

# Advancing the science of Behavioral Health

The Avera Institute for Human Behavioral Genetics will change lives through prevention

BY DONNA FARRIS, AVERA MCKENNAN WRITER/EDITOR

Unique in the nation, the Avera Institute for Human Behavioral Genetics has the potential to change many lives – by limiting the suffering caused by psychiatric illness.

“Behavioral illnesses last an entire lifetime,” said Dr. Matthew Stanley, psychiatrist with Avera University Psychiatry Associates. “Imagine being able to develop wellness programs so that many people never get ill.”

The Avera IHBG initiative combines genetic and environmental principles with an aim toward health and wellness in children, families and communities.

“Our mission is pretty simple,” said Dr. James Hudziak, internationally-known child psychiatrist and genetic researcher, and scientific consultant for the Avera IHBG. “We want to keep well children and families well.” Other missional aspects are to protect children and families at risk for emotional and behavioral illness, and intervene on behalf of those who are ill or become ill.

While certain genes can predispose people to psychiatric disorders, research indicates that environmental factors play a role – to either cause a greater risk, or provide protection from illness.

“We don’t understand everything about the development of illness yet, but it’s our very strong belief that it is a combination of genetic and environmental impacts,” Dr. Stanley said.

“Imagine being able to test kids early in life through genetic samples,

identify children who would otherwise be at very high risk, and put them in the right environmental structure so they never develop that illness,” Dr. Stanley said. “What a huge impact this would have, even if we could do it for one person. What

if you could find the genetic predisposition and create interventions for thousands and thousands across the United States, and even the world?”

This probably sounds too incredible for some, Dr. Stanley recognizes.

## Genetic research will trace susceptibility for illness



Human beings are so different, and yet so alike – 99.9 percent alike to be exact.

Since the sequencing of the human genome was completed in 2000, we now know that human beings are genetically identical by 99.9 percent. The remaining 0.1 percent accounts for all our differences in physical features, as well as susceptibility to different diseases.

“Only a tiny change in our DNA gives us these susceptibilities. We are almost identical, yet some develop diseases and some don’t,” said Dr. Gareth Davies, director of scientific operations for the Avera Institute for Human Behavioral Genetics.

Dr. Davies, who also serves as assistant professor with the South Dakota State University College of Pharmacy, has a background in unlocking the genetics related to complex diseases, specifically in the area of diabetes.

The development of all diseases, whether it is diabetes or schizophrenia, is believed to stem from genes or changes in genes which make people more susceptible, and environmental factors which trigger those genes, Davies said.

“If you have presence of certain genes or a change in a gene associated with a particular disease, it doesn’t diagnose you, it means you are at higher risk if you have a certain trigger or environmental event that could kick off this susceptibility,” he said.

Dr. Davies’ work will involve testing genetic samples, usually collected through saliva, in research conducted by the Avera IHBG.

Allowing scientists to conduct this testing is advanced technology such as the Applied Biosystems 3130 Genetic Analyzer, which sequences the nucleotide bases within a person’s DNA, and the Roche AmpliChip® Cytochrome P450 genotyping test, which helps physicians personalize treatment options according to their genetic makeup.

“If we can identify environmental risk factors and those genes that interact with those risk factors, it would be a phenomenal breakthrough for the field of behavioral disorders,” Dr. Davies said. “It’s a wonderful opportunity for this area and for psychiatric medicine.”

“It’s the kind of thing you think of as happening at Johns Hopkins or Stanford. But I think we’re going to show that not only can we do it, we will do it here.”

### The vision takes shape

The vision began in the minds of Dr. Stanley and his colleague, Dr. Timothy Soundy, child and adolescent psychiatrist with Avera

University Psychiatry Associates, as Avera was planning its state-of-the-art 100,000 square foot, 110-bed Behavioral Health Center, which is now the region’s premier facility for behavioral health services.

“Dr. Soundy and I had the belief and vision that in psychiatry, genetics is going to play a larger and larger role.

It is a new field – a field that no one has

cornered,” Dr. Stanley said.

The physicians shared their vision with Fred Slunecka, Avera McKennan regional president, who also saw the possibilities. “It’s an exciting prospect. Together we can build a stronger framework for social health. Together we can design a better prevention and treatment approach for children and families with psychiatric disorders,” Slunecka said. A commitment from

## Both genetic and environmental factors place children at risk



Nature or nurture? Genes or environment? Which are responsible for mental health conditions, such as depression, anxiety, bipolar disease or addiction?

