Introductory Neuroscience and Neuro-Instrumentation
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Lecture No. 23
23 Different Event Related Potentials

Introductory Neuroscience and Nero-Instrumentation: ERPs but different event-related potentials.

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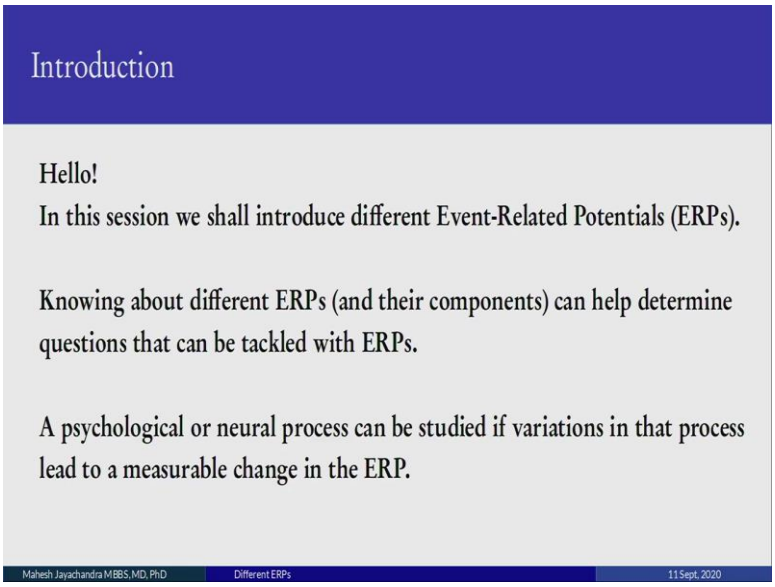

Hello! In this session, we shall introduce different event-related potentials. Knowing about different ERPs and their components can help determine questions that can be tackled with appropriate ERPs. A psychological or neural process can be studied if variations in that process lead to a measurable change in the ERP.

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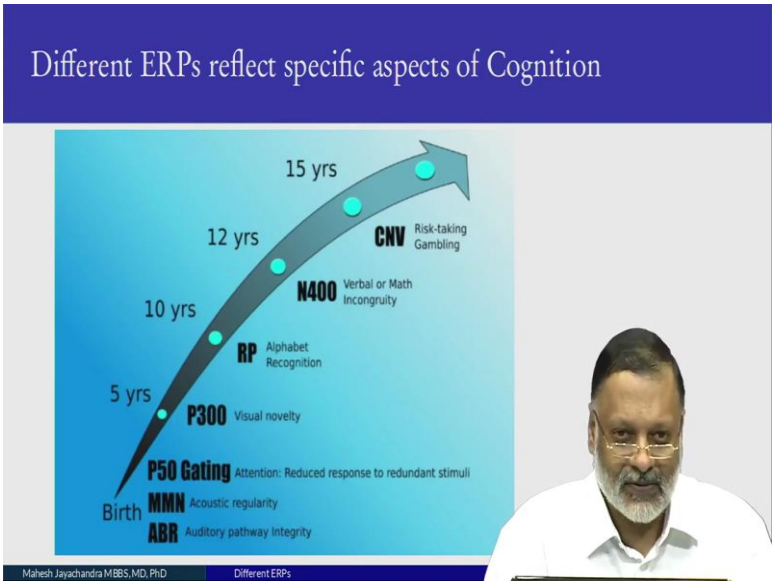

So, this is just a brief overview of commonly used event-related potentials. There are many more but we cannot possibly cover every single one of them. So, I shall be focusing on the important ones and the ones generally used in clinical research. So, ERPs, all of them are not present all the time. Some of them are present at birth but most of them develop as the brain develops through age.

So, at birth we have MMN, MMN is the first cognitive ERP present at birth. We have discussed MMN in previous lectures. We also have ABR, it is an evoked potential, is not event-related potential strictly speaking and it checks the auditory pathway integrity. MMN shows acoustic indicates acoustic regularity or short-term auditory echoic memory, it is an auditory MMN. So, P50 gating is also present at birth and this relates to attention and reduced responses to redundant stimuli.

Around 4 or 6 years of age you get the P300, whereas any novelty in the visual environment evokes a response between 300 to about 450-500 milliseconds. Around 10 years of age you get the recognition potential where you start recognizing alphabets. Around 12 years of age you have the N400 evoked event-related potential. This occurs when there is some incongruity in verbal or math stimuli.

Later, at around about 15 years you have the contingent negative variation which is used to evaluate how much risk-taking a subject would indulge in. So, by putting all these things together you could get a brain function index which is what I am working on in my lab at St. John's.

