Advanced Neural Science for Engineers
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National Institute of Mental Health and Neurosciences (NIMHANS)
Lecture - 41
Newborn Hearing Screening - II

Hi welcome to this second part of the lecture on the neonatal hearing screening and now what we are looking at is where we stopped and we move from there. So, if you recall we were talking about the gaps in neonatal hearing screening. The gold standard is ABR which is Auditory Brainstem Response and in the gold standard we only look for first 10 milliseconds, but what I said in the last class is that if you go for a mismatch negativity.

Then there can be an additional biomarker which will not only look till the auditory thalamus, but also the auditory cortex that means that we will have a way of looking at the complete entire auditory pathway right from outer ear all the way to the auditory cortex and how can we do that? We can do that by looking at the further signals which are till 200 millisecond and so on. So, in those things we will look at P1, N1, P2, N2.

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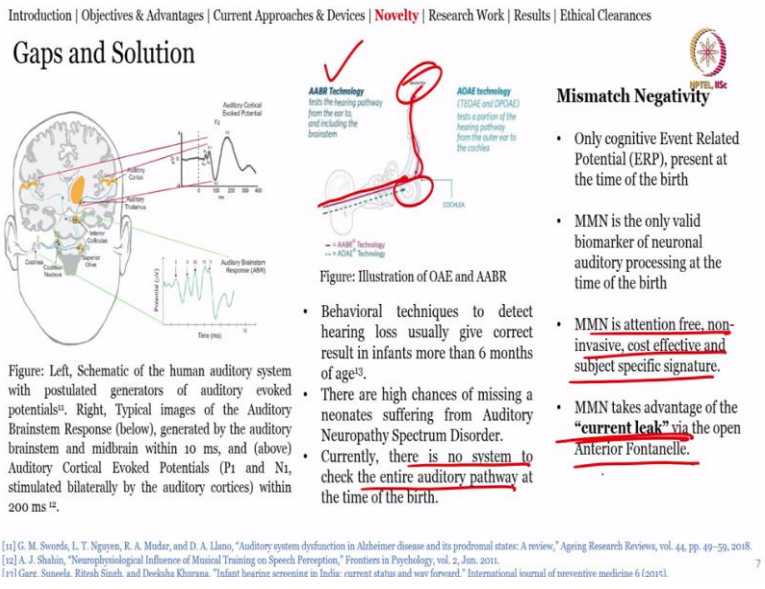

So, if you see the slide we were discussing that from the hearing it goes to the auditory thalamus and if you further look into that it can raised to auditory cortex. So, can we add one more marker which we call mismatch negativity to not only look at ABR, but also to look at the MMN. So, this is what it is and we have also seen that in case of the ABR there are 7 peaks for normal subjects.

And if the subject has a difficultly in hearing then it would be different and particularly if we pick number 5 is what is generally of interest in the case of the hearing. Now, if you look at this particular image we have AABR technology and AAE technology. So, O is otoacoustic emission, ABR is Auditory Brain Response, brainstem response. So, now you can see that it goes, it goes to the cochlea, it goes cochlea to the brainstem and that is it there we stop.

But if we can go one step further then it will be helpful. So, we have seen that there is no system to check the entire auditory pathway. Mismatch negativity is attention free, is non-invasive, cost effective and takes advantage of the current leak. I told that the skull is not completely diffuse and that is why there is a current leak because what we call in technical terms as anterior fontanelle.

And that is open and that is why it is easier for us to look at the mismatch negativity because that is the only cognitive event related potential that is present at the time of birth. So, we need to look into that particular aspect as well. Mismatch negativity is the only valid negative biomarker of the neuronal auditory processing at the time of birth.

