Brain Matters

NEWS FROM THE FLOREY INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH

PROFESSOR GRAEME JACKSON AND RACHEL VELLA

Life-changing epilepsy surgery

SCHIZOPHRENIA
Florey researchers talk about prevention and better treatments (see pages 4 & 5)
**Mourning Aaliyah**

We, the Florey community, send our thoughts to the family of baby Aaliyah Meehan, who died in May. Aaliyah was a patient of Professor Ingrid Scheffer, a senior principal research fellow at the Florey and paediatric neurologist at Austin Health.

Aaliyah was the beloved daughter of Romina and Justin Meehan and sister of Jabe, 4. In her short life, Aaliyah lived with a rare and severe form of epilepsy caused by a defective sodium channel gene known as SCN2A. Her small body was simply unable to cope with the number of epileptic seizures occurring often many times per day.

“...I knew there was a problem when she had her first seizure when she was eight hours old,” says Romina. Neurologist Dr Lindsay Smith cared for Aaliyah throughout her journey. “We first heard of Ingrid Scheffer when we were asked if we would like to participate in some research. Of course, we agreed and gave blood.”

Neither Romina nor Justin carry the defective gene. Aaliyah’s problem was simply the result of bad luck – a new abnormality in her SCN2A gene.

As Aaliyah grew, the seizures were relatively well controlled by medication but at 18 months, it became clear she was losing skills. She lost interest in eating as the seizures became increasingly frequent. “We were just hanging on, hoping she would get better. I think I was a bit delirious, hoping she’d recover.” Sadly, Aaliyah died while sleeping between her parents, at home and with her brother asleep in the next room.

A few weeks later and the family is surrounded by loving family, friends and kinder teachers who are taking special care of Jabe.

“I feel as though Aaliyah was just waiting to meet Ingrid, to receive her help and to give us the support to perhaps have another child one day,” Romina and Justin are determined to keep Aaliyah’s memory alive and to help other families avoid the sort of heartache they have endured. The Aaliyah Fund will help Ingrid and her research team to investigate this horrible disease – with the ultimate aim of preventing it from affecting other families.

If you would like to donate to the Florey’s Aaliyah Fund here are the bank details for a direct deposit – BSB 083 170 account 8743 08161 or visit florey.edu.au and hit the donate button on the home page.

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**Professor Scheffer honoured**

The Florey would like to congratulate Professor Ingrid Scheffer who has been recognised in the Queen’s Birthday Honours with an Officer (AO) of the Order of Australia.

Together with colleagues including Professor Sam Berkovic AC, Ingrid’s research has helped uncover several genes responsible for epilepsy. Her energy is particularly focussed on the serious and debilitating epilepsies. “It means patients all over the world can be diagnosed and their doctors can investigate for genetic abnormalities,” Ingrid says. “We describe these new diseases, figure out the causes of devastating disorders of the brain, as well as ways to prevent or cure them. Florey neurologists, Professor Ingrid Scheffer and Professor Graeme Jackson, provide inspiration on these pages as we connect. We want to discover the immune system’s response to disease, to our thoughts, dreams and imagination. From the human genome project, this research area of “connectomics” allows pinpoint accuracy and isolation of the seizure centre, far left. The third image shows a PET scan with low blood supply in the area until a seizure begins when the blood flow increases (far right).

Despite the risk, Rachel decided to take a punt to be the beneficiary of the Florey’s world-first imaging techniques developed by Graeme, PhD student Mangor Pederson and Professor Alan Connelly and his team. The researchers were confident they had “boosted” the power of the MRI, finding previously “invisible” epilepsy centres. The technique has been hailed as a game-changer and allows precise and minimal intervention during surgery.

Rachel went under the scalp of experienced surgeon, Professor Gavin Fabinyi from Austin Health. The team of neurologists searched for the abnormality in her brain, guided by images that led them through the veins, folds and valleys of brain tissue.

Eventually, a tiny sliver of tissue was removed from Rachel’s brain from just above the ear, an abnormality known as the Bottom of Sulci, Dysplasia. In recovery, the team held its collective breath until Rachel awoke and spoke quietly but clearly.

“Talking too much” to its local environment. After four years of nightly seizures from epilepsy, Rachel Vella, 18, decided she had endured enough.

“I hope my story encourages other people with epilepsy to feel brave and to realise there is help available.”

