

Summary of presentations by Dr. Shelli Kesler,

Presented at the 5th Biennial Family-focused Conference on TS “Understanding and Appreciating Turner Syndrome” held in Vancouver, BC on Oct. 27th 2007

(Based on the work of Allan Reiss, MD, Shelli Kesler, PhD, Joachim Hallmayer, MD, Kirk Neely, MD, Booil Jo, PhD and Bria Dunkin, MS at the Center for Interdisciplinary Brain Sciences Research, Stanford University, School of Medicine)

Summary by Jaye Kerzner, B.C. Chapter, Turner Syndrome Society of Canada

Note that Dr. Kesler will be speaking on “Neurobiology of and Treatments for Learning Difficulties in TS” at the 27th Annual Conference of the Turner Syndrome Society of Canada May 24th, 2008

Dr. Kesler began her presentation by outlining the age-old debate in science, that is, “How much does nature (genetics) or nurture (environmental factors) affect who we become? Most researchers would now agree that both nature and nurture affect an individual. In the case of Turner Syndrome (TS) the question becomes to what extent does the missing ‘X’ affect the behaviour and thinking (cognition) of a girl or woman with TS and, to what extent do environmental factors (prenatal events, parenting, education, peer group, nutrition, etc.) affect behaviour and thinking? The position of this research team is that TS is a “risk factor” for certain cognitive-behavioural problems; but TS does not “cause” those problems. *[Editor’s note: This is a subtle, but important difference because it suggests that the behavioural and thinking challenges associated with TS are not solely due to gene differences.]*

Dr. Kesler then posed the question, “When attempting to understand the thinking and behavioural problems in TS, are descriptive diagnoses such as Nonverbal Learning Disabilities (NLD) and Attention Deficit Disorder (ADD) helpful? This research team believes that these labels are not at all helpful because, in their words, “TS is a diagnosis with clear biological markers and increasingly well understood disease mechanisms ... whereas NLD and ADD are descriptively defined” (meaning that a diagnosis of NLD and ADD are made by observing certain behaviours). The team thinks that NLD and ADD may have different neurobiological and neurogenetic factors underlying them and that using the NLD label to describe the cognitive and behavioural challenges of people with TS distracts from the real issues of TS. To put it another way, the concern is that, although the learning challenges evident in girls with TS may look similar to NLD, effective strategies for dealing with each may be different. Therefore, the approach of these researchers has been to first, focus on the neurobiology of TS (what is going on in the brain of TS girls) and then to try to identify strategies to enhance their thinking processes based on those observations. This led into the second keynote address by Dr. Kesler.

The second presentation started with a review of the known cognitive features of TS, namely, that girls with TS: 1) nearly always have a normal IQ (individuals with TS who have severe learning problems may have unusual genetic characteristics), 2) tend to have a higher verbal IQ than performance IQ, 3) often have a strength in verbal skills and 4) often show a weakness in visual memory, visual-spatial skills and executive functioning (planning and organizing skills). The psychosocial features of girls and women with TS were also summarized. Dr. Kesler noted that physical well-being (how healthy the person is), the pattern of sexual maturation and height clearly affect behaviour. She also noted that the literature suggests that individuals with TS are at increased risk for 1) attention problems, 2) impaired face and emotion processing (difficulty “reading” social cues), 3) problems with peer relations, and perhaps 4) anxiety and depression – although this last point is not clearly established in current research literature.

Dr. Kesler moved on to pose the question, “What can we **do** about the thinking and behavioral problems of TS girls if they are present?” She then listed some recognized general strategies for addressing thinking and behavioural challenges, namely, early identification of problems, family or parental counseling and guidance, treatment of behavioral problems with therapy and (sometimes) medication and placement in an optimal educational environment. Treatments for psychosocial challenges are not as clear cut, since there has been little research in this area. It appears that these strategies may be helpful: 1) general coping and adaptive skills training (focusing on dealing with medical issues), 2) social skills training (focusing on face processing & body language interpretation), 3) stress management training, 4) efforts to improve self-esteem and 5) developing effective learning and organizational strategies to compensate for cognitive weaknesses. The research team that Dr. Kesler is part of believes that much research still needs to be done to find new ways to identify early on whether a girl with TS will have some of the thinking challenges associated with TS and, research also has to be done to find ways to help girls and women with TS optimize their thinking and develop their social skills. They feel that the guiding questions for future research are:

- What are the specific genetic, biological and environmental factors that contribute to cognitive and behavioral strengths and weaknesses?
- Can we identify brain correlates of these factors and use them to improve treatment specificity and effectiveness?
- Which of these factors predict response to particular treatments?
- What treatments are most likely to be of benefit?
- Who is most likely to benefit from early identification and treatment?
- How can we increase the likelihood that each individual with TS will achieve their maximum potential?
- What is the brain structure and function in TS and how can we develop a model for understanding this?

Dr. Kesler went on to describe some of the work that their team are working on at Stanford University. *[Editor's note: One of the key researchers of this team, Dr. Allan Reiss, has been involved in brain imaging research for about 20 years, much of it trying to discover how the brains of those with certain genetic conditions function differently than “typical” brains in an effort to understand differences and to formulate effective treatments for dealing with thinking challenges and behaviours which are problematic for these individuals. Dr. Reiss has also been a medical advisor on the US TSS board for many years].*

Currently the research team at Stanford is using brain imaging (pictures obtained by using magnetic resonance imaging or MRI) to see what parts of the brain are being used when subjects are given certain tasks. They have discovered that people with TS have certain differences in their brains and that they used their brains differently. They have determined that the volume of the parietal lobe (where visual spatial processing occurs) tends to be smaller and the temporal lobe (where verbal processing happens) tends to be enlarged in girls with TS. In a study of math function, TS girls also showed greater activation in frontal-parietal regions of the brain during simple math tasks but less activation during harder tasks (Kesler et al. 2006 *Cerebral Cortex*). A study of verbal and visual-spatial working memory led to the conclusions that there is some frontal-parietal dysfunction in TS and that its active storage of material in the working memory is impaired. Collectively, the brain imaging results suggest “network” issues – certain pathways or connections in the brain are not as well developed in girls with TS. There appears to be a “disconnection” between parietal and frontal regions associated with visual spatial-executive function in TS. People with TS tend to engage the parietal- temporal lobe of the brain (where verbal skills reside) and do not tend to engage the parietal-frontal pathways (where visual skills arise) when doing visual-spatial tasks or executive functioning (organizing) tasks. This way of using the brain shows that they are compensating, but they are less efficient and this compensation may only work for lower level tasks.

The team is also working on developing cognitive Interventions for girls with TS. They are trying to find out if they can “increase parietal-frontal connectivity in individuals with TS, thus improving planning ability and math skills”. They are doing this by using a cognitive intervention that they have developed which involves asking the individual to perform specific skills and then asking that person to practice the skill in small, increasingly difficult steps [which the author of this summary likens to “brain physical therapy”]. The researchers believe that this intervention works by taking advantage of the brain’s neuroplasticity – the ability of the brain to develop new connections between different parts of the brain by exercising the brain, much as you would exercise a muscle. As the brain encounters mental challenges it learns new things and develops more efficient and effective brain networks, a process that can then be measured with functional MRI images. Early results of their work demonstrate that girls with TS can be taught to achieve much higher accuracy on certain cognitive tasks and improve the efficiency or speed in which they perform correct tasks. MRI comparisons show that the girls can actually be taught to activate different parts of their brain! Continued research is being done to determine how long this effect will last.

The team is currently recruiting additional volunteers for their ongoing study of brain function and TS. A flyer with study inclusion criteria, a brief outline of what is required of participants, and contact information can be obtained by contacting: Bria Dunkin briad@stanford.edu toll free 888-411-2672

[Final Editor’s note: I have tried to capture accurately the flavour of this presentation from my own notes and recall and the presentation slides. This information should not be reproduced in any other format without the header and footer noting the date of the presentation and the conditions under which this summary was made. Readers are encouraged to attend the National Conference in Toronto – May23-25th, 2008 if they would like to hear Dr. Kesler’s presentation in person.]