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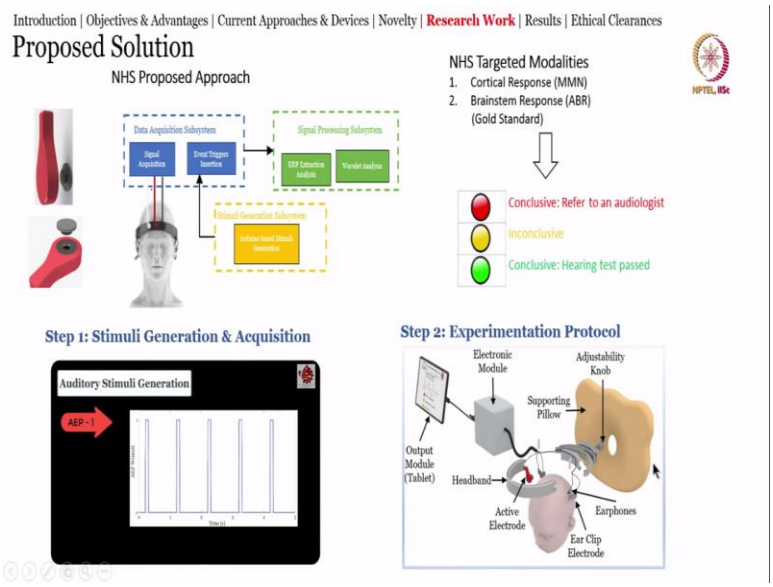

And now we have seen this particular thing where we were able to see that how we can generate a different auditory stimuli, so that to capture the ABR or to capture the mismatch negativity or AEP or P 300. Now, here we are talking about only AEP and then MMN and then P 300. So, P 300 is positive milliseconds that arises for the unexpected event in our general ecosystem.

So, here you can see that we apply the stimulation to the ear and we acquire the signal, process the signals and then we can understand how to reduce the number of cycles so that it run faster so that can be done with the help of the wavelet analysis. Now, let me just play once again for all of you that how the auditory stimuli generation sounds like this is AEP 2 mismatch negativity see every fifth one P300 randomly.

So, this is how it is done that we have AEP, MMN, P 300 and the stimuli can be generated with the help of heart beat. We can also use other ways to generate the stimuli. Now, what we want to do is if we have a similar band for a neonate then if we get the signal proper like EEG signal we can say that it is conclusive hearing test pass or in conclusive or conclusive refer to an audiologist. So, if yellow and red light is there that means that the audiologist has to intervene for the green thing no need to worry about it. So, can we make a band that can be placed at every primary health center that is our idea.

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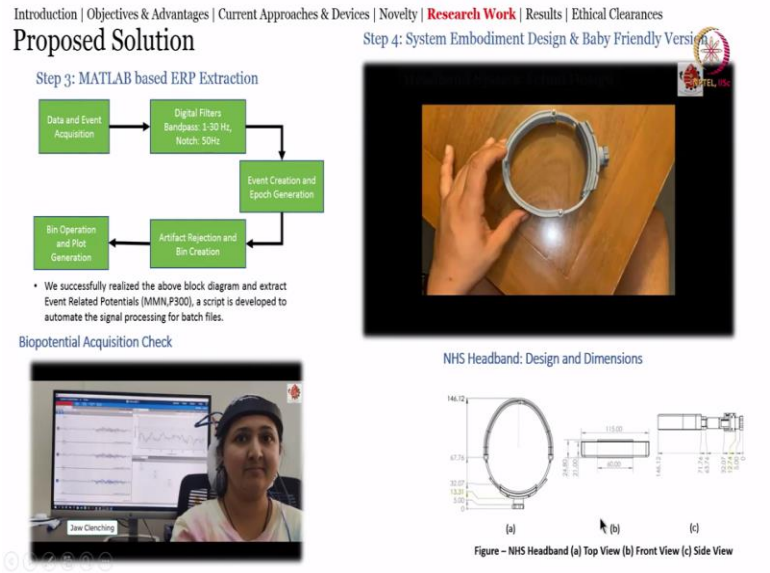

Now, here you see on the left-hand side which is on here where my mouse is there the MATLAB based ERP extraction technique is there where data and event acquisition occurs where you follow it up by the filters. Bandpass filter between 1 to 30 hertz and notch filter at 50 hertz so that you can event creation and epoch generation and then there is artifact rejection followed by the bin operation and plot generation.

So, here we have successfully realize the event related potential which is MMN and P300 a script we have designed and this is used to automate the signal processing for the batch files. Now, here let us see this video. So, what exactly you see in this video this has the waves that

are coming up. So, whenever sea clinches sea clinching the signals are different. When this is blinking the signals would be different okay I will just play it again you see that.

