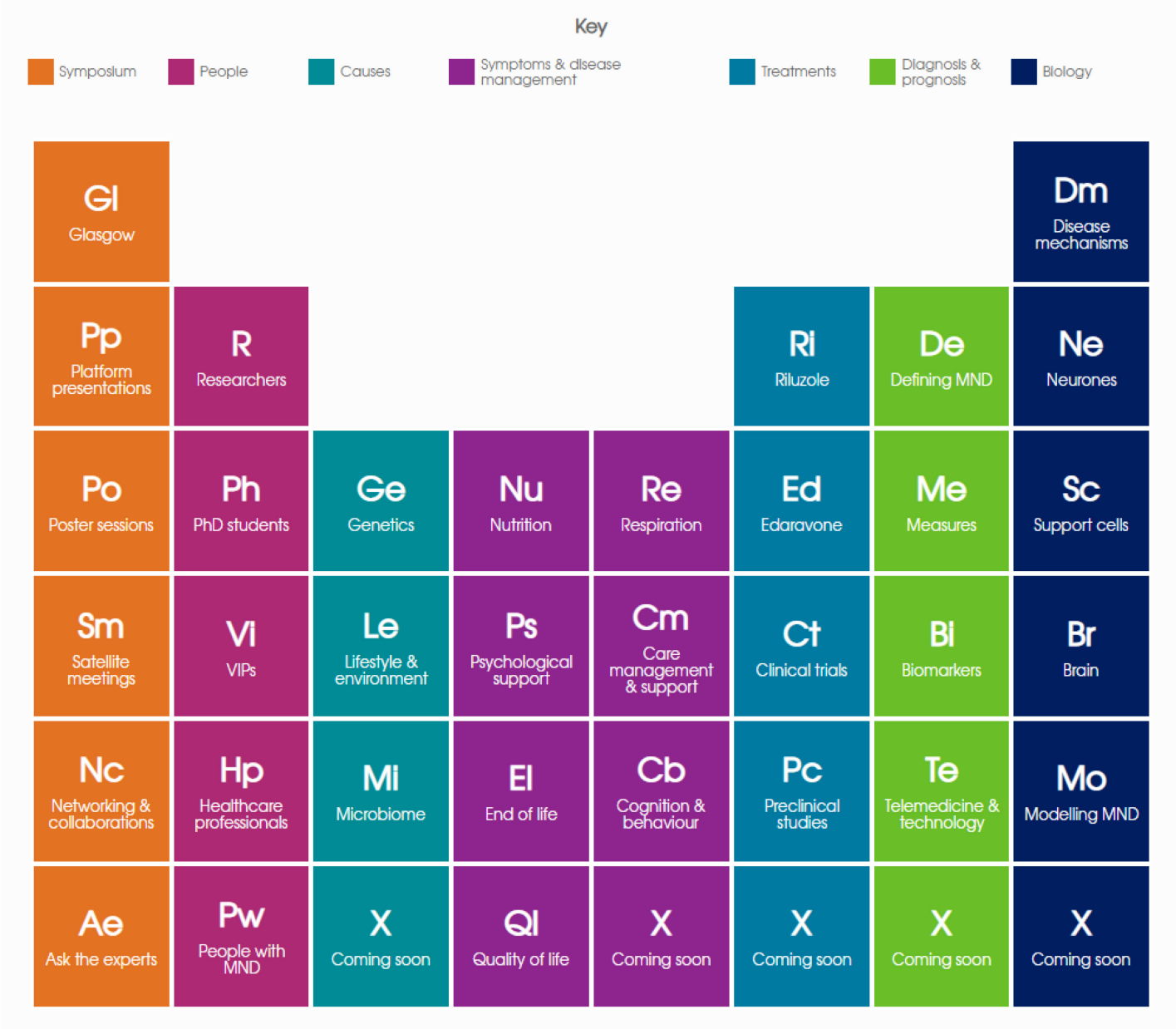
Periodic Table of MND Research

Glasgow 2018

In this document, you can find the complete Periodic Table of MND Research for the 29th International Symposium on ALS/MND in Glasgow, 2018.

Click on a tile below and read more about the content discussed at the Symposium or watch interviews (▶) with selected delegates and speakers. You can also scroll through this document to browse all topics within the Periodic Table. To get back to this page, click the 'back up' symbol (⬆) anywhere in the document.

For a current version of the Periodic Table, please visit
symposium.mndassociation.org/symposium-live



Symposium ⬆

Find out more about the International Symposium on ALS/MND, where is it held, how researchers present their work at the conference, other meetings that complement the Symposium, and an interactive session that everyone can take part in!

People ⬆

Read about the people coming to the Symposium this year, without whom the event wouldn't be possible.

Causes ⬆

Read about the factors scientists study to find out more about what causes MND.

Symptoms & disease management ⬆

Understanding, managing and improving the care of people with MND and their supporters.

Treatments ⬆

From bench to bedside. Covering medicines from those currently available to people with MND to those in development and into the future.

Diagnosis & prognosis ⬆

What is MND anyway? Find out about current status of diagnosis, the search for biomarkers to diagnose and measure disease progression, and how technology available now and in the future will impact MND.

Biology ⬆

The science of life. The main players involved in making us tick, from cells, molecules, nerves to the whole brain!

Glasgow (Gl)

Organised by the MND Association, the International Symposium on ALS/MND is the largest medical and scientific conference specific to MND/ALS in the world. Held annually at venues around the world, this year's 29th Symposium sees us returning to Glasgow on 7-9 December 2018, after 21 years.

Each Symposium is hosted by an ALS/MND Association from the home country, and this year's hosts are **MND Scotland**, the leading charity in Scotland providing care and support to people affected by MND, as well as funding vital research into finding a cure.

Voted the friendliest city in the world, you're guaranteed a warm welcome in Glasgow. From top class attractions, some of the best shopping outside of London in the UK, great food and drink and legendary nightlife, you are sure to have a trip to remember.

Video resources

- Welcome to Glasgow – MND Scotland
- Sally Light – The importance of our Symposium
- Kaye Stevens – Symposium experience
- Sally Light – Symposium 2018 wrap up

Platform presentations (Pp)⬆

Those who would like to present at the Symposium have to submit an abstract – an overview of their research and findings – to be judged by the Programme Committee and rated 'oral', 'poster', 'work in progress', or 'reject'. Out of the abstracts submitted some will be awarded **platform (oral) presentations** – the chance to present to an audience from the stage; others may be offered a poster – the chance to display their work in the form of a poster at a dedicated session.

You can **read all the accepted abstracts online**. All platform presentations have a code beginning with '**C**' followed by a number (e.g. C50). This will help you locate the specific abstract mentioned throughout the periodic table topics.

Platform presentations are prestigious, and Glasgow will hear **109 talks** over the three days. These talks will be split between three sessions; biomedical (A), clinical (B), and alternative mixed (C) session. Each session is organised by specific themes, such as genetics, clinical trials or neuroimaging. **See the full programme for this year's Symposium**.

Alongside these presentations we also invite several **plenary (keynote) speakers** who are the world experts in their respective fields. Their talks complement the Symposium sessions by providing an overview of a variety of topics across the ALS/MND research and clinical management spectrum.

Poster sessions (Po)

Those who would like to present at the Symposium have to submit an abstract – an overview of their research and findings – to be judged by the Programme Committee and rated 'oral', 'poster', 'work in progress', or 'reject'. Out of the abstracts submitted some will be awarded platform (oral) presentations – the chance to present to an audience from the stage; others may be offered **a poster** – the chance to display their work in the form of a poster at a dedicated session.

You can **read all the accepted abstracts online**. All poster presentations will have a code composed of three letters and a number (e.g. GEN-12, referring to poster number 12 in the Genetics and Genomics section). This will help you locate the specific abstract mentioned throughout the periodic table topics.

This year, **523 abstracts** have been awarded poster presentations. These are split into biomedical and clinical posters. This allows presenters to create an A0 sized poster describing their work and gives them the opportunity to talk through this with colleagues at two poster sessions on Friday and Saturday.

Poster Prize

To celebrate the high quality of posters presented by early-career researchers during the Symposium, the MND Association presents the **International Symposium on ALS/MND biomedical and clinical poster prize**. The winners of the poster prize are announced during the Joint Closing session of the Symposium, and are presented with a certificate, engraved glass paperweight, and offered a free space at the next Symposium. One prize is awarded for a clinical poster and one for a biomedical poster. You can **find out more about the Poster Prize here**.

