## Introductory Neuroscience and Neuro-Instrumentation Professor. Rathin Joshi Indian Institute of Science, Bengaluru Lecture No. 60 Epilepsy Classification using EEG data

Welcome to the course Introductory Neuroscience and Neural Instrumentation. We are in the week 10, so for the final 3 weeks, we have decided to touching up on some of this topic which are currently in neuroscience and neuro instrumentation or neuro computation research. So, so far you have been taught about different systems to acquire EEG, how different kind of cognitive experiment performed, how different types of microfabrication process works.

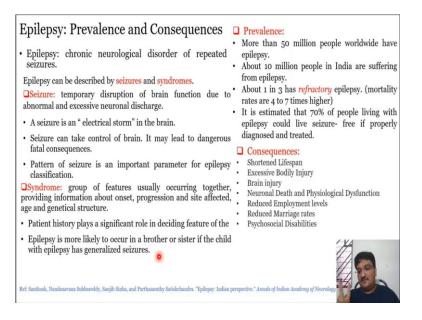
So, building upon this basic fundamentals, here we will see how we can leverage those fundamental process to convert it into clinical applications. So, basically the main agenda behind taking this recent advances in neuroscience and neural instrumentation module is to let everyone know that how this concepts can be translated into clinical or neurological applications. So, for today's this module we will be covering epilepsy classification using EEG data.

So, for epilepsy patient or epileptic subject, EEG is considered as a gold standard, of course it depends on the prognosis of the disease and what is the actual status of the patient, but this is the normal clinical practice that if somebody have a seizure that person should undergo a video EEG or a long-term EEG test with respect to specific triggers and they will measure the brain waves record it as per system, there are many protocols and so they will observe or analyze basically. A neurophysiologist or a experienced neurologist will particularly analyze the trace and finally they will provide an impression that this person is epileptic and of course they will provide medication and sketched the further way of treatment.

So, this is the normal procedure when it comes to dealing with a person with epilepsy. So, why epilepsy classification using EEG data is required? So, in India there are very very very few registered neurophysiologist and compared to that the patient who are suffering from epilepsy are huge in number. So, if statistically if we talk it is around 1000s of patients for 1 neurologist so practically it's impossible for a neurologist to check each and every patient's data and come up with an impression.

So, this is an ongoing research in the field of neuroscience that your EEG can be recorded for that you do not require the neurophysiologist, there can be a technician who can record your EEG and further that EEG data can be fit to some algorithm or some logic device which can tell you that finally the outcome of the patient or this person has epilepsy and this person has this kind of epilepsy. So, this is one of the ongoing research in the field of epilepsy classification. So, let us first see what epilepsy is and we will, I will provide you a basic introduction about the disease epilepsy.

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So, epilepsy is a chronic neurological disorder of repeated seizure, now the seizure term is frequently used in the literature of epilepsy, it means that your body will become rigid, there will be a contraction of your muscles and basically a subject or epileptic subject will not have a control total control of his like his movement and further it can be it can result in very adverse consequences.

So, this is basically the prevalence how prominent the disease has spread so far. So, more than 50 million people are already affected in epilepsy and this is a data which has been taken almost a few years back so and if I talk about India it is around 10 million people who are already affected in epilepsy, the worst thing is that about 1 in 3 has a refractory epilepsy. So, refractory epilepsy is that there are to combat epilepsy to eliminate epilepsy you have anti-epileptic drugs.

So, ideally the assumption is when epilepsy is found you will give the anti-epileptic drug to a particular patient and that patient should be survived. But there are a kind of epilepsy which

would not respond or which would not get recovered by a specific entry of known antiepileptic drugs. So, these are epilepsy known as refractive epilepsy who does not respond to antibiotic drugs. So, if I talk about refractory epilepsy then the rates are 4 to 7 times higher than what is being observed in normal epilepsy.

Further, the key point or the idea or the motivation is that most of them can live seizure-free life if diagnosed and treated at the proper time. So, of course there is a treatment gap because not all patients can get the advice of doctors as a timely advice of doctors exactly during the some onset or after some episode it should be detected or observed by doctor. So, this is basically there is a significant observable treatment gap exists in terms of epilepsy and suppose if not detected, how, what can happen to a patient? A question might arise.