Whenever sea is blinking any effects signals are different. Now, whenever sea is clinching it will be different you see. Now, this is just to understand that what are the noise in the signals. We just do not want to understand the only signals, but what are the noise in the signals so that we can remove all those noise and focus only on the data. Now, you see this one this is the baby friendly version of the device.

So, you have seen how this neonatal hearing band can be designed, we have also shown you the blown-up diagram of the same bed and you can create this or you can fabricate this device or you can develop this device using additive manufacturing which is the 3D printing technique. Of course, there are electronic modulus that we have been discussing as a part of this course separately. And signal that is acquired a preprocessing has to be done, post processing has to be done to remove the noise and only look at the signals. These are the NHS head band top view, front view and side view, the engineering drawing what we call.

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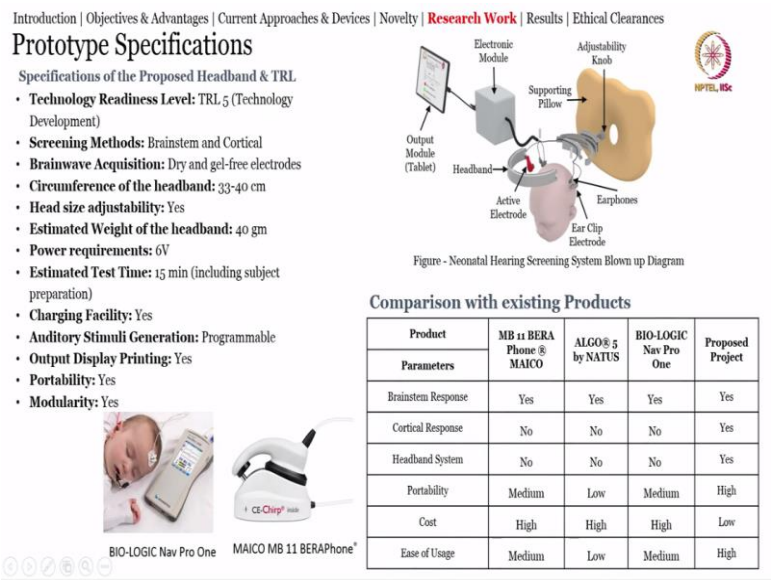

Product / Parameters	MB 11 BERA Phone ® MAICO	ALGO® 5 by NATUS	BIO-LOGIC Nav Pro One	Proposed Project
Brainstem Response	Yes	Yes	Yes	Yes
Cortical Response	No	No	No	Yes
Headband System	No	No	No	Yes
Portability	Medium	Low	Medium	High
Cost	High	High	High	Low
Ease of Usage	Medium	Low	Medium	High

So, let us go to the next slide. Now, here what we see here we see that there is a prototype specification. Now, once you develop a system you need to understand that you need to compare the system with the existing system. So, this is a Nav Pro One you can see a system, you can see here for the baby there is another one MB 11 BERA phone. Both of this are extremely costly technique.

But at the same time a technology readiness system of our system here is about TRL 5, screening method is brainstem and cortical, brainware acquisition is dry and gel free, circumference of the head band 33 to 40 centimeter we can change the shape and then you can go further head size adjustability is possible, estimated weight of the band is 40 grams. Power requirements is 6-volt time how much time it takes 15 minutes.

And this is including subject pressure. So, in reality when we go for only ABR it is released less than a minute, if it is MMN it is a bit time consuming, but we can reduce this further by using as I told you earlier. Can you recharge the batteries yes or Auditory Stimuli generation is programmable, output printing is yes, portability yes, modality yes. So, this is a way of looking at it.

You can see that putting patches at different area of on the baby's face is not really advisable because baby skins are very soft sometimes using the tape also affects the skin. So, we need to be very careful about how to use this system. Now, these are comparison about what kind of parameters can we look at. Brainstem response our system can do, cortical response yes. Headband system is yes. Portability yes very high, cost is extremely low compared to the existing cost of this commercial products and ease of usage is extremely high, it will be very easy to use it.

