Introductory Neuroscience and Neuro-Instrumentation
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Lecture 19
Introduction to Event-Related Potentials (ERPs)

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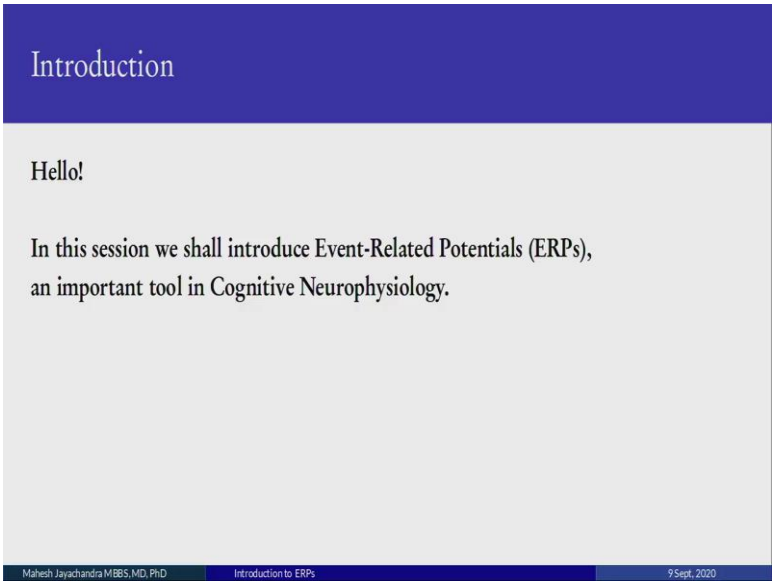

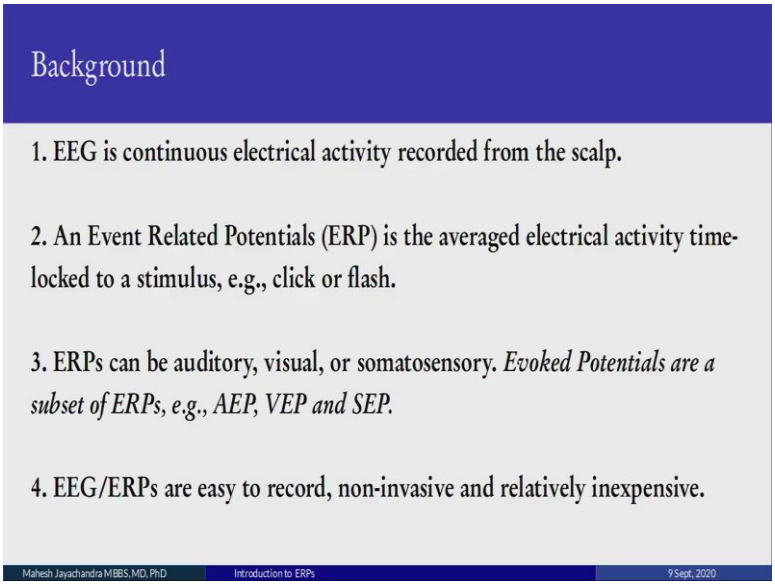

Introductory Neuroscience and Neuro-Instrumentation: Introduction to Event-Related Potentials. So, hello, in this session we shall introduce ERPs Event-Related Potentials and a very important tool in Cognitive Neurophysiology. So, the next 2 lectures are the heart of the course, so far you have got the background on the brain little bit of its anatomy, a little bit of its physiology, a little bit of how cells, nerve cells can be stimulated etcetera.

So, now we would get into Event-Related Potentials, where we record activity from the scalp. It is non-invasive and it is tolerated very well by most people. So EEG, electroencephalography is the continuous electrical activity recorded from the scalp. An Event-Related Potential, on the other hand, is the average electrical activity which is time-locked to a specific stimulus, it could be a tone, it could be a click or it could be a flash.

So it could be, ERPs can be auditory, visual, or somatosensory that is touch. Evoked potentials are used in neurology and there is a subset of ERPs and they are the auditory evoked potential, the visual evoked potential, and the somatosensory evoked potential. So, they are easy to record, they are non-invasive and they are relatively inexpensive, relatively inexpensive compared to fMRI. So, another technique to look at brain function.

