NEUROSCIENCES CONNECT:
HUMAN RESEARCH NEWSLETTER

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Department of Neurosciences
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Vice Chair of Human Clinical Research
Dr. Jennifer Graves

Department Chair
Dr. James Brewer

Dear Colleagues,

Welcome to the Spring edition of our *Neurosciences Human Research Newsletter*. Spring is a season of renewal and growth, offering the perfect time to reflect on our progress and look ahead to exciting discoveries. It is also a time to embrace new opportunities for collaboration, innovation, and continued advancement in human research.

In this issue, we highlight UC San Diego's outstanding achievements in neuroscience research, including its recognition as a Tier 1 institution for research by *U.S. News & World Report* and its ranking as the No. 5 public medical school for NIH funding. Among these accomplishments, we celebrate a groundbreaking publications from our colleagues, including a recent paper from UC San Diego's Autism Center of Excellence, led by Dr. Eric Courchesne, Dr. Kuaikuai Duan, and a multidisciplinary team of collaborators. This top-ranked study, published in *Nature Communications* (2024), used innovative brain cortical organoid technology to uncover biological origins of autism subtypes. Ranked in the top 99th percentile among more than 339,000 publications worldwide, the study has garnered international attention and advanced understanding of autism's early developmental pathways.

We also share highlights from our inaugural *Neurosciences Seminar*, a preview of upcoming workshops on digital tools in research and the role of sex differences in neuroscience clinical studies.

Additionally, as we reflect on *Black History Month* in February and *Women's History Month* in March, we highlight the achievements of women scientists whose groundbreaking contributions continue to shape the field, including those who have overcome historical barriers to advance scientific discovery. It is also *Multiple Sclerosis Awareness Month*, reminding us of the importance of advancing research to better understand this complex condition and develop more effective treatments.

Collaboration is at the core of our work, and I encourage you to engage, share insights, and help build an inclusive, innovative research community. Thank you for your ongoing commitment to excellence and for being part of this incredible community.

With gratitude,

Jennifer Graves, MD, PhD, MAS
Vice Chair of Human Clinical Research

In This Issue

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News Spotlight

Top Honors: UCSD Health Top 20 in National Rankings & No. 5 for NIH Funding in 2024!

UC San Diego continues to be a leader in biomedical research, with the School of Medicine securing over $725 million in sponsored research for the 2024 fiscal year**,** representing approximately 44% of the university's total research funding**.** Among the university's many research-driven departments**,** Neurosciences stands out as the No. 1 NIH-funded department in the nation, receiving an impressive $41.97 million in the most recent rankings in 2023. While Blue Ridge Institute for Medical Research (BRIMR) rankings for 2024 have not yet been released, the department's history of securing substantial federal research support suggests it remains a leader in the field. Continued progress from 2025 and beyond depends on sustained federal investment.

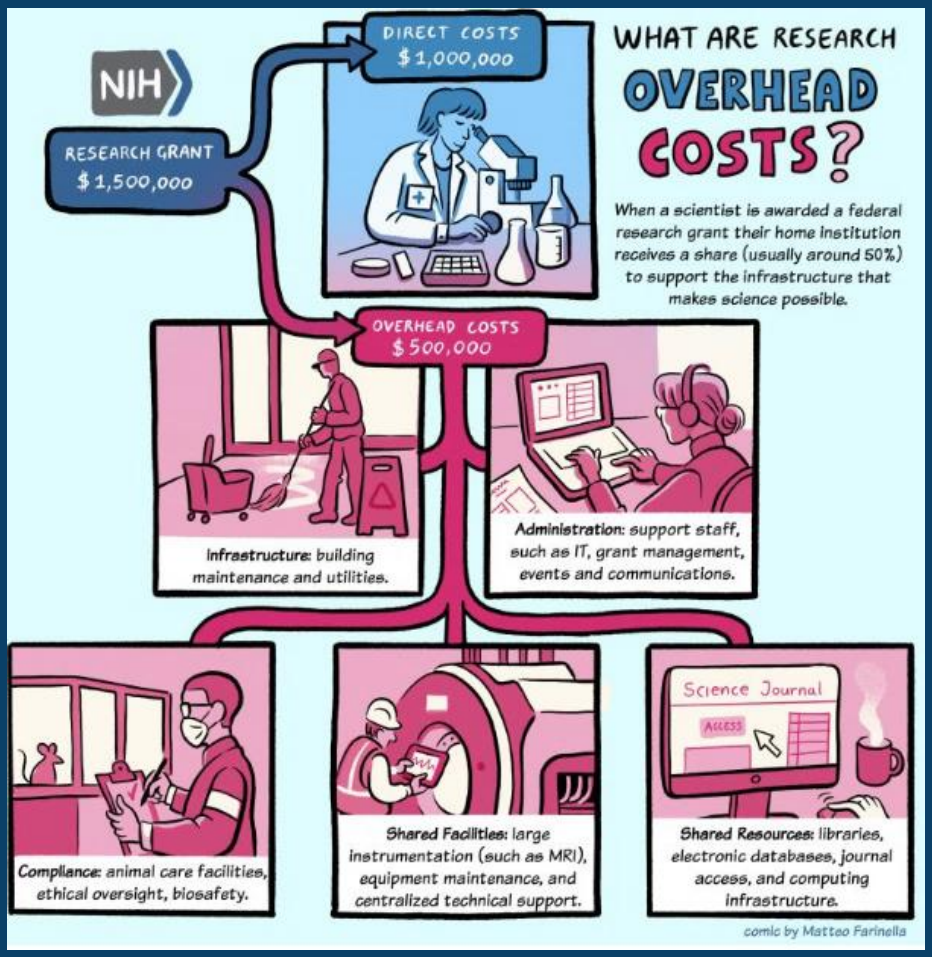
Current proposed NIH overhead funding cuts threaten to slow the momentum of life-saving discoveries and hinder the resources that support scientific advancement, affecting labs, equipment, and critical infrastructure. To protect this vital work, we need everyone's voice.

