

Neuroscience: What's the difference?

Mary Hayek, Clinical Operations Manager



"Neuroscience is the last frontier of medical research and its been something of a mystery package until recently. But the breakthrough came with imaging in the 1980s and that led to an incredible explosion in knowledge and therapy."

Geoff Donnan



Introducing The Florey

(Institute of Neuroscience and Mental Health)

The largest Brain research capability in the Southern Hemisphere and one of the world's top 10 Brain Research Centres.

We are world leaders in imaging technology, stroke rehabilitation and epidemiological studies.

An amalgamation of 4 Research Institutes united in finding cures for brain disease

- National Stroke Research Institute
 - Brain Research Institute
- Howard Florey Research Medical Institute
 - Mental Health Research Institute

Our state of the art facilities, over 3 campuses in Melbourne Australia, include platforms such as laboratories (including diagnostic laboratories for the assessment of amyloid and tau proteins), pre-clinical work, imaging facilities (MRI, PET) and translational research.

Parkville



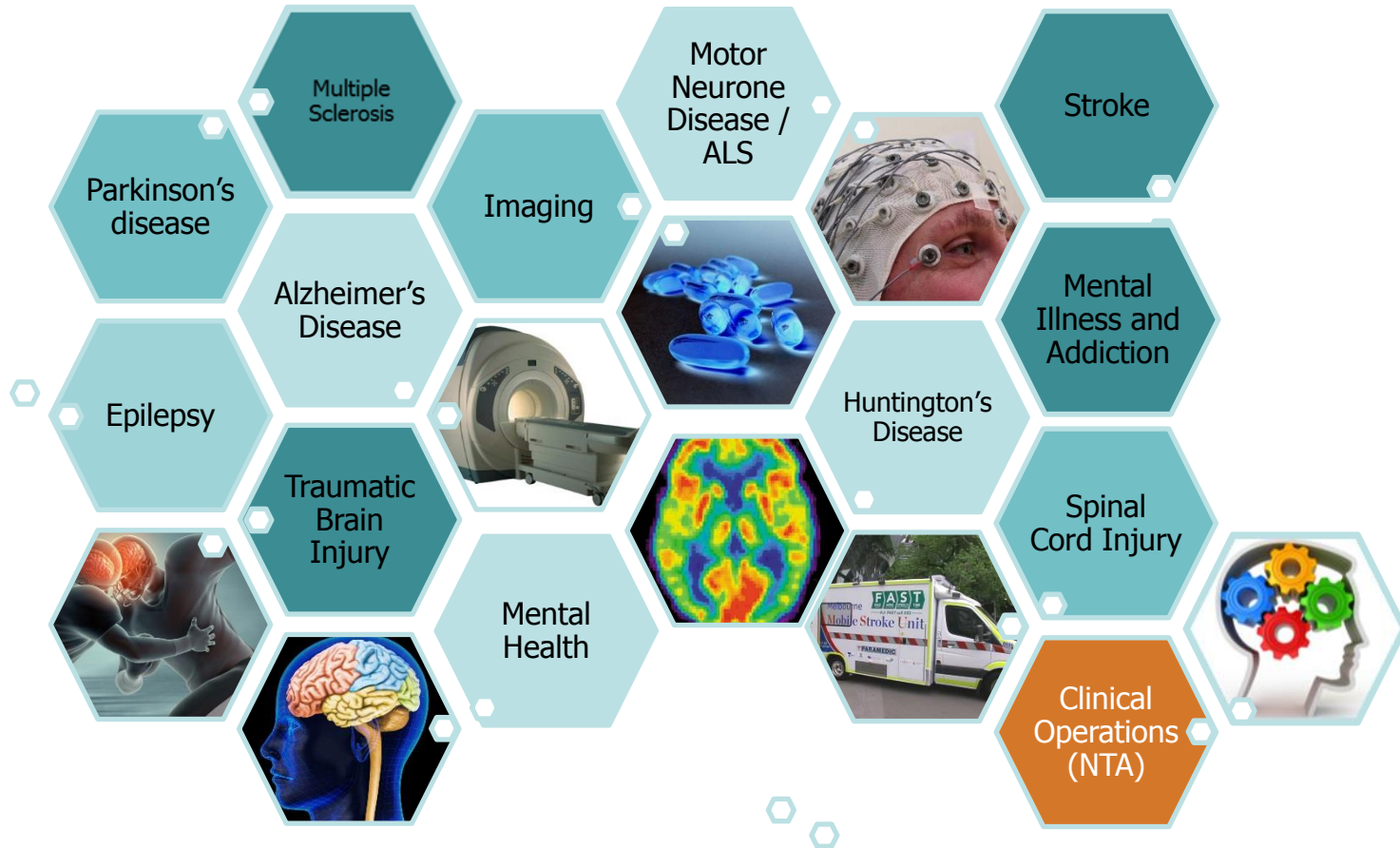
Heidelberg - Austin



Royal Melbourne Hospital



Florey Teams



NTA: Our place in the world

THINKING GLOBALLY,
WORKING LOCALLY.
INNOVATIVE NEUROSCIENCE RESEARCH

neuroscience trials australia

- ❑ Neuroscience Trials Australia (NTA), is a business within The Florey Institute of Neurosciences and Mental Health (<http://www.neurotrialsaustralia.com>)
- ❑ A niche, not-for-profit CRO
- ❑ A team of clinical research professionals with an average of 12 years experience (Pharma, Biotech and CRO experience across local and Global companies)
- ❑ Operating within markets and on projects that are both local and global, sponsored and investigator-led.
- ❑ **~75% of projects are Commercial**
- ❑ **~70% from overseas Clients**

