

# Seminar Day 2018

### Program Book



17 AUGUST 2018 - MELBOURNE

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### Welcome to the ABSS Seminar Day 2018



Dear colleagues and friends,

On behalf of the organising committee, it is my pleasure to welcome you to the inaugural Australasian Brain Stimulation Society seminar day, as we take this opportunity to celebrate the launch of the newly formed Society.

The Society was established with the purpose of promoting excellence in scientific research and clinical practice using brain stimulation, in order to advance our understanding of the brain and improve wellbeing for people with brain related impairment.

I'd like to thank my colleagues, the founding members of the Executive Committee for their energy and enthusiasm to date in not only setting up this important initiative, but also for organising this inaugural meeting. I'd also like to thank our founding sponsors for their financial backing and confidence in the goals that we have set out to achieve as a society.

Today, we are pleased to welcome two outstanding international keynote speakers, who have both contributed significantly to important basic and clinical areas in our field and who will, I expect, help to shape some interesting conversations throughout the day.

The running of this seminar day was one of the key aims of the Society in our first year and the Executive Committee thanks you for your support. We look forward to working with all of our members in the future as we plan meetings, training opportunities, and foster communication between members of the Society.

We very much look forward to your participation today, and hope you have an enjoyable and rewarding day.

**Professor Mike Ridding** 

President

Australasian Brain Stimulation Society

## ABSS 2018 Committee



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**Professor Michael C Ridding** University of Adelaide



Vice- President **Dr Ann-Maree Vallence** Murdoch University



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Committee Member

Professor Paul Fitzgerald Epworth Healthcare & Monash University



Committee Member **Professor Winston Byblow** University of Auckland



Committee Member

**Professor Colleen Loo** University of New South Wales



Committee Member **Dr Martin Sale** The University of Queensland

### General information

#### **Australian Brain Stimulation Society**

The Australasian Brain Stimulation Society (ABSS) was founded in 2018. The ABSS is made up of a diverse group of researchers, scientists and clinicians from across Australasia. Our goal is to promote excellence in scientific research and clinical practice using brain stimulation, in order to advance our understanding of the brain and improve wellbeing for people with psychiatric or neurological illness.

#### The purposes of ABSS are to:

- Promote the understanding and use of brain stimulation in scientific research and clinical practice.
- Foster communication and collaboration between research groups and clinical groups across Australasia who use brain stimulation.
- Support students, early/mid-career researchers, and clinicians who use brain stimulation.
- Provide opportunities for high quality education and training of members.
- Convene regular meetings of members and facilitate workshops on the use of brain stimulation.

ABSS is committed to ensuring equitable participation that is representative of the diversity of our field across all its activities.

#### **Registration Desk**

The Registration Desk is located at the entrance of the Epworth Auditorum and will be open for registration from 8:00am to 9:30am.

#### Name Badges

Delegates are asked to wear their name badges at all times during the seminar day.

#### **Program Changes**

Whilst we will try to minimise any changes to the program, there are sometimes circumstances beyond our control. Any changes to the program will be made available at the registration desk. Chairpersons will also announce any changes in sessions.

#### Catering

Morning tea, lunch and afternoon tea will be served in the foyer area.

#### **Mobile Phones**

We appreciate your cooperation in ensuring that your mobile phone is switched to silent as a courtesy to speakers and other delegates. We do encourage you to tweet about the conference using #ABSS2018

### Getting to the venue

#### Epworth Auditorium

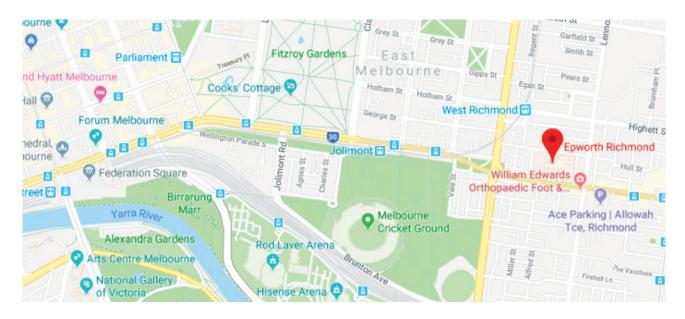
Epworth Hospital - Level 2, 89 Bridge Road, Richmond 3121

Epworth Richmond is only 15 minutes from the city center and easily accessible via public transport

- Trams: If you are coming to Epworth Richmond from the city by tram catch tram 48 towards North Balwyn from Collins Street or tram 75 towards East Burwood from Flinders Street and get off at tram stop number 15.
- Trains: By train the closest station to Epworth Richmond is West Richmond station which is on the South Morang and Hurstbridge Lines. Richmond station on Swan Street is a 15 minute walk away.

For further information regarding train, tram & bus information & timetables visit ptv.vic.gov.au

### Conference venue



#### **Epworth Auditorium**

Level 2, Epworth Hospital Richmond 89 Bridge Road, Richmond 3121

#### Visit google map

Epworth Richmond is only 15 minutes from the city center and easily accessible via public transport