Take action today! Help ensure that UC San Diego and the Department of Neurosciences remains at the forefront of medical breakthroughs by urging your federal legislators to prioritize NIH funding. It takes just one minute to make a difference. [Protect Biomedical Research | University of California]

Together, we can continue advancing groundbreaking research, driving innovation, and transforming the future of healthcare. Thank you for standing with us in support of scientific discovery.

Why NIH Overhead Cost Cuts Matter to Us All

Research breakthroughs rely on a network of people and resources supported by "overhead costs," which fund essential infrastructure like lab and participant space, maintenance, technology, and safe workspaces. While research grants cover project-specific expenses, overhead ensures that research can happen at all. Recent changes in NIH funding for overhead costs present challenges but also highlight the importance of our interconnected community. Every role—whether in administration, facilities, IT, or research support in any capacity, contributes to advancing discoveries. By collaborating, improving efficiencies, and advocating for these vital roles, we can continue to thrive as a hub for innovation and discovery.



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WALK MS: San Diego 2025 – Support the MS Community

Walk MS: San Diego will take place on Saturday, April 12, 2025, at the Preble Field, NTC Park in Liberty Station. This annual event unites the community to raise awareness and funds for multiple sclerosis (MS) research and support services.

- **Event Opens - 8:00 am**
- **Ceremony Starts - 9:15 am**
- **Walk Kickoff - 9:30 am**

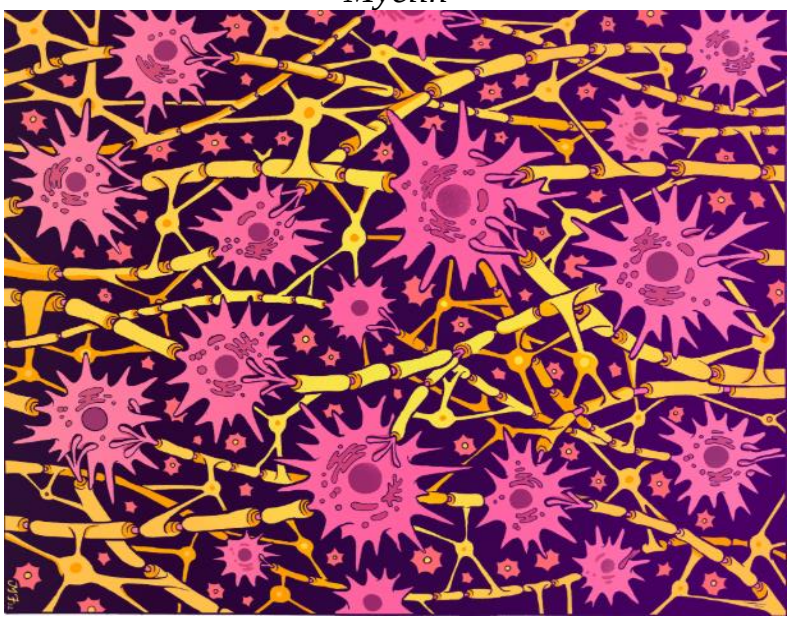
Participants can choose between a 1-mile or 3-mile route, both accessible and welcoming to all mobility levels and devices.

Fundraising Initiative: Participants who raise $100 or more by March 8, 2025, will receive an exclusive MS T-Shirt mailed ahead of the event. Those reaching the goal after the date will receive their T-shirt post-event.

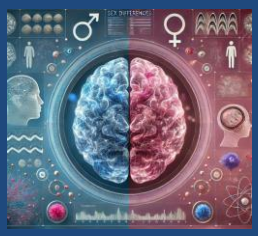
Get Involved: Whether walking individually or with a team, participation helps advance MS research and support services. To register, volunteer, or donate, visit the official webpage at WALK MS: San Diego 2025

The artwork below, *Myelin*, by Matteo Farinella and inspired by the style of artist William Morris, vividly illustrates the intricate structure of myelin, a crucial component of the central nervous system. Myelin acts as an insulating layer around nerve fibers, ensuring the swift and efficient transmission of signals between the brain and the body. In multiple sclerosis, the immune system mistakenly attacks this protective sheath, disrupting nerve communication and leading to a wide range of challenging symptoms. This visual serves as a powerful reminder of how essential myelin is for healthy nerve function and highlights the importance of continued research, advocacy, and community support in the fight against MS. By sharing this piece, we hope to inspire greater awareness and empathy for those affected by the condition.

Myelin



Feature Events



Digital and Wearable Tools & Sex Differences in Neurological Diseases Research Workshops – Planning Underway!

Exciting progress is being made in the development of two upcoming research workshops: Digital and Wearable Technology and Sex Differences in Neurological Diseases.

On January 24, 2025, faculty members interested in these topics gathered for a pre-planning meeting, where they collaborated to establish a structured framework for organizing both workshops. As a result of this discussion, the first seminar, focused on digital tools and wearable devices in research and clinical applications, is scheduled for **May 2, 2025.**

The Digital and Wearable Technology Workshop will explore how these tools can improve real-time data collection, and integrate innovative platforms into clinical trials. Participants can look forward to:

- **Engaging Sessions:** Insights from thought leaders and innovators in wearable technology and digital research tools.
- **Hands-On Demonstrations:** Opportunities to interact with technologies being implemented in research.
- **Collaborative Networking:** An opportunity to connect with colleagues who share a passion for advancing technology in human research.

Following this event, we will apply key takeaways from the Digital Tools Workshop to the upcoming Sex Differences in Neuroscience Research seminar, ensuring it receives the attention and engagement it deserves.

If you are interested in participating in either of these workshops, please email **irubio@health.ucsd.edu** to be added to the attendee list.