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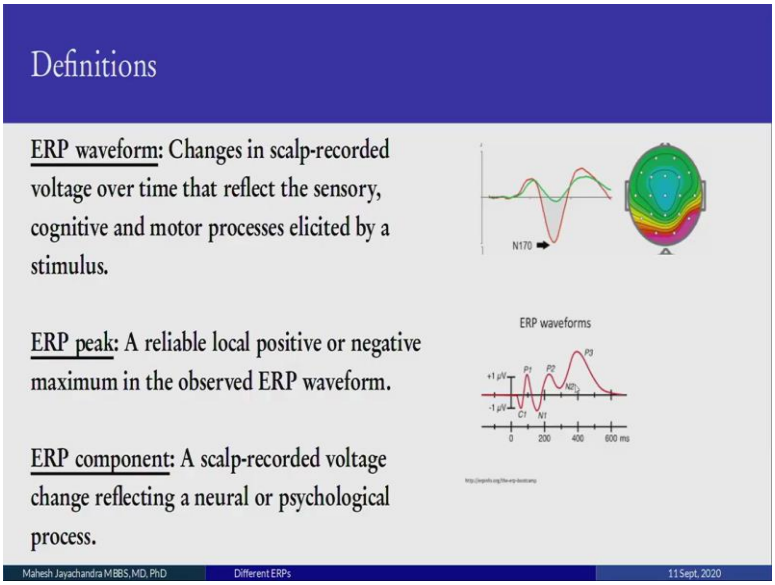

So, definitions. So, just to reiterate event-related potential waveforms, these are changes in scalp-recorded voltage over time. You record over the scalp, this is a heat map and over time. That reflects sensory, cognitive, or motor processes elicited by a stimulus. A peak is exactly what it says, you have different peaks. And the logic here is positive-up. So, the first peak is called P1, the second one, P2, and the third one, P3 which relates to the P300.

And similarly, you have N1, N2, and so forth. Now each peak may be made up of many, probably is made up of many subcomponents and all these components merge and give rise to the peak.

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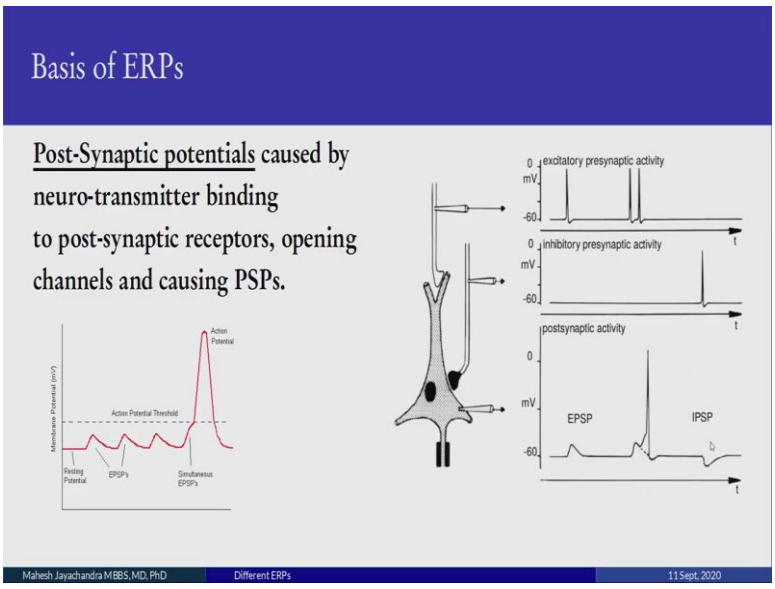

So, again to refresh your mind, how do ERPs occur? So, post-synaptic potentials caused by neurotransmitter binding to post-synaptic receptors opens channels and cause post-synaptic potential. So, if you see over here, you have the resting memory and potential and then you have an excitatory post-synaptic potential, another one here, another one here, and then they come simultaneously and they reach the threshold and you have an action potential. So, these guys cause the EJ.

This is not, it does not, is not recorded by scalp electrodes. So, looking at in a little more detail here you have a classic pyramidal neuron without the dendritic tree because that would make it very busy. So, you have a synapse over here, an excitatory synapse. You have an inhibitory synapse over here and together these things merge and give rise to the post-synaptic activity.

