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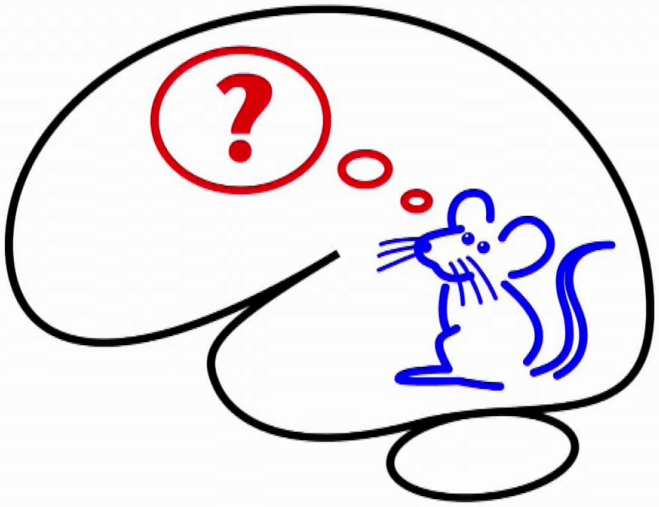
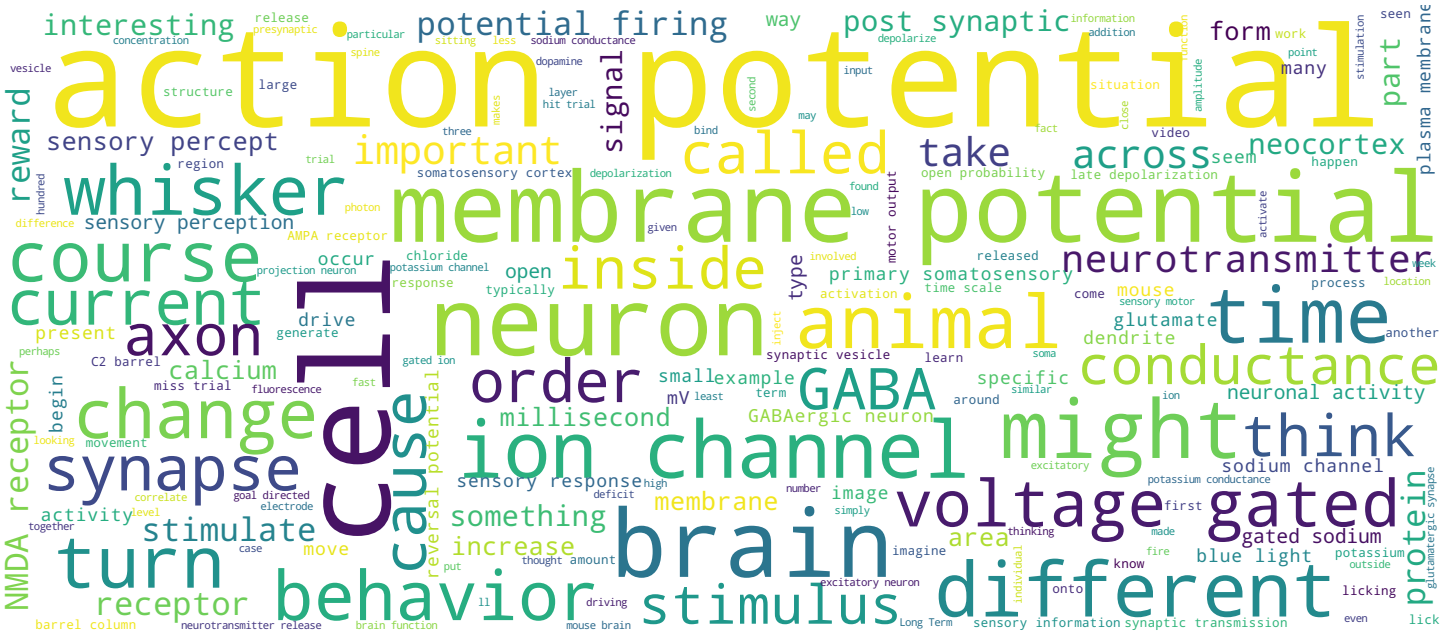


7.2 Sensory perception

Cellular Mechanisms of Brain Function

Prof. Carl Petersen



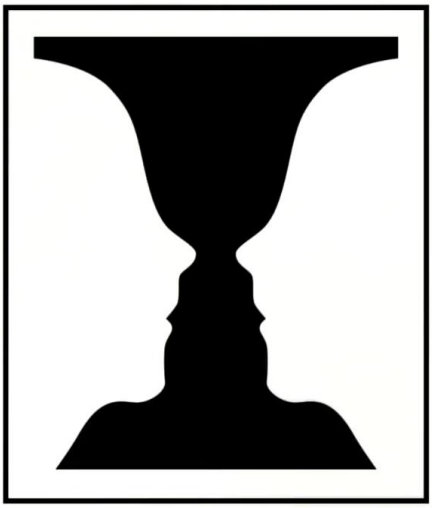
Search MOOC

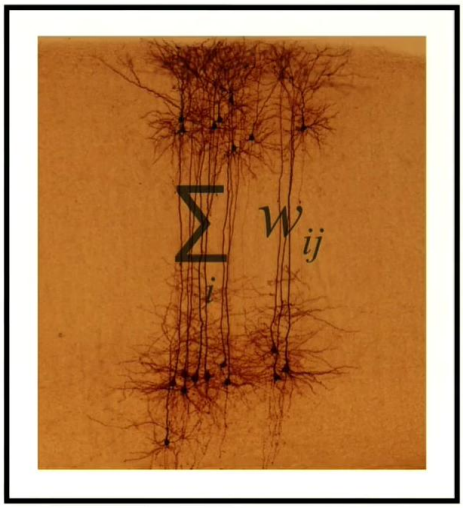
Video

EPFL

Sensory percepts are subjective

Sensory percepts are internal contructs, created by neuronal activity.





Lefort, Tomm, Sarria & Petersen, 2009

Cellular Mechanisms of Brain Function

When we first think about sensory perception, it seems trivial. We look at the world around us, and we see objects. We listen and we hear sounds. We sniff, and we smell fragrances. And it all fits together in one unified world view: our perceived reality. However, when we start thinking about the underlying neuronal mechanisms, it turns out that we're only just beginning to get our first clues as to how sensory perception works. Sensory perception is an active process in at least two different ways. Firstly, motor control is very important for sensory perception. We actively gather sensory information. And that's what we discussed in the last video. We make eye movements and head movements to see specific parts of the visual field. And we move our hands and fingers to touch objects, actively get tactile sensory information. It turns out that sensory perception is active in another way of thinking also, in which our neuronal activity actively generates our sensory percepts. That sensory percepts are subjective, can easily be seen by looking at images like this that evoke bistable percepts. We have one set of photons that fall upon the retina, but if you stare at this image for long enough, you'll see two alternating percepts.

