

Modifiable lifestyle factors in MS Workshopping the next steps

MS Research Australia recently held a workshop on modifiable lifestyle factors in MS, with delegates attending from around the world and representing a large variety of research disciplines and people with MS.

The Research Priorities survey conducted in 2016 confirmed this as a theme of strong interest. It is an area that people with MS can control themselves to help manage and potentially minimise the impact of MS on their lives, providing a sense of empowerment and hope.

While much is already known about the role of lifestyle factors in the risk of developing MS, this workshop focussed on whether lifestyle factors could impact progression and disease course in MS. The workshop aimed to discuss the current evidence for the effect of modifiable lifestyle factors on MS, determine the knowledge gaps and identify priorities and opportunities for both further research to strengthen the evidence and the best way to design this type of research for the most meaningful outcomes. A key aim of the workshop was also to identify opportunities to translate and implement the current evidence to provide the most appropriate advice to the MS community.

The workshop opened with a brief overview of the current evidence on the environmental risk factors that contribute to MS onset and progression and also included a presentation from Tara King about her personal MS journey and the positive lifestyle changes that she has made. She discussed the difference it has made to her and her thoughts on what the MS community are looking



for in the way of guidance and support to make positive lifestyle changes for themselves.

The first session covered the current evidence for the role of lifestyle factors such as diet and physical exercise in MS. While research in this area is difficult, studies have shown that a healthy diet and exercise is of benefit for quality of life and disease outcomes in MS. Delegates heard from Associate Professor Ingrid van der Mei, Menzies Institute of Medical Research TAS, about her research into lipids in MS and the influence that other health conditions (known as co-morbidities) can have on MS outcomes. Dr Lucinda Black, Curtin University WA, discussed the role of diet in MS and the

evidence that diets with higher levels of fruit and vegetables, less fat and sugar can improve outcomes such as disability and quality of life.

The second session covered ways that evidence of lifestyle factors had been implemented into the MS community and aimed to learn from similar initiatives in other diseases and in the general population. Ms Jodi Haartsen, from Eastern Health VIC, spoke about the Brain Health Initiative which aims to improve the understanding of people with MS on how they can keep their brains as healthy as possible and request the highest possible standard of care from healthcare professionals. Professor Mark Harris, University of NSW, described the

(continued next page...)



A WORD FROM OUR CHIEF EXECUTIVE OFFICER

The month of May and World MS Day was all about Multiple Sclerosis research.

Largely due to the incredible fundraisers and Ambassadors of the *Kiss Goodbye to MS* campaign, *Red Lab Coat Day* and the comprehensive range of social media activities designed to bring the research community firmly into the spotlight.

We brought you up close and personal with some of Australia's best and brightest MS researchers through a series of videos that captured a clear message of hope and commitment to solve this disease. The MS researcher profiles provided a glimpse into who they are and the *"Battle Of The Labs"* enabled the community to marvel at the diverse talent of our researcher community.

We were also delighted to have held a workshop focussed on how lifestyle factors can impact on the MS disease course and progression, with the thanks to a very generous corporate grant. The participants represented a wide variety of research specialties and MS community representatives and whilst a large number of topics were discussed it was encouraging to see the delegates come together to agree that a diet and exercise guideline needs to be developed to assist people living with MS as well as consensus on a clinical trial design.

As we head to the end of the financial year, I naturally encourage you to consider donating to MS Research Australia to help us continue to make a positive impact on the lives of people with MS. Together we can make real change. We are the only national, not-for-profit, MS-dedicated organisation committed to funding the best and brightest researchers to find better treatments, prevention and the cure for MS, and we need your help to continue the progress that has been made.

Dr Matthew Miles, CEO

Modifiable lifestyle factors in MS continued...

implementation of SNAP, which are guidelines for smoking, nutrition, alcohol and physical activity for use by general practitioners to help people manage general health and long term health conditions. Professor Kaarin Anstey from NeuRA, NSW, spoke about the successes and failures of implementation of lifestyle research outcomes in dementia.