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**World-first imaging - a brave teenager takes a punt**

Rachel dared to proceed with an operation that would remove part of her brain. There were several risks associated with the procedure and these were carefully described to her by Florey neurologist, Professor Graeme Jackson. Graeme was able to tell Rachel exactly where the seizures were coming from. He had high-resolution images from the Florey’s MRI machine – images that offered better clarity than any before. These images told him the seizures were originating from Rachel’s language centre. Surgery could result in a loss of speech – and there was the risk of a stroke during the procedure.

Professor Graeme Jackson and Rachel Vella, post-surgery.
Schizophrenia

Professor Brian Dean and his team of researchers are taking a wide-ranging approach to the treatment of schizophrenia. Here, we investigate several areas offering hope.

Schizophrenia directly affects about 15 out of every 1000 Australians – that’s approximately 345,000 people. This figure balloons when you include their families, friends, colleagues and carers.

What’s clear from talking to families is that even when people recover from the condition, and about 20 per cent do spontaneously, the experience changes their basic personality forever. This is likely to be due to subtle brain chemistry changes, and is one of several areas Professor Brian Dean and his group have been working on for many years.

Schizophrenia is not one condition, but a collection of syndromes. Most people are familiar with the obvious symptom: visual and aural hallucinations. These are called ‘positive’ symptoms, because they ‘add on’ to your personality. Less well known are the ‘negative’ personality and cognitive effects for sufferers. Negative symptoms ‘take away’ from someone’s personality, so that emotions are deadened and people don’t experience the same pleasure they used to. Cognitive effects include the inability to plan and think ahead, stick to a schedule or modulate appropriate interpersonal behaviours – like talking too loudly at a very close distance.

The brain’s cognition systems are driven by a number of molecular signaling systems. One of the main systems is called the cholinergic system, in which a signal, acetylcholine, binds to its receptor to tell a brain cell to fire. Cognition is critically important, so Brian and his team have focused their research in this area. Several years ago the team showed that about 25 per cent of sufferers had a 75 per cent decrease in the level of their receptors for acetylcholine. Lower levels of the receptors not only mean that sufferers had a 75 per cent decrease in the level of their receptors for acetylcholine, but patients with two copies of the gene mutation perform less well on cognitive tests, indicating that the mutation disrupts the receptor’s function. If the team can discover a method to restore function to the receptor, patients may recover some cognitive ability.

Finally, Brian’s team aims to identify the environmental factors that are absolutely required for people to develop full-blown schizophrenia. Foetal stress during the third trimester of pregnancy seems to be important – perhaps the mother catches influenza or suffers severe stress, but the exact causes and mechanisms remain a mystery. Similarly, there is no definitive way yet to actually diagnose someone as being ‘schizophrenic’. Clinicians are very good at doing so once someone presents at the hospital, but Brian’s team hopes to develop a diagnostic kit that examines the chemical signature in blood to tell if someone has the disease and possibly which type. If a doctor had some warning, they could help the patient by introducing them to cognitive behavioural therapy, art or music therapy, all of which have been shown to be effective in treating schizophrenic symptoms.

There is a long road ahead for the researchers trying to combat this terrible condition, but new technologies such as PET imaging, genomic sequencing and gene association studies, and large scale biochemical analyses are giving hope to scientists, and the schizophrenia community.

The team is now developing, in conjunction with Professor Chris Rowe at Austin Health, a method to image receptor levels in living patients using PET scanning. This will mean that a patient’s current treatment regime can be taken into account when analysing the results of imaging studies, and paves the way for a measurable outcome when patients are given new therapeutic drugs.

The team has made another exciting finding. Some patients have a mutation in the gene that codes for one particular type of brain cell receptor. This mutation doesn’t appear to affect the levels of the receptor in the brain, but patients with two copies of the gene mutation perform less well on cognitive tests, indicating that the mutation disrupts the receptor’s function. If the team can discover a method to restore function to the receptor, patients may recover some cognitive ability.

Dr Rachel Hill and her research team have found that a brain-derived growth factor plays a key role in cognition and in brain development during the adolescent years.

A specific growth factor, a protein that helps cells grow, is thought to be disrupted in some young people during important development periods. This leads to altered brain development and behavioural abnormalities. Worryingly, the changes occur in a part of the brain which we know stops working properly in those living with schizophrenia.

