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Optimizing Antiepileptic Therapy in Comatose Patients Through EEG-Guided Administration

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1. Identification and Definition of Problem

Coma is a state of unconsciousness from which patients cannot regain consciousness even with the strongest stimulus[1]. On top of this it is a life threatening condition with high mortality rates. Seizures are common in coma patients, affecting up to 20% of individuals [2]. These seizures can further worsen the prognosis and contribute to the already high mortality. Studies have shown that coma patients experiencing seizures have a mortality rate as high as 60% compared to 32% for those without seizures [6].

Currently, there are many challenges regarding managing seizures in coma patients. The current treatment for seizures in coma patients involves Antiepileptic Drugs (AEDs) [3]. AEDs work by binding to specific nerves in the brain and inhibiting abnormal electrical activity. However, the use of AEDs presents several challenges. The optimal dosage of AEDs varies between patients due to individual differences in drug metabolism and tolerance, which can lead to unexpected side effects when the dosage is too small or too large [4]. A study published in Epilepsia found that nearly 30% of patients with epilepsy experience breakthrough seizures due to underdosing of AEDs [7]. On the other hand, overdosing can lead to adverse side effects in up to 70% of patients, according to a meta-analysis published in Neurology [3]. Another issue is that current methods for monitoring the effects of AEDs, such as visual observation for seizures or MRI scans, are limited. Visual observation may miss subtle seizures, and MRI scans are time-consuming, expensive, and cannot be used continuously or often due to radiation concerns [5]. Studies have shown that a significant portion of AED-induced side effects, like minor indicators of possible seizure and cognitive impairment, go undetected with traditional monitoring methods [5]. This delay in detecting adverse side effects can lead to prolonged exposure to potentially harmful medication.

Therefore, there is a pressing need for a more efficient and continuous monitoring system to optimize AED therapy in coma patients. This system should ideally provide real-time feedback

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on brain activity, allowing for precise medication titration and prompt identification of adverse effects that don't exist with current technology such as MRI's that are being used in the field today.

2. Information Gathering

Coma, a state of prolonged unconsciousness, is a serious medical condition affecting thousands of individuals annually. Estimates suggest 3-4 people per 10,000 experience coma each year, with a wide range of underlying causes. Traumatic brain injury (TBI), stroke, and metabolic disorders are just a few examples. A significant complication of coma is the development of seizures, which can occur in up to 20% of patients. These seizures can be particularly concerning because they are often difficult to detect, especially when lacking the typical motor convulsions associated with seizures outside of a coma. Seizures in coma patients pose a major threat for several reasons. First, they can exacerbate existing brain damage. The brain is already in a vulnerable state during a coma, and seizures can further compromise neurological function and hinder recovery. Second, undetected and untreated seizures can lead to a condition known as status epilepticus. This is a prolonged seizure that can have life-threatening consequences. Studies have shown a clear link between status epilepticus and increased mortality in coma patients. Unfortunately, current methods for detecting seizures in coma patients have limitations. The primary approach relies on visual observation for signs of motor activity, such as jerking or twitching. However, this method is often unreliable. Coma patients can experience non-convulsive seizures, which lack external signs, making them easily missed. Additionally, relying solely on visual observation requires constant monitoring by healthcare professionals, placing a significant burden on already strained resources. Another option is magnetic resonance imaging (MRI) scans. While MRIs can detect subtle changes in brain activity indicative of seizures, they are expensive and time-consuming. This makes them impractical for continuous monitoring. Furthermore, repeated exposure to MRI radiation raises safety concerns, limiting its use for long-term monitoring of coma patients.

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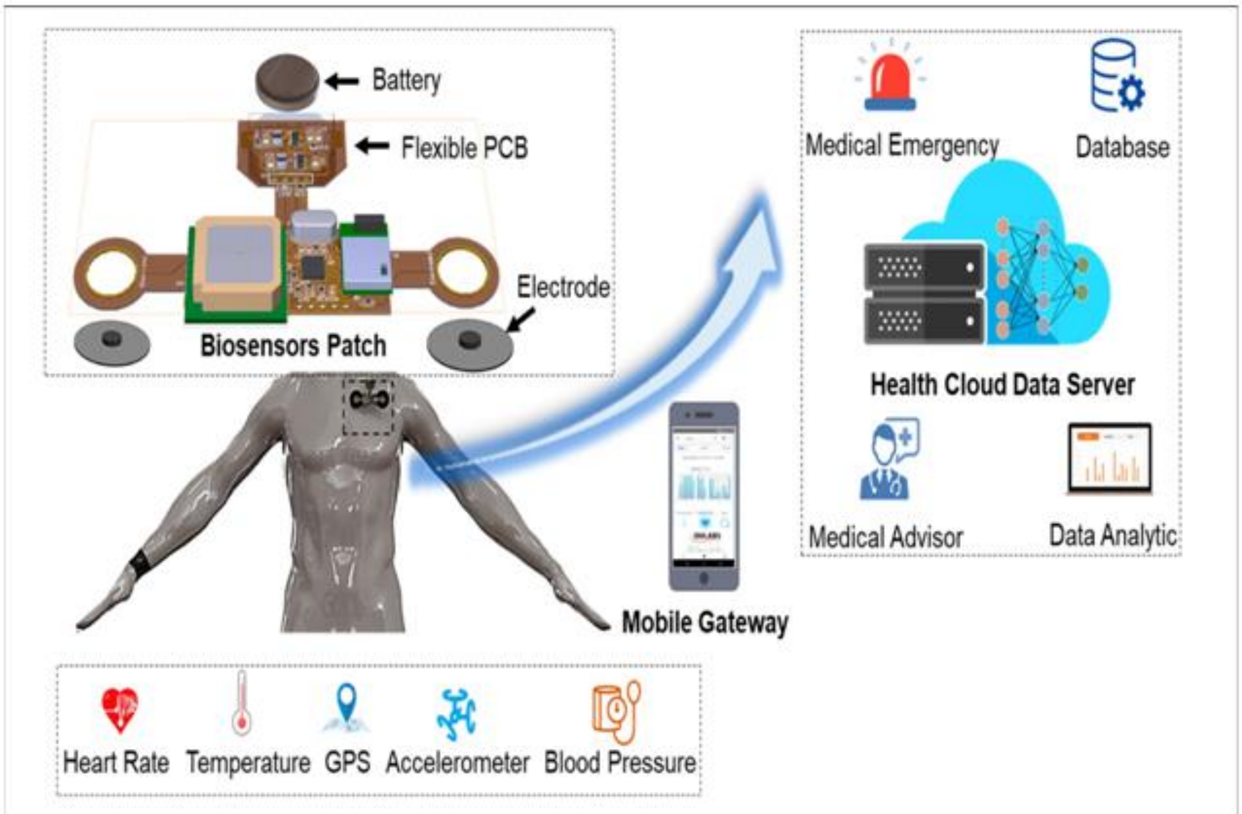
3. Possible Solutions

