
Separate Zoom links will be used for each day of the symposium, which will be emailed to all registered participants before the symposium.


## Welcome to the 2nd Annual ISFTD Early-Mid Career Researcher online symposium!

On behalf of the ISFTD Early–Mid Career Researcher (EMCR) Committee, it is my great pleasure to welcome you to the **2nd Annual ISFTD EMCR Online Symposium**. Since our committee was founded in 2022, we have been driven by a shared mission: to champion, connect, and empower early- and mid-career researchers within the ISFTD community. Over a short but incredibly productive period, we have launched webinars, coordinated conference meet-ups, curated quarterly newsletters, and proudly established the ISFTD EMCR Online Symposium as a dedicated platform to showcase EMCR-led science. Our committee represents the breadth of the FTD field—spanning clinical research, neuropsychology, neuroimaging, genetics, neuropathology, and translational neuroscience—and we hope this growing network continues to foster learning, collaboration, and meaningful career development for EMCRs working tirelessly to advance our understanding of FTD.

Building on the success of our inaugural symposium in 2023, we are excited to be establishing this meeting as an **annual EMCR-focused event** held early each year. Our vision is to spotlight the outstanding work being conducted by EMCRs, highlight emerging research methods and discoveries, stimulate engagement across FTD and related disorders, and catalyse new collaborations through open exchange of ideas.

This year's symposium takes place over **three days of bite-sized, accessible sessions**, designed to accommodate global time zones as inclusively as possible. Each day features a diverse mix of topics relevant to FTD and allied conditions, ensuring there truly is something for everyone. We are delighted to present an exciting program that includes internationally renowned keynote speakers alongside EMCR keynote presentations, EMCR and PhD short talks, and dynamic data blitz sessions.

We hope you find this symposium inspiring, intellectually stimulating, and rich with opportunities to connect. We also look forward to seeing these new conversations and collaborations continue as we gather again in person at the annual ISFTD conference in **Philadelphia, 8–11 October**. Thank you for being part of this vibrant and growing EMCR community.

Sincerely,
Jessica L Hazelton
ISFTD EMCR Chair
On behalf of the ISFTD EMCR committee

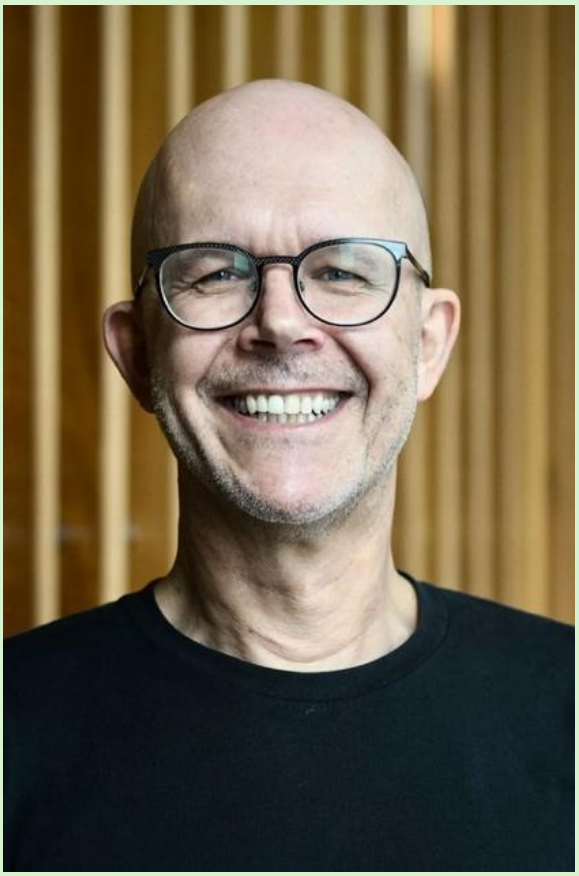
ISFTD EMCR symposium organising committee

| | | |
|---|---|---|
| Jessica L Hazelton | Celine N. Sakran | Anna Gilioli |
| Jackie Poos | Jordan Sibley | Gaia Santi |
| Indira García Cordero | Allegra Sheppard Kawles | Michèle Masson-Trottier |

ISFTD EMCR committee members:

| | | | |
|---|---|---|---|
| Jessica L Hazelton (chair) | Maxime Montembeault | Anna Gilioli | David Foxe |
| Elise Marson (past chair) | Enrico Premi | Indira García Cordero | Qihui Zhou |
| Shelley Forrest (past chair) | Lucy Russell | Gaia Santi | Oriol Dols |
| Nadia Dehghani | Ramon Landin-Romero | Adam Staffaroni | Veronica Ryan |
| Jackie Poos | Ignacio Illan-Gala | Celine N. Sakran | Daniel Ohm |
| Paolo Chibotti | Anke Dijkstra | Sylvia Josephy | Sterre De Boer |
| Chirstopher Morrow | Manizhe Eslami-Amirabadi | Adam Martersteck | Rebecca Williams |
| Emily Feneberg | Aitana Sogorb Esteve | Martina Bocchetta | |
| Hidetomo Tanaka | Maura Malpetti | Emma Rhodes | |

## Message from the ISFTD president



It is my great pleasure to welcome you to this 2nd ISFTD EMCR online symposium. The richness of the program reflects the progress that has been made in FTD research in recent years. Advances in our understanding of the clinical, genetic, and pathophysiological mechanisms of FTD are truly remarkable. Over the next three days, the symposium will cover topics that include improving and refining diagnostic criteria, genetic testing for familial forms, and sophisticated pathological, neuroimaging, digital technologies, speech analysis, and fluid biomarker tools. This work is transforming how we understand FTD and monitor disease progression. Importantly, these advances are also paving the way for therapeutic development, with clinical trials now in preparation or actively underway.

Equally inspiring is the growth of our research community over the past several years. The increasing number of early- and mid-career researchers entering the FTD field, is bringing fresh ideas, new methodologies, and tremendous energy to solving complex and pressing challenges in the FTD space. They represent the future of our discipline and will play a central role in driving earlier diagnosis, improving care, and ultimately delivering effective treatments for people living with FTD and their families.

In recent years, the global collaborations and multidisciplinary work in FTD has been astounding, and truly reflective of the capabilities of our research community. On behalf of the ISFTD board, I thank you for your commitment to this field and for being part of this collaborative, international effort. I wish you an engaging, thought-provoking, and rewarding symposium.

**Professor Olivier Piguet**
President of ISFTD
On behalf of the Board of Directors

# Program

**ISFTD EMCR**
**Annual Online Symposium**
**April 14–16, 2026 | Online**

## Day 1

| | |
|---|---|
| **00:00 - 00:05** | General Welcome |
| **00:05 - 00:10** | Welcome by Chairs |
| **00:10 - 00:40** | Keynote speaker: Eino Solje |
| **00:40 - 00:45** | *Break* |
| **00:45 - 01:00** | Short Talk 1: Olaiya A. Aro |
| **01:00 - 01:15** | Short Talk 2: Amelia Blesius |
| **01:15 - 01:30** | Short Talk 3: Gaia Chiara Santi |
| **01:30 - 01:45** | Short Talk 4: Jackie Poos |
| **01:45 - 02:00** | Short Talk 5: Charlotte Graafland |
| **02:00 - 02:05** | *Break* |
| **02:05 - 02:35** | EMCR keynote speaker: Maura Malpetti |
| **02:35 - 02:40** | Datablitz 1: Sophie Farley |
| **02:40 - 02:45** | Datablitz 2: Simona Aresta |
| **02:45 - 02:50** | Datablitz 3: Luna Nordenstrom |
| **02:50 - 02:55** | Datablitz Q&A |
| **02:55 - 03:00** | Day 1 Closing Remarks |

## Day 2

| | |
|---|---|
| **00:00 - 00:05** | Welcome by Chairs |
| **00:05 - 00:10** | *Open space for comms* |
| **00:10 - 00:40** | Keynote Speaker: Suvarna Alladi |
| **00:40 - 00:45** | *Break* |
| **00:45 - 01:00** | Short Talk 1: Sam L. Warren |
| **01:00 - 01:15** | Short Talk 2: Manisha Narasimhan |
| **01:15 - 01:30** | Short Talk 3: Jordan Sibley |
| **01:30 - 01:45** | Short talk 4: Sherry Chen |
| **01:45 - 02:00** | Short Talk 5: Sophie Matis |
| **02:00 - 02:05** | *Break* |
| **02:05 – 02:35** | EMCR keynote speaker: David Foxe |
| **02:35 - 02:40** | Datablitz 1: Julie Behenska |
| **02:40 - 02:45** | Datablitz 2: Ting Shen |
| **02:45 - 02:50** | Datablitz Q&A |
| **02:50 - 02:55** | |
| **02:55 - 03:00** | Day 2 Closing Remarks |

## Day 3

| | |
|---|---|
| **00:00 - 00:05** | Welcome by Chairs |
| **00:05 - 00:10** | *Open space for comms* |
| **00:10 - 00:40** | Keynote Speaker: Lea Grinberg |
| **00:40 - 00:45** | *Break* |
| **00:45 - 01:00** | Short Talk 1: Isis So |
| **01:00 - 01:15** | Short Talk 2: Victoria Helmly |
| **01:15 - 01:30** | Short Talk 3: Adam Martersteck |
| **01:30 - 01:45** | Short Talk 4: Linde Assendelft |
| **01:45 - 01:50** | *Break* |
| **01:50 - 02:20** | EMCR keynote speaker: Joaquin Migeot |
| **02:20 - 02:35** | Short Talk 5: Lize Jiskoot |
| **02:35 - 02:50** | Short Talk 6: Franco Ferrante |
| **02:50 - 3:05** | Short Talk 7: Arabella Bouzigues |
| **03:05 - 03:10** | Datablitz 1: Ivan Caro |
| **03:10 - 03:15** | Datablitz 2: Federico Castano |
| **03:15 - 03:20** | Datablitz 3: Loreece Haddad |
| **03:20 - 03:25** | Datablitz Q&A |
| **03:25 - 03:30** | Day 3 Closing Remarks |
| **03:30 - 03:40** | Prizes |
| **03:40 - 03:45** | Conclusion and Wrap Up |

**Program**
**Day 1: 14th April 9 am – 12 pm UTC +3**
(Please note all program times start from 00:00)

**General welcome** (00:00-00:05)
Jessica L. Hazelton (University of Sydney, Australia), Chair of the ISFTD EMCR committee

**Day welcoming by chairs** (00:05- 00:10)
Dr Jackie Poos (Erasmus MC University Medical Center, Rotterdam, The Netherlands )
Jordan Sibley (University of Sydney, Australia)

**Keynote – Associate Professor Eino Solje** (00:10- 00:40)
Title: What population-based real-world data reveal about frontotemporal dementia
Affilitation: Brain Research Unit - University of Eastern Finland, Memory Center - Kuopio University Hospital

**Short Break 1** (00:40- 00:45)

**Short talk 1 –** Olaiya A. Aro (00:45-01:00)
Title: Automated Connected Speech Classification in Prodromal Behavioural Variant Frontotemporal Dementia
Affiliation: Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Short talk 2 –** Amelia Blesius (01:00-01:15)
Title: Early changes in heart rate variability in asymptomatic FTD mutation carriers
Affiliation:University College London

**Short talk 3 –** Gaia Chiara Santi (01:15-01:30)
Title: Automated Multidimensional Analysis of Written Language in Italian non fluent and logopenic variants of Primary Progressive Aphasia
Affiliation: Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy

**Short talk 4 –** Jackie Poos (01:30-01:45)
Title: Smartphone-based Assessment Of Startle Response In Frontotemporal Dementia And Alzheimer's Disease
Affilitation: Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Short talk 5** – Charlotte Graafland (01:45-02:00)
Title: Ethically relevant features of onset prediction in genetic FTD
Affilitation: Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Short Break 2** (02:00-02:05)

**EMCR keynote – Dr Maura Malpetti** (02:05-02:35)
Title: Lighting the Path(ology): Inflammation Brain-body Cross-talk in Frontotemporal Dementia - A Multimodal Perspective
Affilitation: Department of Clinical Neurosciences, University of Cambridge, UK

**Datablitz 1 –** Sophie Farley(02:35-02:40)
Title: Investigating apathy across disease stages and genetic groups in frontotemporal dementia (FTD)
Affilitation: University College London, UK

**Datablitz 2 –** Simona Aresta (02:40-02:45)
Title: Multimodal Acoustic and Linguistic Analysis for Early Detection of Primary Progressive Aphasia using AI
Affiliation: Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy

**Datablitz 3 –** Luna Nordenstrom (02:45-02:50)
Title: Online keyboard tapping as a digital biomarker for FTD
Affilitation: University College London, UK

**Datablitz Q&A** (02:50-02:55)

**Day 1 closing remarks** (02:55-03:00)
Dr Jackie Poos, Jordan Sibley

**Day 2: 15th April UTC +5**
(Please note all program times start from 00:00)

**General welcome** (00:00-00:05)
Jessica L. Hazelton (University of Sydney, Australia)
Gaia Chiara Santi (Istituti Clinici Scientifici Maugeri IRCCS)

**Open space for comments** (00:05- 00:10)

**Keynote speaker – Professor Suvarna Alladi** (00:10- 00:40)
Title: Frontotemporal Dementia: Priorities for clinical research in the Global South
*National institute of Mental health and neurosciences, Bangalore, India*

**Short Break 1** (00:40- 00:45)

**Short talk 1 -** Dr Sam L Warren (00:45-01:00)
Title: Exploring Neuropsychiatric Symptom Heterogeneity in Frontotemporal Dementia
Affiliation: *The University of Sydney, Brain and Mind Centre, Australia*

**Short talk 2 -** Dr Manisha Narasimhan (01:00-01:15)
Title: Movement disorder in frontotemporal lobar degeneration
Affiliation: *The University of Sydney, Brain and Mind Centre, Australia*

**Short talk 3 -** Jordan Sibley (01:15-01:30)
Title: From Apathy to Action: Investigating the Neurocognitive Bases of Volitional Behaviour
Affiliation: *The University of Sydney, Brain and Mind Centre, Australia*

**Short talk 4 -** Dr Sherry Chen (01:30-01:45)
Title: Cerebellar degeneration and its integrative network contributions to language function in Chinese-speaking primary progressive aphasia
Affiliation: University of California San Francisco, USA

**Short talk 5** - Sophie Matis (01:45 - 02:00)
Title: Tau- and TDP-43-specific grey and white matter degeneration in frontotemporal lobar degeneration
Affiliation: *The University of Sydney, Brain and Mind Centre, Australia*

**Short Break 2** (02:00-02:05)

**EMCR keynote - Dr David Foxe** (02:05-02:35)
Title: Modernising FTD Assessment: Improving Brief Cognitive Measures for Better Detection, Subtyping, and Disease Monitoring
Affiliation: *University of Sydney, Brain and Mind Centre, Australia*

**Datablitz 1- Julie Behenska** (02:35-02:40)
Title: An ecological home-based assessment of apathy and anhedonia in younger-onset dementias
Affiliation: *Paris Brain Institute, France*

**Datablitz 2- Dr Ting Shen** (02:40-02:45)
Title: Transcriptomic Signatures of Cortical Atrophy in Genetic bvFTD
Affiliation: *University of Pennsylvania, USA*

**Datablitz Q&A** (02:45-02:50)

**Day 2 closing remarks** (02:50-03:00)
Jessica L. Hazelton (University of Sydney, Australia)
Gaia Chiara Santi (Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy), member of the ISFTD EMCR committee

**Day 3: 16th April 9am – 12:45pm (UTC -4)**
(Please note all program times start from 00:00)

**General welcome** (00:00 - 00:05)
Indira Garcia Cordero **(**Universidad de San Andrés, Argentina)
Celine N. Sakran **(**University of Toronto, Canada)

**Open space for comments** (00:05 - 00:10)

**Keynote – Professor Lea Grinberg** (00:10 - 00:40)
Title: Navigating an Evolving FTD Landscape: Scientific Frontiers, Collaboration, and Career Choices for Early Investigators
Affiliation: Laboratory of Medicine and Pathology, Mayo Clinic, Florida, USA

**Short Break 1** (00:40 - 00:45)

**Short talk 1 - Isis So** (00:45 - 01:00)
Title: Longitudinal neurodevelopmental and neurodegenerative outcomes in genetic FTD
Affiliation: Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

**Short talk 2 - Dr Victoria Helmly** (01:00 - 01:15)
Title: FTD and the Criminal Legal System: An Examination of Experiences and Policy
Affiliation: Georgia State University, USA

**Short talk 3 - Dr Adam Martersteck** (01:15 - 01:30)
Title: Longitudinal tau PET progression follows language network spread in primary progressive aphasia
Affiliation: University of Chicago, USA

**Short talk 4 - Linde Assendelft** (01:30 - 01:45)
Title: Validation of the Story-Based Empathy Task in Frontotemporal and Alzheimer's Dementia: Cognitive and Affective Theory of Mind
Affilitation: Erasmus MC University Medical Center, Rotterdam, The Netherlands **Short**

**Break 2** (01:45 - 01:50)

**EMCR Keynote - Dr Joaquin Migeot** (01:50 - 02:20)
Title: Social determinants and biological embedding in Frontotemporal Lobar Degeneration
Affiliation: *Universidad Adolfo Ibanez, Santiago, Chile; Global Brain Health Institute (GBHI)*

**Short talk 5** - **Dr Lize Jiskoot** (02:20 - 02:35)
Title: Cross-linguistic evaluation of the Mini Linguistic state examination (MLSE)
*Affiliation:* Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Short talk 6 - Franco Ferrante** (02:35 - 02:50)
Title: Addressing heterogeneity and the language blind spot in bvFTD through automated analysis in Latin America
Affiliation: *Universidad de San Andrés, Argentina*

**Short talk 7 - Dr Arabella Bouzigues** (02:50 - 3:05)
Title: Survival rates in genetic FTD
Affiliation: *The Douglas Research Centre, Canada*

**Datablitz 1- Ivan Caro** (03:05 - 03:10)
Title: Evaluating Digital Speech Biomarkers for Dementia in Latin America
Affiliation: *Universidad de San Andrés, Argentina*

**Datablitz 2 - Federico Castano** (03:10 - 03:15)
Title: A meta-analysis on cognitive and behavioral impairments in primary tauopathies
Affiliation: *Universidad Católica Argentina*

**Datablitz 3 - Loreece Haddad** (03:15 - 03:20)
Title: Divergent Mechanisms of Anomia in Alzheimer's Disease versus FTLD-TDP-C with Primary Progressive Aphasia
Affiliation: *Mesulam Institute for Cognitive Neurology and Alzheimer's Disease at Northwestern University*

**Datablitz Q&A** (03:20 - 03:25)

**Day 3 closing remarks** (03:25 - 03:30)
Indira Garcia Cordero**,** University of Toronto - Canada
Celine N. Sakran**,** University of Toronto - Canada

**Prizes awards** (03:30 - 03:40)
Jessica L. Hazelton (University of Sydney, Australia)

**General conclusion** (03:40 - 03:45)
Jessica L. Hazelton (University of Sydney, Australia), ISFTD EMCR committee chair

## Organising committee and Session chairs

**Dr Jackie Poos**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Bio:**
Dr. Jackie Poos is an Assistant Professor at the Alzheimercenter Erasmus MC in Rotterdam, the Netherlands. Her research is focused on digital approaches to improve early diagnosis and monitoring in young-onset dementias, with an emphasis on FTD.

**Jordan Sibley**
**The University of Sydney, Australia**

**Bio:**
Jordan Sibley is a current PhD candidate at FRONTIER, FTD research clinic in Sydney Australia. He is currently training in Clinical Neuropsychology and has a particular interest in the cognitive processes that facilitate intentional, goal-directed behaviour. By better understanding these processes, Jordan aims to provide neurocognitive insights and intervention strategies to address apathy, loss of drive, and reduced volition in frontotemporal dementias.

## Organising committee and Session chairs

**Dr Jessica L. Hazelton**
**ISFTD EMCR Chair**
**The University of Sydney, Australia**

**Bio:**
Jessica L. Hazelton completed her Psychology Bachelor's degree with honours at the University of Wollongong, Australia in 2015. She worked for several years as a research assistant at FRONTIER, the younger onset dementia clinic in Sydney, Australia, before starting her PhD in 2019 under the supervision of A/Prof Fiona Kumfor and Prof Olivier Piguet. In 2023, she moved to Buenos Aires, Argentina, to complete a neuroimaging postdoctoral fellowship under the supervision of Dr Agustín Ibañez. In 2025, she returned to The University of Sydney as a Clinical Neuroimaging Postdoctoral fellow under the supervision of A/Prof Ramon Landin-Romero. Jessica's work investigates structural and functional neuroimaging techniques to investigate allostasis, interoception, and symptom profiles in neurodegenerative diseases.

**Dr Gaia Chiara Santi**
Laboratory of Neuropsychology
Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy

**Bio:** Gaia Santi is a clinical neuropsychologist and post-doctoral researcher at the Laboratory of Neuropsychology, Maugeri, Bari (Italy). Her work focuses on the assessment and rehabilitation of language disorders in neurodegenerative conditions, with a particular emphasis on primary progressive aphasia (PPA). She employs multimodal and AI-driven approaches to characterise cognitive-linguistic deficits and develop personalised interventions, while also promoting strategies to support caregivers and improve everyday communication. She was a visiting researcher at the Memory and Aging Center at the University of California, San Francisco, where she specialised in cross-linguistic assessment of PPA. She contributed to large-scale data collection involving over 120 individuals with PPA across five language cohorts and healthy controls, strengthening her expertise in cross-linguistic assessment and the role of linguistic diversity in shaping clinical presentation.

## Organising committee and Session chairs

**Dr Indira Garcia Cordero**
*Universidad de San Andrés, Argentina*

**Bio:**
Indira García Cordero is a PhD researcher affiliated with the National Scientific and Technical Research Council (CONICET), Argentina and Universidad de San Andrés, Buenos Aires, Argentina. She is particularly interested in the pathophysiological mechanisms underlying cognitive decline and behavioral changes in frontotemporal dementia. Her work uses multimodal approaches that combine structural and functional neuroimaging, fluid biomarkers, and clinical data to study disease progression and develop tools to improve diagnosis and prognosis.

**Celine N. Sakan**
*University of Toronto, Canada*

**Bio**
Celine Sakran is a PhD candidate in Neurology at the University of Toronto, working with Prof. Carmela Tartaglia at the Tanz Centre for Research in Neurodegenerative Diseases. Her research focuses on agitation in Frontotemporal Lobar Degeneration, aiming to deepen understanding of its clinical presentation, improve clinical differentiation, and inform better treatment interventions. Alongside her research, Celine is a lead contributor to mixed-methods curriculum research on graduate professional development at the University of Toronto, and is an active member of the International Society for Frontotemporal Dementias, contributing to its communications team and early-mid career research group.

## Organising committee and Session chairs

**Dr Anna Gilioli**
San Raffaele Scientific Institute, Milan, Italy

**Bio** Anna, PhD, is a clinical neuropsychologist and post-doctoral researcher at IRCCS San Raffaele, specializing in Frontotemporal Dementia. After graduating from the University of Padua and training at the Besta Neurological Institute, she earned her PhD in Neuroscience, building upon research conducted at the University of Texas at Dallas regarding memory retrieval deficits. During her doctoral studies, she joined the Memory and Aging Center at the University of California, San Francisco, where she focused her expertise on the right-sided semantic variant of FTD. Her current work integrates psychophysiology and neuroimaging to investigate social and emotional processing in neurodegenerative diseases. Additionally, Anna is completing a specialization in Cognitive-Behavioral Psychotherapy, further refining her clinical perspective. This dual expertise allows her to apply a deeply integrated approach to understanding socio-emotional behavioral alterations in neurodegenerative conditions.

**Allegra Sheppard Kawles**
*Mesulam Center for Cognitive Neurology & Alzheimer's Disease*
*Northwestern University, Chicago, USA*

**Bio**
Allegard is a fourth-year clinical neuropsychology PhD student and her research focuses on examining the correlation between clinical features in FTD and neuropathologic changes observed in postmortem human brain tissue.

## Organising committee and Session chairs

**Dr Michèle Masson-Trottier**
University of Queensland, Australia

**Bio:** Michèle is a certified speech-language pathologist and postdoctoral research fellow working at the intersection of clinical neuroscience, neuroimaging, and speech-language pathology. Her research focuses on communication disorders associated with neurological conditions, particularly post-stroke aphasia and neurodegenerative diseases such as primary progressive aphasia. She combines behavioural approaches with neuroimaging methods to better understand therapy-induced neuroplasticity and improve evidence-based rehabilitation. Currently based at the University of Queensland, she also contributes to open science initiatives that develop accessible and reproducible neuroimaging workflows for clinical researchers and clinician-scientists.