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### Sponsors

We would like to acknowledge the foundation sponsors of ABSS









MONASH MEDICINE, NURSING AND HEALTH SCIENCES

# Keynote speaker

### Prof Sarah H Lisanby

National Institutes of Mental Health



### Biography

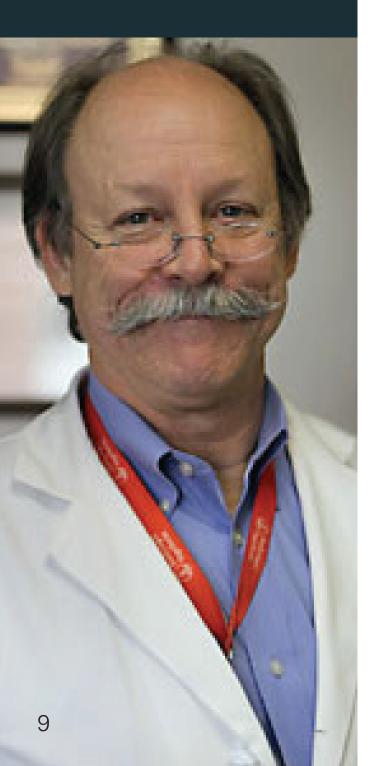
Dr. Lisanby is an internationally recognized expert in the field of brain stimulation. Her work is translational, spanning nonhuman primates, healthy humans, and clinical populations. JP Gibbons Endowed Professor with Tenure and former Department Chair of the Duke Department of Psychiatry, she founded and directed the Duke Brain Stimulation and Neurophysiology Division that encompasses interdisciplinary research labs spanning technology development, preclinical modeling, translational neuroscience, clinical trials, and clinical application. Prior to being recruited to Duke as Department Chair, Dr. Lisanby founded and directed the Columbia Division of Brain Stimulation, where she was Professor of Psychiatry. Dr. Lisanby been Pl on a series of NIH and DARPA funded studies on the development of novel neuromodulation technologies, including studies on the rational design of magnetic and electrical seizure therapies. Her team pioneered magnetic seizure therapy (MST) as a novel depression treatment from the stages of animal testing, first in human, and now international clinical trials. An experienced NIH-funded researcher, she has been PI of a series of R01 and U01 mechanisms involving transcranial magnetic stimulation (TMS) and other devices. Dr. Lisanby was PI of the series of studies that established the fMRI-guided TMS during working memory training to improve working memory performance in healthy volunteers, and to remediate working memory deficits following sleep deprivation. This paradigm has been extended to mitigate the effects of age-related decline in working memory. In October 2015, she took a leave of absence from Duke to serve as Director of Translational Research at NIMH. where she founded and directs the Neuromodulation Unit in the Experimental Therapeutics Branch in the NIMH Intramural Research Program. The Neuromodulation Unit specializes in the use of noninvasive neuromodulation tools to measure and manipulate neuroplasticity to improve human health. Dr. Lisanby co-led and presently serves on the NIH BRAIN Initiative Team on large-scale recording and modulation devices.

### Session 1 9:30 am - 10.30 am

# Keynote speaker

### Prof Mark George

Medical University of South Carolina



#### Biography

Trained as both a psychiatrist and neurologist, Mark George, M.D., always has had a primary interest in studying emotion in the brain. Working as both a clinician and researcher, George has been able to bring an innovative technology to the hospital called Transcranial Magnetic Stimulation or TMS, which non-invasively stimulates the brain by applying magnetic stimulation to the scalp.

George was featured in the PBS show, "NOVA scienceNOW," on his work treating depression and pain using TMS. He got involved with this technology while doing a research fellowship in London in 1989. At the time, this was the only hospital that had this machine and the idea of brain stimulation was a radical idea. He then spent four years at the National Institutes of Health (NIH) in Bethesda, Maryland, which also had advanced brain imaging and new brain stimulation methods like TMS. He performed the firstever studies of TMS for depression while at the NIH. He purchased a TMS machine after beginning his job at MUSC in 1995 and has been using the technology ever since.

This new technology not only answers questions on how the brain works, but is also used to treat patients with depression. In October 2008, almost 13 years after George began his research, TMS became an FDA-approved treatment for depression.

"There are now between five and 20 patients every day in the United States who are now free of depression, who never would have been if this technology hadn't made it to market," he said. "I just hope these technologies are nothing but stepping stones to the next generation of technologies that are even better."

Although the technology's potential still is being discovered, its success in treating depression has been one of the most rewarding successes in George's career.

"I was talking to a patient who had been struggling with depression for five years, and she just now got better with the help of TMS. I swear that is just as good as any award, even better in some ways. If you're lucky, you can get those kinds of rewards nearly every day."

### Session 2 1:20 pm - 2.20 pm

### ABSS ECR Award Winner

### Dr Bernadette Fitzgibbon

Senior Research Fellow, Monash University

#### Biography

Dr Bernadette Fitzgibbon is a Senior Research Fellow at Monash University where she holds a National Health and Medical Research Early Career Fellowship. She is the head of the Pain and Affective Neuroscience Unit within the Therapeutic Brain Stimulation division of MAPrc. She has received several awards for her research including the national 2014 Bethlehem Griffiths Research Foundation Young Investigator of the Year award, a 2014 Young Tall Poppy Science Award through the Australian Institute of Policy and Science and in 2018 was selected for the Veski inspiring women STEM side-by-side program. Bernadette is also the elected chair of Australian Brain Alliance EMCR Network and an Executive Member of the Australian Brain Alliance, an initiative of the Australian Academy of Science to bring together strategic brain research across Australia.

Bernadette's research program aims to better understand the mechanisms underpinning how pain can become chronic as well as novel therapeutics to treat persistent pain. Her work is driven by the integration of psychosocial and biological processes linked to the development and maintenance of pain which are integrated into her application of brain stimulation approaches. Her research uses a range of techniques, including Theta-Burst Stimulation (TBS), Transcranial Magnetic Stimulation (TMS), transcranial Direct Current Stimulation (tDCS), transcranial Alternating Current Stimulation (tACS), electroencephalogram (EEG), concurrent TMS-EEG, Magnetic Resonance Imaging (MRI), Electrocardiography (ECG) and Galvanic Skin Resistance (GSR).

### 11:20 am - 11.40 am



# Program and abstracts

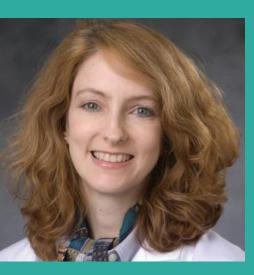
### ABSS Seminar Day / Program



9:20 am – 9:30 am	Welcome A/Prof. Kate Hoy	
9:30am – 10:30 am	International Keynote: Prof Sarah H Lisanby Chair: Prof. Paul Fitzgerald	KEYNOTE
10:30 am – 11:00 am	Brain Stimulation and Cognitive Impairment Chair: Prof. Peter Enticott	SESSION 1
	<b>Dr Mitchell Goldsworthy</b> (20 min) Daily activity compositions are associated with cortical connectivity in older adults without dementia.	
	<b>Dr Melanie Emonson</b> (5 min) Neurobiological effects of transcranial direct current stimulation in younger adults, older adults and mild cognitive impairment.	
	<b>Dr Donel Martin</b> (5 min) tDCS combined with cognitive training for improving memory in people with amnestic mild cognitive impairment (aMCI)	
11:00 am – 11:20 am	MORNING TEA	
11:20am – 11:40 am	ABSS ECR Award Presentation: Dr Bernadette Fitzgibbon Chair: Dr Ann-Maree Vallence	
11:40 am – 12:30 pm	Measuring the Neurobiological Effects of Brain Stimulation Chair: Dr Ann-Maree Vallence	SESSION 2
	<b>A/Prof Marcus Meinzer</b> (20 min) Behavioral and neural effects of high-definition transcranial direct current stimulation	
	<b>Dr Hannah Filmer</b> (20 min) Structural and neurochemical predictors of individuals' response to prefrontal electrical stimulation.	
	<b>Mana Biabani</b> (5 min) Disentangling cortical responses from sensory inputs in TMS-evoked EEG recordings	
	<b>Nicholas Bland</b> (5 min) Recovering the M/EEG from tACS artefacts: A nonlinear problem.	
12:30pm – 1:20 pm	LUNCH	



