THE NEWSLETTER FOR PROFESSIONALS INTERESTED IN **ENCEPHALITIS**

CONNECT PROFESSIONAL

EDITION 10 **AUTUMN 2022**

ENCEPHALITIS 2022: Speakers revealed

ENCEPHALITIS SOCIETY
The brain inflammation charity

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IN THIS ISSUE:

Welcome

Welcome to the latest edition of Connect Professional.

We write to you in the final few weeks before the return of Encephalitis 2022 – our annual conference.

On Thursday, 1st December, we will again be returning to the Royal College of Physicians in London for a full day devoted to encephalitis research.

We have put together an amazing and diverse programme this year (see pages 8-11) with speakers from ten countries, including our keynote lecturers who hail from Australia and the USA.

We have a further 40 poster presentations and the potential for an interesting debate between Dr Thomas Pollak and Assistant Professor Janet L Cunningham.

And for young researchers, we also have a day of satellite meetings on Wednesday, 30th November, which includes a very useful workshop of applying for grants and fellowships (see page 11).

As always, we would love you to join us in London, but we realise that the journey may be too costly in terms of money or time for many of you reading this.

Thankfully, technology means the conference can be viewed online, with all presentations available to watch for 30 days afterwards.

We do hope to see you there – be it in London or online – for what will be an interesting and thought-provoking conference.

Elsewhere in this magazine, we have an in-depth feature on the work of Assoc Professor Maarten Titulaer and the work of the Erasmus MC Autoimmune Encephalitis Research Group (see pages 19-23), an article on the neurological complications of Monkeypox, and a reflection on the almost one-year anniversary of the release of our Global Impact Report.

It would be remiss of us not to take this opportunity to champion the work of the Encephalitis Society.

Anecdotally, we have heard from several medical professionals that they are unaware of the support that we can provide for their patients.

As a result, and starting with this issue, we will begin to put our support services under the spotlight for you to read and fully understand the ways in which we can help (see pages 6 and 7).

Please do take the time to read it and to share with any of colleagues or patients who you believe may benefit from our support.

Finally, World Encephalitis Day 2023 is on the horizon – and we need your help!

We always want to make a splash with our global awareness day, but 22nd February 2023 will be cause for an even bigger splash as it will be the 10th anniversary (see page 5).

If you can go #Red4WED, are interested in taking part in our BrainWalk step challenge or can help us to light up a landmark on World Encephalitis Day, please get in touch.

Thank you and with very best wishes,

Dr Ava Easton
Chief Executive
Encephalitis Society
@encephalitisava

Dr Nicholas Davies
Chair - Scientific Advisory Panel
Encephalitis Society

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Pictured overleaf: Dr Charly Billaud, of Aston University, shares his research at Encephalitis 2021

HONOUR: (left) Professor Tom Solomon receives his CBE from the Princess Royal, and with his wife, Dr Rachel Kneen.

Pride at CBE honour for Professor Tom Solomon

Many congratulations to Professor Tom Solomon who received his CBE from the Princess Royal at an investiture ceremony held at Buckingham Palace.

It is a well-deserved honour for Professor Solomon, the President of the Encephalitis Society, who has done so much to further the understanding of encephalitis.

"I am truly honoured by this award, which reflects the tremendous support I have had from family and friends, plus the enormous efforts of a very large group of colleagues over many years," he said.

"Not least among these is my wife, Dr Rachel Kneen, a paediatric neurologist at Alder Hey Children's Hospital, who has made major contributions to the work.

"When I first started working on emerging infections in Asia 25 years ago, many people thought this was a rather esoteric and niche subject. But over the last two and a half years we have all seen the enormous impact such infections can have, and how important an area this is."

After the investiture at Buckingham Palace, Professor Solomon celebrated with family, friends, and work colleagues at the Academy of Medical Sciences in London, where he is Vice President – International.

Dr Ava Easton, our Chief Executive, said: "This was an extremely proud day for everyone at the Encephalitis Society.

"Tom has been a leading figure for the Encephalitis Society for over 20 years. His work as a researcher has been invaluable to improving our understanding of encephalitis, he has used his expertise to guide us, raise awareness of encephalitis, and, of course, raised tens of thousands of pounds to support our work.

"We are lucky to have him as a President and I am sure you are all as proud of him as I am. Many congratulations, Tom!"

Professor honour

Congratulations are in order for Professor Benedict Michael, the Vice Chair of our Scientific Advisory Panel.

Professor Michael has recently been appointed to the position of Professor of Neuroscience at the University of Liverpool.

The honour is in recognition of his stellar work as a Medical Research Council Clinician Scientist and lead of the Infection Neuroscience lab at The NIHR Health Protection Research Unit for Emerging and Zoonotic Infection at Liverpool.

Professor Michael's career has been devoted to furthering understanding of encephalitis, zoonotic infection, neurology and pandemics. As well as co-chairing the Global Neuro-Research Coalition and sitting on the WHO Expert Forum on Neurology and Covid-19, he is leading the £2.3m Covid-Clinical Neuroscience Study which is investigating the neurological complications of SARS-CoV2. Professor Michael is also an Honorary Consultant Neurologist at The Walton Centre, Liverpool.

Information week focuses on measles

The Encephalitis Society recently marked its second annual Encephalitis Information Week with a campaign urging parents to get the facts about measles.

Our media awareness drive, which ran between October 17 and 21, reached approximately 9.5 million people in the UK on radio and television. It was complemented with a global social media campaign targeting English, Spanish, Portuguese, French and German speakers.

Dr Ava Easton, our Chief Executive, said: "We felt that it was vital to reach out to parents and guardians and ask them to seek advice about the MMR vaccine and other routine childhood vaccinations.

"We emphasised that measles is so contagious that just one person with measles can infect another nine people who do not have immunity.

"As we all know, a measles infection is not a harmless childhood illness and can, for the unvaccinated, lead to complications such as ear infections, severe diarrhoea, blindness, pneumonia, and encephalitis, which can require hospital treatment and lead to long-term disability or death."

"Sadly, data reveals that the MMR vaccination rate in the UK has dropped to its lowest level in a decade with more than one in 10 five-year-olds not up to date with their two doses of the vaccine. Globally, it is just as bad with Unicef and the WHO reporting that measles cases nearly doubled globally in the first two months of 2022, compared to the same period in 2021."

Professor Benedict Michael, Chair of Infection Neuroscience at the University of Liverpool and Vice Chair of our Scientific Advisory Panel, said: "Even before the COVID-19 pandemic in 2019, the UK had lost its WHO measles-free status so we are far from achieving the vaccination status needed in our communities.

"The belief among my NHS colleagues is that there might be many reasons why parents have not had their child vaccinated against MMR including because they didn't realise the NHS was offering appointments following the COVID-19 outbreak or that they didn't want to burden the NHS during the pandemic.

"With this campaign, we wanted to reassure everyone that it is safe to go and have your vaccinations, protect your children and, in turn, anyone who is not immune."

Refresh your neurology skills with the NeuroPRACTICE team

Are you looking to refresh your knowledge of neurology in clinical practice?

NeuroPRACTICE on Friday, 18th November is running an intensive one-day update on the latest ideas in the management of neurological presentations. They will focus on the key skills required for clinical assessment, investigation, and management of common neurological and neurosurgical presentations.

The course, organised by the University of Liverpool, is aimed at primary and secondary health professionals and is relevant to anyone who sees common neurological presentations. This includes but is not limited to GPs, ANPs, A&E doctors, and junior doctors.

Topics that are discussed in the course generally cover

- Headache, migraine, or not?
- Transient neurological symptoms
- Approach to movement disorders
- Acute and chronic back pain
- Functional Neurological Disorders

Additionally, at the end of the day, there will be an opportunity to ask the questions you have always wanted to ask of an expert in neurology.

NeuroPRACTICE takes place at Aintree University Hospital, Liverpool, on Friday 18th November.

SIGN UP TODAY: www.liverpool.ac.uk/neurosciences-research-unit/neuropractice

WED 2023: We Need YOU!

World Encephalitis Day (WED) is returning on Wednesday, 22nd February - and we need YOU to help us shine a light on encephalitis.

Medical professionals around the world have been fantastic in raising awareness of encephalitis since its launch in 2014 - playing a key role in helping us to reach 294 million people globally.

This coming year will be the 10th anniversary of our awareness campaign and to celebrate we want to continue to shine a light on encephalitis.

How can you get involved? Well, it is as easy as **One**, **Two**, **Three**.

ONE: Go #Red4WED

Every year we ask healthcare professionals to wear something red on World Encephalitis Day and then share their photos or videos on social media, telling their followers about why they are wearing red.
Wearing something red could mean anything - a red bow tie, red hat, red nails, red trousers or even one of our official World Encephalitis Day T-SHIRTS.
Do you and your team want an official World Encephalitis Day t-shirt? Email comms@encephalitis.info and we can put some in the post to you today!

TWO: BrainWalk

BrainWalk is our fun step challenge which asks supporters to walk, jog, or run as many steps as possible throughout February – raising money for the Encephalitis Society at the same time.
You will be able to enter from the 1st January and set a daily, weekly or total step goal for February as you battle it out to top the BrainWalk leader boards.

THREE: Light up a Landmark

On 22nd February 2023, we are asking supporters to help us turn the world #Red4WED by lighting up well-known local landmarks red.

In 2021, 156 landmarks and buildings around the world went #Red4WED, including Niagara Falls, The Optus Stadium in Perth, Australia, the Liver Building in Liverpool, Cameroon's Reunification Monument and Rani Pokhari in Nepal, to name a few!

How can I get involved?

Do you live near a famous local landmark? Or can your hospital or place of work light up #Red4WED? Then please get in touch and help us to shine a light on encephalitis! If you are able to secure a building lighting up #Red4WED, please email comms@encephalitis.info and let us know so we can count it towards our official WED buildings portfolio!

Email comms@encephalitis.info if you need any t-shirts or information about World Encephalitis Day

How we can help your patients

The Encephalitis Society provides support to people directly and indirectly affected by encephalitis from all over the world. Patients, family members, carers and medical professionals are all welcome to contact us for advice and support. Whether you need information about encephalitis, advice about recovery or rehabilitation, signposting to appropriate services, or simply to speak to someone who understands this condition, we are here to help.

Telephone and Online

We provide a telephone and online service run by knowledgeable staff with expertise in encephalitis who can give comprehensive information and signpost to relevant services. We can arrange for interpreters if English is not a patient or family member's first language.

Meeting Others Affected

The support service facilitates regular weekly and monthly regional virtual groups across the world, as well as some in-person support groups within the UK. Additionally, we have a global connection scheme that enables people affected by encephalitis and their families to contact with others in similar situations to themselves. There is also a support forum for our online community where encephalitis members can connect and support each other.