Video

Dr Nick Cole & Rachel Boothman – Poster Prize Winners announcement

Satellite meetings (Sm)

Whilst the main Symposium runs over three days, Friday to Sunday, there are also several **satellite meetings** in the days before as well as during the Symposium itself. The International Alliance of ALS/MND Associations organises meetings to serve the broader ALS/MND community: **The Annual Alliance Meeting**, on the 4-5 December and **Allied Professionals Forum** on the 5 December.

The Annual Alliance Meeting is attended by representatives of ALS/MND associations from around the world and provides the opportunity for these associations to meet and share knowledge of supporting people living with ALS/MND. It is also an opportunity for representatives from around the world to discuss developments and planning from their organisations, patient care and funding, and the role and activities of the Alliance and its Board of Directors.

The Allied Professionals Forum is for healthcare professionals, such as physiotherapists, nutritionists, speech-language therapists and more, who specialise in ALS/MND. It is an educational and training forum and offers healthcare professionals from around the world an opportunity to share ideas about good practice in the daily care management of people living with ALS/MND.

During the Symposium there is also a number of smaller meetings covering several subject areas that delegates can attend, encouraging further knowledge sharing and collaborations.

Video

Dr Nick Cole – Satellite meetings

Networking & collaborations (Nc) ⬆

One of the main advantages of the Symposium is the opportunity to have the best and brightest scientists, researchers and clinicians in the world of MND research in one place at the same time. This gives attendees the opportunity to network with those who work in similar research as well as those working in different areas, allowing new collaborations and ideas to form.

These connections are vital in pushing forward research development – a simple chat waiting in the coffee queue can go a long way and start an important project that will lead to a key breakthrough.

Ask the experts (Ae)

Every year the International Alliance of MND/ALS Associations invite the host association to organise a free `**Ask The Experts'** session. It is designed specifically for people living with MND and their caregivers to attend an afternoon of presentations by neurologists and researchers and then participate in a `question and answer' session afterwards.

This year, we will hear from **Professor Orla Hardiman** (Trinity College Dublin, Ireland), **Professor Dame Pamela Shaw** (University of Sheffield, United Kingdom), and **Dr Arpan Mehta** (University of Edinburgh, United Kingdom).

This session is live-streamed on Facebook, and so anyone from around the world can attend and ask questions online.

Symposium update

The 2018 Ask the Experts session took place on Wednesday 5 December from 14.30. A panel of five research and clinical experts gave presentations on four different topics on MND research, and answered questions from the audience in the room and online. The first speaker was **Dr Brian Dickie**, Director of Research Development at the MND Association, who explained why it is extremely difficult to find out the precise cause of MND, by looking at the environmental, lifestyle and genetic factors that together lead to a person developing the disease.

Following on from there, **Professor Dame Pamela Shaw** of the Sheffield Institute for Translational Neuroscience took us through the mechanisms that go awry in motor neurones of people with MND and therapies that are currently being tested to prevent these.

In the third talk, **Dr Bhuvaneish T. Selvaraj and Dr Arpan Mehta** from the Euan MacDonald Centre took us through the process of creating motor neurones from induced pluripotent stem cells and how these can be used to tackle some of the toxic processes that occur in MND.

Finally, **Professor Orla Hardiman** from Trinity College Dublin, outlined the objectives we need to fulfil in order to find an effective treatment for all the different types of MND – these included developing and implementing a set of biomarkers to measure disease progression, improving clinical trial design, and a combined effort across countries to develop a dataset that would help reveal subgroups of people with MND. You can watch the full session below:

Video

Ask the Experts – 5th December 2018

Researchers (R)

The key to defeating MND lies in fostering strong collaborations between leading researchers and sharing new understanding of the disease as rapidly as possible – this is the main aim of the Symposium.

Researchers from all around the world arrive at the Symposium every year representing the energy and dynamism of the global MND research community. It is the largest medical and scientific conference specific to ALS/MND and is the premier event in the MND research calendar for discussion on the latest advances in research and clinical management. It gives delegates the opportunity to present their work, hear about progress, share knowledge and most importantly collaborate with their peers.

Videos

Dr Hiroshi Mitsumoto – MND Symposium experience

Dr Rickie Patani – IPG Award winner

Dr Angela Genge – Forbes Norris Award winner

PhD students (Ph)

At the MND Association we are proud to fund a number of PhD studentships, ensuring that high-calibre graduates can undertake a PhD training in MND-related research. These students are the people who will be pushing research in the future so it's vital that they have the support they need to be able to do this.

The Symposium is a fantastic and rare opportunity for students to make significant connections with others that share their passion for finding treatments and a cure for the disease. Over the three days they will be able to listen to presentations from the best in their field, network with peers who are working on similar or different areas and importantly promote their own research to others.

Two of our funded PhD students, **Matthew Nolan**, from the University of Oxford, who investigates the toxic TDP-43 protein in brain tissue, and **Sarah Opie-Martin** from King's College London, who works on the **MND Register** and analyses epidemiological (environmental and lifestyle) data, shared a bit about their research and why attending the Symposium is important to them.

Videos

Sarah Opie-Martin

Matthew Nolan

VIPs (Vi)

This year we are privileged that HRH The Princess Royal, the Royal Patron of the MND Association and MND Scotland, is attending the Opening Session of the Symposium. She is a regular supporter of both charities and the development of research in MND.

The Princess Royal attended the Symposium in 1997 – the last time it was held in Glasgow.

Healthcare professionals (Hp)

As well as researchers attending the Symposium a large number of clinicians (healthcare professionals) also attend the event to help expand their existing knowledge on MND. All fields are represented at the Symposium from respiratory experts to physiotherapists. It is a chance for them to hear innovative talks from experts in their field from nutritional support to quality of life and learn about new techniques and ways to improve their practice.

Helping to educate clinicians (Health and Social Care Professionals) is a priority for the MND Association as this will help those affected by MND have a better multi-disciplinary care plan, as well as a higher quality of life. As part of this education the Association runs conferences, study days and online learning for professionals on a range of topics. Find out more about these **events for healthcare professionals**.

Videos

Marjolein Cleaver – APF presentation

People with MND (Pw)

People living with MND, their carers and families are at the heart of everything we do, and our reason for organising the Symposium every year. Whilst the event is aimed primarily at scientists and healthcare professional, there is an opportunity for people with MND to attend, via the **Patient fellows programme** managed by the ALS Therapeutic Development Institute (ALSTDI). This allows some people with MND to be funded to attend the Symposium and then share their experiences via an article or social media. Find out more about **this year's patient fellows** Sunny, Keith and Bruce.

Everyone involved in MND research is extremely thankful to all those affected by the disease who take part in various research studies, helping us to get closer to finding the cure.

Videos


Doddie Weir – My Symposium experience


Sunny Brous – My Symposium experience


Catherine Collet – Patient Fellowship Programme

Genetics (Ge)

Around 5-10% of people with MND have a family history of the disease known as **familial, or inherited, MND**. This is caused by a mistake in the genetic code that holds the instructions for making every protein in our bodies. This mistake may be passed down from parent to child.

To date, about 70% of the genes known to cause inherited MND have been identified. The most common of these are **SOD1, TARDBP, FUS** and **C9ORF72**. Other extremely rare causative genes have also been identified. These discoveries represent major breakthroughs because they can provide important clues as to how motor neurones are damaged in MND and may advance our understanding of all types of the disease.

At the Symposium

Christopher Shaw will present a plenary talk (C8) in which he will discuss the possible ethical and logistical issues of genetic testing, and whether this should be offered to people without a family history of MND. In another session, **6A: Genetics and Genomics**, **Tobias Moll** (C45) will talk about a novel gene recently identified by researchers at the University of Sheffield.

In an associated poster theme, **1: Genetics and genomics**, **Lauren Cairns** (GEN-16) will talk about genetic testing in ALS and FTD, while other presenters will focus on more specific genes, including the recently identified KIF5A (GEN-21,22) and ANXA11 (GEN-24,25).

Videos

Prof Ammar Al-Chalabi – ALS Gene Scanner

Prof Christopher Shaw – MND gene testing

Dr Russel McLaughlin – Project MinE & Understanding MND genetics

Lifestyle & environment (Le) ⬆

The causes of MND are still not fully understood. Around 90% of people with MND have a sporadic form of the disease – when the disease appears for no apparent reason and with no known familial link. Sporadic MND is thought be caused by a combination of genetic, environmental and lifestyle influences.

