Module:
Biological Foundations of Mental Health

Week 2
Building blocks of the brain

Topic 2
From embryonic NPCs to AHN – part 4 of 4

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Lecture transcript

Slide 2

So can we modulate neurogenesis? And if so, how?

Slide 3

So here is a little quiz for you. So think if the behaviours I will give you can increase hippocampal neurogenesis in the adult or decrease adult hippocampal neurogenesis. You will have a few seconds to think in between each behaviour I'm going to present you.

So what do we think about learning? Will it increase neurogenesis or decrease neurogenesis? Yes, learning will increase neurogenesis.

How about stress? Stress will decrease the level of adult hippocampal neurogenesis, especially chronic stress.

How about social interaction? Social interaction will be associated with a higher level of adult hippocampal neurogenesis. And conversely, in rodents, social isolation is going to lead to decreased neurogenesis in the hippocampus.

How about chronic sleep deprivation? Yes, chronic sleep deprivation is going to decrease the level of neurogenesis in the hippocampus.

What do we think about running and exercise? Running will increase the level of adult hippocampal neurogenesis, and I will highlight that in a few slides.

And finally, what about getting older? As we get older, neurogenesis is still occurring. However, the rate of neurogenesis is going to decrease as we age.

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And this is beautifully illustrated by the work from Villeda, et al. So this is an example of how ageing influences adult hippocampal neurogenesis. And more precisely, how the ageing systemic milieu, or blood and serum, modulate adult hippocampal neurogenesis.

So this is a 2011 Nature article by the lab of Wyss-Coray using a parabiosis approach, which means

fusing the circulatory system of an old and a young mice. So they have isochronic control - young and young in yellow. We have an old and old isochronic pair in grey. And then they have their heterochronic young, old pair in the middle. And they let them attach for three months and then look at their brain and look more precisely at the adult hippocampal neurogenesis.

So what we see when we look closely, and they label the newborn neurons or neuroblasts with doublecortin, and we see that in the isochronic mice - young and young - we have a nice level of neurogenesis. Then when we look at our heterochronic young brain that was fused with an old brain, we see that there is a decrease of the level of neurogenesis. When we look at how old isochronic pair - both brains - we see that there's a dramatic reduced level of neurogenesis. But then if we look at the heterochronic old brain that was fused with the young animal, we see that compared to the old animal it has an increased level of neurogenesis. And it is nicely quantified in the C section of the figure and D section of the figure, where we see that our young mice that was fused with old mice has a decreased level of neurogenesis. Whereas the old mice that was fused with a young animal actually has an increased level of neurogenesis.

And they could recapitulate that experiment by simply injecting the plasma. So if we look on the right side of the figure, and they take a young mice as a control and then inject young mice with the young plasma, and then they take an old blood plasma that they inject into young mice. Then we look at the level of neurogenesis. And you see that the young mice injected with the young plasma have a normal level of doublecortin of neuroblast.

But then if you look at the brain of the young mice injected with the old plasma, you see this dramatic decreased level of neurogenesis. And we could correlate that with, actually, their learning and memory abilities.

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So because of the functional role of adult hippocampal neurogenesis on learning and memory, and mood and depression, and the fact that we can modulate adult hippocampal neurogenesis, we think that neurogenesis in the adult hippocampus emerges as a target of choice to enhance learning and memory and mood, or prevent their decline. So we have already done a quiz and know how neurogenesis can actively be modulated, such as with running.

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So now, I want to highlight this article published in the Gage Lab - from the Salk Institute showing for the first time that neurogenesis can be modified by an intervention such as running.

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So here we see the hippocampus of a control mouse not having access to a running wheel. The cells labelled in black are neural stem cells proliferating that will lead next to neurogenesis. And compare this to the amount of black cells in mice who did run in D. We have nearly an increase of 30%, so showing that running is probably a very efficient intervention to increase the level of neurogenesis in the adult hippocampus.

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So let's summarise what we have seen so far. So we know that learning, exercise is going to increase neurogenesis. We have not discussed particularly enriched environment. But be aware that by enriched environment, I mean putting toys, for example, in cages of rodent will increase the level neurogenesis, and in line then will increase their learning and memory abilities and improve their mood.

Diet also can have a positive impact, but equally another type of diet can have a negative impact. We talked about ageing can decrease the level of neurogenesis. Chronic stress will decrease

neurogenesis. Chronic sleep deprivation will decrease the level of neurogenesis.

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So what we do can have an impact, but also what we eat can modulate the production of new neurons.

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So here you see all the diets that have been shown to modulate neurogenesis, and I'm just going to point out a few. So limiting calorie intake of 30% or doing intermittent fasting - so eating every other day - increased neurogenesis. Flavonoids contained in cocoa and fruits with dark skins like blueberry will increase neurogenesis. Omega-3 fatty acid contained in oily fish like salmon will increase the production of new neurons.

Conversely, diets rich in saturated fat will decrease neurogenesis. Alcohol will also be detrimental to the production of new neurons. However, resveratrol contained in red wine has a positive effect.

So now for a quirky one. There are entire groups of Japanese scientists fascinated about the role of food texture, and they have shown that soft food will decrease neurogenesis. So these data are derived from animal work, but actually the same diets that have been shown to impact memory and mood in human studies, and food modulates behaviour in the same direction as food-modulated neurogenesis, such as decreasing calorie intake, intake of flavonoids, Omega-3 fatty acid, has increased the production of new neurons, will improve cognition and mood. Conversely, diets rich in saturated fat will decrease learning and memory abilities and exacerbate symptoms of depression. And some food seems to be linked to poor learning and memory abilities.

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Therefore, we have more and more evidence that suggests that neurogenesis mediates the effect of diet on mental health.