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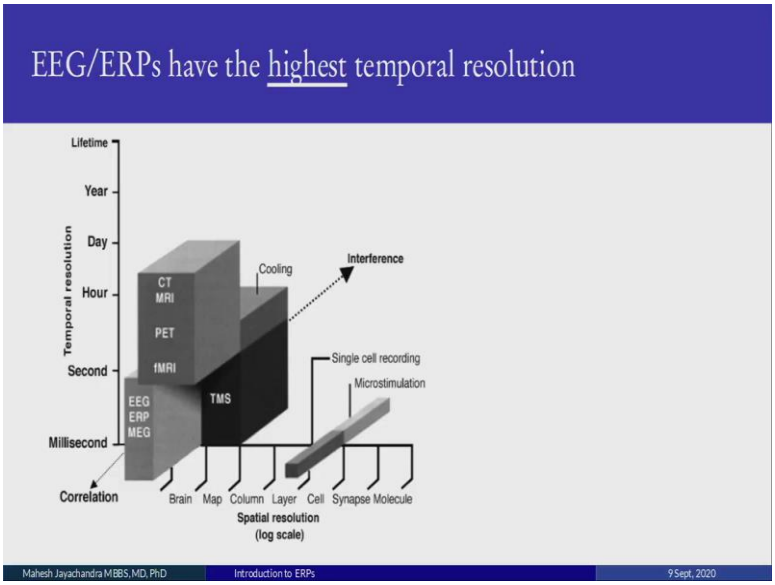

So, they have the highest temporal resolution, resolution measured in milliseconds. So, EEG, ERP, MEG are right up there and they have millisecond resolutions. Further down you have MRI, PET, fMRI, and these look at brain activity in multiple seconds of tens of seconds. And finally, you have singe cell recording and microstimulation, we are not talking about that over here.

So, as far as whole-brain recordings are concerned EEG ERPs are the best. MEG is magnetic, recording the magnetic fields of the brain, if you remember your Flemings laws, the electrical field is perpendicular to or orthogonal to the magnetic field, except that is you need a special recording setup using squids, not the squid we are talking about but superconducting quantum interference devices and that makes it very expensive to deploy on a large scale. So, EEG ERPs remain the simplest and the most cost-effective tool to look at brain function.

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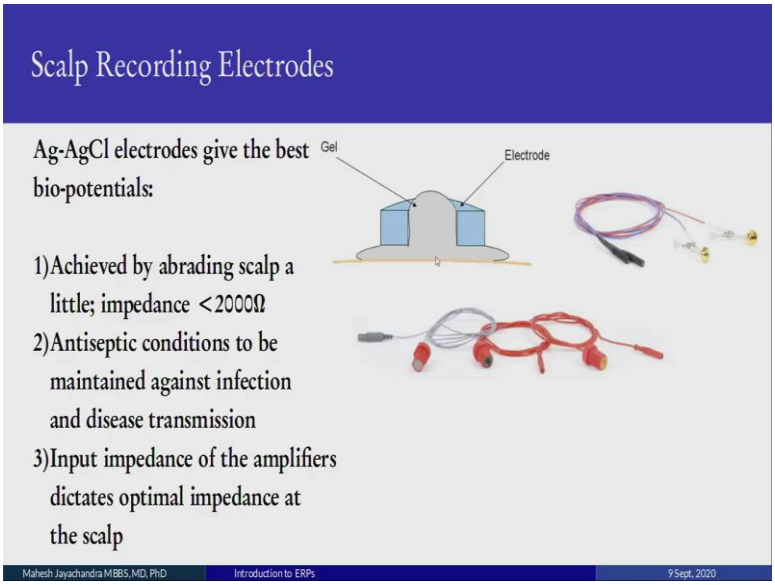

So, let us start with the electrodes. What are the best electrodes to use? You want electrodes that do not take part in the phenoma contribute to the electrical activity and thus far we have found that silver electrodes are the best. Now silver form a layer of silver chloride between the silver and the scalp and this with this bio-potentials are not distorted, they are easily recorded.

And between the electrode and the scalp we over here, we use conductive gel, this is something which conducts is got salt in it and it provides a good interface between the electrode and the biological tissue, in this case, the scalp. On the side you see gold plated electrodes which are alternative, they are inert and they are typically used in clinical practice. So, what we do is first we clean the scalp and abrade it slightly. So, that the impedance of the scalp is less than 2000 ohms.

We, it is important to use antiseptic precautions because you can cause infection if the electrodes are contaminated by previous recordings and typically the infection one is worried about in clinical practices Hepatitis, Hepatitis B infection. And the input impedance of the amplifiers tells us what would be the optimal impedance we need over here. So, typically this impedance has to be much less compared to the input impedance of the amplifiers. So if it is 2k, the input impedance of the amplifiers would be probably like 10 megs.

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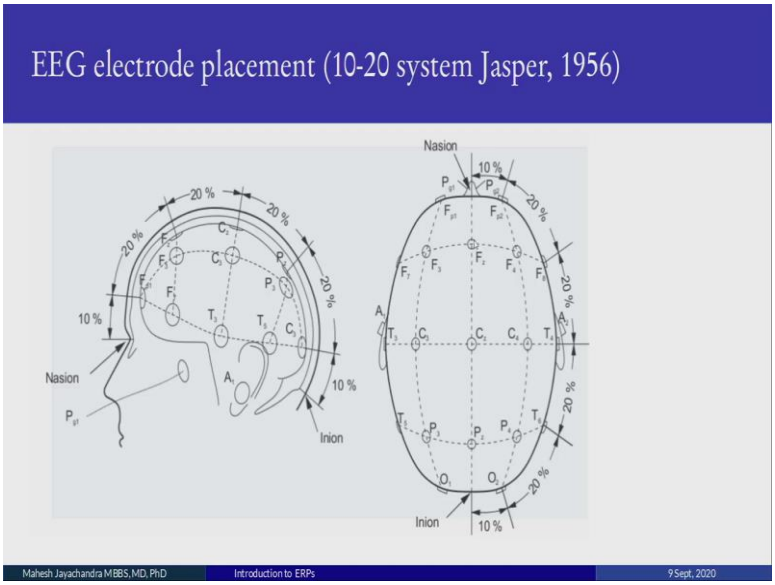