**Keynote speaker**

**Associate Professor Eino Solje**

**Talk: Day 1 Tuesday 14th April**

**Talk title:** What population-based real-world data reveal about frontotemporal dementia

**Talk summary:** Population-based real-world data are reshaping how we understand FTD. This talk highlights novel evidence showing that sociodemographic factors and even premorbid behaviors, such as criminality, may precede clinical onset—opening new possibilities for earlier recognition of FTD.

## Bio:

Dr. Eino Solje is an Associate Professor (tenure track) of Clinical Research at the University of Eastern Finland, Director of the Brain Research Unit, and Chief Neurologist of the Memory Center at Kuopio University Hospital. His research focuses on frontotemporal dementia (FTD), with particular expertise in C9orf72-associated disease. He also leads the national DEGE-RWD early-onset dementia real-world project. He heads the Frontotemporal Lobar Degeneration and Early Onset Dementia research group and is actively involved in several international consortia, including GENFI and NIC-FTD.

## Keynote Speaker

**Professor Suvarna Alladi**

**Talk: Day 2 Wednesday 15th April**

**Talk title:** Frontotemporal Dementia: Priorities for clinical research in the Global South

**Talk summary:** Emerging research on Frontotemporal dementia has advanced our understanding of disease neurobiology and clinical manifestations across diverse contexts. This talk will focus on advances in diagnosing FTD across cultural, linguistic, educational, and ethnic contexts. Differences in clinical manifestations, complexity of genetic diagnosis and opportunities for research to fill these critical gaps will be discussed.

**Bio:**
Dr. Alladi is Professor of Neurology at the National Institute of Mental Health and Neurosciences in Bangalore, India where she coordinates a multidisciplinary service for persons living with dementia. Her main areas of interest are Cognitive Neurology and Brain Health. Dr. Alladi's team focuses on investigating the complex influence of life-course experiences, especially bilingualism, education, gender, social engagement and skills, on the development of resilience against dementia. To overcome the limited availability of diagnostic tests for dementia in diverse linguistic and educational contexts, she coordinated a country-wide effort to adapt and validate a neurocognitive battery, the ICMR Neurocognitive toolbox for different Indian languages. She leads The Karnataka Brain Health Initiative, an innovative public health project of the Government of Karnataka, which aims to provide a model of care for neurological diseases in low-resource settings and to promote brain health at the grassroot level. She is World Dementia Council Member, Chair of The Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) International Advisory Council. Dr. Alladi co-founded the Hyderabad Deccan chapter of the NGO Alzheimer's and Related Disorders Society, which provides support, and advocates for families of persons living with dementia. Dr Alladi is Executive Member of the World Federation of Neurology Speciality Group on Aphasia, Dementia and Cognitive disorders. She is committed to collaborating with cognitive neurologists and allied specialists and building a robust network and a platform for advancing clinical care, training and research in cognitive disorders in India.

**Keynote speaker**

**Professor Lea Grinberg**

**Talk: Day 3 Thursday 16th April**

**Talk title:** Navigating an Evolving FTD Landscape: Scientific Frontiers, Collaboration, and Career Choices for Early Investigators?

**Talk summary:**
Drawing on her extensive work in neuropathology, tau biology, and population-based brain banking, Dr Grinberg will share insights into emerging scientific directions in FTD, the importance of collaboration, and practical perspectives on career development for early investigators working in this rapidly evolving field.

**Bio**
Dr Gringberg is a neuropathologist (MD/PhD) with specialized training in clinical aspects of dementia and neuroanatomy. Her research focuses on neurodegenerative diseases, emphasizing their early, pre-symptomatic stages. After completing a residency in Pathology, she pursued a PhD in Neuropathology of Aging and Dementia, a research-oriented fellowship in Aging Neurology, and a post-doc in Neuroanatomy. She has a strong record of funding and publication, investigating neuropathological aspects of Alzheimer's disease, tauopathies, and other age-related dementias, with a particular emphasis on early disease mechanisms, selective vulnerability, and deep phenotyping using histological and morphological methods. She founded and co-directed a prolific population-based brain bank specializing in age-related brain conditions in São Paulo, Brazil. I co-lead the UCSF/MAC Neuropathology Core and Neurodegenerative Disease Brain Bank within the UCSF Alzheimer's Disease (AD) Research Center and lead the Neuropathological Core for the NIA-funded U01 LEADS project. Additionally, she directs a human validation core of an NINDS/U54 Center Without Walls for Tau Biology. Beyond her research, she conducts brain autopsies, provides diagnostic reports for neurodegenerative diseases, consults for extramural institutions, and actively participates in workgroups establishing diagnostic criteria for these conditions. She has a particular interest in tau deposition effects in the neuromodulatory subcortical system and has authored several papers on this topic. She is also the founder and first chair of the Neuromodulatory Subcortical Systems Professional Interest Area. In May 2025, she relocated with her whole lab to the Mayo clinics in Florida. She will also direct an initiative to modernize the Mayo's Department of Neuroscience's Brain Bank.

**EMCR keynote speaker**

**Dr Maura Malpetti**

**Talk: Day 1 Tuesday 14th April**

**Talk Title:** Lighting the path(ology): Inflammation brain-body cross-talk in frontotemporal dementia – a multimodal perspective

**Talk Summary:** This talk will highlight how multi-tracer PET, blood-based biomarkers and post-mortem pathology together "light up" inflammatory signatures across brain and body in people with frontotemporal dementia and related conditions. I will show how these multimodal markers track symptom progression, interact with proteinopathies and neurodegeneration, and help to disentangle heterogeneous disease trajectories. Finally, I will discuss how defining individual inflammatory "fingerprints" could enable smarter trial design and personalised immunomodulatory strategies for people living with frontotemporal dementia.

**Bio:**
Dr Maura Malpetti is an Assistant Research Professor and Race Against Dementia Alzheimer's Research UK Fellow at the University of Cambridge and an Emerging Leader at the UK Dementia Research Institute. She trained at Vita-Salute San Raffaele University and University of Cambridge, and as visiting researcher at UCSF and LMU Munich. Her research focuses on PET imaging and fluid biomarkers to study frontotemporal dementia, aiming to identify markers and therapeutic targets for early diagnosis and treatment. She leads the Open Network for Frontotemporal Dementia Inflammation Research (ON-FIRE) study, connecting 20+ UK centres to accelerate clinical research in FTD.

**EMCR keynote speaker**

**Dr David Foxe**

**Talk: Day 2 Wednesday 15th April**

**Talk title:** Modernising FTD assessment: improving brief cognitive measures for better detection, subtyping, and disease monitoring

**Talk Summary:** In this talk, David will make the case that brief cognitive screening remains important for dementia assessment and clinical management. He will outline how advances in statistical and machine-learning methods open up opportunities to develop smarter, interactive tools for analysing patient cognitive data. David will present his Addenbrooke's Cognitive Examination-III (ACE-III)–based tools, which i) improve detection of non-Alzheimer dementia presentations compared with healthy ageing, and ii) differentiate the primary progressive aphasia variants and typical Alzheimer's disease using item-level ACE-III performance profiles. He will conclude with a discussion of their clinical utility and limitations.

**Bio:**
David Foxe is a post-doctoral researcher with the FRONTIER Research Group at the Brain and Mind Centre, University of Sydney. He has a background in clinical neuropsychology and over 15 years of experience in dementia research. His work focuses on improving the diagnostic process and clinical experience of people with neurodegenerative conditions. David has a particular interest in primary progressive aphasia (PPA); his doctoral research examined ways to improve both diagnosis and management for individuals living with PPA.

**EMCR keynote speaker**

**Dr Joaquin Migeot**

**Talk: Day 3 Thursday 16th April**

**Talk Title:** Social determinants and biological embedding in Frontotemporal Lobar Degeneration

**Talk summary:** Social determinants of health are well established contributors to dementia risk, particularly in Alzheimer's Disease, yet their role in FTLD remains poorly understood and with mixed results. Compared with other dementias, FTLD differs in its earlier age of onset, stronger genetic contribution, and preferential involvement of socioemotional brain networks. This suggests that social adversity may influence FTLD through mechanisms distinct from those typically proposed for Alzheimer's disease. Chronic social stress may contribute to FTLD vulnerability through allostatic overload, particularly affecting interoceptive–allostatic brain systems involved in homeostatic and emotional regulation. This presentation will highlight the need to integrate social determinants, biological embedding, and network vulnerability to better understand how social adversity may shape the risk and expression of FTLD.

**Bio:** Joaquín Migeot is a researcher at the Latin American Brain Health Institute (BrainLat), Universidad Adolfo Ibáñez, where he leads research at the intersection of social neuroscience, cognitive aging, and equity in brain health across Latin America. He is also an Global Brain Health Institute (GBHI) Atlantic Fellow for Equity in Brain Health. He has authored over 25 peer-reviewed publications in leading international journals, including Nature Medicine, Nature Communications, Nature Aging, Trends in Neurosciences, and Alzheimer's & Dementia. His work integrates social determinants of health, exposome science, and neurobiological markers to understand how structural inequality and lived environments shape brain aging and dementia risk. Methodologically, he combines multimodal neuroimaging, biomarkers, and advanced statistical and machine-learning approaches to model mechanisms linking adversity, allostatic load, interoceptive dysfunction, and neurocognitive decline. He contributes to large-scale regional collaborations, including the ReDLat Consortium, where he leads the integration and analysis of social, clinical, cognitive, and neuroimaging datasets across multiple Latin American countries. His contributions span empirical, theoretical, and meta-analytic work aimed at advancing equitable brain health and reducing disparities in dementia outcomes.

**EMCR speakers Day 1**

**Olaiya A. Aro**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Bio:** Olaiya is currently pursuing her PhD in the Department of Neurology at Erasmus MC University Medical Center in Rotterdam, the Netherlands. Her research focuses on exploring digital health technologies, such as eye-tracking and automated speech analysis, to enhance early diagnosis of Frontotemporal Dementia.

## Automated Connected Speech Classification in Prodromal Behavioural Variant Frontotemporal Dementia

**Background:** Individuals with frontotemporal dementia (FTD) may experience symptoms that violate social norms and may be considered “criminal.” As a result, persons living with FTD may be more vulnerable to interactions with the criminal legal system, including arrests and incarceration. There is little data on individuals’ or their care partners’ experiences in navigating the criminal legal system and the policies that shape these experiences.
**Methods:** We conducted semi-structured interviews with care partners of individuals with FTD who have been in contact with the criminal legal system in the United States due to the accusation or conviction of a crime. We analyzed interview transcripts using a team-based thematic analysis approach. To complement the qualitative data, we are conducting a legal mapping analysis of state laws that can potentially affect how people with dementia navigate the criminal legal system.
**Results:** Interviews with care partners (n=27) revealed many challenges for this population, including navigating the complexity of the legal system. Care partners also shared the resources that they used, including calling upon their social networks for help. One of the salient themes was the challenge of determining decision-making capacity or competency for a person with FTD, including a person’s competency to stand trial. Care partners shared challenges in being trusted as a credible source of information about their loved one’s condition and navigating court-ordered competency assessments.
**Conclusion:** Care partners of people with FTD are under-resourced and unprepared to navigate the criminal legal system and are faced with barriers. The legal system generally lacks the education needed to appropriately respond to people with dementia. More awareness about dementia and increased collaboration between systems is a potential solution to these challenges. Further, it could foster greater trust in care partners as reliable sources of information. Using legal mapping methods, we are currently exploring the theme of competency through a policy analysis of state laws related to the issue of competency to stand trial. Significance Statement: Findings reveal how interactions with the criminal legal system affect care partners and people living with FTD, including how they navigate the challenges. Evidence from state laws will shed light on the policies in place that potentially affect a person with FTD who is processed through the court system in the U.S.

**EMCR speakers Day 1**

**Amelia Blesius**
University College London

**Bio:** Amelia is a PhD student at University College London working on the Genetic FTD Initiative. Her research focuses on using wearable devices and speech analysis to detect early cognitive and behavioural changes in genetic FTD.