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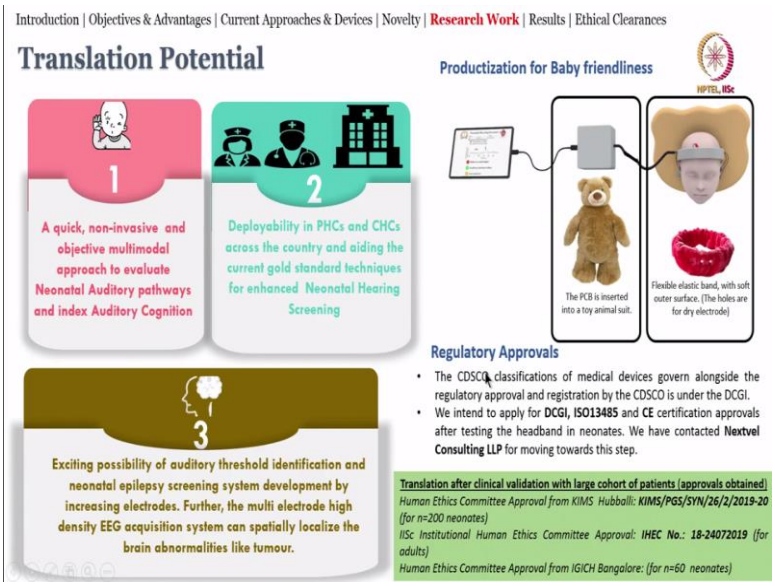

So, the translation potential if you look at the translation side of this particular work then a quick non-invasive and objective multimodal approach to evaluate, neonatal auditory pathways and index auditory cognition. There is a deployment in PHC which is Primary

Health Centers and CHCs across the country and aiding the current gold standard we are not removing anything you do understand this thing none of the technology that I teach you has to do anything with removing or replacing a clinician.

We should not be replacing the clinician, we should aid them, we should help them, we should empower the semiskilled personnel like ASHA workers. So, that they can use this technology and where clinicians cannot be reached where the technology which is this costly technology, like, 14 lakh, 15 lakh cannot be commissioned, cannot be placed then in that cases we can use our technology which is much more affordable, can be easily used.

Can be used for screening neonates which are right now not screened at all. So, the technology that we are generally focus on is to aid, to help, to empowers always remember that. The technology should not be developed to replace; the replacement is difficult job we should empower. Finally, the third one is exciting possibility of auditory threshold identification.

And neonatal epilepsy screening system development by increasing number of electrodes. If we increase number of electrodes similar to 10-20 system, we can not only look at the epilepsy in the young adults, but also in the neonate as well and that is the advantage of this particular system. A high-density EEG acquisition system can specially localize the brain abnormally like tumor. We require approvals like CDSCO, we intend to apply ISO 13485, CE certification and lot more.

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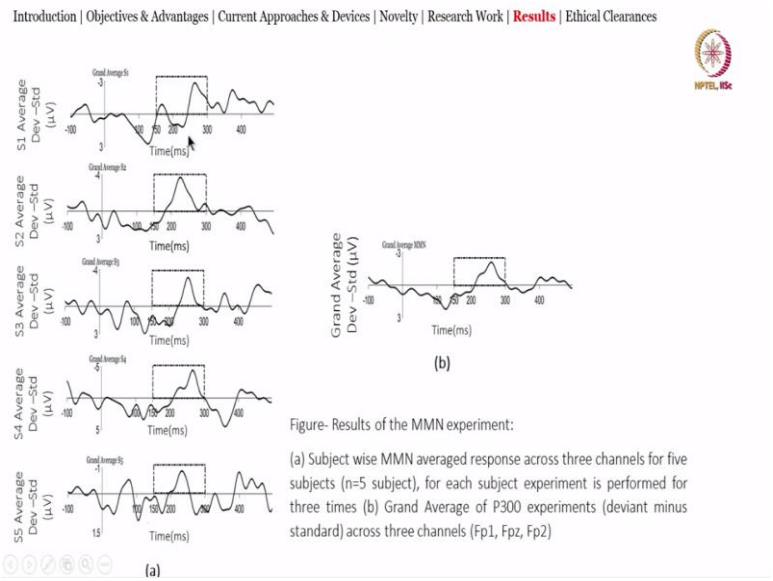

So, if you see the signals you can very easily see the mismatch negativity. Generally, it is between 200 and 300 milliseconds and every time you can see there is a peak coming up here. Even the grand average also you can see a peak at this particular point this is a negative up as you can see here.