And where do we place the electrodes? So, this was a system for easy electrode placement which was first propagated and popularized by Jasper, a Canadian EEG researcher. So, here you have, this is from the top and this is looking at the left side of the brain. So, from the top, your central electrode is, central electrodes the ones over here are all denoted C with the subscript depending on whether on the left side in which case is an odd number, and on the right side it is an even number. So, in front of Cz anterior root of the frontal electrode, and Fp 1 and Fp 2 are electrodes on the forehead. Behind you have the parietal electrodes.

And right behind you have occipital electrodes. So then, what the convention is that on the left side we have odd numbers, on the right side we have even numbers and the central electrodes have a subscript of z or z so you have Pz or Pz which is central line parietal electrode Oz is not shown over here it is below, so it is an occipital electrode. Central electrode, Cz is probably the most important electrode in this central electrode. Frontal Fz is midline frontal electrode and so on and so for.

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So, traditionally you have to clean each area and then affix the electrode on it so that the impedance goes down but now we have advanced first of all we have caps where the electrode positions are already pre-marked. Just put on the cap and you do not have to measure it because with the Fz, I mean with the electrode placement convention you have to measure the distance between the nasion, the inion, between the two pre-oracular ridges over here, join these two lines and then you get Cz.

And now you take 10 percent and 20 percent of this length and there, with that you get the other electro positions. So, it is a painstaking method, especially when you have 40 electrodes or more, we have to mark each electrode and make sure that you are in the correct position. Current day technology you have a cap where these electro positions are pre-marked. So you just put on the cap. And also they use dry electrodes, with dry electrodes the impedance is very high of the electrodes, anywhere from 50 to 150 k.

But correspondingly, the input impedance of the amplifiers are much much higher 10 to the 12 for example, a k. So, you get recordings, they will be slightly noisy, but very good recordings within seconds. This ENOBIO is made by neuro electrics, it is an FDA approved and C certified system which we use in our lab both at Saint Johns and at IISC. It is a little expensive but if you want to do it yourself and get good recordings but on a bare born system, I strongly recommend Open-BCI. This is not certified for regular clinical use but it is okay for doing research. And these are also, even though it uses wet electrodes, dry electrodes also work pretty well.

This is an electro EEG cap for a child. We make it differently by putting a Mickey mouse overlay on it. And finally, I have to mention a gamer system, systems used by gamers like Emotiv and Neurosky where you can record EEG and ERPs. However, these tend to be noisy and usually neuro-scientist hesitate to use them in an official study because they are not certified for clinical or research purposes. But again, in a pinch, you could use these and many people have many students and researchers have used these systems.

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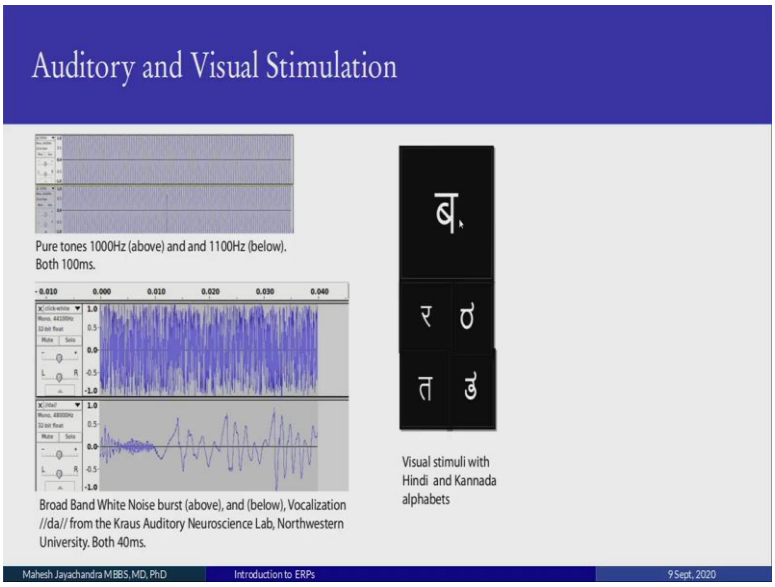

So, what are the stimuli? So, we went through the electrodes, we went through the impedances, we went through the positions, now coming to the stimuli. So, for auditory stimuli, we typically use clicks, which is a square way of 1 millisecond or point 1 millisecond, or we use tones, discrete tones of particular frequencies 500, 1000 hertz. And this is a tone, it is a pure tone, above it is 1000 and below it is 1100. It is too close for us to make out a difference and, these were generated using the open-source program audacity.