Glia and Neuroinflammation Seminar Series

Sidar Aydin, PhD
Daneman Lab, UCSD
"The role of retinol transporter Stra6 in modulating neuroinflammation"

Celina Nguyen, PhD candidate
Coufal and Glass Lab, UCSD
"Myocyte Enhancer 2C maintains homeostasis in human microglia"

Date: March 27, 2025
Time: 4-5 PM
Place: Liebow Auditorium BSB

To be added to the distribution list please contact: Tamara Shabi at trshabi@health.ucsd.edu

Research Highlights: Publications

2024/2025 Publications from PubMed Search Featuring Faculty and Staff from our Department

Exploring bradyphrenia in Huntington's disease using the computerized test of information processing (CTiP)

Georgia M Parkin [1], Braden Culbert [1], Emma Churchill [1], Paul E Gilbert [2], Jody Corey-Bloom [1]

Bradyphrenia, or slowed thinking, is common in neurological disorders but remains underexplored in Huntington's Disease (HD). Researchers used the Computerized Test of Information Processing (CTiP) to assess cognitive processing speed in 211 participants, including HD-ISS Stages 0-3 and healthy controls.
The CTiP comprised three subtests: Simple Reaction Time (SRT): Measures baseline motor function, Choice Reaction Time (CRT): Introduces a decisional component and Semantic Search Reaction Time (SSRT): Adds a conceptual element.

By subtracting SRT from CRT and SSRT scores, researchers obtained a motor-corrected measure of cognitive processing speed, allowing for a clearer assessment of bradyphrenia. Significant differences emerged between HD groups and HCs ($p < 0.0001$), with bradyphrenia worsening as HD progressed. An ROC analysis demonstrated that these motor-corrected differences could reliably distinguish early-stage (0+1) from advanced-stage (2+3) HD (AUC = 0.72, $p < 0.0001$).

This study provides quantifiable evidence of bradyphrenia in HD, which worsens with disease progression. Given its potential impact on daily life, further research into its effects and mitigation strategies is warranted.

Sex Differences for Regional Pathology in People with High Likelihood of Lewy Body Dementia Phenotype Based on Underlying Pathology

Ece Bayram [1 2], David G Coughlin [2], Shunsuke Koga [3 4], Owen A Ross [3 5], Irene Litvan [2], Dennis W Dickson [3]

This study explored sex differences in clinicopathological correlations in Lewy body dementia (LBD), analyzing brain tissue from 357 individuals with a high likelihood of LBD based on autopsy findings. The study found significant sex-based differences in both pathology and clinical diagnosis. Females were less likely to receive a clinical LBD diagnosis despite having higher levels of Lewy bodies, neurofibrillary tangles (NFTs), and senile plaques in several brain regions compared to males. Specifically, females had more Lewy body pathology in the superior temporal, inferior parietal, and entorhinal cortices, along with increased NFT and senile plaque counts in the hippocampus, amygdala, and nucleus basalis of Meynert. Interestingly, the study found that the presence of Lewy bodies in specific brain regions, such as the middle frontal, cingulate, and entorhinal cortices, was more strongly associated with a clinical diagnosis of LBD in males than in females. This suggests that the pathological burden needed for a clinical diagnosis may be higher in females or that the presentation of symptoms differs between sexes. After adjusting for regional pathology differences, the likelihood of an LBD diagnosis became similar between males and females, further emphasizing the role of pathology in diagnostic disparities.

These findings highlight the potential for underdiagnosis of LBD in females and underscore the need for sex-specific approaches to diagnosis and disease management. Understanding these differences could improve clinical recognition, lead to more tailored diagnostic criteria, and ultimately enhance care for individuals affected by LBD. Further research is needed to explore the underlying mechanisms contributing to these sex differences and how they might inform future diagnostic and therapeutic strategies.

Highlighting a Significant Publication in Autism:

Embryonic Origin of Two ASD Subtypes of Social Symptom Severity: The larger the brain cortical organoid size, the more severe the social symptoms

Embryonic brain overgrowth dictates autism severity, new research suggests

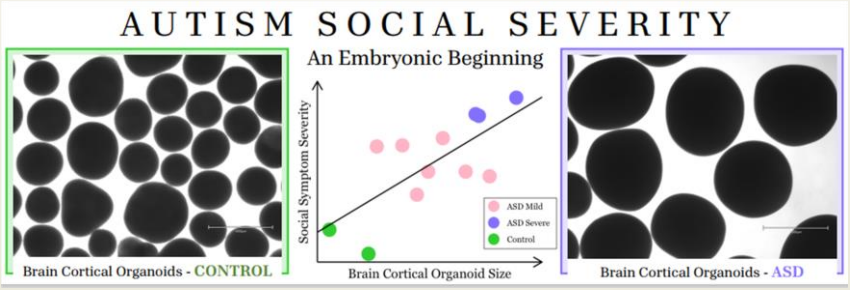
Eric Courchesne [1], Vani Taluja [2], Sanaz Nazari [2], Caitlin M Aamodt [3], Karen Pierce [2], Kuaikuai Duan [2], Sunny Stophaeros [2], Linda Lopez [2], Cynthia Carter Barnes [2], Jaden Troxel [2], Kathleen Campbell [2], Tianyun Wang [4 5], Kendra Hoekzema [6], Evan E Eichler [6 7], Joao V Nani [3 8], Wirla Pontes [3], Sandra Sanchez Sanchez [3], Michael V Lombardo [9], Janaina S de Souza [3], Mirian A F Hayashi [8], Alysson R Muotri [10 11]

A groundbreaking study from UC San Diego's Autism Center of Excellence, led by Dr. Eric Courchesne, and a multidisciplinary team of collaborators, has uncovered the biological origins of autism spectrum disorder (ASD) through innovative brain cortical organoid (BCO) research. Published in *Nature Communications* (2024), the study made a significant global impact, ranking in the top 99th percentile among over 339,000 publications worldwide and receiving widespread media coverage (Press Release Courchesne et al ASD BCO Overgrowth.pdf). This collaborative effort included experts from UC San Diego's Departments of Neurosciences, Pediatrics, and Molecular and Cellular Medicine, along with partners from Rady Children's Hospital, the University of Washington, Peking University, and the Istituto Italiano di Tecnologia. Their collective expertise has provided unprecedented insight into the early neurodevelopmental pathways underlying autism's clinical diversity.

The research involved analyzing 4,910 embryonic-stage BCOs derived from toddlers with ASD and typically developing controls. It revealed two distinct autism subtypes emerging during early brain development. Toddlers with *profound autism*, characterized by severe social, language, and cognitive impairments, had significantly enlarged BCOs, growing nearly three times faster than controls. This accelerated growth correlated strongly with more severe social symptoms and reduced IQ. In contrast, toddlers with *milder autism* exhibited more moderate BCO enlargement and less pronounced cognitive and social challenges.