Solution 1 - AI Biosensors



One solution to address the challenges of continuous monitoring and optimization of Anti-Epileptic Drug (AED) therapy in coma patients involves the use of wearable biosensors and artificial intelligence (AI) algorithms.Wearable biosensors, such as smartwatches or patches, can continuously monitor physiological parameters relevant to seizure activity, such as heart rate variability, perfusions, respiratory rate, and blood oxygen levels. These biosensors can collect real-time data non-invasively and wirelessly transmit it to a central monitoring system. Artificial intelligence algorithms can then analyze the data collected by wearable biosensors to detect patterns indicative of seizure activity. By leveraging machine learning techniques, these algorithms can learn from historical data to improve the accuracy of seizure detection and minimize false alarms. AI algorithms can integrate data from wearable biosensors with other clinical information, such as medication dosages and patient history, to personalize AED therapy. By considering individual patient characteristics and real time physiological data, these algorithms can optimize AED dosages and treatment regimens to minimize seizure frequency and adverse effects. The combination of wearable biosensors and AI algorithms offers a holistic

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approach to continuous monitoring and optimization of AED therapy in coma patients. By providing real time insights into seizure activity and medication response, this solution has the potential to improve patient outcomes and enhance the quality of care in coma management.

Solution 2 - Continuous Glucose Monitoring Systems (CGMS)

CGMS systems offer real-time insights into glucose levels, empowering both patients and healthcare professionals with crucial data for managing diabetes and related conditions.

At the heart of CGMS lies its ability to continuously monitor glucose levels, providing a comprehensive picture of fluctuations throughout the day. By utilizing sensors placed subcutaneously, CGMS captures data at regular intervals, offering a nuanced understanding of glucose dynamics beyond traditional intermittent measurements. This continuous stream of data enables personalized treatment adjustments, enhancing glycemic control and reducing the risk of complications associated with diabetes.

One of the key advantages of CGMS is its capacity to detect trends and patterns in glucose levels, facilitating proactive interventions to prevent hypo- and hyperglycemic episodes. By analyzing this data, healthcare providers can tailor treatment plans to individual patients, optimizing medication regimens, dietary recommendations, and lifestyle modifications for improved outcomes. Furthermore, CGMS holds promise in enhancing patient engagement and self-management. With access to real-time glucose data via smartphone apps or wearable devices, individuals with diabetes can make informed decisions regarding their health, fostering a sense of empowerment and autonomy in managing their condition. Additionally, CGMS enables remote monitoring, allowing healthcare providers to remotely assess patients' glucose trends and intervene promptly when necessary, thus fostering a collaborative approach to diabetes management.

Beyond diabetes care, CGMS technology has the potential to revolutionize research and clinical practice in related fields. By capturing continuous glucose data, researchers can gain valuable insights into the physiological mechanisms underlying metabolic disorders, paving the way for novel therapeutic approaches and precision medicine strategies.

In conclusion, Continuous Glucose Monitoring Systems represent a paradigm shift in health informatics, offering real-time, personalized insights into glucose dynamics for individuals with diabetes. With its potential to improve glycemic control, enhance patient engagement, and drive innovation in research and clinical care, CGMS stands poised to significantly impact the landscape of diabetes management and beyond.