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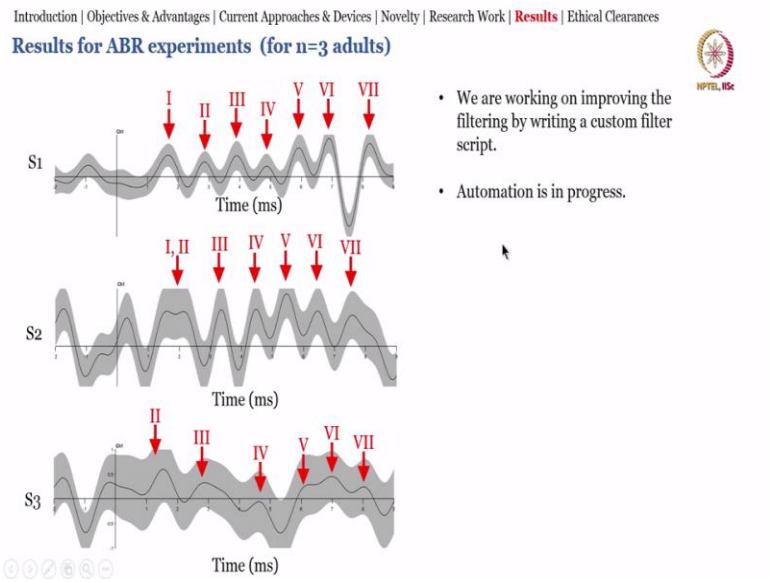

These are the 7 peaks that generally are supposed to observe in the adults and peak 5 is of more interest, peak 5, peak 5 here and then peak 5 here. We are working on improving the filtering by using some custom filter script and also atomization is in progress. So, these are some of the things how we get it done.

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Institutional Human Ethics Committee Approval from IISc, Bangalore Dr. Hardik J Pandya and Dr. Mahesh Jayachandra

Ethical Clearance for 200 neonates from KIMS, Hubballi Dr. Manjunath D

Now, like I said that ethical committee clearance is very important without having this clearance you should never use any human subject or even the samples of the human subject without ethical clearance and without the consent it is prohibited, it is not allowed, it is against the ethics. So, it is always to good get ethical clearance before you start working on it. We have a collaborator from Indra Gandhi Institute of child health.

And we have collaborator from KIMS Hubballi Doctor Manjunath Dandi, from Indra Gandhi we have Doctor Pratik as our collaborator and also Pratik Senior he is also there for us to utilize the system or to put the system on neonates head and to screen those neonates. So, these are two clearances as you can see here and this is end of this particular module. So, what we will do in the next module.

We will look into something called implantable MEA for recording potentials. So, now we move one step further until now what we are looking at, we are looking at what is EEG, how EEG is generated, how EEG can be used if we understand EEG signal then if there is a normal subject versus elliptic subject then how the EEG signals would vary then types of epilepsy, generalized, absence, focally generalized good.

Next step if you want to use this as a system then can you use it for hearing screening. So, yes how can we develop a band this is how we develop a band and how we give the stimulus. These are the different stimulus that we can look at. Now, we would go one step further and we talk about when the epilepsy is intractable epilepsy that means that even by taking the drugs the person is not free of epilepsy in those cases the way to do is by implanting a electrode.

And then waiting for the episode to occur and exactly where the episode occurs then the tissue is dissected and also it is one way of looking at it. The another side of it is that if there is a new drug that if other pharmacy comes up with how can we test the efficacy of the drug that means that the testing of efficacy of drug is very important since some drug maybe more effective compared to others.

So, this is generally done in ammeter model which is inside the laboratory then followed by the ex vivo model which is a tissue taking that from the animal or blood or other samples and then test it with lab and then goes to in-vivo model. Invivo models can be animal models, can be Espino models like rodents, it can be rabbit, it can be a pig or it can be a monkey non-human primates before which requires lot of clinical trials and then move further.

Now, my point is that if the drug that is developed or formulated by a pharmaceutical industry then can we understand the effect of that drug, how that drug would be effective. If it is effective it will treat epilepsy, but it is not effective then no point. So, with that purpose in mind we again focus on epilepsy, but in this case what we are talking about micro electro array that can be implanted in a brain. And that from the implant we will know when there is epilepsy and if the episode is there or not or if you give the drug whether you can recover the baseline. So, let us understand from the slide.