So, there are several very adverse consequences are there. So, of course, epilepsy can be fatal, so there are different type of epilepsies, in some of the epilepsy patient will not remain in consciousness like currently I am talking with you within 10 seconds I will be totally blank, I will not say anything, I do not know what is going on around me after 10 seconds suddenly I will be incomplete consciousness. So, this loss of consciousness is known as epson seizure and this becomes very very very dangerous when you are driving a vehicle. So, this kind of epilepsy can easily result in a fatal consequences.

Further, as I mentioned you do not have a control of your body, so it might happen that you may fell down. So I have seen patients of epilepsy from very closely so I can say that they might have fall down from different in different scenarios like I have one, I know one of the epileptic patient who has fallen down from a motorbike like this like his head is he has fallen down to the back side of the bike and his head was fallen was stucked on the road.

So, basically the idea of providing all these examples is that a person will not have its own control his own consciousness as a result of that there are chances of very very excessive body injury. If it hurts on some of the body parts it can be recovered considering the degree of injury but if something happened to your brain and if some of the cortex or some of the main part tissues of your brain will get damaged, it can affect your sensory system, it might happen that after falling down your head is stuck on to some something in such a way that you might lose your vision or you might loss your memory.

So, again a very very difficult scenario if not treated by time you might face as I mentioned some of the physiological dysfunction you would not be able to sense or you would not be able to hear something based on your damage due to epilepsy. Further, if I talk about the social aspect of epilepsy disease, it has been reported epileptic person will soon find will soon lost the interest in their spouses, so there are marriage rates and of like epilepsy has affected the marriage as well as that person will not find himself, you would not get attracted towards the social crowd and all the person will start remaining separated from the crowd.

So, in general it is a very difficult situation to handle if not detected on time. So, how do we detect epilepsy? And what how do a neurophysiologist or neuro physician neurologist approach for any epileptic patient? So, I already mentioned that in the preliminary cases or at initial level EEG would be advised and then the traces or final data stream would be observed and impression would be provided to the subject, epileptic subject or affected subject but if I talk in detail, so epilepsy can be described by two things one is a seizure otherwise syndrome.

So, in medical science syndrome plays a very vital role basically syndrome or symptoms will provide you the details, the history how the disease irrespective of epilepsy for any any disease symptoms or features or syndrome plays a major role in medical science when a subject will provide an information, the patient history is a vital thing for any disease, especially for epilepsy, what are the things they will measure is that when the episode happen? When the seizure happened? What are the consequences next time when the thing is happen? What was the consequences?

So, and one more thing for specific set of human beings there are different kind of seizures, like some of the seizures can only be observed in child, some of the seizures can observe in aged person like that. So, all these thing will be taken into consideration for syndrome, that is why if I talk about a seizure, seizure is more of a technical term, it is basically abnormal discharge of electrode from your brain, so seizure you can observe, verify, validate using an EEG like.

One more thing I would like to clarify here very important is when a person will be having experiencing a seizure it is very difficult to record EEG because for each recording you are placing electrodes on the head of the subject. Now when you place the electrode on head and seizure comes the person will surely have muscle contraction, stiffness, you will feel stiffening and all. So, it is very difficult for a person to remain as it is and when the person will move if I am telling you that person will move like anything that person will you know

feel like jerks and all. So, what will happen is that there will be a lot of muscle movements for that function results in EMG.

Now EMG is basically a muscle biopotential which has a far higher value than EEG, so there are very very high chances that your biopotential EEG will get eliminated in between this EMG, basically the prominent waveform which you can see outside would be the EMG and which is not able, EEG would be there but in a very small term very difficult to extract EEG from EMG when a person is throwing a seizure. So, why in that case, why EEG is advisable?