Alternatively, these are pure tones. Alternately, we can have a white noise burst like sshh, or we can have a vocalization like “da”. So, this is a white noise burst and this is “da” which is a stimulus developed by Professor Nina Kraus’ lab at Northwestern University, both of them are approximately 40 milliseconds. Notice the complex structure of 40 milliseconds of “da”. You can also use visual stimuli, I happen to use alphabets over here, Hindi and Kannada, but you can use English alphabets, pictures, faces, what have been.

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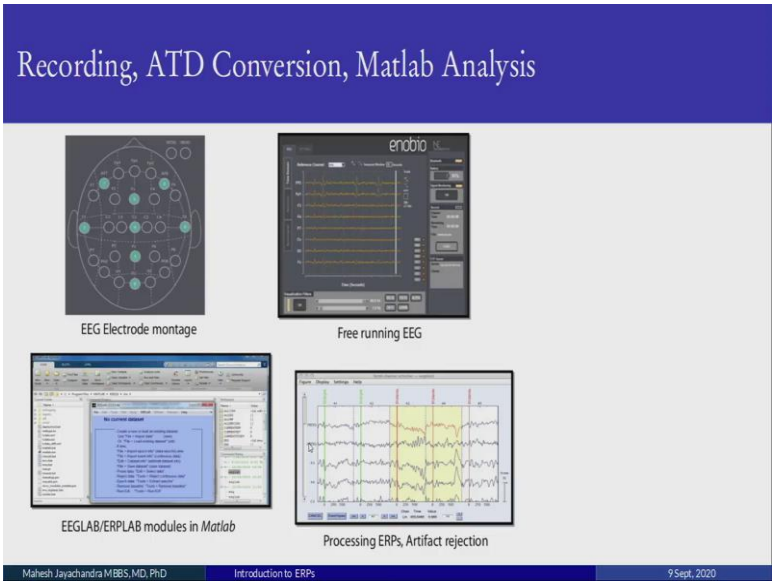

So, this is from our lab, where this is the electrode montage. So, here we have midline electrodes and we have some temporal electrodes and electrodes on the headband on the side. This is the free-running EEG. Once we record the raw EEG, we do the processing, this is the choice. We do the processing in ERP lab or EEG lab which are open source modules that work on Matlab and they have been there for more than a decade and they are designed to analyze ERPs and evoke potentials.

And after (proce) we have to do the processing. Typically, what we do is we have a stimulus. So, we take an epoch time logged to the stimulus a little before the stimulus began forgetting the baseline and then for about a 1 second to get the phenomena of interest. Then we reject all the artefacts which are eye blinks, movements, all these are muscular artefacts that will swamp the EEG. So, we keep a window and windowing threshold plus minus 100 microvolts, for example, something above or below, we throw it out and then we filter it.

The EEG frequencies of interest which we record from the scalp are all below 100 hertz. So, we can use a filter usually a bandpass filter 1 to 30 hertz and that gets us all the information we need for ERPs. So, typically what information we need? We need amplitudes, we need latencies, and so on. When after you have done all this, we average it. Why do we average it? We average it so that when we are doing the ERP experiment, the person is thinking a lot of different things are happening in the brain, besides listening or paying attention to the tone or the visual stimulus.

So, when you average, only the common features of the stimulus invoke response remains, all the other stuff is thrown out. So we, that is the importance of averaging. So, in the free-

running EEG, it is we have stimuli coming in at regular intervals, so time log, so we create epochs, we reject the artefacts, we filter, and then finally we average. So, in brief is how we analyze the raw data to get ERPs.

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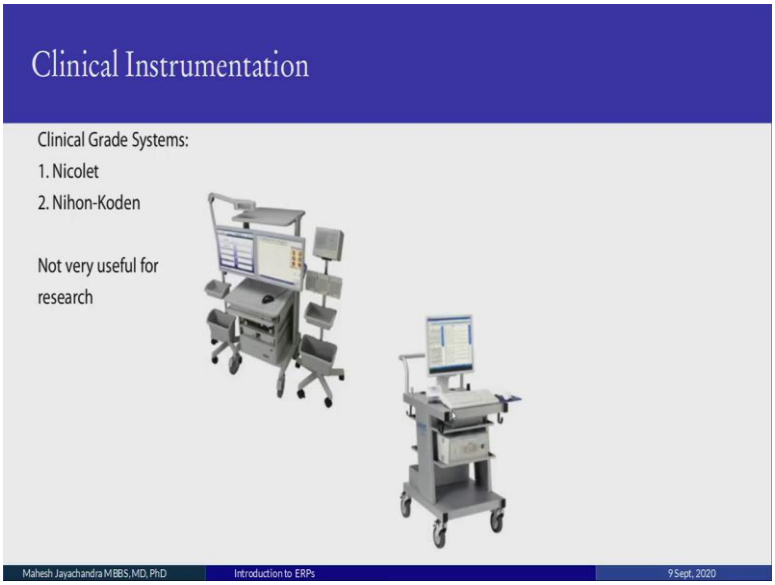

One point, as a (pers) a person in bioinstrumentation or medicine, you will often encounter clinical-grade EEG systems, some models, or Nicolet and Nihon-Koden. They are very very good for clinical work. They are not very useful for research because you have to be able to have complete control over the stimulus modality, modify it, get external triggers so on and so forth. And these do not do that.