> There have been times when I have wondered who else knows how much it takes to fight the fatigue. After today, I realise I am not alone.

Events

There are various annual events across the year for members affected by encephalitis. Our next event will be My Brain My Medicine on 24 April 2023 at the Royal Society of Medicine, London, which provides a powerful space where speakers affected by encephalitis tell their story in the company of others affected by encephalitis, raising support and giving inspiration to all. Attendance can be in-person or virtual.

Retreats

We provide UK-based retreats for both children and adults affected by encephalitis. This gives an opportunity for relaxation, confidence building, and meeting those who share the effects of encephalitis. This year we held the Young Persons Weekend in an inclusive adventure park for children and their families. Our adult retreats offer respite and wellbeing activities such as walks, yoga, meditation.

Information

We have a range of peer reviewed factsheets and guides tailored to a range of audiences, including individuals with encephalitis and their families, professionals, GPs/family doctors and teachers. These are available in both digital and hardcopy from our website and can be translated into different languages. Visit www.encephalitis.info

Videos and Podcasts

We have a YouTube channel and podcast which showcases interviews and discussions with world leading experts in the field alongside people with lived experience of encephalitis. The Encephalitis Podcast is available on all good podcast channels and our YouTube channel by visiting www.youtube.com/encephalitissociety

> What a relief it is to hear others speak of things that have held us in isolation for years. Now I am in tears, so grateful to still be here. It's a wonderful thing that you are doing to help us all... there are no words to express enough thanks."

How patients can get in touch

Telephone/Skype/Zoom

Our support team are available from 9am to 5pm (BST/GMT), Monday to Thursday, and 9am to 4.30pm (BST/GMT) on Fridays on +44(0)1653 699599. We try to be flexible and can pre-arrange out-of-hours telephone appointments, particularly for people in other time zones around the world. If your patient would like to use Skype/Zoom please email support@encephalitis.info to book an appointment.

Email and Online

If your patient would like to contact us online, please refer or signpost them to support@encephalitis.info. We try to respond to all our emails and online enquiries within 48 hours.

Website Instant Online Chat

We provide instant messaging under the "Let's Talk – Chat Online" button on www.encephalitis.info. You can talk to us and ask us questions here. This is subject to staff working hours and the service may not be available all the time, particularly around holidays.

Virtual Gatherings

To register and find out dates and times of our worldwide virtual gatherings, please visit our website: www.encephalitis.info/virtual-gatherings

Connection Scheme

If your patient would like to be put in touch with a person similarly experiencing encephalitis, they can sign up to our Connection scheme. They can find out more and sign up at www.encephalitis.info/connection-scheme

> I came away feeling upbeat and with more understanding that my feelings are normal for me and others. Thank you so much for arranging this, I'm looking forward to the next meeting

Online Forum

To access our online forum community for peer-to-peer support, visit www.encephalitis.info/encephalitis-support-forum

Events

For current updates on all our events, including dates, availability and bookings, please see the events website page www.encephalitis/events-and-activities or contact our office on admin@encephalitis.info.

Social Media

You can find us and our community on various social media platforms. These provide an opportunity to connect online with us and other people with similar experiences, find out the Society's news, encephalitis advances, and how to get involved with the Society. Simply search for the Encephalitis Society on any of our channels, including Tik Tok, Facebook, Twitter, Instagram and YouTube.

We manage all personal information in the strictest of confidence. Our confidentiality and data protection policies can be found on our website: www.encephalitis.info/privacy-policy

Join us at Encephalitis 2022

Speakers from around the world will be sharing their latest research when the Encephalitis Conference returns on Thursday, 1st December.

Attendees are invited to join us at the Royal College of Physicians, London - or virtually - for talks which cover hot topics, critical research questions, and approaches to the key clinical challenges informed by the latest research.

The programme for the conference has been put together by the Encephalitis Society's staff and Scientific Advisory Panel, members of which will be chairing the sessions during the day.

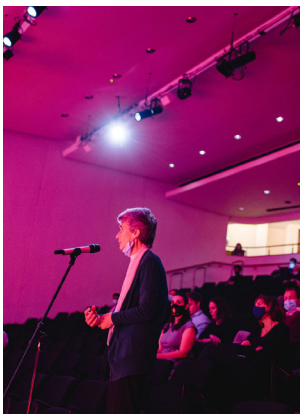
This year's keynote lectures will be delivered by Assist Prof Stacey L Clardy, from the University of Utah and Salt Lake City, and Professor Russell Dale, from the University of Sydney and the The Children's Hospital at Westmead, with invited guest lectures coming from Professor Tom Solomon CBE, President of the Encephalitis Society, and epidemiologist, Dr Julia Granerod.

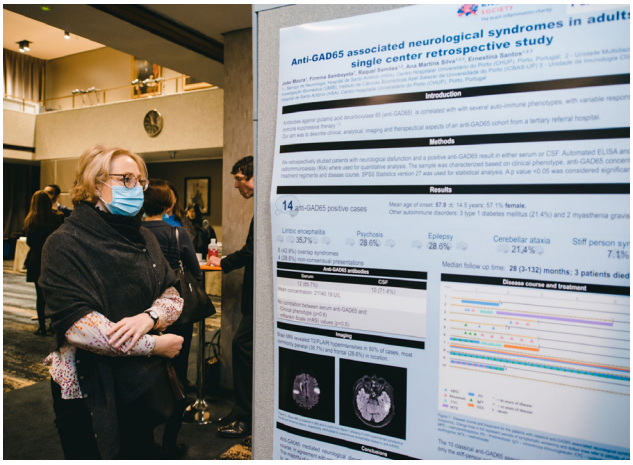
There is also a thought-provoking debate chaired by Professor Sarosh Irani, Head of the Oxford Autoimmune Neurology Group, and based around the statement: "This House believes that too many patients with psychiatric illness are being unhelpfully diagnosed with brain autoimmunity".

Ten countries are represented on the speaking panel with a further 40 poster presentations arriving from researchers all over the globe. This year's conference also includes free admission to Satellite meetings on Wednesday, 30th November, which include a session on how to be successful when applying for a grant or fellowship and a data-blitz poster presentation.

Dr Ava Easton, Chief Executive of the Encephalitis Society, said: "We have put together a packed programme which we believe will be of interest to all medical professionals involved in the clinical care or research of encephalitis. There is so much interesting research which is being carried out around the world, it would be a shame to miss out."

The Encephalitis Conference, as in recent years, will be recorded with all talks available to watch on demand afterwards for anyone who is unable to join us virtually or in-person on the day.





Tickets: www.encephalitis.info/conference

Tickets include access to all video presentations for 30 days after the conference

ENCEPHALITISCONFERENCE

CHAIR: Prof Arun Venkatesan
Johns Hopkins Encephalitis Center; The Johns Hopkins University School of Medicine, Baltimore, USA

CHAIR: Prof Benedict Michael
Institute of Infection, NIHR HPRU for Emerging and Zoonotic Infection; The Walton Centre NHS Foundation Trust, Liverpool, UK

9.35am: **KEYNOTE LECTURE** - Updates on Paediatric Encephalitis: Infections and autoimmunity
Prof Russell Dale, The University of Sydney and The Children's Hospital at Westmead, Australia

10.05am: Biomarkers of neurological complications of COVID-19
Dr Cordelia Dunai, University of Liverpool, UK

10.20am: Outcomes of adult patients with meningo-encephalitis requiring intensive care: the international prospective multicentre EURECA study
Prof Romain Sonneville, Bichat Claude-Bernard Hospital, Intensive Care Medicine, INSERM U1337, Université Paris Cité, France

10.35am: **INVITED GUEST LECTURE** - Do Steroids Improve the Outcome in Herpes Encephalitis - a 25-Year Odyssey
Prof Tom Solomon CBE, Pandemic Institute, University of Liverpool and Brain Infectious Group, UK

Session One

Professor Tom Solomon CBE

CHAIR: Prof Frank Leypoldt
Kiel University, Kiel, Germany

CHAIR: Prof Tom Solomon CBE
Pandemic Institute, University of Liverpool and Brain Infectious Group, UK

Session Two

Dr Julia Granerod

11.30am: Human anti-CASPR2 autoantibodies impact synaptic transmission and neuronal excitability
Prof Ana Luisa Carvalho, University of Coimbra, Portugal

11.45am: The blockade of bacterial-neuron interaction as a new therapeutic strategy to prevent neurological sequalae caused by central nervous system pneumococcal infections
Assoc Prof Federico Iovino, Karolinska Institute Stockholm, Sweden

12pm: The spectrum of immune checkpoint inhibitors-related encephalitis: clinical features and outcome according to the antibody status
Dr Antonio Farina, Hospices Civils de Lyon and Université Claude Bernard Lyon, Lyon, France

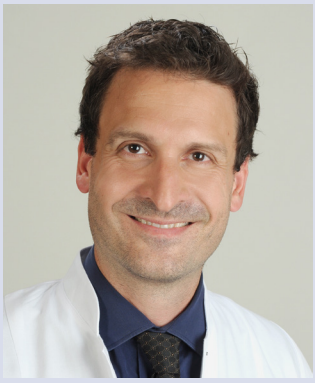
12.15pm: Neuropsychiatric factors influencing outcome in patients with encephalitis admitted to neurorehabilitation - a 6-year retrospective analysis
Dr Sonali Polakhare, Thames Brain Injury Rehabilitation Unit, Blackheath; King's College Hospital, London, UK

12.30pm: **INVITED GUEST LECTURE** - A Global Perspective of Encephalitis: Where Are We Going and When?
Dr Julia Granerod, Epidemiologist, Independent Consultant, UK

Session Three

CHAIR: Assist Prof Stacey L Clardy
University of Utah and Salt Lake City VA, USA

CHAIR: Dr Nicholas Davies
Chelsea and Westminster Hospital, London, UK


Dr Frank Leypoldt

2.15pm: Long-term clinical outcome and relapse rate in a Dutch anti-CASPR2 encephalitis cohort
Ms Marie Vermeiren, Erasmus Medical Center, Rotterdam, The Netherlands

2.30pm: Experiences of persons with acute brain infections and their caregivers – a qualitative exploration
Ms Vasundharaa S Nair, NIMHANS, Bengaluru, Karnataka, India

2.45pm: Orthostatic polymyoclonus and other myoclonus syndromes can be the main and presenting syndrome in CASPR2 autoimmunity
Prof Frank Leypoldt, Kiel University, Kiel, Germany

3pm: The disconnected hippocampus: structural brain lesions and functional network alterations follow distinct routes to recovery in patients with NMDAR encephalitis
Dr Josephine Heine, Charité – Universitätsmedizin Berlin, Germany

Session Four

CHAIR: Dr Ava Easton
Chief Executive - Encephalitis Society

CHAIR: Prof Sarosh Irani,
Oxford Autoimmune Neurology Group and John Radcliffe Hospital, Oxford, UK