At the molecular level, the study identified elevated activity of Ndel1, a key regulator of cell proliferation and neurogenesis, as a driving factor behind abnormal brain growth in ASD. These findings demonstrate that the biological foundations of autism are established during embryogenesis, offering unprecedented insight into the neurodevelopmental pathways underlying autism's clinical diversity.

This landmark discovery not only enhances understanding of ASD's origins but also opens new avenues for early diagnosis and personalized interventions, reinforcing UC San Diego's leadership in autism research.



Research Highlights: Publications

2024/2025 Publications from PubMed Search Featuring Faculty and Staff from our Department

Mapping Neurodegeneration Across the Huntington's Disease Spectrum: a five-year longitudinal analysis of plasma neurofilament light

Georgia M Parkin [1], Elizabeth A Thomas [2], Jody Corey-Bloom [3]

A five-year longitudinal study has identified plasma neurofilament light (NfL) as a critical biomarker for tracking Huntington's disease (HD) progression. Published in *EBioMedicine* (2024), the study analyzed 108 participants, including 78 individuals with the HD mutation and 30 healthy controls, using two staging systems—the HD-Integrated Staging System (HD-ISS) and the PIN score-Approximated Staging System (PASS).

The study found that plasma NfL levels increased steadily with disease advancement, with annualized rates of change rising from 10.55% in early-stage HD to 15.62% in advanced stages, compared to 8.32% in healthy controls. This increase was particularly notable in later stages, where NfL levels surged alongside worsening cognitive and motor symptoms. Elevated NfL levels were closely associated with lower performance on the Symbol Digit Modalities Test (SDMT), a measure of cognitive processing speed, and higher Total Motor Scores, reflecting disease severity.

Importantly, the study demonstrated that plasma NfL can provide valuable insights into both clinical and pathological progression, offering a non-invasive and easily measurable biomarker for monitoring disease trajectory. This advancement paves the way for more personalized disease management, earlier intervention strategies, and improved evaluation of therapeutic efficacy in clinical trials.

Laser Interstitial Thermal Therapy for the Treatment of Mesial Temporal Lobe Epilepsy in Children

Aditi M Trivedi [1,2], Maria A Montenegro [1,2], David Gonda [1,2], Olivia Kim-McManus [1,2], Neggy Rismanchi [1,2], Aliya Frederick [1,2], Natalie Guido-Estrada [1,2], Anuja Jindal [1,2], Shifteh Sattar [1,2]

The effectiveness of laser interstitial thermal therapy (LITT) for treating drug-resistant mesial temporal lobe epilepsy in children and adolescents was evaluated in this retrospective cohort study included 19 patients (12 girls, 7 boys), with a mean epilepsy onset age of 9.9 years and a mean surgery age of 15.1 years. All patients underwent comprehensive presurgical evaluations, and treatment decisions were made by a multidisciplinary team. The procedures were performed using the Visualase laser ablation system, and patients were classified into lesional (hippocampal sclerosis) and nonlesional groups based on MRI findings.

Overall, 73.5% of patients achieved seizure freedom (Engel 1 score), with significantly better outcomes in the lesional group (90%) compared to the nonlesional group (55.5%). Younger age at seizure onset was associated with better postsurgical outcomes, while other potential predictors, such as sex and additional MRI findings, did not show significant associations. The study also found that the procedure was generally safe, with no major complications reported.

The findings suggest that LITT is a safe and effective minimally invasive treatment option for drug-resistant pediatric epilepsy, particularly for patients with hippocampal atrophy. It offers a promising alternative to traditional epilepsy surgery, especially for children with identifiable lesions, supporting improved seizure control and quality of life.

Research Highlights: Publications

2024/2025 Publications from PubMed Search Featuring Faculty and Staff from our Department

Study of the Association Between Menarche and Disease Course in Pediatric Multiple Sclerosis

Kristen M Krysko[1,2,3], Michael Waltz[4], Tanuja Chitnis[5], Bianca Weinstock-Guttman[6], Gregory S Aaen[7], Anita Belman[8], Leslie A Benson[9], Mark P Gorman[9], Timothy E Lotze[10], Soe S Mar[11], Manikum Moodley[12], Jayne M Ness[13], Mary Rensel[14], Moses Rodriguez[15], John W Rose[16], Alice Rutatangwa Edwards[17], Teri L Schreiner[18], Yolanda S Wheeler[19], Bradley J Barney[4], Emmanuelle Waubant[17], T Charles Casper[4], Jennifer S Graves[20]; as the US Network of Pediatric MS Centers

A recent study led by Dr. Kristen M. Krysko, Dr. Jennifer Graves, and collaborators from the US Network of Pediatric MS Centers, including UC San Diego, highlights puberty as a critical period for increased multiple sclerosis (MS) activity in female pediatric patients. Published in *Neurology* (2025), the study analyzed 736 girls with pediatric-onset MS, comparing relapse rates across premenarche, perimenarche, and postmenarche periods. Findings showed that relapse rates peaked during the perimenarche period, with a 1.52-fold increase compared to postmenarche ($p = 0.0049$). MS onset most commonly occurred around 2.8 years after menarche, emphasizing puberty as a potential trigger. High-efficacy disease-modifying therapies (DMTs), particularly oral and infusion treatments, significantly reduced relapse risk ($p < 0.001$).

These results underscore the importance of closely monitoring disease activity during puberty and considering more aggressive treatment strategies during this transitional period. Future research measuring sex hormone levels could provide further insight into the biological mechanisms driving this increased risk.