Because anyway when the seizure happened you would not be able to get the EEG which you want but there have been evidence in the literature it has been known that in between two episodes of your epilepsy your EEG, your biopotential will provide some of the information about the epilepsy and type of epilepsy. So, basically you had a seizure you had some injury, injury and all would have been recovered but before your next episode that can be after 1 month, after 1 year, after 2 year, after 5 years or if you have been provided a correct proper antiepileptic drug it would not happen as well.

So, before the second episode your EEG would have been taken it would have had a footprint it would that your EEG will show that a person will have some form of problem or the person will have specific it can be region-specific as well like person's occipital lobe or right side of the occipital lobe has some activity there is some issue there, person's frontal lobe has some issue or it might be that your entire head had some issue. So, based on the progression of your disease or based on where you are observing uh abnormal discharge, okay this excessive neuronal it can be identified that which kind of epilepsy you have.

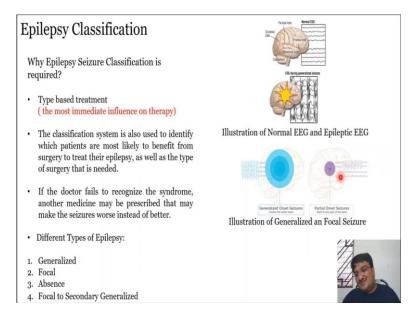
So, we quickly run through this details the seizure is basically an electronics electrical storm which I already mentioned, it will be a discharge of your discharge observed from the scalp electrode. It can take a control of brain and may lead to dangerous fatal consequences noted down here. Further, pattern of seizure is an important parameter for epilepsy classification which kind of as I mentioned from which region it is and how prominent and all. So, and patients history I have already mentioned that plays a vital role.

And one more important thing is that there are as I mentioned two types of epilepsy, one is it can be across your brain where one is in the particular part of your brain, so it is named as generalized epilepsy and focal epilepsy, focal epilepsy means your epilepsy focus would be a particular region of your brain it is limited to a particular region of your brain, whereas generalize would be everywhere. Generalized epilepsy mostly occur due to some imbalance of your neuron, it can be genetic as well.

Whereas focal epilepsy mainly happens because of some brain injury or some basically so that is why it can occur anywhere in your head injury, in head injury it can occur any place so might result in some epilepsy or focal epilepsy, that is why if your brother or your relative would be having a generalized seizure there are high chances of direct brother or sister would have the same because it can be due to the genetic properties of a subject.

So, talking in the nutshell about this slide, epilepsy can be characterized by two things, one is, two things, one is seizure and one is syndrome. Doctor, when you approach a doctor they will ask probation history everything using that they will decide the syndrome as well as they will obtain the EEG ask to go through EEG test, they will check your data stream and they will tell that okay you have this kind of epilepsy.

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So, further we will see specifically that why epilepsy classification is required. So, there are different kind of as I mentioned focal, generalize, I already told about absence seizure, so the different type of epilepsy accordingly there is a different type of medication. And if at all you misclassify a subject or if you give a general patient, generalized epilepsy patient medication which should be given for focal there are high chances of the person who has generalized seizure will have more issues.

Or in the other way a person's only one particular part is damaged or as issue focal portions if you give generalized anti-epileptic drug might happen that person will start observing a generalized seizure. So, type like type based medication is very very important and this type is medication has the most influence in a recovery rate or in you know coming out of epilepsy which is very difficult, so it has the most influence on the therapy of epilepsy recovery.

So, further, how do we differentiate a normal subject from epilepsy? Because like I mentioned there will be a abnormal discharge, there will be a different form of wave, but how can a we make a difference from a normal EEG compared to the EEG provided by when it is taken from epileptic subject? So, this is a very nice illustrative diagram if you can see that here if you see this is a normal EEG, so nice baseline is going on there is nothing no much movement, of course this is illustration whereas, if you talk about here, here there is some onset this yellow color structure shape is just showing that this is the onset of your seizure.

So, at that time you can clearly see that there is a lot of movement, so this is this is at the time of seizure if you take intricate like in between two seizure, if you take recording, then also you will find a clear difference in the patterns. So, now, the idea is how we can screen or out of you as I mentioned there are many 1000s of patients for one neurologist, so which 100 patients or the neurologist should see the first? So, that is being decided when you have one screening algorithm for epilepsy.