3.45pm: **THE ENCEPHALITIS SOCIETY FUNDED RESEARCH: DATA BLITZ SESSION**

Implementing an hospital-based encephalitis surveillance in Senegal to decipher main causes of viral encephalitis in a West-African low-income country
Dr Jamil Kahwagi, Clinique de Neurosciences Ibrahima Pierre Ndiaye, Dakar, Senegal

Dissecting the selective vulnerability of dopamine neurons to SARS-CoV-2 infection using human stem cell model
Dr Oliver Harschnitz, Neurogenomics Research Centre, Milan, Italy

4pm: **DEBATE:** "This House believes that too many patients with psychiatric illness are being unhelpfully diagnosed with brain autoimmunity"

For: Dr Thomas Pollak
King's College London, UK

Against: Assist Prof Janet L. Cunningham, Uppsala University Hospital and Uppsala University, Sweden

Chair: Prof Sarosh Irani, Oxford Autoimmune Neurology Group and John Radcliffe Hospital, Oxford,UK



Assist Prof Janet L. Cunningham and Dr Thomas Pollak

4.30pm: **KEYNOTE LECTURE** - The Landscape of Clinical Trials in Autoimmune Encephalitis
Assist Prof Stacey L Clardy, University of Utah and Salt Lake City VA, USA

As part of Encephalitis 2022, we are also offering free admission to our Satellite Meetings on Wednesday, 30th November.
These meetings were introduced by the Encephalitis Society's Scientific Advisory Panel to offer advice and feedback to researchers who are in the early stages of their careers.
"One of the aims of the Encephalitis Society's Scientific Advisory Panel is to help the next generation of researchers through sharing our expertise and offering advice," said Professor Benedict Michael, the panel's Vice Chair.

How to Get Your Fellowship or Grant

Wednesday, 30th November – 1.30pm to 2.30pm GMT

Hybrid session: face-to-face (Royal College of Physicians, London) and virtual

This workshop is for researchers from junior to intermediate level who are beginning their research careers and will share advice on how to apply for funding as well as develop Fellow- ship and grant application writing skills.

By attending this workshop, attendees will:

- Know how to find grant funding opportunities.
- Gain advice on important tips on writing, along with guidance on what reviewers will be looking for.
- Explore the most common mistakes made by the applicants.
- Hear from Clinical Academics about obtaining funding to support research in both high and medium-low income countries.

This workshop will be delivered by:

Professor Benedict Michael
NIHR HPRU for Emerging and Zoonotic Infection, and Institute of Infection, Veterinary and Ecological Science, University of Liverpool; UK

Assist Prof Omar Siddiqi
Harvard Medical School, USA; University of Zambia School of Medicine, Zambia.

Dr Mark Ellul
Clinical Infection Microbiology & Immunology, University of Liverpool

Data Blitz Poster Presentation

Wednesday, 30th November – 3.00pm to 5.30pm GMT

The Encephalitis Society has invited several researchers who submitted posters for this year's conference to share their re-search with members of the Scientific Advisory Panel. Confirmed posters at the time Connect went to press, include:

Risk of seizure activity in patients with encephalitis regional and volumetric analysis of cerebral oedema and development of a multivariable prediction model
Dr Jian PK Chen, National Hospital for Neurology and Neuro-surgery, UCLH NHS Trust, London, England

Assessment of CASE and NEOS scores in a Danish National NMDAR-encephalitis cohort
Ms Andrea Gestsdóttir, Dept of Neurology, Odense University Hospital, Odense, Denmark

Development and validation of a clinical prediction score for the risk of autoimmune encephalitis
Dr Marion Le Marechal, Johns Hopkins Encephalitis Center, Johns Hopkins University, Baltimore, Maryland, USA

Laboratory diagnostic strategies for identification of antibodies against neuronal surface antigens in autoimmune encephalitis
Dr Matteo Gastaldi, Neuroimmunology Research Unit, IRCCS Mondino Foundation, Pavia, Italy

Peripherally- derived monoclonal LGI1 antibodies cause epileptic seizures in a passive transfer animal model
Dr Sukhvir Wright, Institute of Health and Neurodevelopment, Aston University, Birmingham, UK

Encephalitis and poor neuronal death mediated control of her-pes simplex virus in human inherited RIPK3 deficiency
Dr. Zhiyong Liu, St. Giles Laboratory of Human Genetics of Infectious Diseases, The Rockefeller University, New York, NY, USA

Changing the global landscape of encephalitis

Dr Ava Easton, Chief Executive of the Encephalitis Society, shares an update on our progress and work with the WHO and other global stakeholders

Nearly one year ago, we published an ambitious in-depth report which identifies a range of difficulties and solutions to the global impact of encephalitis.

Encephalitis: an in-depth review and gap analysis of key variables affecting global disease burden – or the Global Impact Report to give you its short name – covers epidemiology, incidence, and the economic impacts of encephalitis through to prevention, diagnosis and treatment, and the needs of patients and families.

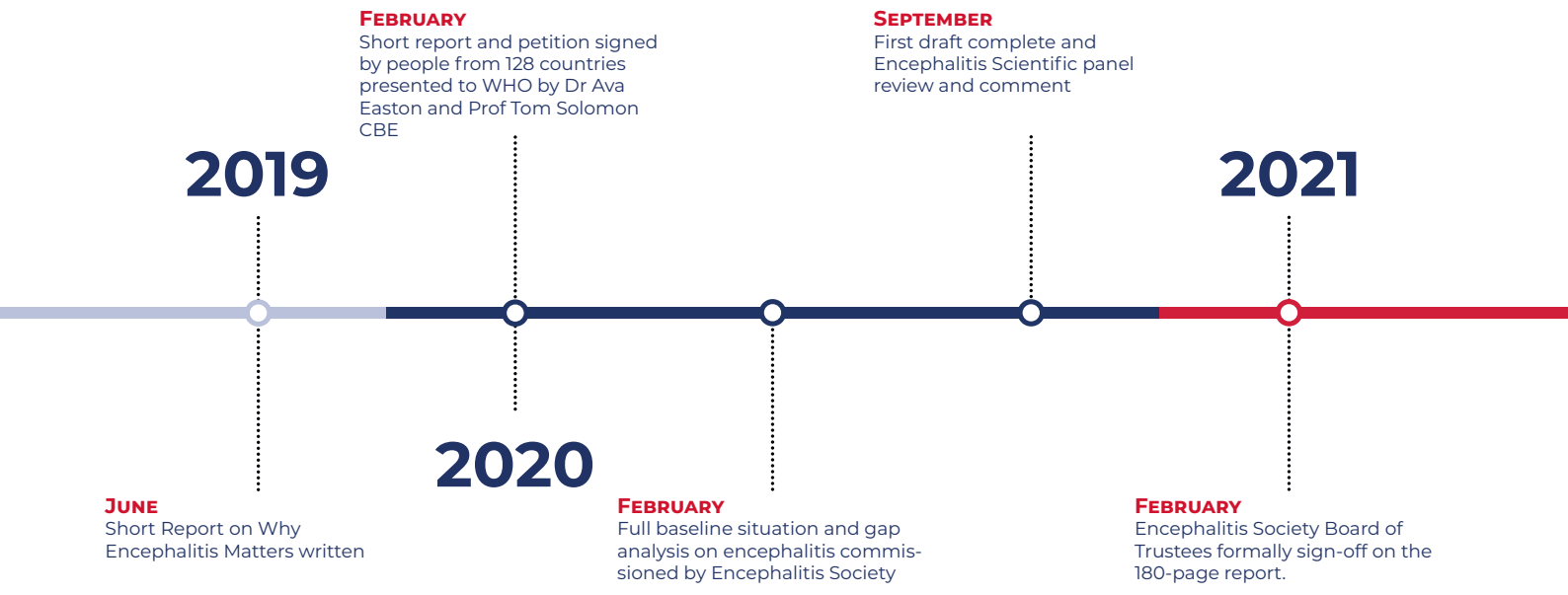
We believe the 180 page report could save lives and improve the treatment and after-care of millions of people in the future. It was initially inspired by a short report called Why Encephalitis Matters which was written in June 2019.

This report – together with a petition signed by 28,000 people from 128 countries – was transported to the Geneva headquarters of the World Health Organization by myself and Professor Tom Solomon ahead of World Encephalitis Day 2020. This visit would be the spark that led to us commissioning the Global Impact Report shortly afterwards, featuring a panel of experts including myself, Tom, Dr Julia Granerod, Alina Ellerington, Dr Nicholas Davies, and Professor Benedict Michael.

The first draft was completed in September 2020 with several months of reviews needed before it was formally signed off and presented to our stakeholders, including the World Health Organization's Brain Health Unit, at the beginning of the following year.

Discussions with all interested parties would continue throughout the year before it was officially announced in a Lancet Neurology correspondence piece for World Encephalitis Day 2022 and followed up by two global stakeholder events, one of which was hosted by the WHO.

Global Impact Report: Timeline



GLOBAL IMPACT REPORT

We had already given some supporters a taste of what to expect when we launched our Changemakers Initiative at the Royal College of Physicians in December. This is designed to be the fundraising arm of the Global Impact Report in the years to come.

A huge amount of work has been achieved on such a mammoth project in a short period of time and we are so proud. Our next steps include the drafting of a meeting report following a two-day global stakeholder meeting in June.

Following this, it is anticipated that a Technical Briefing will be created which will target to policy-makers, health programme managers and planners, health-care providers, researchers, people with the condition specified and their carers to support the implementation of the WHO intersectoral action plan on epilepsy and other neurological disorders.

This latter action plan is the umbrella under which any work on encephalitis will likely sit. It is envisaged that certain actions to address various encephalitis global challenges will be identified and from this we can begin to make a difference, cautiously and strategically, in the encephalitis landscape.

In addition to the above we are currently working up an article on our original 180-page baseline and gap analysis which we aim to publish in a high-impact, peer-reviewed journal.

We are also very pleased that our second Changemakers Collaborative event was held at the House of Lords on 27th October - to celebrate what has been a very successful year!

Become a Changemaker

We are coming to the end of our first year of the Changemakers collaborative which was launched to gather financial support so we can make our Global Impact Report a reality.

If you or your organisation want to help us tackle the global impact of encephalitis, please get in touch with calum@encephalitis.info and join our army of Changemakers today!

2022

March
180-page report presented to Brain Health Unit, WHO, and discussions continue throughout 2021.

December
Changemakers Collaborative – a funding initiative to support this global work formally launched at the Royal College of Physicians.

February
180-page report formally announced in a correspondence piece for World Encephalitis Day in the Lancet Neurology

March
A small global stakeholder event led by the Encephalitis Society held to discuss the report.

