



Allostatic Load and Medical Illness 5

Written Video Transcript

Well, now I'm going to define a new term. Well, if allostatic load is the price you pay is there some way that we can oppose that load? And to stick with the metaphor I've chosen the term is allostatic support. So, if there is some way that we can oppose the [00:00.20.00] load can we not just neutralize the impact of PTSD and traumatic stress but can we even go beyond that and protect ourselves? Can we build in a situation whereby we're going to be less likely to develop PTSD or all of the medical consequences [00:00.40.00] if we're in the wrong place at the wrong time and are exposed to a traumatic situation? And I maintain that this is a way of defining resilience. That allostatic support, however you can acquire it, is another word for resilience because you're opposing [00:01.00.00] allostatic load. Now, to carry this a step further. So, to think about interventions that prevention—prevention would be any activity that would increase allostatic support in advance. And obviously that's a particularly important thing to consider for those of us who work in professions [00:01.20.00] where we know we're going to be exposed to traumatic situations whether we're in the military, we're police on the police force, firefighters, whether emergency medical technicians or if we're mental health professionals that work with traumatized folks. [00:01.40.00] We're all a high risk group and so we have to think about allostatic—so that would be prevention. And obviously treatment would be after the fact. Treatment would be anything that's going to correct or reduce the amount of allostatic load that has been produced by the PTSD and the traumatic situation. Okay. [00:02.00.00] Well, here are some things that we can do. I mean, you know, this applies to life in general but it certainly applies to PTSD as well. I mean having good habits, exercising, good interpersonal relationships, these do increase allostatic support. And there's actually some interesting work on social support [00:02.20.00] and allostatic load suggesting that the more social support you can really reduce this. Okay. Here's a second one. If, as I said during the previous question period, that the hallmark of PTSD in terms of its differentiating it from depression and [00:02.40.00] pointing towards the particular medical problems that may be more unique to PTSD than to say depression is hyperreactivity. There's some very interesting speculation. Roger Pitman, Scott Orr and that group have led the way suggesting [00:03.00.00] that people with PTSD are hyperreactive to start off with. It's a chicken or egg issue isn't it? We don't really know yet. But one interesting hypothesis would be what differentiates a person who is more liable to develop PTSD when exposed to traumatic is that he or she is more hyperreactive. [00:03.20.00] That his stress system is going is going to flare up at a much higher degree and maybe recover less quickly than someone who won't develop PTSD. So, obviously if we can reduce hyperreactivity, if we can reduce conditionability in terms of fear conditioning that would be another way of achieving [00:03.40.00] allostatic support and that would be a behavioral approach or a psychotherapeutic approach. Normalizing HPA function, well that really begins to raise some very



interesting questions about certain pharmacological interventions. Certainly a very important class of drugs that is currently under investigation are the [00:04.00.00] CRF antagonists. There I think the people developing them are thinking more in terms of depression but I would argue that certainly PTSD is another area where we might expect a CRF antagonist to be a particularly effective, particularly in the earlier stages. I mean the sooner you can [00:04.20.00] neutralize this cascade of biological events and the sooner you can stop the wear and tear of the cumulative allostatic load obviously the better outcomes you're going to have. Well, here's another one which I think is really interesting. I'm going to show you some data in a second [00:04.40.00] about why I'm very bullish on neuropeptide Y. But if you recall, neuropeptide Y is a neuropeptide that is one of the body's own anxiolytic substances. When given to people it reduces anxiety. It also [00:05.00.00] neutralizes the impact of CRF and of norepinephrine. So, that's a real exciting one. Increased anabolic factors, this is something I haven't talked about very much but I'll take a minute or two to talk about this. On the one hand we talked about how normal growth and development [00:05.20.00] might be adversely affected by the impact of the psychobiological abnormalities induced by PTSD. One of the very important findings is, as I said earlier, that people with PTSD seem to have a reduced hippocampal volume. [00:05.40.00] That also happens to be a finding in depression and in Cushing's syndrome for that matter. Well, and there's additional research suggesting that the reduced hippocampal volume is clinically significant and functionally significant because people with PTSD seem to be less able to perform cognitive [00:06.00.00] tasks that rely on hippocampal function. Now one of the very exciting things that's happening in psychopharmacology in general is the discovery—and Ron (Duman) and his group at the National Center and at Yale Medical School have shown that effective antidepressants as a group [00:06.20.00] seem to promote neural growth, neural regeneration. And even if it doesn't promote the regeneration of the neurons themselves, although it may, it certainly promotes the improved dendritic sprouting. So that the—so whereas stress can kill neurons, [00:06.40.00] particular in the hippocampus, and can reduce the branches, the dendritic branches, in hippocampal cells, antidepressants seem to promote neurogenesis, regrowth of these important structures. And if it's certainly important to depression it's equally important [00:07.00.00] in PTSD. So, and interestingly enough (certinergic) drugs in addition to working at the synapse in the conventional ways do some other things for a living through the five HT1A receptors seem to promote neural growth. Well, insulin-like [00:07.20.00] growth factor one, is another neurotropic factor that—and there has been some work with spinal cord injuries in animals where administration of IGF1 can actually promote neural growth. So, again, [00:07.40.00] if chronic stress, PTSD can suppress it perhaps some way to either promote or even administer the IGF (denovo) might be one way of promoting regeneration and maybe even stopping the destruction [00:08.00.00] of hippocampal cells or hippocampus dendrites and maybe even regenerating some of them. Okay. Now, I'm going to end by showing you an extraordinary experiment that I believe indicates [00:08.20.00] the allostatic load model and shows how this information really does have some perhaps clinical utility. This is some very extraordinary work that has done by Andy Morgan and collaborators of the National Center for PTSD. [00:08.40.00] And one of our general strategies in the National Center has been we have been doing more and more research



