Introductory Neuroscience and Neuro-Instrumentation
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Lecture No. 24
Lecture 24: Different Event-Related Potentials-2

So, Introductory in Neuroscience and Neuro-Instrumentation: Different event-related potentials part 2.

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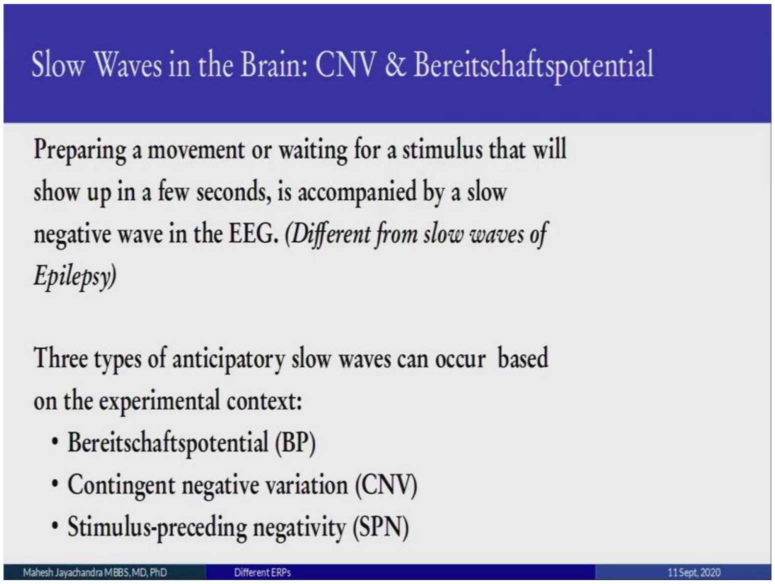

So, now we will consider slow waves in the brain, specifically the CNV, the contingent negative variation, and the bereitschaftspotential, also called the readiness potential. Slow waves mean DC shift. So, one point to note is if you are going to record slow waves, you have to change your filter settings so that it is DC to 100 hertz or 30 hertz or whatever. If you put it at 1 or 2 hertz, you will, to 30 hertz, which we normally do for other evoked potentials, you will miss the slow-wave. So, bear in mind that you have to record from DC to 30 hertz or 100 or 50 hertz, because the DC will allow you to record slow waves.

So, preparing a moment or waiting for a stimulus that will show up in a few seconds is accompanied by a slow wave in EEG. You also get slow waves in epilepsy and these are slightly different. This is pathology, pathological slow waves. We are talking here of normal slow waves. So, 3 types of anticipatory slow waves occur based on the experimental context. One is the bereitschaftspotential or the readiness potential. The other one is the contingent negative variation. And there is a stimulus preceding negativity. We will focus on the BP and the CNV.

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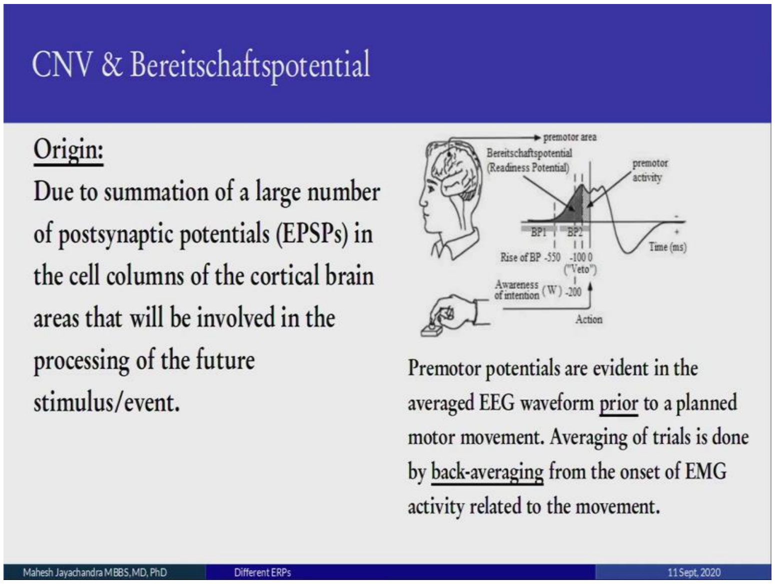

So, the bereitschaftspotential and the CNV are due to the summation of a large number of postsynaptic potentials, EPSPs in the cell columns of the cortical brain areas that will be involved in the processing of future stimuli or events. So, consider this schematic on the right. It is over the premotor area that is in front of the central sulcus of the motor area, in front of it you have the premotor area. So, the bereitschaftspotential experiment is very simple. You tell the subject to please press the key of the mouse, or joystick, or whatever whenever you feel like it. There is no stimulus.