The answer is both, according to Dr. James Hudziak, internationally-known child psychiatrist and genetic researcher, and scientific consultant for the Avera Institute for Human Behavioral Genetics. Hudziak is affiliated with the University of Vermont College of Medicine and Vrije Universiteit at Amsterdam, The Netherlands.

“This gives us the argument for why we do genetic-environmental research,” said Hudziak, as he explained his involvement in a number of published genetic studies covering problems such as attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, smoking and substance abuse, autism spectrum disorders, anxiety/depression, obsessive-compulsive disorder and juvenile bipolar disorder. “In every instance, we cannot find any illness that’s purely genetic, or any illness that’s purely environmental.”

Hudziak brings with him to the

Avera IHBG the premise of using genotyping to bridge the gap between emerging research on gene-environment interaction, and child psychopathy, and implementing that research in clinical community settings.

“We’re never going to have genes that diagnose ADHD, or genes that diagnose depression. We’re going to have genes that tell you the relative risk that the child or family has to develop these outcomes,” Hudziak said.

That understanding can help scientists see which genes and which environmental influences predict risk for, or protection from, psychiatric illness.

The “old genetics” is the understanding that one gene causes one disorder, such as Huntington’s disease, cystic fibrosis or muscular dystrophy. “These are rare genes causing rare conditions in a small percentage of the population,” Hudziak said.

The “old genetics” has nothing to do with modern medicine, and the study of common conditions such as hypertension, diabetes, obesity – and psychiatric illness. “The old genetics is over. The new genetics involves common genes – genes we all carry that don’t cause illness, but put you at a greater risk,” he said.

So a child with ADHD develops it because he carries the genes, and has some type of environmental trigger.

Environmental risk factors may

include varied situations, such as trauma, abuse, conflict in the home, growing up with a depressed mother or even seeing too much violence on TV.

On the other hand, environmental factors such as a peaceful home, involvement in sports and music, good nutrition, and quality family time can protect children from illness.

“Genes matter and environment matters, but in different ways at different times for boys and girls. These sources of variance must be taken into account when treating a child and a family,” Hudziak said.

Psychiatric illnesses have been shown to run in families. A family-based approach means not just treating a child with ADHD individually, but also assessing the all members of the family.

By improving the home environment, parents may be able to improve the health of their children. In some cases, if a parent is treated, perhaps for depression, her child may get better without any treatment at all.

“We do this work because we’re devoted to developing strategies to reduce the suffering of children and families. These are medical conditions influenced by gene and environmental factors. They are not someone’s fault,” Dr. Hudziak said. “We predict our work will lead to new diagnostic and treatment strategies to help children, families and communities.”

Avera McKennan of \$1.5 million over three years is supporting the project, along with grants and contributions from philanthropic donors.

Drs. Stanley and Soundy heard a conference presentation by Dr. Hudziak, who connected with the idea, and agreed to work as a consultant on the project. Together, the team has shaped and honed the vision.

“We’re talking about very real, very interventional studies. We see ourselves providing a service to the community immediately, but at the same time drawing research out of it so that our efforts will have an even greater impact in the future,” Dr. Stanley said.

### **Key partnerships**

Collaboration and partnerships are key in the success of the Avera IHBG venture. Partners include the South Dakota State University College of Pharmacy, the University of South Dakota, University of South Dakota Sanford School of Medicine Department of Psychiatry, and other local community partners, currently in development.

The structure of Avera IHBG consists of a central core of child behavioral specialists, educators and scientists serving in two major areas of focus – community-based research programs and Centers of Excellence for Child and Adolescent Emotional Behavioral Problems.

Through a family-based approach, community-based programs will focus on maternal health, early childhood and school-age children, at-risk families and special populations.

Although most families who participate in the community-based centers will be well or at risk, there will be those who suffer psychiatric illness. For them, Avera IHBG visionaries hope to create state-of-the-art Centers of

Excellence to improve the health of the most at-need children and families, and at the same time contribute to the research database to advance the understanding of these disorders.

These Centers of Excellence will focus on specific disorders such as autism and pervasive developmental disorders, attention deficit hyperactivity disorder, obsessive compulsive and anxiety disorders, mood and bipolar disorders and substance abuse.

“We believe these will be cutting-edge treatment centers, and a resource that would draw people from across the country to be seen in these specialty clinics,” said Ryan Hansen, director of clinical research for the Avera Research Institute and interim chief operating officer for the Avera IHBG. “It’s a lofty goal, but an exciting goal and I believe we’re building the infrastructure to make it successful.”