with the military. Because we feel that it's with healthy young men and women entering an arena which is [00:09.00.00] potentially quite traumatic that this is the place to look for resilience, vulnerability. If we can identify people that may be vulnerable, a place to intervene early in the game in terms of [00:09.20.00] promoting resilience or promoting allostatic support as I'm using the term. For example, if we could—if it were true, for example, if it were true that people [00:09.40.00] who are most vulnerable to PTSD are people who are most physiologically reactive, okay as a hypothesis, would it be possible—and let's say we could identify these people in basic training, basic military training, basic police training, basic firefighter training, etc., [00:10.00.00] basic EMT training for emergency medical technicians, could we take a person who is hyperreactive and through conditioning protocols make them less reactive? Thereby promoting some allostatic support so that when they are exposed to the inevitable traumatic situation they're not going to have [00:10.20.00] the huge amount of hyperreactivity and therefore they're going to be somewhat protected? So it's in that kind of spirit that I think that these concepts such as allostatic support hopefully there's some meat on the bones, there's some real-time clinically relevant, very practical down and dirty kinds of applications that one might think about. Anyway, this is about a collaboration [00:10.40.00] at Fort Bragg, North Carolina. And one of the things that they have at Fort Bragg is a special training for Special Forces. And this special training is I'm told absolutely terrifying. It includes a mock captivity where the recruit [00:11.00.00] is captured, is tied up, is subjected to a very, very intolerable interrogation, etc., etc. And you know it's basically trying to find the people with the right stuff. Okay. [00:11.20.00] Now, we've got two groups here. We have Special Forces for the—your Green Berets, your Navy SEALs, etc.. And then you have your garden variety general grunt, military recruit. And so these are the two comparison groups, 10 in the one group and 11 in the other. [00:11.40.00] And what we're measuring here is neuropeptide Y. Well, as you can see, we're measuring a baseline and during the acute stress. At baseline these two groups are essentially the same. There's really no significant difference between their baseline levels of neuropeptide Y. Okay. [00:12.00.00] So, if you were just going to look at people, take their neuropeptide Y temperature, as it were, to try to identify people that might be more or less resilient you're not going to find any—it won't do you any good. During the acute stress however, look at the difference between these two groups. The Special Forces are able [00:12.20.00] to really mobilize under a peptide Y. This is a very, very significant difference in terms of the capacity to mobilize neuropeptide Y. And there's really very, very little overlap between these groups. And even though there's only 10 and 11 subjects in each group [00:12.40.00] it's really quite a remarkable finding. Okay. Now, this is the same experiment. We've got more folks in this particular—we did this several times and depending on when they would let us get the blood samples which is why there's some differences in the numbers here. But again [00:13.00.00] the baselines are the same. However, here we're talking about recovery. So, this is I believe 48 or 72 hours after this interrogation. And what you see is that the folks, the non Special Forces are way back down which would suggest that [00:13.20.00] some of this is maybe anticipation of the adverse situation (because) the Special Forces are able to keep the neuropeptide Y up there. And let me show you one more thing and then we'll talk about it. What we're measuring here is all of the subjects. And



[00:13.40.00] this is neuropeptide Y levels and this is a dissociation scale. Okay? So that the higher the number here the greater the amount of dissociation. And what you see is that [00:14.00.00] the folks with the greatest amount of neuropeptide Y (mobilization) were the ones that were least likely to disassociate. What's really interesting about it is that's there been a lot of military research on this because obviously you know the military is always trying to figure out, you know, who are the best people? [00:14.20.00] Who has the right stuff? Who are the people that we want to send into these very difficult assignments? And their own dissociation measures that the military's developed are very, very good predictors of performance and map on very well with our own disassociation scale. So, what this would suggest is that one predictor [00:14.40.00] of coping capacity, of resilience, of allostatic support if you will, is the capacity to mobilize neuropeptide Y. Now, to apply this to some kind of a preventive strategy it might suggest that let's say you've got someone who really would be fabulous [00:15.00.00] for some kind of a risky job but he or she has some genetic or otherwise caused inability to mobilize their neuropeptide Y sufficiently for you to feel confident sending them in. This is space age conjecture but I think it's a good way to think about the [00:15.20.00] hypothesis. Well, maybe we need to think about getting our pharmaceutical companies to develop neuropeptide Y antagonists. If someone can't develop it himself or herself maybe we ought to give them a hand the same way that we would use insulin or we would use other kinds of things for people that have other kinds of [00:15.40.00] deficiencies but they can't—but are correctible. So, the suggestion here is in the true spirit of medicine. By understanding the path of physiology of PTSD, by understanding which components of those abnormalities make people vulnerable to medical problems or to psychological [00:16.00.00] inability to function we—if we can identify and explicate and operationalize the particular vulnerability there may be in many and many of these people we can actually give them the tools [00:16.20.00] so that they can increase their resilience, they can increase their capacity by themselves.

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