Nottingham Multiple Sclerosis Research Group

Research portfolio 2020

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Nottingham Multiple Sclerosis Research Group

Our work, our ethos

The **Nottingham Multiple Sclerosis Research Group** (MSRG) is an interdisciplinary collaboration between the University of Nottingham, Nottingham University Hospitals NHS Trust, and the Institute of Mental Health.

Our research focuses on (i) diagnostics, (ii) investigating disease modifying therapies, and (iii)symptom management. Straddling these three foci are our Neuroimaging and our Clinical implementation themes. Our Patient and Public Involvement (PPI) activities are core to all our research.

Our research investigates diagnostic developments, treatment optimisation, rehabilitation practices, and health services and implementation strategies. Given the COVID-19 pandemic, we have also started conducting research to examine the impact of COVID-19 on people with MS. We conduct basic sciences and laboratory research, large-scale multi-centre randomised controlled trials, systematic reviews, cohort studies, and qualitative and implementation research.

In 2019/20, we have a portfolio of 32 studies. Our research grant income of over £27 million, is from major funders including the UK National Institute for Health Research (NIHR), the UK MS Society, MRC and PCORI from the USA. We also undertake commercial trials. Since 2012, our research has led to over 100 publications in leading scientific publications.

The MSRG supports and trains the next generation of clinicians and researchers interested in MS. In 2019/20, we have 4 postdoctoral researchers, 18 doctoral students, 4 MSc students, and 2 undergraduate medical students working on our projects.

Welcome to our research world.

Prof Roshan das Nair
Professor of Clinical Psychology & Neuropsychology

Dr Nikos Evangelou
AssociateProfessor of Neurology

Co-Leads of the Nottingham MSRG

Nottingham Multiple Sclerosis Research Group

MSRG in numbers

£ 24.5 million
in research grants 2015-2020

18 Doctoral students
2019/2020

100 +
Publications

12
Principal Investigators & Award winners

4
Postdoctoral researchers
2019/2020

32
On-going studies

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Diagnostics

Diagnosis of multiple sclerosis is frequently easy but over-reliance on the detection of white matter lesions in the brain has led on many occasions to misdiagnosis. At the very beginning, MS brain lesions can be few and sometimes not typical, leading to a delay in diagnosis and sometimes a delay in treatment. We work in collaboration with the team at Sir Peter Mansfield Imaging Centre. Our work aims to provide a safe, simple and reliable diagnostic tests and procedures that can help patients and clinicians plan effective treatments.

Nottingham Multiple Sclerosis Research Group

Diagnostics

1. DiagnosE using the Central veIn SIgn. A prospective diagnostic superiority study comparing T2* MRI and lumbar puncture in patients presenting with possible Multiple Sclerosis (DECISIVE)

A number of patients complain that lumbar puncture is an invasive procedure and encouraged us to find better way to diagnose MS. This research aims to change the way people are diagnosed with MS and reduce the number of lumbar punctures used. Our team will recruit a large number of people from different hospitals whose doctors suspect they may have MS. We will invite them to have a new MRI scan we have developed here in Nottingham and is based on the detection of a central vein in MS lesions, a very characteristic finding. We will compare the accuracy, speed, costs and acceptability of the different tests needed to make a diagnosis of MS and establish if most lumbar punctures can be replaced by a slightly longer MRI scan.

Funder: NIHR Research for Patient Benefit

Contact: Christopher.Allen@nottingham.ac.uk

2. MAGNIMS/RIMS study

We recently collaborated with the MAGNIMS group in Europe and reported the prevalence of veins as detected by clinical scanners across the continent. The study of lesions with paramagnetic iron rims (IRs), which are dark, ring-like features on edges of some MS lesions, has gained attention. Many believe that they are the MRI signs for active white matter lesions as seen in pathology. We work together with our European network of MS centres to put together hundred of scans and find how common this MRI sign is and if we can use it in the diagnosis and prognosis of MS.

Funder: Saudi Government supported by MAGNIMS collaboration

Contact: msxaa113@exmail.nottingham.ac.uk (Amjad Ibrahim AlTokhis)

3. RADAR-CNS

Wearable and smartphones technology might be used to track the course of conditions such as MS and help patients and clinicians to make clinical decisions and to track the value of new drugs once they are released for clinical care. RADAR-CNS is the largest EU Horizon 2020 grant ever given for health, which has been used to develop on open source operating system to work with wearables and android phones to track symptoms in patients with MS with and without depression, or epilepsy across Europe. In particular researchers in Nottingham will be examining the value of such disease monitoring across care pathways for clinical and research purposes.

Funder: EU Horizon2020

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4. AI gets real: using routine clinical data and Artificial Intelligence to predict worsening of MS despite treatment (AIMS)

A wealth of clinical and MRI data from patients with MS are acquired every year in clinical practice, but only part of these data are used for clinical decision making. We propose that a set of structural characteristics extracted from the MRI brain scans of people with MS are related to biological changes which are meaningful to MS, and may therefore act as predictive markers for outcome. In this study, we aim to use whole-image brain MRI scans processed with AI techniques and detect the clinical and MRI profiles that predict accumulation of MS-related disability or cognitive impairment. We will take advantage of our MS clinic and the Nottingham MS Society Register. Using clinical information which patients have consented for us to use, and the MRI images before starting treatment, we will train a computer to use mathematical models to predict whether a person's MS will determine accumulating disability or cognitive impairment over the long term. Furthermore, we seek to see if the profile can predict development of disability in other patient groups, by validating the models in large sets of MRI scans obtained from other groups of people with MS using different scanners. We will use a large group of patients from the United States, and also align with a clinical trial ongoing in UK and US, which compares treatments for MS with different strengths.

By identifying early, at diagnosis, who is likely to fare worse over the long term, we could offer them a more tailored treatment approach.

Funder: MRC & NIHR

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Nottingham Multiple Sclerosis Research Group

Disease Modifying Therapies

One of the main foci of our research is to explore new avenues in MS treatment and to gain a greater understanding of how best to use our current disease modifying therapies (DMTs). There are 9 approved DMTs in the UK and more are becoming available every year. All of them aid in decreasing inflammation and it is thought they might even protect neurons. All DMTs work with the overall aim to improve the clinical outcome of people with MS.

DMTs have been found to decrease the number and severity of relapse, slow the development and progression of brain and spinal cord lesions, and reduce disabilities. However, there is currently little to no evidence on which type of DMT is best, for which patients, and when would be the most beneficial time to use them to get the best results.

Stronger treatments are usually associated with riskier side effects. Therefore, the question is, can we find the right balance of effectiveness and side effects? Our aim, working with many other MS research teams across the world, is to provide this evidence in order to find the best treatment for each patient.

Nottingham Multiple Sclerosis Research Group

Disease Modifying Therapies

1. WIRMS (Worms for Immune Regulation in MS)

Epidemiological, experimental and limited clinical evidence indicates that gut helminths are protective in MS. Taking advantage of unique immunoparasitology experience at University of Nottingham and experience with therapeutic helminth trials, we conducted the largest randomised controlled trial on hookworm infection in relapsing MS. 71 patients received either hookworm larvae through the skin or placebo over 9 months, undergoing monthly MRI and immunology tests. We show that considerably more hookworm-treated MS patients had no new disease activity on MRI, and that hookworm increased regulatory cells that suppress inflammation. Follow up studies optimising the outcome measures, the target patient population, and hookworm dose are planned.

Funder: MS Society; Bayer; Forman Hardy Charitable Trust

Contact: cris.constantinescu@nottingham.ac.uk, radu.tanasescu@nottingham.ac.uk

2. WIRMS - virology/EBV

Previous experimental evidence in mice shows that infection with gut parasites increases the risk of reactivation of gamma herpesvirus, the mouse equivalent EBV, the virus strongly associated with MS. We looked for EBV reactivation in MS during hookworm infection, and showed that there was no reactivation, and no differences from placebo.