Overview

NEUROLOGICAL DISEASES

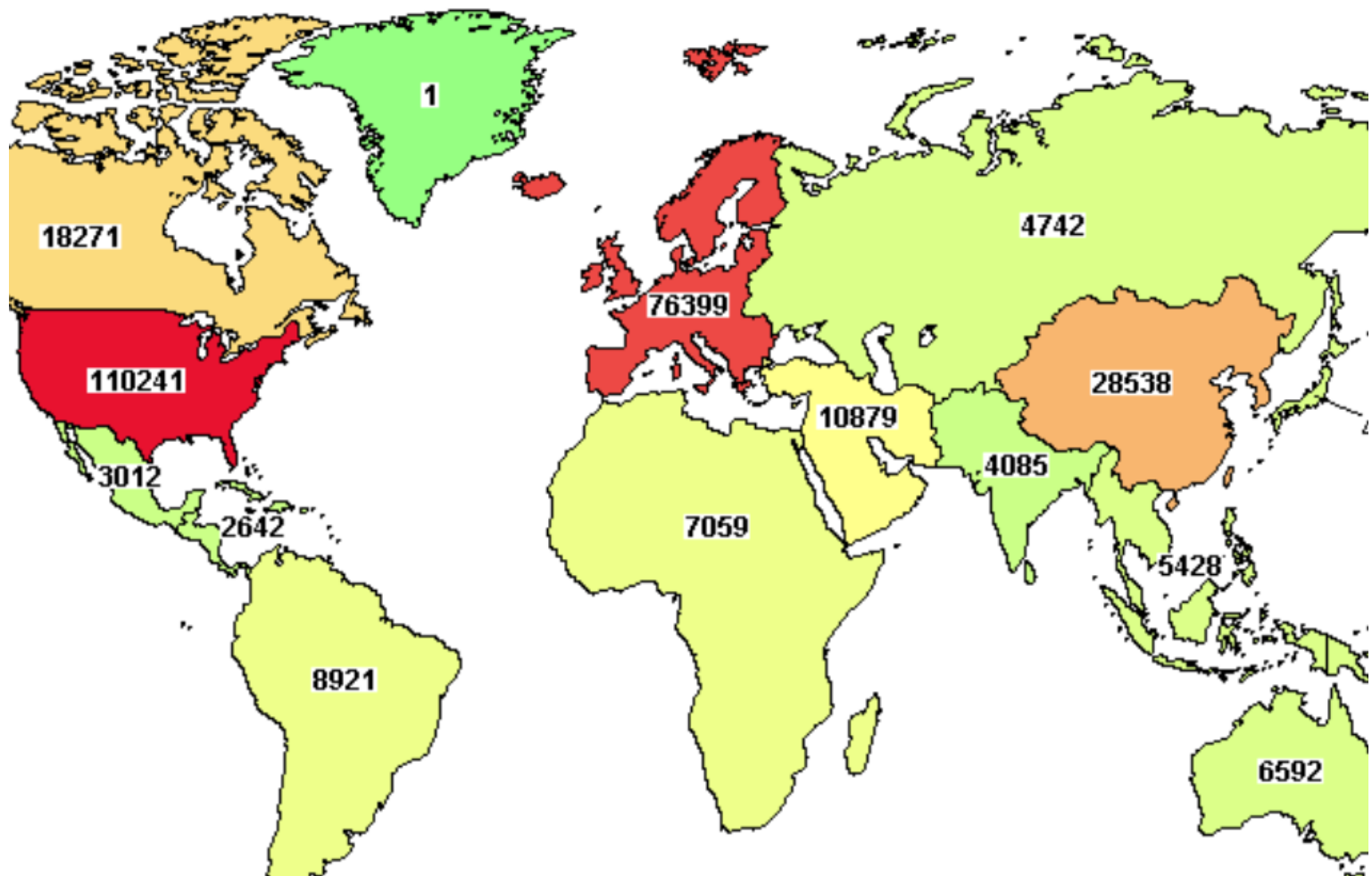


Neurological Diseases

- **100s millions of people worldwide are affected by neurological diseases**
- **Involves brain:** spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles
- **Specific causes of neurological problems vary, but can include:** genetic disorders, congenital abnormalities or disorders, infections, lifestyle or environmental health problems including malnutrition, and brain injury, spinal cord injury or nerve injury
- **Complex etiology**



Recruiting Clinical Trials



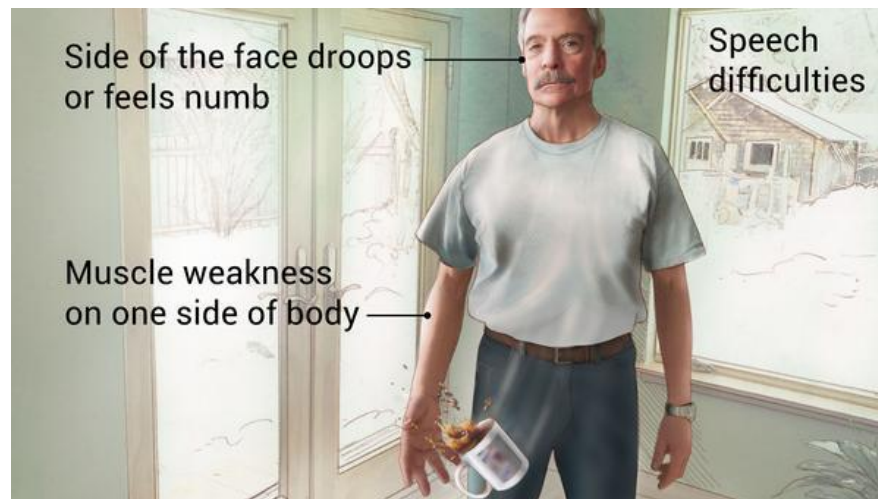
All recruiting clinical trials global total **57,904**₇

Recruiting Clinical Trials

Indication	Global	Australia
All	57 904	6592
Oncology	15 933	495
Depression	1143	12
Stroke	1140	18
Dementia	610	22
Schizophrenia	469	6
Parkinson's Disease	444	44
Alzheimer's Disease	422	19
Epilepsy	318	13
Spinal Cord Injury	302	3
Traumatic Brain Injury	291	2
MND / ALS	161	2

Stroke Today

- *More than 6 million die by stroke each year*
- In 2017 there were almost 56,000 new and recurrent strokes globally—that is one stroke every 9 min
- 65% of stroke survivors suffer a disability which impedes their ability to carry out daily living activities unassisted
- Strokes cost Australia an estimated \$5 billion each year





Stroke

Stroke Clinical Trial Challenges

- Early diagnosis and treatment
- Requirement for 24hr study staff to identify potential subjects
- Consenting to clinical trials – up to 8 information sheets available for 1 stroke study being conducted in Victoria
- Acute versus chronic treatment
- A new research trend is to combine treatment and rehabilitation requiring multidisciplinary teams

Stroke

- 1st Mobile Stroke Unit (MSU) in the Southern Hemisphere was launched in Melbourne November 2017.
- Crewed by stroke nurse, radiologist, 2 paramedics and a stroke neurologist.
- Allows patients to be diagnosed on location with immediate administration of time critical stroke therapy.
- 2 clinical trials utilizing the MSU.



