ANGELMAN SYNDROME ASSOCIATION

www.angelmansyndrome.org

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"West Coast Angels"

9th Biennial Australian National Angelman Syndrome Association Conference
Friday 2nd – Sunday 4th October 2009

Summary of Presentations by Professor Bernard Dan, Laura Jones and Dr Ellie Smith.

For a full report see the Conference Report on the National ASA website (www.angelmansyndrome.org) or the ASA of WA website (www.angelmanwa.com.au)

1. **Professor Bernard Dan** presented his keynote address. This was extremely informative and a recording will be available so I will attempt to be brief. He stated...Angelman Syndrome is known as an 'orphan' disease because pharmaceutical companies are reluctant to 'adopt' treatments because the financial return does not justify the investment as the numbers involved are small- less than 7.5 people in 10,000 (US) or less than 5 people in 10,000 (EU). However support groups can have a great influence on policy making and research. Families need to start with the Clinical diagnostic criteria as reviewed by Williams et al in 2006 and then confirm the diagnosis with genetic testing. All genetic abnormalities are a result of reduced expression of the UBE3A gene. The five mechanisms were described. Statistically, individuals who are deletion positive may have greater problems with motor skills, communication and epilepsy as several genes may be affected but there are individually wide variations in presentation across the different classes. Development = maturation + experience so we don't regard atypical development as 'incomplete' or 'slow' but rather as 'alternative' development which very often is less functional. The difficulty in AS can be from a lack of filtering, so there is impaired information processing. The possibilities for learning in AS persist for a long time especially as adolescents and adults when they tend to be less overactive. In some ways, individuals with AS have exceptional visual perception, eg knowing how to scan a room but they often have a squint or low vision caused by not being able to focus with both eyes.

Communication People with AS have communication skills but they are less functional. They want to communicate and we need to be open to these communication avenues. Sophisticated electronic devices may be appropriate for some but are not necessarily better than pictures or invented signs. People with AS want to be looked at.
Sleep Usually reduced total sleep time, increased sleep onset latency (they need to relax and let themselves go) and a disrupted sleep architecture-frequent awakenings, reduced REM sleep, leg movements. However there seems no significant interference with daytime alertness... Professsor Dan then answered questions relating to epilepsy and non-convulsive status epilepticus, tremor and mouse models used in research.

2. Introduction to Conductive Education and Communication presented by **Laura Jones**, Teacher Conductor. Every child can learn and it is a problem of teaching if they can't. Conductive Education (CE) is holistic covering every area of development as well as comprehensive. CE views motor disorders as a learning problem. The *key principles* comprise: a. belief in human potential and open expectation—pedagogic optimism; b. the primary goal is 'orthofunction' - developing a 'can do' attitude and teaching the ability to cope, adapt and be spontaneous; c. CE is a comprehensive, complex and unified system of teaching; d. Learning occurs in groups as learning is a social process; e. Active learning (links to Piaget and Vygotsky)—CE seeks ways to help the child be more actively engaged in their tasks and f. A whole life approach, an ongoing intervention.
Key Issues for learning associated with AS include movement issues such as: ataxic gait and limb tremor with flexed arm position; stability and balance; weight bearing and weight shift; asymmetry; gravity; fatigue; 'hypermotoric behaviours' or associated reactions. Other key issues are sensory processing difficulties, motor planning difficulties, complex communication, social and emotional needs and medical/health issues.

3. **Dr Ellie Smith** presented her Summary of Dr Weeber's talks from his visit to Australia in July 2009. She said AS is the second human cognitive disorder in which a genetic rescue with a mouse model has been achieved. Neurofibramatosis is the other. The gene responsible for AS, UBE3A, was discovered in 1997. In mice, expression of the UBE3A is in the hippocampus and cerebellum. It is not important in the cortex. (Ref: Jiang Neuron 1999) In human brains, the hippocampus (responsible for memory) is very small in area proportionally compared to its big proportion in a mouse brain. The cerebellum is responsible for balance and gait. The nerve cell (neuron) has a very different shape compared with normal cells. In a three year old brain there are 100 billion neurons and 10^{16} synapses. Dr Weeber is interested in the long term potentiation or spread of the nerve impulse across the synapses. He says the mouse model is good for studying learning and memory because we know all of the genes (it is fully sequenced), the genes are easy to manipulate, the genes are conserved (= to humans) and the genes are made of the same types of proteins (may be structural, enzyme or housekeeping). There are now huge numbers of mouse models. Dr Weeber showed the ways of testing mice comparing AS mice with wild type mice. They include: a) rotorod for motor co-ordination and balance; b) fear conditioning—the more memory the mouse has the more it will 'freeze' in the conditioning chamber; c) water maze to demonstrate spatial learning memory and d) electrophysiology—looking at spike and waves after a shock to see the electrical response in pre and post-synaptic long term potentiation. A slice of hippocampus is taken and given a shock to look

at responses. The shock can be varied and pre-treatments can be given. An overview of the genetics behind AS covering testing and the five classes of AS was provided. The ubiquitination process was described. Dr Weeber says the UBE3A gene codes for a house-keeping protein called ubiquitin ligase which is an enzyme that targets other proteins that have ceased to function properly and need to be recycled. Dr Weeber said the expression of UBE3A is in the cerebellum and cortex in the mouse but humans have the expression in the whole brain. Dr Weeber performed plasticity testing and found the more pre-synaptic input given, the greater the output. His team decided to look at particular enzymes to do with learning and memory. One of them is CAMK11 which is very important at the synapse, very sensitive to calcium, can be inactive, active or very active. Dr Weeber was able to make a 'double mutant mouse' which showed improvement.