The final session discussed different types of study design for lifestyle factors in MS, as this has a major impact on the quality of the conclusions that can be drawn from the research. In this session, Professor Anne-Louise Ponsonby, Murdoch Children's Research Institute VIC, spoke about her upcoming clinical trial which will investigate if specific supplements that support mitochondria (the energy powerplants of cells) could improve fatigue and depression in MS. Professor Terry Wahls, University of Iowa, USA spoke about her clinical trial design which will compare two specific diets, the Wahls Diet and the Swank Diet, on outcomes in MS, especially fatigue. Professor George Jelinek, University of Melbourne, VIC discussed research into lifestyle interventions that combine several aspects, such as nutrition, exercise, medications and stress reduction. This type of research can be very complex as many lifestyle factors are considered at once, providing additional challenges for study design. Dr Yvonne Learmonth from Murdoch University, WA spoke about the points to consider when designing research studies into physical activity in MS.

Following each session, time was set aside for in depth discussion on the many points raised, allowing all delegates to contribute their perspectives,

thoughts and expertise. Themes of the discussion included the strength of the current evidence for various modifiable lifestyle factors such as diets and exercise, as well as the best ways to improve this area of research and fill the gaps. The final discussion session aimed to draw together all the threads and themes that had been explored during the day, to arrive at some clear next steps to move the field forward.

One clear outcome was the imperative for MS professionals to develop communication materials to provide consistent guidance to people with MS based on the best-available evidence about modifiable lifestyle factors. Following the workshop, a working group will be convened to develop and produce these guidelines.

There was also much discussion of future research avenues. These included controlled clinical trials of interventions in MS that could compare people making changes to diet or exercise or both with others who did not make the changes or make smaller changes. Some of the simplest interventions would be to find ways to support people with MS to follow the current Australian Healthy Eating Guidelines and physical activity guidelines. Ultimately developing a framework for use in the MS clinic to identify what changes would be beneficial and achievable for individuals and assist them to stick with these changes in the long-term, to give them the best chance of success.

MS Research Australia considers it incredibly important to bring together the MS scientific community to discuss this important topic and believes the outcomes of the workshop will help people with MS to live as well as possible with their MS.



Prioritising the Panacea

It's unlikely I need to tell you how frustratingly unpredictable living with MS can be.

While we've made huge strides in the laboratories and can feel incredibly proud of our researchers in this country, time and again we hear those living with MS feel a sense of control when they can explore lifestyle factors that assist in managing the disease. It may be choosing to follow a certain dietary plan, taking up a form of physical exercise that better suits their symptoms or even committing to meditation to calm the nervous system.

The type of modifiable lifestyle factors to adopt has been a hot topic of debate for decades. The internet has made it easy for the newly diagnosed to find more information than ever; some of this information can be comforting but conversely, some can be confusing and misleading. Certainly, the positive effects of many modifiable lifestyle factors in treating MS is a tremendously under-estimated topic.

To set the scene for the debate, let's examine the pathway for getting a disease modifying therapy (DMT) to the patient.

In Australia, clinical trials must conform to the Ethical Principles of the Declaration of Helsinki and to international Good Clinical Practice guidelines. Before a trial can go ahead it needs to be approved by independent ethics committees that operate according to the guidelines issued by the National Health and Medical Research Council (NHMRC Guidelines).

The pathway for being able to recommend a certain diet or style of exercise should be a no-brainer. But it just isn't for the MS community.

In simple terms, the panel of speakers at the recent MS Research Australia Modifiable Lifestyles workshop asked themselves one overarching question; 'Can we alter the natural history of multiple sclerosis with non-drug factors?' In essence,

this is the role that modifiable lifestyle factors play in MS research.

Using the same clinical trial protocol as DMTs to provide evidence around the efficacy for modifiable lifestyle factors is logistically problematic. Take a trial for a particular diet; you would need to have a significant number of participants, each provided everything they would be allowed to consume – day in day out – in a controlled environment and then recorded for many years. It's not impossible but it's wildly impractical. The workshop discussed different trial methodologies to overcome

this 'wildly impractical' barrier. It facilitated good discussion about some ways we can look at generating strong and defensible evidence with different types of trial designs.

And does that matter? While it would be difficult for anyone to argue against the need for efficacy, I think there's a happy medium to be embraced, where people with MS consider the notion of using modifiable lifestyle factors to prioritise and obtain quality health rather than fighting disease.

So where to now?

In the interim to undertaking clinical trials for MS-approved modifiable lifestyle treatments, I think the research community would do well to develop a set of practical guidelines for healthy living for people with MS.

From a personal point of view, I believe language has a significant role to play in the adoption of lifestyle factors. In developing guidelines, careful and considered language and advice will set people living with MS on a path of well-informed options in striving for good health.

“Certainly the positive effects of many modifiable lifestyle factors in treating MS is a tremendously under-estimated topic.”