1:20 pm – 2.20pm	International Keynote: Prof Mark George кеумоте Chair: Prof. Paul Fitzgerald	
2.20 pm – 3:10pm	Optimizing Effects of Brain Stimulation SESSION 3 Chair: Prof. Winston Byblow	
	<b>Prof. Janet Taylor</b> (20 min) Paired corticospinal-motoneuronal stimulation to increase motor output	
	<b>Dr James Coxon</b> (20 min) Effect of cardiovascular exercise on the response to iTBS.	
	<b>Dr Aron Hill</b> (5 min) Exploring an 'activity-selectivity' approach to neuromodulation of the dorsolateral prefrontal cortex with HD-tDCS.	
	<b>Joshua Hendrikse</b> (5 min) Examining the effects of multi-day rTMS on neurometabolite concentrations.	
3.10pm - 3:25pm	AFTERNOON TEA	
3.25 pm – 4:20pm	Broad applications: from preclinical to clinical SESSION 4 Chair: Dr Nigel Rogasch	
	<b>A/Prof Jenny Rodger</b> (20 min) Preclinical studies of brain stimulation: can we learn from animal models?	
	<b>A/Prof Paul Sowman</b> (20 min) The dorsolateral prefrontal cortcies and suscpetibiliy to hypnosis	
	<b>Dr Gillian Clark</b> (5 min) Dissociable implicit sequence learning mechanisms revealed by continuous theta-burst stimulation.	
	<b>Bhedita Seewoo</b> (5 min) Effects of low-intensity repetitive transcranial magnetic stimulation on rodent resting-state networks: A longitudinal fMRI study.	
	<b>Rohan Puri</b> (5 min) Response expectancy has distinct effects on corticospinal excitability and interhemispheric inhibitory mechanisms: a TMS study in young and older adults.	
4:20pm – 4:40pm	ABSS Launch Prof. Michael Ridding	



Chair: Prof. Paul Fitzgerald

# Keynote presentation

9.30 am - 10:30 am

**Prof Sarah H Lisanby** National Institutes of Mental Health

### Chair: Prof. Peter Enticott

# Brain Stimulation and Cognitive Impairment

Dr Mitchell Goldsworthy Dr Melanie Emonson Dr Donel Martin



### SESSION 1 Brain Stimulation and Cognitive Impairment



### Daily activity compositions are associated with cortical connectivity in older adults without dementia

### **Dr Mitchell Goldsworthy**

University of Adelaide

Abstract: Regular engagement in physical activity (PA) may provide some protection against late life cognitive impairment and dementia. However, neither the mechanisms responsible for the beneficial effects, nor the optimal intensity or type of exercise for brain health are fully understood. To further understand these mechanisms, we characterised the relationship between daily activity patterns and cortical connectivity using a novel compositional data analysis approach and a combined transcranial magnetic stimulation (TMS) – electroencephalography (EEG) paradigm. Objectively measured 24-h activity was captured over 7 days in 28 older adults without dementia (67.6  $\pm$  7.3 years, range 53-82, 14 males). Average daily time spent in sleep, sedentary behaviour, light PA and moderate-tovigorous PA were calculated using pre-defined cut-points (COBRA software, UniSA). Connectivity of the dorsolateral prefrontal cortex was quantified for both left and right hemispheres separately by determining the number of EEG sources involved by TMS (i.e. a measure of the spread of cortical currents evoked by TMS). When accounting for age, sex and cognitive performance (Addenbrooke's Cognitive Exam Score), time spent in light PA was positively correlated with the number of detected sources (r=0.46, P=0.02). Additionally, compositional data analysis revealed more time spent in Light PA at the equal expense of sleep, sedentary behaviour and moderate-to-vigorous PA was associated with more sources, but only for TMS applied to the left hemisphere (P=0.04). These findings suggest light PA promotes cortical connectivity in older adults and provides further evidence for the cortical mechanisms underpinning the effects of regular PA on the brain.

**Biography:** Dr Goldsworthy is an NHMRC-ARC Dementia Research Development Fellow at the University of Adelaide. His research employs various non-invasive brain stimulation (TMS, tES) and recording (EEG) techniques to characterise the neurophysiological determinants of cognitive function in healthy ageing and dementia. The overarching aim of this research is to provide new mechanistic insights into the roles of brain connectivity and plasticity in supporting later life cognitive health, with the potential to inform novel strategies for dementia prevention and therapy.

### SESSION 1 Brain Stimulation and Cognitive Impairment



### Neurobiological effects of transcranial direct current stimulation in younger adults, older adults and mild cognitive impairment

#### **Dr Melanie Emonson**

Monash Alfred Psychiatry Research Centre

Abstract: Transcranial direct current stimulation (tDCS) has been investigated as a way to improve motor and cognitive functioning, with largely variable results. Currently, relatively little is known about the neurobiological effects, and possible drivers of variability, in either healthy or clinical populations. Therefore, this study aimed to characterise the neurobiological effects to tDCS in younger adults, older adults and adults with mild cognitive impairment (MCI), and their relationship to cognitive performance. 20 healthy younger adults, 20 healthy older adults and 9 individuals with MCI participated in the study. All completed neuropsychological tasks and TMS-EEG, prior to and following delivery of 20 minutes of anodal tDCS to the left dorsolateral prefrontal cortex (DLPFC). EEG was also recorded during the 2-Back working memory task. Following tDCS, younger adults demonstrated alterations in early TMS-Evoked Potentials (TEPs), namely P30 and P60. Both younger and older adults exhibited a larger task-related N250 amplitude after stimulation, with contrasting relationships to cognitive performance. The MCI group showed no change in TEPs or ERPs over time. Comparisons between the groups revealed differences in the change in amplitude of early TEP (P60) and ERP (N100) peaks between younger and older adults. Our findings indicate that tDCS was able to modulate cortical activity in younger and older healthy adults, but in varying ways. These findings suggest that varied response to tDCS may be related to factors such as age and the presence/absence of pathology, and these factors should be considered when assessing the effectiveness of tDCS in healthy and pathological aging.