So, consider this stress, this is the microelectrode that has been put in here and pre-synaptic excitatory terminal, and each timer it fires, you have an excitatory pre-synaptic activity. Here you have a spike and you have two more potentials over here. Here it is inefficient, so it is the opposite. Together they give rise to the EPSP and IPSP. So, the EPSP looks like this, the IPSP looks like this. This is recorded from the pyramid itself. When you record from the pre-synaptic whether it is excitatory or inhibitory, it kind of looks the same.

So if two of them merge or come close to each other, the postsynaptic cell reaches the threshold, and then it fires an action potential. Again, the action potentials are not recorded on the surface, it is only the EPSPs and the IPSPs. Excitatory postsynaptic potentials and inhibitory postsynaptic potentials.

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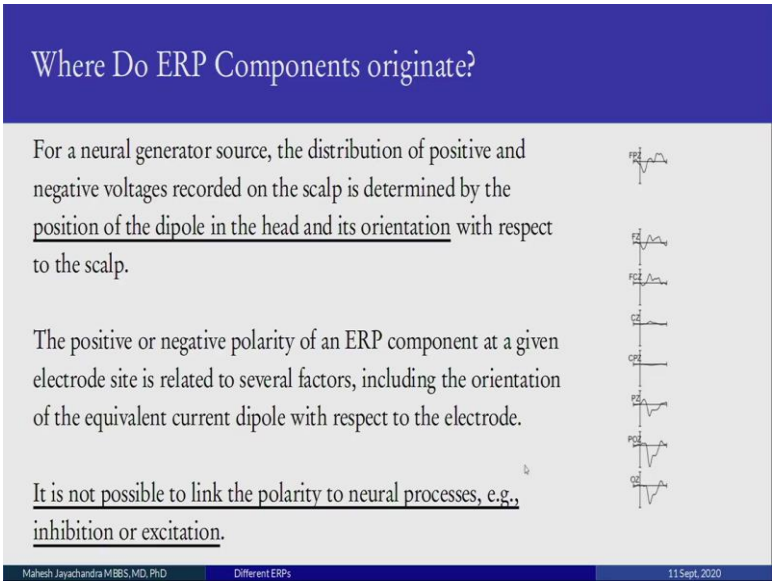

Where do the components of the ERP originate? For a neural generator source, the distribution of positive and negative voltage is recorded on the scalp, is determined by the position of the dipole in the head and its orientation. So, when groups of neurons fire and they are all aligned in one particular axis, they can be considered or they act as a dipole, like a magnet with north and south. The positive or negative polarity of an ERP component at a given electrode site is related to several factors including the orientation of the equivalent current dipole concerning the electrode.

So, all the individual dipoles sum up and we can consider them as an equivalent current dipole. So, it is important to note that the polarity of a process is going up or down, P1N1, P2N2 does not relate to inhibition or excitation, it may but it may not. On the right over here, these are recordings from my lab using a neuro-scan cap. I am just showing the midline electrodes, fpz on the four head, fz, fcz, cz, cpz, pz, poz and oz. So, as you can see there is an inversion and the inversion occurs if you look at this first component over here, it gets less over here, it gets even less at cz, you can barely see it.

Cpz you cannot see it. pz it comes but is inverted and as we go down to the occipital region, it gets more and more inverted. So, likewise with the second component. So, here you see it going up, upward deflection and when we go to the posterior electrodes, it goes down. So, we can think of a dipole happening in this central area which changes polarity from front to back.

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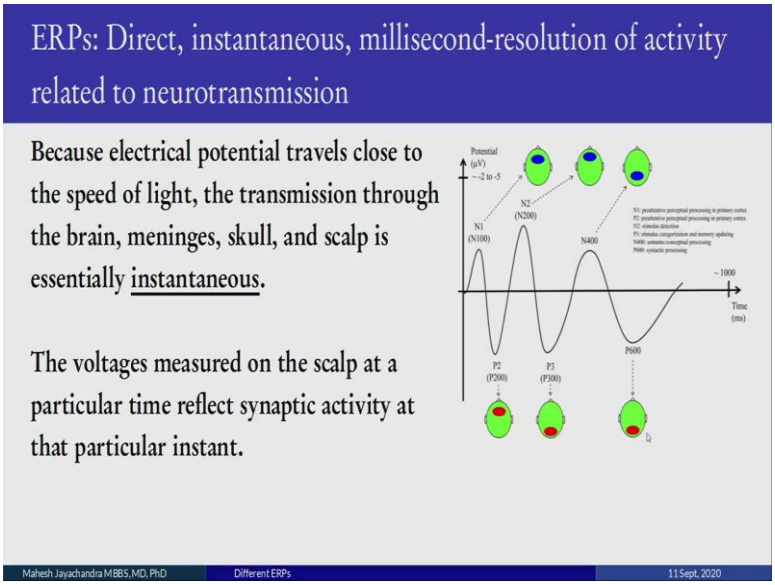

So ERPs, so their direct instantaneous millisecond resolution of activity related to neurotransmission. Because the electrical potential travels close to the speed of light, the transmission through the brain, the meninges, the skull, and the scalp is essentially instantaneous. And the voltage is measured on the scalp at a particular time reflect synaptic activity at that particular instant.