## Early changes in heart rate variability in asymptomatic FTD mutation carriers

**Introduction:** Digital health technologies (DHTs) offer promising tools for remote symptom monitoring, contributing to the early detection of frontotemporal dementia (FTD). The Genetic FTD Initiative (GENFI) has implemented DHTs to enhance detection and develop outcome measures for clinical trials. One approach is the use of wearables to monitor heart rate variability (HRV), which reflects changes in parasympathetic nervous system function.
**Methods:** Participants attended their GENFI research visit at UCL and completed the CDR+NACC-FTLD during their clinical examination. After the visit, a Fitbit was provided for at home use. Resting HRV was measured through average root mean square of successive differences (RMSSD) per person over 28-days. Mutation carriers were classified based on CDR+NACC-FTLD stages: asymptomatic (0; n = 18, mean age = 34.8, SD = 8.5), prodromal (0.5; n = 40, mean age = 44.2, SD = 10.7), and symptomatic (≥1; n = 7, mean age = 62.9, SD = 5.7). Differences in average RMSSD between these groups and 27 mutation-negative controls (mean age = 46.2, SD = 13.0) were analysed using a linear regression model, adjusting for age.
**Results:** Asymptomatic mutation carriers had greater HRV with significantly higher RMSSD scores (mean=49.2, SD=23.7), compared to mutation negative controls (mean=30.6, SD=9.80, $p<0.01$). No significant differences were found between controls and prodromal mutation carriers (mean=32.8, SD=12.7, p=0.93) or between controls and symptomatic mutation carriers (mean=20.5, SD=2.60, p=0.36), although there was a trend to a lower RMSSD in the latter group.
**Conclusion:** Significant differences in HRV were observed at the asymptomatic stage, with carriers showing increased HRV compared to controls. This variability may reflect heightened physiological stress in response to early neurodegenerative changes. However, HRV declined at later disease stages, suggesting progressive parasympathetic dysfunction.
**Significance statement:** These findings support DHTs as potential biomarkers for tracking physiological changes across FTD stages, while facilitating remote, unsupervised monitoring before and after symptom onset. This is the first study exploring stage-specific HRV changes in FTD, highlighting the potential of DHTs as early biomarkers.

**EMCR speakers Day 1**

**Dr Gaia Chiara Santi**
Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy

**Bio:** Dr. Santi is a clinical neuropsychologist and post-doctoral researcher at the Laboratory of Neuropsychology, Maugeri, Bari (Italy). Through international collaborations, she uses multimodal and AI-driven approaches to characterise and rehabilitate language disorders in neurodegenerative conditions.

## Automated Multidimensional Analysis of Written Language in Italian non fluent and logopenic variants of Primary Progressive Aphasia

**Background:** Primary Progressive Aphasia (PPA) is characterized by impairment in both oral and written communication. Despite limited attention, written production offers a valuable means of identifying non-fluent (nfvPPA) and logopenic (lvPPA) variants, overcoming the complex phonemic–phonetic distinction in speech disorders. It may also reveal grammatical, linguistic, and graphomotor deficits less evident in speech1. This study aims to characterise written profiles in nfvPPA and lvPPA, identifying features that distinguish patients from healthy controls (HC) and between variants.
**Methods:** Forty-eight Italian PPA patients (25 nfvPPA; 23 lvPPA) and 48 matched HCs completed the SAND writing assessment2. Twenty-three features were automatically extracted using a Python pipeline and CLAN, covering graphomotor, orthographic, lexico-semantic, morpho-syntactic, and informativeness domains. Group differences were tested with Mann–Whitney U or t-tests with FDR correction. Feature selection used LASSO, and Firth's logistic regression identified features discriminating PPAvsHC, nfvPPAvsHC, lvPPAvsHC, and nfvPPAvslvPPA.
**Results:** Compared to HC, the PPA produced fewer words and utterances, increased letter spacing, abandoned words, retracing, unintelligible words, and agrammatic utterances. LASSO identified total and agrammatic utterances as significant predictors of PPA ($p<0.01$; $p<0.001$). The lvPPA group showed fewer utterances, more retracing, and agrammatic utterances than HC. LASSO selected agrammatic and total number of utterances, and morphological errors, with the latter two predicting lvPPA ($p<0.01$; $p=0.04$). The nfvPPA group showed reduced word and utterance counts, and more agrammatic and verbless utterances than HC. LASSO selected letter spacing, total, and agrammatic utterances, with agrammatism predicting nfvPPA ($p=0.01$). Compared with lvPPA, nfvPPA showed greater word spacing and reduced production of conjunctions. LASSO regression selected tremor, size, word spacing, mean length of utterances, and conjunctions, but none significantly contributed to variant differentiation.
**Conclusions:** This study characterized the written profiles of Italian individuals with PPA, revealing the roles of graphomotor and morpho-syntactic domains in distinguishing impaired individuals and suggesting their role in differential diagnosis as well.
**Significance statement:** This approach represents the first applications of an automated, multidimensional analysis of writing in the PPA population and highlights the value of writing assessment in characterizing the language profiles of nfvPPA and lvPPA beyond speech analysis.

## EMCR speakers Day 1

**Dr Jackie Poos**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Bio:** Dr. Jackie Poos is an Assistant Professor at the Alzheimercenter Erasmus MC in Rotterdam, the Netherlands. Her research is focused on digital approaches to improve early diagnosis and monitoring in young-onset dementias, with an emphasis on FTD.

### Smartphone-based Assessment Of Startle Response In Frontotemporal Dementia And Alzheimer's Disease

**Background:** Prepulse inhibition (PPI) refers to the attenuation of the startle reflex to an intense stimulus when preceded by a non-startling prepulse. Deficits in PPI have been documented in people with Alzheimer's disease (AD) and frontotemporal dementia (FTD). However, this evidence is based on a limited number of studies due to the costs and laboratory-based nature of traditional PPI assessment methods. To address these limitations and extend research to presymptomatic populations, this study evaluates whether the eye blink component of the startle reflex, quantified via smartphone video and computer vision, can differentiate people with dementia, presymptomatic FTD mutation carriers, and cognitively unimpaired people.
**Methods:** A total of 15 people with dementia (8 primary progressive aphasia, 4 with AD, 3 with behavioural variant FTD), 15 presymptomatic FTD mutation carriers, and 7 control participants were tested. Participants watched a 20-minute audio normalised video while eyelid startle responses to intermittent startle pulses were automatically recorded. The peak amplitudes of eyelid startle responses were compared between groups using Kruskal-Wallis tests and post hoc comparisons. Participants were also classified as responders or non-responders to the startle stimulus.
**Results:** The amplitude of startle responses to the startling stimulus without a prepulse differed significantly between groups ($H=7.6$, $p=0.02$), with post hoc tests indicating a substantial difference between people with dementia and control participants ($p=0.02$). Mutation carriers did not differ from people with dementia ($p=0.28$) or control participants ($p=0.29$). Non responders to the startle stimulus were predominantly people with dementia ($n=7$), followed by mutation carriers ($n=6$) and one control participant ($n=1$). Although a visual trend suggested differences between groups in PPI, the difference did not reach significance ($H=2.7$, $p=0.27$).
**Conclusion:** Our preliminary results suggest that a smartphone-based application for measuring eyelid startle response in a PPI paradigm can distinguish people with AD and FTD from control participants. This paradigm is the first demonstration of the potential to assess sensorimotor reactivity remotely in dementia, which may facilitate research into oculomotor changes associated with dementia progression. The next step is to increase sample sizes (~30 per group) to shed more light on sensorimotor changes in presymptomatic FTD mutation carriers.

**EMCR speakers Day 1**

**Charlotte Graafland**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

**Bio:** Charlotte Graafland is a PhD student in medical ethics at Erasmus MC in Rotterdam, the Netherlands, working on ethics of onset prediction in genetic FTD.

## Ethically relevant features of onset prediction in genetic FTD

**Background**
Recent research has shown that biomarkers such as neurofilament light chain and thalamic volume are predictive of FTD symptom onset in persons with a pathogenic FTD variant in the next few years. “Onset-predictive biomarker tests” (OPBTs) could be used to recruit at-risk individuals who are close to onset for preventive clinical trials, which would involve communication of OPBT results to potential participants. This raises ethical issues, as a prediction of onset in the next few years could cause psychological harm. Yet it could also provide personal utility. This study aims to identify ethically relevant aspects of OPBTs that may help researchers and clinicians understand and anticipate the impact of emerging OPBTs on individuals at risk of genetic FTD.

**Methods**
We conducted a comparative analysis of ethically relevant aspects of OPBTs in FTD and other autosomal dominant neurodegenerative diseases (Huntington’s disease and spinocerebellar ataxia), drawing on existing literature and our previous interview studies on OPBTs with Dutch and American individuals with a (50% risk of a) pathogenic FTD variant.

**Results**
We developed a framework of ethically relevant features that may influence the value and impact of OPBTs; features of the disease, the onset-predictive test, the individual and the context. For current OPBTs in genetic FTD, the most important features are the lack of treatment options, emerging opportunities to participate in clinical trials (for some genetic variants), the limited positive predictive value of onset predictions, the lack of legal protections against (mis)use of biomarker information, the high prevalence of anosognosia in early FTD stages, and the individual’s prior knowledge of their genetic status.

**Conclusions**
Researchers planning to implement OPBTs for the purpose of clinical trial recruitment can use the framework of features as a tool to identify ways to mitigate psychological impacts of OPBT results and maximize personal value for decision-making for individuals at risk of genetic FTD, through test design and development of guidance for communication of OPBT results.

**Significance statement**
This study advances insights into ethical aspects of OPBTs in genetic FTD and aims to assist the FTD research field with ethically responsible implementation of onset prediction technologies.

**EMCR speakers Day 1**

**Sophie Farley**
University College London, UK

**Bio:** Sophie is a Research Assistant at University College London (UCL), working with the GENFI team in Professor Rohrer's lab. In her role as a Site Qualification and Liaison Coordinator, she supports the onboarding and training of GENFI sites across Europe and Canada, acts as a UCL site liaison for the Global FTD Prevention Initiative (FPI), and contributes to participant visits and clinical trial recruitment at UCLH. Her research interests focus on improving clinical rating scales in FTD, particularly to better capture behavioural and functional changes.

## Investigating apathy across disease stages and genetic groups in frontotemporal dementia (FTD)

**Introduction:** Apathy is a key symptom of frontotemporal dementia (FTD) and has a substantial impact on patients and caregivers. The brief informant-rated Dimensional Apathy Scale (b-DAS) assesses apathy severity across emotional, executive and initiation domains. However, its application in FTD remains limited, and the trajectories of apathy across disease stages and genetic subtypes remain poorly characterised.
**Methods:** We examined b-DAS scores in 515 participants from the GENFI cohort (mean age 50.3 [13.4] years; 43% male; education 15.1[3.25] years), including 184 C9orf72, 104 GRN, 53 MAPT mutation carriers, and 174 non-carriers. Mutation carriers were classified as asymptomatic (FTLD-CDR+NM=0), prodromal (0.5), or symptomatic (≥1). Cross-sectional analyses compared b-DAS total and subdomain scores across disease stages and genetic groups using linear regressions adjusted for age, sex, and education, with bootstrapping to account for non-normality. In a subset of participants (N = 353), associations between apathy (b-DAS total scores) and cognition were assessed using correlations with an executive function z-score composite derived from standardised measures (TMT-B Time, Digit Symbol, Digit Span Backwards, Stroop Ink Naming). **Results:** Apathy progressively increased across disease stages in all mutation groups. Symptomatic carriers exhibited significantly higher b-DAS total and subdomain scores ($p < .001$), and prodromal carriers also demonstrated elevated scores on b-DAS total and Initiation subdomain scores, compared with non-carriers ($p < .05$). Notably, MAPT carriers showed increased Initiation-Apathy relative to non-carriers even at the asymptomatic stage ($p = .025$). Across all genetic groups, higher total and subdomain apathy scores were associated with poorer executive function ($p < .001$), although the effect size was modest.
**Conclusions:** Apathy emerges early in genetic FTD, progressing from the prodromal phase, and is associated with executive dysfunction. These findings support the b-DAS as a sensitive tool for early detection and disease monitoring, although further analyses across longitudinal data are required.
**Significance Statement:** This study demonstrates that apathy emerges early in genetic frontotemporal dementia and progresses across disease stages, with domain-specific changes detectable even before clinical symptom onset. By applying the brief Dimensional Apathy Scale in a large GENFI cohort, these findings highlight its utility for early detection, phenotypic characterisation, and monitoring of behavioural change in FTD.

**EMCR speakers Day 1**

**Simona Aresta**
Istituti Clinici Scientifici Maugeri IRCCS, Bari, Italy

**Bio:** Simona Aresta, a bioengineer at the Laboratory of Neuropsychology at Maugeri Institute of Bari and a PhD student at the University of Advanced Study IUSS Pavia. Her work explores how artificial intelligence can be used to better understand language impairments in neurodegenerative disorders.

