them?”

**LA:** “I think recognizing that physical health and mental health are connected is very important. For example, there have been recent advancements in neuroimmunology, the study of how the problems with the immune system actually impact neural function and create risk for autism. There was this naive view that the brain is separate from the rest of the body in a way, but we now know that that’s not the case. The impacts on the brain are really dramatic. We now know about exposure to pollutants and how that impacts the brain. I think one of the consequences of the pandemic is that opportunities for neuroscientists to collaborate with other professionals and specialists will increase and that neuroscience will be even more central than now.”

**VN:** “How will current ‘social distancing’ measures impact interactions in the post-COVID-19 world, that is once the number of cases has decreased to a safe and manageable level?”

**LA:** “I think that people, at least for a little while, will feel nervous. You might not see people hugging each other quite as often as they would before, and I think people are going to have lasting skittishness over this. Again, it’s going to take time and some reassurance that we are better prepared for the next pandemic or next threat we have. People will definitely be nervous for a while. First of all, although we’re going to see a decrease in the number of infections across the United States, different regions will be at different time scales, so I think the psychological transition will be gradual in that sense. I think it’s also going to be gradual in that people will have some lingering fear and concern.”

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**Figure 4.** Illustration of a neuroimmune pathway that can lead to autism spectrum disorder (ASD) [3]
VN: “There have been studies showing that recovered COVID-19 patients are left with lasting lung damage [4]. What are the psychological implications of their ‘post-COVID-19’ life?”

LA: “In any case, whenever your physical health is severely impacted, you have a high risk for depression and other things like that. I think that we have to just see how we can help people, for example through any sort of occupational therapy, to regain as much function as possible, and we must recognize that they’re going to have long-term psychological consequences and that we need to provide support for those people. Fortunately, patients with lasting losses of lung function make up a relatively small portion of all the COVID-19 patients, but certainly, it still is a significant number of people.”

VN: “Within the United States, how much can we trust politically sponsored drugs, such as hydroxychloroquine and zinc and, in general, the political perspective of things during this time, considering how divided the United States is regarding partisan politics?”

LA: “Well, I think that’s one of the reasons for [having] the Food and Drug Administration. They’re supposed to be a nonpartisan organization that has established rules for testing pharmaceuticals and other medical devices for safety and efficacy. I think all of those things are in place. I have colleagues who are part of clinical trials and trying to test some of these therapeutics. I trust science, and I think that science and medicine will be objective and will give us evidence; we just have to recognize that it takes time and doesn’t happen overnight. We feel an urgency to help, but we can’t just give a drug known to have positive effects in mice and assume it’s going to be efficacious and safe for humans. I think we are going to recognize that we need to spend some time on this. I think the clinical trials are ongoing in a number of areas, and I think that the US government is putting resources into this, but it’s going to take some time. It’s hard to deliver bad news to someone, so I think that you have to recognize that false hope can be very damaging. I think you need to be honest and open, but we also have to recognize when we don’t know things and then figure out how we can find the answers to that.”

VN: “How do you think people can continue to stay happy and maintain good mental health during this time?”

LA: “We have to maintain social distancing, so that puts some constraints on what we do. I think thinking about things that you could do to reach out to other people or organizations that you care about that are going to be in trouble can be really beneficial. For example, for kids that have to be in school to get good meals because their family doesn’t have the income to always feed them nutritious meals, I think figuring out ways for you to spend time problem-solving with these organizations and possibly making donations to these organizations would be helpful. Think about what you care about the most and have some impact on that, whether it’s the arts or children or families or the fact that restaurants are going to go out of business because they’ve been closed too long. I think you have to decide what is the most important thing for you and try and find a way to do that, even if it’s volunteering to do a Zoom [meeting] and reading books for little kids. Anything
that will help and also shows that there’s someone who cares about them is really important, but it’s hard because we’re stuck at home.”