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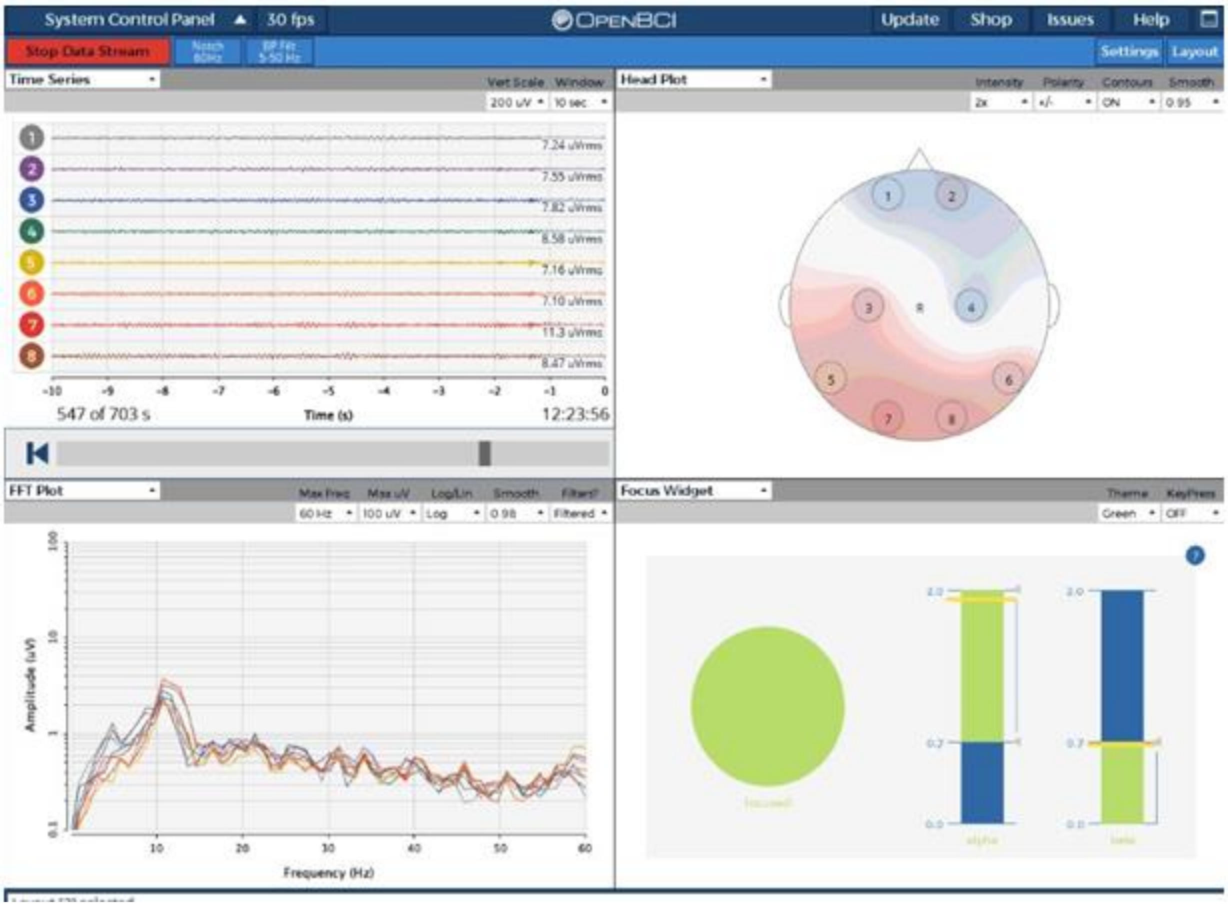
Solution 3 - Electroencephalogram (EEG)



Another innovative solution relating to constant monitoring is leveraging Electroencephalograms (EEGs) to address a critical issue in patient care, particularly in the use of Anti-Epileptic Drugs (AEDs) on coma patients experiencing or displaying signs of seizures. By integrating EEG technology into clinical practice, we can significantly enhance a doctor's ability to successfully treat patients rehabilitating them at a much higher rate in returning to pre-coma state. EEGs, used for their ability to capture brainwave patterns, offer a precise method for assessing neurological activity.

Over 20% of all coma patients face some form of seizures. To treat this AEDS (Anti-Epileptic Drugs) are used to treat the patients.

The problem that arises is that every person requires a different amount, meaning that there is no one shape that fits all ways to administer these drugs. On top of this the over use of AEDs may create an inverse effect, even increasing a patient's chance/severity of seizure. To work around

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this doctors slowly administer drugs in increments testing for negative effects either through visual symptoms or MRIs which can only be administered a couple times due to health effects on top of which is expensive. This makes it so doctors can only have a couple increments and must play it safe in order to not further affect the patient making it so the threshold the patient is able to take is being missed. Our approach involves utilizing EEGs to constantly monitor coma patients' brain activity in real-time, specifically targeting nodes sensitive to drug reactions. By strategically placing electrodes at key locations dependent on the drug such as F3, F4, Cz, P3, P4, O1, and O2, we can detect any abnormal spikes indicative of potential adverse reactions to Anti-Epileptic Drugs (AEDs). This proactive monitoring allows healthcare providers to titrate medication dosage accurately, mitigating the risk of seizures while best optimizing the AEDs effects benefits.

4. Chosen Solution - Neurowatch

4.1 NeuroWatch Application

NeuroWatch improves on the “guess and check " method that doctors use now. The current method using AEDs is imprecise - too high a dose can worsen seizures. Doctors administer them slowly while relying on infrequent MRI scans or visual signs to monitor for side effects, both of which are limited. On top of this, doctors often underdose the drugs in hopes to not worsen symptoms. Here's where NeuroWatch comes in: it's a technology using EEG (electroencephalogram) that continuously monitors brainwave activity. By analyzing these waves for specific patterns linked to the medication's effect (we call them nodes), NeuroWatch allows real-time monitoring. Using a proprietary ML Model we empower doctors to maximize the AED dosage to a patient's threshold as quickly as possible. This is beneficial as it highly reduces the long term effects as well as hightenes chances of awakening.

4.2 Science of EEG’s

An Electroencephalogram (EEG) entails the placement of electrodes on a patient's scalp to capture the collective electrical signals generated by groups of neurons firing synchronously within the cerebral cortex. Unlike methods focused on individual neuron activity, EEG provides a macroscopic view, primarily measuring postsynaptic potentials reflective of changes in membrane potential triggered by neurotransmitter activity.

The resulting EEG data is visualized real time as waves characterized by varying frequencies, amplitudes, and shapes, offering a comprehensive depiction of brain activity. These waves are classified into categories such as Alpha (8-13 Hz), Beta (>13 Hz), Theta waves (3.5-7.5 Hz), and Delta waves (<3Hz). The Alpha and Beta waves corresponded to conscious brain activity while Delta and Theta waves represented unconscious brain activity making them a smaller frequency.

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Next the 10-20 method covers all portions of a person's head: Frontal, Parietal, Temporal, Occipital. It does this by utilizing science in polysomnography. This is helpful to accurately place the electrode wires on the correct nodes, in order to acquire accurate and precise data. Through proper electrode placement, an EEG helps pave the way for enhanced diagnostic capabilities and advancing health informatics.