So, if you see on the right, there is a canonical ERP representation, negative-up. So N1, that is around about 100 milliseconds. It generally reflects pre-attentive perceptual processing in the primary cortex. P2, pre-attentive processing the primary cortex and you can see if you look at the heat map where the activity shows, N1 is there, P1 is here. And N2 is also over there and it reflects stimulus decision, etcetera. N4 is semantic, conceptual processing, and here the activity moves behind, the occipital areas.

P3 is the P300 it is there behind and P600 is syntactic processing, again the principal thing is behind. So, these are kind of averages, the consolidated sum of all the processes happening in the brain at that particular time.

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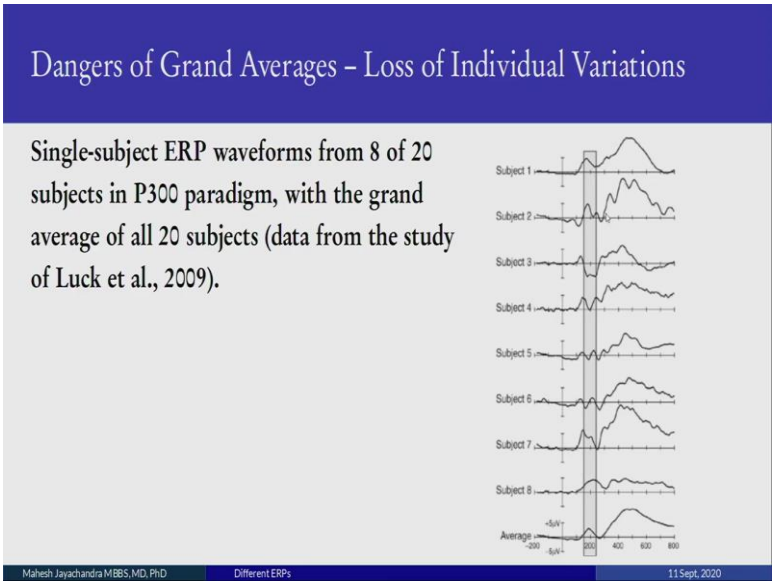

So, one of the methods used to display data is grand averages. Here you take the averages of many subjects so that if you look at the last trace over here, it looks nice and smooth. It is really pretty but there is a problem here. These are, this is the grand average of 8 subjects, this is from the study by Steven Luck. And you see the variation between subject 1 and subject 2, subject 3, subject 4, subject 5. It generally follows this pattern but there are very significant individual variations.

So, you have to be careful. If you do grand averages, you get lovely statistics but you lose all the individual variations. So, if you use the individual variations then it is very noisy data. So, you have to kind of compromise and the kind of analysis you do depends on the questions you are asking.

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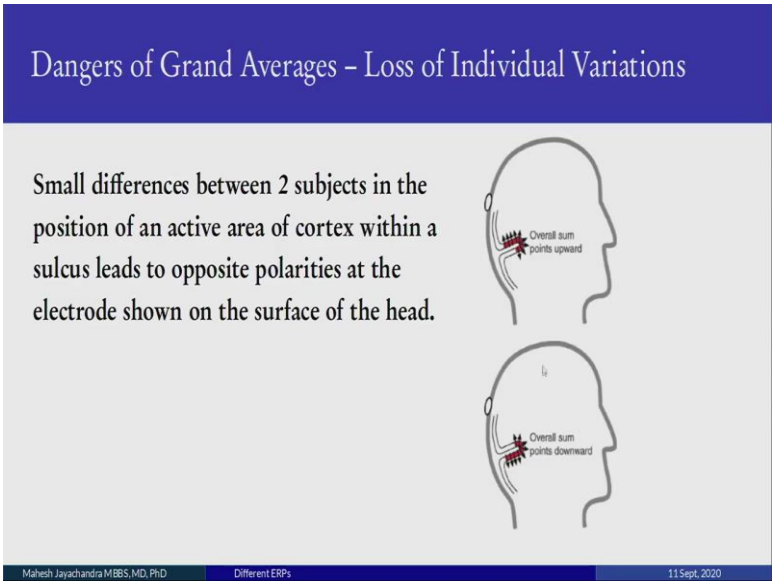

So, small differences. So, consider an electrode over here on the scalp and another subject electrode at the same place. So, these two subjects, there is a sulcus over here. So there are slight variations. Here the dipoles are like this, so most of them on the top and a few of them below, it is the opposite over here. So, the resultant or the equivalent dipole over here points up. Here it points down. So, that is why you have significant differences between subjects because the brain, the sulcus gyral patterns are very variable between subjects.