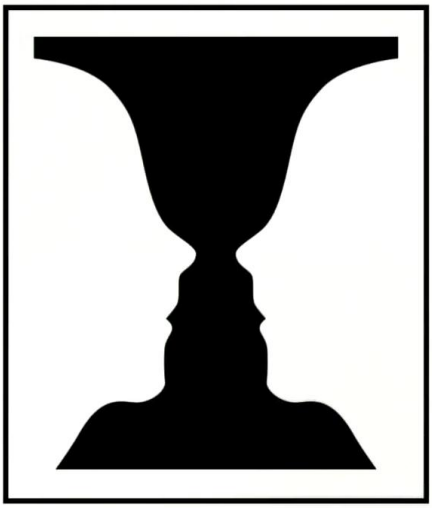
Notes

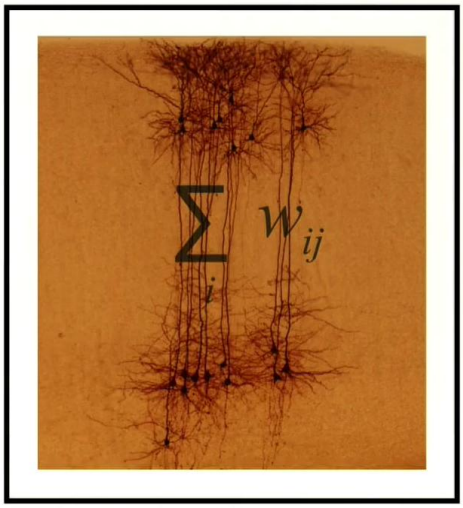
Summary

0m 05s

Sensory percepts are subjective

Sensory percepts are internal contructs, created by neuronal activity.





Lefort, Tomm, Sarria & Petersen, 2009

Cellular Mechanisms of Brain Function

Either you see the two white faces looking at each other, with their noses almost touching, or you see the black cup in the middle. And it's one set of light that falls on the retina, but the brain generates two distinct percepts from it. Clearly, sensory percepts are internal constructs that are generated by neuronal activity. And right now, neuroscientists think that it's largely the activity of neurons in the neocortex that generate our sensory percepts. And so for that causal and mechanistic insight into how sensory percepts occur, we need to look at the activity of individual nerve cells and how they talk to each other, perhaps with a particular focus upon what's going on in the neocortex.

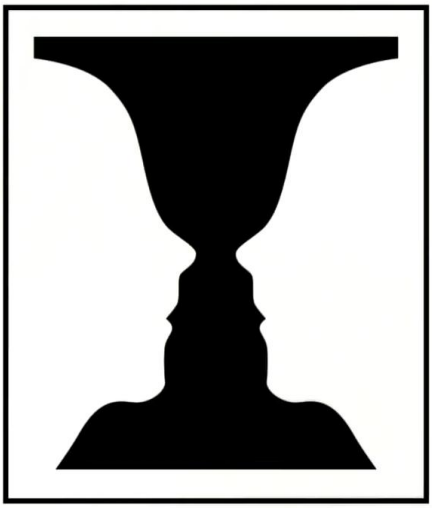
Notes

Summary

1m 39s

Sensory percepts are learned

Sensory percepts are learned through experience.



We can recognise objects because we have previously seen closely-related images.

We learn to see the world.

Cellular Mechanisms of Brain Function

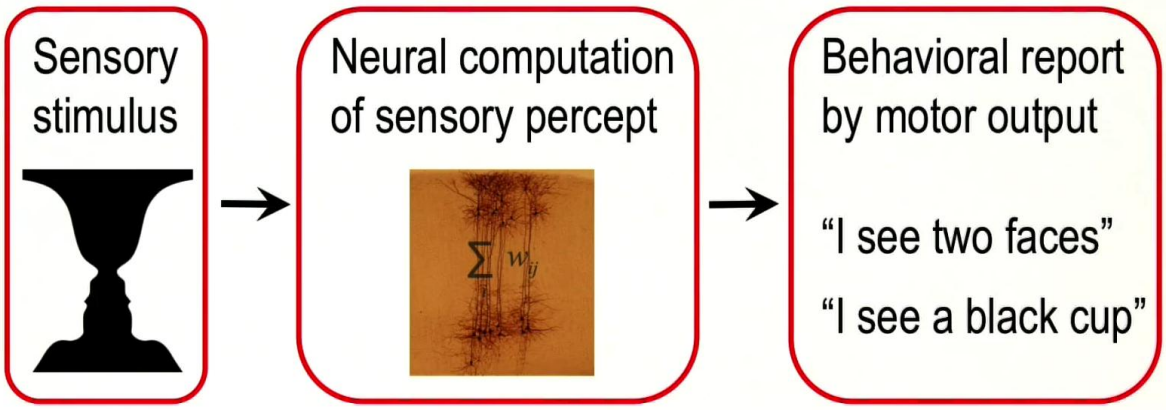
So sensory percepts are not just out there in the world, but they're actively generated by the internal activity of our brain. Sensory percepts are also learned through experience. And it's because we've seen many silhouettes before, that we recognize this as a silhouette of a human. And so the reason we recognize objects is because we've seen many closely related images before, images of faces and people from many different angles. And our brain has managed to extract the appropriate statistics that associate that information. And so, as we are all aware of from watching young babies, we don't immediately know how to perceive the world, but we learn to see the world around us. And the same is true of course, for all of our other sensory inputs.

Notes

Summary

2m 25s

Experimental investigation of sensory perception



Sensory percepts must be reported through motor output to allow experimental investigation. Learned abstract sensorimotor transforms are therefore minimal essential core features of sensory perception.

Cellular Mechanisms of Brain Function

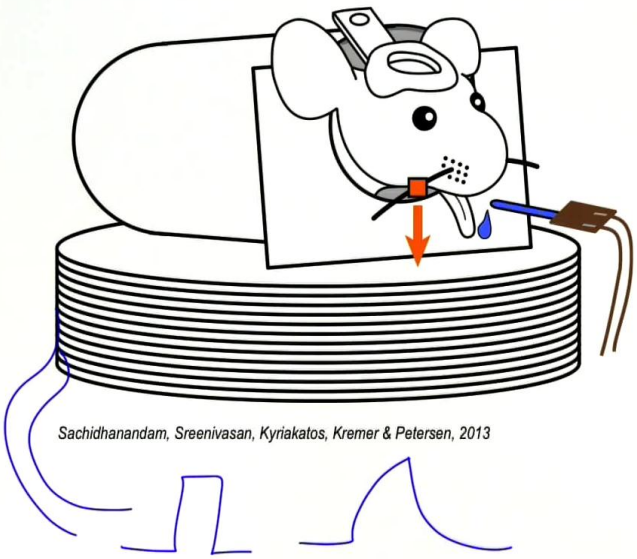
So how are we going to investigate subjective, learned, sensory percepts? Well, we clearly need to be able to deliver well controlled sensory stiumuli. That's then going to evoke neuronal computations inside the brain. And those are going to depend upon context, learning, and also the goals of the particular moment. And if we're going to experimentally investigate the subjective percept, then we also need the subject to report what it is that it's feeling. And so we need to have a motor output where behavior reports the subject to percept. And so if this were a human psychophysics experiment, we would have two buttons. One that the human observer would push if he sees two faces, and another button if he sees the black cup. And he would then be pushing in alternation these two buttons as a percept flickered from one to the other. And so, an important concept in terms of experimental investigation, is that sensory percepts must be reported through motor ouput. And we might consider this, all together, as a learned, goal-directed, sensory motor transformation. And that then, might represent the minimal, essential core feature of sensory perception, that it has to form a learned, perhaps relatively abstract sensory motor transform.