Stroke



When it comes to a stroke,
TIME = BRAIN





Epilepsy

- More than 50 - 65 million people have epilepsy worldwide
- There are around 40 different types of epilepsy and epilepsy syndromes, many are not convulsive
- Seizures can vary from the briefest lapses of attention, confusion or unusual behaviours to severe and prolonged convulsions
- Seizures can also vary in frequency, from less than 1 per year to several per day or thousands per month.
- Cross therapeutic areas in same patient
- No known cure but in some instances can be controlled
- Most trials now focus on drug-resistant epilepsy (approx. 33% of patients)

Cerebral Therapeutics example



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Herald Sun, Melbourne

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World-first trial of treatment to beat epilepsy and other brain disorders

GIFT OF LIFE



BRIGID O'CONNELL

A WORLD-first trial will deliver medication directly into the brain of epilepsy patients to sidestep the devastating side-effects of tablets.

The pioneering treatment aims to be a game-changer for neurological conditions more widely by getting a drug directly where it is needed.

The St Vincent's Hospital team has implanted a pump in their first patient. The pump sends anti-epileptic medication from the stomach, through a tiny tube, into a cavity in the brain where it can diffuse into the areas causing the "electrical storm".

Natalie Kellalea's seizures are so severe and unpredictable that she cannot walk to the letterbox or take a

shower on her own. The 27-year-old from Numurkah has tried every combination of every anti-epileptic medication without success, and has been in hospital for almost the past three months for her own safety.

After the world-first surgery by neurosurgeons Michael Murphy and Kristian Bulluss to implant the device earlier this month, Ms Kellalea had the first medication, Epilim, administered this week through the pump.

If her violent drop seizures can be reduced to episodes of visual illusions, she hopes this will allow her to finally start a family with husband Alex.

"With the life I have now, I'm willing to try anything," Ms Kellalea

(above) told the Herald Sun.
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- World first drug and device trial
- Therapy is the combination of a complex precise medication delivery pump which administers a reformulation pharmaceutical delivered through a catheter implanted directly into the fluid around the brain
- Project team includes Project Manager, Clinical Research Associate and Clinical Field Engineer, , Neurosurgeons, Neurologists, Study Coordinators, Blinded raters

Parkinson's Disease

- Affects 80, 000 Australians
- Mainly affects people older than 50 with 1 in 5 patients being under 50
- Progressive disease that impacts movement and causes stiffness and tremors
- No definitive diagnostic blood test or scan
- Drugs versus devices: e.g Global Kinetics corporation



Parkinson's Disease



EXCLUSIVE Melbourne surgeons inject stem cells into man's head in world-first Parkinson's trial

BRAIN REBOOT

3D RECREATION OF PATIENT'S SKULL

STEM cells have been injected into the brain of a Victorian patient as part of a world-first trial to treat Parkinson's disease.

In experimental surgery, Royal Melbourne Hospital neuroscientists transplanted millions of cells at 14 injection sites via just two 1.5cm holes in the skull.

The cells, which can metamorphose into brain cells, had been

LUCIE VAN DEN BERG

frozen and flown in from the United States, in a global collaboration. It is hoped the cells will boost levels of the neurotransmitter dopamine, a lack of which causes tremors, rigidity and slowness.

The therapy, which pushes the frontiers of science and surgery, had shown great promise in pre-

clinical trials, paving the way for human trials.

The identity of the patient, 64, remains private while he recovers from the pioneering surgery.

Months of planning, which involved designing the operation from scratch, winning regulatory approval, and importing a machine that has never been used in Australia, was required.

Using a three-dimensional model of the patient's brain, neurologist Andrew Evans and neurosurgeon Girish Nair spent weeks doing "dummy runs", devising a way to enter the brain.

Hospital staff donated their time for the eight-hour operation.

