Introduction

[Dr. Briggs] So this is a very exciting day for NCCAM. This is the inauguration lecture of our wonderful new Scientific Director, and it's a great pleasure for me to introduce Dr. Bushnell. She'll be speaking today about the neural basis of mind-body therapies. She is our Scientific Director and Director of the Intramural Research Division, and she is responsible for establishing a new state-of-the-art program, which will be the focus of our intramural program, and will collaborate extensively with others across this campus, both for the wonderful neuroscience expertise on the campus and for the substantial interest in pain management. She comes to us from McGill University, where she was the Harold Griffith Professor of Anesthesia and professor in dentistry and neurology and director of the McGill Alan Edwards Center for Research in Pain. She is, however, returning to the NIH because her scientific career began here in the lab; so she's an NIH insider in many ways. She holds a Ph.D. and master's degree in experimental psychology from American University, where I had the pleasure of jogging this morning, so I really feel that Catherine knows this city and I am very proud of our recruitment efforts that have brought her back to the NIH and to Washington. So with no further ado, it is a great pleasure to introduce Dr. Bushnell.

[applause] >>

[Dr. Bushnell] Well thank you, Josie. It is a pleasure to be back here. I had dinner with a friend of mine from Montreal who was in town last night and he was talking about the minus 25 weather and the 4 feet of snow and I was thinking it's nice being back here. But also intellectually, NIH is a wonderful place to be.

Okay. So I'm going to be talking about the neural basis of mind-body pain therapies, and I will talk some about my own research as well as some other research that's been funded by NIH to address these issues. I didn't know if I need to do this here, but I will. And it was mentioned to me that there may be CME credit and I needed learning objectives, but this doesn't apply to you.

Complex Brain Circuitry Underlying Pain

So first of all, pain is a very complex experience, and as such, there is complex brain circuitry underlying pain. There's not one pain spot in the brain. It's really the activation of a number of areas, pathways, multiple pathways coming from the spinal cord up to the midbrain, the thalamus, ascending projections to multiple cortical areas including somatosensory areas, limbic areas. As I said, there's a lot going on in the brain, even with the simplest of a pain experience. We can get into peoples' brains now using functional MRI or positron-emission tomography where we can actually look what's happening in the brain when a person is experiencing pain. So here's an example, a very simple one. You put a small thermode on the leg and heat it up to a temperature that gives a burning sensation but is not hot enough to damage the skin, in the range of 47 to 49 degrees centigrade. This is the type of temperature if you're cooking, if you have a pan on the stove, it's a hot pan, and you pick it up and you carry it over to the sink and it has a burning sensation, but you can hold on to it for 5 seconds while you take it over to the sink, that's the type of pain this is. So it's not a profound pain, yet despite that it's short duration and simple and something we're familiar with, it activates multiple parts of the cerebral cortex.

So this just shows the anatomical MRI, and the colors in this case are just color representations of statistics showing areas where there's significantly more activation when you heat this thermode up to this burning temperature in the range of 48 degrees as opposed to when you just have it at warm skin temperature. And you see here that there are activations—this is primary somatosensory cortex, contralateral to the stimulated leg, what we call secondary somatosensory cortex, which is on the upper bank of the lateral sulcus. And even though this is a small discreet unilateral stimulus, you're getting activation on both sides of the brain in the secondary somatosensory cortex. Parts of the limbic system, the anterior cingulate cortex, a midline structure, and again bilateral activation, and in the insular cortex, again profound activation bilaterally despite the fact that this is a very simple unilateral stimulus.

Now in addition to having this multiple representation of the pain sensation, we also, within the brain, there are pathways—descending modulatory pathways that are going to control the afferent flow. And so now we know that we have an afferent signal, as we said before, that goes up through the midbrain, the thalamus and to the cortex, but we also have an efferent flow starting in the cortex region such as the anterior cingulate prefrontal cortex, down to an area called the periaqueductal gray matter that's been studied extensively in animal studies. We show the projections from

the PAG down to the rostral ventral medulla down to the spinal cord, that modulate pain and there's been a lot of animal work showing in pharmacology, showing how these pathways are involved in either the enhancement or the dampening of the afferent pain signal. And because we know about these pathways through multiple animal studies, there's been a lot of work done about how the neurotransmitters that are involved and how various—these can be involved when we give analgesic drugs to modify pain.

So that when we give opiates, which are the most powerful analgesic drugs, they work at the periphery, they work at the level of the spinal cord, they work at the level of the PAG, and they even work (not shown here) at the level of the anterior cingulate cortex. NSAIDs, the non-steroidal anti-inflammatories—they work peripherally, but they actually even have a central activation in the PAG. And then other drugs that are used for chronic pain, the cannabinoids, the various antidepressants—the TCAs, the SNRIs—are activating in this descending system, as well as the antiepileptic drugs that are used for chronic pain. So we can see how various centrally acting drugs, analgesic drugs, are activating a naturally occurring endogenous modulatory system in the brain. But the systems are not there in order that we can take drugs, right? They've evolved for some other purposes, so there should be natural ways to activate these systems.