Exposure to these factors has been extensively studied. This is known as epidemiology. Epidemiological studies have identified possible links with prior exposure to mechanical and/or electrical trauma, military service, high levels of physical activity, agricultural chemicals and a variety of heavy metals. However, these are all only suspected contributory risk factors and the evidence from studies is often circumstantial or conflicting and offers no clear conclusions.

Understanding the causes and mechanisms of motor neurone degeneration is essential to the development of new treatments. Only by understanding what goes wrong in MND can scientists identify potential drug targets and other therapies.

Highlights from the Symposium

In the Epidemiology session (5C), several talks focused on the risk associated with various lifetime events, and the demographics of people who develop MND categorised by onset at various body regions. **Susan Peters** (C37) and her colleagues studied a group of 1,500 people with MND and 3,000 control participants, and found that people who had suffered head trauma after the age of 55 had an increased risk of developing the disease compared to those without this type trauma. They further found reduced risk in people currently/recently taking antihypertensive and cholesterol-lowering medication, but this risk was significantly increased in people who were taking these medications earlier in life. These findings now need to be explored further to investigate the underlying mechanisms that would explain these differences.

Adriano Chio (C39) presented his data on the development of different motor variants within MND (e.g. bulbar, flail arm, upper motor neurone), and how these are likely to be driven by various mechanisms, depending on factors such as age, sex, and genetics. For example, his findings show that the bulbar variant of MND is more often observed in older age groups (especially over 80 years of age), females, and those with the C9ORF72 genetic variation. The fact that different variants of the disease can be dependent on specific factors proposes that the disease mechanisms might vary across people living with MND.

We have also heard from **Jane Parkin Kullmann** (C40) who discussed her study looking into the impact of psychological stress using a newly-developed questionnaire ALS-Quest, which asked 850 people about any potentially stressful life events. While the findings did not show any impact of stress on the development of MND, people with the disease were found to be more resilient compared to healthy controls, showing their increased ability to respond to life stressors. The reasons for this association now need to be looked at further, as resilience is thought to be linked to biological, social, and environmental factors.

In the final talk of the Symposium, **Pamela Shaw** (**C109**) took us through the anecdotal reports and studies looking at the connection between physical activity and MND, highlighting that the evidence has been quite conflicting. In one study, increased physical activity in adulthood (such as daily 20min jog) was associated with increase odds of developing MND, which was also confirmed by other studies. Other studies, however, failed to find such association and in some, reduction of risk was observed instead. Professor Shaw concluded by saying that physical activity may amplify the disease mechanisms known to contribute to the development of MND, however, this might only be the case in people who are more susceptible, with genetics playing an important role. Therefore, while for some people exercise will not lead to MND, those with a specific genetic variation might be more likely to develop the disease following increased exposure to physical activity. Further work will now focus on the interaction between environmental and genetic factors to confirm this theory.

Further research studies were presented in the poster session, where **Jane Parkin Kullmann** (**EPI-09**) and her team found that exposure to mercury from eating seafood or from having dental fillings containing mercury did not increase risk of developing MND, and any associated link could be due to other sources of exposure or due to increased susceptibility to mercury toxicity in some people.

You can read abstracts of other poster presentations that focused on Epidemiology online.

Videos

- Prof Ammar Al-Chalabi – Smoking and MND
- Prof Ammar Al-Chalabi – Physical activity and MND
- Dr Roger Mills – The TONiC study: Smoking and history of MND

Microbiome (Mi)

Recent studies have found that microbes living in our gut (**microbiome**) might have an effect on the rest of the body, including the immune and nervous systems. It is possible that the microbiome may be able to communicate with and affect the immune cells in the brain and spinal cord, called microglia.

Microglia have a naturally protective effect on motor neurones and the rest of the nervous system. Therefore, if the microbiome has the potential to affect the way microglia are behaving in the brain and motor neurones of people with MND (and other neurodegenerative diseases such as Parkinson's and Alzheimer's disease), the microbiome could become an important treatment target.

Researchers are currently trying to focus on the possible differences in the gut microbes of people with MND compared to people without the disease, in order to establish the possible connection between gut microbes and MND (and other neurodegenerative diseases).

At the Symposium

John Cryan will give a plenary talk (C2) on the up-to-date evidence of the effect of the gut microbiome on the brain throughout our lives and show the ways future research on the connection between MND and the gut microbiome might be explored. Researchers from Canada will present a poster (TST-01) about their work studying the genes that might be influenced by microbiota in an MND worm model, confirming the link between microbiota and MND.

Video

Dr Nik Sharma – Microbiome study

Nutrition (Nu)

Swallowing problems affect at least two-thirds of people with MND during their illness. This is due to a weakening of the muscles in the mouth and throat. If MND affects a person's ability to swallow, it becomes harder for them to eat and drink. As a result, they are likely to experience dehydration and weight loss.

Adaptations to the way a person eats and drinks may be needed to ensure they get the nutrition and fluid their body needs. Some people with MND choose to have a gastrostomy – a surgical opening through the abdomen into the stomach. This allows tube feeding – a way of passing specially prepared fluid straight into the stomach.

At the Symposium

Nimish Thakore will present a talk (C102) on gastrostomy, rates of decline of ALSFRS-R subscores and BMI, and survival in session **10B: Respiratory and nutritional support**. He will discuss whether gastrostomy placement (as it is currently performed) has a beneficial effect on decline or survival in MND.

During the associated poster session, **12: Respiratory and nutritional management**, presenters will look at whether weight before a diagnosis is a good indicator of disease progression (RNM-34), and the effect of artificial nutrition on survival and risk of death (RNM-43).

Videos

Prof Ammar Al-Chalabi – Lipids and diet

Dr Fred Steyn – Hypermetabolism, appetite and weight loss

Respiration (Re) ⬆

MND can affect the way a person breathes by weakening the muscles that control breathing. Although this cannot be reversed, there are treatments that can help reduce symptoms such as disturbed sleep, fatigue and anxiety, and enable the person to breathe more effectively.

When breathing becomes weaker a machine may be used to support breathing. This is known as assisted ventilation. There are two types of assisted ventilation: **non-invasive ventilation**, where a machine supports breathing by boosting the intake of normal air through a mask, and **tracheostomy ventilation**, where a tube is inserted into the windpipe through the front of the neck, which enables a ventilator to support breathing.

The use of ventilation may not be suitable for everyone. If appropriate, it may help to relieve breathing problems but will not stop the progress of the disease.

At the Symposium

In session **10B: Respiratory and nutritional support**, **David O'Brien** (C105) will present his systematic review study on enhancing the efficacy of non-invasive ventilation in MND, highlighting the need for active preparation and ongoing monitoring if NIV is to be used successfully for people with MND. In another talk, **Emily Plowman** (C106) will present her study on the impact of a combined expiratory and inspiratory respiratory strength training programme in MND.

A presentation by **Andrew Geronimo** (C33) in session **5B: Technology and ALS/MND** will look at the possibility of remote monitoring of pulmonary function, to reduce the number of clinic visits, and potentially increase the number of people participating in clinical trials as a result.

Many more presentations on respiration will also be given in poster session **12: Respiratory and nutritional management**.

Resources

- Information sheet: Support for breathing problems
- Information sheet: Ventilation for motor neuron disease
- Information sheet: Withdrawal of ventilation with MND
- MND Research Blog: Choices around tracheostomy ventilation
- MND Research Blog: Withdrawing ventilation support at the request of the patient: the clinical, moral and legal issues
- Video: Dr Esther Hobson (University of Sheffield) on gastrostomy, non-invasive ventilation, and utilising telemedicine in MND care

Psychological support (Ps)

MND has a huge impact on the psychological and emotional welfare of people living with the disease and those around them who are affected by it, particularly when it comes to thinking about death and end of life decisions. It is normal to feel heightened emotions when facing end of life decisions and every individual will have a different set of circumstances, needs and preferences.

With support from health and social care professionals, difficult feelings usually become more manageable over time, and support is needed for both the person living with MND and those who care for them. Referral to a palliative care team or hospice may provide access to wider services to help with end of life decisions and manage the impact on the person with MND and those close to them.