Differences in Regional Brain Structure in Toddlers with Autism are Related to Future Language Outcomes

Kuaikuai Duan[1], Lisa Eyler[2,3], Karen Pierce[4], Michael V Lombardo[5], Michael Datko[4], Donald J Hagler[6], Vani Taluja[4], Javad Zahiri[4], Kathleen Campbell[4], Cynthia Carter Barnes[4], Steven Arias[4], Srinivasa Nalabolu[4], Jaden Troxel[4], Peng Ji[7], Eric Courchesne[8]

A major publication from UC San Diego's Autism Center of Excellence has identified early-age brain alterations in toddlers with autism that predict future language outcomes. Published in *Nature Communications* (2024), the study leveraged 372 longitudinal MRI scans from 166 autistic toddlers and 109 typically developing toddlers, with findings validated in an independent cohort of 75 toddlers.

Researchers found that, compared to typically developing peers, toddlers with autism exhibited distinct structural differences in brain regions associated with language and social processing. These included larger or thicker temporal and fusiform regions, smaller or thinner inferior frontal and midline structures, larger callosal subregions, and a smaller cerebellum. Importantly, these alterations were closely linked to autism symptom severity and cognitive impairments at early ages.

The study demonstrated that incorporating these brain measures significantly improved the prediction of future language abilities at a six-month follow-up, surpassing models based solely on clinical and demographic factors. This discovery underscores the potential of MRI-based biomarkers to guide early diagnosis, prognosis, and personalized intervention strategies for children with autism.

Research Highlights: Publications

2024/2025 Publications from PubMed Search Featuring Faculty and Staff from our Department

A Useful Cognitive Motor Dual Task Paradigm in Prodromal and Manifest Huntington's Disease

Emma Churchill [1], Shelby Hughes [2], Andrew Hall [3], Braden Culbert [3], Daniel J Goble [4], Jody Corey-Bloom [3], Paul E Gilbert [5]

A recent study from UC San Diego, published in *Parkinsonism & Related Disorders* (2024), demonstrates how a cognitive-motor dual-task (DT) paradigm can effectively uncover balance deficits in individuals with Huntington's disease (HD) and those in the prodromal stage (Pro-HD). Researchers evaluated balance in 68 participants—30 with HD, 17 with Pro-HD, and 20 healthy adults (HA)—using the BTrackS Balance Plate alongside the Paced Auditory Serial Addition Test (PASAT).

While single-task (ST) balance assessments showed significant impairments in the HD group compared to healthy controls, Pro-HD participants performed similarly to healthy adults. However, the dual-task condition, which added a cognitive challenge, revealed substantial balance deterioration in both the HD and Pro-HD groups. The Dual Task Cost (DTC), a measure of balance decline from ST to DT, was significantly higher in both HD and Pro-HD participants compared to healthy controls.

These findings suggest that cognitive strain amplifies subtle motor impairments in individuals transitioning from prodromal to manifest HD. The study highlights the potential of dual-task assessments as biomarkers for early disease progression, fall risk evaluation, and clinical trial outcome measures. Further studies is recommended to validate these promising results.

Intranasal Oxytocin for Apathy in People with Frontotemporal Dementia (FOXY): A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Adaptive, Crossover, Phase 2a/2b Superiority Trial

Kristy K L Coleman [1], Scott Berry [2], Jeffrey Cummings [3], Ging-Yuek R Hsiung [4], Robert Laforce [5], Edward Huey [6], Simon Ducharme [7], Maria Carmela Tartaglia [8], Mario F Mendez [9], Chiadi Onyike [10], Kimiko Domoto-Reilly [11], Mario Masellis [12], Nathan Herrmann [13], Anton Porsteinsson [14], Michelle A Detry [2], Chloe Stewart [15], Anna L Bosse [2], Anna McGlothlin [2], Bryan Dias [16], Sachin Pandey [17], Michael Mayich [17], Stephen H Pasternak [18], Ramiro Ruiz Garcia [19], Miguel Restrepo-Martinez [20], Howard Feldman [21], Adam L Boxer [22], Elizabeth C Finger [23]

A recent multicenter, randomized, double-blind, placebo-controlled trial investigated the effectiveness of intranasal oxytocin for treating apathy in people with frontotemporal dementia (FTD). Conducted across 11 clinics in the U.S. and Canada, the study enrolled 94 participants, aged 30 to 80, with probable FTD and significant apathy. The trial was conducted in two stages to identify the optimal dosing schedule. Results showed that administering 72 IU of oxytocin every third day significantly improved apathy scores on the Neuropsychiatric Inventory, with an estimated reduction of -1.32 points compared to placebo (p=0.010). The treatment was well tolerated, with no serious adverse events attributed to oxytocin. Mild side effects included upper respiratory infections (5-6%) and headaches (3-7%). These findings suggest that intermittent intranasal oxytocin could be a promising approach for managing apathy in FTD, warranting further trials with more potent formulations.

Other Highlights (cont.):

Inaugural Neurosciences Research Day – September 6, 2024

Inaugural Neurosciences Human Research Day: Recap

The 1st Neurosciences Human Research Day, held on September 6, 2024, at the ACTRI Auditorium, was a resounding success, bringing together 92 attendees from across the neuroscience research community. The event provided an invaluable platform for scientific exchange, collaboration, and inspiration.

The day began with a warm welcome from Dr. Jennifer Graves, setting the stage for thougt provoking presentations on the latest advancements in human neuroscience research. Highlights included presentations from K-Award Recipients, featuring innovative projects led by Drs. Coughlin, LaBuzetta, Longardner, and Yang, followed by insightful contributions from research staff and pediatric neurology teams.

Senior faculty sessions showcased research from our colleagues and leaders, including Drs. Shih (Epilepsy), Graves (Neuroimmunology), Hemmen (Stroke), Gundogdu (Motor Neuron/ALS), Tuszynski (Neural Repair), Galasko (Alzheimer's Disease), and Litvan (Movement Disorders). These presentations sparked lively discussions and identified potential areas for cross-disciplinary collaboration.

The BLITZ presentations featured dynamic, fast-paced research highlights from Drs. Desplats, Gholipour, Laverty, Kim-McManus, Morlett-Paredes, and Schulte, offering a glimpse into cutting-edge studies shaping the future of neuroscience.

Attendee feedback was overwhelmingly positive, with many expressing appreciation for the opportunity to connect with colleagues, explore potential partnerships, and gain insights into groundbreaking studies. The event fostered new collaborations, setting the foundation for continued research excellence.