Jillian Kingsford Smith

@JillianKS, Journalist, Author,
MS Research Australia Writer in Residence
and Kiss Goodbye to MS Ambassador



Decoding MRIs

What are MRIs?

Most people with MS are very aware of MRI or Magnetic Resonance Imaging, often having regular MRIs to diagnosis and monitor their MS. Most people don't love them, but MRIs are a marvel of modern medicine, allowing us to visualise what is going on in the human body and a rare opportunity to peer beneath the skin.

MRIs use strong magnets and radiofrequency pulses to generate signals from the body. These signals are in turn detected by the machine and are processed by a computer to create pictures of the inside of our bodies.

How does MRIs work?

The human body is largely made of water molecules. Each water molecule is comprised of two hydrogen and one oxygen atom and due to the chemical properties of these atoms, water molecules (and other molecules in the human body) act like miniature weak bar magnets with a north and south magnetic pole. Normally these molecules are just randomly jumbled up in the body. However, in an MRI machine the human body is placed in a huge magnet which causes the water molecules to all align up in one direction. The MRI machine then changes the direction of the pulses causing the molecules in the human body to flip orientation. How quickly they change depends on the chemical composition of each molecule and on what other chemicals are around it. The MRI machine then detects these billions of minute changes and how long they last and builds up an image of the composition of the body.

The magnetic field is created by passing electricity through coils within the machine, which can cause the coils to vibrate, resulting in a knocking sound inside the scanner. These noises can be loud and concerning but are completely normal.

MRIs and MS

MRI can be used to look at most types of tissues and body parts and can diagnose a variety of conditions. In MS, MRIs are used to look at the brain and spinal cord (the central nervous system).

By detecting the subtle differences in body composition, MRIs can identify areas of inflammation and damage within the central nervous system. In MS these are the result of the immune system attacking and damaging the insulating layer of nerve cells, known as myelin.

Myelin helps nerves to conduct their electrical signals very quickly, as well as acting as a protective layer and supplying nourishment to the cells beneath it. Loss of myelin results in failure of nerve signals and can ultimately result in the death of nerve cells.



MRIs can help detect these areas of inflammation and can also detect the scarred patches where cells have died. MRIs however, may also be able to detect other more subtle effects of MS on the brain, with studies over the last few years revealing another important emerging measure and that is changes in brain size or volume known as brain atrophy.

Areas of inflammation and damage in the brain or on the spinal cord leave marks on the MRI images that look like spots and are referred to as lesions.

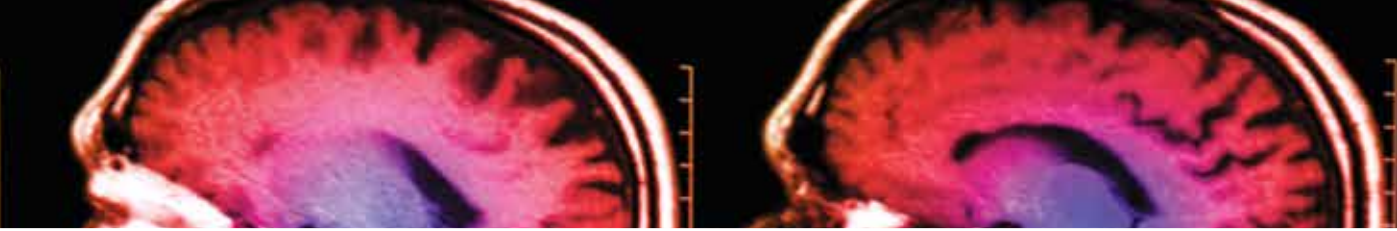
The positions of these spots can give an indication of symptoms, for example lesions on the spinal cord, can indicate numbness or loss of movement of some of the limbs. However, often spots cannot be linked to specific symptoms and may be referred to as asymptomatic or 'silent'. It is thought that as many as 9 in 10 lesions do not result in a bout of symptoms or a relapse. Stopping new lesions is considered to be the main goal of treatment, however in some cases this doesn't prevent the continual progression of the disease.

Decoding types of MRI images in MS

The MRI field is awash with acronyms and jargon which refer to the different types of pictures (or sequences). These are generated by changing the strength and duration of the magnetic and radio pulses which cause the magnetic molecules in the body to change their behaviour. The different sequences are a bit like a photographer using different lighting and changing the aperture and lens to capture perfect photos.