4.3 Science of AEDs

AEDs or anti-epileptic drugs are what are generally administered to comatose patients in the event of a seizure. As coma patients are more prone to seizure with some statistics showing that around 20% of coma patients experience seizures, significantly increasing their mortality rate, professional monitoring is often required. In the event of a seizure, the doctors administer AEDs through a needle directly through the blood or into the IV. These then work to counteract the seizure. Though mainly positive the use of AEDs has two main flaws:

- First, there is no set amount to treat patients and can vary seizure by seizure even in the same person.
- Second, the over use of AEDs can lead to adverse effects even worsening the seizure.

In effect that leads to doctors having to guess with minimal amounts and test for possible side effects either through physical signs or timestaking MRI scans. This leads to more malpractice, long term side effects as the seizure lasts longer, and sometimes underdosing which hurts a patient's chances of fully recovering.

4.4 Specifications of NeuroWatch

NeuroWatch operates as a streamlined process designed to optimize seizure management in comatose patients. It begins with the application of electrodes to the scalp of the comatose individual, facilitating the collection of EEG data. This data is then processed, and FFT graphs are generated in real time, with a new graph outputted every five seconds.

In the event of a seizure, the FFT graphs offer critical information which is then fed into our proprietary machine learning model. By analyzing the graphs, doctors can determine the appropriate dosage of Anti-Epileptic Drugs (AEDs) tailored to the patient's current neurological state. This targeted approach minimizes the risk of overdosing, ensuring optimal effectiveness of the medication while mitigating potential adverse effects.

4.5 Use of Machine Learning

The major problem with the current method of treatment for coma patients is the large reliance on guesswork and large margin for error. Requiring the doctors or healthcare professionals to make

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this determination increases the guesswork and margin of error NeuroWatch works to eliminate.

NeuroWatch uses a machine learning model from TensorFlow and Keras called VGG16 to solve this problem. It compares the patients EEG data to datasets of FFT plots from both seizure and coma patients. This allows for a quantitative measurement of when AEDs should be administered.

4.6 Methodology of Usage

NeuroWatch would be used in hospital intensive care units (ICUs) where coma patients are being treated. Statistics show that around 20% of coma patients experience seizures, significantly increasing their mortality rate. The current method of treating these seizures relies on AEDs, but finding the right dosage is tricky. Too low and the seizures continue, too high and the medication itself can trigger more seizures. Doctors are essentially flying blind, monitoring patients visually for signs of seizure or using infrequent MRI scans which take a long time and can't be done repeatedly due to radiation risks. This is where NeuroWatch comes in. By continuously monitoring brainwave activity through EEG technology, NeuroWatch acts like a real-time map of the patient's neurological state. When a specific brainwave pattern (like a unique node) indicates the drug is nearing its limit, doctors can immediately stop administration, potentially preventing further seizures and allowing for a more targeted and effective use of AEDs. This could significantly improve patient outcomes and reduce the high mortality rate associated with seizures in coma patients.

4.7 Affected Professions

Neurocritical care specialists, who typically care for coma patients, will find themselves with a much easier task as their dosages will no longer be determined through immense probability related calculations as real time vital updates will be delivered to coma care takers allowing them to make decisions without any major side effects for the patient.

4.8 Costs Associated

In theory, NeuroWatch doesn’t actually present any new costs other than possible purchase of EEG’s, which are fairly inexpensive. However, this too isn’t normally a cost as most ICU units where coma patients are stored already own EEG’s.

4.9 Future Applications and Relation to Prompt

Advancing health informatics is about using technology to improve patient care, and that's exactly what NeuroWatch does for coma patients at risk of seizures. Currently, doctors struggle to find the right dose of AEDs (anti-epileptic drugs) because too high a dose can trigger more

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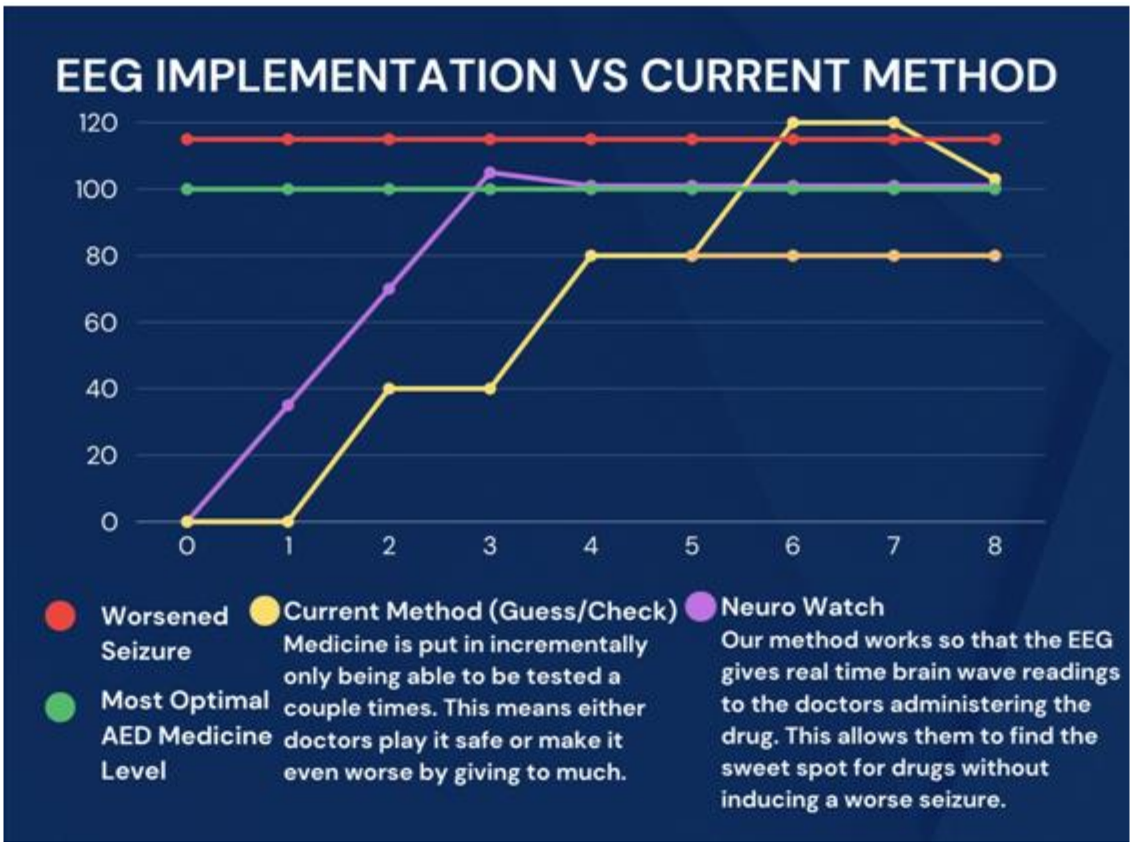
seizures. They monitor patients visually or with infrequent MRI scans, which are slow and limited. NeuroWatch solves this by continuously tracking brainwave activity through EEG. By analyzing these brainwaves for specific patterns (nodes) that indicate the medication is reaching its limit, doctors can immediately stop administration and prevent further seizures. This real-time data analysis translates complex neurological information into actionable insights, perfectly aligning with the goals of advancing health informatics. Ultimately, NeuroWatch empowers doctors to use AEDs more effectively, potentially reducing the high mortality rate in coma patients with seizures.