We extend our gratitude to all speakers, and participants for contributing to this successful event. Below is a fantastic image that perfectly captures the day's strong attendance and collaborative spirit of the day. Special thanks to Chi Kim from the ADRC for generously volunteering his time, providing exceptional technical support and capturing the event through outstanding photography, ensuring everything ran smoothly for the organizers. THANK YOU CHI!

Clinical Research Studies: Referrals Welcome!

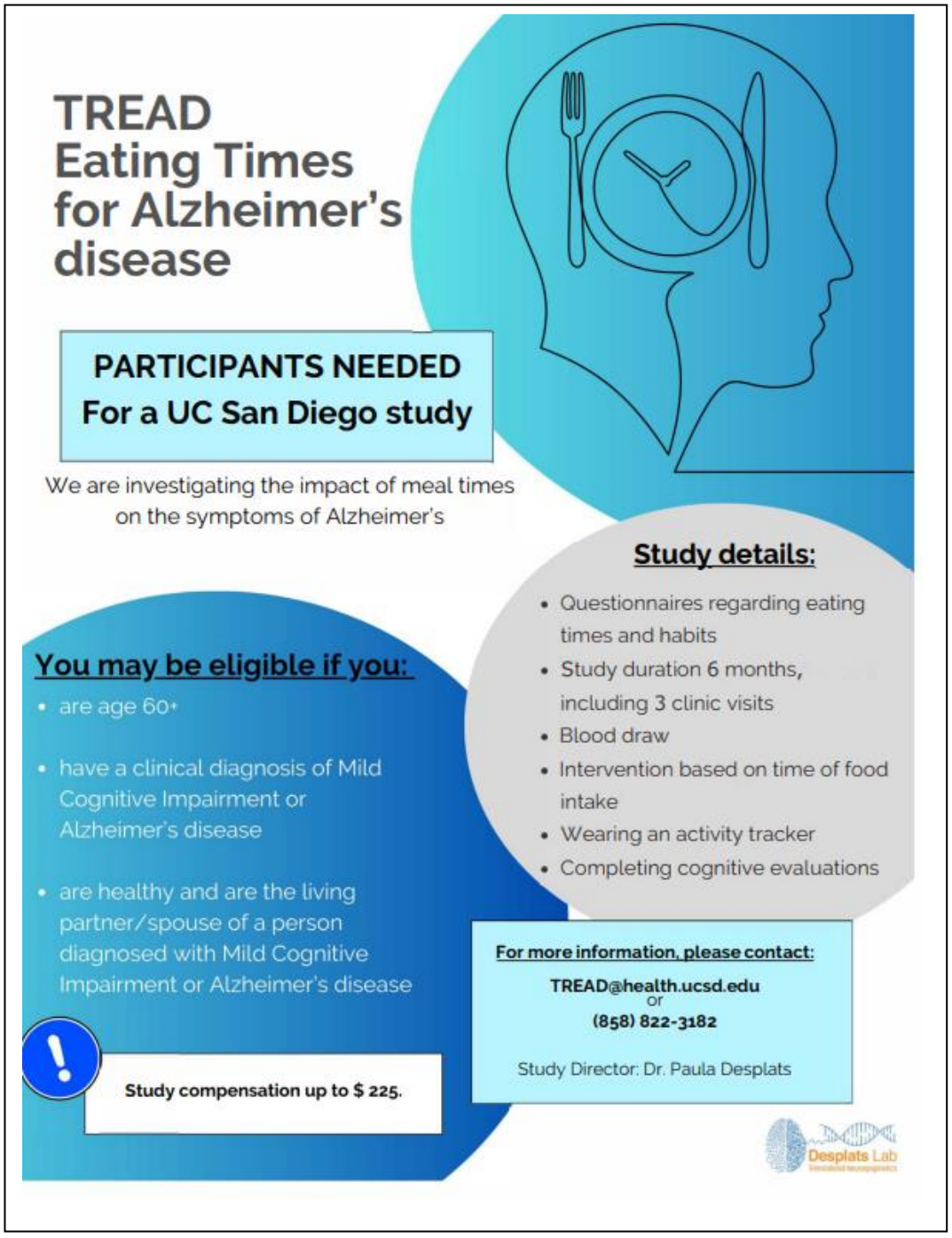
Currently Enrolling

TREAD: Time-Restricted Eating for Alzheimer's Disease

The UC San Diego Alzheimer's Disease Research Center, in partnership with the Desplats Lab, is conducting the TREAD study to explore whether a 14-hour nightly fasting regimen is feasible and beneficial for individuals with mild cognitive impairment (MCI) or Alzheimer's disease (AD). This research builds on promising preclinical findings showing that time-restricted eating can reduce Alzheimer's pathology, improve sleep quality, and enhance cognitive function in animal models (Cell-Metabolism)

The 6-month study involves only three in-person visits, each lasting under 2 hours. These visits include cognitive evaluations, questionnaires, a fasting blood sample, and actigraph monitoring to assess sleep patterns and activity levels. Participants can earn up to $225 in compensation.

The study is currently enrolling individuals aged 60 and older with a clinical diagnosis of MCI or AD. Healthy caregivers of participants are also invited to co-enroll, providing an opportunity to engage in the fasting protocol alongside their loved ones. Participants will receive weekly support from the study team to address any challenges and help establish a sustainable nightly fasting routine.



For more details, visit the ClinicalTrials.gov listing at TREAD Criteria or contact the TREAD team at TREAD@health.ucsd.edu or 858-822-3182.

Clinical Research Studies: Open Studies (cont.)

Enrolling, referrals welcome!

Dr. Corey-Bloom continues recruitment for Enroll0HD: A prospective Registry Study in a Global Huntington's Disease Cohort

- For more information, complete list of inclusion/exclusion criteria or to refer participants please contact: Dr. Corey-Bloom at jcoreybloom@health.ucsd.edu

Inclusion Criteria

- Carriers: Male or female ≥18 years old who carry the HD gene expansion mutation
- Controls: Male and female ≥18 years old participants who do not carry the HD mutation.