Work will take place on two fronts: First, genetic research, and secondly, clinical prevention and intervention. Dr. Gareth Davies from the SDSU College of Pharmacy is heading up scientific operations, and Dr. Manish Sheth is assuming oversight of clinical operations. Dr. Hudziak will continue his role with Avera IHBG long-term as a key consultant at both the clinical and scientific levels.

### **Unique and innovative**

Avera IHBG is cutting edge in many ways.

It is set apart merely by its location within a 110-bed behavioral health facility, with a large team of mental health professionals under the same roof.

Even more unique is the potential involvement of the local school system.

“The current scientific and clinical expertise that we have today, and the rapid development of key community

## **Research will have immediate community benefits**

The Avera Institute for Human Behavioral Genetics is set apart from other research institutions by its family-based, community-focused approach.

“There has been a lot of research done in psychiatric genetics but it has not actually come down to the bedside,” said Dr. Manish Sheth, director of clinical operations for the Avera IHBG. A board-certified psychiatrist, he also holds a doctorate in basic biomedical sciences.

The goal is to have four to five studies at any given time conducted in the community with the help of partners, such as the school district or community organizations.

An initial focus will be on at-risk preschool children.

“We are told that by the time these children are going to kindergarten, it’s already too late,” Dr. Sheth said.

After a database is created, enrolled children will be followed over a period of three to five years, and provided support and treatment if needed through a family-based approach.

“Our goal is to keep the well healthy. We will have the resources available for children and their families so that if anything is noticed, we can intervene before it becomes an illness,” Dr. Sheth said.

At-risk families will be counseled, and children in need of psychiatric services will be referred to disorder-specific treatment programs.

This program will encourage wellness strategies such as involvement in sports, music or dance programs. Mental health

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## Research will have immediate community benefits (cont.)

experts will offer workshops for parents or school personnel, and support groups may play a role.

“Some of these same types of programs are offered by others in the community, but they operate in isolation. We intend on working cooperatively with these community programs in a very comprehensive program, all done under the umbrella of behavioral health,” Dr. Sheth said.

Another area of study will involve cytochrome genotyping, which determines genetically how a person will metabolize drugs.

This test will help physicians prescribe the correct medication and dosage, rather than the trial and error of seeing whether a drug will work, and whether or not side effects will be tolerable.

“That would be a phenomenal improvement in the way we practice psychiatry,” Dr. Sheth said.

A third area of focus will look into whether or not genetic testing promotes a willingness to accept psychiatric treatment.

“We all know there is a stigma attached to psychiatric care,” Dr. Sheth said. While no one gene or combination of genes directly cause an illness, certain genes along with environmental risk factors or childhood issues can lead to the development of a mental health condition, Sheth said.

The first study being designed involves attention deficit hyperactivity disorder in women. Because females with ADHD are more often inattentive than hyperactive, they often stay below the radar and are not treated.

Participants in the study will undergo genetic and clinical testing, and offered treatment based on symptoms.

The clinical work of the Avera IHBG could expand in different directions as the program matures, Dr. Sheth said.

It’s hoped that by the time the initial preschool children in the early childhood study enter kindergarten, the positive results will be obvious, with less intervention needed at that point.

It’s also hoped that treatment options can improve for those suffering from mental health conditions, locally, nationwide or worldwide as results at some point in the future are published.

“We don’t know where this will lead us. We have some very audacious goals, but we are confident we can reach them because our intentions are right,” Dr. Sheth said.

partnerships are aspects that make us truly unique. That’s what will make us one of a kind, and it’s something that I believe we should be proud of,” Hansen said.

The practical application also distinguishes the Avera IHBG from most traditional research programs, in which results don’t benefit patients for years or even decades to come. “The gap between research science and clinical practice is huge. When a discovery is made it takes decades to get into clinical practice,” Dr. Hudziak said.

The Avera IHBG will be among pioneers of a form of research called translational research. “It’s taking basic research in the form of genetics and attaching a clinical application. So you’re progressing the research science, but more importantly you’re actually benefiting the community right away,” Hansen said.

What’s special about the Avera IHBG team is their desire to do something to help people now, not in 10 or 20 years, Dr. Stanley said. “We want to come down out of the ivory tower and be providing treatment from Day 1. Genetics is a whole new universe in the field of psychiatry. There are so many opportunities.”

Ultimately, work through the Avera IHBG could change the way psychiatrists treat patients.

Psychiatrists and psychologists at the Avera Behavioral Health Center provide the best care the field of psychiatry is able to offer, Dr. Stanley said. “But there are still people who are very sick. What I would love to be able to do is see people early enough, and have enough information from their genetic profile to be able to prescribe an environmental change so they will be well.”



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