“The growth factor has been shown to be low in post-mortem brain tissue of schizophrenia patients,” says Rachel.

Schizophrenia is a severely debilitating disorder which leads to a lifetime of disability and distress for individuals and their families. It’s considered a neurodevelopmental disorder and usually first appears during late adolescence.

Although many people living with schizophrenia first go to hospital in their early to mid-20s, symptoms may be noticed for a long time before they are identified as needing medical care. Several studies have found that structural changes in brain circuitry involved in schizophrenia may begin several years earlier. “Indeed, when compared to unaffected siblings or school mates, schizophrenia sufferers tended to exhibit poorer motor skills, a lower IQ and a generally lower academic performance in school,” Rachel says.

“Learning and memory deficits may start to develop during adolescence – well before the onset of the first episode.”

Our capacity to learn and remember are crucial skills, especially when integrating with the community or holding down a job.

Only 20 per cent of patients with schizophrenia find employment and job tenure, with schizophrenia patients faring much worse in the workforce than patients with other mental disorders.

“It can also lead to poor medication compliance and the likelihood of relapse.”

Sadly, there is no current treatment that significantly improves cognitive ability in schizophrenia patients.

The Florey’s latest research focuses on the role of the growth factor, known as brain derived neurotrophic factor, in specific brain regions during adolescent development.

If we can identify why the growth factor is disrupted during adolescence, we may be able to prevent – or at least delay – these disruptions by intervening early. This may represent an exciting new preventative therapeutic approach.

Intriguingly, a naturally-occurring compound has been discovered which activates the same signaling pathways as the growth factor, making it an unlikely but possible drug therapy.

Prevention – by offering a drug to ensure the growth factor is present – is a promising option given the problems with current drug options and side-effects given to people once the disease has taken hold.

“We’re a long way from a drug therapy of this type but we’re working tirelessly to exploit this idea for all it’s worth.”
One of our greatest successes is our research into how our brains influence our immune system. This research is yielding fascinating results.

We have identified that the brain can influence our immune system by releasing cytokines and neurotrophic factors. These factors can affect immune cell differentiation and activation, impacting immune responses. This cross-talk between the nervous and immune systems plays a crucial role in maintaining homeostasis and can be dysregulated in various diseases, such as autoimmune disorders and neurodegenerative diseases.

As new neurotransmitters are discovered, our understanding of their functions continues to evolve. This highlights the complexity of the brain-immune interface and the importance of ongoing research in this field.

We are committed to supporting our researchers in their pursuit of innovative and impactful discoveries. Together, we are pushing the boundaries of knowledge and making significant contributions to advancing our understanding of the brain-immune relationship.

This exciting research area offers endless opportunities for collaboration, translation, and translation. By investing in our researchers, we are equipping them with the tools and resources needed to unlock the secrets of how our brains influence our immune system and pave the way for future breakthroughs in medical treatments.

If you would like to support our research teams and continue to drive progress in this vital field, visit our website to learn more about the work we are doing and how you can contribute to our mission.

Thank you for your continued support, and let's work together to make a difference in the lives of those affected by neurological conditions.
The Florey Institute of Neuroscience and Mental Health invites you to this year’s Culinary Charity Challenge!

FRIDAY, 7pm
15 AUGUST 2014
BOOK VIA WWW.FLOREY.EDU.AU

Competing on the night will be teams led by Guillaume Brahimi, soon to open his new restaurant Guillaume’s in Paddington and Scott Pickett of Saint Crispin’s, voted best new restaurant in Melbourne in 2013.

The gala will be judged by a panel of elite chefs and noted food critics, once again chaired by Jacques Reymond - all in the name of raising money for vital research into diseases of the brain and mind.

While much of the emphasis in treatment of Parkinson’s disease is on prescribed medications, there are many important steps people can take to reduce its impact on their lives.

Proudly supported by Parkinson’s Victoria and the Florey.

The lecture will be recorded and posted on our website for those unable to attend.

City2Sea
Planning to get fit for summer?

Then join us for The Sunday Age City2Sea – a 5km or 14km running event.

When: Sunday, November 16

Sign up at www.thecity2sea.com.au or call Jane for more information on 03 8344 1824.

If you want to help find a cure for Alzheimer’s disease, join the Albert Park Rotary Club team or if interested in running for mental illness research, join the One in Five team.

Special thanks to our partners