So, what is the idea or how you can screen a particular patient for epilepsy is you will just observe this spike as waveforms here, there are some of the patterns in the waveform which is a characteristic biomarker or a pattern which is a signature for a different type of epilepsy. So, what you can see here is by just a normal vision like if you I can see here with the naked eye I can clearly make out a difference between normal and generalized seizure EEG patterns.

So, same thing you can model you can perform some algorithmic check you can take a benefit take a use of mathematical algorithm like fast Fourier transform, time frequency analysis and further to come to a conclusion that this person have this kind of epilepsy, this is in between a normal EEG and epileptic EEG. Now how do we differentiate in between two epileptic subjects, whether the subject has generalized epilepsy or focal epilepsy or absence epilepsy or there is one more type here it is written focal to secondary generalized.

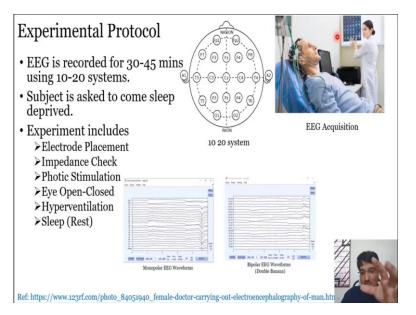
So, I have already told about focal generalized absence a different type of epilepsy which I have mentioned when I was going through the consequences of fatal consequences of epilepsy, so here focal to secondary generalized epilepsy is nothing but we can consider it as intermediate stage in between focal to generalize. So, in general all focals all focal epileptic cases are generalized but with a very small degree of generalization. So, that is the neurophysiological basis behind this and we would not go into the detail because idea here to let you know about what are the difference in EEG or if you can see the pattern by yourself you would be able to at least detect that this person has epilepsy or this person has this kind of epilepsy.

So, these are the 4 major types. Further there is a international league against epilepsy they have come up with their own classification in 2017, so I would like all of you to just have a look at that after understanding the details so far you would be able to understand this thing that thing very clearly that they have basically 3 sections, focal, generalized and unknown onset based on onset they have divided into three parts, it is a good read you can go through it international journal of epilepsy.

Now coming back here that this is useful to differentiate between normal and EEG, how do we delineate between partial seizure and generalized seizure or a focal seizure and generalization? So, it is why I included this thing in the presentation here is a very nice illustration of how you can get the information or how you can differentiate between generalized and focal seizure.

So, if you see here only two of the channel is observing an activity whereas here, entire all 4 channels all 4 electrodes are observing irregularities. So, basically it is starting from here and spreading everywhere that is what this particular image or this sky blue colored circles wants to show whereas, here if you can see here this is a small circle so this is a focus to a particular area that is why it is basically a focal seizure.

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So, further we will see how EEG is recorded and what basically specifically up people do for easy recording or for epilepsy screening or. So, further this is the experimental protocol that it is recorded generally from 30 to 45 minutes, and what do they do for this 30 to 45 minutes time period?

So, first and foremost thing if you go for any epilepsy EEG test they will ask you to come sleep deprived, so what they will ask you is you complete your 4 to 5 hours of sleep and come back come to come for test, why that is required is because sleep deprivation is one of the kindling factor for epilepsy, if your sleep is not finished, if your sleep is not finished very there are very very high chances that you will show some epileptic behavior or your brain will discharge some of the biopotentials in higher rate compared to a person who has a sound sleep.

Anyway, one more thing for any in general epileptic patient is that they are advised to maintain 3 things very properly, the food intake timings, the sleep and the medication very important all 3 things should be and must be followed in as regular manner as possible in order to eliminate the further chances of episode. Anyway sleep deprivation is one of the main cause of epilepsy. So, a subject is being asked to come sleep deprived so that in between they can when they record EEG they will get this kind of signature using which they can identify that this person has this type of epilepsy.