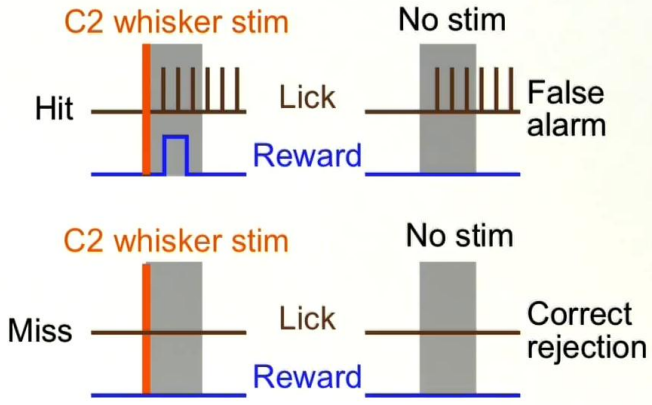
Notes

Summary

3m 20s

Whisker detection task





Cellular Mechanisms of Brain Function

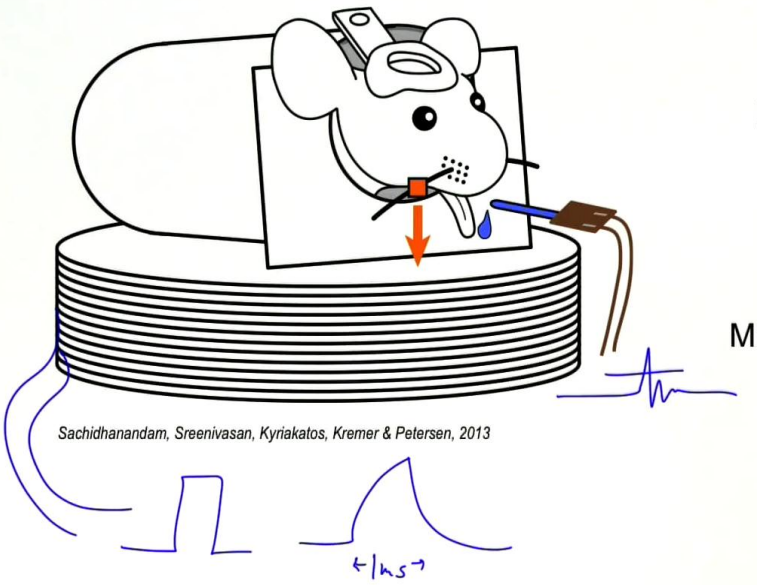
Now, sensory perception is rather complicated, and it might be a good idea to start with very simple forms of sensory perception, if we want to get to the detailed, mechanistic and causal insight into how it actually works. The simplest form of sensory perception is detection. Simply to say, is there a stimulus or not? And that's what we're going to investigate here, in the whisker sensory system. We implant metal head holders onto the head of mice, so we can head-restrain them, make recording chambers that allows us to do electro-geological and imaging experiments at high resolution. The animal sits inside a cardboard roll where it feels relatively comfortable, and in addition, we have a plate here in front that restrains the movement of its forepaw, so it can't for example, scratch its nose. Onto the whisker we place a small piece of metal. And the whole animal site on top of a electromagnetic coil. We can then drive current pulses through that electromagnetic coil that generates magnetic fields, and those magnetic fields, act upon the metal particle and cause a force to be applied. And we can make these magnetic pulses relatively short, about one millisecond in duration, and so a one millisecond impulse is applied to the whisker, and that occurs at a random time.

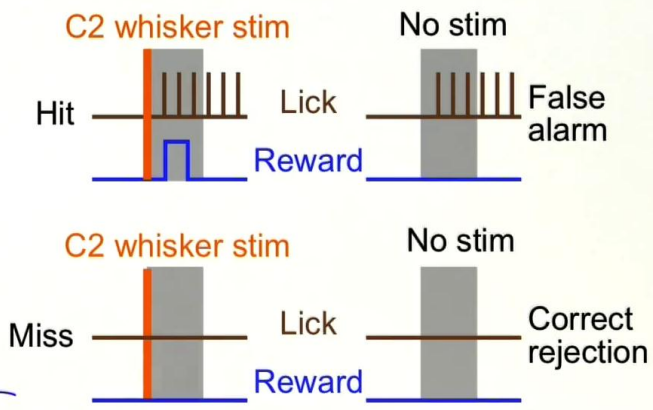
Notes

Summary

4m 50s

Whisker detection task





Cellular Mechanisms of Brain Function

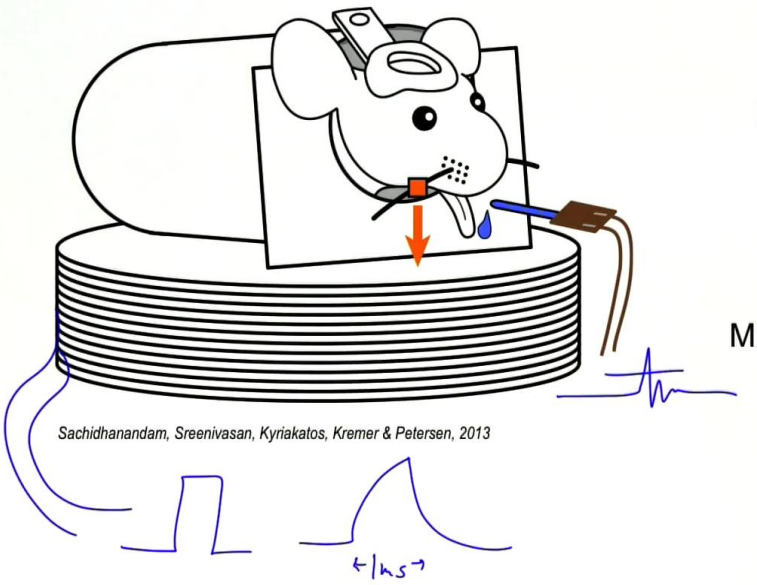
The animal has no cue to tell us when that stimulus is coming. So the animal is waiting, waiting, waiting, and every now and then, there's a brief one millisecond pulse on the whisker, and what the animal has to learn in this behavior, is that that one millisecond whisker stimulus means that reward is available from this licking spout. And if it licks immediately after the whisker stimulation, then it gets a droplet of liquid reward. And we monitor the tongue contacting the spout here through so called piezo film, that then gives us a little electrical signal when the tongue touches the spout. And we can threshold that, and use that to open a valve and deliver liquid water. And so for the trials in which we stimulate, there are two different outcomes. If the animal licks during the reward window, which we set at one second, then we open the valve and the animal gets a reward. On other trials, we give the same stimulus but the animal fails to lick. And this is then a miss trial and of course, there's no reward that's delivered. And so as the first indicator, we can quantify performance as a so called hit rate-- the fraction of trials where the animal licks, compared to the total number of trials where we deliver a stimulus.

