SUSANNAH TYE: Hello, my name is Dr. Susannah Tye and I'm a researcher within the Department of Psychiatry and Psychology at Mayo Clinic, where we are working towards optimizing our treatments for depression. Our department is eager to find and develop promising new treatments for treatment-resistant depression. Many patients with depression do not respond effectively to first line antidepressant treatments. And for those who do respond, it usually takes at least three weeks, from the time of starting treatment to receiving any clinical benefit. Currently, our treatment process is trial and error. We are actively working to improve this process.

We want to understand why some patients do not get better with current treatments, and how we can overcome this and improve the process to recovery. We are also striving to find ways to identify these patients early in the course of their clinical treatment through biomarker discovery. This is something that requires a concerted team effort and is a key priority for our Depression Center, where we have a multidisciplinary team working together to resolve these critical clinical issues. Our overall goal is to individualize treatments for patients with depression so that we can get the right treatment to each patient at the outset. And to improve the rate of recovery avoiding the trial and error process that delays recovery from what is a seriously debilitating and life threatening illness.

One of the promising treatment approaches that we are pursuing here at Mayo is development and optimization of ketamine as an intervention treatment for treatment-resistant depression. Ketamine is an anesthetic that works by blocking a glutamate receptor, which is abundantly expressed throughout the brain. This is the NMDA receptor. However at very low sub-anesthetic doses, ketamine has been shown to have rapid acting antidepressant effects, significantly improving symptoms of depression, sometimes within hours or days. A very interesting and important finding in the field is that ketamine has been shown to be particularly effective for patients who are experiencing feelings of suicidality.

We are engaged in a variety of research projects aimed at understanding how ketamine is able to induce such rapid depressant effects, as well as which patients will be most effectively treated with ketamine, how we can optimize the depressant actions of this treatment and the best practice for integrating ketamine treatment into our Depression Center within Mayo clinic. There's a lot that we still do not understand about each of these important points. It is critical for basic science researchers and clinicians that are working at the front of psychiatric care to join forces, so that we are able to achieve this. At Mayo Clinic, we have done just this through development of a translational neuroscience research program.

At the recent Society for Biological Psychiatry meeting in New York, Dr. Mark Frye, the chair of psychiatry at Mayo, and director of our Mayo Clinic Depression Center, together with myself and doctors Pierre Blier from the University of Ontario and James Murrough from the Icahn School of Medicine at Mount Sinai, presented our recent data on these important topics in a symposium called Translational Biomarkers of Ketamine Response. This was chaired by Dr. John Krystal, the chair of psychiatry at Yale University. In this symposium, we presented both preclinical and clinical data on the neurobiological actions of ketamine in animal models as well as on its clinical efficacy in treatment trials.

Doctor Pierre Blier presented data on the effects of ketamine, on dopamine and norepinephrine neuronal firing in rats and glutamate receptor mechanisms that mediate this. Dr. Mark Frye presented recent clinical data from the Mayo Clinic trial on the safety and efficacy of intravenous ketamine for patients with severe treatment-resistant depression and raised important clinical considerations for the field as we move forward to develop ketamine treatments. Dr. James Murrough presented his research related to ketamine and other glutamate modulators in depression, and discussed the potential pitfalls and promises of these approaches. The work I presented pertained to data from the pre-clinical research that we have been conducting at Mayo, that shows that there is a clear correlation between activation of mTOR signaling in the brain and the antidepressant responses to ketamine.

Collectively, our symposium was able to highlight these findings on the mechanism of action of ketamine, treatment response biomarkers, and clinical efficacy. This provided the forum an opportunity for discussion of how the field can best integrate ketamine treatment into its clinical practice. The rapid antidepressant responses of our severe treatment resistant patients to ketamine is providing the field with a paradigm shift. It is underscoring the neurobiological nature of depression and that this is a serious illness that must be treated effectively. In this way, it may also help us to reduce the stigma associated with mental illness, and encourage people to take the medical care that they need rather than try to battle the illness alone.

Importantly, it is informing our understanding of the mechanisms mediating rapid antidepressant responses, which is providing us with critical clues to the mechanisms we need to target to improve responses, and the biomarkers that can help us identify those who will respond most effectively to this treatment. We still have much to learn about how to optimize ketamine treatment for treatment resistant depression. As we work to better understand this, it still remains clear that this treatment has great potential to save the lives of seriously ill patients. Thank you very much for the opportunity to present our work today. And I hope it has been useful for your practice.