The stimulus is from inside, from the person. So, it is called a self-willed key press. So, just before the person presses the key, you get the slow rise in negativity, negative up. And the initial part is called BP 1, bereitschaftspotential 1, or readiness potential 1. And it starts more than half a second before you press the key. You are only aware of the intention of pressing the key much later and then there is a sharp rise and that is BP 2, readiness potential 2 and after that, you have your keypress and then it goes down.

So, this whole complex is the bereitschaftspotential, this BP 1 and BP 2. So, this is fascinating because before you are aware of the intent to press, the brain already has started doing it.

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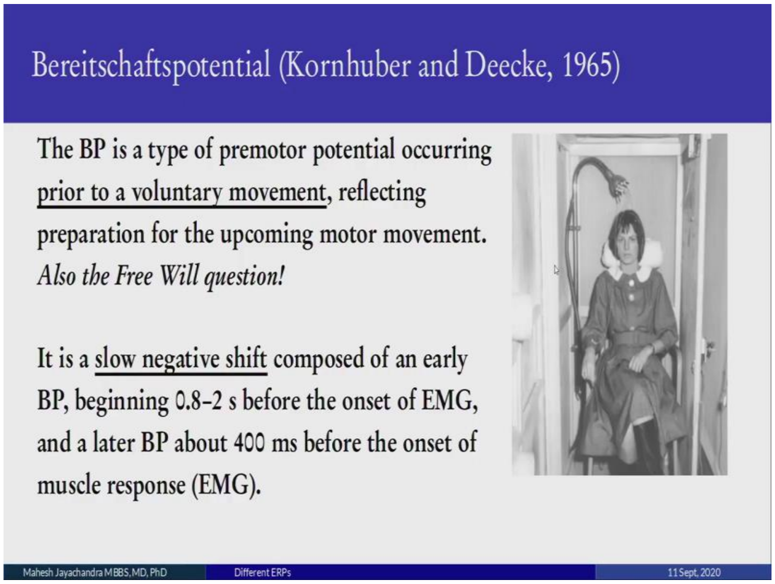

So, the question is, do you have Free-Will, because this was a huge philosophical question. If you are not aware of something, while in the brain this activity can be recorded, which means the brain starts doing its stuff before you intend to do something. I mean that is one possibility. So, this was a very big controversy or debating point and it still is. One of the problems with the bereitschaftspotential is it is a very delicate potential. It rises over here and you need DC recording amplifiers. And it is very very sensitive to any kind of artifacts, AC noise, and stuff.

So, this is one of the first experiments done in Austria, Germany and you see the subject. He is inside a faraday cage. So, the faraday cage is basically, it is a wooden frame and it is chicken mesh, copper mesh inside which is grounded. So, it prevents interference, any electrical interference from outside. So, it has to be, it can be recorded only with stringent recording conditions. It is not as easy to record as an auditory evoked potential or visual evoked potential.

And part of the difficulty in recording contributed to the controversies because some people could not find it and so forth. So, again, the bereitschaftspotential is a premotor potential occurring before voluntary movement and then reflects preparation for upcoming voluntary movement. So, it is a slow negative shift and there are two components. There is an early BP and then there is a late BP.

So, the Free Will question, do you have Free Will, or is there a green man inside your brain, things, has now come to rest, in this, because one of the things is our consciousness, the resolution of consciousness is in 100s of milliseconds. If you look at the P3 100, or even if you look at the MMN, it is the minimum time is 150 milliseconds, the P3 100 is supposed 300. So, our consciousness is not, does not have a resolution shorter than that. We cannot resolve things less than 100 milliseconds or 10 milliseconds.