At the Symposium

Poster session **11: Cognitive and psychological assessment and support** will cover a large range of issues relating to psychological support. In his poster presentation (COG-14) for example, **Luke Williams** will ask 'What are MND patients really distressed about?'**,** highlighting that the NICE guideline for MND states 'during multidisciplinary team (MDT) assessments and other appointments, discuss the psychological and emotional impact of MND and ask whether they *(the person with, or affected by, MND)* have any psychological support care needs.'

Videos

Dr Francesco Pagnini – Web-based mindfulness intervention and meditation in MND

Prof Carolyn Young – The TONiC study: Psychosocial factors

Care management & support (Cm) ⬆

Aside from finding out the causes of the disease and ways to treat it, it is vital that people who are living with MND receive top-quality care. Current research is looking into ways of improving their wellbeing and managing disease symptoms including physiological changes, such as problems with breathing, weakening of postural muscles, cramps or joint stiffness.

When someone is diagnosed with MND, the changes affect not only the person with the disease but also those close to them. Becoming a carer for someone with MND can be very challenging and, over time, the level of care needed will increase – sometimes rapidly.

Supporting someone with MND can often feel emotionally overwhelming but there can be many positive emotions, such as satisfaction when a task or challenge is successfully completed, especially if this has involved both the carer and the person with MND. It is important that the carer takes time to look after their own needs, even if this feels impossible when facing the challenges of supporting someone with MND.

At the Symposium

One platform session, **6B: Clinical support and quality of life** and one poster theme, **13:Clinical management and support**, will look into the way care is managed across multiple disciplines, and ways this can be improved and standardized. In one of the talks, **Sile Carney** (C52) will talk about the limited amount of information there is on how caregivers minimise their own psychological distress even though this is recognised as a consequence of caring for a person with a neurodegenerative disease. The aim of this study was to examine the relationship between coping styles, positive aspects of care-giving and psychological distress in MND in informal caregivers.

Resources

- Information sheets: Symptom management
- Guide: Caring and MND: support for you guide
- Video: How can the MND Association help you?
- MND Research Blog: Recognising and supporting the role of informal carers

End of life (EI) ⬆

This section talks openly about death and end of life decisions.

Palliative care is of utmost importance in MND and focusing on managing symptoms and improving quality of life of people living with the disease is a priority of healthcare professionals. Because of the nature of the disease, it is important for those affected by MND to know about the symptoms they should expect as the disease progresses, and how best to manage them. Research is always ongoing to find out how best to manage symptoms and when to utilise life-sustaining measures.

The decision to end one's life is a highly sensitive and difficult one both for the person considering this option and their family, as well as for clinicians who are approached about this. A person's wish to end their life is an often-discussed topic, relevant in all countries, not only for MND but all terminal illness. The legality of euthanasia varies across the world. Currently, active euthanasia is legal in Canada, Colombia, the Netherlands and Luxembourg, with assisted suicide being legal in Switzerland, Germany, the Netherlands, and in eight US states.

The MND Association's position on assisted suicide is neutral, you can read our policy statement here.

At the Symposium

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Resources

- Information sheets: Symptom management
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- Video: How can the MND Association help you?
- MND Research Blog: Recognising and supporting the role of informal carers

Cognition & behaviour (Cb) ⬆

Up to half of people with MND experience changes to how they think and behave, and these affect people in different ways. For some they will have little effect on daily life, while others will need significant day-to-day support. In a small number of cases, people with MND develop frontotemporal dementia (FTD).

People with MND may experience changes to their thinking and learning, language and communication, and behaviour and emotions. It may become more difficult for them to make and carry out plans, process information and solve problems. They may find it harder to recognise words when reading or writing, have difficulty spelling or find it hard to follow conversations. They might also begin to lack enthusiasm, find it difficult to manage emotions and behave inappropriately in social situations.

If a person is affected by FTD they will experience symptoms similar to those already described but with greater severity. With FTD, memory is not usually affected although it may appear that it is due to difficulties with concentration and taking in new information.

Highlights from the Symposium

A history of other mental health conditions or psychiatric disorders within the family, or for the individual, indicates a correlation with MND/FTD. There seems to be a link between this increased history and a risk of apathy. Early screening is recommended where these histories exist. This can help prepare families and enable early discussions with the person diagnosed with MND, so they can make decisions that may be important to them in the future *(C41)* **C McHutchison**.

We are all subject to apathy at times, where we lack motivation to accomplish our goals. However, where cognitive change is involved this can be more marked. Using a five minute questionnaire based on the Dimensional Apathy Scale (DAS), with patients and their care givers, research has found that up to 50% of people with MND/ALS experience apathy throughout the progression of the disease *(C53)* **R Radakovic**. Initiation apathy is most typical which makes it hard to accept new things, such as support from an external care worker. This can impact on burden for care givers and quality of life for both patient and care giver. External stimulation can help, so finding out what motivates the person enables activity and therapy to be customised to individual need. This is consistent with sessions at the Allied Professionals Forum which highlighted the use of music therapy and art therapy *(**Alisa Apreleva, Vivianna Faierman**)*. Also, volunteers working with people who have cognitive change to stimulate interest (***Marjolein Cleaver***).

With cognitive change there is a greater burden on care givers than with physical demands of care support alone. Early screening and recognition of signs may help to prepare and improve the support given to carers, for example, metabolic changes and overeating indicate the potential for cognitive change. Also, making unexpected decisions about finance, wills or end of life planning that conflict greatly with previous views. Those with the gene C9orf72 may be more predisposed

towards frontotemporal dementia and the MND/FTD combination is more likely to have a genetic cause *(C64)* ***J Hodges***.

People with cognitive change are more likely to drop out of studies and trials. When looking at why this attrition occurs, factors common to cognitive or behavioural change became apparent, such as advancing disease stage, age of onset, fewer years of education and the presence of the genetic mutation C9orf72 *(C65)* ***C Crockford***. There was a recommendation that cognitive assessment should take place during diagnosis, be monitored throughout the disease course and featured as standard in any further work on defining the stages of MND.

Typically, there isn't a great deal of emphasis on memory decline in MND. However, a study has shown that clinicians should pay attention to memory function in older patients with cognitive impairment where episodic memory deficits may be a notable feature *(C66)* ***J Machts***. Those intact at the start are unlikely to show deficits, whereas those already impaired at the start are more likely to develop deficits in, as yet unaffected areas.

If there is a past family or personal history of mental disorder or alcohol abuse, men with MND/FTD are more likely to develop psychosis. This psychosis should possibly be considered as a distinct behavioural subtype, which appears to be made up predominantly of males with the genetic mutation C9orf72 and FTD. Surprisingly, survival in this subtype seems to be prolonged. There needs to be prompt referral to psychiatric services and this form can be very difficult for carers to manage *(C67)* **R Ahmed**.

All presentations in this section indicate the need for early screening to prepare families, relieve care giver burden through better support and enable opportunities for decision making before impairment progresses.

Resources

- Booklet: Cognitive change, frontotemporal dementia and MND
- Booklet: Making the most of life with MND
- Information sheet: Will the way I think be affected?
- Information sheet: How do I support someone if they way they think is affected?
- Information sheet: Managing emotions
- MND Research Blog: MND and the mind-who is affected?
- MND Research Blog: Are there differences between FTD alone and FTD-MND?

Quality of Life (QI) ⬆

The aim of hospice and palliative care is to give the best possible quality of life with a life-shortening illness. For maximum benefit to people with MND, this type of care is recommended from the point of diagnosis onward.

Palliative care refers to specialised care services that focus on quality of life and symptom control when an individual has an illness that can't be cured. This includes practical help, medication to ease symptoms and support for the individual and their family. Palliative care isn't just for end of life. It may be given earlier in a person's illness in conjunction with other therapies treating the condition.

The Trajectories of Outcome in Neurological Conditions (TONiC) is the largest study in the UK examining the factors that influence quality of life in patients with neurological conditions, including MND. TONiC aims to have a significant positive impact on the lives of all people living with neurological conditions, regardless of symptoms, stage of illness, age or social status.

Highlights from the Symposium

From the expected to the unexpected, such as studies which considered the effect of gut health on brain and mood. (C2) **John Cryan** – As stress and other factors such as medications can affect gut bacteria, there is a need to maintain a healthy microbiome. This led to a recommendation for sharing refined human poo. Coming your way soon could be 'Crapsules' and supplements such as 'Poopulate'.