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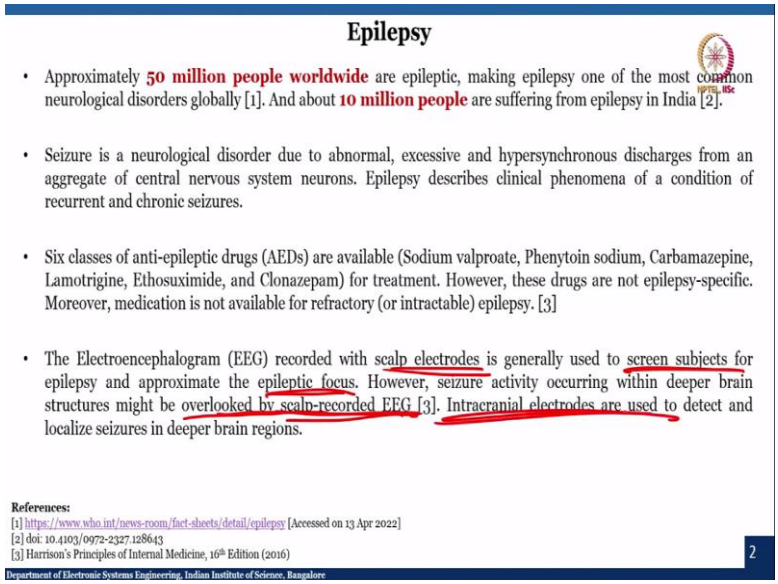

If you see the slide we can see that approximately 50 million people worldwide are epileptic and making epilepsy one of the most common neurological disorder and you see close to 10 million people are suffering from epilepsy just in our country. Now, this is a low number because this number would be way more, this data is from 2016 and 2014 the epilepsy effect is from 2022, but the data about the Indian epilepsy in India is a bit older.

So, my point is that this epilepsy increases for several reasons. One of the few reasons for you to understand because you are the future and is that sleep well if you sleep well and if the stress level is less then less chances of having this kind of depression, seizures and epileptic episodes. If you do not sleep for 5 days, 6 days, 7 days, 8 days, 9 days suddenly you will see that everything will come up.

So, as important as for you is keep your hearts strong, equally important is to keep your mind strong and to keep your mind strong you need to sleep the best medicine is to sleep, 8 hours is what is recommended if you can find 8 hours in your life and sleep well then, less number of

all the other kind of mind related or mental disorders would be there. Let me again tell you since we are taking the advantage of our advantages towards some advance neural science.

We particularly that includes me also are brought up in a society where we think that going to a psychiatrist is a bad thing you are mad, you are mental. It is not that guys, it is absolutely not that. If I go let us say if I break my mind I go to doctor oh he broke his hand it is okay. If I have some health-related problems where I cannot breath well or I cannot walk well I had to go to doctor it is fine.

But if I cannot sleep well, if I do not feel well I go to whom, who is the doctor? A psychiatrist; psychiatrist is a doctor. So, I go to that person and he gives me a treatment then going to a psychiatrist is bad, but going for all the physical health related activities and complaints to a doctor it is fine that is how we have accepted it. It is wrong practice since we are looking into the important applications in neural engineering.

Do understand that your mind is as important as your heart and going to a doctor if do not feel well which is a psychiatrist is absolutely 100 percent okay, talking to someone, understanding it improving the sleep. If somebody helps by talking to you and gives you a medicine which will improve your sleep, which will give you a mental peace, which will make you feel better, which will relieve your stress why not to go.

So, that is why my request to all of you that change that mindset, change the mindset, start telling people going for a mental health checkup is as important as going for a physical health check up that is our body is no separate than mind. So, do understand that when you say that why number of cases are increasing, why epilepsy episodes are increasing? Because people are stressed, people do not sleep like they used to sleep.

So, sleeping is one of the most important jobs at your stage particularly do not leave that 8-hour cycle, try to catch that sleep well, be healthy. Now, coming to that number of cases in epilepsy 50 million worldwide 10 million in India and then in epilepsy we already know seizure is a neurological disorder due to abnormal excessive and hypersynchronous discharges like from an aggregate of neural or central nervous systems or neurons.