Exclusion Criteria

- Individuals with chorea movement disorders in the content of a negative test for the HD gene mutation.
- For Community Controls: Individuals with a major central nervous system disorder, such as stroke, Parkinson's disease, multiple sclerosis, etc. Has 2 or more relatives with history of MSA.

In preparation for the activation of a Phase 2b clinical trial, Dr. Gabriel Leger is prescreening potential participants for a multicenter, randomized, placebo-controlled, double-blind study. This trial will assess the efficacy, safety, and immunogenicity of JNJ-64042056, a phosphorylated tau-targeted active immunotherapy, in individuals with preclinical Alzheimer's disease.

- For more information please contact: Barbara Johnson at b4johnson@health.ucsd.edu

Inclusion Criteria

- Elevated brain tau pathology defined as Braak 3 region of interest standardized uptake value ratio (ROI SUVR) greater than (>) 1.1 on a screening tau PET scan, reviewed centrally by a qualified reader
- Clinical Dementia Rating (CDR) global score of 0 at screening and baseline
- Mini Mental State Examination (MMSE) greater than or equal to (>=) 27 (with educational adjustment)

Exclusion Criteria

- History consistent with or known autosomal dominant AD (mutation identified in the family and/or participant)
- Fulfills diagnostic criteria for Alzheimer's Dementia or non-Alzheimer's Dementia, including, but not limited to Frontotemporal Dementia (FTD), Diffuse Lewy Body Dementia (DLBD), Vascular Dementia (VAD), alcoholic dementia, Parkinson's dementia, Korsakov, Creutzfeldt-Jakob or other prion diseases, Posterior Cortical Atrophy
- Diagnosis of Mild Cognitive Impairment (MCI)

Hidden Figures & Pioneers: Women in Neurosciences

Shinning the light on women whose groundbreaking contributions have shaped the field of Neurosciences

February marked *Black History Month*, and March brings the celebration of *Women's History Month*.

Spring is the perfect time to reflect on the recent celebration of Black History Month in February and the ongoing recognition of Women's History Month. In this spirit, we want to highlight the remarkable contributions of women who shaped the field of neuroscience. These trailblazers not only advanced our understanding of the brain but also paved the way for future generations of researchers and clinicians.

1. **Mary Putnam Jacobi (1842–1906)**
   First woman admitted to the Academy of Medicine in 1872. Physician and advocate for women's health, she championed gender equality in medical education.
2. **Cécile Mugnier Vogt (1875–1962)**
   Neuroanatomist whose work on brain cytoarchitecture advanced understanding of brain structure and function. Her groundbreaking contributions remain foundational in neuroscience. Nominated for the Nobel Prize 13 times.
3. **Rita Levi-Montalcini (1909–2012)**
   Discovered nerve growth factor (NGF), a key protein for nerve cell survival, earning her the 1986 Nobel Prize. Her work revolutionized neurobiology and influenced treatments for neurological disorders.
4. **Brenda Milner (1918–Present)**
   A founder of modern neuroscience, Milner's research with patient H.M. revealed the hippocampus's role in long-term memory, transforming understanding of memory and brain function.
5. **Audrey S. Penn (1934–Present)**
   First woman president of the American Neurological Association in 1994 and an expert in neuromuscular disorders. She also served as Deputy Director of NINDS.
6. **Patricia Goldman-Rakic (1937–2003)**
   Mapped the prefrontal cortex, demonstrating its role in working memory and executive function. Her work advanced understanding of cognitive disorders like schizophrenia and ADHD.
7. **Candace Pert (1946–2013)**
   Discovered the opiate receptor in 1973, explaining how the brain processes pain, pleasure, and addiction. Her work influenced modern pain management and neuroscience. Also known by her fans as the "Goddess of Neurosciences"
8. **Alexa Canady (1950–Present)**
   First African American woman neurosurgeon in the U.S. in 1981. Specializing in pediatric neurosurgery, she advanced treatments for hydrocephalus and spina bifida.

Ethics & Compliance Highlights

COI Training for UC San Diego Researchers

All investigators and senior/key personnel involved in PHS-funded research or with agencies following PHS Financial Conflict of Interest (FCOI) regulations are required to complete the Ethics and Compliance Briefing for Researchers (ECBR) training.

- Before engaging in new PHS-funded research
- Every four years while participating in PHS-funded projects
- Immediately if new to the institution, if UC policies change, or if an individual is found noncompliant

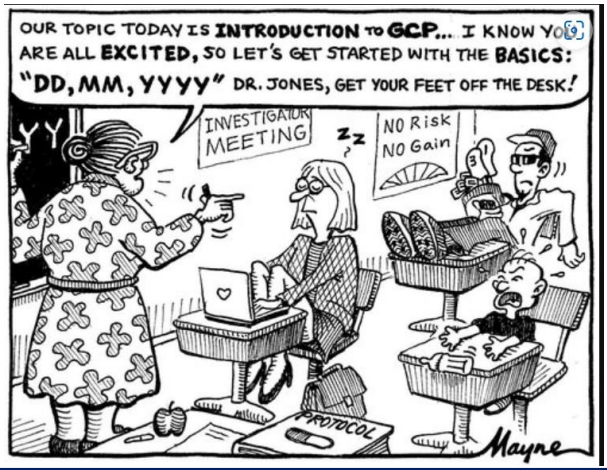
Launched by the UC Office of the President (UCOP) on October 4, 2021, the ECBR training satisfies both the UC training requirement for recognizing ethical and conflict of interest (COI) issues and the NIH COI training requirement.

The course is available through the UC Learning Center and aims to:

- Raise awareness of the UC Statement of Ethical Values and Standards of Ethical Conduct
- Provide guidance on COI regulations when accepting extramural research funds
- Ensure compliance with PHS FCOI requirements

The ECBR online course is available online through the UC Learning Center and takes approximately 30-60 minutes to complete. UC San Diego employees identified by the UC Office of Ethics, Compliance, and Audit Services will receive will receive a system-generated notification. You can also find the assignment listed in your Required Training analysis in the UC LEARNING SINGLE SIGN-ON portal. To access the training: 1. Log in with your Single-Sign-On (SSO) credentials. 2. Locate the ECBR training under your "To Do List or Assigned Training" and 3. Click the course link to begin the briefing.