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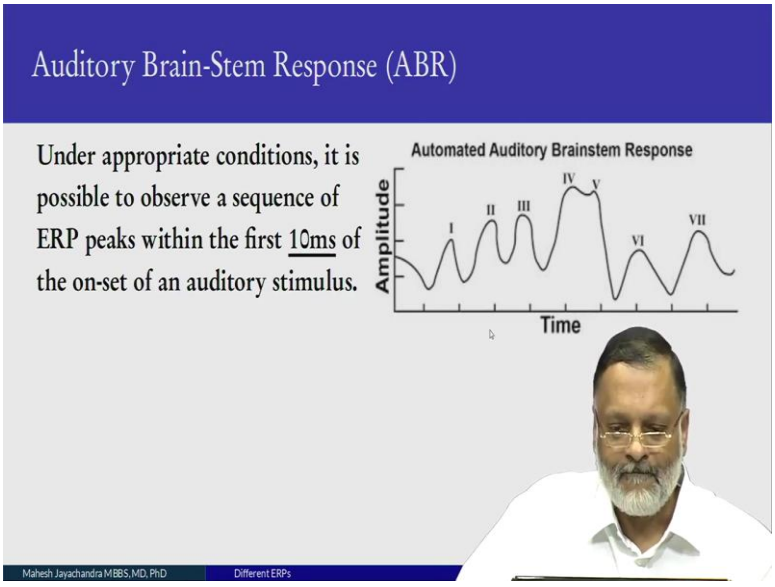

So, now let us look at the auditory brain stem response in detail. So, under appropriate conditions, it is possible to observe a sequence of ERP peaks within the first 10 milliseconds of an auditory stimulus. So, this is just 10 milliseconds and you have these following peaks,

1, 2, 3, 4, 5; 6, and 7 are a little difficult to record but this is the auditory brain stem response. And this is the basis of checking for hearing loss or auditory dysfunction in units.

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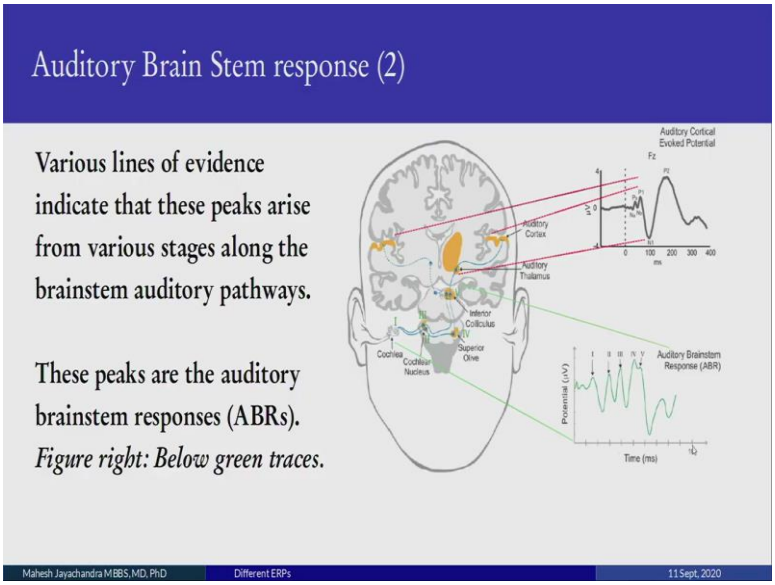

So, various lines of evidence indicate that these peaks arise from the various stages along the auditory pathway. So, you have a stimulus coming in here. First, you have the cochlea then you have the cochlea nucleus and you have something called the superior olive, then you have the inferior colliculus and then you have the auditory thalamus, the medial geniculate body, and then finally, the auditory cortex.

So, the response from the tympanic membrane, the eardrum to the brain stem, all these different way stations gives rise to these potentials. So, if there is a problem, one of these components would be delayed or even absent. And this is the auditory brainstem response and again it is between 0 and 10 milliseconds, the green traces.