So, it, it maybe a strawman, this whole Free Will question, it maybe that a resolution of our, when we are of consciousness is in chunks of 300 milliseconds. So, it is not such a big deal that this, it starts at half a second before the keypress.

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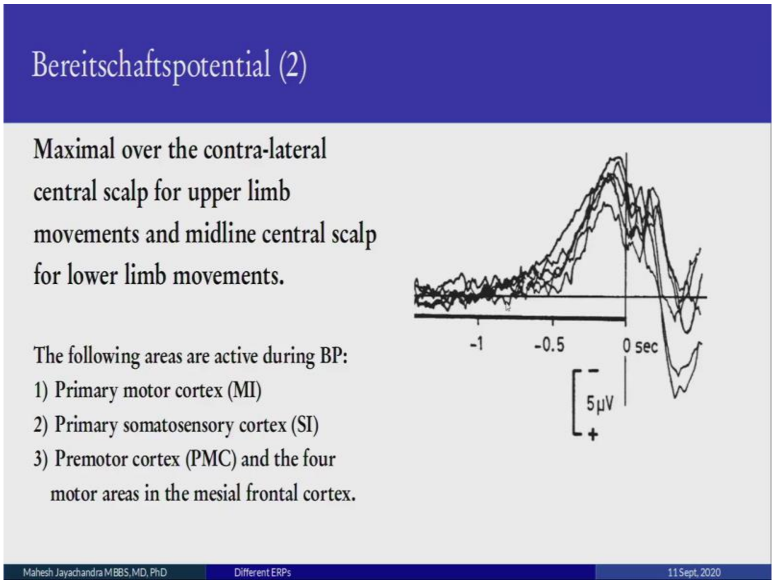

So, this is a classic bereitschaftspotential. You have individual, individual responses, very good recordings, there is no noise at all. And it is maximal over the opposite side of the scalp for upper limb movements. And comes in the midline for lower limb movements. That is because of the way the hand and the leg are represented on the opposite side of the brain. So, the following areas are activated during BP, one is the primary motor cortex, then the primary somatosensory cortex, which is on either side of the central sulcus, which you studied in macroscopic anatomy. And also the premotor cortex and 4 motor areas in the mesial frontal cortex which is in between, the hemispheres and it comes in between, so this area is in between.

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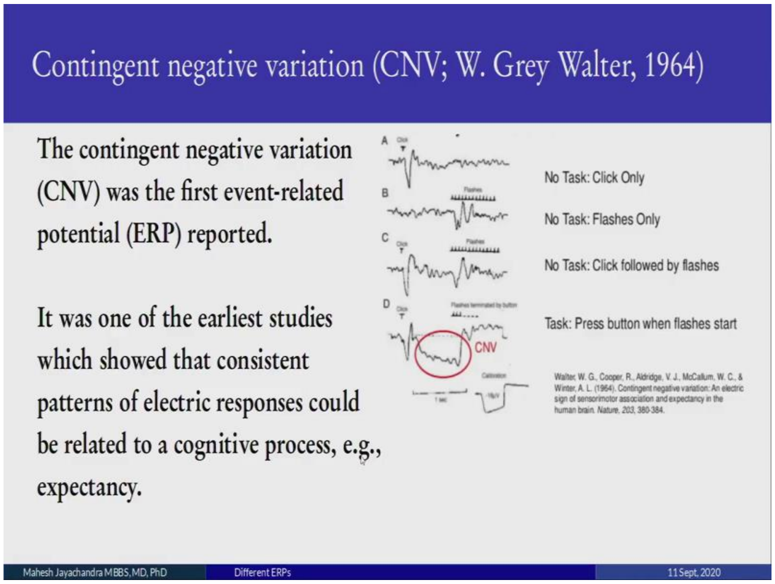

So, let us consider the contingent negative variation. So, this is very similar to the bereitschaftspotential. In the bereitschaftspotential, it is a self-willed key press. You press, press the key whenever you feel like. The contingent negative variation on the other hand, as you press it, it is contingent on a stimulus before. So typically the experiment is like this, you have one stimulus called S1, which could be a click or a tone or a flash of light, and after about 2 or 3 seconds, which this is to prepare you, after about 2 or 3 seconds, you have the second stimulus to which it could be anything, again a click or a tone or a flash, to which you like a keypress.