They are meant for technicians which are set over there, you have pre, pre-made evoke potential stimuli, mostly, auditory work potential, visually evoke potential and some other sensory evoke potential and that is person sits over there, punches a few buttons after placing the electrodes and gets the data. But they are very good clinical systems, they can take a lot of abuse in the clinical wards and hospitals if they have ERP EEG setup, it is one of these or something similar.

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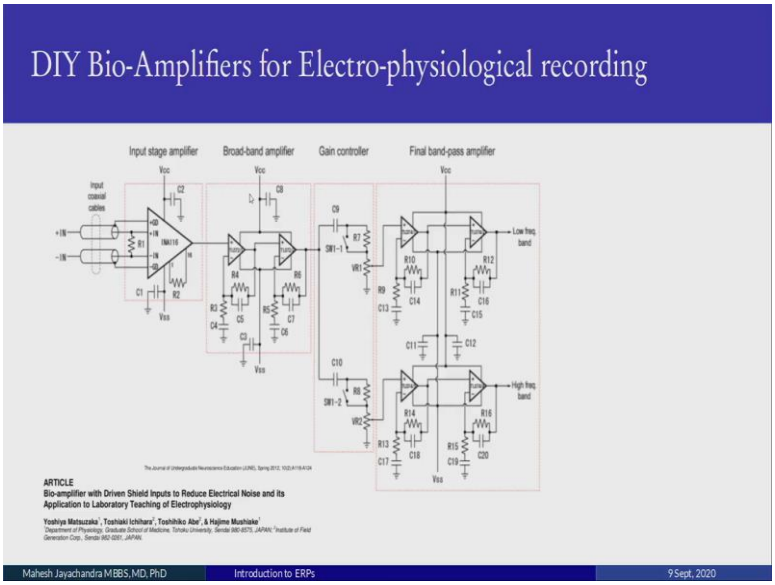

If you are, if you have the talent and you are matured and you want to do it yourself, it is possible. You can build bio-amplifiers that do all this stuff. So, this is from a Japanese group, Matsuzaka Atayal, and all amplifiers, biological amplifiers have this similar kind of meta schematic. You have your electrodes over here and they have to be shielded because otherwise, they will pick up AC. Then you have an input stage amplifier which kind of basically impedance matches between the electrodes and the rest of the signal conditioning circuit.

There is no real amplification over here. In the next stage, you have a broadband amplifier of the particular usually it is of the, of a particular level 1000, 2000, 10000 like that. If it is too much, you can cut the gain, so you have a gain control stage where you can modify the gain, and finally, you have bandpass amplifiers where you look, filter, and look at only the frequencies of interest. So, this is a general biological signal conditioning circuit for EEG.

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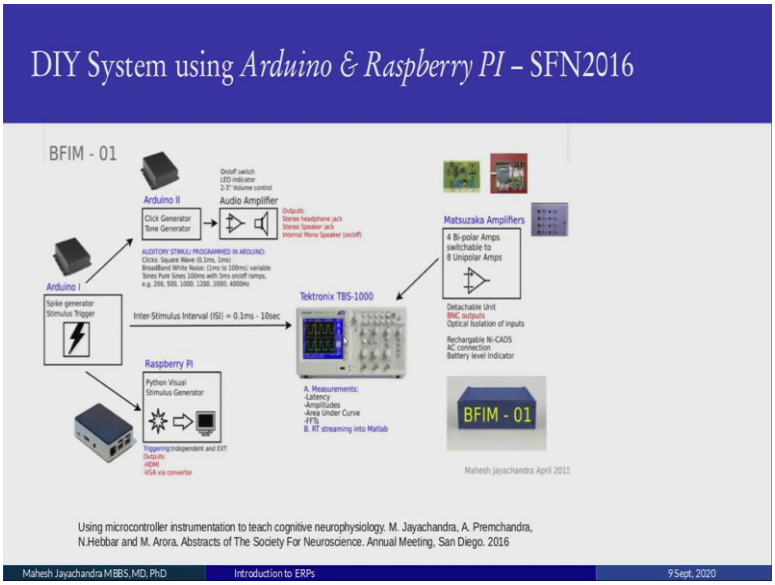