5. Iteration Process - Narrative for a Means of Testing the Solution

After proposing our idea to OpenBCI, a leading company in neurotechnological research.

They were willing to supply us with the Cyton Biosensing Board (EEG). This allowed us to be able to run tests with the EEG and provide us with real time data that would be used to support our solution.

To conduct these tests we used the Cyton Sensing Board (Fig 1.), a laptop that had the Python and EEG files downloaded, electrodes (Fig 3.), a bluetooth transmitter (Fig 2.) that would relay the data to the laptop, and a conductive paste (Fig 4.) that would help with attaching the electrodes to the head sample.

Materials:

Fig 1. Cyton Sensing Board (EEG)

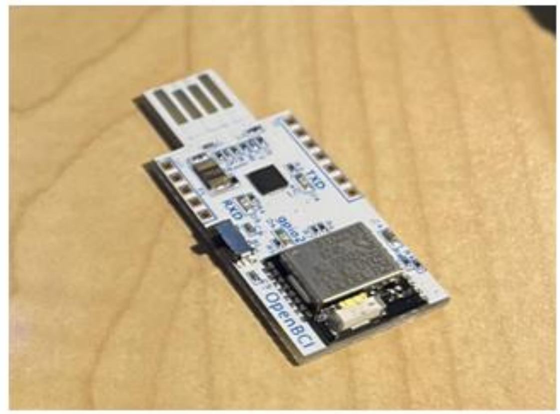


Fig 2. Bluetooth Transmitter

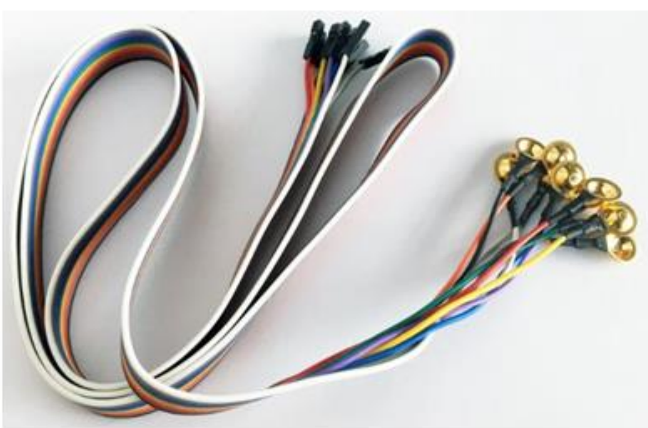


Fig 3. Electrodes

Fig 4. EEG Conductive Paste

Procedure:

1. Connect the electrode wires to the Cyton Sensing Board.
2. Next, apply the electrode heads to the patient's head using the conductive paste.

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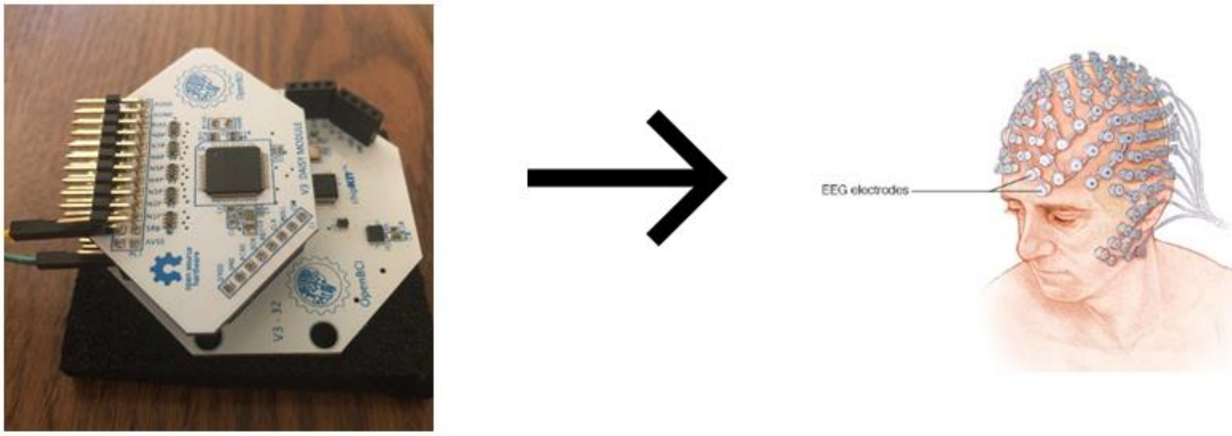
Fig 5. Electrode Wires Connected To EEG