**VN:** “The United States will be having the 2020 presidential election in a few months. How might the psychological consequences of this pandemic impact the election, in terms of both the voters and the candidates?”

**LA:** “I think it’s going to depend on what life is like post-COVID-19. I think if the predictions about the economy and unemployment continue to be true, you’re going to have a lot of people that are unemployed, that are struggling, and I think that’s going to really set a negative tone. Now that may hurt the incumbents because we look for change usually when we’re upset, and so we’ll have to just wait and see. I also think that there’s probably going to be a lot of promises made from all, independent of the party, when you’re running for office about how you’re going to fix life post-COVID-19 and point blame problems at other people. I think the [candidates] that make the most compelling stories there will make the largest impact as well. I think the people are going to be herding and looking for help, and so whoever seems to have a plan that is going to be the most helpful [will be] the ones that are going to be the most successful. It’ll be interesting to see.”

**VN:** “Are people with neurological or mental disorders more susceptible to the SARS-CoV-2 virus in any way?”

**LA:** “No, not that we know of; unless there’s some sort of comorbid immune system problem, we don’t really know that there’s any sort of physical vulnerability, other than those we talked about before, that is going to make you have a higher risk of being infected. In general, the answer is no. If you talk about those with depression, anxiety, or autism, there’s no evidence that suggests that they would be more at-risk unless there was some sort of accompanying immune issue that really made them more susceptible. It would be the immune issues that make them more at risk, not the brain-based piece of it, as far as we know.”

**VN:** “Many younger students are yearning to go back to schools, as they miss their teachers, friends, and the school system. What are some strategies for parents to calm them down and help them engage in other activities at home?”

**LA:** “I have a lot of my younger colleagues who are all at home and trying to be productive with home and also help their kids. I think that one of the things that parents have tried to do is to really explain to their kids the best they can that there are ‘germs’ out there that can make you really sick and that they have to stay in more and can’t get close to people, but they can FaceTime their friends, with the help of their parents, or do other things to connect with them, [as] we talked about previously. Social interaction is going to be important for the kids, just as it’s going to be important for the adults, and maybe even more important for the [younger] kids, as they’re going to worry about what this means. ‘Is my friend okay?’ ‘Is my teacher okay from preschool?’ I think using these kinds of platforms so that they can interact and see that the person is okay will be really important.”
VN: “What might the role of spirituality be during this pandemic?”

LA: “That’s a tricky question, in terms of issues of religion. I can give my own personal view. I think that having faith is comforting to people, and I think that comfort is a good thing. Also, as a scientist, I think that we’re at a point now where we have to take action to stem the pandemic and to find cures and ways to prevent future pandemics, and I think that’s going to require action on the part of science and government and everything else. As for prayers at the individual level, people can find comfort in whatever beliefs they have about a god or anything. I think that’s fine, but my own view is that we don’t want that to be our response as a society, and we need to do more than that.”

VN: “Are there any current research efforts in UC Davis concerning the COVID-19 pandemic and as it may relate to neuroscience and psychology?”

LA: “The University of California (UC) system has five universities with medical centers, and the UC system is putting money into supporting small projects to start looking at COVID-19 and its impact in lots of different ways, including in non-neural development and neural functioning. I think that there’s starting to be a lot of research. I think the idea is that if they can seed small projects and get things started, then these scientists will be able to apply for more funding from the National Institutes of Health, which is really the biggest funder of health-related research in the [United States], so I think that you’re going to see a lot of it. I think we have some studies that are starting at UC Davis; in fact, I just saw a little email that said that they funded ten projects at UC Davis related to COVID-19. Now I don’t know what those ten are necessarily [about], but I think you’ll see more and more of that, and you’ll be hearing more. Some of it’s basic science, perhaps using animal models, or at the cellular level, so I don’t know if we’re at the point where any of these ten projects necessarily are involving human patients yet, but clinical trials are still being conducted.”

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