So, it is also possible, now all these systems are very expensive, typically they cost 50 thousand to 100 thousand dollars. So, you can also build it yourself. So, using a judicious combination of Arduino and Raspberry Pi. So, we presented, our group presented circuit where we use Arduinos to generate the trigger and then we use another Arduino to generate clicks or tones and that goes from the audio amplifier and the outputs are a stereo headphone or a speaker heard by the subject. That is for auditory stimuli

For visual stimuli, we use a single board computer typically a Raspberry PI and you can run psycho PI which is a program from professor Jonathan Peers and that generates auditory and visual stimuli. The electrodes are, you could use the previous circuit, this circuit, Matsuzaka circuit and we made this circuit in our lab. So, these get the inputs from the electrodes and you combine these, you integrate the triggers from the stimulus trigger generator with the responses and you do the analysis either on oscilloscope which is the traditional way to do it or you can take it through a DAC an A to D conversion and take it into your laptop and do the analysis.

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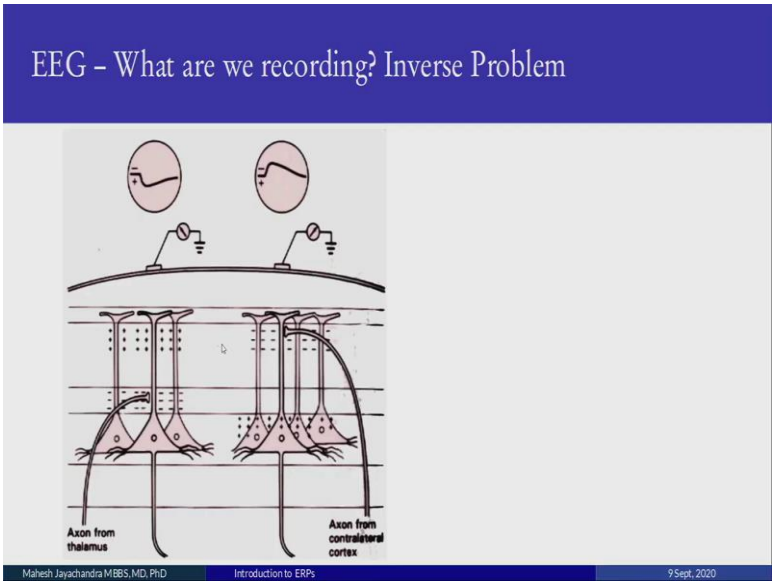

So, what are we recording when you put an electrode on the head? So, there is something called the inverse problem. There is a whole lecture on it, which would be done in a subsequent week, but briefly, you have all the pyramidal cells if you remember the pyramidal cells, the cortical column, and stuff. So, you have an axon coming from a lower area, the thalamus. It goes just above the soma and depolarises it.

So, soon as it depolarises here, this area gets hyperpolarised. So, there is a dipole that is formed. And if you have the electrode on top, you have a positive deflection. Now this is an interesting tradition in neurophysiology, negative is often shown is up and positive is down. Keep that in mind. So, this is a positive deflection. Alternatively, you can have inputs to the pyramids from the opposite side, the contralateral cortex and then the opposite phenomena happen, it depolarises this area, the dendritic branches and it does hypo polarization over here.

So, here you get the opposite deflection. And there are many combinations. But roughly, this is what is recorded and we do not record action potentials, we record postsynaptic potentials, typically excitatory postsynaptic. Action potentials occur but the scalp access a low pass filter. It just filters out all the high-frequency action potentials and you only get the low frequencies. So, the current understanding is that the EEG ERPs, all the stuff you record on the scalp are due to postsynaptic potentials.

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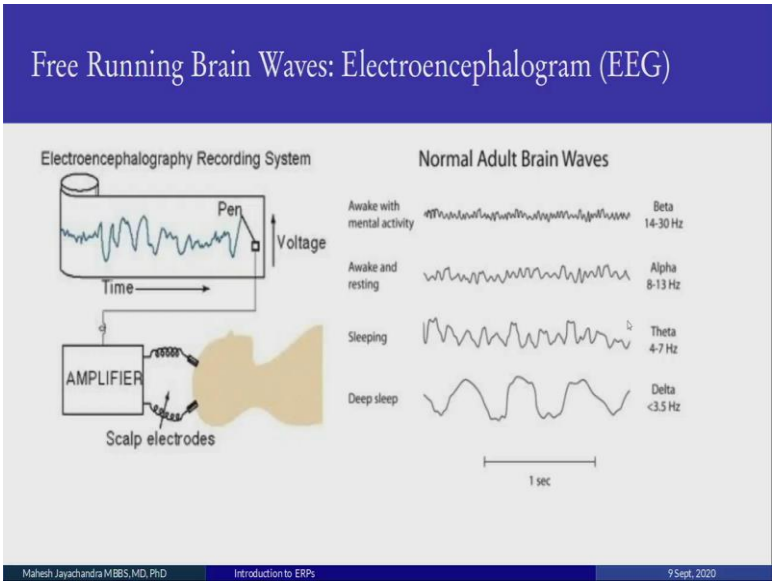

So, free-running EEG brain waves. So, this is a traditional way of recording EEG, you put two electrodes on the scalp, amplifier, and in the old days, they used a stylus and a running paper sheet which the stylus would track the EEG on it. So, you have different frequencies and they are all low frequencies. So, in deep sleep, you have frequencies less than 3, 4 hertz. When you are drowsy and kind of getting there a little sleepy, you get the theta band which is 4 to 8 hertz.