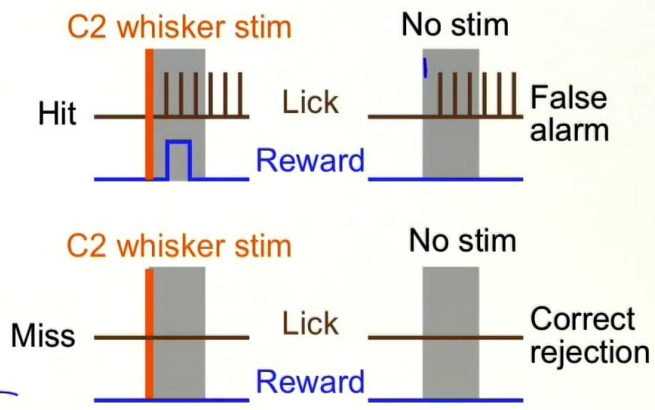
Notes

Summary

6m 18s

Whisker detection task





Cellular Mechanisms of Brain Function

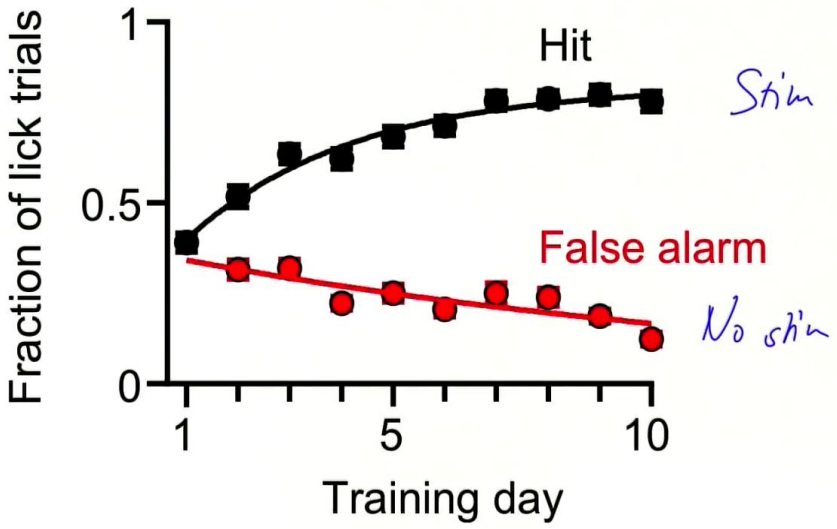
We can also look at another trial type where we don't stimulate, and sometimes the animal will spontaneously lick. We can think of those as false alarm trials. And these might also be very interesting to analyze. Perhaps the animal is dreaming of a whisker stimulus being delivered. And something in the neuronal activity then makes it lick. And we can think of other trials where we don't stimulate-- the animal doesn't lick, and those are then correct projection trials.

Notes

Summary

7m 42s

Learning



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

Cellular Mechanisms of Brain Function

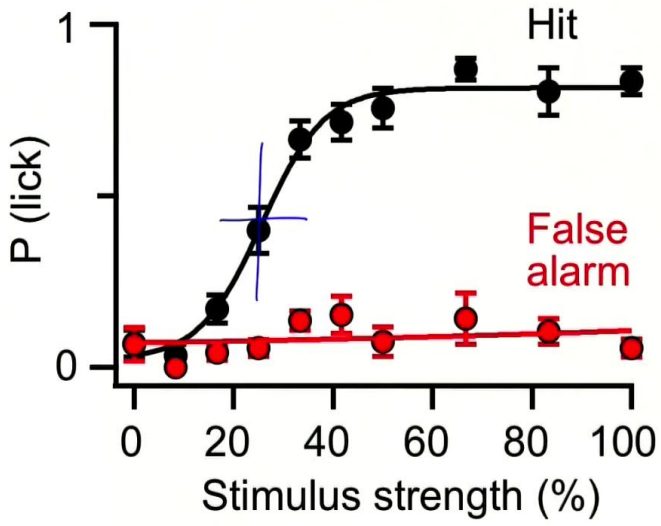
On the first day, when the animal goes into the behavioral apparatus, the animal knows that licking is a good thing, that it sometimes gets reward when it licks, but it doesn't know when. It has no idea that the whisker stimulation is a cue to initiate licking, and that when there's no stimulation, there's no reward that's going to happen. And so it licks just as much on stimulation trials, as on no stimulation trials. Through trial and error and reward-based learning, the animal learns that licking after a stimulus is a good thing, and it begins to pick up something like 70 to 80 percent of the trials in which we stimulate, and licks in response to that stimulus. It also learns that when there's no stimulation, there's no point in licking. And so it learns to suppress the licking in the absence of a stimulus. And it 's really the divergence of these two curves, that tells us that the animal has learned the behavior.

Notes

Summary

8m 10s

Psychophysics



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

Cellular Mechanisms of Brain Function

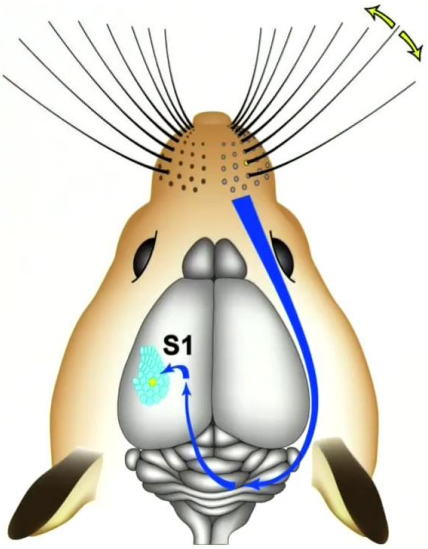
We can also look at the psychophysics of this behavior where we plot the stimulus strength against performance of the animal. And as we turn the stimulus strength down, the fractional trials in which the animal perceives a stimulus and gives a motor output in licking, goes down. And somewhere here, we're at about half way in performance, and that's a so called psychophysical threshold. As we decrease the stimulus even further, there's no licking above the false alarm rate, and so here the stimulus is undetectable. And so this s a standard psychometric function for any given behavior.