Here are some of the most common types of MRIs in MS;

- **T2/Flair images.** When radiologists carry out a T2/Flair sequence MS lesions stand out as bright spots which are often referred to as hyper intensities. These show spots of both new and old damage. In MS these tend to cluster deep in the brain and these pictures are used to determine how active the disease currently is.
- **T1 with contrast images.** To help identify active lesions, the radiologist may use a contrast agent or a chemical which shows up brightly on an MRI, a commonly used agent is a



chemical known as Gadolinium (GAD) which is injected into the vein prior to the MRI. GAD does not normally enter the brain or spinal cord however when the blood vessels are 'leaky' due to inflammation it can leach out of the blood vessels and show up as an area of brightness in the MRI image. This indicates an active lesion. Typically, these are only visible for a couple of weeks to a couple of months and often then revert to a T2/Flair scar.

- **T1.** These images are carried out in a similar way to the previous sequence but without a chemical agent. On these images, areas where there has been damage to the myelin coating and nerve cells appear as black holes.

Reading MRIs is a complicated endeavour, and not all lesion like marks appearing on MRIs are due to MS. Things like injury, infection, and blood vessel blockages can all also show up as spots on an MRI.

Traditionally neurologists have used the presence of new lesions in the MRIs of a person with MS as a sign that a change in medication may be needed, but more sensitive measures are also now being included in the assessment of MRI images.

Other MRI measures

While lesions have been the critical measure considered on the MRI images, more recent research has revealed that brain atrophy, or shrinkage in brain volume, may be a more accurate measure which potentially correlates more closely with disease progression and disabilities than lesions and relapses.

Brain atrophy or brain shrinkage is a normal process of ageing, but it can be accelerated in people with MS. On average we lose between 0.5% and 1% of our brain volume per year and this varies greatly from person to person, however for

people with MS, shrinkage can be slightly higher.

Measuring the rate of brain atrophy is slightly challenging, it requires regular high-quality MRI scans that are done in a comparable way every time. Changes in volume are small and are therefore difficult to detect on images which were taken on different MRI machines and by different radiologists.

Recent research into both relapsing and progressive MS has shown that people with more brain atrophy have a poorer outcome and studies have shown that this is independent of the number of lesions.

Research also shows that the spinal cord can shrink too, and that this is more marked in primary progressive MS than in relapsing remitting MS. Additional research has also shown that atrophy of certain subsections of the brain may be more important than overall atrophy. Importantly, studies have also shown that some MS medications can slow the rate of atrophy bringing it more in line with normal ageing.

Brain volume measures are becoming more accessible in clinics but further work is required to establish a unified way of taking MRI pictures and to assess them to accurately measure atrophy. MS Research Australia funded researchers such as Dr Heidi Beadnall, Brain and Mind Centre, NSW have been working on sensitive and automated tools to help improve the routine detection of atrophy in clinical practice.

The current goal of therapies is now to achieve no evidence of disease activity (known by the acronym NEDA). Traditionally, treatment of relapsing remitting MS has focused solely on reducing the number of relapses, however given the activity seen on MRI, we know there is additional activity other than relapses which we need to treat to achieve NEDA, and that includes lesions seen on MRIs and potentially also atrophy.



The Future of MRI

The field of MRIs has exploded. It was only in the early 1980's that saw the introduction of MRIs and since then we have seen the rapid evolution of this technology. Over its relatively short existence, MRI has become the imaging technique of choice for the study and clinical evaluation of MS and other diseases, with more than 60 million clinical MRI scans performed annually on over 25,000 MRI systems world-wide.

The introduction of more powerful machines has given even more detailed vision into the human brain and has brought about the possibility of measuring brain and spinal cord shrinkage. Future advancements will only further enhance this and allow us to peer into the brain and gather even more information on health and disease. Combining detailed imaging with big data on clinical outcomes, also provides potential for artificial intelligence computing to sift through hundreds of scans and detect subtle changes even earlier and more accurately, accelerating and enhancing the diagnosis of MS and management of MS.

**Dr Hamish Campbell, Research Development Coordinator,
MS Research Australia @DrHCampbell**

Making a difference through rehabilitation research

The 3rd Scientific Congress of the International Progressive MS Alliance was held in Toronto in May with the theme ‘Progressive MS – making a difference through rehabilitation and symptom management.’

MS Research Australia is a managing member of this global Alliance which aims to raise the profile, highlight the unmet needs (including strategies to deliver new treatments as well as to enhance wellbeing) and find solutions for people living with progressive MS.