So, the first one is a delta band less than 4, then is a theta band which is less than 8, 4 to 8. Then you are awake but you are resting and sometimes your eyes are closed, you get this (stipikle) typical alpha activity 8 to 13 hertz and that is recorded best on the occiput, the back of the head. Right on top is a beta activity which is a normal mental activity, 15 to 30, 14 to 30 hertz.

And the beta activity is high frequency, high frequency by EEG standards but low amplitude, while all the rest the lower the frequency gets, the amplitude increases. So, Hans Berger showed alpha waves and use a physiatrist from Shiv Jena in Austria and he won the Noble Prize, he was the first guy to show electrical activity, it could be recorded from the scalp. Of course, no one believed him so it took many years for people to come around and independently replicate it, and before they believed.

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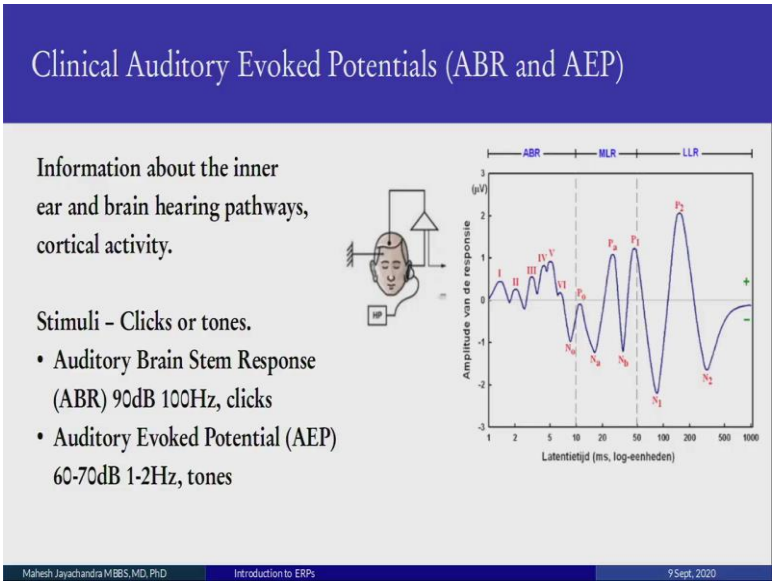

So, let us start with the auditory system. So, this gives us, we have clicks and as soon as we have clicks, we record from the scalp and this test the pathways, the auditory pathways right from the periphery, the tympanic membrane, the eardrum through the cork layer, through the brain stem, multiple pathways, and primary auditory cortex, the whole auditory pathway is checked by the auditory evoked potential. So, the stimuli are typically clicks for auditory brain stem responses at 90 dB and 100 hertz, or the auditory evoked potential, you have tones.

Tones of a 100-millisecond duration usually abort 65-70 dB. And these tones should have on-ramps and off-ramps otherwise if they are abrupt when you do FFTs you might get edge effects. So, on the, in the middle, you see a typical circuit where you have recording electrodes, one on the top, one on this ear and there is a ground and you hear the sound and the sound is given by an hp click or tone generator and you get recordings like these.

Please note that this is a logarithmic X-axis, so 1 to 10 milliseconds is where you get the auditory brain stem responses you have a set of wave station if you will 1 to 7, 6, 7 waves. Then you have the middle latency responses and then you have the auditory evoked responses what we usually record and are most important potentials are, are components are p1, n1, p2, n2, p3. So, p1, p2 etcetera stands for the first positive comp, component n1 is the first negative component. That is the nomenclature used in ERP component analysis.

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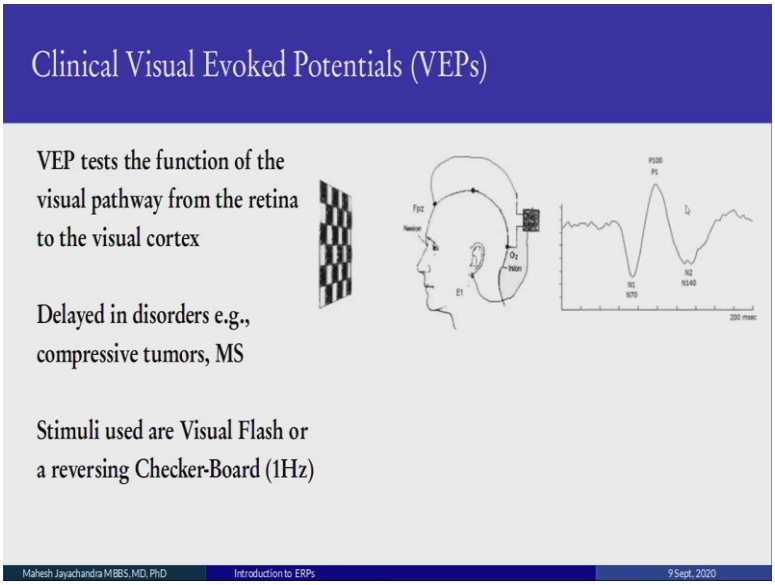