**Biography:** Melanie completed her Doctor of Psychology (Clinical Neuropsychology) at Monash University in 2018 under the supervision of A/Prof Kate Hoy, Prof Paul Fitzgerald and Dr Nigel Rogasch. Her thesis investigated the neurobiological and cognitive effects of transcranial direct current stimulation in healthy aging and mild cognitive impairment. Melanie had previously completed her Honours Degree of the Bachelor of Behavioural Neuroscience at Monash University in 2011. Her research project involved the use of transcranial direct current stimulation (tDCS) in the enhancement of working memory. Melanie is the current Research Co-ordinator of the Cognitive Therapeutics Research Program and a Research Psychologist for the Therapeutic Brain Stimulation Team at the Monash Alfred Psychiatry Research Centre. Current research interests include healthy aging, Alzheimer's disease and Mild Cognitive Impairment.

### SESSION 1 Brain Stimulation and Cognitive Impairment



# tDCS combined with cognitive training for improving memory in people with amnestic mild cognitive impairment (aMCI)

#### **Dr Donel Martin**

Black Dog Institute, University of New South Wales

**Abstract:** Abstract: Currently, there is no effective intervention available for people at increased risk for dementia. While recent reviews have highlighted promising results for cognitive training (CT), randomised controlled trials (RCTs) in people diagnosed with mild cognitive impairment (MCI) have shown modest efficacy for memory improvement. Transcranial direct current stimulation (tDCS) is a safe, non-invasive technique, which can enhance cognitive functioning. This double-blind, sham-controlled, parallel group RCT examined whether tDCS + CT is more effective than CT alone for improving memory. Older participants diagnosed with amnestic MCI (aMCI) were randomised to receive either Active tDCS + CT or Sham tDCS + CT during computerised CT for 15 sessions given over a period of 5 to 6 weeks. The primary outcome measure was the California Verbal Learning Task 2nd Edition (CVLT-II). Outcomes were administered at baseline, end treatment and 3 month follow-up. Results from the completer sample (N = 59) for the primary outcome measure will be presented.

**Biography:** Donel Martin is a practicing Clinical Neuropsychologist and academic researcher based at the Black Dog Institute. He is the leader of the Neurocognition research stream of the Sydney Neurostimulation Centre (SyNC). Dr Martin is also the senior project officer for the Clinical Alliance and Research on ECT (CARE) Network, a large network of national and international hospitals which collects a common set of clinical data with an aim to improve ECT clinical practice. His research interests include investigating novel treatments for psychiatric disorders, including novel brain stimulation techniques (e.g. transcranial direct current stimulation tDCS), and using brain stimulation to enhance cognitive functioning. Dr Martin has won two internationally competitive early career researcher awards to fund research in the area of therapeutic brain stimulation. In 2014 he conducted a workshop on the cognitive enhancing effects of brain stimulation at The International Society of ECT and Neurostimulation annual meeting in New York. Since 2015 he has been a lecturer and demonstrator at SyNC's TMS and tDCS courses and a guest lecturer on non-invasive brain stimulation at postgraduate university courses.

### ABSS ECR Award Presentation

### 11.20 am - 11:40 am



### Beyond nociception: Using non-invasive neuromodulation to treat pain

#### **Dr Bernadette Fitzgibbon**

Senior Research Fellow, Monash University

The perception of pain is a complex and uniquely personal experience. Defined as an unpleasant sensory and emotional experience caused by real or potential tissue damage, pain is characterised by considerable inter-individual variability. Unsurprisingly, pain has proven to be one of the most complex medical symptoms to manage to date with the high rates of individuals living with pain now considered a "global crisis". In recent years, non-invasive neuromodulation has emerged as potential treatment tool in the management of persistent pain. However, the overall outcomes of this field have had limited clinical translation likely due to heterogeneity both within the application of neuromodulation as well as the heterogeneity of the experience of pain. In this presentation, I will discuss the experience of pain, how it is different to nociception and why one person's pain differs from another. I will then provide a brief overview of non-invasive neuromodulation for pain to date, including the presentation of a 4-week left dorsolateral prefrontal cortex rTMS randomised control trial (RCT) for fibromyalgia and preliminary findings from our subsequent Theta Burst Stimulation RCT for fibromyalgia. I will then present a proposed model using TMS-EEG to better understand what makes someone vulnerable or sensitive pain to pain, and the mechanisms that are driving this susceptibility. In doing so, develop an understanding of pain that goes beyond nociception and is able to identify the mechanisms underlying pain phenotypes. I will argue that biotypes and the individualisation of neuromodulation is fundamental to the future of this area.

11:40 am - 12:30 pm

### Chair: Dr Ann-Maree Vallence

# Measuring the Neurobiological Effects of Brain Stimulation

A/Prof Marcus Meinzer Dr Hannah Filmer Mana Biabani Nicholas Bland



Measuring the Neurobiological Effects of Brain Stimulation



### Behavioral and neural effects of high-definition transcranial direct current stimulation.

### A/Prof Marcus Meinzer

University of Queensland

Abstract: High-definition transcranial direct current stimulation (HD-tDCS) has recently received substantial attention in experimental and clinical research, because it allows for more targeted current delivery than conventional set-ups. I will (a) review recent behavioral studies from my group demonstrating regional and task specific effects of HD-tDCS across cognitive domains and (b) discuss ongoing studies that use modelling of electrical current flow and simultaneous brain imaging to investigate the neural mechanisms underlying these behavioral effects.

**Biography:** I am currently appointed as Associate Professor and Principal Research Fellow at the Centre for Clinical Research of the University of Queensland in Brisbane. My group uses behavioral, neuroimaging and brain stimulation techniques to investigate the neural mechanisms underlying language, cognition, social behavior and motor function across the lifespan. By building on these studies, my group develops novel intervention protocols to counteract age-associated functional decline and to improve treatment outcome in patients with common age-associated neurological conditions (e.g. stroke, dementia and its precursors, Parkinson's disease).

Measuring the Neurobiological Effects of Brain Stimulation



### Structural and neurochemical predictors of individuals' response to prefrontal electrical stimulation

### **Dr Hannah Filmer**

The University of Queensland

**Abstract:** There is now considerable evidence that applying a small electrical current to the cerebral cortex can have wide ranging effects on cognition and performance, and may provide substantial benefit as a treatment for conditions such as depression. However, there is variability across subjects in the extent to which stimulation modulates behaviour, providing a challenge for the development of applications. Here, we employed an individual differences approach to test if baseline concentrations of the neurochemicals GABA and glutamate, and the structure of the cortex, can predict an individual's response to brain stimulation. Using a decision-making training paradigm, we identified key correlates of variance in the response to stimulation: baseline levels of neurochemical excitability, and cortical thickness, in prefrontal cortex. This work represents a substantial step forward in developing models to predict stimulation efficacy, and provides a unique insight into how trait-based properties of the targeted cortex interact with outcomes from stimulation.