And epilepsy describes clinical phenomenon of a condition of recurrent and chronic seizures. Now, this is very difficult because person cannot control sometimes if the person is driving and having the episode there can be accident while walking a person can fall, while climbing

a stairs a person can fall. So, epilepsy has detrimental effect. Six classes of anti epileptic drugs are available you can see the screen.

Now, where you can see that there is a sodium valproate, there is a phenytoin sodium and then so on and so forth. So, these are further treating the epilepsy for treatment. However, these drugs are not epileptic specific. Moreover, medication is not available for refractory or I said intractable epilepsy here the medicine will not work and the only thing will work is to resect the tissue from the brain. The EEG or electroencephalogram records with the scalp electrodes we have seen 10, 20 systems generally used to screen subjects for epilepsy and approximate the epileptic focus. However, seizure activity occurring with the deeper brain structure might overlook by scalp electrode EEG. So, intractable electrodes intracranial electrodes are used to detect and localize seizure in deep brain regions.

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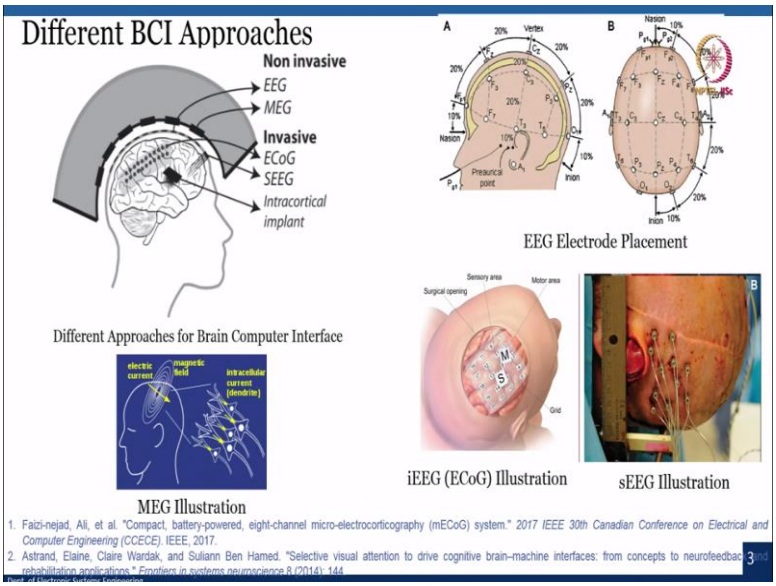

So, these are different BCI approaches. What you see on the left side which is here is a non-invasive when you go for EEG and MEG for invasive when we go for Electrocorticography or stereo EEG that is by implanting the electrodes inside the brain and then intracortical implant you put that implant inside the brain forever, different approaches. So, now what happens is that in this kind of activity you can have either non-invasive or invasive methods.

This is again the same thing 10, 20 system the way the electrodes are placed on the head. Now, I said there is something called intractable epilepsy you can see here in this case there

is a Craniotomy that means that removing the part of the skull and when you remove the part of the skull you will reach dura when you open the dura you will see the brain; brain is floating in a cerebrospinal fluid has a pulsating effect, there is brain pulsate.

Now, if I had to place this micro electrode array on the brain and switch OFF the entire thing back then I can get signals from each electrodes like each electrodes I will get signals from. So, you can cover the motor area, you can cover the sensory area and these are the grids so these are about 20 electrodes in this particular MEA Micro Electrode Array. These are example of the sEEG stereo EEG illustration. So, electrodes are placed inside the brain. So, this much we understood about how to plant the electrodes whether it is inside the brain or it is non-invasive then it is either MEG or it is EEG approaches.