June
A two day global stakeholder event on the report and encephalitis hosted by the WHO

Neuroimmune disorders in COVID 19

Abstract: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the aetiologic agent of the coronavirus disease 2019 (COVID-19), is now rapidly disseminating throughout the world with 147,443,848 cases reported so far.

Around 30–80% of cases (depending on COVID-19 severity) are reported to have neurological manifestations including anosmia, stroke, and encephalopathy. In addition, some patients have recognised autoimmune neurological disorders, including both central (limbic and brainstem encephalitis, acute disseminated encephalomyelitis [ADEM], and myelitis) and peripheral diseases (Guillain–Barré and Miller Fisher syndrome). We systematically describe data from 133 reported series on the Neurology and Neuropsychiatry of COVID-19 blog (https://blogs.bmj.com/jnnp/2020/05/01/the-neurology-and-neuropsychiatry-ofcovid-19/) providing a comprehensive overview concerning the diagnosis, and treatment of patients with neurological immune-mediated complications of SARS-CoV-2.

In most cases the latency to neurological disorder was highly variable and the immunological or other mechanisms involved were unclear. Despite specific neuronal or ganglioside antibodies only being identified in 10, many had apparent responses to immunotherapies. Although the proportion of patients experiencing immune-mediated neurological disorders is small, the total number is likely to be underestimated. The early recognition and improvement seen with use of immunomodulatory treatment, even in those without identified autoantibodies, makes delayed or missed diagnoses risk the potential for long-term disability, including the emerging challenge of post-acute COVID-19 sequelae (PACS). Finally, potential issues regarding the use of immunotherapies in patients with pre-existent neuro-immunological disorders are also discussed.

Arino H., Heartshorne R., Michael B.D., et al. (2022)
Neuroimmune disorders in COVID 19
Journal of Neurology; 269:2827–2839 (DOI: 1007/s00415-022-11050-w) OPEN ACCESS: http://creativecommons.org/licenses/by/4.0/

Immunotherapy in autoimmune encephalitis

Trewin et al.(2022) evaluate acute and long-term treatments for autoimmune encephalitis (AE) and demonstrate how understanding of disease pathogenesis can lead to targeted therapy while outlining the challenges of defining disability outcomes.

The study examines recent large cohort studies, meta-analyses and registries to outline current evidence for contemporary therapeutic advances in autoimmune encephalitis.

A recurring theme from the studies is the importance of prompt diagnosis to enable the rapid administration of first-line immunotherapies such as corticosteroids and plasma exchange to improve outcomes. Emerging evidence shows second-line immunotherapies (rituximab) help to reduce relapse rates, but optimal timing for commencing it is not yet established. However it is important to balance risks and consequences against long-term deficits in patients who were only partially responsive to first-line immunotherapies. Clinical, radiological, and serological biomarkers would help selection and escalation in deciphering which patients require immunotherapy, as life-long immunosuppression is not typically considered for relapsing autoimmune encephalitis patients compared to other anti-body- mediated neurological diseases with higher relapse rates.

The authors also emphasise that currently used outcome measures have limitations and are insufficient to identify and track the efficacy of specific immunotherapeutic agents on consequences such as fatigue, pain, mood, cognitive impairment and quality of life. They propose further outcome measures to help monitor treatment response more accurately and enable comprehensive comparisons between international multicentre cohorts, systematic reviews and meta-analyses.

Trewin B. P., Freeman I, Ramanathan S, et al. (2022)
Immunotherapy in autoimmune encephalitis
Wolters Kluwer Health, Current Opinion Neurology, 35:399–414 (DOI:10.1097/WCO.0000000000001048)

Clinical characterisation of patients in the post-acute stage of anti-NMDA receptor encephalitis: a prospective cohort study and comparison with patients with schizophrenia spectrum disorders

Guasp et al. (2022) describe the clinical features of the post-acute stage of anti-NMDAR encephalitis, it's similarities with schizophrenia spectrum disorders, and the factors that predict cognitive–psychiatric outcomes and could serve as prognostic biomarkers.

A prospective cohort study at Hospital Clínic de Barcelona (Barcelona, Spain) recruited 28 participants aged 12–60 years with anti-NMDAR encephalitis during the post-acute stage. The patients undertook comprehensive neuropsychiatric evaluations three times (at study entry, six months, and twelve months). Evaluations of 27 age-matched participants with schizophrenia spectrum disorders and 27 age- and sex-matched healthy participants recruited from the same location were also carried out. The study investigated the distinctions between and within groups in the longitudinal follow-up using multilevel linear mixed-effect models, adjusting for group, age, sex, and socioeconomic status to control for possible confounding.

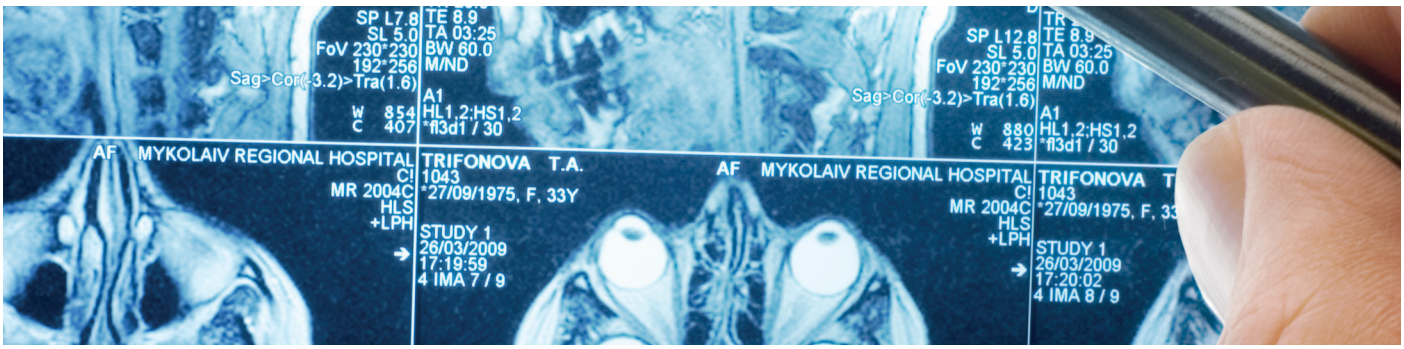
Deficits in at least one cognitive domain occurred in 25 participants (89%) with anti-NMDAR encephalitis, of which 15/22 cognitive domain variables were impaired in the first study entry compared to just eight at six months. Schizophrenia spectrum disorder participants shared 22 (50%) variables with anti-NMDAR encephalitis. These variables were impaired at study entry and without change at 12 months.

Two of the acute-stage anti-NMDAR encephalitis characteristics - decreased consciousness and no improvement within the first four weeks of treatment - predicted cognitive domain outcomes. A visuospatial task, (serial biases) at study entry showed potential in predicting learning and memory outcomes. Comparing participants with anti-NMDAR encephalitis with those with schizophrenia, although initially all psychiatric symptoms were similarly altered, only individuals with anti-NMDAR encephalitis subsequently improved.

Participants with anti-NMDAR encephalitis showed the most cognitive psychiatric improvements. Within the first six months, four (14%) patients with anti-NMDAR encephalitis would have fulfilled the diagnostic criteria of schizophrenia if cerebrospinal fluid (CSF) antibody studies or anti-NMDAR encephalitis were not explored. The cognitive–psychiatric symptoms of anti-NMDAR encephalitis in the post-acute stage resembled those of stabilised schizophrenia, but only those in participants with anti-NMDAR encephalitis progressively improved, predominantly during the first six months.

The authors conclude that these findings are important for clinical trials on anti-NMDAR encephalitis and suggest that prompt, intensive cognitive–psychosocial rehabilitation within the first six months may be a valuable intervention. They advise that the similarity of these alterations with those of individuals with schizophrenia spectrum disorders needs to be considered in the differential diagnosis of patients with psychiatric disorders and when applying the current diagnostic criteria of schizophrenia

Guasp M., Rosa-Justicia M., Muñoz-Lopetegi A., et al. (2022)
Clinical characterisation of patients in the post-acute stage of anti-NMDA receptor encephalitis: a prospective cohort study and comparison with patients with schizophrenia spectrum disorders
The Lancet Neurology 21: 899–910. (DOI: 10.1016/S1474-4422(22)00299-X)



Epileptic phenotypes in autoimmune encephalitis: from acute symptomatic seizures to autoimmune associated epilepsy

Matricardi et al. (2022) set out to explain the clinical and paraclinical findings, treatment options and long-term outcomes in autoimmune encephalitis (AE), focusing on epilepsy. Patients with AE and new-onset seizures were enrolled in a retrospective observational study which compared clinical and paraclinical findings in patients with and without evidence of antibodies.

In total, 263 patients (138 females; median age 55 years, range 4-86) were followed up for a median time of 30 months (range 12-120). More than a half of patients (63.50%) had antineuronal antibodies identified. A higher prevalence of episodes of status epilepticus (SE) was found in the antibody-negative group. Although 88.60% of patients received immunotherapy, 61.80% of patients responded to it. The study found that AE-associated epilepsy was the long-term sequela in 43.73% of patients with AE with a higher prevalence in antibody-negative patients. In 81.73% of the patients, it was also associated with cognitive deficits and psychiatric disturbances. Risk factors of developing epilepsy included difficult to treat seizures at the onset with numerous prescribed antiseizure medication, persisting interictal epileptiform discharges at follow-up and poor response to immunotherapy during the acute phase. The authors conclude that the severity of seizures at onset is a major risk factor for the development of chronic epilepsy in AE. This finding may be a driver for understanding the pathophysiological mechanisms of acute seizure through identifying specific seizure biomarkers.

The authors warn clinicians about the need of maintaining a high level of suspicion in the evaluation of patients with new-onset seizures as AE can be associated with other symptoms of brain dysfunction and could remain under-recognised. Antibody-negative patients and cases in whom seizures may be associated with subtle signs of encephalitis represent important yet challenging clinical groups. This study provides class IV evidence for management recommendations.

Matricardi S., Casciato S., Bozzetti S., et al. (2022)
Epileptic phenotypes in autoimmune encephalitis: from acute symptomatic seizures to autoimmune associated epilepsy
J Neurol Neurosurg Psychiatry: 0:1–8. (DOI: 10.1136/jnnp-2022-329195)

Consensus clinical guidance for diagnosis and management of adult COVID-19 encephalopathy patients

A common complication of patients hospitalised with COVID-19 is encephalopathy. These patients can present with prolonged encephalopathy as a result of severe complications like inflammation of the brain parenchyma with or without cerebrovascular involvement, demyelination and seizures, all of which are not always proportionate to COVID-19's severity. This condition can be challenging to manage and impact negatively on the prognosis.