## Multimodal Acoustic and Linguistic Analysis for Early Detection of Primary Progressive Aphasia using AI

**Background:** Primary progressive aphasia (PPA) is characterised by progressive language impairment with distinct variants, including nonfluent/agrammatic (nfvPPA) and logopenic (lvPPA). Accurate identification is crucial for management, and digital language analysis enables more objective differentiation. This study uses Machine Learning (ML)-based digital language markers from connected speech to distinguish Italian nfvPPA from lvPPA, improving diagnostic accuracy and understanding language decline patterns.
**Methods:** In this cross-sectional study, 50 Italian patients with PPA (nfvPPA = 27; lvPPA = 23) and an equally sized group of age-, sex-, and education-matched healthy controls (HCs) completed an audio-recorded picture description task from the Screening for Aphasia in Neurodegeneration (SAND). Audio recordings were collected using Audacity, transcribed with OpenAI's Whisper, and manually quality-checked. Transcripts were subsequently analysed using Computerized Language ANalysis (CLAN) software to extract 24 linguistic features. An ML pipeline based on a Support Vector Machine (SVM) was implemented to classify PPA variants versus healthy controls (HCs) and to differentiate between PPA variants. Finally, an explainability analysis based on SHAP was performed.
**Results:** The SVM models achieved sensitivities/specificities of 96/85% for lvPPA vs HCs, 96/85% for nfvPPA vs HCs, and 85/92% for nfvPPA vs lvPPA. Explainability analysis showed that reduced speech rate and noun production, along with increased pause time, disfluencies, and agrammatic utterances, increase the probability of being classified as lvPPA. Conversely, lower articulation and speech rates, preposition use and vocabulary span, and higher disfluency increase the likelihood of being classified as nfvPPA. In differentiating PPA variants, greater articulation rate, adverbs, utterances, and morphological errors, together with reduced motor speech impairment, increase the probability of being classified as lvPPA.
**Conclusions:** This study introduces a promising digital tool for PPA identification, enabling objective and scalable assessments beyond traditional clinical settings. These findings may help address current challenges in PPA treatment development, supporting the use of sensitive outcome measures in clinical trials and personalised language assessments.
**Significance statement:** We applied natural language processing to perform ML classification on connected speech from Italian-speaking individuals with PPA. This approach, applied for the first time to the Italian PPA, identified key linguistic markers distinguishing the PPA variants.

**EMCR speakers Day 1**

**Luna Nordenstrom**
University College London, UK

**Bio:** Luna is a Research Assistant at the Dementia Research Centre, UCL, working on the Early Detection of FTD (EDoF) study, which uses digital technologies to identify and measure early signs of FTD, particularly in motor function.

## Online keyboard tapping as a digital biomarker for FTD

**Introduction:** Frontotemporal dementia (FTD) is primarily characterised by behavioural or language impairments but shows notable clinical and genetic overlap with amyotrophic lateral sclerosis (ALS), including shared genetic causes such as the C9orf72 repeat expansion. There remains a need for early and objective markers of FTD which has led to the development of digital investigations for frequent and precise assessment.
**Methods:** The online BRadykinesia Akinesia INcoordination (BRAIN) tap test, originally developed for Parkinson's disease, involves alternate tapping between two keys of a computer keyboard for 30 seconds. Output measures, computed as the mean between left and right hands, include the kinesia score (KS, number of taps) and akinesia time (AT, mean dwell time). The test was completed by 269 participants whose motor function, cognition, behaviour, language, and neuropsychiatric symptoms were assessed using the CDR® plus NACC FTLD-NM scale (0=normal, 0.5=minimally impaired, and ≥0.5=impaired). Participants included healthy controls (HC; n=157), asymptomatic (n=23) and prodromal (n=54) genetic carriers, and people with symptomatic behavioural variant FTD (bvFTD, n=19) and ALS (n=16). The aim was to investigate whether the BRAIN Tap Test could be used across the FTD–ALS spectrum to detect early changes in motor function.
**Results:** After adjustment for age, sex, and education, both mean KS and AT significantly differentiated healthy controls from symptomatic individuals with bvFTD (KS $p < 0.001$; AT $p < 0.001$) and ALS (KS $p < 0.001$; AT $p = 0.001$). Symptomatic individuals performed significantly fewer taps and exhibited significantly longer dwell times. The metrics also significantly correlated with plasma neurofilament light chain (NfL) levels (KS $p = 0.0011$; AT $p = 0.0136$).
**Conclusions:** The BRAIN Tap Test, particularly its KS and AT metrics, detected differences in motor function in symptomatic individuals with bvFTD and ALS compared to healthy controls. It also demonstrated significant correlations with other physiological and clinical markers, including plasma NfL levels.
**Significance statement:** The BRAIN Tap Test shows promise as a sensitive, digital tool to detect motor changes in both bvFTD and ALS. These findings align with observed upper limb motor deficits across the FTD-ALS spectrum and underline the value of monitoring motor function in bvFTD.

**EMCR speakers Day 2**

**Dr Sam L Warren**
*The University of Sydney, Brain and Mind Centre, Australia*

**Bio**
Sam is a postdoctoral researcher in cognitive neuroscience at the Brain and Mind Centre, the University of Sydney. He is part of the Irish Lab and Frontier research center, working under Professor Muireann Irish.

## Exploring Neuropsychiatric Symptom Heterogeneity in Frontotemporal Dementia

**Background:** Neuropsychiatric symptoms are prevalent in younger-onset neurodegenerative disorders. While there is a sizable literature focusing on key neuropsychiatric symptoms (e.g., apathy and depression), the full web of neuropsychiatric symptomatology is often poorly characterized.
**Methods:** Here, we used an unsupervised, data-driven approach to investigate neuropsychiatric symptom profiles in 898 individuals with FTD across three international dementia cohorts. A transdiagnostic approach was used comprising behavioural-variant FTD (bvFTD; n=592), progressive nonfluent aphasia (PNFA; n=129), semantic dementia (SD; n=122), and right temporal variant FTD (rtvFTD; n=55). The Neuropsychiatric Inventory (NPI) was used to determine the presence and severity of neuropsychiatric symptoms. Clustering was performed using a latent class analysis (LCA) that was fit using five-fold cross-validation, covarying for age, sex, and overall cognitive impairment.
**Results:** This LCA identified 4 distinct clusters of neuropsychiatric symptomatology using the ALLFTD dataset, centring on apathy, appetite, irritability, and disinhibition. The clusters were best separated by the probability of neuropsychiatric symptoms occurring, showing a clear grading where symptoms were most prominent in bvFTD, then SD, and then PNFA. We externally validated the LCA model using a harmonised clinical sample from the Alzheimercentrum Amsterdam (Netherlands) and FRONTIER research clinic (Australia). The resulting model showed considerable generalizability, with the same four clusters holding up across all datasets. Observed diagnostic-group differences were confirmed with post-hoc statistical analysis, such as the neuropsychiatric similarity between rtvFTD and bvFTD, not SD.
**Conclusions:** Our findings highlight the ability of LCA to uncover unique NPS profiles that can assist with diagnostic confidence in the face of FTD heterogeneity.
**Significance statement:** This study is the first of its kind to apply data-driven machine-learning methods to categorise neuropsychiatric symptoms across FTD syndromes. Such findings highlight the importance of symptom profiles and potential of machine learning for person-centred modelling in the clinic.

**EMCR speakers Day 2**

**Dr Manisha Narasimhan**
The University of Sydney, Brain and Mind Centre, Australia

**Bio**
Manisha is a Neurologist and PhD candidate at FRONTIER, The University of Sydney, Brain and Mind Centre. Manisha is interested in movement disorders in frontotemporal lobar degeneration, and the intersection between motor neuron disease and FTD.

## Movement disorder in frontotemporal lobar degeneration

**Background:** The presence of movement disorder in frontotemporal dementia (FTD) syndromes is being increasingly recognised and may cause diagnostic difficulty. Equally, the atypical parkinsonism syndromes (AP), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS), may present with cognitive and language difficulty, without the characteristic motor features described in established diagnostic criteria. The objective of this study was therefore to determine the prevalence of movement disorder on initial presentation across the spectrum of frontotemporal lobar degeneration (FTLD).
**Methods:** This was a retrospective cohort study between 2008 and 2020 conducted by the FRONTIER research clinic, the University of Sydney. Patients were included if they met diagnostic criteria for syndromes known to be associated with FTLD pathology: behavioural-variant frontotemporal dementia (bvFTD), progressive nonfluent aphasia (PNFA), semantic dementia (SD), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS). The presence of movement disorder symptoms at initial presentation was recorded. Changes in functional, behavioural and cognitive domains were documented using revised Cambridge behavioural inventory (CBI-R) subscores, total Addenbrooke's cognitive examination III (ACE III) score, and multiple cognitive assessments.
**Results:** A total of 325 patients were recruited into the study out of whom 74 (23%) patients had movement disorder (MD) at initial presentation. MD occurred in 15/150 (10%) of bvFTD, 7/45 (15.6%) of PNFA, 16/25 (64%) of PSP and 36/41 (87.8%) of CBS patients, but was not observed in patients with SD. Patients with both AP syndromes displayed cognitive, behavioural and functional impairment profiles which were similar to or worse than those in the two FTD syndromes, bvFTD and PNFA. The presence of MD had a negative effect on cognition in PNFA.
**Conclusions:** Movement disorder is an important clinical feature in FTLD related clinical presentations and links FTD and AP. Cognitive disturbances are common in AP and a proportion of patients do not have movement disorder on initial presentation.
**Significance statement:** These findings demonstrate the shared symptomatology across FTD syndromes, and PSP and CBS with regards to cognition, language and movement disorder. Identification of movement disorder and accompanying neuropsychological profiles provide a useful way to recognise FTLD clinical subtypes.

## EMCR speakers Day 2

**Jordan Sibley (01:15 - 01:30)**
*The University of Sydney, Brain and Mind Centre, Australia*

**Bio**

Jordan Sibley is a current PhD candidate at FRONTIER, FTD research clinic in Sydney Australia. He is currently training in Clinical Neuropsychology and has a particular interest in the cognitive processes that facilitate intentional, goal-directed behaviour. By better understanding these processes, Jordan aims to provide neurocognitive insights and intervention strategies to address apathy, loss of drive, and reduced volition in frontotemporal dementias.

### From Apathy to Action: Investigating the Neurocognitive Bases of Volitional Behaviour

**Background:** Behavioural apathy, marked by difficulties initiating and sustaining goal-directed behaviour, is a prominent symptom of frontotemporal dementias. However, existing clinical measures lack specificity for identifying the cognitive processes driving these deficits. This research integrates neuroimaging, cognitive testing, and a novel informant-report measure to examine the neuroanatomical and executive function foundations of behavioural apathy.
**Methods:** Participants with behavioural variant frontotemporal dementia (n = 34), semantic dementia (n = 18), Alzheimer's disease (n = 37), atypical Parkinsonism syndromes (n = 7), and healthy controls (n = 30) underwent magnetic resonance imaging and neuropsychological testing of four executive functions. A cortical thickness analysis was conducted to examine the cortical correlates of the novel measure of behavioural apathy. A subsequent neuroimaging conjunction analysis identified cortical areas showing transdiagnostic overlap between behavioural apathy and each of four executive functions, controlling for age, global cognition, and diagnosis.
**Results:** Distributed regions spanning the bilateral frontal lobes, the right temporal lobe, and the right parietal lobe were identified as cortical correlates of behavioural apathy. Analysis of transdiagnostic overlap between behavioural apathy correlates and executive functions revealed that inhibitory control was uniquely associated with the cortical network underlying behavioural apathy, showing convergence in the right anterior insula, left ventrolateral prefrontal cortex, and left medial prefrontal cortex.
**Conclusions:** Inhibitory control may represent a unique neurocognitive marker of behavioural apathy in frontotemporal dementias, with implications for understanding self-initiation, functional independence, apathy-inhibition dynamics, and behavioural accountability in clinical and forensic contexts. These results refine neurocognitive models of apathy and identify specific cortical regions as potential transdiagnostic targets for detection and intervention.
**Significance Statement:** These results provide preliminary neurocognitive evidence towards further explaining the characteristic co-occurrence of reduced inhibitory control and elevated apathy in behavioural variant frontotemporal dementia. These results carry implications for the assessment of behavioural apathy in frontotemporal dementias, for understanding its neurocognitive basis, and for the development of targeted interventions.

## EMCR speakers Day 2

**Dr Yu (Sherry) Chen**
University of California, San Francisco, USA

**Bio**
Dr. Yu (Sherry) Chen is a neurologist and cognitive neuroscientist, currently a postdoctoral scholar at the UCSF Memory and Aging Center. Her research focuses on cerebellar-cerebral network mechanisms underlying social cognition, particularly in neurodegenerative diseases such as frontotemporal dementia. Using multimodal neuroimaging and advanced network approaches, her work aims to better understand how brain systems support behavior and clinical progression.