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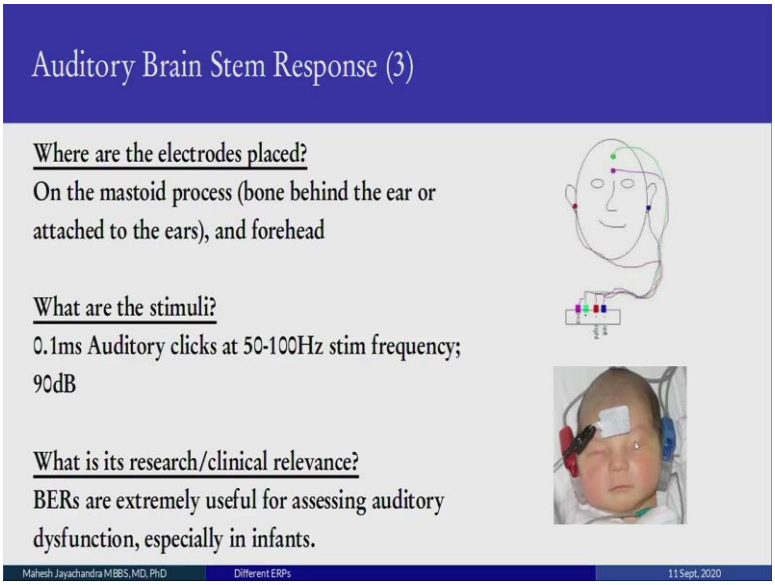

So, getting into a little more detail, where are the electrodes placed? So, below is the baby, you have usually three electrodes, one on the forehead, two on the behind the ears, the mastoid prominences, or the mastoid bone and then you have ground and a reference. And the stimuli are very different. Since it is 10 milliseconds, the stimuli are much shorter, it is 0.1 millisecond or 1 millisecond and they are clicks.

And they occur, we give them at 50 to 150 hertz, that is what come drrrrrr. Like that. But the brain can distinguish and do, I am, the cochlea and the brainstem can distinguish individual stimuli at that frequency and the frequent the amplitude is pretty high, 90 dB. This normal hearing, can cause damage to the ears but since the stimuli are so short, 0.1 milliseconds, it does not cause any damage.

And the clinical relevances, babies, many babies are born with the auditory dysfunction and for example, they have thyroid hormone dysfunction and if we find out that there is abnormal ABR and then we do the bloods of the baby and find out there is a problem with TSH, T3, T4, the thyroid hormone, then we can immediately add a thyroid supplement to the nutrition of the baby. And as simple as that.

If you do not do it and this continues for months then the baby has congenital deafness. And once it is deaf, then it is very difficult to treat it once it sets in. So, the sooner we catch it and we treat it and the baby is perfectly normal and has a perfectly normal life. So, that is why it is important. The second thing is you do not need any responses from the baby. It can sleep, does not matter. These responses occur even if the baby is asleep.

And also sometimes it is used in monitoring auditory function during surgery if you have a brain stem tumor. So, you cannot simply apply, monitor the ABR during surgery to make sure that no damage occurs to the brainstem pathways due to surgery.

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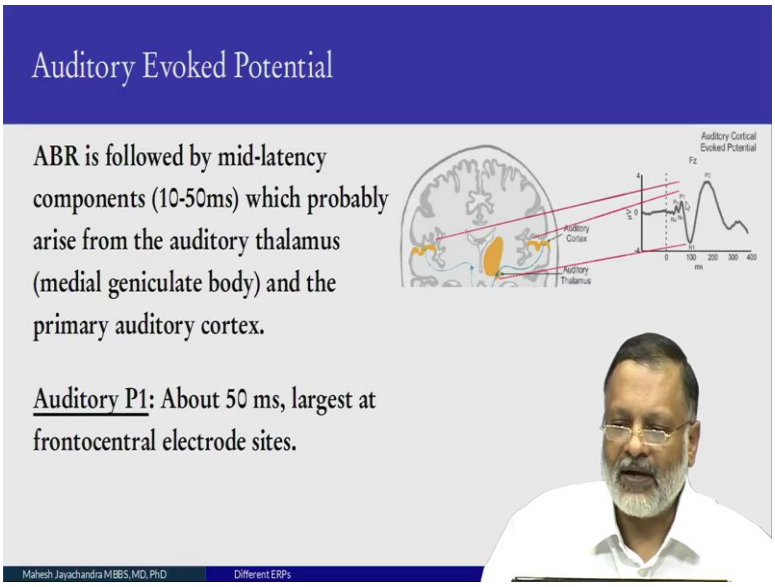

So, the ABR is followed by mid-latency potentials which probably arise from the auditory thalamus, the medial geniculate body, and just before the primary auditory cortex. So, over here just before P1 is the mid-latency potentials. These are mainly of research interest, have not seen too many applications of this in clinical neurophysiology. P1 is the largest potential after the mid-latency potentials. It occurs around about 50 to 60, 70, 80 milliseconds and it arises from the auditory, primary auditory cortex. And it is largest at frontocentral sites. So, this is a classic auditory evoked potential and you have the P1 and then you have the N1 and P2.