3. Attach the Bluetooth transmitter to the laptop containing the EEG files, OpenBCI GUI and Python code.
4. Run the OpenBCI GUI and the Python program

Fig 6. OpenBCI GUI

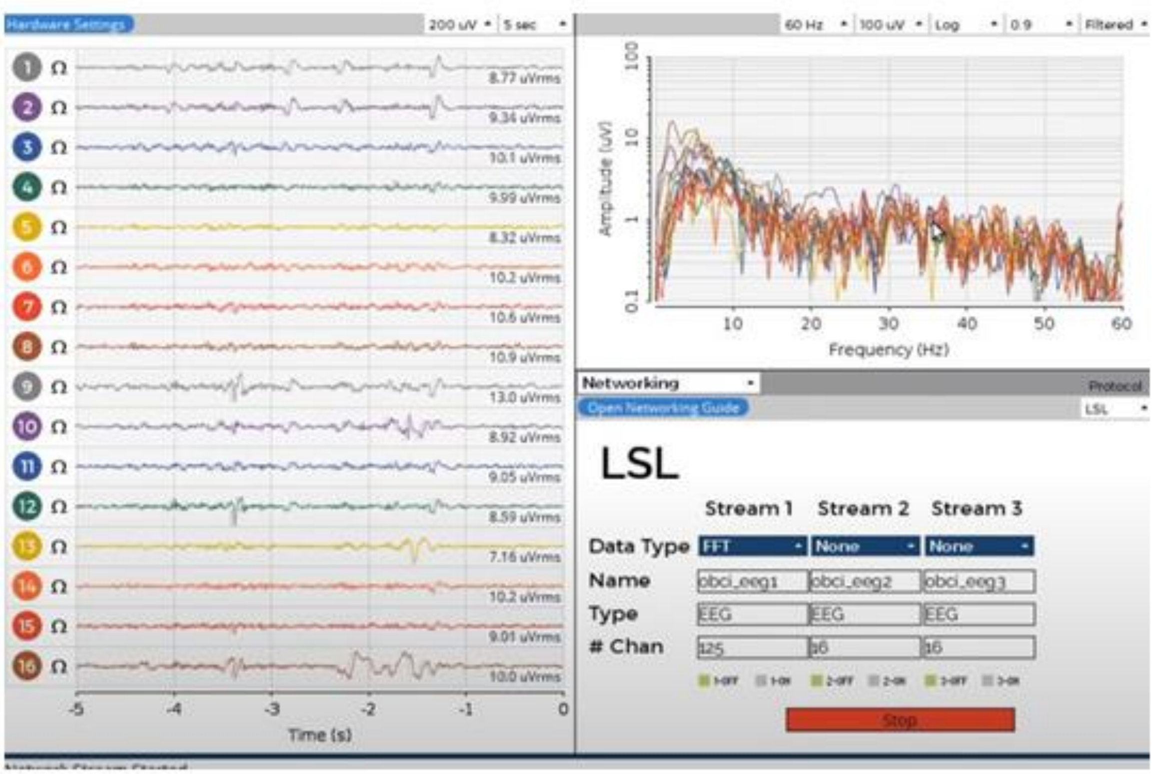


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Fig 7. Python code that gathers the FFT plot from the OpenBCI GUI

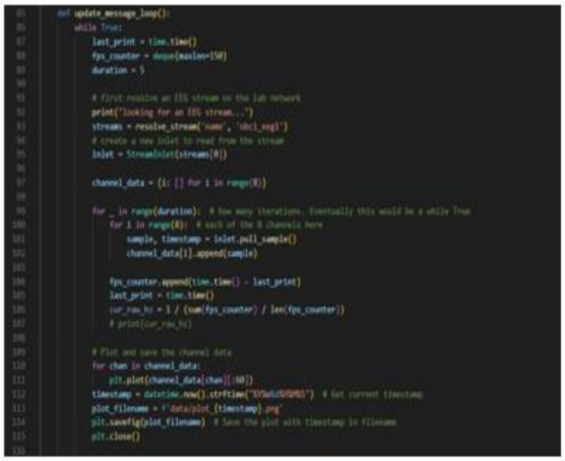
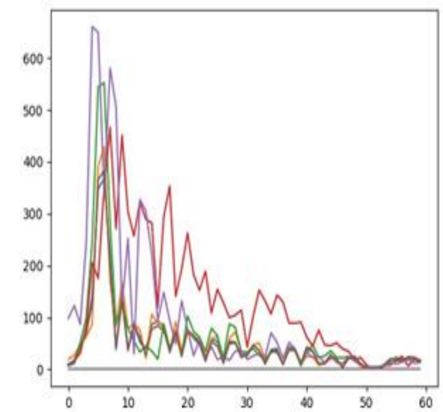


Fig 8. FFT plot



5. The program will then proceed to collect an FFT graph around every five seconds
6. Using a machine learning model from TensorFlow and Keras, each FFT graph is compared to a folder of example EEG data of patients in coma versus seizure.