**Cerebellar degeneration and its integrative network contributions to language function in Chinese-speaking primary progressive aphasia**

**BACKGROUND.** The cerebellum is densely interconnected with cerebral language networks and is increasingly recognized as contributing to higher-order cognitive and speech processes. However, its role in primary progressive aphasia (PPA) remains insufficiently characterized, particularly in Chinese-speaking populations. As current models of language network disruption are largely derived from Indo-European languages, brain-behavior relationships underlying features absent from these languages, such as lexical tone, remain poorly understood. To address this gap, we investigated network-level contributions of cerebellar subregions to language function in Chinese-speaking individuals with PPA.
**METHODS.** The study included 33 individuals with PPA (14 logopenic, 10 nonfluent/agrammatic, 9 semantic variants) and 31 healthy controls from the Chinese Language Assessment in PPA (CLAP) project. Five language tasks were analyzed: single-word comprehension, semantic association, sentence repetition, a tone-twister task, and tone production errors during tonal phrase repetition. Volumes of cerebellar subregions linked to social-linguistic, multiple-demand, and motor networks were extracted using a functional parcellation. Cortical volumes from language-relevant networks (control, limbic, temporoparietal, somatomotor) were included. To assess cerebellar contributions while accounting for collinearity with cortical atrophy, we applied sequential regression and partial least squares correlation (PLSC), followed by dominance analysis to quantify relative contributions.
**RESULTS.** Adding cerebellar measures significantly improved prediction of language performance beyond models including only cortical volumes and demographics. PLSC identified a dominant latent dimension explaining 89.3% of shared brain-behavior covariance. Cerebellar contributions were specific to tone production errors, with no significant covariance for semantic tasks or sentence repetition. This latent dimension showed strong loadings from right-lateralized cerebellar subregions spanning social-linguistic, multiple-demand, and motor (mouth) networks, alongside weaker cortical contributions within the phonological loop. Dominance analysis further showed that cerebellar subregions accounted for 86.8% of explained variance in tone production errors after controlling for cortical contributions.
**CONCLUSIONS.** In Chinese-speaking PPA, cerebellar degeneration and its interaction with cerebral language networks play a critical, domain-specific role in tone production, a function not captured by cortex-centric models based on non-tonal languages. These findings highlight cerebello-cerebral interactions as a key substrate of language impairment and emphasize the importance of studying linguistically diverse populations. Right cerebellar subregions may represent promising targets for future neuromodulatory and behavioral interventions.

## EMCR speakers Day 2

**Sophie Matis**
*The University of Sydney, Brain and Mind Centre, Australia*

**Bio**
Sophie Matis is a PhD candidate at the University of Sydney's Brain and Mind Centre and an NHMRC Postgraduate Scholar. Her research focuses on developing advanced neuroimaging biomarkers to characterise pathology-specific mechanisms across the frontotemporal dementia spectrum.

### Tau- and TDP-43-specific grey and white matter degeneration in frontotemporal lobar degeneration

**Background:**
Frontotemporal lobar degeneration (FTLD) is driven by distinct proteinopathies, most commonly misfolded tau (FTLD-tau) and TAR DNA-binding protein 43 (FTLD-TDP). Despite different molecular mechanisms, these pathologies often produce overlapping clinical syndromes, leading to frequent misdiagnosis and limited ability to stratify patients for clinical trials. In the absence of reliable molecular imaging markers, conventional MRI cannot distinguish underlying pathology in vivo. This study aimed to apply advanced grey and white matter imaging techniques to identify pathology-specific network degeneration patterns in FTLD.
**Methods:**
We included fifty individuals with an in vivo diagnosis of frontotemporal dementia, MRI, and confirmed post mortem pathology (FTLD-tau; n=24, FTLD-TDP; n=26), matched for age, sex, and disease duration. Grey and white matter alterations were quantified using cortical thickness analysis and fibre-specific diffusion MRI metrics. Group differences were evaluated using whole-brain voxel- and fixel-based general linear models.
**Results:**
Distinct patterns of neurodegeneration and clinicopathological correlations were identified in each group.
FTLD-tau showed predominant degeneration in motor-related networks, including the right brainstem, cerebellum, and left motor tracts. White matter changes were primarily reflected by reduced fibre density, indicating microstructural damage. Clinically, approximately 75% of these cases presented with motor syndromes.
In contrast, FTLD-TDP showed right-lateralised frontotemporal and parietal grey and white matter degeneration. White matter changes were mainly reflected by reduced fibre cross-section, consistent with macrostructural fibre loss. This group showed mixed language and motor presentations.
Behavioural syndromes occurred at similar rates in both groups (~25%).
**Conclusion:**
Although FTLD-tau and FTLD-TDP show overlapping patterns of grey and white matter degeneration, advanced structural and diffusion MRI revealed pathology-specific differences in regional distribution and the scale of white matter damage. These findings indicate that sensitive imaging measures can detect protein-specific neurodegenerative signatures within shared atrophy patterns, refining mechanistic models of FTLD and improving our ability to interrogate disease biology in vivo.
**Significant Statement:**
By identifying distinct network and fibre-level degeneration patterns across FTLD-tau and FTLD-TDP, this work demonstrates that sensitive MRI markers can capture underlying proteinopathy in vivo, strengthening mechanistic models of FTLD and supporting biologically informed patient stratification.

**EMCR speakers Day 2**

**Julie Behenska**
*Paris Brain Institute, France*

**Bio**
Julie is a joint PhD Candidate at the FrontLAB at Paris Brain Institute and Irish Lab at the University of Sydney.

## An ecological home-based assessment of apathy and anhedonia in younger-onset dementias

**Background:** Apathy (i.e., a reduction in goal-directed behaviour) and anhedonia (i.e., a decreased ability to experience and to pursue pleasure) are prominent motivational symptoms significantly undermining autonomy and quality of life. These symptoms often co-occur in people with Alzheimer's disease (AD) and behavioural variant of frontotemporal dementia (bvFTD). Currently, they are primarily assessed in clinical settings using standardised scales that fail to capture the complexity of these symptoms. There is therefore a need for validated and reliable digital markers of these symptoms from ecological settings to ensure robust disease monitoring and to inform the development of targeted interventions.
**Methods:** The ECOCAPTURE@HOME.V2 project aims to develop novel digital biomarkers of apathy and anhedonia based on everyday experience. These symptoms are studied within the dyadic ecosystem consisting of the person with dementia and their carer.
Digital biomarkers will be derived using machine learning techniques that will combine behavioural and physiological data from smartwatches with ecological momentary assessment data and targeted behavioural questionnaires. Apathy and anhedonia profiles will be characterised at the group and individual level.
We hypothesise that apathy and anhedonia can be reliably identified and tracked using ECOCAPTURE digital biomarkers. Specifically, we propose that apathy markers will exhibit momentary fluctuations contingent on context and environment, whereas anhedonia will remain relatively stable over the course of the day.
**Conclusions and significance statement:** This project will generate novel, objective behavioural indices of apathy and anhedonia that can be deployed in real-world home environments. Importantly, apathy and anhedonia are dynamic rather than static symptoms; this approach will capture their fluctuations over time, enabling a more nuanced understanding of their expression. These digital biomarkers will provide critical insights to identify optimal windows for intervention. Furthermore, this approach will support the monitoring of targeted therapeutic interventions, with the potential to enhance autonomy in people with dementia, reduce caregiver burden, and facilitate ageing in place.

**EMCR speakers Day 2**

**Dr Ting Shen**
*University of Pennsylvania, USA*

**Bio**
Dr. Ting Shen is a postdoctoral researcher at the FTD Center, University of Pennsylvania. Her work integrates multimodal neuroimaging, multi-omics data, and computational approaches to dissect disease heterogeneity in neurodegenerative disorders.

**Transcriptomic Signatures of Cortical Atrophy in Genetic bvFTD**

**Background:** Cortical atrophy is a common manifestation in behavioral variant frontotemporal degeneration (bvFTD), exhibiting spatial heterogeneity across various genetic subgroups, which may be driven by distinct biological mechanisms.
**Methods:** We employed an integrative imaging transcriptomics approach to identify both disparate and shared transcriptomic signatures associated with cortical thickness in bvFTD with C9orf72 repeat expansions or pathogenic variants in GRN or MAPT. Functional enrichment analyses were conducted on each gene list significantly associated with cortical thickness. Additionally, we mapped neurotransmitter receptor/transporter density maps to the cortical thickness maps, to uncover different correlation patterns for each genetic form. Furthermore, we examined whether the identified genes were enriched for pathology-related genes by using previously identified genes linked to TDP-43 positive neurons and genes associated with tau pathology.
**Results:** For each genetic form of bvFTD, we identified cortical thickness signatures and gene sets associated with them. The cortical thickness associated genes for GRN-bvFTD were significantly involved in neurotransmitter system and circadian entrainment. The different patterns of spatial correlations between synaptic density and cortical thinning, further confirmed the critical role of neurotransmission and synaptic signaling in shaping brain structure, especially in the GRN-bvFTD group. Furthermore, we observed significant overlap between genes linked to TDP-43 pathology and the gene sets associated with cortical thickness in C9orf72-bvFTD and GRN-bvFTD but not the MAPT-bvFTD group providing specificity for our associations. C9orf72-bvFTD and GRN-bvFTD also shared genes displaying consistent directionality, with those exhibiting either positive or negative correlations with cortical thickness in C9orf72-bvFTD showing the same direction (positive or negative) in GRN-bvFTD. MAPT-bvFTD displayed more pronounced differences in transcriptomic signatures compared to the other two genetic forms. The genes that exhibited significantly positive or negative correlations with cortical thickness in MAPT-bvFTD showed opposing directionality in C9orf72-bvFTD and GRN-bvFTD.
**Conclusions:** Overall, this integrative transcriptomic approach identified several new shared and disparate genes associated with regional vulnerability with increased biological interpretation including overlap with synaptic density maps and pathologically-specific gene expression. These findings illuminated the intricate molecular underpinnings contributing to the heterogeneous nature of disease distribution in bvFTD with distinct genetic backgrounds.
**Significance Statement:** Using an integrative imaging transcriptomics approach, this study reveals

distinct and shared transcriptomic signatures associated with cortical thinning across genetic forms of frontotemporal degeneration (C9orf72, GRN, MAPT), linking regional vulnerability to neurotransmitter systems and pathology-specific gene expression, with implications for biologically informed therapeutic stratification.

**EMCR speakers Day 3**

**Isis So**
Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

**Bio**
Isis So is an MD/PhD student and CIHR Canada Graduate Scholar at Western University in London, Ontario, Canada. She previously studied neurodegeneration in traumatic brain injury during her MSc at the University of Toronto, and currently works with Dr. Elizabeth Finger at Western University to investigate potential neurodevelopmental effects of genetic variants associated with FTD.

## Longitudinal neurodevelopmental and neurodegenerative outcomes in genetic FTD

**Background:** Converging evidence hints at neurodevelopmental effects in genetic frontotemporal degeneration (FTD). For some genes, young adult FTD variant carriers show cross-sectional differences in brain volumes and cognition compared to familial non-carriers. However, longitudinal trajectories may more sensitively capture FTD-related neurodevelopmental vs. neurodegenerative changes than cross-sectional approaches. This study examined longitudinal trajectories of brain volumes, executive function, and plasma biomarkers in young adult carriers compared to familial non-carriers, as measures of neurodevelopmental and neurodegenerative outcomes of FTD-causing variants.
**Methods:** This longitudinal cohort study comprised participants, aged 18-30 years, from the FTD Prevention Initiative across Europe, Canada, and the USA. Genetic groups included C9orf72 (47%), MAPT (30%), and GRN (23%). Linear mixed-effects models were computed to assess longitudinal outcomes across age between groups, controlling for sex, scanner (for brain volumes), and education (for executive function); random effects accounted for between-subject variability nested within family membership.
**Results:** Variant carriers (n=147) and familial non-carriers (n=113) did not differ in age (mean±SD, 25.9±3.2 years), sex (53% female), or number of visits (2.1±1.7). Young adult C9orf72 carriers exhibited smaller thalamic volumes than non-carriers with large effect size (b=-982.8mm3, SE=317.0, p=0.0046, f2=0.32), with relatively stable trajectories across ages 18-30. Trajectories of rostral anterior cingulate volumes differed in C9orf72 carriers and non-carriers across age with small-to-medium effects, where carriers showed relatively stable trajectories and non-carriers showed age-appropriate declines (b=64.4mm3, SE=29.9, p=0.035, f2=0.07). For MAPT and GRN, there were little to no differences in total brain, cortical, or subcortical volumes between groups and over time. No longitudinal differences were observed between carriers and non-carriers in executive function, or plasma NfL or GFAP for any genetic group.
**Conclusions:** C9orf72 repeat expansions were linked to smaller average subcortical volumes and stable trajectories between ages 18 to 30, potentially supporting neurodevelopmental origins. The absence of neurodegeneration biomarkers and executive function differences suggests minimal early

neurodegeneration and potential compensation in young adulthood.
**Significance Statement:** Findings from this study support neurodevelopmental effects of some forms of genetic FTD. It highlights the importance of longitudinal studies in youth FTD variant carriers and non-carriers (<18 years) to distinguish developmental resilience and vulnerability from emerging neurodegeneration.