And between S1 and S2, you have this negativity. Here it is negative down, so it is kind of going down over here. But this is the contingent negative variation. And this was one of the earliest studies which showed a consistent pattern of electrical response related to a cognitive process. In this case, expectancy. It was also the first-ever event-related potential which was reported. Grey Walter is an American neurophysiologist who worked in England. And he was the person who found this potential.

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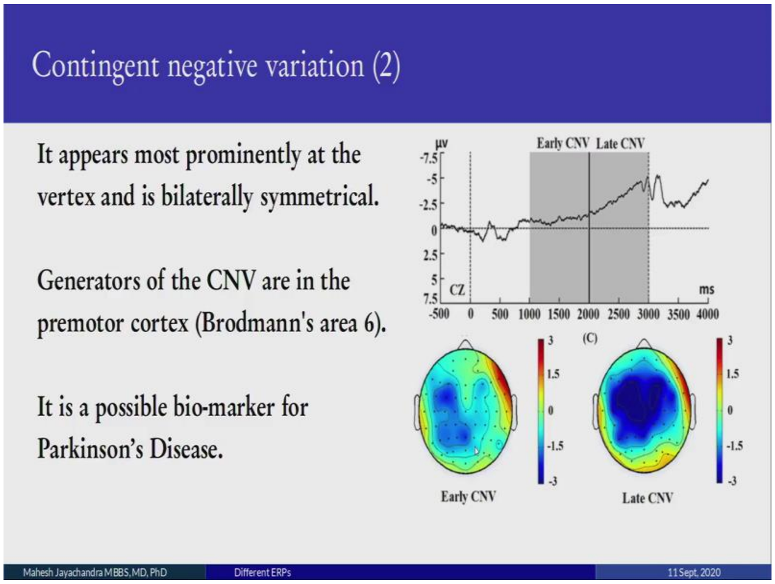

It is most prominent in the vertex and it is symmetrical on both sides. And again, there are, it can be divided into two parts, an early contingent negative variation, and a late CNV. So, the early CNV has a heat mapped distribution, like so. And the late contingent negative variation has a heat mapped distribution, like so. So, the generators as I mentioned are in the premotor cortex, a Brodmann's area 6. And also some of these areas which are activated during the bereitscaftspotential are supposed to be involved in the contingent, in the generation of the CNV.

So, the thing about the CNV is, it could be a possible biomarker for Parkinson's disease. Now Parkinson's disease is basically, there is a symptom called start hesitation. You tell a person to start walking, they take some time. Once they are walking, you tell them to stop, they take some time, they cannot stop immediately like they have a starting problem. So, these are classic symptoms of Parkinson's disease, it is a disease affecting the motor system.

And here, you have a stimulus S1 and you have to get ready and then you have to press the button at S2, and there would be a delay in Parkinson's patients or it would be abnormal the CNV thing. So, it could be used as a biomarker for Parkinson's disease.

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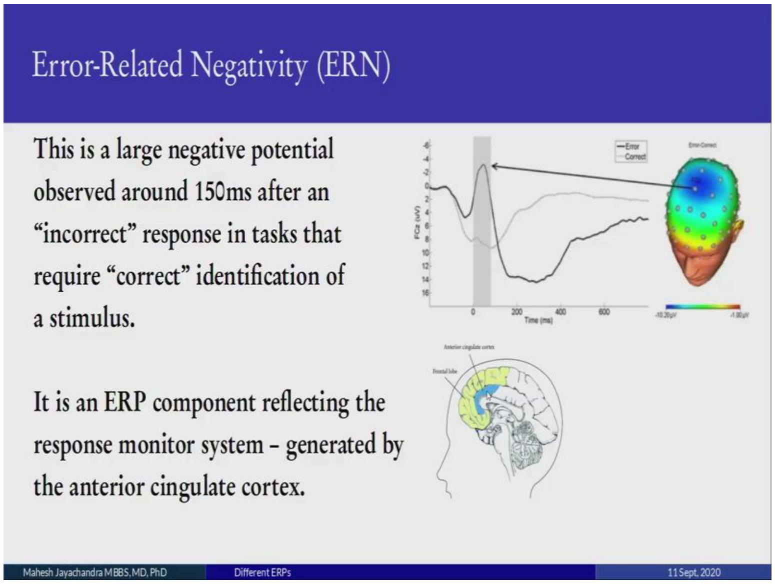