In conclusion, Dr Weeber says that CAMK11 appears to be the end point of UBE3A loss. This is not produced until after birth in the mouse so AS is not necessarily developmental—it is not an abnormal structure of the brain but abnormal biochemical processes important for learning (plasticity, long-term potentiation) disrupt normal synaptic communication. Dr Ellie Smith says that not all genes are expressed when you are born - they are there but the expression gets developed later, for example with adult haemoglobin. There is potential for treatment such as by putting the gene back in eg transfect with adenovirus, target all areas affected by UBE3A and turn on the paternal genome. Ellie said that going from research to therapy is usually a very long process even if this work is validated as submissions must be made and clinical trials performed.

In terms of AS therapeutics currently, there has been some success with melatonin, but no success with folic acid. Levodopa /carbidopa has been used for movement disorder and Reelin (a neuromodulator) helps potentiation against synapse meaning that it helps information travel across the synapse- the more input to the synapses the better. Ellie thinks stem cells could offer some potential to work on. She said that imprinting is there for a purpose, not random. It may be to stop a foetus from getting too big. Ellie said that in the human, other parts of the brain (such as the cortex) are involved with learning and memory. It is not just the hippocampus.

Newsletter by email

If you would like your newsletter emailed (PDF format) to you instead of being posted send a note to Leticia Grant at secretary@angelmanwa.com.au requesting that your future newsletters be emailed to you. This is not only cheaper for the association but faster for our secretary who volunteers her time while, like us all, juggling work, family and life with an angel.
Editor

National Disability Insurance Scheme News

26 Nov 2009

Speaking at the National Disability Awards on Monday night, the Prime Minister announced the Productivity Commission will conduct an inquiry into a national care and support scheme for people with a disability and their families. Assisted by an expert panel, the Commission will examine the feasibility, cost and benefits of replacing the current disability service system with a new national no fault scheme providing long term essential care and support to people with a disability and their families. The inquiry will examine options for the scheme and how it would fit with Australia's existing health, aged care, income support and injury insurance systems. The Commission will report to government in 2011. It is important that the study takes the time to examine all the details fully and gets the answers right. For mre information go to http://www.ndis.org.au

BOOK OFFER!

MacKeith Press, the publishers of Professor Bernard Dan's book, Angelman Syndrome (2008) have made a special offer for parents and families wishing to purchase this book. Please contact Leonora Paasche, Editorial Assistant—Leonora@mackeith.co.uk or www.mackeith.co.uk to buy the book for half-price. (37.50 English pounds). Alternatively, contact Sally Shackcloth.

Father and son smile every step of the way.

By Ewa Kretowicz, Canberra Times
14 September 2009

Keith Bradley crossed the finish line of the 10 km fun run in about 55 minutes, all the while pushing his 68 kg disabled son Callum in a specially built three-wheel pushchair. The 57-year-old's fastest finish was in 1979 when he came in second.

"Callum loves it, but he keeps getting heavier every year. As you get older it hurts a bit more, but when I found out he loved it, well, it was an extra incentive to keep doing it," Mr Bradley said.

"My son can't talk but he was making happy noises and everyone was parting like the Red Sea to let us through...everyone was very kind and encouraging."

Mr Bradley has been a board member of the Heart Foundation since 1981 and said the fun run was a wonderful community event. "I know how important it is to make exercise a part of your day. The incentive of the fun run makes it better."

He first pushed Callum in the fun run when Callum was just six years old.

"Two years ago, as I started the King's Avenue bridge—Callum was 16 and weighed about 45 kg—the steward said, 'You're the first push chair'.

Then about 200 m from the end, a woman-a mother pushing a baby pram with small baby in it—passed me by. I said to her, 'My baby is bigger than your baby,'....She laughed."

He said the spirit of the Canberra community was a wonderful thing on fun run day.

"But I think I've reached my maximum handicap. I hope my son doesn't grow any bigger."

From the Lilydale and Yarra Valley Leader 30 Nov 2009

Montrose mum heads to US to fight for son

Billy, 4, thanks Healesville artist Rex James, who donated his painting Turtle Tales to support Angelman syndrome research.STEVE TANNER N23LE201

A MONTROSE mum is on her way to the United States as part of an effort to set up the first Angelman syndrome research foundation in Australia.