This study investigates the current evidence for definition, epidemiology, and pathophysiology of COVID-19 encephalopathy in order to provide practical guidance for clinical assessment, investigation, and both acute and long-term management via consensus agreement of the Global COVID-19 Neuro-Research Coalition. The study answers the following questions:

- What is the pathophysiology of COVID-19 encephalopathy?
- Which clinical features suggest COVID-19 encephalopathy?
- Which clinical features suggest a primary Central Nervous System (CNS) pathology?
- What investigations should be performed to establish these CNS diagnoses?
- How should patients suffering from COVID-19 encephalopathy be managed?
- What is the prognosis for patients with COVID-19 encephalopathy?
- What is the role of rehabilitation for these patients?

Walton M.B.D., Westenberg E, Garcia-Azorin D., et al. (2022)
Consensus clinical guidance for diagnosis and management of adult COVID-19 encephalopathy patients
J Neuropsychiatry Clin Neurosci.: appineuropsych22010002. doi: 10.1176/appi.neuropsych.22010002. Epub ahead of print. PMID: 35872617

Acute seizure risk in patients with encephalitis: development and validation of clinical prediction models from two independent prospective multicentre cohorts

ABSTRACT

Objective In patients with encephalitis, the development of acute symptomatic seizures is highly variable, but when present is associated with a worse outcome. We aimed to determine the factors associated with seizures in encephalitis and develop a clinical prediction model.

METHODS

We analysed 203 patients from 24 English hospitals (2005–2008) (Cohort 1). Outcome measures were seizures prior to and during admission, inpatient seizures and status epilepticus. A binary logistic regression risk model was converted to a clinical score and independently validated on an additional 233 patients from 31 UK hospitals (2013–2016) (Cohort 2).

RESULTS

In Cohort 1, 121 (60%) patients had a seizure including 103 (51%) with inpatient seizures. Admission Glasgow Coma Scale (GCS) ≤8/15 was predictive of subsequent inpatient seizures (OR (95%CI) 5.55 (2.10 to 14.64), p<0.001), including in those without a history of prior seizures at presentation (0R 6.57 (95% CI 1.37 to 3.15), p=0.025).

A clinical model of overall seizure risk identified admission GCS along with aetiology (autoantibody-associated OR 11.99 (95% CI 2.09 to 68.86) and Herpes simplex virus 3.58 (95% CI 1.06 to 12.12)) (area under receiver operating characteristics curve (AUROC)=0.75 (95% CI 0.701 to 0.848), p<0.001). The same model was externally validated in Cohort 2 (AUROC=0.744 (95% CI 0.677 to 0.811), p<0.001). A clinical scoring system for stratifying inpatient seizure risk by decile demonstrated good discrimination using variables available on admission; age, GCS and fever (AUROC=0.716 (95% CI 0.634 to 0.798), p<0.001) and once probable aetiology established (AUROC=0.761 (95% CI 0.6840.839), p<0.001).

Conclusion

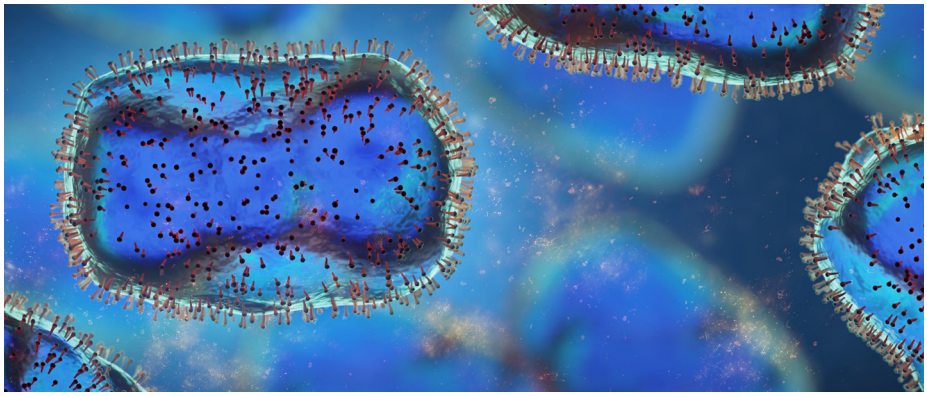
Age, GCS, fever and aetiology can effectively stratify acute seizure risk in patients with encephalitis. These findings can support the development of targeted interventions and aid clinical trial design for antiseizure medication prophylaxis.

Wood G.W., Babar R., Ellul M.A., et al. (2022)
Acute seizure risk in patients with encephalitis: development and validation of clinical prediction models from two independent prospective multicentre cohorts
BMJ Neurology Open;4: e000323. (DOI: 10.1136/ bmjno-2022-000323) Open Access.

Neurological and psychiatric presentations associated with human monkeypox virus infection: A systematic review and meta-analysis

Monkeypox can sometimes lead to neurological complications such as encephalitis, confusion or seizures, finds a new review of evidence.

Several studies incorporated in the systematic review and meta-analysis of evidence, published in eClinicalMedicine, also found that muscle aches, fatigue, headache, anxiety and depression were all relatively common among monkeypox patients.



Across the studies with relevant evidence, 2-3% of patients had severe complications such as seizure or encephalitis, although those studies mainly involved hospitalised patients from previous years. The researchers say there is not yet enough evidence to estimate neurological complication prevalence in the current outbreak.

The team led by researchers at UCL, Barts Health NHS Trust, Guy's and St Thomas' NHS Foundation Trust, King's College London and the Encephalitis Society, looked for any studies reporting neurological or psychiatric symptoms of monkeypox that had been reported up until May 2022, before the outbreak spread globally.

Co-author Dr Jonathan Rogers (UCL Institute of Mental Health, UCL Psychiatry, and South London & Maudsley NHS Foundation Trust) said: "We found that severe neurological complications such as encephalitis and seizures, while rare, have been seen in enough monkeypox cases to warrant concern, so our study highlights a need for further investigation.

"There is also evidence that mood disorders such as depression and anxiety are relatively common for people with monkeypox."

Monkeypox primarily causes skin lesions and fever, and can be fatal, although in the current outbreak, substantially fewer than one in 1,000 confirmed cases have resulted in death.

Although it has been endemic in parts of Central and West Africa for decades, with sporadic outbreaks elsewhere, 2022 has been the first time the virus has spread globally, attracting increased attention to an infectious disease that was previously relatively neglected.

The review incorporated 19 studies, with a total of 1,512 participants (1,031 of whom had a confirmed infection), in the US, Nigeria, Democratic Republic of Congo, Republic of Congo, and the UK.

By pooling data from across a sub-set of studies with relevant evidence, the researchers estimated that 2.7% of monkeypox patients experienced at least one seizure, 2.4% experienced confusion, and 2.0% had encephalitis, a serious condition of brain inflammation that can lead to long-term disability. There was very limited evidence for the prevalence of such symptoms, as the review only identified two cases of seizures, five cases of encephalitis and six cases of confusion (although other preliminary research has identified other cases), so larger studies are needed to better ascertain prevalence. The researchers say that further study is also needed to determine how monkeypox can impact the brain.

While the researchers were not able to pool data for psychosocial symptoms due to incomplete evidence, in some studies at least half of patients experienced at least one of myalgia (muscle aches), fatigue, headache, anxiety or depression. The researchers note that monkeypox may cause higher rates of mental ill health than other illnesses due to the presence of potentially disfiguring lesions, while there may also be stigma linked to how transmission is typically from close physical or sexual contact.

The studies reviewed did not have enough long-term follow-up with patients to know whether any of the symptoms last substantially longer than the acute phase of the illness. The researchers also caution that most cases in this review were hospitalised patients, and so the studied symptoms might not be as common in people with more mild cases.

Badenoch J.B., Conti I., Rengasamy E.R., et al. (2022)
Neurological and psychiatric presentations associated with human monkeypox virus infection: A systematic review and meta-analysis
eClinicalMedicine. 52 (DOI:10.1016/j.eclinm.2022.101644) OPEN ACCESS http://creativecommons.org/licenses/by/4.0/

FOCUS: Erasmus MC Autoimmune Encephalitis Research Group

Associate Professor Maarten Titulaer talks about his research mission in the Autoimmune Encephalitis (AIE) field, and his Rotterdam-based team's work in optimizing care for AIE patients.

As a neurologist with a specialized clinic in autoimmune encephalitis (AIE) and related disorders, I have the privilege of seeing many patients. The stories of these patients have determined the aims of my clinical research. My goal is to improve the outcomes of my patients, and to do so, several things are necessary: 1) early diagnosis, facilitated by an increase in awareness and better diagnostic tools; 2) better understanding of the processes involved in the body and brain that create AIE and its outcome; 3) accurate measurement of the disease, using information patients and caregivers provide themselves as well as biomarkers, and 4) providing treatment options to the individual patients based on the combination of all these factors. This is only possible for us combining our clinical work with the data we obtain in our laboratory. The generous contribution of samples and information provided by over 95% of our patients and the nationwide coverage of our studies are essential to our research.

Dr Juna de Vries and Associate Prof Maarten Titulaer

As an MD PhD student I was involved in the care, tumour prediction and long-term outcomes of autoimmune and tumour–related diseases of the muscles and nerves. I was captured by these newly discovered diseases and the impact of appropriate treatments in the field of Autoimmune Neurology. I joined the lab of Professor Josep Dalmau, a world authority on autoimmune and paraneoplastic disorders affecting the nervous system, who had just discovered several AIE subtypes. First in Philadelphia and later in Barcelona, I started clinical and translational research that formed the basis for my current research in the Netherlands. The study "Treatment and prognostic factors for long-term outcome in patients with NMDAR encephalitis"**1**, showed the clinical presentation and characteristics of a large group of 577 NMDAR patients in detail, and provided evidence that most patients responded to immunothera-

(1) *Titulaer MJ, McCracken L, Gabilondo I, Armangué T, Glaser C, Iizuka T, Honig LS, Benseler SM, Kawachi I, Martinez-Hernandez E, Aguilar E, Gresa-Arribas N, Ryan-Florance N, Torrents A, Saiz A, Rosenfeld MR, Balice-Gordon R, Graus F, Dalmau J.* Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis. *Lancet Neurol. 2013 Feb;12(2):157-65.*

(2) *van Sonderen A, Petit-Pedrol M, Dalmau J, Titulaer MJ.* The value of LGI1, Caspr2 and voltage-gated potassium channel antibodies in encephalitis. *Nat Rev Neurol. 2017 May;13(5):290-301.*

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(6) *van Coevorden-Hameete MH, de Bruijn MAAM, de Graaff E, Bastiaansen DAEM, Schreurs MWJ, Demmers JAA, Ramberger M, Hulsenboom ESP, Nagtzaam MMP, Boukhrissi S, Veldink JH, Verschuuren JJGM, Hoogenraad CC, Sillevis Smitt PAE, Titulaer MJ.* The expanded clinical spectrum of anti-GABABR encephalitis and added value of KCTD16 autoantibodies. *Brain. 2019 Jun 1;142(6):1631-1643.*