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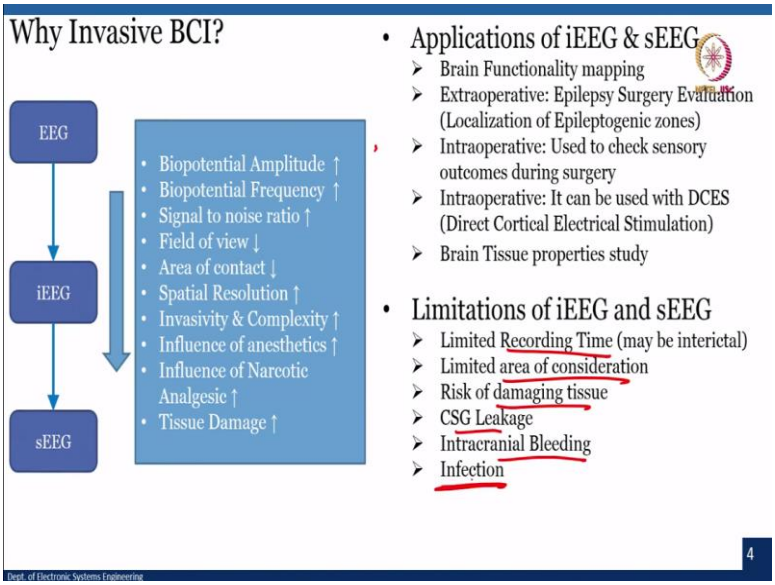

So, why invasive BCI? Why invasive technologies? So, you can go from EEG to iEEG to sEEG. So, one is that the bio potential amplitude increases, the frequency increases, signal-to-noise ratio increase, field of view is less and area of contact is smaller, spatial resolution is better, invasivity and complexity is higher, influence of anesthesia is higher, influence of narcotic and analgesic is higher and tissue damage is higher.

These are the different things as you go from EEG all the way to the sEEG. So, the application, but the application perspective is that it can be used for brain functionality mapping very important, extraoperative because epilepsy surgery evolution can be done, intraoperative can be used to check the sensory outcome during the surgery, intraoperative again it can be used with DCES which is direct cortical electrical stimulation.

Finally brain tissue properties you can study with the help of iEEG and SEG. The limitations are limited recording time, limited area of consideration, risk of damaging the tissues, there is a leakage which is cerebrospinal fluid leakage, intracranial bleeding and there can be possibility of infections. So, there are several limitations associated with the invasive technique as well.

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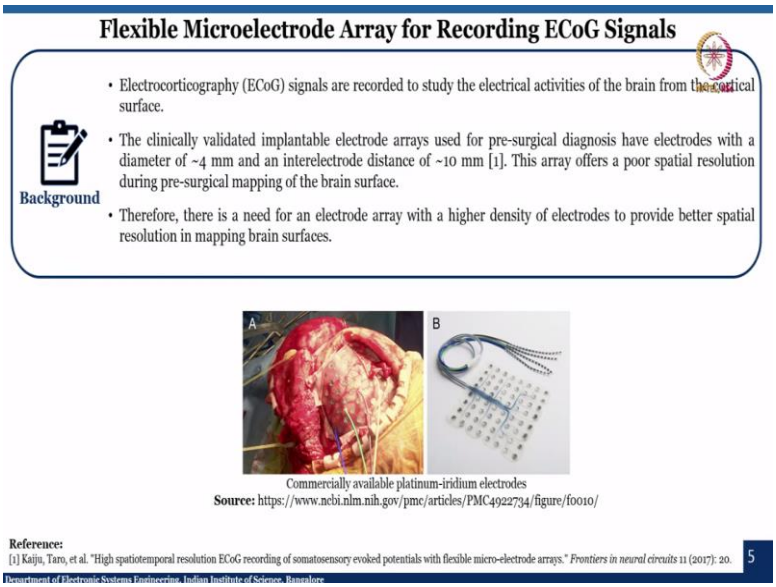

So, let us now take into next class about how to design this flexible microelectrode array for recording ECoG signals. ECoG as I told you is a electro cartography, it is a signals that is taken from the brain. So, we will see that how can be design these implantable electrodes in the next class and then we will see that what are the fabrication technologies of fabrication disc device, what are the casing that we can use.

How to held to be characterized before it can be used in the surgery, how the surgery can be done some videos are there and followed by how the signals are acquired and in the case of antiepileptic drugs, how the efficacy of these AEDs are measured. So, we will do all that in the next class if you have any questions like I said you always are free to ask me in the NPTEL forum. I shall see you in the next class till then you take care bye.