**Biography:** Dr. Filmer is a Research Fellow in the School of Psychology at The University of Queensland. She completed her PhD at the University of Exeter in 2012, followed by a postdoctoral fellowship at The University of Queensland. She has won the Most Highly-Cited Centre Publication Award from the Centre for Integrative Brain Function (2016), and the Trainee Professional Development Award from the Society for Neuroscience (2015). A focus of Dr. Filmer's research is the application of non-invasive brain stimulation techniques (predominantly transcranial direct current stimulation) to investigate cognitive training and executive functions in the prefrontal cortex. In addition to brain stimulation, her work employs imaging approaches (e.g., MRI, magnetic resonance spectroscopy), cognitive paradigms, and psychophysics. Dr. Filmer's work has appeared in Cerebral Cortex, Journal of Neuroscience, and Cortex, among other outlets, and she has a key review paper on applications of transcranial direct current stimulation for understanding brain function, published in Trends in Neurosciences (2014).

Measuring the Neurobiological Effects of Brain Stimulation



### Disentangling cortical responses from sensory inputs in TMS-evoked EEG recordings

### Mana Biabini

Monash University

Abstract: TMS evoked potentials (TEPs) appear as voltage deflections in EEG recordings and are increasingly being used to make inferences about brain dynamics following stimulations. TEPs not only reflect the direct cortical responses to the stimulation, but also sensory potentials resulting from loud acoustic clicks and scalp sensation. The present study aimed to characterize and minimize the contribution of multisensory inputs to TEPs. In total, 25 healthy participants were recruited for this study. TMS was applied over left motor cortex using two different intensities (i.e. suprathreshold and subthreshold) and waveforms (i.e. monophasic and biphasic). As a multisensory control condition, supra-threshold TMS pulses were delivered over left shoulder using both stimulation waveforms. EEG was continuously acquired using a 62-channel TMS-compatible EEG system during stimulations. Temporal and spatial correlations between the potentials evoked by motor cortex stimulations and control conditions were calculated. To decontaminate TEPs from sensory potentials, responses to control stimulations were removed from the potentials evoked by scalp stimulations using three different spatial filtering methods (i.e. ICA, SSP-SIR and linear regression). Results show that late TEP components (>80-100 ms) are highly correlated with sensory potentials evoked by TMS regardless of the intensity and type of stimulation. All three filtering methods substantially altered the topography of the late potentials, while preserving early response thought to reflect activity at the site of stimulation. The findings highlight the necessity for adopting control conditions in TMS-EEG experiments and suggest that employing spatial/temporal filters may help to separate the cortical response to TMS from sensory potentials.

**Biography:** Mana completed her Master of Science at Shiraz University of Medical Sciences in Iran, majoring in physiotherapy and human motor control. Currently, she is a third year PhD student at the Brain and Mental Health Laboratory at Monash University. Under the supervision of Dr. Nigel Rogasch and Prof. Alex Fornito, Mana is investigating brain dynamics using concurrent TMS-EEG technique. Her research particularly focuses on spatiotemporal decoding of EEG signals following stimulations in order to reveal dynamical properties of different brain regions.

Measuring the Neurobiological Effects of Brain Stimulation



### Recovering the M/EEG from tACS artefacts: A nonlinear problem

### **Nicholas Bland**

Queensland Brain Institute, University of Queensland

Abstract: Removing artefacts of rhythmic brain stimulation from the magnetoand electro-encephalogram (M/EEG) is a challenging problem because the endogenous activity we typically wish to recover shares its frequency with that of stimulation (e.g., neural entrainment). For example, transcranial alternating current stimulation (tACS)—where a low-intensity alternating current is delivered via scalp electrodes-contaminates the M/EEG with artefacts several orders of magnitude greater than the underlying endogenous oscillations. Most (if not all) existing methods that attempt to recover the M/EEG assume linear tACS artefacts (invariance over time or sensor-space). However, it has recently been shown that rhythmic changes in body impedance (and position) by heartbeat and respiration nonlinearly modulate the amplitude (Noury, Hipp, & Siegel, 2016) and phase (Noury & Siegel, 2017) of tACS artefacts. This contaminates the power spectrum symmetrically around the frequency of tACS, which may contribute to spurious "entrainment" effects. Using the simultaneous record of heartbeat and respiration, we demonstrate that these nonlinear modulations can be modelled and removed from the M/EEG. We also demonstrate the feasibility of using this approach while remaining naïve to these physiological traces, which are rarely recorded. Our approach will be useful for those wishing to remove tACS artefacts from their own M/EEG data. We thank Nima Noury, Joerg Hipp, and Markus Siegel for providing data used in their previous works.

**Biography:** Nick received his Bachelor of Psychological Science (Honours) from The University of Queensland in 2014, and is currently a postgraduate student at the Queensland Brain Institute. His thesis focusses on [1] high-density transcranial alternating current stimulation (HD-tACS) to manipulate ongoing phase relationships across cortically distributed networks, and [2] statistical approaches to removing tACS artefacts from electrophysiological recordings to study network connectivity online. Nick is due to complete his Ph.D. in January, 2019 under the supervision of Martin Sale and Jason Mattingley.



Chair: Prof. Paul Fitzgerald

# Keynote presentation

1.20 pm - 2:20 pm

**Prof Mark George** Medical University of South Carolina

### Chair: Prof. Winston Byblow

# Optimizing Effects of Brain Stimulation

Prof. Janet Taylor Dr James Coxon Dr Aron Hill Joshua Hendrikse





### Paired corticospinal-motoneuronal stimulation to increase motor output

#### **Prof Janet Taylor**

Edith Cowan University

Abstract: After incomplete spinal cord injury (SCI), impaired corticospinal drive contributes to weakness. The spinal end of corticospinal neurones are a possible target for plasticity to improve strength by amplifying residual cortical input to motoneurones. Transcranial magnetic stimuli paired with strong peripheral nerve stimuli and delivered repeatedly (paired corticospinal-motoneuronal stimulation, PCMS) can induce plasticity in the motor pathway at a spinal level. Depending on interstimulus intervals, motor responses elicited by cervicomedullary stimulation are increased or decreased, as is voluntary motor output during weak contractions (1). These changes likely reflect potentiation and depression of corticospinalmotoneuronal synapses, and facilitation from PCMS depends on NMDA receptors (2). In able-bodied people, PCMS can increase voluntary activation during brief maximal contractions of the thumb (3). This suggests that PCMS affects synapses onto high-threshold as well as low-threshold motoneurones. In people with chronic incomplete SCI, PCMS directed to hand muscles can increase evoked motor responses and improve motor performance for submaximal tasks (4). However, PCMS for the elbow flexor muscles has failed to show increases in maximal force or voluntary activation. Like many plasticity protocols in humans, responses to PCMS are variable and the sources of variability are unknown. Thus, PCMS has potential to improve motor output in people with inadequate corticospinal drive but needs to be harnessed reliably to be useful clinically.