So, coming to another potential, called error-related negativity. One thing to bear in mind with the contingent negative variation, the BP, and all the cognitive potentials is that they are all uniformly across the board, depressed in disorders of higher mental function, for example, schizophrenia, or bipolar disorders. So, these are very sensitive indicators of dysfunction, but they are not specific. So, you have to bear that in mind.

So, coming to error-related negativity. Consider a task, you have to make a correct response to a task, it could be anything, count the number of dots on the screen for example. Now, if you make a mistake, you get a response called the ERM, the error-related negativity, which comes about a 150 milliseconds after the mistake. And it is a component that is supposed to arise from the anterior cingulate cortex. This is looking at the hemisphere, the right hemisphere with the left hemisphere removed, looking at it from the left side.

And this is the area, the anterior cingulate cortex. The anterior cingulate cortex is a much-storied cortical area, some neuroscientists feel that one of the seeds of conscious as it were, is in the anterior cingulate. So this ERN, is an ERP component reflecting the response monitor system and it tells you whether you made a mistake or not, so you can imagine, it is useful to know that you have made a mistake.

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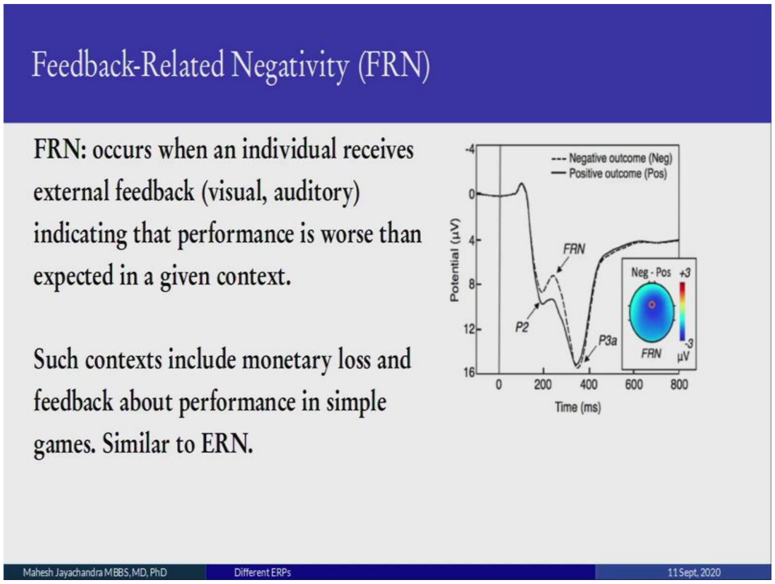

A very similar potential related to ERN is the FRN, which is feedback-related negativity. This occurs when an individual receives external feedback, it could be either visual or auditory indicating that the performance is worst than expected. So for example, consider a simple gambling task. So, you have to gamble and you have two responses. And if you choose one, you will always get a reward. You choose another, you may or may not get a reward. But when you do get a reward, it is huge.

Like for example, the first time you choose the response, the lower the reward condition, you get 10 rupees. The second time, the second condition is, and you get it 95 percent of the time, 10 rupees always, when you choose, you get 10 rupees. When we choose the other option, you get a (100), a 1000 rupees, but very rarely, you do not get it always. So this, what you get is the index for this is the feedback-related negativity and it occurs around between 150 to 300 milliseconds.

So, on this graph on the right, you see a negative outcome which is shown by the dotted line. And the positive outcome, which is shown by the solid line. So, the negative outcome between 150 to 250 is the feedback-related negativity. So, it comes as indicated in paradigms which include monetary loss, feedback about performance in simple games etcetera and it is very similar to the earlier error-related negativity. And you like at the heat map on top, it is front centro parietal distribution.