Dr Peter Maple, a virologist with interest in herpesviruses including EBV performed this research as part of his MRes in immunology. We found that a substantial proportion of MS patients, unlike healthy controls, have a continuous reactivation of EBV (regardless of treatment). Moreover, we found an inverse correlation between CMV infection and EBV responses, suggesting a protective action of CMV. Indeed, fewer patients with MS than controls were positive for CMV.

Funder: MS Society through WIRMS; Forman Hardy Charitable Trust

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3. WIRMS- microbiota

The gut microbiota is increasingly implicated in MS. Therapeutic helminths act in part by modifying the gut microbiota in a beneficial way. The WIRMS trial offered the opportunity to obtain one of the largest collections of gut microbiota samples in MS. The composition of the gut microbiome was investigated in collaboration with colleagues at Cambridge University. The placebo arm provided information about the composition and stability of the microbiota in untreated MS, while the helminth arm provided unique information on the effect of helminth treatment of MS on the gut microbiota. Changes associated with the treatment response, with relapses and with MRI activity were detected.

Funder: MS Society through WIRMS

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Disease Modifying Therapies

4. MSC MSC (mesenchymal stem cells in MS and controls)

Mesenchymal stem cells (MSC) have immunomodulatory and potential neuroregenerative capacity. There is almost no information on the effect of the interaction of MSC from people with MS with immune cells from the same donor, and how that differs from healthy volunteers. We have pioneered a study investigating these interactions and found that MSC from people with MS have diminished immunomodulatory activity on immune cells from the same donor, and in fact can enhance inflammatory responses. We have identified key factors involved in this faulty interaction. These factors can be targeted in the future, allowing MSC transplants to regain their immunomodulatory capacity.

Funder: MS Society

Contact: nanci.frakich@nottingham.ac.uk

5. GM-CSF in MS

Recent evidence implicates pro-inflammatory cytokine GM-CSF as a key factor in MS pathogenesis, likely to be more important than the traditional Th1 and Th2 cytokines. In a first trial of its kind, the safety, tolerability and immunogenicity of an anti-GMCSF antibody was tested in a phase I international trial led from Nottingham.

The primary outcomes were reached, and there was suggestion an immunomodulatory action warranting further study.

Funder: Morphosys

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6. GM-CSF in MS - effect on Oligodendrocytes

Radhika Patel completed a MRes investigating the effect of GM-CSF on human ligodendrocytes, the cells that produce myelin. GM-CSF suppressed production of myelin proteins, providing a mechanism for the demyelination seen during inflammation in MS, and suggesting that blocking GM-CSF for example through an antibody may facilitate remyelination.

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Disease Modifying Therapies

7. THRIFT-MS (Tysabri High Resolution Imaging and Function of T cells in MS)

In this study, we investigated whether subtle changes in white and grey matter integrity still occur despite no new lesion development over 1 year of treatment with the potent DMT Tysabri. Reassuringly, even when imaging at ultra-high field (7 Tesla) we did not find such changes. Tysabri reduced some T cells subgroups that are damaging in MS more successfully than interferon beta.

Funder: Biogen

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8. Interactive effects of Teriflunomide and repurposing molecules on a model of blood brain barrier

We study the effects and interactions of disease modifying treatments such as Teriflunomide, and molecules with potential of repurposing in MS, on transporter proteins and cytokine expression in a cultured primary human brain microvascular endothelium as a model of the human blood brain barrier. We aim to detect mechanisms of actions which can improve immunomodulation in MS.

Funder: Genzyme Pharma

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9. Determining the Effectiveness of Early Intensive versus Escalation Approaches for the Treatment of Relapsing-Remitting Multiple Sclerosis - (DELIVER-MS)

DELIVER-MS is a study coordinated by Nottingham and the Cleveland Clinic in the USA is comparing two treatment strategies in 400 people with relapsing-remitting MS who have never taken a disease-modifying therapy. The study is recruiting at 30 centres in the United States and United Kingdom. One strategy is an “escalation” approach, in which individuals start taking a less-powerful therapy with the option of switching to a more potent one if disease activity continues. The other strategy involves starting with a strong therapy that is potentially more effective, but also carries greater risk for significant adverse effects.

Funder Patient-Centered Outcomes Research Institute (PCORI)

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Nottingham Multiple Sclerosis Research Group

Disease Modifying Therapies

10. Spinal cord, MS, & diabetes - The SpINDLE study

Our group has pioneered the measurement of spinal cord atrophy in MS and its use in longitudinal studies of MS DMT. In the SpINDLE study, we are applying our imaging techniques to diabetes with or without neuropathy, in an attempt to determine whether spinal cord area/volume can be used as markers of disease progression. This allows us to compare changes and rates of atrophy with those of people with MS.

Funder: NUH Charity

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11. Cardiff-Nottingham DMT analysis

Is the current treatment of MS significantly better than the one we used 10 years ago? There is an optimism in MS clinics that patients currently receive stronger treatments earlier and as a result the long-term outcomes are better. We set up a study with the University of Cardiff to explore if this is true and we plan to analyse clinical data from our clinics.

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Symptom management

The symptom management theme focuses on understanding, assessing, and treating symptoms of MS. We mainly focus on (i) cognition, and (ii) psycho-social adjustment and psychological wellbeing. Finding effective treatments for cognitive problems is a top 10 research priority for people with MS (as identified by a James Lind Alliance/MS Society priority setting exercise). We are developing new research projects into management of other symptoms, particularly fatigue and spasticity. We are affiliated with the Institute of Mental Health, which enables us to recruit large samples and access to expert knowledge in the areas of psychological wellbeing and mental health.

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i. Cognition

Up to 70% of people with MS can experience cognitive problems. These are persistent and debilitating to the person with MS, and can adversely affect their personal, social, and professional lives. Unsurprisingly, the MS Society with the James Lind Alliance identified finding treatments to improve cognition as a top 10 research priority. Our portfolio of cognition research focuses on (i) understanding the cognitive and neural mechanisms that underpin the cognitive problems that people with MS face, and (ii) finding ways to treat or support people with cognitive problems, so that they can continue to participate in activities of daily life.

1. Neuropsychological Evaluation and Rehabilitation in Multiple Sclerosis (NEuRoMS)

The NEuRoMS is a 6-year programme that aims to develop a neuropsychological evaluation pathway, to routinely assess all people with MS for cognitive problems attending NHS MS clinics, and to develop and test a brief neuropsychological rehabilitation programme for people with MS with mild cognitive problems.

Funder: NIHR Programme Grant for Applied Research

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2. Cognitive Rehabilitation of Attention and Memory in Multiple Sclerosis – II (CRAMMS-II)

CRAMMS was an NIHR/HTA-funded trial that determined the clinical and cost-effectiveness of a 10-session group rehabilitation programme. We recruited 449 people with MS and cognitive problems, 229 were randomly allocated to receive cognitive rehabilitation in addition to usual care and 240 to receive only usual care and 240 to receive only their usual clinical care, and outcome measured at 6 and 12 months. Results can be found in Clinical Rehabilitation and the Health Technology Assessment Monograph.

In CRAMMS-II, we are determining who benefits most from cognitive rehabilitation, and based on this classification, we will conduct a new trial of the CRAMMS intervention, to prospectively test whether our new classification system yields better outcomes when compared to providing the intervention to everyone with cognitive problems.

Funder: MS Society

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3. Digitising cognitive tests

Increasingly, tests to assess people's cognition is being delivered online or on computerised formats. This has made administration and scoring of these tests much easier, but some of these tests have not undergone rigorous testing to establish their psychometric properties or they are expensive to purchase.

This makes it difficult to use these in routine NHS clinics, where they are most needed. Hannah's PhD research has examined all cognitive tests used in MS research, and she has sought patient and clinician views on various tests. Based on this information, she has been working with MindTech to digitise two tests, is collecting normative data, and is determining how these new digitised tests compared to their traditional paper-pencil counterparts.