Jo Davis, mother of four-year-old Billy who has the neuro-developmental condition, will attend the Foundation for Angelman Syndrome Therapeutics charity gala ball in Chicago later this week..“The aim of this is twofold: one is to raise awareness about Angelman in Australia and to help support research,” Ms Davis said.“The other reason is that we want to establish a foundation in Australia. Essentially it would be the Australian chapter of FAST, but all the money raised would stay here and support research here.”While there are some Australian support groups, there has been little local research into potential treatments for the genetic condition, which affects balance and speech and is often associated with seizure disorder. “Already, in the US, researchers have identified a protein associated with Angelman, and they are now hoping to find a way to replace that protein and treat the condition,” Ms Davis said. She said she hoped the localised foundation would also spread awareness about the condition. “Most people with Angelman don’t start walking until between four or six, but about 10 per cent will never walk. Billy has started walking, but he had a really bad lot of seizures last month, which has slowed his progress,” she said..

Ms Davis said she would organise local fundraising events in 2010. As part of the Chicago gala, which will be attended by Hollywood actor Colin Farrell, a father of a child with Angelman, Ms Davis will be entering a painting donated by Healesville artist Rex James (and an Australian timber cheeseboard set donated by the ASA of WA Editor’s note) into the silent auction.For information about Angelman syndrome, visit cureangelman.org or billythestory.com

Girl in a Tent

Nicole sleeps every night in a tent. No—we don’t put her in the backyard! When Nicole got too big for her cot, we faced the dilemma of how to keep her safe at night. We didn’t want her wandering about the house but preferred not to shut her bedroom door. For us the answer was a 3-man tent, and we put a padlock on the zip each night (leaving the key in the lock for quick access if needed). Underneath the tent are foam sleeping mats, and some blankets and quilts are layered on the base of the tent to weigh it down and provide a comfortable bed for sleeping. Each night Nicole is quite happy to get into her special bed. All sides are mainly fly-screen so she can see out. The base of the tent is 1.5mx2.1m with a self-supporting crossframe so no ropes or pegs required. It came with a fly-sheet that’s not needed inside and would reduce ventilation. We have been on several holidays including a 6 week trip with our tent. We stayed mainly In motels and an apartment on the Gold Coast. When booking ahead etc. we say we have a disabled daughter who needs a special bed that we bring with us, and enquire if there is enough spare room on the floor. This has worked well and Nicole is quite happy to curl up in her own bed on holidays. Heather James (SA)

PRESIDENT'S REPORT

Welcome to our final newsletter for 2009.Thanks to our new editor Sally Shackcloth who has agreed to take on this role as Kerri Monaghan steps down for a break. I have been re-elected as National President for another term and together with our new committee hope to work on some improvements and projects for our association over the coming 12 months. I wish to acknowledge the hard work of our outgoing treasurer, Robert Church, who has resigned after 7 years of performing this role. He has maintained financial records on behalf of both the National & NSW branch of the Association with diligence and honesty and deserves a well earned break now having served so long in this position. In addition, I would like to acknowledge the tireless efforts of the committee both past and present, who work behind the scenes whilst juggling family life, work and other responsibilities. I thank them for their ongoing support.

The national committee will continue to hold internet meetings several times a year where issues are discussed and decisions are made on behalf of our members. If you have any issues or concerns to raise- please don't hesitate to contact your state Vice President to raise these on your behalf. During this past year several states have developed their own Associations and websites, such as Queensland Angelman Association and Angelman Syndrome Association of WA. These will hopefully offer further assistance and support to families who reside in these states.

On behalf of all our members, I extend a big thank you to the conference committee in WA who have excelled by organizing a fantastic conference in Perth in October, which was well attended and highly successful and professional!

Congratulations!

Finally I wish to take this opportunity to wish you all a safe and happy Christmas break and happy, healthy new year!

Regards Anne Funke

Victorian Family Picnic Day

Where? Becketts Park, Parring Rd, Balwyn

When? Sunday 14 February 12 am

BYO picnic lunch and drink, picnic blankets and chairs etc.

Angelman Syndrome Association Victorian Branch ph(03) 977 97600 or heyjod@gmail.com

Angelman Syndrome Association Committee:

President: Anne Funke

Vice-Presidents:

Karina Harris (NSW),Jo Davis (Vic) Sally Shackcloth (Tas), Heather James (SA), Kellie Wild (WA), Alison Bennett-Roberts (Qld) Dave Hall (ACT)

Secretary: Leticia Grant

Treasurer: Kevin Kennedy

Committee: Liz Stanley (WA) Lysandra Warren (WA) John Hannaford (Qld) Kerri Monaghan (SA) Fiona Lawton (Qld)

WA Family Picnic Day

Where? 17 Kishorn Rd Applecross

When? Sunday 17 January 11am-3 pm

BYO Picnic lunch, soft drinks & Angel-friendly activities provided. Ph. 9315 2636 or secretary@angelmanwa.com.au

Correspondence to:
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Newsletter articles to -
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