

**Week 4** Answer to Question 4  
Step 5.3 Ask Mark

Ok. Question 4, a short one. It says:

**Question 4:** is depression simply a lesser amount of the encephalitis lethargica? I've got it that people suffering from depression have lost motivation for seeking, etc. Not finding enough meaning in life.

And these things that are lacking in depression, the questioner is referring to the fact that these, this seeking, this finding meaning, this engaging with the world, this optimistic, enthusiastic expectation that something good is going to happen out there, that's why I'm going to throw myself into the mix, and see what happens, something good might happen, it might happen to me, let me check it out, and so on. This system, this dopaminergic system, this seeking system, this intentionality system, is the system that was severely compromised in the encephalitis lethargica epidemic just after the first world war. And yes, those patients, therefore fundamentally what they suffered from - those encephalitis lethargica patients - was a very severe form of what, in the functional disorder of depression, we see also. I think that is correct.

I think not - of course the disease process is entirely different. There's a disease, in fact it was an autoimmune disease we think, in response to the flu epidemic of the nineteen twenties - nineteen eighteen, nineteen twenty - we think that that's what caused encephalitis lethargica. That's a disease, that disease doesn't happen in depression. But that disease in encephalitis lethargica which burnt out the seeking system, it affects the same system as depression does. In depression, for functional reasons - that is to say for different etiological reasons - that system is shut down. And that's why in depression too we see a lack of energy, a lack of motivation, a lack of hopefulness, a lack of positive expectancy, a lack of enthusiastic engagement with the world, a lack of capacity to find pleasure in social and other object related interactions.

So I - as long as you take the caveat seriously that I'm reminding you that etiologically they have nothing to do with each other, then that aside, I agree with the questioner. He's right. The normal - the brain system that is compromised in depression is the same system that is normally shutdown in the despair response in mammals in response to the loss of an attachment object.

That's not to say that that's always what happens in depression, but that's the normal phenotype for it. And that's important, because it gives us important insights into what is going on in the brain during depression, which gives us a basis for new drug development, but also for understanding better what it is we're treating psychotherapeutically. And for understanding this sort of otherwise really difficult to comprehend situation that the depressed patient finds him or herself in, where they feel so hopeless, where they have no energy etc etc. They're not just making it up. You know, they really don't have it, because that system has been shut down, and that's its consequence.

So thank you, as usual, for the many interesting questions - the mentors have great difficulty selecting only four every week. And I - as I've told you before - really enjoy answering them. Thanks a lot, see you next week. Bye bye.



Mark Solms 2016

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