Funder: MS Society

Contact: hannah.elwick@nottingham.ac.uk

4. Cochrane review: Memory rehabilitation for people with MS

Cochrane reviews bring together the best and latest evidence of effectiveness of a particular treatment. We completed this review in 2016, and now that there are a number of new studies on memory rehabilitation in MS,
we felt it was time to update this review. We believe this will be the biggest update yet of this review. This update is part of Lauren's PhD research.

Funder: MS Society

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5. Medication adherence in people with cognitive problems

Up to 70% of people with MS can have cognitive problems. We also know that many people with MS are on a complicated regimen of medications and treatments, and many times, people forget to take these treatments on time. Working with the UK MS Register, Sarah's doctorate project will identify strategies related to disease modifying treatment (DMT) adherence amongst people with MS with associated cognitive deficits, and whether the barriers and strategies related to DMT adherence differ between those who are adherent vs non-adherent.

Funder: Health Education England (as part of the DClinPsydegree)

Contact: sarah.thomason@nottingham.ac.uk

6. SMART Rehab: Exploring the effects of Strengthening Mental Abilities with Relational Training on Executive Functioning for People with MS.

There is some evidence that 'brain training' exercises are helpful for improving cognition, but the evidence is not robust. Strengthening Mental Abilities with Relational Training (SMART) is computerised intervention that aims to improve cognition The program is based on theoretical developments in Relational Frame Training, an established theory of language and cognition.

RFT proposes that many cognitive processes are underpinned by our ability to 'relate' concepts together, and that this ability is learnt (starting in infancy) and develops over time as the individual interacts increasingly with their environment. In this mixed-methods, multiple-baseline across participants Single Case Experimental Design Rupert will examine the feasibility and effectiveness of the SMART intervention for people with MS reporting cognitive problems.

Funder: Health Education England (as part of the DClinPsydegree)

Contact: rupert.burge@nottingham.ac.uk

7. Neuromodulation with Connectivity-Guided Intermittent Theta Burst Stimulation for Cognitive Impairment in MS: A Feasibility Trial

In this feasibility trial, we will test the feasibility of MRI-guided intermittent theta burst stimulation (iTBS) as a treatment for improving cognitive status in people with MS. We will test the feasibility of recruitment, participant retention and experience of the procedure. We will also collect preliminary evidence of efficacy and for different administration protocols to allow us to optimise the design of a subsequent planned fully RCT.

Funder: MS Society

Contact: rob.dineen@nottingham.ac.uk

8. Development of a self-report measure of cognitive abilities for people with MS

There are a few self-report measures of cognitive abilities for people with MS, but these tend to be long, complex, lack validity and input from people with MS, or are expensive. Therefore, we cannot use these in routine clinical practice in NHS MS clinics. Furthermore, increasingly, there is a call to use robust patient-reported measure in clinical trials. Therefore, it is vital that we have one that is suitable for use for these purposes. In this study, Heather will develop an item pool based on qualitative research into cognitive problems faced by people with MS, from people with MS, clinicians and other stakeholders. This item pool will be used in a Delphi study to develop the scale, which will then be assessed for its psychometric properties. We will test whether respondents understand each item as it was intended to be understood, using cognitive interviews with people with MS.

Funder: Health Education England (as part of the DClinPsydegree)

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Nottingham Multiple Sclerosis Research Group

ii. Psychosocial adjustment and psychological wellbeing

There are key moments in the lives of people with MS that they find more stressful than others. However, we also know that many people with MS experience longer-term problems with anxiety and depression. These have a knock-on effect on their MS and other aspects of their lives. Our portfolio of studies explores how best to support people at the points of diagnosis and transition to secondary progressive MS, and people with low mood. We also examine how people manage their invisible symptoms and how to best support people with MS to remain in work.

1. Providing Emotional support around the point of Multiple Sclerosis diagnosis (PrEliMS): A feasibility randomised controlled trial

Diagnosing MS can be a lengthy and stressful process. Difficulties during this challenging period may influence people's perception of MS, their relationships with the healthcare team, and can contribute to ongoing MS adjustment. Therefore, providing support to people with MS around diagnosis is important, but does not routinely happen in NHS MS clinics. In this feasibility trial, we are testing standard care with two new psychosocial interventions, which were developed following stakeholder consultations: (i) delivered by MS nurse specialists and (ii) delivered by MS nurse specialists and MS Society volunteers.

Funder: MS Society

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2. Behavioural Activation for Low mood in Multiple Sclerosis (BALMS)

People with MS a lifetime prevalence of depression of around 50%, and people with advanced MS are more likely to experience clinically significant depression than those with minimal disease symptoms. Behavioural Activation aims to reduce behaviours that aintain or exacerbate depression by promoting counteracting behaviours, using strategies such as activity monitoring and scheduling. In this mixed-methods study, Lloyd will (i) adapt an existing behavioural activation protocol for people with secondary progressive MS, and (ii) evaluate the new adapted intervention using multiple single-case experimental design and a follow-up change interview. The Hospital Anxiety and Depression Scale will be used to investigate changes in depression.

Funder: Health Education England (as part of the DClinPsy degree)

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Nottingham Multiple Sclerosis Research Group

ii. Psychosocial adjustment and psychological wellbeing

3. Acceptance Based Telephone Support around the time of Transition to Secondary Progressive Multiple Sclerosis: A Feasibility Randomised Controlled Trial

There is good evidence that those transitioning to secondary progressive MS (SPMS) feel an increasing sense of loss, frustration and worry. We also know that people with SPMS are more likely to have depression compared to those with other MS subtypes. Acceptance and Commitment Therapy (ACT) is now a well-established psychological intervention, but is still resource intensive, so is not routinely offered in NHS MS clinics. In this mixed-methods feasibility trial, Chris is evaluating the feasibility of providing a low-resource acceptance-based telephone support intervention around the time of transition to SPMS, and assessing the efficacy of this intervention compared to usual care. Furthermore, with the support of the UK MS Register, he is examining the association between psychological flexibility and distress in those with SPMS.

Funder: Health Education England (as part of the DClinPsy degree)

Contact: christopher.meek@nottingham.ac.uk

4. Seeing the invisible: An exploration of living with, and how people manage, invisible symptoms of MS

Many of the symptoms people with MS face are considered 'invisible symptoms' because they are not visible to others, and indeed, sometimes to the people with MS themselves. In this project Le-Sharn uses photo-voice as an interview technique and research practice to explore the experience of living with these invisible symptoms and how people manage these invisible symptoms in daily life. Participants take photos on their mobile phones of these two aspects and send them to the researchers, who use the photographs as a starting point for wide-ranging discussions around invisible symptoms.

Funder: Health Education England (as part of the DClinPsy degree)

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Nottingham Multiple Sclerosis Research Group

ii. Psychosocial adjustment and psychological wellbeing

5. Preventing job loss in people with MS

The average age of onset of MS is around 30 years of age, when people are at the beginning of their professional career and seeking to live independently. Work is an important part of most people's lives. After 10 years with MS, fewer than 50% remain at work and this figure decreases to 20% after 15 years.
Blanca's PhD research aims to develop and test a job retention vocational rehabilitation intervention for people with MS. As part of her PhD, Blanca has reviewed various vocational rehabilitation programmes offered for people with MS across the world, and is adapting these for use in the UK context. She is currently evaluating this newly developed intervention as a series of case studies.