**EMCR speakers Day 3**

**Dr Victoria Helmly**
Georgia State University, USA

**Bio:** Victoria Helmly is a postdoctoral fellow in the School of Public Health at Georgia State University in Atlanta, GA.

## FTD and the Criminal Legal System: An Examination of Experiences and Policy

**Background:** Individuals with frontotemporal dementia (FTD) may experience symptoms that violate social norms and may be considered "criminal." As a result, persons living with FTD may be more vulnerable to interactions with the criminal legal system, including arrests and incarceration. There is little data on individuals' or their care partners' experiences in navigating the criminal legal system and the policies that shape these experiences.
**Methods:** We conducted semi-structured interviews with care partners of individuals with FTD who have been in contact with the criminal legal system in the United States due to the accusation or conviction of a crime. We analyzed interview transcripts using a team-based thematic analysis approach. To complement the qualitative data, we are conducting a legal mapping analysis of state laws that can potentially affect how people with dementia navigate the criminal legal system.
**Results:** Interviews with care partners (n=27) revealed many challenges for this population, including navigating the complexity of the legal system. Care partners also shared the resources that they used, including calling upon their social networks for help. One of the salient themes was the challenge of determining decision-making capacity or competency for a person with FTD, including a person's competency to stand trial. Care partners shared challenges in being trusted as a credible source of information about their loved one's condition and navigating court-ordered competency assessments.
**Conclusion:** Care partners of people with FTD are under-resourced and unprepared to navigate the criminal legal system and are faced with barriers. The legal system generally lacks the education needed to appropriately respond to people with dementia. More awareness about dementia and increased collaboration between systems is a potential solution to these challenges. Further, it could foster greater trust in care partners as reliable sources of information. Using legal mapping methods, we are currently exploring the theme of competency through a policy analysis of state laws related to the issue of competency to stand trial.
**Significance Statement:** Findings reveal how interactions with the criminal legal system affect care partners and people living with FTD, including how they navigate the challenges. Evidence from state laws will shed light on the policies in place that potentially affect a person with FTD who is processed through the court system in the U.S.

**EMCR speakers Day 3**

**Adam Martersteck**
University of Chicago, USA

**Bio**
Dr. Adam Martersteck is a biomarker neuroscientist and an Assistant Professor of Neurology at the University of Chicago. His work focuses on PET and MR imaging, using computational approaches to unravel the heterogeneity in FTD, AD/ADRD, and successful cognitive aging.

## Longitudinal tau PET progression follows language network spread in primary progressive aphasia

**Background:** Primary progressive aphasia (PPA) is a clinical dementia syndrome characterized by selective vulnerability of the (usually) left-lateralized language network and is often caused by underlying Alzheimer's disease (AD) neuropathologic change. PPA is less frequently diagnosed compared to 'typical' amnestic sporadic late-onset AD, and fewer studies have examined the change in AD tau over time with PET imaging.
**Methods:** 27 PPA participants with positive AD biomarkers (PPA-AD) underwent 18F-flortaucipir (FTP; Tauvid) PET and MR imaging at baseline and repeated 1-3 years later. Analyses used 80–100-minute post-injection frames, motion corrected and registered to FreeSurfer's unbiased within-subject native space. Partial volume correction was not used. Region-wise multiple comparisons were controlled by false discovery rate (FDR; 68 Desikan-Killiany regions, q=0.05).
**Results:** PPA participants (mean age 66.7) had mild-to-moderate language impairment (average WAB-AQ=80.0%). 17 were subtyped logopenic, 3 agrammatic/nonfluent, and 7 mixed/unclassifiable. Baseline FTP was elevated in left perisylvian temporal cortex (PSTC) and left precuneus. Over a median follow-up of 1.8 years, frontal regions and right-hemisphere PSTC homologues showed the largest increase in FTP standard uptake value ratio (SUVR; Figure 1B). Younger age related to higher baseline SUVR in inferior parietal and inferior frontal regions and to greater SUVR increase across cortical regions (Figure 2A). Baseline FTP showed no sex or APOE effects, but SUVR increases were higher in parietal cortex in females and near the temporoparietal junction in non-ε4 carriers, although the APOE association did not survive FDR.
**Conclusions:** Longitudinal FTP in PPA-AD indicates spread from left perisylvian/precuneus toward frontal and contralateral language regions, consistent with network-based progression and supporting tau PET for staging and prognosis. Younger age, and a possible female effect, tracked with faster tau accumulation, while APOE associations require follow-up. These patterns may inform trial stratification and outcome selection in atypical AD.
**Significance statement:** This study shows that in PPA caused by AD, tau spreads over time through the language network and into connected regions. The findings support tau PET as a useful tool for tracking disease progression (e.g., for clinical trial target engagement monitoring). More broadly, the methods presented here may be used for future PET radiotracers targeting proteins linked to PPA or FTD caused by underlying FTLD pathology.

**Linde Assendelft**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

## Bio

Linde is a PhD student at the Alzheimer Center of Erasmus MC University Medical Center, with a background in neuropsychology. Her research focuses on social cognition in dementia, including the validation of new and innovative tests and she investigates the theoretical framework/constructs of social cognition. She aims to improve understanding of changes in social behaviour in people with dementia.

## Validation of the Story-Based Empathy Task in Frontotemporal and Alzheimer's Dementia: Cognitive and Affective Theory of Mind

**Background:** The Story-based Empathy Task – Dutch version (SET-NL) is a novel, non-verbal Theory of Mind (ToM) task based on comic cartoons designed to measure the attribution of intention and emotion.
**Methods:** We examined the preliminary psychometric characteristics of the SET-NL and its ability to differentiate between patients with behavioural variant frontotemporal dementia (bvFTD; n = 19), Primary Progressive Aphasia (PPA; n = 24), Alzheimer's dementia (AD; n = 17) and control participants (n = 83). We examined the SET-NL's psychometric properties, investigating internal consistency, between-group differences, and construct validity.
**Results:** Internal consistency was good (Kuder-Richardson-20; KR-20 =0.80). Small to moderate correlations with age and years of education were observed. All patient groups scored lower on the SET-GS than the control group. There was an overall significant main effect ($F(3, 137) = 32.35$, $p < 0.001$, $\eta p2 = 0.42$) with controls outperforming all patients and both AD and FTD showing lower total scores than PPA. On SET-EA controls had higher scores than all patient groups. In contrast, on SET-IA controls outperformed patients with AD and FTD, and the AD and FTD groups scored lower than PPA. For SET-CI, controls outperformed AD and AD scored lower than PPA. The total score SET-GS correlated significantly with measures of processing speed, shifting and memory($rs = 0.41$; 0.37; 0.52, all $p < 0.05$), but not with emotion recognition ($rs = 0.19$, $p = 0.32$). SET-EA showed a specific correlation with verbal fluency ($rs=0.30$, $p < 0.05$). SET-IA correlated with memory ($rs = 0.44$ $p<0.05$).
**Conclusions:** This preliminary analysis of the SET-NL showed adequate internal consistency. The SET-NL was able to discriminate between persons with dementia and control participants. Notably, cognitive ToM (IA) was comparable between control participants and individuals with PPA, whereas all patient groups showed lower performance in affective ToM (EA) compared with controls. SET-NL correlated with cognitive functions (speed, shifting, fluency, memory) but not with emotion recognition.
**Significance statement:** These preliminary findings show results of a novel ToM in a Dutch dementia population. Data collection and analysis in larger samples will clarify between-group patterns of affective and cognitive ToM and their relation with underlying cognitive constructs.

**EMCR speakers Day 3**

**Lize Jiskoot**
Erasmus MC University Medical Center, Rotterdam, The Netherlands

## Bio

Lize Jiskoot is a clinical neuropsychologist and Assistant Professor at Erasmus MC, specializing in early and presymptomatic stages of FTD. Her work focuses on developing sensitive cognitive and language markers to improve early diagnosis and disease tracking.

## Cross-linguistic evaluation of the Mini Linguistic state examination (MLSE)

**Background:** Differentiating between primary progressive aphasia (PPA) subtypes is complicated by the lack of good language assessment tools. In reaction, Patel et al. [2022] developed a comprehensive PPA screening test, the Mini-Linguistic State Examination (MLSE). The MLSE consists of 11 different subtests, the total score is 100. Five error types are scored (motor speech, phonology, semantic, syntax, working memory). The current study aimed to develop and validate the Dutch version of the MLSE (MLSE-NL).
**Methods:** We administered the MLSE-NL to 50 patients with a clinical diagnosis of PPA (22 semantic variant, 15 non-fluent variant, 13 logopenic variant) and 170 healthy controls. We investigated its psychometric properties. The control's cumulative frequencies and percentile scores were calculated. We compared between-group differences, controlling for sex, age, and education. We investigated the MLSE-NL's classification abilities by means of receiver operating curves (ROC) analyses.
**Results:** Internal consistency ($\alpha$=0.71-0.88) and interrater reliability (ICC=0.91-0.98) were good. The MLSE-NL cutoff was <91. MLSE-NL total scores were 33-94 (74.3±13.6) in patients and 83-100 (97.2±2.7) in controls. Patients with PPA scored lower than controls on MLSE-NL total and all subtests ($p<0.001$). Lowest MLSE-NL total scores were measured in patients with nfvPPA. Patients with nfvPPA had more motor speech, phonology, and syntactic errors than lvPPA/svPPA, patients with lvPPA had more working memory errors than nfvPPA/svPPA, and patients with svPPA had more semantic errors than nfvPPA and lvPPA ($p<0.05$). ROC analyses revealed that semantic knowledge was the best predictor for the diagnosis of semantic variant PPA, that motor speech was the best predictor for the diagnosis of non-fluent variant PPA, and that motor speech, phonology and working memory were the best predictors for the diagnosis of logopenic variant PPA (all $p<0.05$).
**Conclusions:** The MLSE-NL shows to be a promising language screening tool, showing good psychometric properties and differential diagnostic abilities in patients with PPA. Further investigation and validation across larger memory clinic cohorts, including presymptomatic FTD, atypical forms of PPA and other FTD spectrum disorders, are currently ongoing.

**EMCR speakers Day 3**

**Franco Ferrante**
*Universidad de San Andrés, Argentina*

## Bio

Franco J. Ferrante is a biomedical engineer, CONICET doctoral fellow, and PhD student at the Faculty of Engineering of the University of Buenos Aires (FIUBA), based at the Center for Cognitive Neurosciences (CNC) of the Universidad de San Andrés, Argentina. He researches automatic linguistic markers in neurodegenerative diseases, including bvFTD, by applying natural language processing and data science to improve clinical diagnosis and monitoring.