The Congress was an incredibly energetic environment that really hit its goal of getting everyone thinking strategically about how we can collectively enhance research into this field. It set out to understand the perspectives of people living with progressive MS and what is needed to improve their wellbeing and quality of life. It aimed to explore the current state of research and evidence in this area and importantly to learn from other fields of rehabilitation research.

It brought together an inspiring collection of speakers and delegates and provided ample discussion time to deeply explore the themes raised. The topics covered included fatigue management, cognitive rehabilitation, physical rehabilitation and exercise, management of other chronic health conditions, mental health, the biological mechanisms of rehabilitation, and the need for a personalised approach to rehabilitation.

It was incredibly rewarding to see Australian researchers contributing to the discussions and collaborative thinking. Balance and falls researchers Professor Stephen Lord and Dr Phu Hoang, NeuRA, NSW and Dr Anna Hatton, University of Queensland, psychology researcher Dr Litza Kiropoulos, University of Melbourne and heat sensitivity

“The idea of ‘pre-habilitation’ was also discussed with the goal of saving function before it is lost.”

researcher Georgia Chaseling, University of Sydney all presented their work in the poster sessions.

We heard from researchers in stroke and spinal cord injury about the successes and challenges they have faced in the drive to harmonise research in their fields to increase the chances of success. Both the ‘dose’ (or amount) and intensity of an intervention is potentially one of the most important consideration



for success along with identifying the optimal window(s) for rehabilitation. The idea of ‘pre-habilitation’ was also discussed with the goal of saving function before it is lost.

How best to harness the property of neuroplasticity, the ability of the brain to ‘rewire’ around areas of damage, was explored along with intriguing discussion of how potential drug treatments that target the biology of plasticity could work synergistically with physical rehabilitation to restore function.

One of the most crucial messages to come from the meeting was the importance of co-designing research studies with people affected by a chronic health condition to maximise success. We need to work together to identify the outcome measures, functions and qualities of life that make a real difference in day to day life.

In the words of Alliance Scientific Steering Committee Chair, Professor Alan Thompson, “we achieved what we set out to do in this unique meeting – we demonstrated excellence in the field, successfully engaged across disease fields and identified the opportunities for the Alliance to make a difference.”

Lay-member of the Scientific Steering Committee, Alexis Donnelly galvanised us all with the quote from George Bernard Shaw - “The reasonable man adapts himself to the world: the unreasonable man persists in trying to adapt the world to himself. Therefore, all progress depends on the unreasonable man.”

There was agreement that we need to continue to be ‘unreasonable’ together to overcome the notion that loss of function is inevitable, and ultimately achieve the best possible outcomes for people with progressive MS.

**Dr Lisa Melton, Head of Research,
MS Research Australia @lisameltonMSRA**





The world comes together to Kiss Goodbye to MS!

This year the Kiss Goodbye to MS global community really came together as one, working side by side as part of the worldwide efforts to raise funds for MS research.

The Aussie founded campaign was held in 15 countries across the globe and we couldn't be more proud. We joined forces again with Canada, United States, Norway, Finland, Denmark, Spain, UK, Netherlands, Greece, Ireland, France, New Zealand and we were thrilled to welcome Egypt and Lebanon to Kiss Goodbye to MS.

Seeing our campaign grow each year and being celebrated all over the world, makes us feel very confident and excited for the future landscape of MS research and the lasting impact our combined efforts will have for people living with MS. Kiss Goodbye to MS doesn't know any cultural or geographical boundaries. We all work as one in order to strengthen and grow our momentum, to increase funding for MS research. We embrace different ideas and beliefs and take learnings from each other to maximize the impact of Kiss Goodbye to MS globally.

This year's campaign ran a variety of activations which were celebrated internationally, including Red Lab Coat Day which kicked off Kiss Goodbye to MS and MS awareness month on May 1st. We saw researchers from the Netherlands, Ireland, New Zealand and Australia change their white lab coats to red lab coats and our Kiss Goodbye to MS community joined us in celebrating their hard work. We changed it up a little this year and introduced the 'Battle of the Labs' to our Aussie researchers

and asked them to create videos showcasing their MS research. Nine fabulous and highly creative videos were submitted and the MS community voted for their favourite on our website. Red Lab Coat Day is our annual day where we stop for a moment to say thank you to our MS researchers across the world and

highlight the significant contributions and invaluable work of our Australian researchers to find a cure for MS.