Fig 9. Example coma EEG dataset

Fig 10. Example seizure EEG dataset

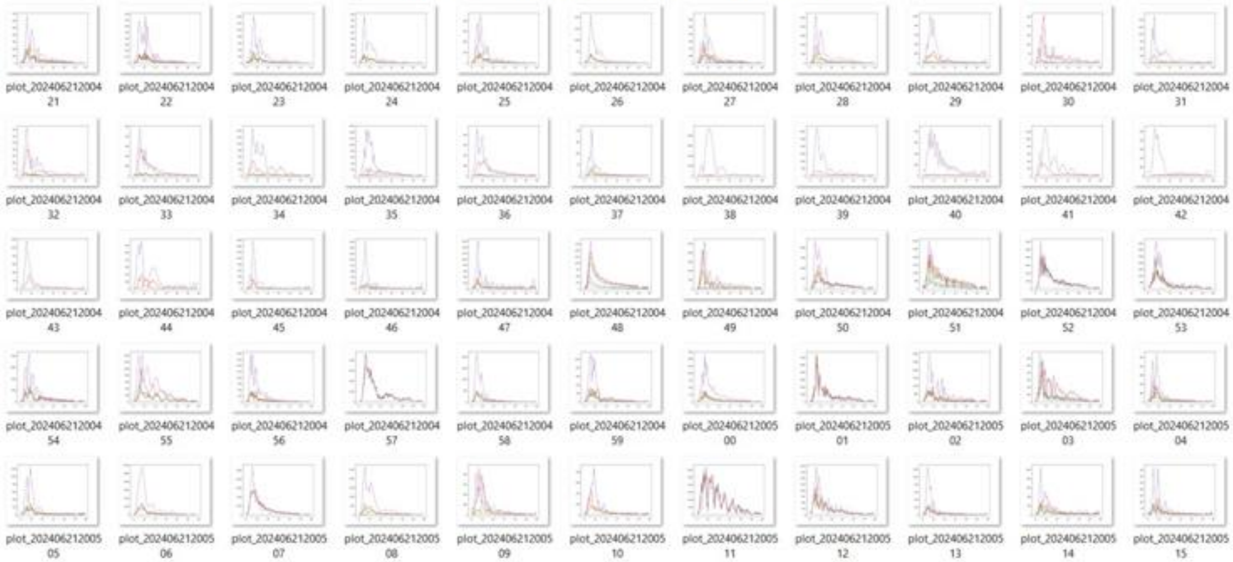


Fig 11. Machine learning code to compare FFT plots to datasets

```
base_model = VGG16(weights='imagenet')
model = Model(inputs=base_model.input, outputs=base_model.get_layer('fc1').output)

def extract_features(image_array, model):
    image = cv2.resize(image_array, (224, 224))  # VGG16 expects 224x224 pixels
    image = img_to_array(image)
    image = np.expand_dims(image, axis=0)
    image = preprocess_input(image)
    features = model.predict(image, verbose=0)  # Suppress progress bar
    return features.flatten()

def compare_images(input_features, folder_path, model):
    similarities = []
    for filename in os.listdir(folder_path):
        image_path = os.path.join(folder_path, filename)
        image = cv2.imread(image_path)
        if image is None:
            continue
        features = extract_features(image, model)
        similarities.append(features)
    return similarities

def determine_similarity(input_image, seizure_folder, coma_folder, model):
    input_features = extract_features(input_image, model)

    seizure_features = compare_images(input_features, seizure_folder, model)
    coma_features = compare_images(input_features, coma_folder, model)

    seizure_similarities = [cosine_similarity([input_features], [feat])[0][0] for feat in seizure_features]
    coma_similarities = [cosine_similarity([input_features], [feat])[0][0] for feat in coma_features]

    avg_seizure_similarity = np.mean(seizure_similarities)
    avg_coma_similarity = np.mean(coma_similarities)

    if avg_seizure_similarity > avg_coma_similarity:
        return "Give medicine"
    else:
        return "Do not give medicine"
```

7. The code will continuously monitor the patients FFT graph.

8. Once the machine learning model detects a seizure by determining the patient's FFT plot is similar to the seizure dataset, it will instruct the medicine to be given.
9. The model will use a similar technique by comparing the FFT plot similarity to the coma dataset to determine when the seizure reduces.
10. However, to ensure the complete dosage of AEDs are given, the model will wait until it detects the start of another seizure before instructing the medicine to no longer be administered.

In this experiment, we utilized the Cyton Biosensing Board from OpenBCI to assess the accuracy of EEG data collection during sleep. Through a structured procedure, including electrode placement with conductive paste and real-time data transmission via Bluetooth to a laptop running Python scripts, we gathered FFT plots of the patients brainwaves. Using machine learning, we were able to accurately determine when the seizure was active and how it progressed, thus allowing us to administer proper AED dosage to end the seizure.

6. Iteration Process- Refinements to the plan

Initially, our plan to collect data from the EEG was to use the OpenBCI GUI (Fig 6.) that worked with the EEG we were delivered in order to display the data being collected. However, after experimenting with the EEG we realized that in order to interpret the data we would need to create our own GUI because OpenBCI doesn't have a feature where the user would have the ability to interpret the data, and put it to use.