Funder: Joan Browne Legacy Funding

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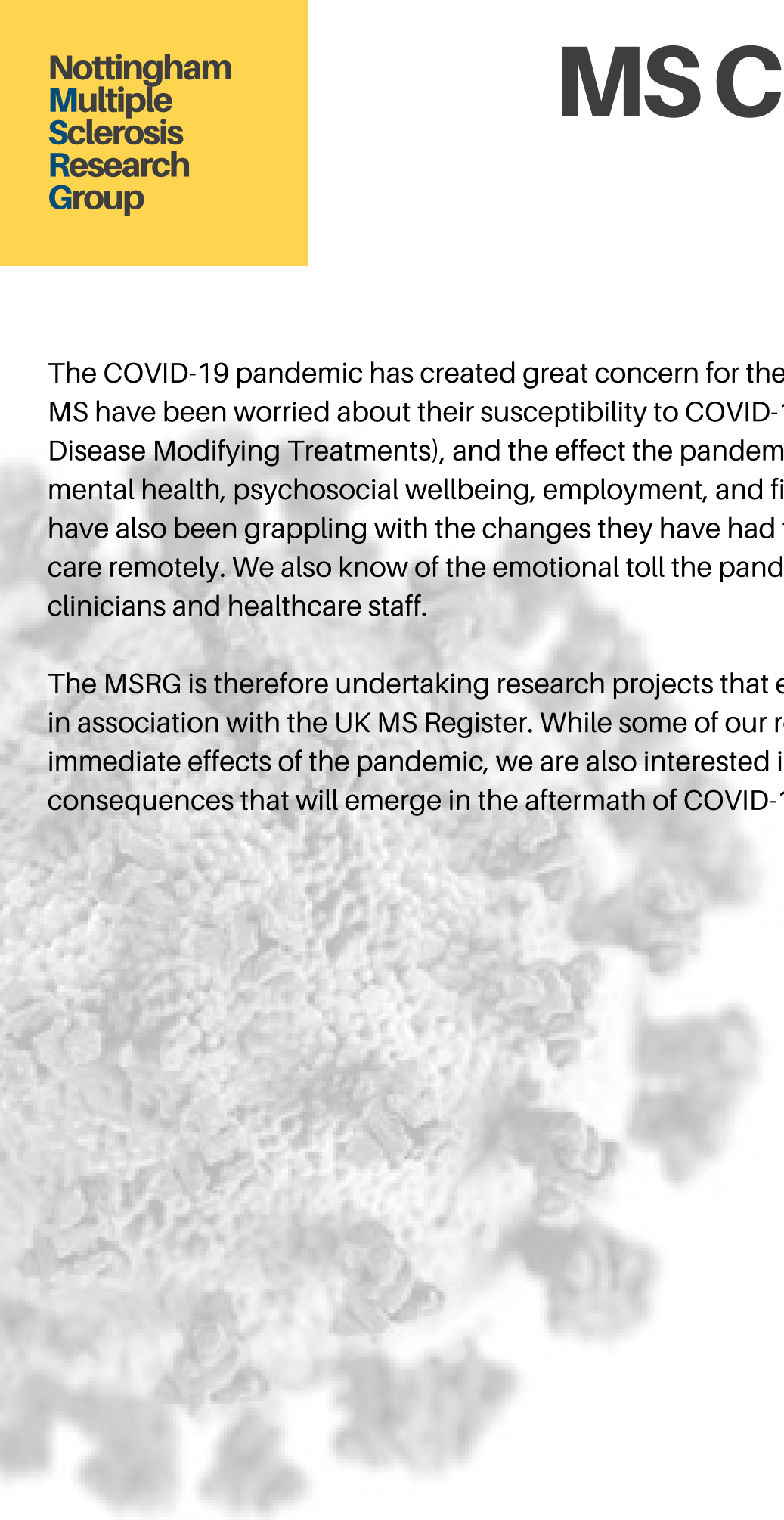
MS COVID-19 studies

The COVID-19 pandemic has created great concern for the MS community. People with MS have been worried about their susceptibility to COVID-19 (particularly for those on Disease Modifying Treatments), and the effect the pandemic will have on people's mental health, psychosocial wellbeing, employment, and finances. Clinical services have also been grappling with the changes they have had to institute to provide clinical care remotely. We also know of the emotional toll the pandemic has had on our clinicians and healthcare staff.

The MSRG is therefore undertaking research projects that examine each of these issues, in association with the UK MS Register. While some of our research is focusing on the immediate effects of the pandemic, we are also interested in the longer-term consequences that will emerge in the aftermath of COVID-19.



Nottingham Multiple Sclerosis Research Group

MS COVID-19 studies

1. Risk of contracting COVID-19 in people with MS and the effect of disease modifying therapies

Funded by the MS Society, and in conjunction with the UK MS Register, this study explores the impact of COVID-19 on people with MS and whether the risk profiles for developing COVID-19 and resultant outcomes differ based on Disease Modifying Therapies (DMTs). Based on data from almost 4000 people, this is the largest MS study to examine this association. This longitudinal survey, with data collected every two weeks is important to offer people with MS and clinicians relevant and timely information about the risks of different DMTs in relation to contracting COVID-19. One innovation is that emerging data/findings are released every two weeks to the MS community, which includes people with MS and clinicians.

Funder: UK MS Society

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2. Mental health and psychological wellbeing in people with MS during the COVID-19 pandemic

A few studies have shown an increase in mood problems, particularly anxiety and depression, during the COVID-19 pandemic. However, we do not as yet know how this pandemic has specifically affected people with MS.

This study examines historically collected mood data from people with MS by the UK MS Register, and prospectively follows people up over the next year to explore whether mood problems have changed, and how these relate to MS symptoms and relapses, while also considering whether lifestyle factors such as exercise, diet, and alcohol intake have altered during the pandemic. The study will also be comparing how people with MS and those without MS are coping during the pandemic.

Contact: roshan.dasnair@nottingham.ac.uk

3. Vitamin D supplementation, serum levels, and susceptibility to COVID-19

It has been hypothesised that low serum levels of 25-hydroxyvitamin D (25(OH)D) act as a risk factor for Coronavirus disease 2019 (COVID-19) susceptibility and severity, and that this in part drives the ethnic disparities that have been observed. This study examines the association between both vitamin D supplementation behaviours and serum 25(OH)D with susceptibility to COVID-19 in a population-based cohort with MS. This is an observational cohort study using prospectively gathered questionnaire (from the UK MS Register) and biological data.

Funding: UK MS Society

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Nottingham Multiple Sclerosis Research Group

MS COVID-19 studies

4. COVID-19 autoethnographic study:

While several COVID-19 related letters and papers have been published, none have considered the challenges of developing, conducting, analysing, and reporting a COVID-19 study as the COVID-19 pandemic unfolds. Based on ethnographic principles, and using data from one of our MS COVID-19 study, this study examines the research processes, the challenges the research team encountered, and the solutions they arrived at, with a view to provide guidance for future researchers developing similar studies during a national and global health crisis.

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Nottingham Multiple Sclerosis Research Group

Commercial trials

Over the years, we have undertaken several commercial trials. We currently have approximately 10 commercial trials of symptomatic (e.g. for spasticity) or disease modifying treatments for MS, funded by pharmaceutical companies. For details of our ongoing commercial trials, please see:

https://www.nottingham.ac.uk/research/groups/clinicalneurology/trials/index.aspx

Contact: Rebecca.Boulton@nuh.nhs.uk

Clinical services

Our research happens across various sites in Nottingham, but primarily linked with our MS Clinic based at Nottingham University Hospitals NHS Trust. This is supported by our multidisciplinary team including 21 neurology and neurorehabilitation consultants, specialist nurses, neurophysiotherapists, and occupational therapists For details of our clinical services, please visit the following sites:

https://www.nuh.nhs.uk/multiple-sclerosis-and-neuroinflammation

https://www.nuh.nhs.uk/meet-the-team

Nottingham Multiple Sclerosis Research Group

Grants

2020

Nicholas, R., Evangelou, N., Middleton, R., Tuite-Dalton, K., das Nair, R., Garjani, A., & Hunter, R. (2020). The Impact of COVID-19 in Patients with Multiple Sclerosis. MS Society, £43,036.