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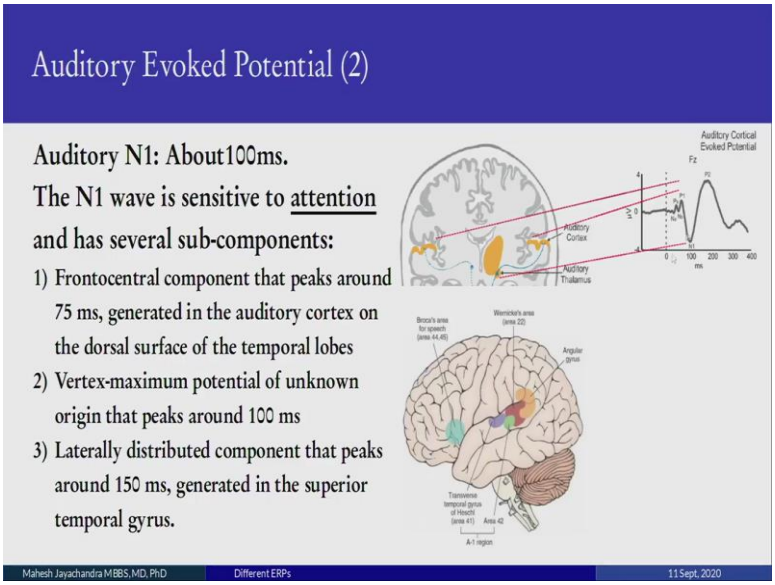

So, coming to the N1, so N1 occurs around 100 milliseconds and this peak has several subcomponents. So, one component is fronto-central, which is over here and it peaks at around about 75 milliseconds and is generated in the auditory cortex over here. This is approximately the auditory cortex. The primary auditory cortex is inside this hassles, this Sylvian fissure over here.

And the stuff on the outside is vernicase area and Broca's area and stuff. So, these are all parts of the auditory system. And following the fronto-central component at 75 milliseconds, you have vertex maximum potential that occurs on 100. And we do not know where this comes from. And then you have a laterally distributed component which peaks at around about 150 which is generated in the superior temporal gyrus, that is over here inside.

So, all these components, these 3 components merge and together they give the N1 which we record at the surface. So, there are 3 different components but you get only one peak.

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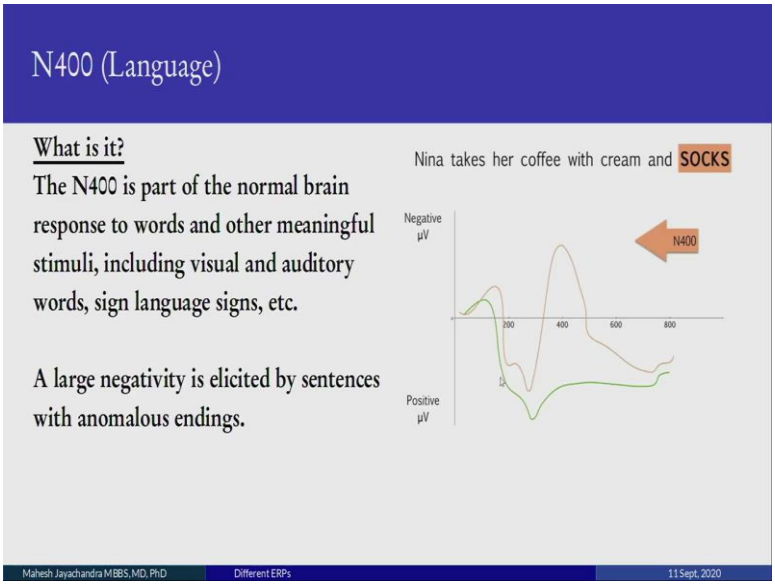

So, coming to N400. So, this is a negative potential at 400 milliseconds and it relates to language. So, the N400 is part of the normal brain response towards and other meaningful stimuli including visual and auditory words, sine language signs, etcetera. So, large negativity is elicited by sentences that have an anomalous, unexpected, or incongruous ending. For example, Nina takes coffee with cream and expects milk or sugar but you get SOCKS, so you have N400 potential over here. So it is negative up, this one.