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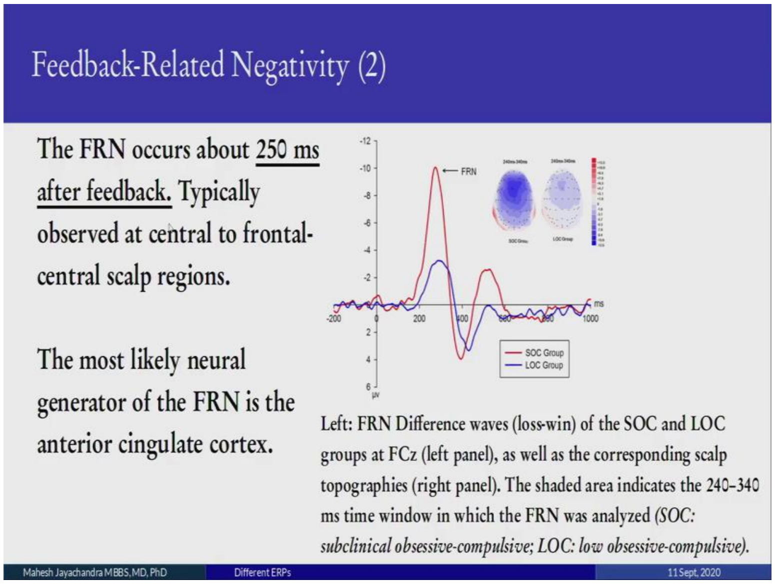

So, typically it occurs 250 milliseconds after feedback, and as I mentioned, this is the central frontal areas. And again the generator most probably is the anterior cingulated cortex. So, difficult to figure this out because it is deep. So, you have to do source modeling, which we will talk about in our next lectures. So, consider the data on the right. So, you have FRN differences loss-win in two kinds of patients. The one patient is, one set of patients were obsessive-compulsive, had obsessive-compulsive disorders.

And the other set were normal. So, the obsessive-compulsive disorder, SOC group is in red. And the normal or the lower obsessive-compulsive is in blue. And you see the obsessive, OCDs, they have a huge FRN. They, their brain reacts majorly to loss. So again, these things, these kinds of potentials could be used, not only to screen obsessive-compulsive disorders but also to see if therapy, they get various drugs, to see if therapy makes a difference.

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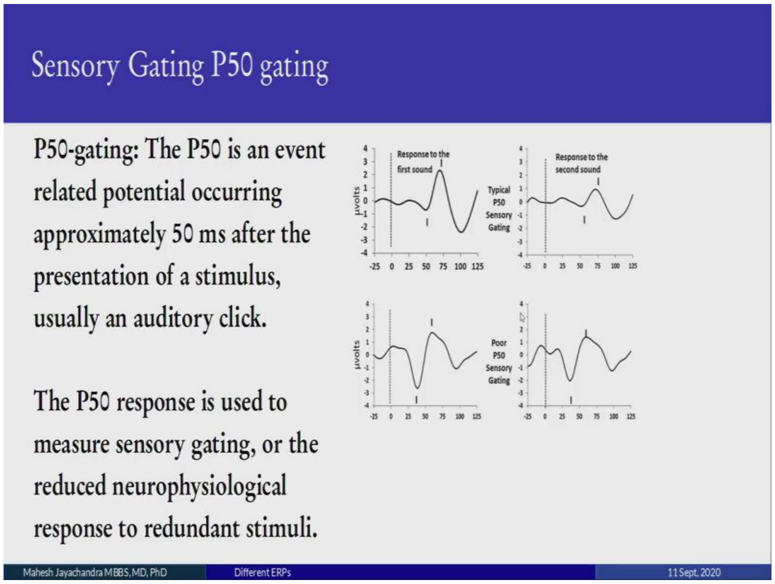

Coming to another potential, and now this potential is very interesting, it is present at birth, it is called P50-gating. So, consider two clicks, click-click. And there is a huge response to the first click. But the response to the second click is kind of muted because there is a little bit of habituation or whatever goes on. So, the P50 event occurs approximately 50 milliseconds after the presentation of a stimulus, usually to click. So, you have one P50 and then you look at the P50 to the next second thing and so, here on top, on the right, you see the response to the first sound.