2019

das Nair, R., Topcu, G., Evangelou, N., Drummond, A., Fitzsimmons, D., Croft, A., Kendrick, D., Martin, J., Moore, P., Leighton, P., Thomas, S., Timmons, S., Vernon, K., & Hoare, Z. (2019). Neuropsychological Evaluation and Rehabilitation in Multiple Sclerosis - Developing, evaluating and implementing a clinical management pathway (NEuRoMS). NIHR Programme Grant for Applied Research, £1,852,239.

Evangelou, N., Allen, C., Dineen, R., Fitzsimmons, D., Craner, M., Tallantyre, E., Schmierer, K., das Nair, R. Morgan, P., Partlett, C., & Bale, C. (2019). Diagnose using the Central Vein Sign: A prospective diagnostic superiority study comparing T2⁎ MRI and lumbar puncture in patients presenting with possible multiple sclerosis. NIHR Research for Patient Benefit. £349,461.

Tanasescu, R., Evangelou, N., das Nair, R., Auer, D., Garibaldi, J., Ontaneda, D. (2019). AI gets real: using routine clinical data and Artificial Intelligence to predict worsening of Multiple Sclerosis despite treatment (AIMS). MRC - NIHR Clinical Academic Research Partnerships. £249,361

Dineen, R., et al. (2019). A Feasibility Trial of Neuromodulation with Connectivity-Guided Intermittent Theta Burst Stimulation for Cognitive Impairment in MS. MS Society. £244,826

das Nair, R., Evangelou, N., Mhizha-Murira, J., & Moghaddam, N. (2019). Determining who benefits most from cognitive rehabilitation. MS Society, PhD studentship. £77,900.

das Nair, R. & Topcu, G. (2019). Building a multiple sclerosis patient and public involvement community for people with multiple sclerosis in Nottinghamshire. Public Engagement Small Grant. Institute for Policy & Engagement. £3,500.

Grants

2018

das Nair, R. & Radford, K. (2018). Preventing job loss in people with multiple sclerosis. Joan Browne Legacy Funding, £75,000.

2017

Dineen, R., Sotiropoulos, S., Auer, D., Morgan, P., Evangelou, N., Constantinescu, C., das Nair, R. (2017). Explaining cognitive impairment in multiple sclerosis through integrated structural and functional networks. Medical Research Council, £97,316.

Ontaneda D & Evangelou N. (2017). Determining the Effectiveness of Early Intensive versus Escalation Approaches for the Treatment of Relapsing-Remitting Multiple Sclerosis (DELIVER-MS), PCORI, $10,630,672.

Evangelou, N. & das Nair, R. (2017). Developing and evaluating psychological interventions for support around the time of multiple sclerosis diagnosis. John Mortimer Shipstone Ratcliff Medical Scholarship, £57,832.

das Nair, R., Topcu, G., Evangelou, N., Drummond, A., Bale, C., Fitzsimmons, D., Vernon, K., & Rose, A. (2017). Intervention to support individuals around the point of multiple sclerosis diagnosis. MS Society, £172,251.

2016

Tanasescu, R., Constantinescu CS. (2016). Interactive effects of Teriflunomide, Simvastatin and Lisinopril on transporter proteins and cytokine expression in cultured primary human brain microvascular endothelium. Genzyme Pharma. £93,960

Dineen, R. A., Lincoln, N., das Nair, R., and Constantinescu, C. S. (2016). MRI markers predictive of treatment response to cognitive rehabilitation in the CRAMMS trial. MS Research, £24,739

Hotopf M, Stewart R, Wykes T, Richardson M, Hollis C, Morriss R, Craven M and 23 other partners (2016-2020). RADAR-CNS. Remote assessment of disease and relapse in central nervous system disorders. EU Horizon 2020, €14,000,000.

Nottingham Multiple Sclerosis Research Group

Grants

2015

Drummond, A., das Nair, R., Thomas, S. (2015). Implementing cognitive rehabilitation for people with MS: Translating research into clinical practice. MS Society PhD Studentship Grant, £64,665.

Gran, B. (2015). Role of innate immunity in neuroinflammation. MS International Federation (supervisor to MSIF MacDonald Fellow). £64,000.

2014

Drummond, A. & das Nair, R. (2014). Delivering cognitive rehabilitation to people with Multiple Sclerosis. MS Society PhD Studentship. £67,468.

Gran, B. (2014). How do infections activate inflammation in MS? Role of TLR2. Italian MS Society. €126,550.

Lincoln, N.B. (Co-CI), das Nair, R. (Co-CI), Drummond, A., Constantinescu, C., Montgomery, A., Morgan, M., & Phillips, C. (2014). Cognitive Rehabilitation of Attention and Memory for people with Multiple Sclerosis: A pragmatic randomised controlled trial. National Institute of Health Research – Health Technology Assessment. £1,167,000.

2013

Dineen, R. A., Constantinescu, C. S. and Auer, D. P. (2013). Brain Network Dysfunction in Multiple Sclerosis. MS Society PhD studentship. £95,794.

2012

Edwards LJ. Constantinescu CS. - Assessment of central and peripheral regulation of inflammation in multiple sclerosis. Anne McLaren Research Fellowship. £58,416.

Gran, B. (2012). Toll-like receptors modulate the balance between Treg and Th17 cells: Implications for multiple sclerosis. Italian MS Society. €28,000.

Grants

Lincoln, N.B., & das Nair, R. (2012). Understanding how group-based interventions work: a social identity approach to adjustment groups for people with multiple sclerosis. MS Society Studentship. £65,669.

Lincoln, N.B., das Nair, R., Hunt, N., & Smale, K. (2012). The contribution of identity processes to psychological adjustment in multiple sclerosis. ESRC studentship. £55,000.

Lincoln, N.B, das Nair, R. & Bateman, A. (2012). Evaluation of Neuropage as a memory aid for people with multiple sclerosis. MS Society PhD Studentship. £73,245.

das Nair, R. (CI) & Lincoln, N. (2012). Comparing individual vs. group psychological adjustment interventions for people with multiple sclerosis: A pilot randomised controlled trial. Pump-priming Competition 2012, Nottingham University Hospitals Charity and R&I. £10,992.

Constantinescu CS, Pritchard DI, Auer DP, Tench RT, Tanasescu RI, et al. WIRMS (Worms for Immune regulation in MS); MS Society £400,000.

Constantinescu CS, Jones RDE, Bath PM, et al. MSC-MSC (Mesenchymal Stem Cells in MS and Controls); MS Society, £60,000

Constantinescu CS, et al. MOR-103 in relapsing MS. Morphosys: clinical trial and ancillary immunology study, ~£100,000

Tanasescu RI, Constantinescu CS, Teriflunomide, simvastatin and lisinopril: effects at the blood brain barrier, Sanofi, ~£100,000.

Constantinescu CS, Pritchard DI: GM-CSF, EBV, and hookworm in MS. Forman Hardy Charitable Trust, £50,000.

2010

Edwards LJ. Biomarkers in multiple sclerosis. MS Society / Fulbright Research Award, £75,000.

Nottingham Multiple Sclerosis Research Group

Grants

2008

Lincoln, N.B., Constantinescu, C., Drummond, A., Armstrong, S., & Phillips, C. (2008). Psychological Treatment for people with Multiple Sclerosis and Low Mood. MS Society. £130,769.

2007

Edwards LJ., Constantinescu CS - Th17 cells in Multiple Sclerosis - Patrick Berthoud Research Fellowship. £163,214.

Edwards LJ, Constantinescu CS – Tetanus vaccination in multiple sclerosis – Mason Medical Research Foundation. £9,500.