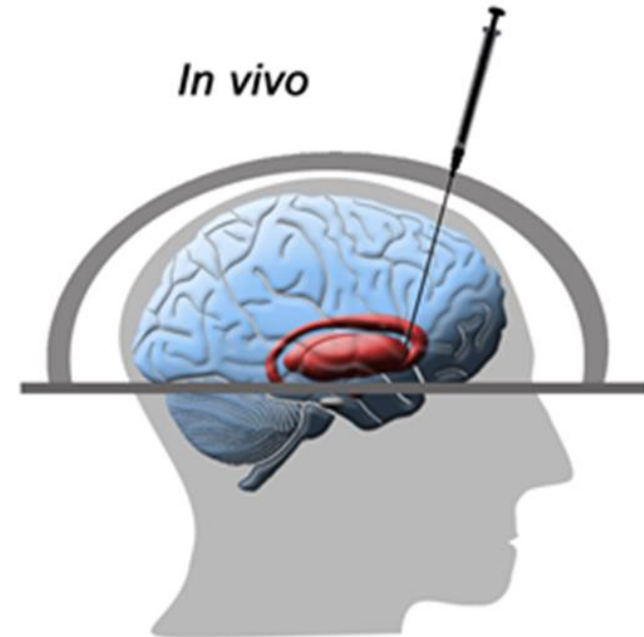
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Source: Herald Sun, 14 September, 2016

Parkinson's Disease

- CTX
- 2 meetings with TGA and 2 with HREC prior to approval with ongoing safety reporting.
- Required the use of experimental devices in combination with experimental treatment
- Extensive team training
- Surgical planning in a public hospital







Motor Neurone Disease / Amyotrophic Lateral Sclerosis

- Progressive terminal neurological disease
- In Australia 2 people are diagnosed and 2 people die each day
- Affects more males than females
- Identification of genetic factors that cause or predispose people to MND is progressing steadily with 10% case now known to be familial
- No cure



AFL legend Neale Daniher reveals his private battle with deadly motor neurone disease: 'There's no prevention. No treatment. No cure'



**FIGHT
MND.**
IT TAKES PEOPLE

- **\$\$ for you project**
- **Access to clinics and patients**

Motor Neurone Disease / Amyotrophic Lateral Sclerosis

- 3 years ago, no clinical trials available.
- Now, 6 trials in various stages available in Australia
- 2 approved drugs globally.



Neurosciences Clinical Trials



<https://goo.gl/images/HR4Hai>



Neurosciences

- Progressive disease for ongoing assessments and site attendance (patient / caregiver)
- Standardising data capture for patient reported outcomes
- Access to central imaging and novel tracers
- Cross therapeutic area KOLs
- Consenting
- Identifying equipment, laboratories, rating scales to support the study



Operational

- Complex skill sets
- Challenges associated with new technology
- Investigational Product logistics
- Adapting changes to studies with new learnings
- Changes can slow clinical trial programs
- Managing expectations of Sponsors, sites and patients
- Availability of intervention post trial



Recruitment via Neuroscience Clinical Trial Networks

- **Australasian Stroke Trials Network (ASTN)** 
- **AC4R** 
- **MS Research Australia** 
- **Movement Disorders Society of Australia (MDSA)** 
- **Australian Epilepsy Clinical Trial Network (AECTN)** 
- **Neurosurgical Society of Australia** 
- **Australasian Neuromuscular I** 
- **Australian Pain Society** 
- **Headache Australia** 
- **Spinal Research Institute** 
- **The Florey Institute of Neuroscience and Mental Health** 



Stakeholders



New Legislation

Guardianship & Administration Act 1986 (Vic)



Effective 12 March, 2018

Provision of medical research procedures to patient without decision-making capacity (Changes include VSM, consent...)

Medical Treatment Planning and Decision Act 2016 (Vic)

What does this mean for trials in neurology?

Mild Cognitive impairment:

- i. Mild
- ii. Moderate
- iii. Severe

Most of the NTA projects are within the first 2 categories however...



New Legislation

Advance Care Directives (ACD)

- Focus has moved from best interests - > personal preferences
- If progressive illness:
 - Would likely make binding ACD which need to be taken into account by the *Medical Treatment Decision Maker (formerly Person Responsible)* and *Medical Practitioner*
 - MTDM needs to be someone in a close and continuing relationship with the patient
- In the process of consulting with PIs and KOLs for their process for locating the ACD as is required in the VSM



New Legislation Impact

Implementation of the MTPD Act (2016)

- ✓ Revision of consents
- ✓ PR -> MTDM
 - New participants -> MTDM consent
 - Talking to KOLs and PIs about implementation of the new Act (VSM offers guidance)
 - Two scenarios:
 - 1) In clinic and progressive illness, request an ACD be considered
 - 2) Emergency Department:
 - i. Administering a medical consent procedure (tricky)
 - ii. What if there is no MTDM?
 - iii. Mild to moderate: Short form consent, continuation consent and consent following Procedural Authorisation (changed)

Thank you



neuroscience trials australia