(7) *van Sonderen A, Schreurs MW, de Bruijn MA, Boukhrissi S, Nagtzaam MM, Hulsenboom ES, Enting RH, Thijs RD, Wirtz PW, Sillevis Smitt PA, Titulaer MJ.* The relevance of VGKC positivity in the absence of LGI1 and Caspr2 antibodies. *Neurology. 2016 May 3;86(18):1692-9.*

(8) *de Bruijn MAAM, Bastiaansen AEM, Mojzisova H, van Sonderen A, Thijs RD, M joie MJM, Rouhl RPW, van Coevorden-Hameete MH, de Vries JM, Muñoz Lopetegi A, Roozenbeek B, Schreurs MWJ, Sillevis Smitt PAE, Titulaer MJ;* ACES Study Group. Antibodies Contributing to Focal Epilepsy Signs and Symptoms Score. *Ann Neurol. 2021 Apr;89(4):698-710.*

(9) *Bastiaansen AEM, van Steenhoven RW, de Bruijn MAAM, Crijnen YS, van Sonderen A, van Coevorden-Hameete MH, Nühn MM, Verbeek MM, Schreurs MWJ, Sillevis Smitt PAE, de Vries JM, Jan de Jong F, Titulaer MJ.* Autoimmune Encephalitis Resembling Dementia Syndromes. *Neurol Neuroimmunol Neuroinflamm. 2021 Aug 2;8(5)*

py and had a 'broadly good' outcome (although the time to recover could well take over 18 months). One of the important factors predicting recovery was an early diagnosis and treatment. To improve recognition and decrease delays has become our mission.

Returning to the Netherlands I had the luxury to build my research on the foundations of 20 years of research into paraneoplastic neurological disorders by Professor Sillevis Smitt at Erasmus University MC, Rotterdam. We first established a national referral centre for autoimmune encephalitis, and actively promoted awareness among neurologist, but also other consultants. Nowadays, we see around 100 patients per year, while counselling is requested for 1000 patients with potential AIE. Optimizing of the diagnostic process involves proper recognition, identification of red flags for these diseases, but also ascertainment of the accuracy of antibody tests. We described the clinical syndrome of LGI1 and CASPR2 encephalitis patients, **2 3 4** resulting in better recognition of these patients. To illustrate, we learned that in LGI1 patients next to faciobrachial dystonic seizures (FBDS), many have subtle focal seizures early in the disease course. To notice these subtle seizures is essential for an early diagnosis and start of treatment, as this will prevent the development of tonic clonic seizures and diminish irreversible cognitive damage. The incidence of anti-LGI1 encephalitis has increased tenfold in the Netherlands over the last decade, at least partially related to all efforts to raise awareness.

In CASPR2 encephalitis we showed that the disease can progress relatively slow, in contrast to the subacute onset of most AIE **4**. More recently, we published that the occurrence of NMDAR encephalitis is less rare in the elderly patients than initially anticipated and the clinical phenotype is less outspoken, making the disease more difficult to recognize in the elderly patients **5**. We established a link between anti- GABAbR encephalitis and rapidly progressive dementia, aside from the known clinical presentation with severe seizures. In these patients, we discovered that the co-occurrence of KCTD16 antibodies points towards an underlying lung cancer and that the addition of KCTD16 improves the sensitivity of the cell-based assay **6**. On the other hand of the spectrum, a VGKC-positive test, while antibodies against LGI1 or CASPR2 are absent, is not associated with a specific clinical picture and lacks specificity to discriminate between patients with and without autoimmune inflammation **7**.

Our journey exploring whether the clinical spectrum of AIE is broader continued, as we estimated the prevalence of AIE as a cause of less fulminant disorders such as epilepsy (see the section 'Latest in Erasmus MC research' about the ACES score), **8** and dementia (see the section 'Latest in Erasmus MC research' about AIE resembling dementia syndromes) **9**. This is currently expanded in large dementia cohorts, including rapidly progressive dementia. Similarly, we try together with tropical medicine specialists to identify immunological causes involved in nodding syndrome and onchocerca associated epilepsy in African children, although the cause of these intriguing diseases are still unclear. **10 11**

I am also part of the international panel for guidelines on Autoimmune Neurology and Paraneoplastic Neurologic Syndromes to safeguard international accuracy and consensus in diagnosis. **12 13** With the CHANCE study group, we validated the current clinical AIE criteria in a Dutch cohort of children with suspicion of AIE. We found that, besides NMDAR encephalitis and ADEM, other AIEs are rare in children and that the AIE guideline are also useful in children. **14**

Besides raising awareness for AIE, the next part of our mission is to understand AIE, the antibodies involved and the role of other parts of the immune system. We found a very strong correlation of LGI1 encephalitis with a specific HLA type, supporting the autoimmune hypothesis, while the absence (albeit rare) could raise tumour suspicion. **15** We have expanded to more translational research into antibody effects, but also proteomics and single cell experiments (see the section 'Present-day research at Erasmus MC, about the UltraAIE research).

Our AIE patients showed us that epilepsy after resolved encephalitis was rare and that seizure freedom is achieved faster and more frequently after immunotherapy. **16** This has taught me several things as it shows professionals can perform research alongside the patients (see the section 'Present-day research at Erasmus

Continued on Page 21

(10) *Hotterbeekx A, Vieri MK, Ramberger M, Jozefzoon-Aghai A, Mandro M, Tepage F, Dusabimana A, Kumar-Singh S, Titulaer MJ, Colebunders R.* No Evidence for the Involvement of Leiomodin-1 Antibodies in the Pathogenesis of Onchocerciasis-Associated Epilepsy. *Pathogens. 2021 Jul 5;10(7):845. doi: 10.339*

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(12) *Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, Cellucci T, Cortese I, Dale RC, Gelfand JM, Geschwind M, Glaser CA, Honnorat J, Höftberger R, Iizuka T, Irani SR, Lancaster E, Leypoldt F, Prüss H, Rae-Grant A, Reindl M, Rosenfeld MR, Rostásy K, Saiz A, Venkatesan A, Vincent A, Wandinger KP, Waters P, Dalmau J.* A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol. 2016 Apr;15(4):391-404. doi: 10.1016/S1474-4422(15)00401-9.*

(13) *Graus F, Vogrig A, Muñiz-Castrillo S, Antoine JG, Desestret V, Dubey D, Giometto B, Irani SR, Joubert B, Leypoldt F, McKeon A, Prüss H, Psimaras D, Thomas L, Titulaer MJ, Vedeler CA, Verschuuren JJ, Dalmau J, Honnorat J.* Updated Diagnostic Criteria for Paraneoplastic Neurologic Syndromes. *Neurol Neuroimmunol Neuroinflamm. 2021 May 18;8(4):e1014. doi: 10.1212*

(14) *de Bruijn MAAM, Bruijstens AL, Bastiaansen AEM, van Sonderen A, Schreurs MWJ, Sillevis Smitt PAE, Hintzen RQ, Neuteboom RF, Titulaer MJ;* CHANCE Study Group. Pediatric autoimmune encephalitis: Recognition and diagnosis. *Neurol Neuroimmunol Neuroinflamm. 2020 Feb 11;7(3).*

(15) *van Sonderen A, Roelen DL, Stoop JA, Verdijk RM, Haasnoot GW, Thijs RD, Wirtz PW, Schreurs MW, Claas FH, Sillevis Smitt PA, Titulaer MJ.* Anti-LGI1 encephalitis is strongly related to HLA-DR7 and HLA-DRB4. *Ann Neurol. 2017 Feb;81(2):193-198*

(16) de Bruijn MAAM, van Sonderen A, van Coevorden-Hameete MH, Bastiaansen AEM, Schreurs MWJ, Rouhl RPW, van Donselaar CA, Majoie MHJM, Neuteboom RF, Sillevis Smitt PAE, Thijs RD, Titulaer MJ. Evaluation of seizure treatment in anti-LGI1, anti-NMDAR, and anti-GABABR encephalitis. *Neurology. 2019 May 7;92(19):e2185-e2196.*

(17) Balu R, Mccracken L, Lancaster E, Graus F, Dalmau J, Titulaer MJ. A score that predicts 1-year functional status in patients with anti-NMDA receptor encephalitis. *Neurology. 2019 Jan 15;92(3):e244-e252.*

(18) van Sonderen A, Arends S, Tavy DLJ, Bastiaansen AE, de Bruijn MAAM, Schreurs MWJ, Sillevis Smitt PAE, Titulaer MJ. The predictive value of electroencephalopgraphy in anti-NMDA receptor encephalitis. *Journal of Neurology, Neurosurgery & Psychiatry. 2018 Oct;89(10):1101-1106.*

During World Encephalitis Day on 22nd February 2021, a total of 156 landmarks lit up red in support of the global awareness campaign for encephalitis. Among the 156 landmarks in 23 countries around the world, we also lit our tower of the Erasmus MC hospital building and, of course, all the members of the AIE research team dressed in red!

Dr. Maarten Titulaer is Associate Professor of Neurology at Erasmus University Medical Centre Rotterdam, the Netherlands.

He combines clinical work with translational research. He has worked at Erasmus MC as well as internationally on autoimmune mediated diseases of the brain, in particular autoimmune encephalitis (AIE). In his clinical work he leads the national referral clinic in Autoimmune Neurology at Erasmus MC, granted as European Reference Network site (ERN-RITA). At Erasmus MC, he closely collaborates with Juna de Vries and residents with a special interest in neuroimmunology.

The clinical team takes care of patients with (a suspicion of) AIE or other autoimmune neurological diseases, in a multidisciplinary approach also involving neuroradiologists, clinical immunologists, pharmacists and psychiatrists.

He is a member of the international panel for guidelines on Autoimmune Neurology and Paraneoplastic Neurologic Syndromes and co-organizer of the European networking conference focusing on AIE.

Continued from Page 20

MC, about the PROMISE study), the importance of immunotherapy cannot be easily underestimated, but also underlines we have a role in the discontinuation of potential harmful treatments that are no longer necessary.

Although AIE only recently entered the ballpark, it is my goal to provide tailored treatment to individual patients based on our understanding of the disease and relevant biomarkers. A modest start was the NEOS score to predict outcome in anti-NMDAR encephalitis, **17** and we are currently updating this for the NEOS2 score. Biomarkers can be clinical items, measurements in blood or cerebrospinal fluid, but also patterns in ancillary tests, like brain imaging or electroencephalography (EEG). **18** We have built a platform for automated harmonisation of EEGs to allow for machine learning approaches.

