Researchers study the brain's link to 'metabolic syndrome'

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SPECIAL TO THE BLADE

also have problems with infertility. Because of the increasing number of patients being treated for both infertility and diabetes, there is intense interest in developing less expensive, combined therapy for these conditions.

At the University of Toledo College of Medicine, formerly the Medical College of Ohio, our research team is focused on the brain because we believe that it is the master regulator of the metabolic syndromes.

Why the brain? What is the connection between the brain and insulin levels in your blood?

We know that specific areas in your brain control how much you eat and how your body responds to high blood sugar. Therefore, our research team is testing the idea that insulin also acts in the brain to regulate metabolic syndrome and related problems such as infertility.

Your brain has multiple regions that control diabetes, obesity, and infertility. One of these regions in the brain is called the hypothalamus, and is further divided into many important subregions. Your brain also contains two types of cells; neurons to communicate messages across the brain and glial cells, whose function has been a mystery until recently.

My research uses a mouse model to study how insulin actions in the brain affect diabetes and infertility. My first experimental step was to delete insulin receptors from specific brain glial cells called astrocytes, which become activated when insulin binds
to their receptors. I wanted to know what would happen when insulin could no longer activate the astrocytes. I discovered that astrocytes without insulin receptors affect fertility, diabetes, and obesity.

My research project is to investigate insulin signaling in the brain and its effect on reproduction (fertility) and metabolism (diabetes). When I studied fertility in this mouse model, I saw a delay in onset of puberty in the sick mouse model without insulin receptors, when compared to control healthy mice. Also, the sick female mice did not have regular menstrual cycles. I also observed a reduction in brain fertility hormone levels as well as ovary and testis hormone levels in the sick mice. I also found that pregnancy rate for the sick female mouse model was reduced dramatically when compared to that of healthy mice. I found similar results of decreased fertility in the sick male mouse model when compared to healthy mice. All of these findings indicate that insulin activity in brain cells affects fertility in important ways.

When I studied diabetes and obesity in this mouse model, as we had suspected, there were profound effects. The sick mouse model showed an increase in body weight from the first month and become outright obese by 6 months of age (equal to a 35-40 year old human).

This was the first hint that the sick mouse model would eventually become diabetic. Indeed, the sick mouse model is also prediabetic at an early age and becomes diabetic by 6 months of age. I also checked overall fat and muscle content in the sick mouse model and, as expected, I measured increased fat and low muscle content, also confirming obesity in the sick mouse model.

These combined findings indicate that insulin in the brain is critical in treating obesity, diabetes, and infertility. We are planning to use these results to help identify new drugs that will target these conditions simultaneously thereby lowering the cost of using of multiple drugs.

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