(C40) **Jane Parkin Kullmann** – In other work on stress, researchers in Australia found that stress is not necessarily a risk factor in the development of MND/ALS, indeed it appears that people with the disease may actually be more resilient. Further study is ongoing to determine whether this might indicate a genetic difference.

In the world's largest study on quality of life and MND (C49) **Carolyn Young**, it was suggested anxiety plays a major part on an individual's sense of wellbeing. This raises the question; is there positive value in therapy on acceptance and treatment for anxiety? Quality of life should also tie into the support given through all disciplines to help ease the impact across daily living. This further underlines the need for multidisciplinary working and how crucial funding is for provision of co-ordinated care.

However, even within the best maintained health and social care team, both patients and carers tend to identify their own 'lynchpin' or key professional, where a trusted relationship is fostered through regular contact (C50, **Esther Hobson**). This has been shown as important for reassurance and the recommendation is to upskill networks and promote the concept of lynchpins.

Of interest with many studies (C32/33/34/35/48), was the increased use of remote technology to record daily activities and symptoms. Psychological and emotional context is being included more and more, including Patient Reported Outcome

Measures (PROMS) on both physical and mental health, quality of life, fatigue and emotional problems. Although this cannot replace detailed clinical face to face assessment, it can provide extra data on disease progression and improve patient/clinician communication.

There is an emerging trend in the use of mindfulness meditation to help relieve depression, anxiety and perception of quality of life (C51) **F Pagnini**. Meditation is the tool, mindfulness is the objective. Mindfulness is about being present in the here and now, and able to adapt, rather than being stuck and repeating unhelpful behaviours. In this study daily exercises appropriate to MND were emailed by the clinician to the patient to improve mindfulness, which indicated over time a significant improvement to the psychological wellbeing of people with MND/ALS.

The Symposium also focused on caregiver burden. The more hours spent caring and the more demands made, the greater the risk of anxiety and depression for the care giver. In a small study (C52) **Silé Carney**, practical and emotional stress also rise from changes to the relationship with the diagnosed person and the new roles the care giver takes on. Exploring ways to find value in the giving of care, along with task oriented coping strategies can help bring balance and reduce a sense of burden.

However, the whole family is affected by the impact of MND. The person with the disease may have changes to mood, a sense of disorder and apathy but those close may also feel anxiety and stress. Sometimes psychotherapy may be at odds with culture, faith or belief and may not be accepted as a form of support. This is where music therapy and art therapy can help families gather together and share their emotional responses together. This can have a healing effect for the family as well as the person with MND/ALS. (Allied Professionals Forum **Alisa Apreleva and Viviana Faierman**)

The key message from these sessions highlights the need for professionals to monitor psychological and emotional wellbeing from diagnosis onwards. This is important for the person with MND and those close to them. Appropriate remedial therapy/support should be offered where possible.

Videos

Prof Carolyn Young – The TONiC study: Study overview

Prof Carolyn Young – The TONiC study: Influence of hope

Dr Zoe Syrimi – The TONiC study: Pain in MND

Resources

- Information sheet: Hospice and palliative care
- MND Research Blog: New research projects agreed to help improve palliative and end-of-life care
- Website resource: Visit the TONiC website
- Booklet: Making the most of life with MND

Riluzole (Ri) ⬆

Riluzole is currently the only drug licensed in the UK for treating MND and is freely available to people who have been diagnosed, although it may not be suitable for everyone.

Riluzole works by suppressing glutamate activity, which is toxic in high concentrations. Glutamate is a chemical messenger in neurones that helps to transmit electrical impulses from one neurone to the next. Riluzole has other actions, too, that are not fully understood, and the observed benefits of the anti-glutamate effect have not yet been proven.

Riluzole is not a cure and does not reverse damage already caused to motor neurones. After 12-18 months of treatment, it may increase survival by an average of three months.

It comes in tablet or liquid form.

At the Symposium

In his talk, **Nimish Thakore** will examine the effect of riluzole across the different disease stages (C82), as recent reanalysis of riluzole trial data suggests that the drug prolongs the later stages of ALS. This topic will also be discussed by **Adriaan Jongh** in his poster (CLT-15), where the focus will be on the way riluzole prolongs survival, and how this information could be important for clinical trial design and counselling.

Video

Prof Carolyn Young – The TONiC study: Riluzole availability across UK

Resources

- Information sheet: Riluzole

Edaravone (Ed) ⬆

Currently licensed in Japan, South Korea, USA and Canada, edaravone (commercially known as Radicut or Radicava) is the second drug approved to treat MND. Originally developed to prevent brain swelling after stroke, edaravone is believed to work as an anti-oxidant which helps remove damaging agents from the body which prevents or delays cell damage. Edaravone is currently awaiting a decision from the European Medicines Agency (EMA) regarding its marketing authorisation in Europe.

In clinical trials, edaravone has been shown to slow the progression of MND in a select group of people in the early stages of the disease, compared to those taking placebo, potentially helping them to preserve function longer. Long-term effectiveness of edaravone is not yet known. Edaravone is provided intravenously, with studies currently investigating the possibility of oral administration of the drug.

At the Symposium

There will be a number of posters looking into the different aspects of edaravone. In the **Clinical trials and trial design theme (7)**, CLT-13 will look at the potential to develop oral formulation of edaravone, CLT-14 will provide an update on the studies requested by the FDA following approval of edaravone in USA, and CLT-15 will review findings on the effect of edaravone based on the different disease stages. Presentations within the **Clinical management and support theme (13)** will explore the effect of edaravone on the different patient subgroups (CMS-10) and patient and clinician experience on accessing and prescribing edaravone and its effectiveness (CMS-12-17). One presentation within the **Clinical work in progress theme (CW)** will look into the investigations of biomarkers to measure the biological effect of edaravone in MND (CW-15).

Resources

- Information sheet: **Accessing unapproved drugs**

Clinical trials (Ct) ⬆

Clinical trials are research studies in human volunteers that determine whether potential treatments are safe and effective. Clinical trials are usually conducted in four progressive phases which check for safety and efficacy, establish the correct dosage and method of delivery and assess the drug's ability to treat the condition it is designed for.

Clinical trials take many years to complete and are often extremely costly. At any stage the drug can be deemed too dangerous, or inefficient, to take into the next phase. To speed up the process, clinical trials are beginning to incorporate a biomarker element (a biological fingerprint) into their design. Monitoring levels of specific biomarkers during a trial will help establish if the drug or intervention being tested is having an effect on disease progression.

Researchers are also looking to 'repurpose' drugs that have failed to show effect for other diseases but have already been shown to be safe in humans, as potential treatments for MND.

Highlights from the Symposium

In the Clinical trials and trial design (**4B**) session we heard from two speakers looking at ways to improve current design of clinical trials. In his plenary talk, **Mahesh Parmar** (**C20**) provided his perspective on the necessity of changes from his experience working on cancer trials, highlighting that any efforts to improve clinical trials should be focused on Phase III where the most money and time is spent. One solution that stuck with a lot of clinicians attending Prof Parmar's talk was the design used in the STAMPEDE trial, a large clinical trial assessing effectiveness of new treatments for people affected by prostate cancer, which has been running since 2005. The innovation of this approach is the ongoing protocol that allows to test multiple treatments within the same established clinical trial, allowing new drug candidates to be tested (relatively) straight away, avoiding the creation of a new clinical trial. This design improves efficacy of testing new treatments, systematic approach to testing, and access to a large pool of participants who could take part in multiple treatment trials over time.

Brian Dickie, the Director of Research Development at the MND Association said: "Prof Parmar's presentation generated a lot of interest amongst clinicians who are regularly involved in MND trials and there was a strong feeling that this is the direction that we need to be taking with MND as it could increase the efficiency and reduce the cost. That said, it will take a while to put the building blocks in place and we certainly wouldn't want to hold up trials that are already in advances stages of planning, so I would expect to see a gradual introduction of changes to trials design over the coming years."

Learn more about the multi-arm multi-stage trial design from Prof Parmar here.

This talk was then followed by **Ruben van Eijk** (**C21**) who showed us the importance of genetic stratification in clinical trials. This came after the finding that the drug

lithium, which was originally found not to be effective for MND, was effective in a subgroup of participants with UNC13A genetic variation, but not in others. Dr van Eijk and his team further looked at the results from trials that tested the efficacy of valproic acid and creatine and found that the distribution of people carrying specific genetic variations (specifically C9ORF72, UNC13A or MOBP) was imbalanced across the placebo and active drug groups. This could lead to unrepresentativeness of each of these subgroups and not enough data to show any potential effect the drug could have on people with a specific genetic variation.

