ALLOCUTION DU PROFESSEUR JOSEPH E. LEDOUX

LAUREAT DU PRIX INTERNATIONAL 2005
DE LA FONDATION FYSSEN

31 mars 2006

I want to thank the Fyssen Family for making such a generous prize available for research on mind and brain. I also want to thank the members of the Fyssen Foundation, especially the Scientific Committee, for choosing me as the recipient of the 2005 award. I am also grateful to Nadia Ferchal for all her help in planning my visit to Paris. I also want to thank Professor Yadin Dudai for nominating me and Professor Eric Kandel for supporting the nomination.

I could not have been recognized for such an award without the contributions of many talented people who have worked with me over the past 25 years. It is as much theirs as mine. Finally I want to thank my wife Nancy and my sons Milo and Jacob, for their love and support over the years. On behalf of all researchers who work on the neural basis of emotions, I am pleased to accept the 2005 Fyssen Prize.

To receive such a wonderful award from a French foundation especially warms my heart. I grew up in the area of Louisiana where French was the primary language of my parent's generation. As you can tell from my speech, though, this tradition did not continue to my generation. Not learning to speak French as a child is one of my only regrets from my childhood. I apologize for my poor command of the French language and ask you to bear with me as I read my remarks.

Few topics in science are as interesting as emotions. It may therefore come as a surprise that the study of emotion was neglected for many years, especially by brain researchers. I became interested in this topic very early in my scientific career, and decided to begin to do research on it. So I applied for a grant to study the Neural Pathways of Emotion. The grant was rejected because, I was told, it is not possible to study emotion in the brain. Emotion is a topic of philosophy not science. This was 1983. I was disappointed but persisted. Eventually I received funding and have been working on emotions and the brain ever since.

Because of the difficulty in studying emotions, I decided to try to find a simple way to study them. I had four requirements. First, I wanted to do the studies in an animal that was easy to experiment on, such as rats. Second, I wanted to study an emotion in rats that is relevant to humans. Third, I wanted to be able to elicit the emotion with a simple,

easily delivered stimulus. Finally, I wanted to be able accurately measure the occurrence of the emotion from the rat's behavior.

These four requirements were satisfied by a behavioral procedure called fear conditioning. This is a variation of Pavlov's famous conditioning procedures. Instead of ringing a bell at feeding time, though, we play a tone prior to a painful experience for the purpose of conditioning fear reactions to the tone. When the rat hears the tone, it freezes, and its blood pressure go up. In humans, muscle tension and autonomic responses also occur. So by using this simple stimulus in a rat we can model something that occurs in humans when we anticipate pain or other traumatic events.

Fear is a particularly important emotion to study because it is so troubling to humans. More people visit mental health professionals each year for problems of fear and anxiety than for any other reason.

Why are we so prone to fear? The answer is found in evolution. The fear system is designed to learn rapidly and to not forget. Animals don't have the opportunity to practice escaping from predators, and once they learn about danger they need to remember. Relearning could be costly. Our brains work the same, not so much because of blood thirsty beasts, but in terms of fears relevant to our lives and especially our

future. Our ability to anticipate the future accounts for mankind's greatest achievements, but at a cost—the ability to worry.

The term fear commonly refers to a conscious experience of being afraid. Can rats feel fear ? No one knows. This is why it is so hard to study emotions. But I have used the term in a different way. For me fear refers to something simpler and more fundamental.

Every organism has to be able to detect and respond to danger. This is true of a bacteria living in a petrie dish and a human living in Paris. This is the function of the fear system. When the brain also has consciousness, then the feeling of fear also occurs. But the feeling is not essential. Fear is an unconscious function of the brain. It simply involves the ability to detect and respond to danger.

Most of the things that are dangerous in life have to be learned about. Fear allows us to learn that stimuli associated with harm are predictive of danger, and thus are in a sense dangerous themselves.

My research on the brain mechanisms of fear have led me to a part of the brain called the amygdala. It was known that the amygdala plays a role in fear, but the exact manner in which this occurs remained unclear. I tried to figure out the brain pathways from start to finish.

That is, I had as my goal to understand the circuit from the sensory pathway that takes the tone into the brain, the auditory pathway, to the motor pathway that takes the response out of the brain and into the muscles. The amygdala turned out to be the centerpiece of this system.

One of most important findings has been that there are two sensory pathways to the amygdala. One is through the cortex. It is slow but provides a very detailed analysis of the eliciting stimulus. The other bypasses the cortex and goes directly to the amygdala from the thalamus. This is fast but imprecise—quick and dirty. It allows you to jump back to avoid being hit by a bus before you consciously know there is a bus.

We have also learned much about the detailed circuits in the amygdala. The lateral nucleus receives the sensory inputs. It communicates with the central nucleus, which controls the responses.

Much of our work in recent years has focused on the mechanisms of plasticity in the lateral amygdala. We have identified neurotransmitters and intracellular signals that lead to RNA and protein synthesis in amygdala cells, with the latter being required to form long term unconscious memories of danger.

All of this would be meaningless if it didn't apply to the human brain. Through studies in which I collaborate with Elizabeth Phelps at NYU we have shown that many of the same basic circuits apply.

Finally, my work has begun to turn to questions about fear and anxiety disorders. Through collaborations with psychiatrists, I am exploring the changes in the brain that take place in people with these disorders, and we are seeking better ways to treat these conditions.

Let me close by again thanking the Fyssen Foundation for this wonderful award. I plan to use it well. I will give some to charity, will use some for the enjoyment of my family and friends. For myself, I will buy a new guitar. Thanks very much.