Module:
Biological Foundations of Mental Health

Week 4
Biological basis of learning, memory and cognition

Topic 3
The effects of activity, experience and deprivation on the nervous system
– Part 3 of 5

Dr Sam Cooke
Lecturer in Neurobiology of Neurodevelopmental Disorders, Basic and Clinical Neuroscience, King's College London

Slide 3:
Now, let's consider a very different event in the postnatal development of the nervous system, that nevertheless requires Hebbian synaptic plasticity. This is the integration of inputs on to shared post-synaptic targets, to create more complex receptive fields. For this purpose, we're going to focus on the postnatal development of binocular vision. As we shall see, this process requires visual experience.

Slide 4:
The important starting point for this section is to take into consideration that after the eyes open, visual stimuli will start to evoke activity in the retinae. This activity is very different from the spontaneous activity occurring during retinal waves for the simple reason that it is highly correlated across the two eyes. Thus, activation of neurons in the visual system will start to reflect the statistics of the environment, and this activity will be shared across the segregated zones.

Slide 5:
We'll now focus on one aspect of the very famous work developed by Canadian neuroscientist, David Hubel and Swedish neuroscientist, Torsten Wiesel, who won the Nobel Prize for their ground-breaking work together at Harvard, in the US, on the development of receptive fields in the visual system. One aspect of the work that they conducted was in coming to understand how neurons in the brain could take on binocular representations that are required for such important faculties as depth perception.

Slide 6:
They worked in carnivore and primate species, which all have excellent binocular vision, unlike some prey species such as mice and deer. This is accounted for by their front-facing eyes, which allows both eyes to serve a match of the same extent of the visual field. One of the species of choice was the cat – the visual system of which is, again, depicted here.

As we discussed before, ocular dominance columns are maintained as separate for each eye within layer 4 of visual cortex – shown here in yellow or blue – but cells from each of these columns then make common contact with other neurons within the cortex, particularly in layers 2 and 3. These neurons then take on a binocular representation – shown in green – as inputs from each eye drive activity in the same binocular neuronal population. But, how does this integration occur?

Slide 7:
A very well used, experimental strategy to study the plasticity of ocular dominance and binocularity was to reversibly close one eye, preventing visual input. This was usually achieved by carefully suturing the eyelids closed. This may sound like a cruel procedure but, when performed with surgical precision, it allows for careful reopening of the eye after several days or weeks without any compromise to the function of the eye. And, assessment of response of the brain to input through that eye compared to the other eye that had remained open. Thus, ocular dominance plasticity could be measured.

The first thing to note is that the ocular dominance columns in cortical layer 4 undergo dramatic reorganisation when the contralateral eye of kittens is sutured for several weeks. Here you can see, using the same radioactive tracer technique described earlier to track ocular dominance columns, that the territory dedicated to the open, ipsilateral eye has dramatically expanded into the columns previously dedicated to the contralateral eye.

Slide 8:
Another important technique was developed by Hubel and Wiesel to record the electrical activity of neurons in visual cortex of anaesthetised cats with tungsten microelectrodes. This revealed an additional striking functional effect of ocular dominance. As we've described in previous slides, neurons in layers 2 and 3 and further intercortical networks of primary visual cortex exhibit binocularity.

Using Hubel and Wiesel's electrophysiology approach and masking visual input through one eye or the other, it could be observed that most neurons in layer 2/3 were either completely or partially binocular in their response to visual inputs, as shown on the right. Just around 10 to 20% of neurons were monocular in their response within this layer in kittens, undergoing normal visual experience.

Slide 9:
However, as Hubel and Wiesel showed, as well as others, such as Colin Blakemore, here in the UK. Monocular deprivation through, lid suture of the contralateral eye, led to a profound shift in these binocular responses so that neurons in layer 2/3 became almost exclusively responsive to the open ipsilateral eye – here depicted in shades of yellow – even after the eye had been reopened.

This effect is known as ocular dominance plasticity as a result of monocular deprivation, and it has been a deeply studied phenomenon – as it likely provides broad insight into how experience and deprivation shape the nervous system.

Slide 10:
An alternative experimental approach was to create an artificial strabismus in kittens, in which the eyes were forced to view different parts of the visual field. This was achieved by surgically cutting one of the muscles around the eyeball. Like monocular deprivation, the strabismus treatment more or less eradicated binocular receptive fields from layer 2/3 neurons.

However, in contrast to monocular deprivation, strabismus led to equal responsiveness through the two eyes as each eye was delivering equal amounts of activity. That activity was just not correlated between the two eyes.

Slide 11:
Importantly, this process of deprivation-dependent plasticity appeared to rely upon Hebbian mechanisms, as work from Wolf Singer's lab showed – in which they blocked NMDA receptors in primary visual cortex with a selective receptor antagonist and prevented the ocular dominant shift resulting from monocular deprivation in kittens.

Slide 12:
Another dramatic observation was that the ocular dominance shift did not occur if both eyes were sutured for the same period as the previous monocular deprivation experiments. Thus, more deprivation did not result in more plasticity or, indeed, much plasticity at all. This was a really important observation because it showed the ocular dominance plasticity is a competitive process that requires not just deprivation of input through one eye but, also, experience through the other.

Slide 13:
So, in summary for section 3, binocular vision is critical for depth perception and survival. Once the eyes open, activity switches from being uncorrelated between the two eyes to being correlated, due to shared visual input from the outside world over much of the visual field. The visual system integrates inputs from the two eyes through experience to form binocular representations – ie neurons that respond to shared visual inputs from both eyes.

In carnivores and primates, intra-cortical synapses originating from segregated ocular dominance columns in layer 4 converge on neurons in layers 2/3 and 5 of primary visual cortex to form binocular receptive fields. Ocular dominance plasticity, which results when vision through one eye is deprived or altered, provides insight into the mechanisms that support binocular integration.

Closure of one eye in kittens or monkeys shifts the response of neurons in layer 2/3 of visual cortex away from the closed eye and towards the open eye. This shift remains even after the eye is opened. Strabismus, in which muscles are cut to prevent the eyes from focusing on the same part of the visual field, has a different effect of forcing neurons in layer 2/3 to become responsive to just one eye or the other.

Hebbian plasticity mediates formation of binocularity. Blockade of the NMDA receptor prevents ocular dominance plasticity. If both eyes are closed, no plasticity occurs, showing the competition between inputs is critical for ocular dominance plasticity.