And you see the response to the second sound, it is being gated or it is being filtered. Now when you have poor gating, the first response is not so big, but the second response is neither small. So, typically, you see this in disorders of higher mental function like schizophrenia. And this has an evolutionary significance that for, you cannot have the same kind of response to redundant stimuli.

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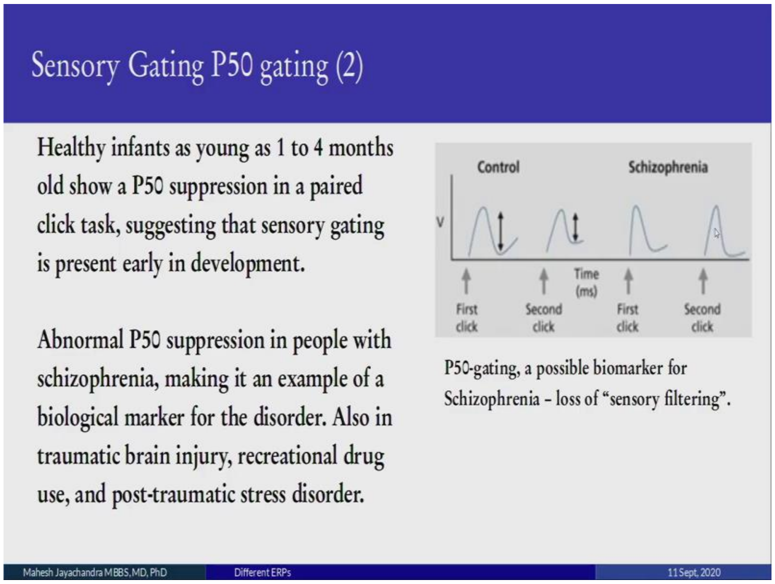

So, in schizophrenia, consider these data over here. You have the controls. This is the first click, the amplitude of the P50-gated, the auditory response for a P50-gating. And then you have the second click and it is smaller. But in schizophrenia, the first one is this big, and the second one is also this big. So, it means that schizophrenics have difficulty in controlling the input of stimuli, so if I am talking to you in hopes you are paying attention to me. But there are a lot of stimuli in your environment, in your crustic space, a schizophrenic will pay attention to everything.

He or she cannot gate and so there is a barrage of sound always, or a sensory input coming to this schizophrenic. And the other interesting thing is healthy infants show this response even when they are between 1 and 4 months, even when they are very young and this shows that sensory gating is present early in development. And the other places where P50 gating can be abnormal is in traumatic brain injury, recreational drug use, and post-traumatic stress disorder like veterans, army veterans, have these problems, they cannot filter stimuli.

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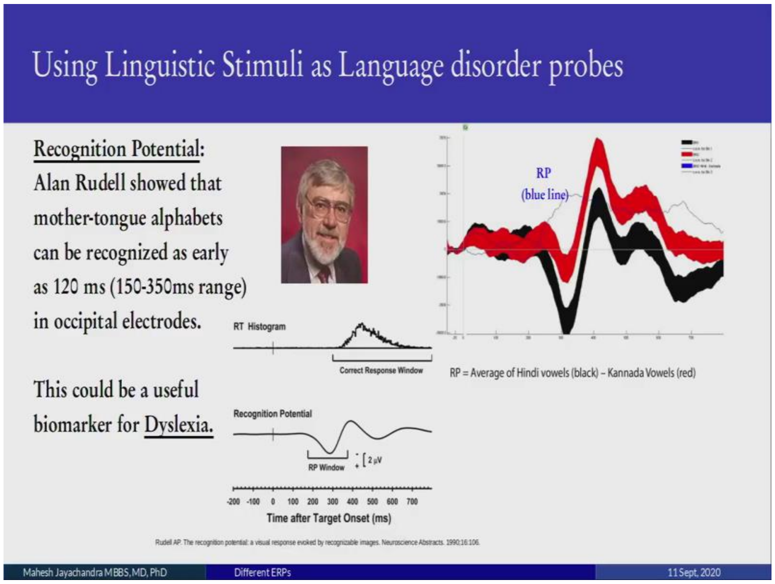

And we considered early on in a previous lecture using linguistic stimuli as language disorder probes where we did LPC, monitoring late positive complex P1 and 1P to monitoring in tribal children in Chhattisgarh. Another way to use this is the, using recognition potential which is discovered by Professor Alan Rudell in Suni Brooklyn, one of my mentors. And he showed that mother tongue alphabets can be recognized as early as 120 milliseconds, in the range of 150 to 300, but as early as 120 milliseconds in occipital electrodes behind.