We also heard from **Robert Miller** (**C23**) who reported on the recently completed Phase 2 clinical trial investigating the drug NP001. While the drug was found to be safe and well-tolerated, no change was observed in disease progression in people receiving the active drug compared to those on placebo.

Looking at some of the poster presentations, **Luis Garcia Gancedo** (**CLT-08,09,10**) showed how biotelemetric monitoring, allowing remote data collection, could provide valuable data assessing the impact of MND on functional capacities and daily living, which could potentially be used as an outcome measure in clinical trials. **Matthew Klein** (**CLT-17**) discussed results from a trial testing safety of the drug EPI-589 which is thought to protect cells from neuroinflammation and oxidative stress. EPI-589 was found to be safe and well-tolerated, with promising improvements on disease progression. Similar findings were also found for the drug ezogabine, as presented by **Brian Wainger** (**CLT-21**), which works by reducing neuronal excitability, thought to affect survival in MND. The Phase 2 trial confirmed that ezogabine reduced excitability, however, due to a small number of participants, any observable effect will need to be studied in a larger clinical trial.

An update was also provided on FORTITUDE-ALS (**CLT-24**), Phase 2 clinical trial investigating effectiveness of reldesemtiv, which is now fully enrolled with first results to be expected in the first half of 2019.

Videos

- Dr Merit Cudkowitz – New way to conduct clinical trials
- Prof Chris McDermott – Changes to MND trials
- Prof Nigel Leigh – MIROCALS clinical trial
- Dr Angela Genge – MND trials

Resources

- MND Research Blog: Journey of a drug

Preclinical studies (Ps) ⬆

Before a drug can be tested in clinical trials, it first has to be examined in a lab to provide an insight into its mechanism (how it is likely to work in the body), safety, and preliminary effectiveness. These studies can be done in cells in a lab dish (*in vitro*), in animals (*in vivo*), or using computer modelling (*in silico*).

While there is only a limited number of clinical trials, there are many compounds currently in investigation that have the potential to be developed into MND treatments.

In general, only an extremely small proportion of compounds tested in pre-clinical studies get to the final drug approval stage, reflecting the rigorous and strict process assuring that only safe drugs of good quality are tested in trials and approved.

At the Symposium

Two sessions will be dedicated to treatments in the preclinical stages: platform session **8A: Preclinical therapeutic strategies,** and poster theme **7: Preclinical therapeutic strategies.** These will include a talk on the results from an investigation of an antisense oligonucleotide (gene therapy) compound and its planned testing in clinical trials (C72), and a study looking into the specific mechanisms of CuATSM, a copper therapy that is currently being tested in Phase I clinical trial (C77), which will also be discussed in the poster session (TST-29,30,31). A number of poster presentations within the preclinical therapeutic strategies theme will also include a review of cannabinoids and their potential effect on treating MND and its symptoms (TST-27,28).

Video

Prof Ammar Al-Chalabi - Cannabis

Resources

- MND Research Blog: Journey of a drug

Defining MND (De) ⬆

It has long been debated whether ALS/MND is one disease, or whether we should look at it as a collection of multiple conditions with similar symptoms and disease mechanisms. We are observing a large amount of variation in terms of speed of disease progression, length of survival, type of onset (bulbar or limb), absence/presence of frontotemporal dementia and its degree, as well as cause of the disease (e.g. involvement of specific genes).

This is especially important when investigating the effectiveness of a new drug in clinical trials, which might not work in the same way across all MND subgroups. A good example is the drug lithium, which was found not to be effective in treating MND, until the data re-analysis found that there was an improvement in people with a specific genetic variation (UNC13A).

At the Symposium

This year, we are opening the Symposium with a debate (C3), where four clinicians (split into two groups) will discuss whether ALS/MND should be seen as one disease or whether a more stratified approach should be adopted. This will be an interactive live debate, where the audience will vote depending on the arguments made by each side.

In another session, **Danielle Leighton** (C9) will talk about guidelines to help clinicians interpret the effect of specific genes on disease progression. **Session 8B: Clinical progression** will specifically focus on the way the disease progresses in different groups of people, including those with late-onset (C78), looking into the characteristics of people with longer survival (C80), or investigating the effect of riluzole across the different stages of the disease (C82).

Further studies on disease subgroups and improved diagnosis will be discussed at the poster session, Theme 10: Disease stratification and phenotyping.

Video

Prof Jeffrey Rosenfeld - Defining ALS/MND: The Big Debate

Resources

- Research talk video: Professor Ammar Al-Chalabi (King's College London) on the progress in understanding and treating of MND in the last few decades

Measures (Me) ⬆

In order for clinicians to diagnose MND and see how fast it progresses, there is a need for reliable measures to diagnose the disease faster and inform of drug effectiveness in clinical trials. While we wait for an established tissue biomarker, measures of clinical progression are currently the standard for monitoring disease progression.

The most widely used measure is the revised ALS Functional Rating Scale (ALSFRS-R), which is a 12-item clinical chart assessing patient's functional abilities. Each item asks about specific abilities (such as speech, swallowing, dressing, or walking) and is rated on a 5-point scale from '0' severe disability) to '4' (normal functioning). A cumulative score gives a physician a considered view on the person's disease status (where 48 marks meansnormal functioning).

Other measures focus on more specific symptoms of the disease, including motor neurone loss, reduced breathing ability, or assessment of behaviour and thinking abilities.

At the Symposium

Some studies have suggested that using the cumulative ALSFRS-R score isn't fully indicative of the disease progression and in one poster presentation (CLT-06), a transformation of these scores is suggested to improve the measure's accuracy. **Hiroshi Mitsumoto** will further introduce the PLSFRS measure (C79), a potentially more sensitive scale to detect changes in people with Primary Lateral Sclerosis (PLS), a rare form of motor neurone disease.

One measure that is thought to be more accurate than ALSFRS-R when it comes to assessing respiration is 'slow vital capacity' (SVC). In her poster presentation (CLT-04), **Lisa Meng** will assess the accuracy of a portable home-based spirometer, which would reduce the need of clinic visits.

In his talk (C53) and poster presentation (COG-12), **Ratko Radakovic** will talk about a different type of measure – the Dimension Apathy Scale, and how specific apathy subtypes affect one's quality of life, wellbeing and care-giver burden.

Biomarkers (Bi)

There is currently no diagnostic test for MND. Because of its relatively rare nature and non-specific symptoms, it is currently being diagnosed by an exclusion method, whereby clinicians have to rule out a whole range of other neurological and muscular conditions before giving a diagnosis of MND.

Finding a simple and pain-free test that would make this process easier and faster, would likely increase the effectiveness of existing and emerging treatments. These tests require searching for what is called a 'biomarker' – a signature of a biological change occurring in a specific disease (or a group of diseases). Some biomarkers have been identified for MND and are being tested to develop them into clinical tests.

Another reason to look for biomarkers is to keep track of the progression of the disease. Researchers are now testing various measures to see how biomarkers might change as the disease progresses, and whether these differ in people with rapid progression from those with a slower progression rate. However, due to the current lack of biomarkers, other measures of functional ability are used in clinics instead. While these are informative and provide us with a good estimate of the disease progression, they are not as accurate as biological markers.

At the Symposium

We first heard from **Rebekah Ahmed** (C83), who presented her data on possible neuroendocrine and metabolic biomarkers. Ahmed and her team analysed several proteins related to these systems in the blood of 127 people with either MND or MND with FTD and compared them to controls. The Neuropeptide Y protein (NPY), which is related to eating habits and food intake, was found to be higher in people with MND and MND-FTD, and lower in people with FTD, shining the light on a possible biomarker. All patients also had an increase in leptin and insulin levels, highlighting the need to examine how these neuroendocrine changes affect underlying disease pathology.

Next, **Valentina Bonetto** (C84) explored the possibility of using extracellular vesicles (EVs) as a biomarker of MND. EVs are like packages that can transport materials between cells, such as proteins and RNA, to facilitate waste disposal and communication between cells. They may also play a part in the spread of disease – several proteins linked to MND play a role in EV activity. An effective biomarker needs to be easy to measure, however, EVs are difficult to isolate and there is no gold standard yet on how to do this. Bonetto presented a new method that the team have developed to isolate plasma EVs, potentially overcoming this challenge. Analysis using this method revealed that people with MND had a significantly higher concentration of EVs compared to healthy people and people with other neurological diseases. The concentration was highest in those with the slow progressing form of MND, potentially showing a biomarker that can distinguish between fast and slow progressing forms of the disease. They also saw that people

with MND had remarkably smaller EVs, and lower levels of a protein called PPIA, which warrants further investigation.