What are the different experiment or different stimuli they will provide? In the further, in the previous modules of mine I have already covered auditory and visual stimuli it is the somewhat different case here but on the whole it remains the same. So, first subject will come they will place electrode and they will check impedance check again, I have covered it into experimental protocol that will check everything is properly working fine and all. So, electrode placement, after electrode placement they will check the impedance they will match the impedance if the impedance is fine. Different system have different input impedance so it should be match with your skin in order to obtain the desired response.

Further they will be presented to subject will be presented to a photic stimulation. So, photic stimulation what they will do is at 1 hertz, 2 hertz, 3 hertz, 5 hertz, 6 hertz they will increase the frequency and they will keep blowing particular light they will keep throwing the light to a subject it may happen sometimes due to this kind of photic stimulation your brain will throw some form of abnormal discharge basically your irregularity in your EEG.

So, all this thing again they will ask you to hyperventilate, hyperventilation is also one of the protocol that has been used in many EEG related studies and these all things like all the different kind of stimuli and all things will happen for 10-15 minutes after that they will ask the subject to sleep or try to sleep. Subject most of the cases as subject has come sleep deprived subject will sleep properly. And when the subject would be resting at that time again there are chances of observing abnormal activities. So, this is basically this thing is basically what will happen when the subject will go for EEG test for epilepsy screening.

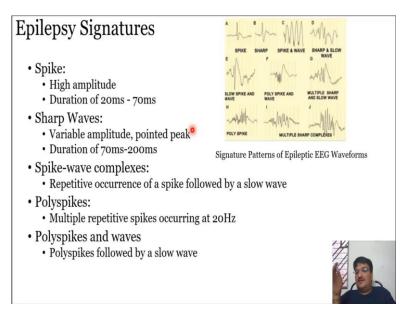
Again, in the course during the course 10-20 system I have also covered once and this is basically I will quickly revise because there are many questions about that, so I will just quickly revise this thing, 10-20 system is nothing but an international standard to record EEG. Now why 10-20 system is required because simply because my head size and your head size would be different. So, you cannot simply say that above your nose or above your nose or nasion you put somewhere after 5 centimeter from your right ear 6 and for me that point would be one point for you that would be some other point.

So, from your nasion to inion, nasion is nothing but this point this point is nasion whereas inion when I just scroll my hand or I move my hand towards the back side of my head there will be a trend there will be a change which you can measure. So, that is at the and near to your neck that is your nasion that would be your inion, this is your nasion from nasion to inion the entire part is divided into different parts of 10 20, 20 20, 20 10 same goes for left ear to right ear divided into 5 parts of 10 20 20 20 10 and this is your final electrode position you can note that all the left side electrodes having odd number all the right side electrodes having even number whereas, this all the electrodes with z represent the midline.

So, this is basically a 10-20 system whenever you go for each recording they will be having a cap supporting 10-20 system. Also you should know that which are the lobes so frontal, central, temporal, parietal, occipital, so there are some of the epilepsy which is specific to a particular lobe. So, if I talk about in US there are very many cases of TLE that is called temporal lobe epilepsy. So, mostly the seizure would be focused around T3 T5 or T4 T6. So, important to know all the nomenclature and why people are using 10-20 system.

Again in 10-20 system, there are different kind of way to record your data I already mentioned before about the montages same thing applies here as well monopolar as well as bipolar and this bipolar EEG waveform is known as a double banana because Fp1 minus F3 F3c b3o1 like that this would be your first banana and this would be the another banana so it is known as a double banana montage and this is how a particular recording, this is just an illustration taken from some content on internet but the idea is to let you people know that this is how basically EEG would be recorded inside the clinical environment.

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So, I think experimental protocols and things are now clear this is how EEG is being recorded, Further, I will tell you how how we can extract the information or looking at EEG how you can say that this person has a problem and this person does not have a problem, how

to see the abnormality, how to quantify the abnormality and how do you see that. So, this is basically a signature to conclude that if a particular person is epileptic or not.

So, what do we measure or what do we see in particular EEG waveform is, this is the main component if you can see the Apart is nothing but your spike B part is your sharp, C part is spike and waves, a small spike is shown along with the wave. D part is sharp and slower. E part is slow spike and wave, here it is a poly spike and the same spike is occurring multiple period of times followed by waves. Again, multiple sharp and slow-wave, poly spike, multiple sharp complexes.