So, this could be useful as a biomarker for dyslexia. So, if you see over here, this is Alan. You see the RP, RP is reaction time, where you have to respond if you guess correctly and it is useful, it is useful to decrease the signal to noise ratio in the data by using only the correct responses and this is the recognition potential. And this is the negative up, and this is the recognition potential window. You only get it with your mother tongue, or with a language, you are very familiar with.

Suppose I flash here Chinese vowels to an Indian child, there will not be any RP. So, we did some pilot experiments in Saint Johns were to a Hindi speaking subject, we showed Hindi vowels and Kannada vowels. I am, to a Kannada speaking subject, we showed Hindi vowels and Kannada vowels. So, the black trace is the response to Hindi. And the thickness of the trace indicates the standard deviation response. Likewise for the Kannada, which is red. If you subtract both of them, you get the RP, which is the thin blue line.

So, you can also use it in an Indian context with Indian alphabets, the vowels, the consonants, and the conjuncts, and you would get the RP. So again, this would be useful in an Indian context because many Indian children learn English late, but they learn their mother tongue first. And we could use their mother tongue to see the screen if they have dyslexia or not. And you might say, what do you do if you find a child has dyslexia? It is pretty easy to reverse. You give them computer games and with feedback and you train them. And within about three weeks, it makes a difference. So they learn, their responses are good. And they get their RPs for their mother tongue.

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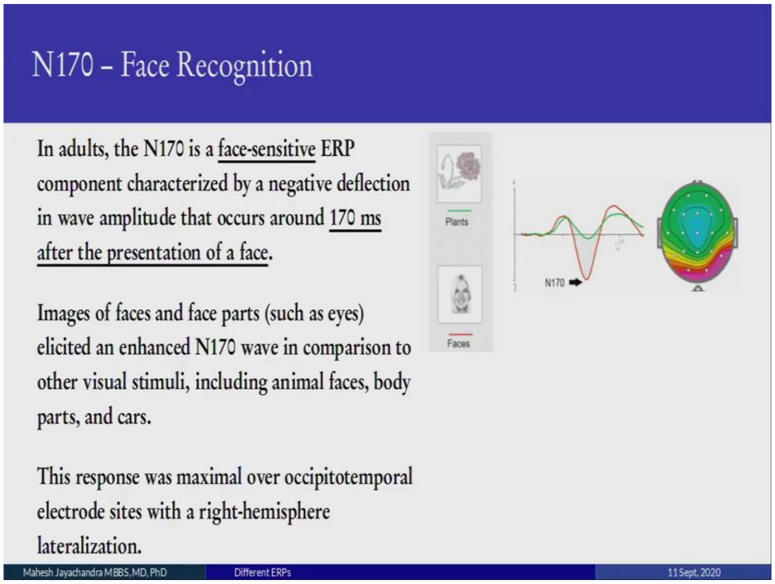

So, one more N170 is for face recognition. So, typically on the right side, the right occiput, there is a face recognition area and this is a face-sensitive event-related potential. It is characterized by a negative deflection at around about 170 milliseconds and this is it. And images or faces or even face parts, which is eyes, elicit and enhance N170 in comparison to other visual stimuli like animal faces or body parts or cars or buses. So, this is very specific to the face and eyes, and it is maximum over the occipital temporal area and more on the right side than the left side. So, here on the right, you see a typical N170 experiment.

So, the green trace is stimuli that are not face related, like plants etcetera. The red is the face, face stimuli and you can see a huge response. And this is the heat map on top showing that most of the activity is in the back and specifically on the right side. So, much of this work was done by a very good French scientist, Stanislas Dehaene and for those who are interested more, I encourage you to go on and check him out on Pubmed. So thank you, that ends our lectures on event-related potentials.