Pam Factor-Litvak (C85) looked at the levels of miRNAs that are packaged within EVs, which are heavily implicated in MND. Her study involved analysis of 100 samples from the United States National US Registry. She isolated miRNAs from the plasma of 100 patients and looked at their activity. Analysis showed that healthy controls, people with Multiple Sclerosis, and people with sporadic MND each had distinct inflammatory miRNA profiles (sets of miRNA that become more active). This suggests that analyzing these sets of miRNA could distinguish MND from other diseases.

Next, **Greg Joilin** (C86) presented on his findings of a unique signature of non-coding RNA from the serum of people with MND. He identified a set of non-coding RNA that could distinguish fast from slow progressing MND in 90% of the cases in the study. Joilin and the team are now carrying out further work to validate this promising signature.

Pierre-François Pradat (C87) next looked at ferroptosis – an emerging new cell death mechanism that occurs via a process of lipid peroxydation. Through studying over 100 patient samples from a recent clinical trial, his study supported that markers of ferroptosis are predictive of functional decline in MND (measured by the ALS-FRS).

Finally, **Osamu Kano** (C88) presented his findings which support that the neuronal apoptosis inhibitory protein (NAIP) is a risk factor and a prognostic biomarker in MND. Through analyzing the changes in NAIP levels over a period of 12 months, Kano found that people with a higher amount of NAIP had a smaller decline in function (measured by ALS-FRS) over 12 months, and vice versa. As NAIP is known to protect neuronal cells against oxidative stress, this suggests that high levels might be protective in MND as well as showing promise as a biomarker.

Further information on this topic was presented at the poster session (Theme 6) where data on many possible tissue biomarker signatures was presented, including a poster by **Daisy Sproviero** (BIO-18) and her team, who found a small group of RNAs in extracellular vesicles that were specific to MND.

Video

Dr Hande Ozdinler – Testing biomarkers specific to site of onset

Resources

- Information sheet: Biomarkers
- Research talk video: Professor Martin Turner (University of Oxford) on the biomarker challenge

Telemedicine & technology (Te) ⬆

Telemedicine is the remote exchange of data between an individual and a healthcare professional to assist in the diagnosis and management of a condition. The ultimate goals of using this technology are to increase access to care for people, decrease the frequency of clinical visits and reduce clinical costs.

For people with reduced mobility, telemedicine means no long commutes to short, but critical, assessments and no waiting around. From previous studies, people taking part in remote assessments expressed higher satisfaction with the overall care they were given and appreciated remaining in the comfort of their own homes.

At the Symposium

Much of the content that was presented related to the use of technology in clinical trials. Trial results and reliability was the theme of our first talk by **Richard Alan Smith** (C32), Director of the Centre for Neurological Study in San Diego. He outlined how computer-based testing of speech gives objective trial results demonstrating outcomes missed by traditional clinical assessments.

Ruben van Eijk (C34) also presented on trial reliability as well as patient participation. Often the success of clinical trials is based upon a questionnaire (such as the ALS functional rating scale; ALSFRS) and this is a rather subjective way of measuring the effectiveness of different treatments. His trial of a hip worn accelerometer has signs of being a reliable data-driven method for tracking disease progression. This method involves sensors which detect motion, the kind common in fitness trackers. His trial captured information on physical activity over a seven-day period and importantly, as people wore the tracker at home, it removed much of the 'trial burden' of attending hospitals or clinics to be assessed. This should mean more patients are willing to sign up for studies using this method and potentially it makes it easier to include those in more advanced stages of disease progression. All of this means richer and more reliable trial data whilst lowering the barrier to patient involvement in trials.

A similar theme was presented by **Jeremy Shefner** (C35) who presented on the reliability of patients and their carers to undertake their own clinical tests in the home and report back using a smartphone app. Their focus was on testing information exchange with health professionals. The trial showed some interesting findings; firstly that patients and their carers can reliably provide accurate data relating to speech, strength and respiratory function using equipment provided by the clinic and used in the home. But also, that people with MND valued the fact that they had a direct involvement in their own health assessment saying they felt more aware of their symptoms and progression and therefore more in control. Having demonstrated data reliability, the Institute's conclusion was that much more frequent measurements are feasible (remember the trial participant can do this at home without the need to attend a clinic), which should make a trial quicker, provide more data and therefore robust results.

This point was also made by **Andrew Geronimo** (**C33**) who presented a study on remote testing of respiratory function with a video connection between patient and healthcare professional. With more frequent measures of lung function, non-invasive ventilation, effective in prolonging survival, can be introduced at the right time improving a patient's quality of life and reducing the risk of emergency hospitalisation due to respiratory decline between infrequent clinic appointments.

Finally, we heard from **Phillipa Rewaj** (**C36**) who gave an update on the Speak:Unique voicebank pilot. This was a great way to wrap up the session as it is a tangible example of technology about to translate into a clinical service. The Speak:Unique pilot, which was part-funded/ by the MND Association, is different to other voice banking technologies in that the recording time is much shorter than the norm (less than 1 hour of recording is required) and it has the ability to 'repair' voices by merging similar voices from volunteers. This is particularly beneficial for people with MND whose voice may have already started to deteriorate by the time they record their voice. Large numbers of Scottish healthy voice donors of different ages, gender and accents have been recorded. These are then combined with the patient voice hence the benefit of a reduced recording time for the person with MND and the 'voice repair' element if voice deterioration has already started. The next steps for Speak:Unique are to expand the voice bank of healthy voices into accents from the rest of the UK, and to work towards the introduction of a clinical service.

Videos

Dr Phillipa Rewaj – The Speak Unique voice banking project

Dr Ruben van Eijk – Remote monitoring of disease progression using accelerometry

Resources

- MND Research Blog: 'There is an app for that' – the wonders of technology in ALS
- Video: Dr Esther Hobson (University of Sheffield) on gastrostomy, non-invasive ventilation, and utilising telemedicine in MND care

Disease mechanisms (Dm) ⬆

Motor neurones are highly specialised, extremely long, single cells that require high levels of co-ordinated energy supply to perform their very complex role in the body. It is likely that their death in MND is caused by 'attacks' from multiple sources. Researchers are working hard to defend motor neurones 'from all sides' and, to do this, they need to know the neurones' weaknesses. They believe there are several ways in which motor neurones are under attack, a few of which are outlined below.

Firstly, proteins are moving out of the 'control centre' of the cell (the nucleus) and into the area around the nucleus (the cytoplasm) where they become toxic by clumping together. Secondly, the highly co-ordinated and essential transport system which carries essential cargo up and down the neurone may fail or work less efficiently. Thirdly, the neurones' energy producing parts (think batteries) called mitochondria become unable to produce the large amount of energy needed to maintain the neurone itself. Finally, the support cells that should protect the neurones 'go wrong' and, instead of protecting, they start attacking the neurones.

If you look at a motor neurone affected by MND down the microscope, you see clumps of proteins (most often the TDP-43 protein) that have clumped together, and are in the wrong part of the neurone – the cytoplasm, instead of the central nucleus. Clues on how they are getting there are found by studying an inherited form of MND, for example the one caused by mutations in the C9ORF72 gene.

Highlights from the Symposium

Several sessions at the Symposium focused on how impairments in key neuronal structures in MND contribute to the development and progression of the disease, and how these could be targeted with therapeutics.

Prof Spires-Jones (C16) opened session 4A with a discussion of the role of synapses in neurodegeneration. Synapse dysfunction and loss is seen in many neurological diseases, including MND, Alzheimer's disease and Dementia with Lewy bodies. The commonality of synapse loss across these diseases makes it a key therapeutic target, and in addition, most neurological drugs work at the level of synapses, making them a very 'druggable' target. Prof Spires-Jones summarised data from her team and others that showed that in MND, synapse degeneration in the frontal cortex is associated with cognitive decline, and damaging TDP-43 protein is found in synapses. Targeting these pathways could be beneficial to prevent or treat MND.