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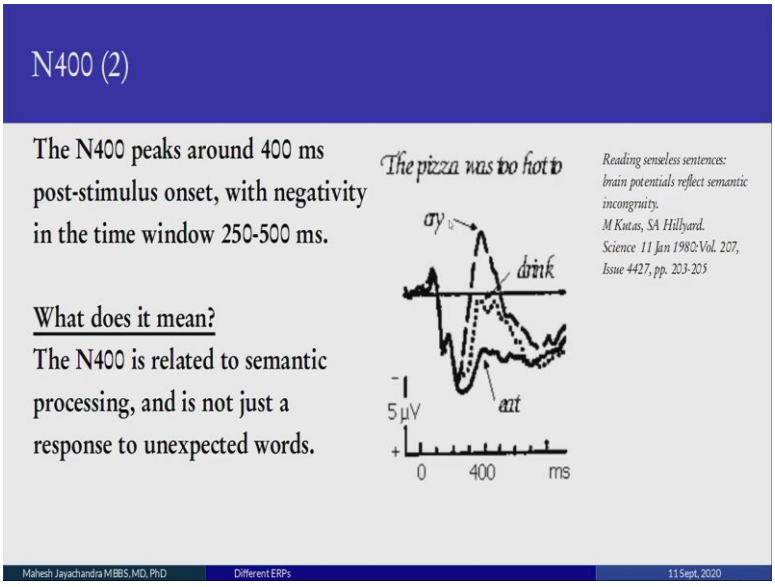

So, it peaks around 400 milliseconds after the stimulus and the negativity is in the time window of 250 to 500. So, what does it mean? It is related to semantic processing and is not just a response to unexpected words. So, this was the original N400 finding by Marta Kutas

and Steven Hillyard. They published it in Science in 1980 and you have 3 sentences; the pizza was too hot to eat, that is fine and negative up. The pizza was too hot to drink, which is a bit weird. So, you have this potential happening over here. And finally, the pizza was too hot to cry, which is completely unexpected. So, you have this N400.

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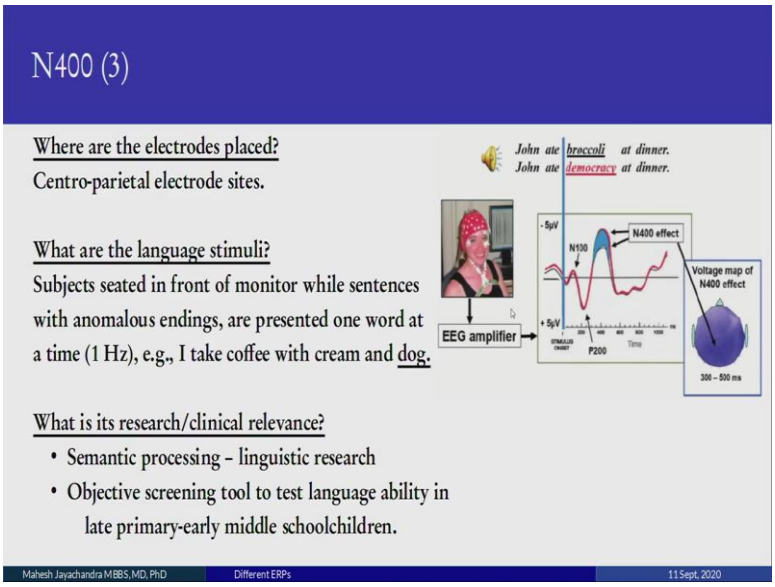

So, where are the electrodes placed for the N400? It is again centro-parietal areas. Centro-parietal areas. And the subject is seated in front of a monitor while sentences with anomalous endings are presented one word at a time, 1 hertz. I take coffee with cream and dough. So, the dough will give you the N400. And here on the right, you see the subject, she has got electrode cap with probably 64 electrodes and the different stimuli which are given, John ate broccoli at dinner and John at democracy at dinner.

So, democracy will give the N400. And here you see the N400 effect over here. And most of the action when you look at the heat map is the fronto-central parietal. This whole area is activated. So, what is use or clinical relevance? So, one is for linguistic research. You can use this as a probe for semantic processing and the other more practical thing is, would be it is an objective screening tool to test for language ability in late primary or early middle school children.

So, if they cannot distinguish between this incongruous or unexpected ending, then you know they have a problem and the teacher can give them extra attention or exercises. So thank you.