Another highlight of this year's campaign saw our Kiss Goodbye to MS community across the world put on their game face to raise awareness for MS research and reach over 400,000 people on social media. People with MS put on their game face every single day, often hiding their many invisible symptoms which come with the disease. We challenged our global community and received hundreds of photos and videos with people applying their game face - young and old, on their own or together, at home or while surfing, our MS Squad took it to the next level and surprised us with their creativity.

The success of our Aussie campaign is a testament to all of the hard work you all put in across the globe to raise the profile of MS and emphasise the importance of research into prevention, better treatments and a cure for MS. This is only the beginning, as we won't stop until we find a cure for MS. Watch Kiss Goodbye to MS take on the world!



Our global video was watched over 400,000 times on social media



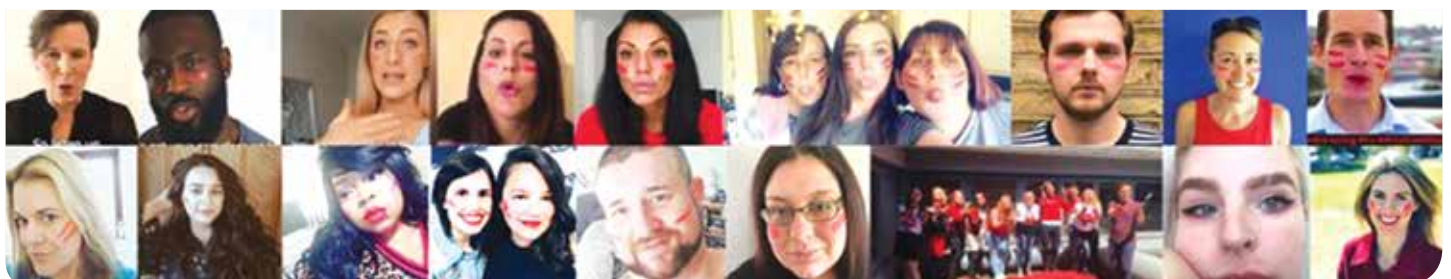
Kiss Goodbye To MS is now in 15 countries



#KissGoodbyeToMS was used over 18,800 times on Instagram



Battle of the Labs videos were watched over 8,300 times



End of Financial Year – the ideal time to make a difference

The financial year is coming to an end creating an opportune time to make a tax-deductible donation.

Your donation to MS Research Australia will help us continue to work towards the mission to accelerate Australian MS research toward the prevention, better treatments and a cure for MS. We receive limited government funding so every precious donation goes towards helping MS Research Australia fund the best MS researchers in Australia.

According to research released by NAB, the rate of charitable giving in Australia increased 1.2% over the past year. There is also a staggering 24% increase in donations in June, compared with other months, as it is not only an easier way to track your donations for tax time, but means claiming your tax deduction is in plain sight.

This year has been a big year for MS Research Australia, with the support of the Macquarie Group Foundation, a new 'paired' Fellowship was created to enable a senior research fellow and a clinician to work together to 'fast-track' research

breakthroughs and improve outcomes for people living with MS. We have also seen, the world's first ever treatment registered for primary progressive MS, and Australia was the second country in the world to register it for use.

“Charitable donations in Australia increased in June 2017 by 24%.”

Source: NAB

This year alone, MS Research Australia awarded 20 investigator-driven grants to researchers at leading universities, research institutes and hospitals across Australia, totalling over \$2 million. This brings the cumulative number of MS Research Australia funded projects to 254. In addition to this, \$1.7 million went to fund our seven large collaborative research platforms. As a Managing Member, we also provided

funding to the International Progressive MS Alliance, which is leading the global fight to solve primary and secondary progressive MS.

Since 2004, \$36.7 million has been invested in Australian MS research across 54 universities and research institutes.

Please take a look at our website www.msra.org.au to see what impacts have been created for people affected by MS with this funding we have mentioned.

Creating change, making discoveries, finding new and better ways to treat or prevent MS and improving our understanding of MS is what we do. Your donation, no matter how small, is absolutely essential to this. We simply cannot do it without you.



HELP MS RESEARCH AUSTRALIA FIND A CURE FOR MS

Donate (Donations over \$2 are tax deductible)

To support MS Research Australia's vital work I would like to:

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- ☐ Make a monthly donation of \$
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- ☐ I have already made a bequest to MS Research Australia in my Will

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