While industry sponsors do not typically require this training, it can be used to demonstrate an investigator's commitment to COI compliance, especially if COI issues have been identified during an investigator monitoring visit (IMV) or sponsor audit. The sponsor may view the training as a proactive step towards ensuring adherence to ethical research practices. If COI concerns arise during an IMV, investigators can provide proof of training completion as part of a corrective action plan (CAPA) or compliance documentation for sponsors or regulatory bodies.



OIA and ACTRI Updates

ACTRI Announces the Opening of the ACTRI@LindaVista Research Clinic

The ACTRI announced the successful opening of the ACTRI@LindaVista Research Clinic, an extension of the Center for Clinical Research in La Jolla, designed to support pediatric and adolescent clinical trials.

The new 1,800 sq. ft. facility, located near Rady Children's Hospital, was introduced to the research community during a well-attended Open House on February 26, 2025. Attendees had the opportunity to tour the state-of-the-art space, meet the research team, and learn more about the specialized clinical services offered.

With this expansion, ACTRI continues to enhance its support for pediatric research, providing investigators with additional resources to conduct high-quality clinical studies.

For more information about the clinic or to explore potential studies that may be a good fit, please contact Bernadette Cale at bcale@health.ucsd.edu.

New sIRB Attestation Process Implemented – What PIs Need to Know

The Office of IRB Administration (OIA) introduced a new sIRB attestation process, effective July 1 2024, to clarify and reinforce the responsibilities of Principal Investigators (PIs) when an external IRB assumes oversight of a study conducted at UC San Diego or RCHSD. This process ensures that PIs are fully informed of their obligations, supporting the integrity and success of their research projects under external IRB oversight.

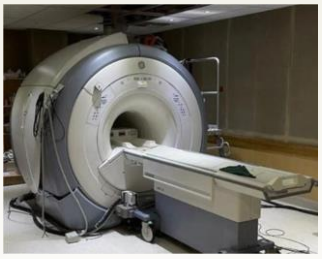
We are sharing this information because many PIs are receiving DocuSign emails related to this attestation but may not be aware of the new requirement or the reason behind the request to complete it.

This process is initiated by the Reliance Team and requires PIs to review reference materials and complete an attestation via DocuSign. Please note that this information will not appear in the Kuali Research Record as some may expect. The attestation serves as a formal acknowledgment of the PI's responsibilities, which include:

- Ensuring compliance with IRB determinations and approvals
- Maintaining site readiness for audits
- Continuing oversight for all study locations
- Promptly reporting any issues or required updates

Additionally, UCSD IRB is seeing increased requests to serve as the sIRB for multi-site studies, and a similar attestation process will apply in those cases. For more details on lead PI responsibilities and the new process, please visit the UCSD IRB reliance page or contact the Reliance Team at: irbrely@ucsd.edu.

MRI Scanner Upgrade CTIMP/ACTRI - What Staff and PIs Need to Know



In March, GE will upgrade both the ACTRI and CTIPM/ROPCC MRI scanners to the MR30.1 RO4 platform. This upgrade will enhance system performance and address and important safety concern. "GE HealthCare has identified that, in certain MR systems, the system-predicted B1+RMS value may exceed the user-prescribed limit when scanning in Low SAR Mode,, potentially resulting in overheating of an MR conditional implant."

Upgrade Schedule:

- ACTRI MRI: March 21, 2025, 3:30 PM – 7:30 PM
- CTIPM/ROPCC MRI: March 26, 2025, 4:30 PM – 8:30 P

Clinical scanning will remain unaffected; however research sequences may be impacted. Although this is a minor update, the imaging center recommends testing research sequences.

Testing Recommendations:

- If your team determines that an imaging protocol requires testing, please contact Fang Zhang for instructions on scheduling testing time with ACTRI imaging operators during business hours. Operator time will be recharged to the study account.
- If your team has its own operator (e.g. trained CRC), testing can be scheduled during weekends or after-hours using the following link: MRI Testing Schedule Weekends and After Hours. There is no recharge for use of space for retests.

Budget Planning Tip:

Moving forward, we recommend that teams include the cost of 1 to 2 annual mandated scanner upgrades when negotiating budgets with sponsors to prevent any financial impact on study accounts.

For questions or assistance, please contact Fang Zhang, Administrative Director, CTIPM.

Upcoming Conferences:

Stay informed about neurology related conferences and other programs that may be of interest.

77th Annual Meeting of the American Academy of Neurology
April 5-9, 2025
San Diego, CA and Online
Registration for the 2025 Annual Meeting in San Diego and online will be available in the fall of 2024

INSAR
International Society for Autism Research

International Society for Autism Research
April 30 – May 3, 2025
Seattle Convention Center
e. info@autism-insar.org

International MSA CONGRESS
Presented by MISSION MSA

Mission Multiple System Atrophy
May 9 – May 10, 2025
Hyatt Regency Cambridge, MA
info@missionmsa.org

International Association of Parkinsonism and Related Disorders

International Parkinson and Movement Disorder Society
May 1-7, 2025
New York City, NY
www.iaprd-world-congress.com

ALZHEIMER'S ASSOCIATION
AAIC 25

Alzheimer's Association
July 27-31, 2025
Metro Toronto Convention Centre
aaic@alz.org

Research Administration Contacts:

Office of the Vice Chair of Human Clinical Research

General Inquiries: irubio@health.ucsd.edu
Tuesdays 9:00 am to 11:00 am - Zoom Meeting Link
Fridays 9:00 am to 11:00 am – in person/4w-217

UCSD Office of IRB Administration (OIA)

General Inquiries: IRB@ucsd.edu | 858-246-4777
Reliance Inquiries: IRBRely@ucsd.edu

Office of IRB Administration – Zoom link and date https://ucsd.zoom.us/j/95259128378
March 12, 2025

Office for Human Research Protections (HHS)

OHRP offers this comprehensive training on human research protections based on the requirements of the revised Common Rule (or 2018 Requirements) HHS Human Research Training. A printable completion certificate is available at the conclusion of each lesson.