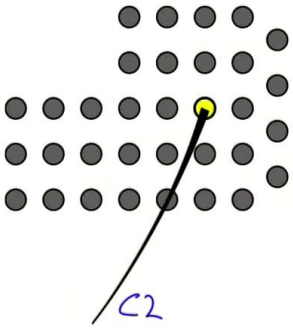
Notes

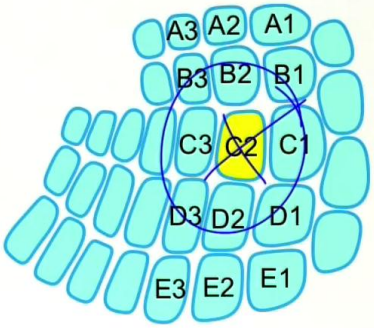
Summary

9m 10s

Primary somatosensory barrel cortex - S1







Cellular Mechanisms of Brain Function

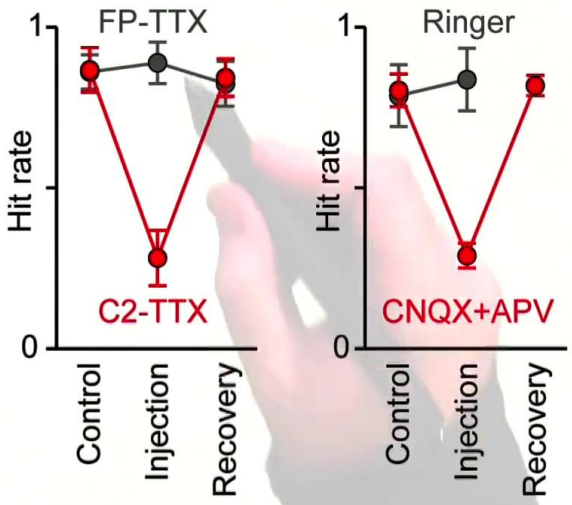
Now, we're interested in the neurobiology of this behavior. What's the neuronal activity that causally drives this learned, goal-directed sensory motor transformation? We've already looked a bit at the sensory pathway where whisker deflection causes depolarization of sensory nerve terminals, and action potential firing down the trigeminal nerve, information crosses the glutamatergic synapses in the brain stem, and action potential takes information to the thalamus, and other glutamatergic synapse then brings the thalamocortical action potential to the neocortex in the primary somatosensory cortex. And then in the primary somatosensory cortex, we have this exquisite one-to-one mapping of the sensory periphery where each whisker is individually represented in an anatomical unit, a so called barrel. And so if we put sensory information here on the C2 whisker, we might then expect that if the neocortex is involved, that the C2 barrel column might be a key area for where this behavior might depend upon. So we can test that by inactivating this part of the brain, and see if that makes any impact upon behavioral performance.

Notes

Summary

9m 50s

S1 is necessary for detection task



Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

Cellular Mechanisms of Brain Function

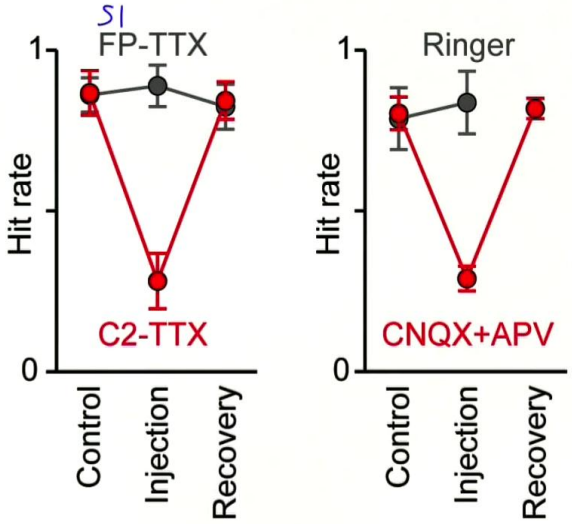
So here we have the animal sitting in the behavioral apparatus, it's performing the task, it's picking up something like 80 percent of the stimuli, and licking in response to them, and at sometime we inject tetrodotoxin into the C2 barrel column of the mouse barrel cortex. And that causes a dramatic and rapid decrement in behavioral performance. TTX is a block of voltage-gated sodium channels. It prevents action potential firing. And so here we've blocked action potential firing, in the primary somatosensory cortex, and that's caused a deficit in behavior. So apparently, action potential firing in the C2 barrel column, is essential in order to perform this task. We can inject other agents like CNQX and APV to block ampa and NMDA receptors. And we see that there's a similar deficit in performance. And so apparently, glutamatergic synaptic transmission, is also essential to carry out this behavior. As control experiments, we can inject the ring of solution that dissolves these agents and that has no impact. Or we can inject the tetrodotoxin toxin into another brain area here, into the primary somatosensory forepaw representation about a millimeter or so away from the C2 barrel column.

Notes

Summary

11m 03s

S1 is necessary for detection task



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Cellular Mechanisms of Brain Function

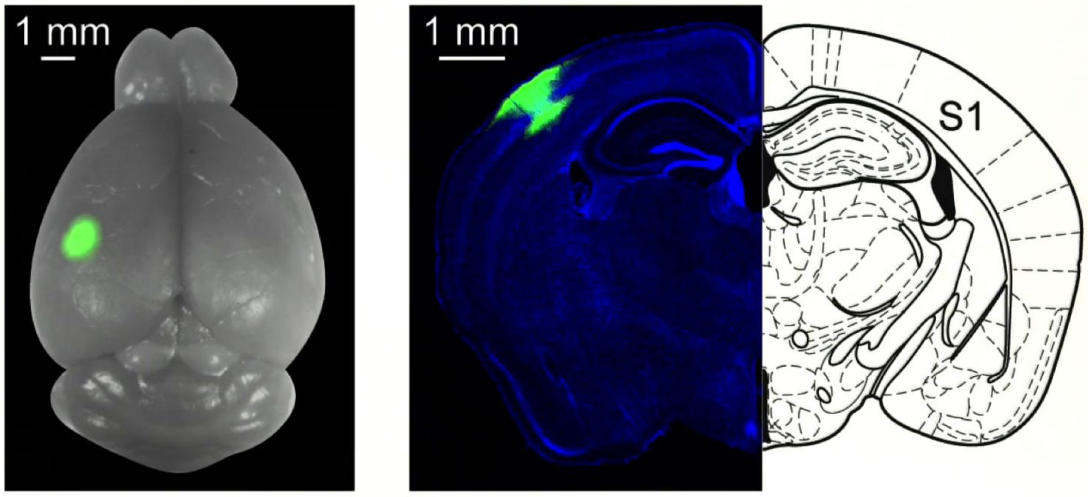
And that also doesn't cause a deficit. So there's some degree of specificity to these pharmacological inactivations. And it seems that action potential firing and glutamatergic synaptic transmission are necessary in order to perform the detection task.

Notes

Summary

12m 19s

Optogenetic substitution for whisker stimulus



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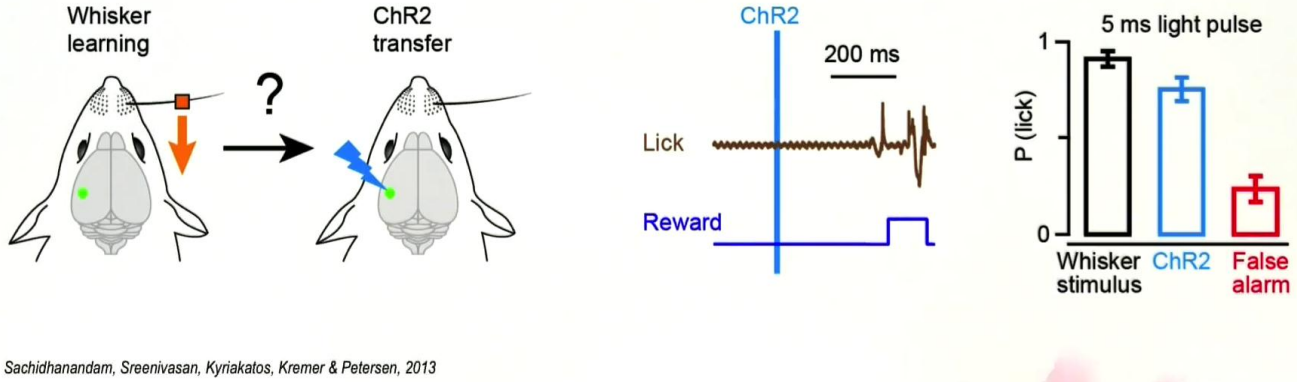
We can then see what happens in the other direction. Can we substitute the whisker stimulation by directly stimulating this area of the brain? And we can do that by expressing channelrhodopsin through injection of viruses that expressed channelrhodopsin here, coupled with a fluorescent protein, so we can see where the area of the brain that's been injected. Here you see it in post-mortem sections, and there's a small localized area of the brain that expresses channelrhodopsin, and that of course corresponds to the C2 barrel column. And here through mass genetics, we've expressed the channelrhodopsin specifically in excitatory neurons.