Now what is the use of defining this many number of patterns? So, basically any EEG, any human EEG for epilepsy can be mapped or can be transformed into 3 basic shapes that is spike, sharp and wave. So, those who know Machine Learning or Artificial Intelligence or those who are in the field of mathematics would be easily able to relate with that that your entire EEG waveform can be mapped into 3 variables and 3 patterns that is spike, sharp and wave.

Those who are not aware are into the detail of Machine Learning or feature extraction in simpler words what I wanted to say is that all the recordings of EEG is a combination of spike, sharp and spike and wave. So, how do you delineate between spike, sharp and spike and wave? Or how do you say that this particular waveform is sharp? So, if you see A and B it looks almost similar, the only thing is the duration the change in time makes it this particular waveform or this particular pattern as a sharp and spike and this as a sharp.

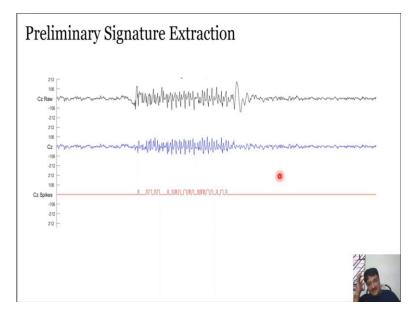
So, there are in literature there are durations of spike and sharp defined. Additionally, when one very important point is spike and sharp you can clearly see it will stand out from your baseline, baseline is nothing but your normal ongoing EEG without much activity but compared to that there will be a change. So, abnormality you can easily catch basically your normal human ongoing EEG it is around within baseline is within plus or minus 10 microvolts.

So, when you target spike or something you can take 3-4 times more amplitude, and then you can check for the duration as well as there is frequency is also defined, what should be the frequency, what are the frequency component beneath it. So, for that a lot of Fourier analysis, frequency analysis is required and further you can perform some another domain analysis like

wavelet analysis and all in order to come up with a better feature type specific feature which will tell you that this particular pattern is spike this particular pattern is sharp and so on.

So, idea behind letting all of you know these different patterns is just that your input EEG, human EEG waveform you convert it into a number of spike, sharp and wave you will be having a features ready for your further epilepsy classification.

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So, I hope this is clear, so what I am trying to say is this is one of the actual human EEG sample recorded. Further it should be pre-processed so this is a row signal recorded in Nicola EEG system it should be pre-processed, why because there are so many that normal recorded human EEG will have so many artifacts, so what is artifacts or noise? Anything apart from your biopotential coming out of your head in other words, anything except the information is your noise.

So, all these noise this can be due to this can be physiological as well as this can be not (physiolo), so it can be due to some issue inside your body or it can be due to some environmental factor like if EEG is being recorded in India, then there are a 50 hertz frequency. Whereas, a powerline artifact which has been observed in US will have 60 hertz frequency, that is one artefact. Whereas, if a person is moving, if a person's eye will be blinking if you move your eye, then also there will be artifact which should be rectified.

Further, it has been reported in some of the subject that there are some thing called ECG artifact your heart pumps inside your body, so that is the effect of your ECG on EAG and

there are literature available to remove your heart's like not exactly ECG but a reflection of your ECG on EEG.

So, all this thing will come into the picture when you talk about the preprocessing of your ECG but once you pre-process it you have to check it for different you can divide this entire trace into particular different segment of time, after dividing your data stream into the different number of section you can check a frequency response also you can check the amplitude whether it is much higher than baseline or not and check for particular assessment what is your frequency response compare it with the frequency response of spike and you can say that okay this particular thing is spike.