We also heard an interesting talk from **Prof Schiavo** in session 5A (C29) on the use of axonal transport as a therapeutic target. Deficits in axonal transport are found in many neurological diseases, including MND. These deficits appear before/at disease onset and are likely to be important in the development of MND. Schiavo talked us through data that showed that the p38 MAPK signalling cascade, which is important for axonal transport, is increased in the SOD1 mouse model of MND, and that long-term treatment with a p38 MAPK inhibitor partially restores physiological function in MND neurones *in vitro* and *in vivo*. Another example showed that inhibition of the insulin-like growth factor-1 receptor (IGF1R) (which is overexpressed

in MND patients) restores axonal retrograde transport in a SOD1 mouse *in vivo,* providing further evidence of the possible beneficial effects of targeting key pathways linked to axonal transport. The take-home message was that axonal impairments are reversible and can be modulated by small molecule inhibitors.

Videos

Prof Giampietro Schiavo – Axonal transport as a therapeutic target

Dr Andrew Tosolini – Axonal transport is impaired in SOD1 mice

Resources

- MND Research blog: Disease mechanisms blog collection
- Nature: Molecular mechanisms of ALS poster
- Video: Dr Emily Feneberg (University of Oxford) on the neurochemistry in MND

Neurones (Ne)

Neurones are cells that form the nervous system. This is split into two sections; central nervous system (CNS) – the brain and spinal cord, and peripheral nervous system (PNS) – branching out from the brain and spinal cord to the rest of the body. The nervous system is important in sending and receiving electrical messages from the brain to other organs and back.

There are different types of neurones in our bodies. Two of the most studied are **motor neurones**, sending signals to the muscles and leading to movement, and **sensory neurones**, responsible for perception of sensation. In MND, motor neurones are affected, while sensory neurones remain intact.

Motor neurones are large cells, consisting of a **body** with the main control centre (nucleus) and important organelles (such as mitochondria), **dendrites** (short projections that receive messages from preceding neurones), and the **axon** – a long projection that carries the incoming message from the dendrites, via the neuronal body to other neurones. Once the electrical signal gets to the end of the neuronal axon, it gets transmitted to another neurone in the form of chemicals passing like messengers in the small spaces (synapse) between two neurones.

In MND, it is suspected that the neuronal body as well as the axon might be affected, leading to degeneration of the motor neurones. Exactly how this happens is of course the subject of extensive investigation.

Highlights from the Symposium

In session **4A: Cell biology and pathology**, one of the plenary speakers, **Tara Spires-Jones** (C16), will discuss the importance of the synapses in neurodegenerative diseases such as Alzheimer's disease and MND, and how these could become a possible therapeutic target.

In another session focusing specifically on the axon part of the neurone, **5A: Axonal degeneration**, one of the plenary speakers, **Michael Coleman** (C28), will talk about the current understanding of axon degeneration and how this is likely to contribute to the development of MND and other related diseases. In the same session, another plenary speaker, **Giampietro Schiavo** (C28), will talk about how transport of important cargo along the axon can disrupt a normal functioning of the neurone, and reveal results of his team's latest study testing a compound that would improve the functioning of axonal transport.

Video

Dr Arpan Mehta – Using stem cells to observe axonal transport

Resources

- Research talk video: Dr Alex Whitworth (University of Cambridge) on axonal transport and RNA biology in MND

Support cells (Sc)

Aside from studying motor neurones directly, researchers are also looking at what happens when the cells that support motor neurones 'go wrong'. Motor neurones are surrounded by support cells called glial cells which normally help protect motor neurones from damage and injury.

Two particular support cells have been studied the most in MND. These are called microglia and astrocytes. In MND, something happens to change these, leading them to attack the motor neurones instead of protecting them. How and why they do this, however, is less well understood.

Motor neurones will grow quite happily on their own in a dish in the lab. However, if astrocytes are grown in the same dish, or motor neurones are grown in liquid that has previously contained astrocytes, the motor neurones die. This suggests that astrocytes are passing something toxic onto the motor neurones.

Highlights from the Symposium

In a platform session dedicated to support cells, **7A: Non-neuronal cells**, we will hear from four speakers on the effect of glial cells on motor neurone degeneration. One of the plenary speakers, **Peter St George-Hyslop** (C60), will discuss the role the neuronal immune system, the microglia, have in various neurodegenerative diseases. In the same session, **Shintaro Hayashi** (C61) will talk about the results from their study that investigated whether there is a sign of glial inflammation in spinal cords of people with MND before they develop symptoms of the disease.

Video

Dr Rickie Patani – Stem cells and MND

Resources

- MND Research blog: Glial cells blog collection
- MND Research blog: It's not just about the neurons

Brain (Br) ⬆

The brain is the main control centre of our body and the nervous system. It is made up of billions of neurones which constantly communicate with each other in order to send messages in the form of electric signals from one part of the brain to another, as well as to communicate with the rest of the body. It controls our thinking, behaviour and the most basic physiological actions (such as breathing, seeing, smelling, or sleeping).

Different parts of the brain are, more or less, dedicated to specific functions, and specific regions of the brain are known to be affected in MND. Two of these regions include the **motor cortex**, responsible for planning and executing our voluntary movements, and the **prefrontal cortex**, involved in our thinking, personality and decision-making. The latter is mainly affected in people with MND who experience cognitive decline and behavioural changes.

Another way to look at the brain is to split it into grey and white matter. **Grey matter** (or the 'cortex') is the 'bark' of the brain or the outside of the brain, while **white matter** is the connections between the different parts of the brain and is generally hidden inside the grey matter.

At the Symposium

In session **4C: Neuropathology**, **Matthew Nolan** (C24) will review the results of his study investigating whether certain subgroups of neurones within the primary motor cortex are more susceptible to accumulate toxic proteins which cause these neurones to die.

In the **Theme 8: Clinical neuroimaging and electrophysiology** poster session**, Matt Gabel** (IMG-19) will present on his work using a novel 'biomarker staging' technique to observe changes in the brain of people with MND over time, with particular focus on the thickness of the cortex. In another poster presentation (IMG-22), **Monica Consonni** will look at the changes in the thickness of the cortex of people with MND and compare the differences between people with cognitive impairment compared to those without.

Modelling MND (Mo)

In order to understand what goes wrong in MND, researchers need to study 'something' that, to all intents and purposes, mimics the biology of the disease. Ideally that 'something' has to be readily available, tangible, accessible, and available with a large enough number of samples so that any findings can be reproduced and confirmed.

There is currently no way to visualise all the complex interactions that happen in MND. For example, observing all of the biology of motor neurones in living people is impossible, and so researchers use models of the disease.

There are generally three types of models that are used to research MND; *in vitro, in vivo* and *in silico*.

In vitro (meaning: 'in the glass') models use isolated cells in a lab dish, with the most widely used being induced pluripotent stem cells (iPSCs). These are skin cells taken from people with MND that are transformed into stem cells – cells with the potential to turn into different types of cells, including motor neurones.

In vivo (meaning: 'within the living') models include testing in living organisms, with the most widely used animals being zebrafish, fruitflies, worms or mice.

In silico (meaning "in silicon" as in silicon microchips) modelling, while not as common, is used to perform a computer simulation.

At the Symposium

In a platform session dedicated to **disease models (Session 9A)** we will hear from four speakers presenting a range of models used to understand disease biology. These include **Sean Sweeney** (C89) using the fruitfly and rat neurones in a dish to identify a novel protein that they have shown protects neurones. **Thomas Moens** (C90) has gleaned a further understanding of the mechanism of C9orf72 (the most common genetic cause of MND) protein toxicity, again using the fruitfly, and further insight into C9orf72 mechanism examined in zebrafish will be discussed by **Tennore Ramesh** (C91). Finally, **Ruxandra Dafinca** (C7) will tell us how calcium buffering is altered in motor neurones derived from patients' cells. Many other presentations will be discussed during the poster session in **Theme 2: In vitro experimental models** and **Theme 3: In vivo experimental models**.

Videos

Dr Barney Bryson – Optogenetics: Using light to restore lost muscle function in MND

Dr Clive Svendsen – Modelling MND in a chip

Prof Kevin Talbot – Studying MND in a dish

Resources

- Website resource: Understanding animal research
- MND Research blog: iPSC collection of blogs
- Video: Dr David Gordon (University of Oxford) talks about modelling MND
- Video: Dr Rickie Patani (University College London) on using stem cells to model human MND