Notes

Summary

12m 35s

Optogenetic substitution for whisker stimulus



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Cellular Mechanisms of Brain Function

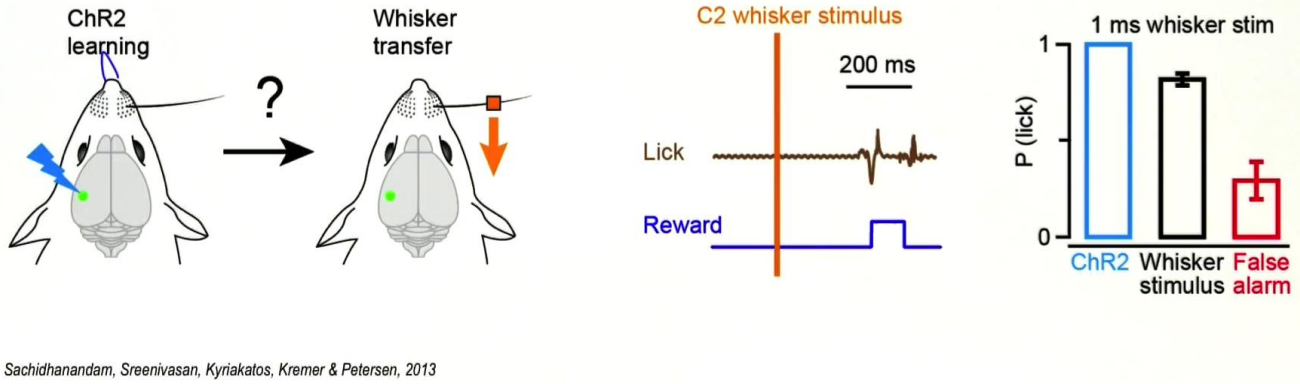
After injection of the virus, it takes a few weeks before the channelrhodopsin expresses. And during that time, we can train the animal, in the standard whisker learning tasks. And so here the animal never sees blue light flashes and we just train it exactly as before, we stimulate the whisker, and the animal learns to lick in response. Then, once the animal performs this task at a high rate, then on a given transfer test day, we ask if we now-- instead of stimulating the whisker, we now make an optigenetics stimulation of cortex, what happens? Does the animal interpret that stimulus as the same as a whisker stimulation? Does it perceive the same? Does that generate the licking motor output? And remarkably, in most of the animals in which we tested, the very first, five millisecond blue light flash drove licking behavior. Here's the light flash. Here's what we're seeing on the piezo trace-- the animal's tongue contacts the spout, Here we open the valve and the animal is now enjoying its reward. This turned out to be a robust phenomenon, where we could replace the sensory peripheral stimulus of whisker with a light stimulation directed at the neocortex.

Notes

Summary

13m 14s

Optogenetic programming of behavior



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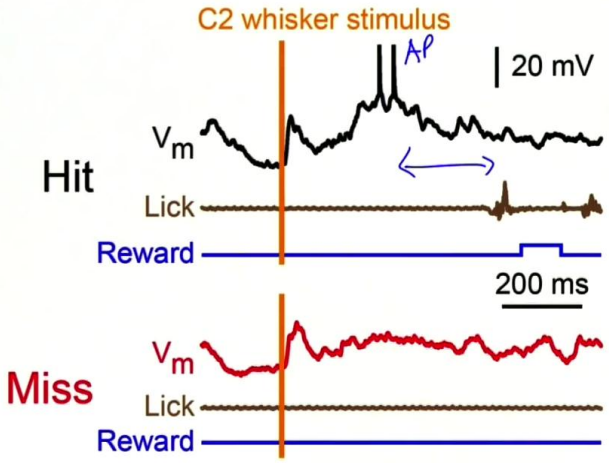
And so we can directly replace sensory stimuli at the periphery by internal stimulation of neurons in the neocortex. We can also examine the learning in the opposite direction. We can train animals first, in the optigenetic detection task, where we now deliver five millisecond blue light flashes to stimulate excitatory neurons in the S1 cortex, the animal learns to lick in response to the S1 stimulation, and after the animals learns that, we then give the very first whisker stimuli. And we then ask, does the animal now interpret that stimulus in the same way, and transform that into a goal-directed, licking motor output? And again, the answer is "yes". We stimulate the whisker, the animal licks, and the replacement from optigenetics stimulation to a real peripheral stimulation is extremely good. And so it seems we can optigenetically program the behavior from S1 cortex. And so these data then tell us that activity in S1 cortex is both necessary and sufficient in order to generate the perception of a whisker stimulus that then gets transformed presumably by downstream brain areas, into a licking motor ouput in order to obtain a reward.

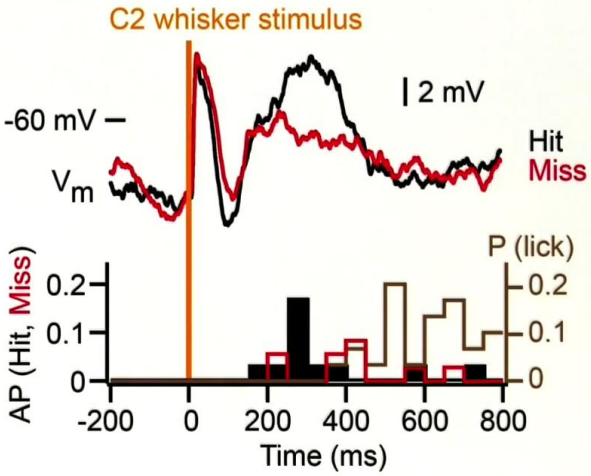
Notes

Summary

14m 28s

Membrane potential correlates of perception





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Cellular Mechanisms of Brain Function