Nottingham Multiple Sclerosis Research Group

Publications

2020

Chou IJ, Kuo CF, Tanasescu R, Tench CR, Tiley CG, Constantinescu CS, Whitehouse WP. Comorbidity in multiple sclerosis: its temporal relationships with disease onset and dose effect on mortality. 2020. Eur J Neurol. 27(1):105-112. doi: 10.1111/ene.14040.

Lincoln, N.B., Bradshaw, L.E., Constantinescu, C., Day, F., Drummond, A.E.R., Fitzsimmons, D., Harris, H., Montgomery, A.A & das Nair, R. (2020). Cognitive Rehabilitation for Attention and Memory in people with Multiple Sclerosis: a randomised controlled trial (CRAMMS). Health Technology Assessment, 24(4):1-182. doi: 10.3310/hta24040.

Meek., C., Topcu, G., Moghaddam, N., & das Nair, R. (2020). Experiences of adjustment to secondary progressive multiple sclerosis: A meta-ethnographic systematic review. Disability & Rehabilitation. DOI: 10.1080/09638288.2020.1734105

Maple PAC, Tanasescu R, Gran B, Constantinescu CS. A different response to cytomegalovirus (CMV) and Epstein-Barr virus (EBV) infection in UK people with multiple sclerosis (PwMS) compared to controls. 2020. J Infect. 80(3):320-325. doi: 10.1016/j.jinf.2019.10.017

Papathanasiou A, Tanasescu R, Davis J, Rocha MF, Singhal S, O'Donoghue MF, Constantinescu CS. MOG-IgG-associated demyelination: focus on atypical features, brain histopathology and concomitant autoimmunity. 2020. J Neurol. 267(2):359-368. doi: 10.1007/s00415-019-09586-5

Parker, L-S., Topcu, D., De Boos, D., & das Nair, R. (2020). The notion of 'invisibility' in people's experiences of the symptoms of multiple sclerosis: a systematic meta-synthesis. Disability & Rehabilitation. DOI: 10.1080/09638288.2020.1741698

Potter, J-J., Golijana-Moghaddam, N., Evangelou, N., Mhizha-Murira, J., & das Nair, R. (2020). Self-help Acceptance and Commitment Therapy for Carers of People with Multiple Sclerosis: A Feasibility Randomised Controlled Trial. Journal of Clinical Psychology in Medical Settings. https://doi.org/10.1007/s10880-020-09711-x

Welton T, Constantinescu CS, Auer DP, Dineen RA. Graph theoretic analysis of brain connectomics in multiple sclerosis: reliability and relationship to cognition. 2020 Brain Connect. February 20, doi 10/1089/brain.2019.0717. Epub

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Publications

2019

Alrouji M, Manouchehrinia A, Gran B, Constantinescu CS, 2019. Effects of cigarette smoke on immunity, neuroinflammation and multiple sclerosis. J Neuroimmunol 329:24-34.

Barker, A., Lincoln, N. B., Hunt, N., & das Nair, R. (2019). The Experience of Identity Change in People who Reported Having a Diagnosis of Multiple Sclerosis: A Qualitative Enquiry. International Journal of MS Care, 21(5): 235–242.

Chou IJ, Kuo CF, Tanasescu R, Tench CR, Tiley CG, Constantinescu CS, Whitehouse WP. Epilepsy and associated mortality in patients with multiple sclerosis. Eur J Neurol. 2019 Feb;26(2):342-e23

Chou IJ, Tanasescu R, Mougin OE, Gowland PE, Tench CR, Whitehouse WP, Gran B, Nikfekr E, Sharrack B, Mazibrada G, Constantinescu CS. 2019 Reduced Myelin Signal in Normal-appearing White Matter in Neuromyelitis Optica Measured by 7T Magnetic Resonance Imaging. Sci Rep, 9: 14378.

Clarke, M.A., Samaraweera, A.P., Falah, Y., Pitiot, A., Allen, C.M., Dineen, R.A., Tench, C.R., Morgan, P.S. and Evangelou, N., 2019. Single Test to ARrive at Multiple Sclerosis (STAR-MS) diagnosis: A prospective pilot study assessing the accuracy of the central vein sign in predicting multiple sclerosis in cases of diagnostic uncertainty. Multiple Sclerosis Journal, p.1352458519882282.

das Nair, R., de Groot, V., & Freeman, J. (2019). Beyond current research practice: methodological considerations in MS rehabilitation research. Multiple Sclerosis Journal, 25(10), 1337-1347.

I-Jun Chou, Radu Tanasescu, Olivier E. Mougin, Penny A. Gowland, Christopher R. Tench, William P. Whitehouse, Bruno Gran, Esmaeil Nikfekr, Basil Sharrack, Gordon Mazibrada & Cris S. Constantinescu, 2019. Reduced Myelin Signal in Normal appearing White Matter in Neuromyelitis Optica Measured by 7T Magnetic Resonance Imaging. Sci Rep 9:14378 https://doi.org/10.1038/s41598-019-50928-0.

Klein, O., das Nair, R., Ablewhite, J., & Drummond, A. (2019). Assessment and management of cognitive problems in people with multiple sclerosis: A National Survey of Clinical Practice. International Journal of Clinical Practice. DOI: 10.1111/ijcp.13300

Lincoln, N. B., Bradshaw, L. E., Constantinescu, C. S., Day, F., Drummond, A. E., Fitzsimmons, D., ... das Nair, R. (2019). Cognitive rehabilitation for attention and memory in people with multiple sclerosis: a randomized controlled trial (CRAMMS). Clinical Rehabilitation. https://doi.org/10.1177/0269215519890378

Maple PAC, Tanasescu R, Gran B, and Constantinescu CS. A different response to Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) infection in UK people with multiple sclerosis (PwMS) compared to controls. 2019. J Infection. pii: S0163-4453(19)30329-9. doi: 10.1016/j.jinf.2019.10.017.

Marck CH, das Nair R, Grech LB, Borland R, Constantinescu CS. Modifiable risk factors for poor health outcomes in multiple sclerosis: The urgent need for research to maximise smoking cessation success. Mult Scler. 2019 Jun 20:1352458519858730.

Mexhitaj I, Nyirenda MH, Li R, O'Mahony J, Rezk A, Rozenberg A, Moore CS, Johnson T, Sadovnick D, Collins DL, Arnold DL, Gran B, Yeh EA, Marrie RA, Banwell B, Bar-Or A, 2019. Abnormal effector and regulatory T cell subsets in paediatric-onset multiple sclerosis. Brain 142:617-632. doi: 10.1093/brain/awz017.

Mowry, E.M., Ontaneda, D., Evangelou, N. and Newsome, S.D., 2019. Pragmatic clinical trials for treating relapsing multiple sclerosis. Lancet Neurol. 2019 Dec;18(12):1075. PMID: 31701890

Papathanasiou A, Tanasescu R, Rocha MF, Singhal S, O'Donoghue MF, Constantinescu CS. 2019. MOG-IgG-associated demyelination: focus on atypical features, brain histopathology and concomitant autoimmunity. J Neurol 2019 doi: 10.1007/s00415-019-09586-5

Ontaneda D, Tallantyre E, Kalincik T, Planchon SM, Evangelou N. Early highly effective versus escalation treatment approaches in relapsing multiple sclerosis. Lancet Neurol. 2019 Oct;18(10):973-980. PMID: 31375366

Sinnecker T, Clarke MA, Meier D, et al. Evaluation of the Central Vein Sign as a Diagnostic Imaging Biomarker in Multiple Sclerosis. JAMA Neurol. Published online August 19, 2019. doi:10.1001/jamaneurol.2019.2478

Tallantyre EC, Evangelou N, Bale C, Chaudhry BZ, Gray EH, LaRocca N, Pavitt S, Miller DM, Planchon SM, Ontaneda D, Manzano A. Achieving effective patient and public involvement in international clinical trials in neurology. Neurology: Clinical Practice. 2019 Sep 26:10-212.