1. Taylor & amp; Martin, (2009) J Neurosci 29:11708-11716; 2. Donges et al (2018) J Neurophysiol 119:652-661; 3. D'Amico et al (2018) J Neurophysiol 119:369-376; 4. Bunday & amp; Perez (2012) Curr Biol 22:2355-2361

**Biography:** Dr Janet Taylor is a Professor of Human Neurophysiology in the School of Medical and Health Sciences at Edith Cowan University. Her research interest is the control of human movement by the nervous system and she has over 170 peer-reviewed publications in the area. Her work focuses on how the motor pathway changes in response to activity such as fatiguing exercise, stimulation of the brain or nerves, and training or practice of motor tasks. Her aim is to better understand how the nervous system contributes to decrements in performance with muscle fatigue, and also to improvements in motor performance with practice in health and disease. Currently, she is a Senior Editor for the Journal of Physiology.



### Effect of cardiovascular exercise on the response to iTBS

#### **Dr James Coxon**

Monash University

Abstract: Regular physical exercise has widespread benefits for the human body, and is known to enhance brain structure and function. Recent studies suggest that even a single bout of cardiovascular exercise can enhance synaptic plasticity in the human cortex; however, the intensity required is currently debated. Here, we investigated the effect of exercise intensity on motor cortex synaptic plasticity following intermittent theta-burst stimulation (iTBS). We hypothesised that highintensity interval training (HIIT) exercise would have the greatest effect on the response to iTBS. Twenty healthy adults (Mage =  $35.10 \pm 13.25$  years) completed three sessions in which measures of cortical excitability and inhibition were obtained before and after a 20-minute bout of either HIIT, moderate-intensity continuous training, or rest, and then again after iTBS. Results showed that HIIT enhanced iTBS plasticity more than rest, manifest as increased cortico-motor excitability (p = .003) and intracortical facilitation (p = .03), and reduced intracortical inhibition (p = .008). In comparison, moderate-intensity cycling tended to show an intermediate effect relative to high-intensity exercise and rest. Analysis of each individual's plasticity response profile indicated that high-intensity exercise increased the likelihood of a facilitatory response to iTBS. Our results suggest that when planning exercise interventions designed to enhance neuroplasticity, HIIT exercise should be considered. Also, high-intensity exercise could be utilised in psychiatric and neurorehabilitation settings, when feasible, as a primer to improve the therapeutic potential of non-invasive brain stimulation.

**Biography:** Dr James Coxon is a Senior Lecturer in the School of Psychological Sciences at Monash University. He obtained his PhD from the University of Auckland in 2007. From 2008-2014 he held competitive postdoctoral research fellowships from the Research Foundation – Flanders (FWO), Belgium; and Aotearoa Foundation, New Zealand. His research interests include the cognitive control of action, motor learning and motor cortex neuroplasticity, and the effects of exercise on brain function. He uses non-invasive brain stimulation and recording techniques to gain insight into the neural control of movement.



# Exploring an 'activity-selectivity' approach to neuromodulation of the dorsolateral prefrontal cortex with HD-tDCS

#### **Dr Aron Hill**

Monash Alfred Psychiatry Research Centre

Abstract: Transcranial direct current stimulation (tDCS) provides a means of non-invasively inducing plasticity-related changes in neural circuits in vivo and is currently experiencing increasing use as a potential tool for modulating a variety of cognitive processes. As tDCS exerts its effects via sub-threshold alterations in ongoing neural activity, outcomes are likely to be contingent on an individual's brain state at the time of stimulation. In this presentation I will highlight key findings from a study which aimed to assess the neurophysiological and behavioural impact of applying stimulation at rest versus during active engagement in a cognitive task. High-Definition tDCS (HD-tDCS) was applied to the left dorsolateral prefrontal cortex (DLPFC) in 20 healthy participants, whilst they either remained at rest, or performed a task engaging neural circuits within the DLPFC and broader working memory (WM) network. In a third condition sham stimulation was administered during task performance. Neurophysiological changes were probed using TMS-evoked potentials (TEPs), event-related potentials (ERPs) recorded during WM tasks, and via resting-state EEG (RS-EEG). Results indicate a degree of neuromodulation of TEP amplitudes following both active stimulation conditions, with changes in ERP (P300) amplitudes observed for the 2-Back task following stimulation delivered during task performance only. However, no changes were seen on RS-EEG for any condition, nor were any group-level effects of stimulation on WM performance observed. Overall, these findings paint a complex picture of neural and behavioural responses to prefrontal stimulation in healthy subjects and highlight some important neurophysiological differences between currents applied to active versus inactive circuits.

**Biography:** Aron is a post-doctoral researcher within the Therapeutic Brain Stimulation team at the Monash Alfred Psychiatry Research Centre (MAPrc). Aron completed an Honours degree at Monash University in 2012 where he used transcranial magnetic stimulation (TMS) to explore the human mirror neuron system. He subsequently completed his PhD in 2018 at MAPrc where he used neuroimaging techniques (EEG, TMS-EEG) to investigate the neurophysiological correlates of transcranial direct current stimulation (tDCS) paradigms aimed at modulating cognitive performance. Aron's current research focusses on studying the effects of plasticity-inducing non-invasive brain stimulation protocols including tDCS, transcranial alternating current stimulation (tACS) and intermittent thetaburst stimulation (iTBS) within both healthy and clinical cohorts. Aron is particularly interested in using these techniques to better understand the neurobiological processes underlying working memory.



### Examining the effects of multi-day rTMS on neurometabolite concentrations.

#### Joshua Hendrikse

Monash University

Abstract: Repetitive transcranial magnetic stimulation (rTMS) has the capacity to induce neuroplasticity and alter the functional dynamics of brain networks. Acute administration of rTMS produces transient changes to neurotransmission in a manner resembling LTP/D-like plasticity and can modulate concentration of the neurometabolite GABA. However, the accumulative, longer-lasting effects of multiple doses of rTMS are not well understood. This study utilised a betweensubject design to examine the effects of multi-day rTMS on the concentrations of GABA and Glx (a glutamate-glutamine-glutathione composite signal) neurometabolites using magnetic resonance spectroscopy (MRS). We hypothesised that excitatory multi-day rTMS would decrease the concentration of GABA at the site of stimulation. A total of 38 (n=19) healthy, predominantly young adults (Mage= 25.8 years; SD = 9.8; 50% female) received four sessions of daily 20 Hz rTMS (2s on, 28s off) to either the left lateral parietal cortex, or the presupplementary motor area. Measures of GABA and Glx were acquired at baseline, and ~24-hrs post multi-day rTMS. We observed no enduring changes to GABA and Glx concentrations following multi-day rTMS. Whilst it is possible that homeostatic mechanisms occlude the induction of long-lasting effects within the healthy brain, multi-day rTMS may also influence brain function on a synaptic scale indiscernible to MRS, or through distinct neuroplastic mechanisms entirely.