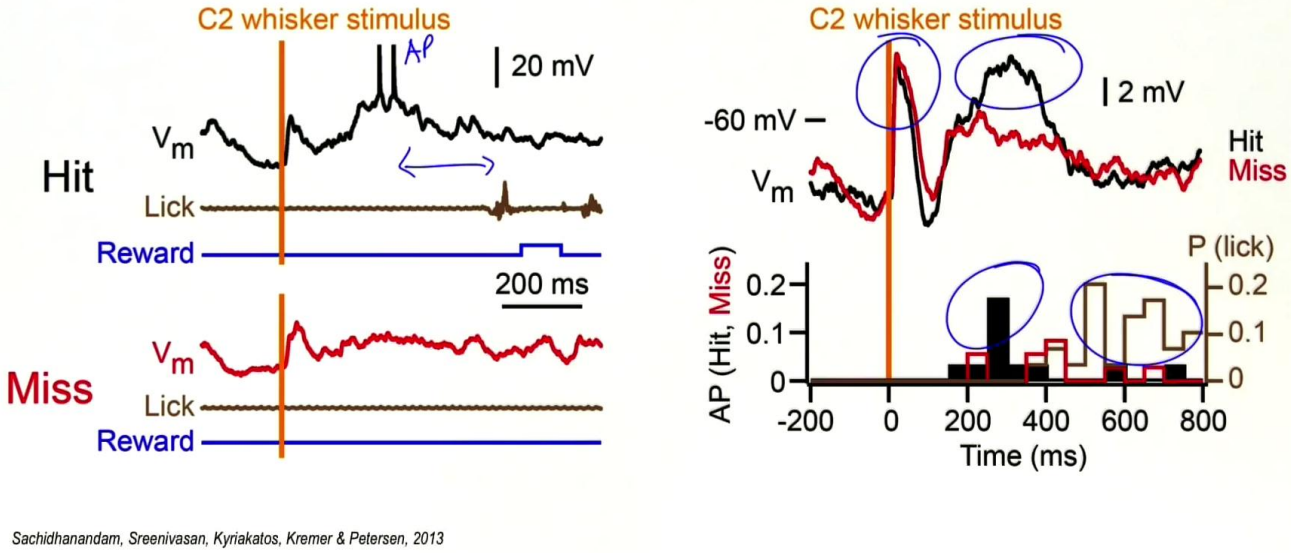
It's therefore clearly interesting to find out what types of neuronal activity are taking place in the C2 barrel column during task execution. And here we're making membrane potential recordings from layer two, three parameter neurons in the C2 barrel column. We stimulate the whisker, and this upper trace is from a hit trial, the animal licks, it gets a reward, and so by definition, this is a hit trial. If we now look at the membrane potential trace, shortly after stimulation we see there is a depolarizing sensory response that is presumably the sensory response driven by the feet forward thalamocortical circuits then at a later time, there's a late depolarization here, with a couple of action potentials riding on top of it, and that late depolarization, nonetheless precedes licking by hundreds of milliseconds. And so there could be a causal relationship between late depolarization and driving the licking motor output. Down below we see a miss trial. We give the same identical stimulus, it drives a depolarizing sensory response, but the late component here seems to be less obvious, and of course, there's no licking and no reward. It's a miss trial. These are just two individual trials.

Notes

Summary

15m 46s

Membrane potential correlates of perception



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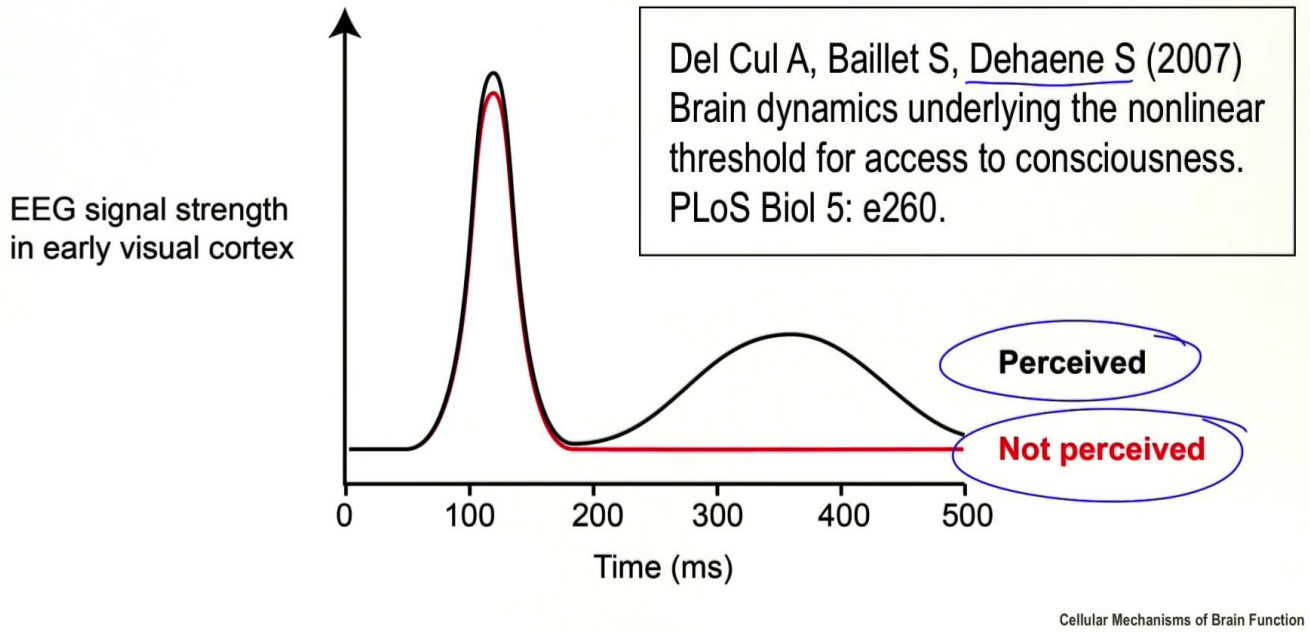
But they turn out to be representative of the average trials for this particular recording. And so here we take all the hit trials together and average them into the black trace. We take all the miss trials, average them together into the red trace, and here at time and stimulus, you see that both hit and miss trials generate large, obvious sensory responses, and there's no obvious difference between the hit and the miss trial. So there's a early, reliable sensory response And that's probably a good thing when primary somatosensory cortex and so you'd expect there to be a good, reliable representation of the periphery. At later times these two traces diverge, with depolarization being more prominent on hit trials than miss trials. And that's accompanied by enhanced action potential firing on hit trials compared to miss trials, and all of that precedes the licking by some hundredths of milliseconds. So here in this late component of activity we have something that correlates with the subject of percept of the animal, as reported by licking.

Notes

Summary

17m 06s

Correlates of perception in humans



Cellular Mechanisms of Brain Function

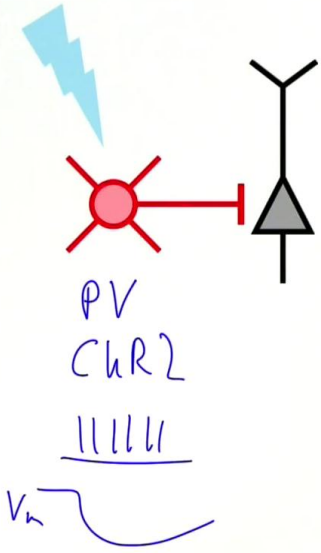
We think that late depolarization, correlating with subjective percept, is interesting, because similar results have been found in humans. And so here in the work of Stanislas Dehaene and coworkers, he has made measurements of the human EEG signal across early visual cortex, and have given visual stimuli that are just at around the threshold for conscience perception. And so some trials are perceived, and that's indicated by the black trace, and other trials are not perceived, and that's represented as a red trace. And what Stanislas Dehaene and his colleagues suggest, is that there's an early, reliable, sensory response in the visual cortex, and that there are late changes to activity in the human brain that correlate with consciously perceived, or not perceived, stimulii. And so it looks like similar might be happening in the human brain, compared to what we've seen in the mouse.