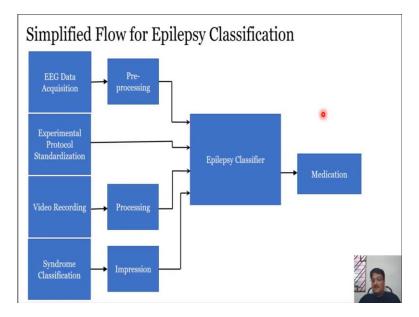
So, similarly here you can see out of this raw data after pre-processing it, you will find this much spike compared to your pre-process data. So, this is just one example which I have provided to extract a spike or how you can get the spike. Similarly, you can perform the analysis for sharp and wave and come to a conclusion that in your input or data EEG file you have this many numbers of spike then you have this many number of sharp and this my number of waves.

Additionally, important thing is that which particular site which electrode is having this kind of waves. One very good thing about EEG is EEG has an excellent temporal resolution. So, if something happens in your brain it will get recorded almost at the same time. Whereas, it would not have that much higher spatial resolution, suppose you have a brain tumor or head injury, then EEG would not be that much useful in that case you should go for FMRI or some intracranial or an invasive EEG when your skull will be open and electrodes will be placed on the affected side.

So, coming back to the epilepsy classification like I have done for spike you can do it for sharp and waves and not only for one channel for multiple channels and finally you can give some impression that this channel is having some activity and further there are some of the one point here I would like to mention is that some of epilepsy will have specific combinations of pattern as a signature, like for absence seizure there is a pattern of spike and wave. So, spike and wave will keep on repeating so then you have to extract spike you have to extract wave and you have to check for the incident where spike is followed by wave.

So, basically, I hope you people have now idea that how you can trace or how you can extract different kind of patterns from your input image signal to conclude the type of epilepsy.

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So, I will show you what can be the simplified flow for epilepsy classification. The motivation behind showing this is to let everyone know that what should be the flow, further there is a lot of mathematics and frequency analysis involved if you want to play with the data or if you want to make a screening tool it would be useful and a lot of literature is available so you can go through some of the epilepsy classification literature, main objective is to automate the process to reduce the load for connection and make a screening tool.

So, this is basically a final classifier which a person should know block background classifier from EEG data it will be pre-processed and it will be give after extracting some of the feature it will be conveyed to a classifier that classifier will also have an input from your experimental protocol like during which period of time you have been provided for the stimulation, during which period of time the patient was hyperventilated?

Now at some point of time the patient will move, so there is one person who sits in observe the entire process so they observe the subject during the entire course of tests that whether a person is moving or not. So, all these inputs are in actual EEG data this has been noted down that person moves at 10 minutes 5 seconds to 10 minutes 15 seconds. So, basically when you see the EEG you can discard those period of time because there will be a moment. So, all these things are the inputs from experimental protocol.

Further, if a person like additionally with this all this detail written by a person and some of the hospitals or units they will provide a video recordings. So, there will be a one constant camera on the face of the person or it will cover the first, it will cover some of its body so some part of the body so then you know they will observe the moment or something so again they can, it is for better interpretation of your EEG data and last but not the least syndrome.

So, syndrome or if you get features if you say symptoms so all this thing, so once all these things are finalized and provided as an input here the epilepsy classifier can tell you that which type of whether the person is having focal whether the person is having generalized seizure or the person is having absence seizure etcetra accordingly medication should be provided.

So, main objective behind this module is to glance through the algorithm or glance through the idea that how you can automate the process of epilepsy classifier currently instead of this epiglottic classifier, one neurologist or neurophysiologist will sit observe and provide his impression. So, can we automate this thing? Can we come up with a better idea? Can we come up with a tool? So, we have a tool to record EEG data, so ca not we come up with a computational unit which can automatically say that, this person has this type of epilepsy or at least reduce the load of clinician.

So, I hope this lecture would have given you some idea about automation regarding epilepsy classification. I will meet you in the next week with one more exciting topic, so far what we have seen is non-invasive energy when sculpted biopotentials or scalp response is recorded. Further, if we go if we open the skull and go inside, will it be more beneficial or should we do that? Or is there what are the significant advantages of invasive EEG techniques.

All this thing and a couple of more applications which has been currently is used or currently in research field it is like ongoing research, all this thing I will discuss in the next week in one of the module, till then all of you take care, bye.