Similarly, with the visual system, you check the visual system from the eye through the various pathways, and you record from the occiput at the back and we could either use a flash or what they do in clinical neurophysiology in the hospital is you have a checkerboard, a chessboard which keeps reversing the squares alternately are whiter black. and again you get an n1 response, a p1 response, and an n2 response. So, first negative component, second negative component, first positive components now these components they are similar to the auditory components but they have, they are just components, they have very different underlying mechanisms and neural tissue involved.

And this potential is delayed if there is a problem with the visual system like for example, multiple sclerosis. We learnt about Millen so sometimes the body destroys its own Millen through an autoimmune process that is a disorder and the conduction failure occurs, first latencies becomes longer then finally you have conduction failure, the nerves do not conduct. But, in the process in the intermediate process when the latencies are getting prolonged you can easily see that here.

In fact, for multiples sclerosis visual evoked potentials, visual evoked potentials are the diagnostic criteria. The other diagnostic criteria are you actually show the antibodies but it is pretty obvious and it very common that you have delayed components visual components in multiple sclerosis and this is because multiple sclerosis can affect the brain randomly. However, 40 percent of the brain arguably deals with the visual system. So, one of the first science that, of multiple sclerosis, is prolonged latencies in the visual evoked potential.

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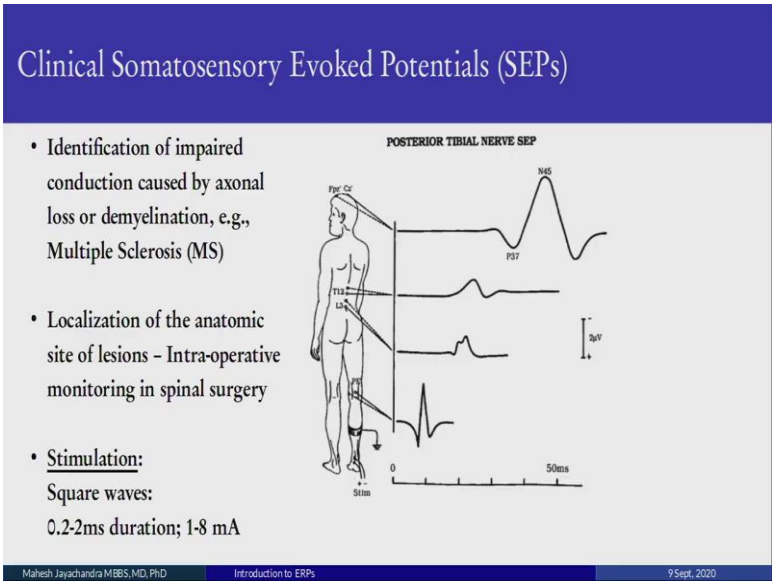

So, we finished auditory, we finished visual. Now we come to the somatosensory. Here we give a brief electrical pulse either to the ankle or we can give it to the median nerve, the wrist and we monitor the potentials as it goes up to the brain. So, right over here at the knee, it is very early than at the spine, at the lambothorasic spine, it is a little later and it gets more delayed as it goes up.

And finally, in the scalp, the brain, you have the somatosensory evoked potentials. So, for the somatosensory evoked potential this would be p1. The 37 indicates the latency in seconds from the stimulus from the time it takes to travel from here to here. And similarly, 45 is the n1 but it takes 45 seconds to go from a milliseconds to go from here to here to record this component. And this is used typically Intraoperative monitoring during spinal surgery.

So, the neurosurgeon is operating somewhere here, is trying to straighten the spinal cord, because people have scoliosis, their spines are bent or it is bent in front kyphosis, so you put rods in the spinal cord and pull the bone back and straighten it. In this process, the spinal cord can get damaged. So, if you are monitoring this continuously before, during, and after surgery, we can tell the neurosurgeon, hey stop because you are doing something which is causing these potentials to go down.

And typically, the neurosurgeons are very good, it occurs very rarely, and typically if they reverse what they are doing within seconds, it comes back to normal. If it is not reversed and then it can become a permanent problem. The problem with doing neurosurgery is that unlike blood vessels if you chop a blood vessel, blood spurts. You know you have done something wrong.

But in spinal surgery, if you chop this spinal cord, there is no indication that anything has happened. It is all just greyish whitish matter. So, this is an important way to monitor you know spinal cord during surgery and make sure that you are not causing problems due to the surgery itself. So, thank you and in the next session, we will get into more details of event-related potentials.