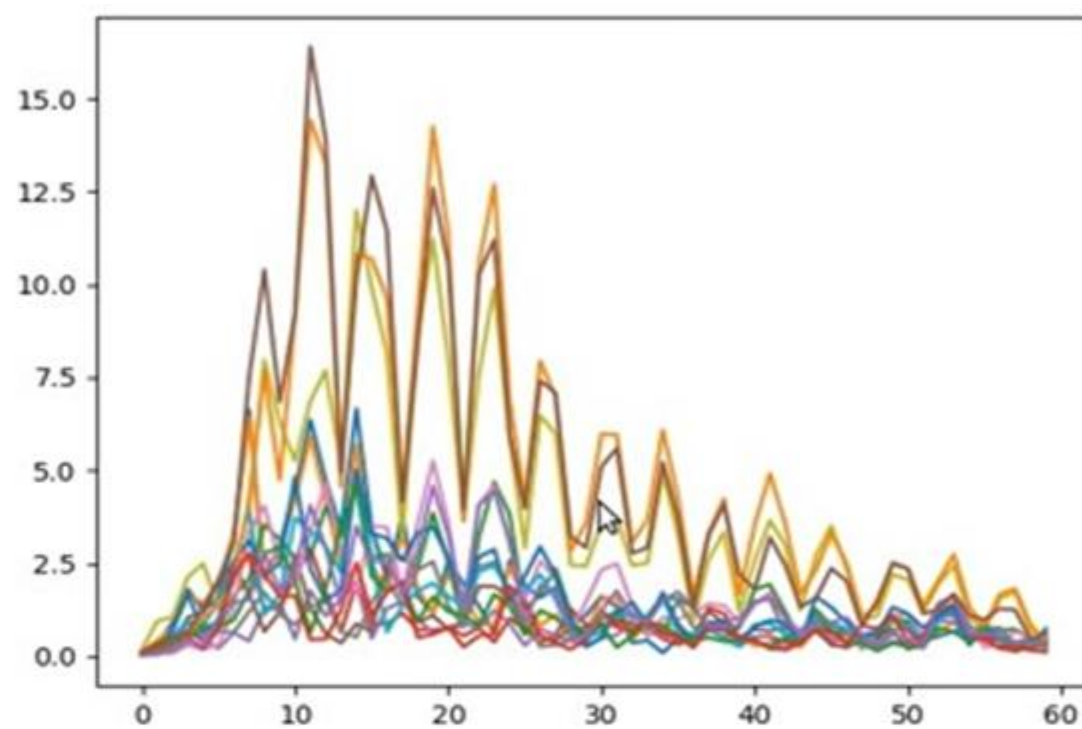
Fig 12. Raw EEG data

At first, we wrote a python script to extract the raw EEG data from the GUI to use. However, we had no way of interpreting or using the data. It was essentially meaningless, impossible for anyone to understand.

In order to organize the data for interpretation we decided to instead pull FFT data from the GUI.

This now allowed us to have the data in a manageable format. The y-axis corresponds to the wave frequency, while the x- axis represents the brain waves' power at each frequency. This organized graph makes it easy for the computer or technicians to interpret the data and explain to healthcare professionals the meaning of the graph.

Fig 13. FFT Graph



However, we ran into our final problem of figuring out a way to precisely interpret the FFT graphs. Our goal was to remove all guesswork from this job so we decided to use machine learning. Our model compared the graphs to a coma (*fig 9.*) and seizure dataset (*fig 10.*). By using the model to determine how similar the FFT plot was to each dataset, we were able to quantifiably determine when to give medicine. The model would output "Give medicine" once it determines the FFT plots show the patient is having a seizure. Using the same technique, it would wait until the patient had reduced back to a coma. However, to ensure adequate AEDs are given, doctors will wait to see when the seizure begins to spike again before stopping the medicine. For that reason, our model will continue to instruct "Give medicine" until it determines a second spike of the seizure is beginning, where it will then output "Do not give medicine." This gives the doctors accurate and reliable instruction on when the best time is to administer AEDs during the seizure to save the patient's life.

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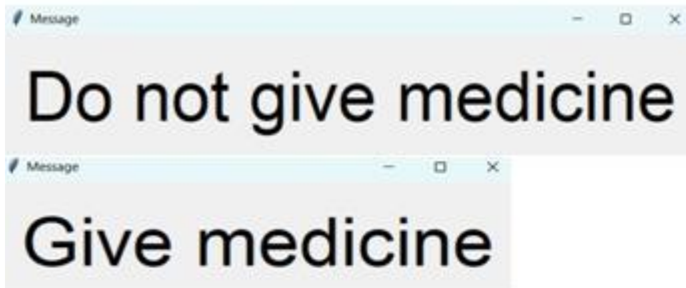
Fig 14. Machine learning model outputs



7. Iteration Process - Reflection

By utilizing the abilities of Electroencephalogram (EEG) technology, in developing a solution for optimizing Anti-Epileptic Drug (AED) therapy in coma patients has been both enlightening and transformative we've embarked on a mission to revolutionize health informatics, particularly in the realm of seizure management in comatose individuals. Our solution addresses the critical need for continuous monitoring systems to optimize AED therapy, offering real-time insights into brain activity that traditional methods like MRI scans cannot provide.

Through a designed experiment, we demonstrated the efficiency of EEG data collection during sleep states, precisely capturing theta and delta waves indicative of coma. By implementing the Cyton Biosensing Board from OpenBCI and crafting a structured procedure involving electrode placement with conductive paste and real-time data transmission via Bluetooth to a Python-scripted laptop, we successfully generated FFT graphs every five seconds. The resulting graphs provided tangible evidence of EEG's ability to monitor brain activity with precision and accuracy, even in unconscious states.

Our iterative process yielded crucial refinements to our initial plan, particularly in the interpretation and presentation of EEG data. Recognizing the limitations of existing GUIs provided by OpenBCI, we developed a solution that tailored to our needs, enabling organized data visualization and interpretation through FFT graphs and machine learning. Through the implementation of both these factors, we eliminated the uncertainty when treating patients. This approach not only enhanced the clarity of EEG data but also empowered healthcare professionals with actionable insights into AED dosage optimization for coma patients.

In conclusion, our solution offers a groundbreaking shift in seizure management for coma patients by leveraging EEG technology to provide continuous, real-time feedback on brain activity. Our experiments serve as compelling evidence of the efficacy and feasibility of EEG-based monitoring systems in addressing the pressing challenges faced in the management of seizures in comatose patients.

8. Iteration Process - Other Issues

A main issue our group was faced with is a restriction in hardware available to us. To use machine learning to compare our EEG data to the datasets requires time and processing power. The lower the processing power, the longer it takes to complete and vice versa. Also, the size of the dataset is directly related to the time and processing power required. However, the larger the datasets, the more accurate the model. Thus, if we were able to have more data in our datasets, our model would only improve and be more reliable. This would only be possible with more processing power in our computers. We had to limit the dataset's size in order to keep the time it takes to process each FFT plot manageable (<5 seconds) as the longer it takes to process the data, the less useful the data will be. In order to increase the accuracy and decrease the time the model takes, better hardware would be required.

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