As AIE are a group of rare diseases, collaborations are essential to achieve sufficient power to really improve treatments and clinical outcomes for AIE patients. I am hopeful that the first European networking conference focusing on AIE I co-initiated (TREAT AIE), supported by the European Joint Program for Rare Diseases and the European Academy of Neurology, has inspired many to further foster European research collaborations. Altogether, this endeavour will improve diagnosis and treatment of patients with AIE in the whole of Europe and beyond.

Latest in Erasmus MC research

The ACES score: Antibodies Contributing to Focal Epilepsy Signs and Symptoms Score.

Diagnosing autoimmune encephalitis (AIE) is difficult in patients with less fulminant diseases such as epilepsy. However, it's recognition is important, as patients require a different treatment strategy with immunotherapy. In this prospective, multicentre cohort study we identified antibodies in patients with focal epilepsy of unknown aetiology, and created and validated a score to preselect patients requiring neuronal antibody testing.

We included 582 patients with focal epilepsy of unknown aetiology and without recognized AIE between December 2014 and December 2017. These patients had a median epilepsy duration of 8 years (interquartile range = 2-18) and were followed for 1 year. Twenty patients (3.4%) had autoimmune aetiology of seizures (AES), of whom 3 had anti-LGI1, 3 had anti-CASPR2, 1 had anti-NMDAR and 13 had high titre anti-GAD65 antibodies. Risk factors for AES as determined by multivariate logistic regression were temporal magnetic resonance imaging hyperintensities, autoimmune diseases, behavioural changes, autonomic symptoms, cognitive symptoms, and speech problems.

The ACES score was created using these risk factors for AES. When assigning each risk factor 1 point, a ACES score of ≥ 2 showed a sensitivity of 100% to detect AES and a specificity of 84.9%. The model was successfully validated in an external cohort of Czech temporal epilepsy patients. Contrary to other available prediction scores, the ACES score was both useful in patient with recently developed and chronic epilepsy, making the ACES score very useful for selecting patients who require antibody testing.

de Bruijn MAAM, Bastiaansen AEM, Mojzisova H, van Sonderen A, Thijs RD, Majoie MJM, Rouhl RPW, van Coevorden-Hameete MH, de Vries JM, Muñoz Lopetegi A, Roozenbeek B, Schreurs MWJ, Sillevis Smitt PAE, Titulaer MJ; ACES Study Group. Antibodies Contributing to Focal Epilepsy Signs and Symptoms Score. Ann Neurol. 2021 Apr;89(4):698-710.

Autoimmune Encephalitis Resembling Dementia Syndromes

Autoimmune encephalitis (AIE) can resemble neurodegenerative dementia syndromes, and patients do not always present with fulminant encephalitis symptoms. In this nationwide observational study we evaluated how frequently AIE mimics dementia and provide red flags for AIE in middle-aged and older patients.

We included patients with anti-LGI1, anti-NMDAR, anti-$GABA_BR$, or anti-CASPR2 encephalitis, who also met 3 additional criteria: 1) age ≥45 years, 2) fulfilment of dementia criteria, and 3) no prominent seizures early in the disease course. Of the 290 patients with AIE, 175 were 45 years or older. Sixty-seven patients (38%) fulfilled criteria for dementia without prominent seizures early in the disease course. Of them, 42 had anti-LGI1 (48%), 13 anti-NMDAR (52%), 8 anti-$GABA_BR$ (22%), and 4 anti-CASPR2 (15%) encephalitis. In 48 patients (76%) a rapidly progressive cognitive deterioration was seen, whereas a neurodegenerative dementia syndrome was suspected in half of the patients. In 17 patients (27%; 16/17 anti-LGI1), subtle seizures had been overlooked. Sixteen patients (25%) had neither inflammatory changes on brain MRI nor CSF pleocytosis. At least 1 CSF biomarker, often requested when dementia was suspected, was abnormal in 27 of 44 tested patients (61%), whereas 8 had positive 14-3-3 results (19%). Most patients (84%) improved after immunotherapy. Based on these findings we concluded that red flags for AIE in patients with suspected dementia are: (1) rapidly progressive cognitive decline, (2) subtle seizures, and (3) abnormalities in ancillary testing atypical for neurodegeneration. Physicians should be aware that inflammatory changes are not always present in AIE, and that biomarkers often requested when dementia was suspected (including 14-3-3) can show abnormal results. Diagnosis is essential as most patients profit from immunotherapy.

Bastiaansen AEM, van Steenhoven RW, de Bruijn MAAM, Crijnen YS, van Sonderen A, van Coevorden-Hameete MH, Nühn MM, Verbeek MM, Schreurs MWJ, Sillevis Smitt PAE, de Vries JM, Jan de Jong F, Titulaer MJ. Autoimmune Encephalitis Resembling Dementia Syndromes. Neurol Neuroimmunol Neuroinflamm. 2021 Aug 2;8(5)

Present-day research at Erasmus MC

The PROMISE study

In the PROMISE study, an acronym for 'Patient Reported Outcomes while Manipulating the Immune System in autoimmune Encephalitis, we (Juliette Brenner, PhD candidate, Juna de Vries and Maarten Titulaer) are working on better outcome measures to represent real outcomes in patients suffering from encephalitis'.

The aim of this study is to determine the clinical outcome and disease burden in treated patients with AIE in the months and years after diagnosis. We measure cognitive outcome, fatigue, effects on mood, behaviour, daily-life functioning and quality of life. We have developed the tools based on literature and our expert opinion we pre-selected questions covering the aforementioned outcomes.

This April we had a very valuable focus group meeting with 12 patients with anti-NMDAR, anti-LGI1 or high titre anti-GAD65 encephalitis. In this group conversation, we listened to the patients telling about the impact the encephalitis still has on their lives, which was very moving to hear. We added missing items to our set of questionnaires, mentioned in this meeting.

We already included over 120 patients, estimating clinical outcome and disease burden in the Dutch population of patients aged 16 years or older with AIE. We will expand to roughly 250 patients. Besides the questionnaires, we also perform a neurological examination, a neuropsychological test battery and determine the mRS and CASE score. From these data we will create a shorter questionnaire encompassing the different domains, which we will use to assess patients in consecutive visits in the prospective phase of the study, following these for several years.

The PROMISE study will raise awareness for residual symptoms these patients suffer. This will assist in more targeted rehabilitation programs to support patients. It will also provide more powerful and relevant outcome measures, making treatment trials or comparison of different treatment protocols in these rare diseases more feasible in the future. This will be an invaluable step towards tailored and optimized care for autoimmune encephalitis patients.

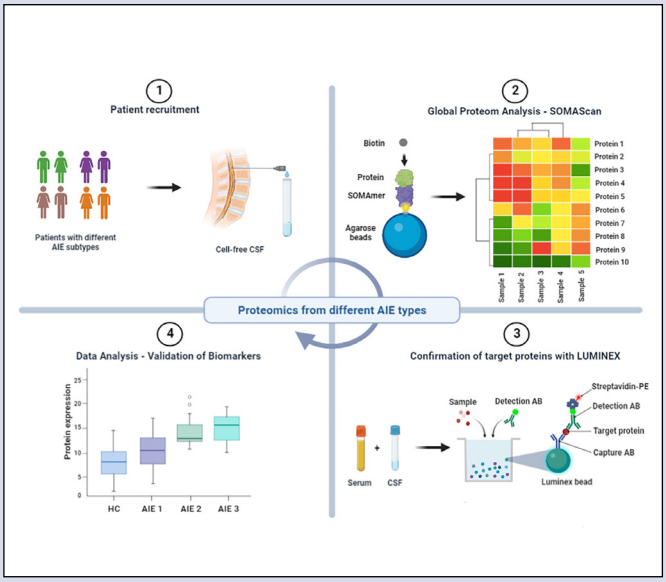
UltraAIE research

Although the antibodies are directly causing the AIE, it is unknown why removal of the antibodies does not lead to complete recovery in patients.

This suggests other pathophysiological mechanisms are also relevant. To investigate these immunological pathways in several subtypes of AIE in depth, we started the UltraAIE consortium, funded by E-RARE, together with the German Universities of Münster (Gerd Meyer zu Hörste), Kiel (Frank Leypoldt), Düsseldorf (Nico Melzer) and Rehovot (Ido Amit, Israel).

We perform single cell RNA-sequencing in paired serum and CSF samples in treatment-naïve patients examining the sequence information from individual cells with optimized next-generation sequencing technologies, providing a higher resolution of cellular differences and a better understanding of the function of an individual cell in the context of its microenvironment.

Our main interest is in the cells of the immune system, and identifying relevant pathways. This analysis has provided clear differences in RNA expression between patients with LGI1 and CASPR2 encephalitis versus healthy controls, in both CSF and PBMCs: B-cells and plasma cells are almost exclusively found in patients, compatible with an antibody-mediated disease.



In addition changes in specific subsets of T-cells and dendritic cells have been identified. There is a difference in genetic expression in patients compared to controls. Result are currently confirmed using other methods, such as proteomics (SOMAscan, liquid chromatography mass spectrometry [LCMS]), Luminex and flow cytometry. Similarly, we use this pipeline to investigate other types of AIE.

Growing new research through seed funding

Researchers in India and Uganda have been awarded grants of up to £10,000 in the latest round of the Encephalitis Society's seed funding project.

Encephalitis Futures - International Research Seed Funding has now handed out eight grants since its launch four years ago.

"Helping researchers to fund their work is something that we are very passionate about," Dr Ava Easton, Chief Executive of the Encephalitis Society. "This year, as with 2021, we wanted to focus on research projects in low-to-middle income countries as we believe our seed funding can go that much further.

Choosing who should receive the grants is never an easy task and involves a lot of soul searching. However, we were very impressed with the proposals submited by Dr John Kasibante and Dr Tina Damodar and wish them the very best of luck with their projects."

Developing a novel host transcript-based test to diagnose scrub typhus in children with acute encephalitis syndrome

Scrub typhus (infection caused by Orientia tsutsugamushi) is a global problem affecting around 1 million people each year, predominantly in southeast Asia. Acute encephalitis syndrome (AES), defined by acute onset of fever and altered mental state, occurs in 37% to 48% of scrub typhus. In India, AES is a serious public health problem majorly affecting children. Scrub typhus is a leading cause of AES in this part of the world associated with high mortality and morbidity.

Commonly used empirical antimicrobials for meningoencephalitis are ineffective in treating scrub typhus, therefore early diagnosis is important to initiate specific antibiotics (e.g. doxycycline) to reduce complications and fatality. Clinical diagnosis is challenging given overlapping features with other endemic infections. Serum IgM ELISA, the most widely used test for scrub typhus, has limitations as IgM antibodies cross-react with other pathogens and persist for long durations post-infection. Moreover, diagnosis in AES hinges crucially on cerebrospinal fluid examination. However, delays in presentation to hospital and sampling, which is a problem in developing countries, lead to poor yield and unreliable pathogen specific test results.