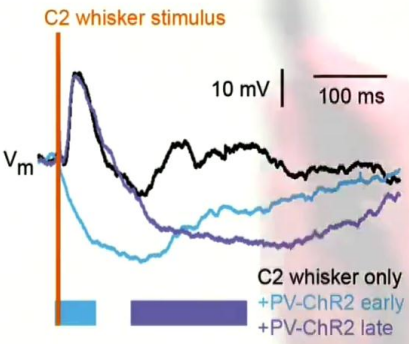
Notes

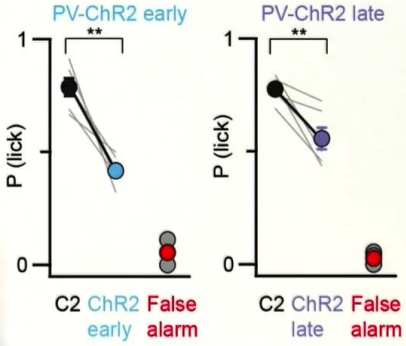
Summary

18m 12s

Late depolarisation contributes to perception







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Cellular Mechanisms of Brain Function

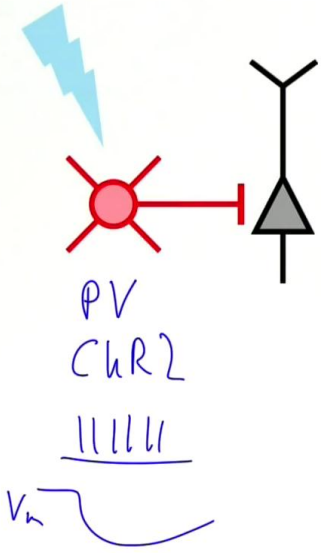
Now, what's difficult in the human situation, is to get a causal perspective on what this late activity might be doing. And that's something that we can do in the mouse system. And so what we need to do then, is specifically inactivate late periods of activtity. And we can do that by using channelrhodopsin optigenetics, and stimulating the GABAergic inhibitory neurons. And so here we take the parvalbumin expressing GABAergic neurons that you might remember are the ones that inhibit perasematically. We put channelrhodopsin specifically inside those neurons using mouse genetics, we can then get blue light flashes and then we can stimulate action potential firing here in the parvalbumin expressing GABAergic neuron. That's going to then release GABA, hyperpolarize the post synaptic cells, the excitatory parameter neurons and then we'll then get a hyperpolarization in the membrane potential of these excitatory neurons. And so we'll be able to shut down primary somatosensory cortex by shining blue light on GABAergic neurons expressing channelrhodopsin. So let's have a look at that in the situation of our experiments.

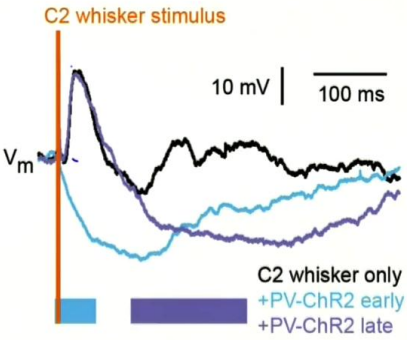
Notes

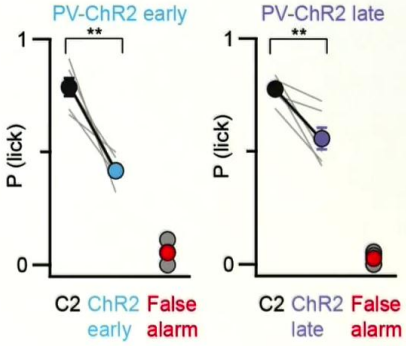
Summary

19m 15s

Late depolarisation contributes to perception







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Cellular Mechanisms of Brain Function

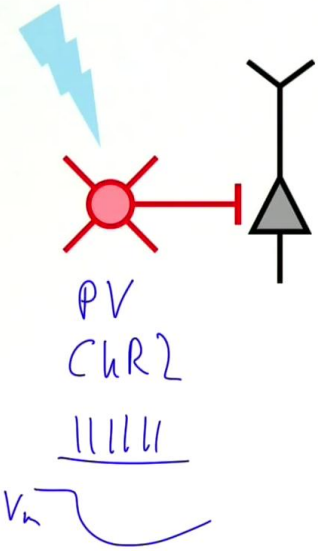
Here's our C2 whisker deflection, here's our sensory response, the black curve is a normal control condition, and if we now turn the blue light on, immediately around the time of stimulation, we get this light blue curve here, we get rid of the early sensory response So now we shut down S1, just at the time where sensory processing of the stimulus occurs, and when we look at the behavioral performance, that causes a deficit in the detection of the sensory stimulus. And so that's really very similar to what we found with the pharmacological inactivation experiments where we injected TTX or [sinqx] and APV into S1 cortex, and found that caused a deficit in detection performance. Here we see the same thing except now, we've done the inactivation on this time scale of 50 milleseconds and so we know that it's a neuronal activity immediately surrounding whisker stimulus that drives sensory perception. The question that we were really interested in, is what happens if we leave that early sensory response in tact, and we only hyperpolarize at late times. And that's what you see in this purple trace. We turn the blue light on, we stimulate the channelrhodopsin, after a hundred milliseconds that causes hyperpolarization at late times, leaving the early sensory response in tact.

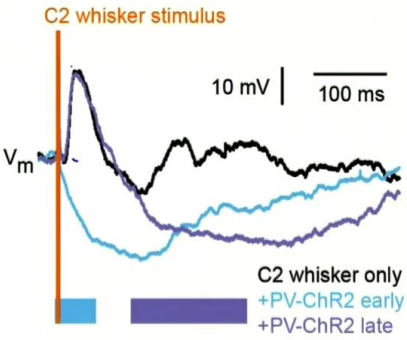
Notes

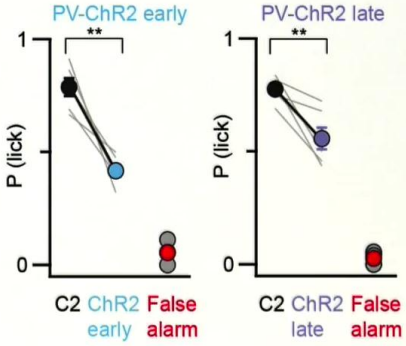
Summary

20m 25s

Late depolarisation contributes to perception







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Cellular Mechanisms of Brain Function

And the question now is, if we just get rid of the late depolarization does that make any difference in behavior? And indeed, it does. It causes a significant deficit in detection. And so that late depolarization not only correlates with the subjective percept of the animal, but it also contributes to driving that sensory percept. And so we're slowly beginning to understand mechanistically, the types of neuronal activity that occur in the mouse brain during subjective sensory percepts.

Notes

Summary

21m 44s

Cellular mechanisms of sensory perception

- Head-restrained mice can be trained to perform simple perceptual tasks, allowing detailed investigation of the underlying goal-directed sensorimotor transformation.
- In a whisker detection task, an early sensory response in S1 reliably encodes stimulus, and a late component codes subjective percept.

Cellular Mechanisms of Brain Function

In this video we've seen that head-restrained mice can be trained to perform simple, perceptual tasks. And over the coming years, we'll get a detailed and mechanistic understanding of how simple, sensory motor loops are performed. In the case of the detection task, we've seen that there appear to be two phases to the sensory processing. An early, reliable response, and a late depolarizatoin that seems to correlate with the subjective percept. In the years to come, it will be important to understand the mechanisms that generate that late depolarization. And also the learning mechanisms that are involved in tying together the sensory input, with the goal-directed motor output. In the next video we'll begin to examine the basis of the learning process.

Notes

Summary

22m 16s