**Biography:** Joshua Hendrikse is a PhD student of the Brain and Mental Health Research Hub at Monash University, supervised by Prof. Murat Yücel, Dr. Nigel Rogasch, and Dr. James Coxon. He completed a Bachelor of Science at the University of Melbourne, and a Graduate Diploma of Psychology at Deakin University. His research employs multi-modal neuroimaging methods to characterise the effects of aerobic exercise and repetitive transcranial magnetic stimulation on neuroplasticity.

### Chair: Dr Nigel Rogasch

# Broad applications: from preclinical to clinical

A/Prof Jenny Rodger A/Prof Paul Sowman Dr Gillian Clark Bhedita Seewoo Rohan Puri



Broad applications: from preclinical to clinical



### Preclinical studies of brain stimulation: can we learn from animal models

#### A/Prof Jenny Rodger

University of Western Australia, Perron Institute for Neurological and Translational Science

Abstract: Repetitive transcranial magnetic stimulation (rTMS), a non-invasive form of brain stimulation, is used in the clinic to promote healthy brain function. Although the mechanisms of rTMS remain unclear, many years of research and treatment in human volunteers and patients suggest it works by harnessing endogenous mechanisms of plasticity to alter connectivity and function. However, a significant challenge in the field is that outcomes are variable both within and between individuals, suggesting that treatment protocols remain suboptimal. This is underpinned by a lack of fundamental mechanistic understanding of rTMS, and very little systematic preclinical evaluation of protocols. My lab has developed custom rTMS devices for stimulation of the rodent brain in order to better understand the cellular and molecular mechanisms of rTMS. We have demonstrated frequency-dependent changes in intracellular calcium levels in neurons and glial cells during stimulation. These calcium changes are associated with changes in gene expression and in neuronal excitability, which likely contribute to the largescale circuit reorganisation and improvement in behavioural function we report in some, but not all, disease models. We have also found evidence for interactions between rTMS and endogenous brain activity that may contribute to the individual variability described in humans. Our recent work using resting state fMRI in rodents indicates analogous changes in rodents and humans following rTMS, suggesting that despite significant differences in brain size and morphology, preclinical studies have translational relevance and may play a useful role in the development of brain stimulation protocols tailored to the disorder and/or patient.

**Biography:** Dr Jennifer Rodger is Associated Professor at Experimental and Regenerative Neurosciences, School of Biological Sciences, University of Western Australia, and is affiliated with the Perron Institute for Neurological and Translational Science. She completed a BScHons in Biochemistry at the University of Bath, UK, followed by a PhD at the University Pierre et Marie Curie, France. Her research team investigates mechanisms of brain plasticity and repair, including preclinical studies of non-invasive brain stimulation in injured and abnormal brain circuits.

Dr Rodger has published over 100 peer-reviewed papers in journals including the Journal of Neuroscience and FASEB Journal and her work is funded by the NHMRC, ARC, Multiple Sclerosis WA and the Neurotrauma Research Program (WA).

Broad applications: from preclinical to clinical



### The dorsolateral prefrontal cortices and susceptibility to hypnotic suggestion

### A/Prof Paul Sowman

Macquarie University

Abstract: According to the Two-Factor theory of delusional belief (see e.g. Coltheart at al., 2011), there exists a cognitive system dedicated to the generation, evaluation, and acceptance or rejection of beliefs. Studies of the neuropsychology of delusion provide evidence that this system is neurally realized in right dorsolateral prefrontal cortex. Many specific delusional beliefs can be created in nonclinical subjects by hypnotic suggestion and it is believed that hypnosis has the effect of temporarily interfering with the operation of the belief system, which allows acceptance of the delusional suggestions. If the belief system does depend on right DLPFC, then disrupting the activity of that region of the brain by the application of repetitive transcranial magnetic stimulation (rTMS) will increase hypnotizability. Dienes and Hutton (2013) have reported such an experiment except that it was left DLPFC to which rTMS was applied. An effect on a subjective measure of hypnotizability was observed, but whether there was an effect on an objective measure could not be determined. We report two experiments. The first was an exact replication of the Dienes and Hutton experiment; here we found no effect of rTMS to left DLPFC on any hypnotic measure. Our second experiment used rTMS applied to right rather then left DLPFC. This right-sided stimulation enhanced hypnotizability (when hypnotic response was measured objectively), as predicted by our hypothesis. These results imply a role for right DLPFC in the cognitive process of belief evaluation, as is proposed in the two-factor theory of delusion. They are also consistent with a conception of the acceptance of a hypnotic suggestion as involving suspension of disbelief.

**Biography:** Paul Sowman graduated with a PhD in Physiology from the University of Adelaide in 2008. Since then he has held fellowships from both the NHMRC fellow and ARC fellow whilst in his current position within the Department of Cognitive Science at Macquarie University in Sydney. His research uses Magnetoencephalography and non-invasive brain stimulation methods to understand cognitive processes underpinning normal and abnormal cognitive development. He has a particular interest in inhibitory control processes and in disorders of inhibitory control that affect motor processes such as stuttering and Tourette syndrome.

### SESSION 4 Broad applications: from preclinical to clinical



### Dissociable implicit sequence learning mechanisms revealed by continuous theta-burst stimulation.

### **Dr Gillian Clark**

Deakin University

Abstract: The primary motor area (M1) has been implicated in visuomotor sequence learning. However, it has been suggested there are multiple neural networks that undertake visuomotor sequence learning. The role of M1 in sequence learning may be specific to learning simple sequences comprising predictable associations between adjacent movements. This study aimed to investigate the role of M1 in learning simple ("first-order conditional") and more complex ("secondorder conditional") sequences. It was hypothesised that continuous theta burst stimulation (cTBS) over M1 would result in poorer learning of the simple sequence only. Forty-eight healthy adults received cTBS to either M1 or the parietal lobe, or received sham cTBS before immediately completing two visuomotor sequence learning tasks. The tasks only differed in relation to the structure (i.e., simple versus complex) of the sequence. The group who received cTBS over M1 demonstrated significantly poorer learning of the simple sequence in comparison to the more complex sequence. The parietal lobe stimulation and sham stimulation did not affect learning of either sequence. This is the first study to show differential involvement of M1 in visuomotor sequence learning, dependent on sequence structure. The study provides new evidence that sequence learning might be supported by different networks in the brain. Specifically, M1 sequence learning appears to be important for learning simple item-to-item associations but not for more complex sequences.