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Publications

2018

Alrouji M, Manouchehrinia A, Gran B, Constantinescu CS. Effects of cigarette smoke on immunity, neuroinflammation and multiple sclerosis. J Neuroimmunol. 2018 Oct 9. pii: S0165-5728(18)30130-9

Aram J, Francis A, Tanasescu R, Constantinescu CS. Granulocyte-Macrophage Colony-Stimulating Factor as a Therapeutic Target in Multiple Sclerosis. Neurol Ther. 2018 Dec 1. doi: 10.1007/s40120-018-0120-1. [Epub ahead of print] Review.

Berti F, Arif Z, Constantinescu CS, Gran B, 2018. Hypothermia in Multiple Sclerosis - beyond the hypothalamus? A case report and review of the literature. Case Rep Neurol Med, 2018 Mar 21;2018:2768493. doi: 10.1155/2018/2768493.

Chou IJ, Lim SY, Tanasescu R, Al-Radaideh A, Mougin OE, Tench CR, Whitehouse WP, Gowland PA, Constantinescu CS. Seven-Tesla Magnetization Transfer Imaging to Detect Multiple Sclerosis White Matter Lesions. J Neuroimaging. 2018 Mar;28(2):183-190

Constantinescu CS, Gershkovich P. Therapeutic cannabinoids in multiple sclerosis: immunomodulation revisited. Eur J Neurol. 2018 Jul;25(7):905-906

Dumitrescu L, Constantinescu CS, Tanasescu R. Recent developments in interferon-based therapies for multiple sclerosis. Expert Opin Biol Ther. 2018 Jun;18(6):665-680

Dumitrescu L, Constantinescu CS, Tanasescu R. Siponimod for the treatment of secondary progressive multiple sclerosis. Expert Opin Pharmacother. 2018 Dec 5:1-8. doi: 10.1080/14656566.2018.1551363. [Epub ahead of print]

Francis A & Constantinescu CS. Gastrointestinal influences in multiple sclerosis: Focus on the role of the microbiome. Clin Exp Neuroimmunol, 2018, 9 (Suppl. 1),(2018) 2–12 https://doi.org/10.1111/cen3.12432

R. Geraldes, O Ciccarelli, F Barkhof, et al Current role of MRI in differentiating multiple sclerosis from its imaging mimics" by Nat Rev Neurol. 2018 Apr;14(4):199-213

Goodwin, R., Lincoln, N. B., das Nair, R., & Bateman, A. (2018). Evaluation of NeuroPage as a memory aid for people with multiple sclerosis: A randomised controlled trial. Neuropsychological Rehabilitation, https://doi.org/10.1080/09602011.2018.1447973

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Publications

AMd J Hossain, E Morandi, R Tanasescu, N Frakich, M Caldano, D Onion, TA Faraj, C Erridge, and B Gran, 2018. The Soluble Form of Toll-Like Receptor 2 Is Elevated in Serum of Multiple Sclerosis Patients: A Novel Potential Disease Biomarker. Front Immunol 9:457.

Kapoor R, et al (ASCEND investigators), 2018. Effect of natalizumab on disease progression in secondary progressive multiple sclerosis (ASCEND): a phase 3, randomised, double-blind, placebo-controlled trial with an open-label extension. Lancet Neurol pii: S1474-4422(18)30069-3.

R.Middleton W.Rodgers J.Chataway et al Validating the portal population of the United Kingdom Multiple Sclerosis Register Multiple Sclerosis and Related Disorders Volume 24, August 2018, Pages 3-10

E Morandi, R Tanasescu, RE Tarlinton, D Constantin-Teodosiu, and B Gran, 2018. Do antiretroviral drugs protect from multiple sclerosis by inhibiting the expression of MS-associated retrovirus? Front Immunol 9:3092.

Proctor, B., Moghaddam, N., Evangelou, N., & das Nair, R. (2018). Telephone-supported acceptance and commitment bibliotherapy for people with multiple sclerosis and psychological distress: A pilot randomised controlled trial. Journal of Contextual Behavioral Science, 9, 103-109. ISSN 2212-1447

Samaraweera APR, Falah Y, Pitiot A, Dineen RA, Morgan PS, Evangelou N. The MRI central vein marker; differentiating PPMS from RRMS and ischemic SVD. Neurol Neuroimmunol Neuroinflamm. 2018 Sep 26;5(6):e496

Tallantyre EC, Whittam DH, Jolles S, Paling D, Constantinescu C, Robertson NP, Jacob A (Correction to:) Secondary antibody deficiency: a complication of anti-CD20 therapy for neuroinflammation.. J Neurol. 2018 May;265(5):1123. doi: 10.1007/s00415-018-8833-8.

Tanasescu R, Constantinescu CS, Tench CR, Manouchehrinia A. Smoking cessation and the reduction of disability progression in Multiple Sclerosis: a cohort study. Nicotine Tob Res. 2018 Apr 2;20(5):589-595

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Publications

2017

Barker, A., Lincoln, N. B., Hunt, N., & das Nair, R. (2017). Social Identity in People with Multiple Sclerosis: An Examination of Family Identity and Mood. International Journal of MS Care, DOI: 10.7224/1537-2073.2016-074.

Bhopale MK, Hilliard B, Constantinescu CS, Phillips SM, Rostami A. DAB389IL-2 recombinant fusion toxin effect on lymphocyte- and macrophage-producing cytokine subpopulation cells in experimentally induced demyelinating disease in mice. Immunopharmacol Immunotoxicol. 2017 Dec;39(6):318-329. doi: 10.1080/08923973.2017.1369099. Epub 2017 Sep 20.

Cerutti C, Edwards LJ, de Vries H E, Sharrack, BM, Nalel DK, Romero, IA. (2017). MiR-126 and miR-126* regulate shear-resistant firm leukocyte adhesion to human brain endothelium. Scientific Reports 7:45284.

Crooks J, Gargaro M, Vacca C, Volpi C, Pirro M, Scalisi G, Turco A, Puccetti P, Rostami AM, Gran B, Fallarino F. Generation of protective immune environment by a CpG type A oligonucleotide in murine models of Multiple Sclerosis. Mediators Inflamm, 2017:1380615. doi: 10.1155/2017/1380615

Klein, O., Drummond, A., Mhizha-Murira, J., Mansford, L., & das-Nair, R. (2017). Effectiveness of cognitive rehabilitation for people with multiple sclerosis: A meta-synthesis of patient erspectives. Neuropsychological Rehabilitation. DOI:10.1080/09602011.2017.1309323

Manouchehrinia A, Tanasescu R, Kareem H, Jerca OP, Jabeen F, Shafei R, Breuer J, Neal K, Irving W, Constantinescu CS. Prevalence of a history of prior varicella/herpes zoster infection in multiple sclerosis. J Neurovirol. 2017 Dec;23(6):839-844

Mhizha-Murira, J., Drummond, A., Klein, O., & das Nair, R. (2017). Reporting interventions in trials evaluating cognitive rehabilitation in people with Multiple Sclerosis: A systematic review. Clinical Rehabilitation. doi: 10.1177/0269215517722583.

E Morandi, R Tarlinton, R Tanasescu, and B Gran, 2017. Human Endogenous Retroviruses and Multiple Sclerosis: Causation, Association or After-Effect? Mult Scler J 23(8):1050-1055.

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Publications

Morandi E, Jagessar SA, 't Hart B, Gran B, 2017. EBV infection empowers human B cells for autoimmunity – Role of autophagy and relevance to multiple sclerosis. J Immunol, 199:435-448. doi: 10.4049/jimmunol.1700178

Morandi E, Tanasescu R, Tarlinton RE, Constantinescu CS, Zhang W, Tench C, Gran B, 2017. The association between human endogenous retroviruses and multiple sclerosis: a systematic review and meta-analysis. PLoS One, 12(2):e0172415.