## Addressing heterogeneity and the language blind spot in bvFTD through automated analysis in Latin America

**Background:** Digital speech biomarkers (DSBs) are emerging as scalable tools for detecting and monitoring Alzheimer's disease (AD) and frontotemporal dementia (FTD). However, their clinical promise is limited by the lack of tests of sociocultural generalizability. Prior inferential studies typically match groups by age, sex, and education, capturing group-level differences without accounting for person-level demographic effects. Machine-learning studies also lose control over these variables because sample balance is often disrupted across cross-validation folds. In addition, no previous work has examined generalizability against social determinants of health (SDH) and dialectal variation. These issues may artificially boost performance through demographic confounds or reduce discrimination through unmodeled variance.
**Methods:** We analyzed 2067 Spanish-speaking participants from the ReDLat consortium, including 820 individuals with AD, 239 with FTD, and 1008 healthy controls (HC). Participants completed six speech tasks, including story retelling, video narration, semantic fluency, and phonological fluency. Speech samples were processed with the TELL app to derive acoustic and linguistic feature dimensions spanning speech timing, prosody, morphosyntax, and lexico-semantics. To isolate disease-related variance, features were residualized for age, sex, education, dialect, and eight SDH composite scores. Machine-learning classifiers were trained to distinguish patients from controls using raw and residualized features, and performance was benchmarked against residualized cognitive scores from the MMSE, TMT, and Digit Span.
**Results:** Before residualization, DSBs showed strong performance for AD-vs-HC and FTD-vs-HC classification (AD-vs-HC: AUC=0.92, balanced-accuracy=0.84; FTD-vs-HC: AUC=0.88, balanced-accuracy=0.78). After residualization, DSB performance improved for AD and remained stable for FTD (AD-vs-HC: AUC=0.94, balanced-accuracy=0.87; FTD-vs-HC: AUC=0.90, balanced-accuracy=0.78). By contrast, cognitive scores declined after the same adjustment (AD-vs-HC: AUC=0.82, balanced-accuracy=0.75; FTD-vs-HC: AUC=0.81, balanced-accuracy=0.75).
**Conclusions:** DSBs retain discriminative value despite sociodemographic heterogeneity and appear less affected by these factors than standard cognitive measures, supporting their utility for equitable precision medicine across diverse populations.
**Significance statement:** This study advances FTD research by showing that speech biomarkers can identify FTD above and beyond major sociodemographic, dialectal, and SDH-related influences in a large Latin American cohort. These findings strengthen the case for scalable, culturally sensitive speech-based tools for FTD detection in underrepresented populations.

**EMCR speakers Day 3**

**Dr Arabella Bouzigues**
*The Douglas Research Centre, Canada*

**Bio**
Arabella is a postdoctoral researcher based at the Douglas Research Centre. She has also been leading the coordination of GENFI, the largest genetic FTD cohort study within Europe and Canada for the past 6 years.

## Survival rates in genetic FTD

**Background:** It is still unknown what drives the heterogeneity of survival rate in genetic frontotemporal dementia (FTD). Understanding the natural history and predictors of disease trajectory are critical for effective care but also therapeutic clinical trial designing and efficacy evaluation.
**Methods:** Using Kaplan-Meier method, we retrospectively assessed survival rates in patients included in the GENFI cohort, carrying a C9orf72 expansion or a mutation in GRN or MAPT genes. Survival was calculated as the time from symptom onset to time of death or censoring date. Cox proportional hazards models were used to identify predictors of survival, which were subsequentially externally validated in an independent cohort. We further designed a Structural Equation Model (SEM) to assess the relationships between predictors, applying a Least Absolute Shrinkage and Selection Operator (LASSO) method.
**Results:** The median survival for all patients with genetic FTD was 6.94 years (95%CIs=6.59-7.80) from symptom onset. The median survival for patients with GRN mutations was 6.63 years (6.08-7.98), for patients with a C9orf72 expansion was 7.04 years (6.45-8.77), and for patients with MAPT mutations was 8.56 years (7.06-13.50). Older age at onset, shorter disease duration from onset to enrolment, clinical phenotype (i.e., FTD-ALS), type of first symptom (i.e., motor or language onset) and geographical area of residency (Central and Southern Europe) were associated with poorer prognosis. Interestingly, we found that genetic group does not directly affect survival rate but that this link is mediated by age at onset and clinical phenotype. We compute a genetic FTD survival risk index which can be used on an individual subject level.
**Conclusions:** Our results highlight that a transdiagnostic approach is required for prognosis in genetic FTD, considering motor impairment in addition to cognitive and behavioural symptoms. Individual risk scores might be of help for patients' stratification in future therapeutic trials.
**Significance Statement:** The available evidence suggests that prognosis in genetic FTD is driven less by the genetic mutation itself than by its impact on age at onset and disease phenotype. This has important implications for clinical practice, indicating that individualised risk assessment should focus on clinical presentation rather than solely on genetic group. For trial design, these findings support transdiagnostic, phenotype-driven stratification approaches, which may improve power and relevance in evaluating disease-modifying therapies. At the health system level, improved prognostic modelling can guide care planning and resource allocation for patients and families. Future studies should validate and refine survival prediction tools by incorporating biomarkers and disease modifiers, ultimately advancing personalised medicine in FTD.

**EMCR speakers Day 3**

**Ivan Caro**
*Universidad de San Andrés, Argentina*

## Bio

Ivan Caro is a a CONICET doctoral fellow and PhD candidate in Neuroscience at the Universidad Nacional de Córdoba in Argentina, based at the Cognitive Neuroscience Center at Universidad de San Andrés. His research focuses on digital speech biomarkers for cognitive decline and Alzheimer's disease and related dementias.

## Evaluating Digital Speech Biomarkers for Dementia in Latin America

**Background:** Monitoring across the Alzheimer's disease continuum (ADC) relies on resource-intensive cognitive testing and neuroimaging. Digital speech biomarkers (DSBs) offer a scalable alternative, but their ability to predict neuropsychological and neuroimaging outcomes across the ADC remains untested in Latino cohorts.
**Methods:** A total of 150 participants across the ADC (17 healthy controls, 55 with subjective cognitive decline, 57 with mild cognitive impairment, and 21 with Alzheimer's disease dementia) contributed speech, cognitive, and neuroimaging measures that were used as features in machine learning regressors. DSB features were extracted from brief fluency recordings using the TELL app, cognitive features were obtained from scores on standardized assessments (Addenbrooke's Cognitive Examination–III [ACE-III], INECO Frontal Screening [IFS]), and brain features reflected gray matter volumes in different regions of interest. Regressors were trained separately to predict ACE-III and IFS scores from either DSB or brain features, and to predict hippocampal and ADD-related atrophy mask volumes from either DSB or cognitive features. Model performance was evaluated using age-adjusted partial Pearson correlations between predicted and observed values. Multiple regression analyses were used to examine associations between DSBs and gray matter volume using a whole-brain voxel-based morphometry approach.
**Results:** Models using DSB features surpassed those using brain features in predicting ACE-III (r = .67 vs. .23) and IFS scores (r = .55 vs. .31), and they outperformed models using cognitive features in predicting ADD-related atrophy mask volume (r = .38 vs. .27), but not hippocampal volume (r = .42 vs. .37). Word frequency was negatively associated with bilateral prefrontal cortex volume.
**Conclusion:** Using a fully automated multivariate pipeline, DSBs captured both cognitive functioning and structural markers of brain health across the ADC. Their favorable performance compared with standard cognitive and neuroimaging measures underscores their promise as a scalable, objective, and low-cost approach for dementia screening and monitoring, with implications for improving equity in large-scale dementia research.
**Significance statement:** This work highlights the potential of speech as a scalable window into neurodegeneration. Automated analysis of brief recordings may enable accessible monitoring of cognitive and brain-related changes, supporting earlier detection efforts and expanding participation in dementia research among diverse and historically underrepresented populations.

**EMCR speakers Day 3**

**Federico Castano**
*Universidad Católica Argentina*

## Bio

Federico Castano is a clinical neuropsychologist and PhD Candidate at Universidad Católica Argentina, focusing on cognitive and behavioral impairment in atypical parkinsonian syndromes.

## A meta-analysis on cognitive and behavioral impairments in primary tauopathies

**Background:** Cognitive and behavioral impairment represent major sources of disability in primary tauopathies such as Progressive Supranuclear Palsy (PSP) and Corticobasal Syndrome (CBS). However, evidence regarding their systematic assessment and quantitative characterization remains fragmented, with substantial variability in instruments and reporting practices.
**Objective:** To synthesize available evidence on cognitive, behavioral, and clinical severity measures in PSP and CBS through a systematic review and meta-analysis.
**Methods:** We conducted systematic literature searches to identify studies reporting summary-level data (sample size, mean, standard deviation) on cognitive, behavioral, or clinical severity outcomes in PSP and/or CBS. Random-effects meta-analyses using restricted maximum likelihood (REML) were performed for outcomes reported in at least four independent studies within a given diagnostic group. Between-study heterogeneity was evaluated using Q and $I^2$ statistics. Sensitivity analyses were conducted using leave-one-out procedures. Small-study effects were examined through funnel plots and Egger's regression. Exploratory meta-regressions assessed associations between study-level demographic and clinical variables and pooled cognitive outcomes.
**Results:** Global cognitive screening measures were the most consistently reported outcomes, particularly the Mini-Mental State Examination (MMSE, n=72), Montreal Cognitive Assessment (MoCA, n=31), and Addenbrooke's Cognitive Examination (ACE, n=26) in PSP, whereas substantially fewer measures were meta-analyzable in CBS. REML models yielded stable pooled mean estimates for MMSE, MoCA, and ACE in PSP despite consistently high heterogeneity. Leave-one-out analyses identified few highly influential studies, and pooled estimates remained largely stable after exclusion. Egger's regression suggested small-study effects for selected outcomes. Meta-regressions indicated that greater clinical severity, lower education, and higher age were individually associated with worse cognitive performance at the study level.
**Conclusions:** This study provides a quantitative synthesis of cognitive and behavioral assessment practices in PSP and CBS, highlighting both robust global cognitive findings and significant heterogeneity, as well as critical gaps in standardized outcome reporting.
**Significance Statement:** This study clarifies the structure and magnitude of cognitive and behavioral impairment in PSP and CBS, demonstrating robust global cognitive differences alongside substantial methodological heterogeneity. The findings emphasize the need for harmonized assessment frameworks to improve comparative phenotyping and future biomarker-driven research in primary tauopathies.

**EMCR speakers Day 3**

**Loreece Haddad**
*Mesulam Institute for Cognitive Neurology and Alzheimer's Disease at Northwestern University*

## Bio

Loreece Haddad is a Research Project Manager at the Mesulam Institute for Cognitive Neurology and Alzheimer's Disease at Northwestern University. She works with Dr. Elena Barbieri on research examining the divergent mechanisms of anomia in Alzheimer's disease versus FTLD-TDP-C with primary progressive aphasia.

## Divergent Mechanisms of Anomia in Alzheimer's Disease versus FTLD-TDP-C with Primary Progressive Aphasia

**Background:** Primary progressive aphasia (PPA) is a progressive language disorder that can be caused by various neurodegenerative diseases including Alzheimer's disease (PPA-AD) and TDP-43 proteinopathy Type C (PPA-TDP-C, see Mesulam et al., 2022). Word-finding difficulties (i.e., anomia) are common to all individuals with PPA but may take different forms, with some participants showing disruption of verbal conceptual knowledge (henceforth "semantic" anomia) and others presenting with difficulties in word retrieval (henceforth "lexical-phonological" anomia). The psycholinguistic sources of anomia were investigated in PPA-AD or PPA-TDP-C.
**Methods:** Thirty-two individuals with mild PPA (i.e., Western Aphasia Battery Aphasia Quotient, WAB-AQ, score ≥ 70) and autopsy-confirmed AD (n=22) or TDP-C (n=10) neuropathological diagnosis were included in the study. Participants were assessed with picture naming (Boston Naming Test, BNT) and word comprehension (Peabody Picture Vocabulary Test, PPVT) tests, as well as with a computerized word-to-picture matching task (Picture Pairs Test, PicPairs). In the PicPairs task, they heard single words depicting objects and were instructed to point to the corresponding object from a selection of two pictures (semantically related or unrelated).
**Results:** While the two groups did not differ in aphasia severity (WAB-AQ) or performance on the Mini-Mental State Examination, the PPA-TDP-C group exhibited lower accuracy and longer Reaction Times (RTs) than the PPA-AD group for related (but not unrelated) items on the PicPairs. Across groups, longer RTs to related (but not unrelated) trials were associated with poor efficacy of phonemic cues in the face of naming difficulty. The PPA-TDP-C group benefited less from phonemic cues than the PPA-AD group, that is they were still unable to name an object even when provided the first sound of a word describing it.
**Conclusions:** Individuals with PPA-TDP-C had greater difficulty understanding verbal concepts denoting members of the same semantic category, while those with PPA-AD showed similar responses to verbal concepts regardless of their semantic association. Limited efficacy of phonemic cues on the BNT and its association with performance on the PicPairs reinforce that in PPA, TDP-C causes anomia by disrupting verbal conceptual knowledge whereas AD interferes with retrieval and phonology.
**Significant statement:** Using identical assessment tools, we show that in PPA, TDP-C causes anomia by disrupting verbal conceptual knowledge whereas AD interferes with retrieval and phonology. Albeit concordant with the PPA subtypes dominating each group, these results offer the first demonstration of the mechanistic difference underlying anomia in neuropathologically confirmed populations.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