Therefore, there is a need for improved diagnostic tests that can quickly and more accurately diagnose scrub typhus in patients with AES. Host transcript-based blood tests can obviate the need for lumbar puncture and are less susceptible to recent initiation of antibiotics or delayed sampling. A novel host-transcript based blood test for scrub typhus meningoencephalitis will enable prompt patient diagnosis, in-turn facilitating faster initiation of appropriate antibiotics, leading to improved patient outcomes, while reducing the burden of unnecessary antibiotic use.

To achieve the aim, the first step is to generate a transcript database on human host response in scrub typhus which is currently unavailable. The key objectives of this study are to measure host transcript expression patterns in pediatric AES patients with scrub typhus, compare (in-silica) the scrub host gene expression pattern against a meta-data set of patients with other bacterial and viral meningoencephalitis, and identify transcripts that discriminate scrub typhus encephalitis from clinical mimics.

Dr Tina Damodar
DBT-Wellcome Trust Early Career Fellow
Department of Neurovirology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, India
(External sponsor for DBT Wellcome trust project: Institute of Infection, Veterinary and Ecological Sciences, University of Liverpool, United Kingdom)

SEEDFUNDING

Differentiating viral encephalitis from its mimics in patients with encephalitis of unknown aetiology.

In Uganda, most cases of encephalitis have no definitive cause. Instead, they are treated as possible TB meningoencephalitis due to limited diagnostics. We have shown that up to 52% of patients treated for tuberculous meningitis have viral pathogens detected on metagenomic next-generation sequencing (Quinn 2020, Ramachandran 2022). However, these diagnoses were done on stored samples and thus could not benefit the patients in real-time. Furthermore, one of the patients in this cohort had multiplex PCR testing done in real-time, which detected Herpes simplex-2 and improved on treatment with oral valacyclovir. Most of the other patients succumbed despite receiving a cocktail of antibacterial, antifungal, and antitubercular therapy in the setting of limited real-time diagnostics.

The scarcity and cost of newer diagnostics that rapidly identify viral pathogens translates into continued utilization of clinical judgment in encephalitis of unknown aetiology care. At Infectious Diseases Institute Makerere university, we accommodate a Biofire® PCR machine. Biofire® meningitis/encephalitis panel can detect seven viral encephalitis pathogens with sensitivity and specificity above 90%. It is cost-effective in encephalitis management elsewhere (Soucek 2017, Hagen 2020). However, its routine utilization in encephalitis management has lagged because of the cost and availability of cartridges. But also, its clinical utility and cost-benefit analysis are yet to be assessed in Uganda.

There is preventable mortality among patients with encephalitis due to limited diagnostics and thus underutilization of targeted and effective antivirals for their treatment. Therefore, this research will utilise Biofire® FilmArray® meningitis/encephalitis panel to describe the viral etiologies of encephalitis among individuals with suspected encephalitis at Mulago National Specialist Hospital and Kiruddu Referral Hospital in Uganda from January 2023 to June 2024. This will document the incidence of different aetiologies of encephalitis to guide treatment options in these public hospitals. We shall also store CSF cell pellets from individuals with encephalitis to provide an opportunity to conduct immunophenotyping studies. We plan to use flow cytometry to understand the immunophenotype of cells in the CSF of these individuals. We will stain using antibodies i.e., leucocyte marker (CD45), T cell markers (CD3, CD4, CD8), B cells (CD19), Natural killer cells (CD16, CD56), Monocytes (CD16, CD14), and cellular activation markers (HLA-DR, OX40, CD25 and CD38).

Although this research will not directly financially support immunology studies, CSF cell pellets will be processed and cryopreserved at -150 0C for immunology studies using flow cytometry to characterize the immune response present. We hypothesize that combining immunophenotyping with molecular diagnostics will enable encephalitis of unknown aetiology to be characterized into distinct subgroups of similar pathogenesis. However, a better understanding of the aetiologies is the first step. Without knowing aetiologies, appropriately describing the diversity of immune responses is less meaningful.

This pilot will yield preliminary data on viral aetiologies of encephalitis in Uganda. This preliminary data will provide a basis for greater availability and use of acyclovir and other antiviral agents in suspected encephalitis. We will also aim for multi-centre randomised clinical trials using antivirals to improve treatment outcomes amongst individuals with suspected encephalitis in Uganda.

Dr. John Kasibante MBChB, MSc
Clinical Immunology (University of Manchester Candidate)
Research Department, Infectious Diseases Institute, Makerere University, Kampala, Uganda.

Seed funding: future funding opportunities

Since the launch of Encephalitis Futures - International Research Seed Funding four years ago, grants have been awarded to researchers in Cameroon, Brazil, the USA, Senegal, India and Uganda.

For future funding opportunities, visit our website www.encephalitis.info/seedfund

Women in Science: Professor Angela Vincent

In a new ongoing feature for Connect Professional, we are asking eminent female medical professionals to share their experiences of working in science. This edition's interviewee is Professor Angela Vincent, Emeritus Professor of Neuroimmunology at the University of Oxford and member of the Encephalitis Society's Scientific Advisory Panel

Name:

Angela Vincent

Occupation:

Emeritus Professor of Neuroimmunology

Professor Angela Vincent - Elected Fellow of the Royal Society (2011)

When did you know you wanted to pursue a career in science?

As a child, I was keen on nature study and messed about a bit – for example, boiling up dead birds to look at their bones, that sort of thing. I was good at art and maths but not a high flyer overall. As a teenager, I started reading books about psychology, mathematics, physiology, not so much to learn but because I was fascinated by the existence of so much knowledge. In fact, I have always had a poor memory and suspect that "disadvantage" makes me a more of an experimental scientist, rather than one who follows the trends.

Where did you study?

I started by studying medicine at Westminster Hospital Medical School in the 1960s. I qualified in 1966 and did one year of "pre-registration" house jobs (ie. the first year as a junior doctor) in general surgery and general medicine, in two less prestigious London hospitals. I enjoyed the surgery and conducted six appendices under supervision as well as a few minor ops. The medicine was routine and not very inspiring; as a result, rather than continuing along a medical career, I did an MSc in Biochemistry at UCL with the intention of being a pure scientist, which I had always felt drawn to.

What is your area of expertise and how did you choose your field of study?

I suppose I slowly became a clinical neuro-immuno-biologist! I was first offered a position as a research assistant at University College London (UCL); the aim was to separate pre- and postsynaptic membranes from rat brain tissue for biochemical studies. At that time there were no clever reagents to use, and I had to spend hours looking down an electron microscope to see if I had achieved separation. It was a hopeless project but it gave me a bit of freedom and I wanted to find a way of labelling the postsynaptic membranes. Ricardo Miledi in the world-famous Biophysics Department at UCL made a radioactive snake toxin that labelled the postsynaptic membrane at the neuromuscular junction; this gave me an excuse to approach him and I worked with him for five years – on the neuromuscular junction. It was great fun and those years provided the scientific basis for practically everything that I have done since.

I made few choices, things just came along. Ricardo wanted to look at the neuromuscular junction from patients with myasthenia gravis, and started collaborating with a neurologist, John Newsom-Davis, at the National Hospital in Queen Square. As a medic, I was the obvious person to collect the muscle pieces and work on the project. Others in the USA identified that myasthenia patients had antibodies in their blood that were responsible for their muscle weakness and fatigue. I started measuring the antibodies in John's patients and then moved to the Royal Free Hospital to help John establish a research group on that myasthenia. Almost all the group moved to Oxford in 1988 and John retired ten years later, leaving me to direct the work. At that stage

we had an international reputation for our work on myasthenia, but we had also begun to move up along the nerve towards the brain. However, it was one particular patient, with insomnia and hallucinations, who made me appreciate that antibodies to a potassium channel protein in the blood could be responsible for brain disease. In the same year we identified two patients with epilepsy and memory loss who had the same antibodies. Importantly these patients and others subsequently identified improved when their antibody levels were reduced by treatments. These were the first cases of what we now call autoimmune encephalitis, which was the focus for the next 20 years.

What inspires you in the workplace?

Antibodies are relatively easy to measure in patient serum and CSF and identifying them and learning about the clinical features from their neurologists, has been very satisfying. I found early on that I loved the atmosphere of the laboratory and I have always tried to visit each day just to chat to people, while informally finding out whether they are working hard enough! So I suppose ultimately what I love(d) was the colleagues, the patients and their clinicians – I miss all three now that I am retired from the lab.

What kind of prejudices, if any, did you have to face?

As long as I was just someone in the lab I never faced any prejudice. Ricardo and John were both very easy to get on with, treated me as an equal, and tolerated my children who often turned up after school. When I became the leader of the group and then, for three years, head of the Neurology Department, everyone within the department was very helpful and collaborative, but a few of the senior people in the clinical faculty, who were all male, were a bit dismissive - I just ignored them. I only twice had to be assertive in order to get what I felt was important for the research group.

In your opinion, which changes, if any, are needed in the scientific system to be more attractive to women in science and possible future scientists?

It's essential to have good science in schools – I was lucky that my girl's boarding school happened to have some good teachers at the time. Flexibility in careers, good childcare possibilities, and appreciating that even if a woman can't be a workaholic during the child-caring years, there is plenty of time afterwards. I describe my career as treading water until my (four) children left home, and only then being able to be more ambitious, creative and exploratory.

What advice would you give to people considering a career in science?

Find out what you are good at and do it as well as you can – a career in science can mean many things, there are huge opportunities, it can be challenging but it is seldom boring.

About Professor Angela Vincent

Angela is Emeritus Professor of Neuroimmunology at the University of Oxford, and an Emeritus Fellow of Somerville College. She holds an honorary position at UCL.

She was previously an Honorary Consultant in Immunology and from 1977 helped to establish and run the Clinical Neuroimmunology service which continues to be an international referral centre for the measurement of antibodies in neurological diseases. She was formerly Head of Department of Clinical Neurology (2005-2008), and was President of the International Society of Neuroimmunology (2001-2004), and an Associate Editor of Brain (2004-2013). She was a co-applicant and group leader of OXION, the Wellcome Trust-funded Integrative Physiology Initiative "Ion channels and Diseases of Electrically Excitable Cells" and led the Neurosciences Theme of the first NIHR Oxford Biomedical Research Centre from 2007. She has received many awards including the Encephalitis Society life-time award in 2017 and the American Epilepsy Society Clinical Science Award (with Josep Dalmau) in 2019.

Her major interests in the past included discovering new antibodies causing neurological diseases, devising new ways to measure the pathogenic antibodies to improve diagnosis, and establishing models in vitro and in vivo for investigating these conditions.

On-going interests include (a) the role of maternal antibodies to different fetal proteins, including CNS proteins, as causes of neurodevelopmental disorders and (b) detailed studies on the role of antibodies to muscle specific kinase in myasthenia gravis.

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