Proctor, B., Moghaddam, & das Nair, R. (2017). Telephone-psychotherapy in Multiple Sclerosis: A systematic review and meta-analysis. Rehabilitation Psychology. DOI: 10.1037/rep0000182

Samaraweera APR, Clarke MA, Whitehead A, Falah Y, Driver ID, Dineen RA, Morgan PS, Evangelou N. The central vein sign: Present in MS irrespective of the MRI scanner or T2* sequence at 3T. J Neuroimaging. 2017 Jan;27(1):114-121

Tanasescu R, Midgley A, Robins RA, Constantinescu CS. Decreased Interferon-β induced STAT-4 activation in immune cells and clinical outcome in MS. Acta Neurol Scand 2017 Sep;136(3):233-238

Zgair A, Lee JB, Wong JCM, Taha DA, Aram J, Di Virgilio D, McArthur JW, Cheng YK, Hennig IM, Barrett DA, Fischer PM, Constantinescu CS, Gershkovich P. Oral administration of cannabis with lipids leads to high levels of cannabinoids in the intestinal lymphatic system and prominent immunomodulation. Sci Rep. 2017 Nov 6;7(1):14542. doi: 10.1038/s41598-017-15026-z.

Zhang Y, Li X, Ciric B, Ma CG, Gran B, Rostami A, Zhang GX, 2017. Effect of Fingolimod on Neural Stem Cells: A Novel Mechanism and Broadened Application for Neural Repair. Mol Ther 25:401-415.

Nottingham Multiple Sclerosis Research Group

Publications

2016

't Hart BA, Kap YS, Morandi E, Laman JD, Gran B, 2016. EBV Infection and Multiple Sclerosis: Lessons from a Marmoset Model. Trends Mol Med S1471-4914(16)30149-6.

Chou IJ, Wang HS, Whitehouse WP, Constantinescu CS. Paediatric Multiple Sclerosis: Update on Diagnostic Criteria, Imaging, Histopathology and Treatment Choices. 2016 Curr Neurol Neurosci Rep Jul;16(7):68. doi: 10.1007/s11910-016-0663-4.

Coclitu C, Constantinescu CS, Tanasescu R. Curr Neurol Neurosci Rep. 2016 Jul;16(7):68. The future of multiple sclerosis treatments. Expert Rev Neurother. 2016 Dec;16(12):1341-1356.

Constantinescu SE, Constantinescu CS. Laquinimod (ABR-215062) for the treatment of relapsing multiple sclerosis. Expert Rev Clin Pharmacol. 2016 Jan;9(1):49-57. doi: 10.1586/17512433.2016.1108189. Epub 2015 Nov 4.

Cronin MJ, Wharton S, Al-Radaideh A, Constantinescu C, Evangelou N, Bowtell R, Gowland PA. A comparison of phase imaging and quantitative susceptibility mapping in the imaging of multiple sclerosis lesions at ultrahigh field. MAGMA. 2016 Jun;29(3):543-57.

das Nair R, Martin KJ, Lincoln NB. (2016). Memory rehabilitation for people with multiple sclerosis. Cochrane Database of Systematic Reviews, Issue 3. Art. No.: CD008754. DOI: 10.1002/14651858.CD008754.pub3.

das Nair, R., Cogger, H., Worthington, E., & Lincoln, N.B. (2016). Cognitive rehabilitation for memory deficits after stroke (An Updated Review). Stroke. DOI: 0.1161/STROKEAHA.116.015377

das Nair, R., Cogger, H., Worthington, E., & Lincoln, N.B. (2016). Cognitive rehabilitation for memory deficits after stroke. Cochrane Database of Systematic Reviews. Issue 9. Art. No.: CD002293. DOI: 10.1002/14651858.CD002293.pub3.

Fallarino F, Gargaro M, Mondanell G, Downer EJ, Hossain MJ, Gran B, 2016. Delineating the Role of Toll-Like Receptors in the Neuro-inflammation Model EAE. Methods Mol Biol. 2016; 1390:383-411.

Harrison, A., das Nair, R., & Moss-Morris, R. (2016). Operationalising cognitive fatigability in Multiple Sclerosis: A Gordian knot that can be cut? Multiple Sclerosis Journal. DOI: 10.1177/1352458516681862

Publications

Hossain MJ, Tanasescu R, Gran B, 2016. Innate immune regulation of autoimmunity in multiple sclerosis: Focus on the role of Toll-like receptor 2. J Neuroimmunol S0165-5728(16)30448-9.

Jagessar SA, Holtman IR, Hofman S, Morandi E, Heijmans N, Laman JD, Gran B, Faber BW, van Kasteren SI, Eggen BJ, 't Hart BA, 2016. Lymphocryptovirus Infection of Nonhuman Primate B Cells Converts Destructive into Productive Processing of the Pathogenic CD8 T Cell Epitope in Myelin Oligodendrocyte Glycoprotein. J Immunol 197:1074-88.

X Li, Y Zhang, Y Yan, B Ciric, CG Ma, B Gran, M Curtis, AM Rostami, and Guang-Xian Zhang, 2016. Neural Stem Cells Engineered to Express Three Therapeutic Factors Mediate Recovery from Chronic Stage CNS Autoimmunity. Mol Ther doi: 10.1038/mt.2016.104. PMID: 27203442

Manouchehrinia A, Tanasescu R, Tench CR, Constantinescu CS. Mortality in multiple sclerosis: meta-analysis of standardised mortality ratios. J Neurol Neurosurg Psychiatry. 2016 Mar;87(3):324-31 pii: jnnp-2015-310361. doi: 10.1136/jnnp-2015-310361.

Mougin O, Abdel-Fahim R, Dineen R, Pitiot A, Evangelou N, Gowland P. Imaging gray matter with concomitant null point imaging from the phase sensitive inversion recovery sequence. Magn Reson Med. 2016 Nov;76(5):1512-1516

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Traboulsee AL, Cornelisse P, Sandberg-Wollheim M, Uitdehaag BMJ, Kappos L, Jongen PJ, Constantinescu CS, Verdun di Cantogno E, Li, DKB. Prognostic factors for long-term outcomes in relapsing remitting multiple sclerosis. Mult Scler J –Exp Transl Clin 2016 2: 1-9.

Tench CR, Tanasescu R, Cottam WJ, Constantinescu CS, Auer DP. Coordinate based meta-analysis does not show grey matter atrophy in narcolepsy. Neurosci Biobehav Rev. 2016 Nov 5. pii: S0149-7634(16)30383-9 (letter)

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Publications

2015

''t Hart B, Van Kooyk Y, Geurts JG, Gran B, 2015. The non-human primate autoimmune encephalomyelitis model; a bridge between mouse and man. Ann Clin Transl Neurol 2:581-93.

Al-Radaideh A, Mougin OE, Lim SY, Chou IJ, Constantinescu CS, Gowland P. Histogram analysis of quantitative T1 and MT maps from ultrahigh field MRI in clinically isolated syndrome and relapsing-remitting multiple sclerosis. NMR Biomed. 2015 Nov;28(11):1374-82.

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das Nair, R., Kontou, E., Smale, K., Barker, A., & Lincoln, N.B. (2015). Comparing individual and group intervention for psychological adjustment in people with multiple sclerosis: A feasibility randomised controlled trial. Clinical Rehabilitation. DOI: 10.1177/0269215515616446.

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Hossain MJ, Tanasescu R, Gran B, 2015. TLR2 – an innate immune checkpoint in multiple sclerosis. Oncotarget 6:35131-2. PMID 26459385

Jean-Gilles L, Braitch M, Latif ML, Aram J, Fahey A, Edwards L, Robins RA, Tanasescu R, Tighe P, Showe L, Gran B, Alexander S, Chapman V, Kendall D, Constantinescu C, 2015. Effects of pro-inflammatory cytokines on cannabinoid CB1 and CB2 receptors in immune cells. Acta Physiol 214:63-74; PMID: 25690155

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