**Biography:** Gillian Clark is a post-doctoral researcher in Deakin University's Cognitive Neuroscience Unit. Working with Prof Peter Enticott, she is currently investigating the development of the social brain in children, using EEG. Gillian also uses a range of techniques including tDCS and TMS to investigate neural mechanisms related to memory, language, and sensorimotor learning. Gillian completed a PhD in 2018, under supervision of A/Prof Jarrad Lum at Deakin. She investigated the relationship between implicit sequence learning and language, in children with developmental language disorder. Gillian's research interests include using cognitive neuroscience techniques to investigate the development of language, memory, and social functioning in typical and atypical populations.

Broad applications: from preclinical to clinical



### Effects of low-intensity repetitive transcranial magnetic stimulation on rodent resting-state networks: A longitudinal fMRI study.

#### Bhedita Seewoo

University of Western Australia

Abstract: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neuromodulation technique used to treat many neurological and psychiatric conditions. Even though rTMS is being used in a clinical setting and animal studies are increasingly identifying potential cellular and molecular mechanisms, little is known about how these mechanisms relate to clinical changes. This knowledge gap is further amplified by the difficulty of aligning the different experimental approaches used in human (non-invasive: functional magnetic resonance imaging (fMRI), positron emission tomography (PET), TMS) and preclinical animal studies (invasive: cellular and molecular outcomes). This project aims to bridge this gap by using non-invasive resting-state fMRI (rs-fMRI) to examine the effects of low-intensity rTMS (LI-rTMS) in rats, setting the scene for direct comparisons between rodent and human studies. rs-fMRI data were acquired at 9.4 Tesla before and after 10 min of 1 Hz LI-rTMS delivered to the right brain hemisphere of anaesthetised Sprague-Dawley rats using a circular stimulation coil. The cumulative effect of daily 10 min stimulations over a period of two weeks was examined by performing weekly imaging. Independent component analysis was used to identify the resting-state networks (RSN) and uncover the immediate and cumulative effects of stimulation. Considerable LI-rTMS-related changes were noted within the RSN immediately after stimulation. However, after 2 weeks of daily stimulations, this effect seemed to decrease as the pre-stimulation RSN was similar to the post-stimulation RSN. Our results suggest that homeostatic or compensatory changes in the brain may occur in response to repeated rTMS, reducing the impact of sequential stimulations.

Biography: Ms Bhedita Seewoo is a second year PhD student in Neuroscience in the School of Biological Sciences at The University of Western Australia (UWA) and a Graduate Research Assistant at the bioimaging facility in the Centre for Microscopy, Characterisation, and Analysis (CMCA) at UWA. Upon completion of a Bachelor's degree in Biomedical Science at Murdoch University in 2015, she was awarded the university medal for being in the top seven graduating students across all disciplines. In 2016, she completed her honours project with an upper first class outcome, following which she was awarded a prestigious Forrest Research Foundation Scholarship to continue with her PhD, building on her honours project. She uses different MRI techniques (e.g., functional MRI, Magnetic Resonance Spectroscopy, Diffusion Tensor Imaging) to study changes in brain activity, chemistry and structure in rats following low-intensity repetitive transcranial magnetic stimulation (rTMS). The aim of her project is to use noninvasive imaging methods in animal models, as used in human rTMS studies, in order to allow for direct comparison of animal and human data, which will potentially improve the efficacy of rTMS as a therapeutic tool.

Broad applications: from preclinical to clinical



Response expectancy has distinct effects on corticospinal excitability and interhemispheric inhibitory mechanisms: a TMS study in young and older adults.

#### **Rohan Puri**

University of Tasmania

**Abstract:** The current study investigated the neural mechanisms subserving our ability to utilise goal-relevant information to select and execute the appropriate response from multiple possible actions.

Young and older participants performed a choice response task; a warning stimulus (WS) indicated with 70% accuracy whether the imperative stimulus (IS) required a left- or right-hand response. Dual-coil TMS applied to M1 bilaterally investigated how corticospinal excitability (CSE) and interhemispheric inhibition (IHI) varied during movement preparation and execution. Responses were faster, and more accurate, when the WS correctly cued the response (ps<0.001). During preparation, CSE was significantly suppressed relative to baseline, however this suppression was attenuated in the hand more likely to have to respond (p=0.011). Similarly, there was a greater release of IHI in the hand more likely to have to respond (p=0.002). These results indicate preparatory changes to neural mechanisms in response to the WS that may be associated with faster execution of the expected alternative. During execution (100 ms post IS), only in young adults, greater CSE was observed in the hand that had been expected to respond, regardless of whether the IS indicated a response was subsequently executed by that hand (p=0.003). In contrast, a greater release of IHI in the hand expected to respond was observed when the IS indicated that this hand should respond, compared to when the IS indicated that this hand should not respond (p=0.007). These results show distinct neural responses to the IS, with only IHI reflecting IS-specific changes in the hand required to respond.

Biography: I completed a Bachelor of Biomedical Science (Neuroscience) from the University of Melbourne, following which, for my Honours year at The Queensland Brain Institute, I investigated the effects of spiritual practices, such as meditation, on the brain using electroencephalography. From 2012 to 2016, I worked as a research assistant in Prof. Jeffrey Summers' Human Motor Control lab (University of Tasmania) on Australian Research Council (ARC) and National Health and Medical Research Council (NHMRC) grants. Our research primarily involved utilizing transcranial magnetic stimulation to test the effects of brain stimulation techniques (transcranial direct current stimulation and theta burst stimulation) and training paradigms on cognitive and motor functioning of older adults, and whether individual differences, such as genetic factors, predicted responsiveness to these techniques. Currently, I am undertaking a PhD (Psychology) program at The University of Tasmania, under the supervision of Dr. Mark Hinder and Prof. Andrew Heathcote, during which I am investigating the neural correlates of various aspects of rapid-choice motor actions (i.e., movement preparation, execution, and stopping) and how it is influenced by cognitive processing and the healthy ageing process.



### Seminar Day 2018

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