

**NIDUS**Network for Investigation of
Delirium : Unifying Scientists

March 2022 NIDUS Newsletter

Network for Investigation of Delirium: Unifying Scientists

In this issue:

- 10th Annual NIDUS Delirium Boot Camp – Call for Applicants!
- Recent Mentoring Webinars Recap
- 2022 NIDUS II Collaborative Awards
- New NIDUS Blog Posts

Apply to attend the 2022 NIDUS Delirium Boot Camp

Our 10th Annual NIDUS Delirium Boot Camp ***"Building Blocks to Clinical Trials"*** will take place Sunday, November 13 to Tuesday, November 15, 2022 at the University of North Carolina-Chapel Hill.

Applications for the 2022 Boot Camp are now being accepted until **July 22, 2022 at 5pm EST**. Visit the [NIDUS Delirium Boot Camp page](#) to download and complete the 2022 NIDUS Boot Camp Application today.

2022 NIDUS Mentoring Webinars

January Webinar - Career Development Award Research

*Featuring Dr. Thomas M. Gill, Dr. Esther Oh, and Dr. Nicholas Reed;
moderated by Dr. Jan Busby-Whitehead*

Dr. Gill kicked off this mentoring session by offering guidance on identifying a

career development plans, research plans, and the importance of specific aims.

Next, Dr. Reed shared stories from preparing and securing his own K23 grant. Flowing out of an experience with a personal friend, Dr. Reed's K23 changed direction from his original plan. Not only that, but he was funded on his first try. In addition, Dr. Oh spoke about the process of helping Dr. Reed build his team and develop his submission.

Preparing the Grant

- Grant writing training
 - Graduate Training in Clinical Investigation (PhD program)
 - Two grant writing courses (quarter 2, and quarter 4) separated by intense methodology courses
 - Conceptually: writing the framework and then filling in the approach with the appropriate course sequence
 - Lots of feedback from peers without any experience in your field

1/26/2022 Cochlear Center for Hearing and Public Health

Nicholas Reed

Dr. Nicholas Reed presents at the January 26 webinar

February Webinar - Being Truly Responsive: How to Win Over Your Reviewers

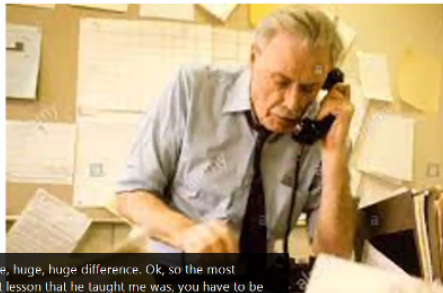
Featuring Dr. Sharon Inouye; moderated by Dr. John Devlin

In this mentoring session, Dr. Inouye introduced a response method called 'the Kassirer Method.' Based on instruction and mentorship from Dr. Jerome Kassirer, a former editor of the New England Journal of Medicine, she encouraged session attendees to get 'into the head of the editor or reviewer.' Also, Dr. Inouye advised attendees not to treat the review as a personal attack; instead, see it as a collaboration and a chance to clarify the paper.

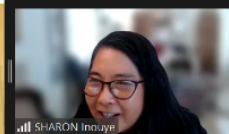
She also highlighted the importance of changes to the manuscript, even if small, for all comments. She also offered concrete examples of how to respond to reviewers. In addition, Dr. Inouye said this approach has increased her acceptance rate from less than 50% to nearly 100%.

The most important lesson...

- Put yourself into the mind of the harried editor—juggling so many papers and balls.
- Keep this image in your mind at all times as you respond
- Understand that your job is to make the re-evaluation of your paper as easy and painless for the editor as possible



So, a huge, huge, huge difference. Ok, so the most important lesson that he taught me was, you have to be in the head.



Dr. Sharon Inouye presents at the February 16 webinar

March Webinar - Pilot Awards: Developing a Competitive LOI/Submitting a Successful Application

Featuring Dr. Michael Avidan and Dr. Tammy Hshieh; moderated by Dr. John Devlin

In this mentoring session, Dr. Michael Avidan shared strategies for developing strong pilot grant LOIs and applications. Using examples from prior NIDUS pilot grant awardees, he compared and contrasted pilots and feasibility studies. Also, Dr. Avidan presented NIDUS resources which can assist applicants in their pilots.

Next, Dr. Tammy Hshieh shared from her own personal experience with NIDUS pilot awards. She detailed the process of reevaluating her original concept to better fit her pilot study. Dr. Hshieh also talked about critical choices like which delirium instruments to use and how she refined the scope of her study.



NIDUS | Objectives

- On Pilot and Feasibility Studies
- How to develop strong NIDUS II LOIs
- How to develop strong NIDUS II pilot / feasibility grant applications
- An example of a NIDUS funded pilot / feasibility grant
- Your questions about your current pilot award application or the NIDUS II pilot / feasibility LOI/application process



We're going to try to cover these areas pretty briefly, and my main focus actually is going to be giving you some conceptual insight.



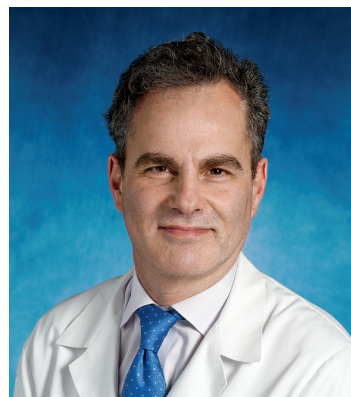
Dr. Michael Avidan presenting at the March 7 webinar

2022 NIDUS II Collaborative Awards

Below are the recipients of our 2022 Collaborative Awards along with a summary of their proposed research.

Machine Learning Prediction and Detection of Intensive Care Unit Delirium

Robert D Stevens, MD, Johns Hopkins University School of Medicine



Collaborators:

Kirby Gong, MSE (Johns Hopkins)

Heidi L. Lindroth, PhD, RN (Mayo Clinic)

There is a need for pragmatic models which can accurately and reliably predict the onset of delirium in critically ill patients. Such models could guide the delivery of targeted therapies aimed at reducing delirium and its deleterious downstream effects.

We hypothesize that specific features derived from high-resolution clinical and physiological data routinely acquired in the ICU are signature of delirium risk, and the latter are identifiable using machine learning. We have demonstrated this using an external multisite dataset.

Here, we will leverage a granular data platform acquired at Johns Hopkins called Precision Medicine Analytics Platform (PMAP) and validate using a similar dataset from co-investigators at the Mayo Clinic. The core objective is to generate discriminative tools for clinical decision support and intervention. Implementation of the latter is expected reduce the burden of ICU delirium and associated harm and costs.

Delirium, Long-term Cognitive Impairment and Bacterial Infection-induced Endothelial Proteopathy

*Department of Anesthesiology
University of Alabama at Birmingham*



Collaborators:

Brant Wagener, MD, PhD (University of Alabama)

Christian Balabanoff-Acosta, MD (University of Alabama)

Troy Stevens, PhD (University of South Alabama)

Michael T. Lin, PhD (University of South Alabama)

Multi-center clinical studies have implicated that ICU survivors and especially patients who develop hospital-acquired bacterial pneumonia suffer from pervasive delirium and long-term cognitive impairment.

Dr. Pittet has developed a scientific collaboration with Drs. Stevens and Lin from the University of South Alabama to better understand how bacterial infections contribute to end-organ injury in rodents and humans. Together, they have discovered that pneumonia-causing bacterial pathogens elicit the production of lung endothelial cell-derived amyloids (EC-amyloids).

Lung endothelia exposed to clinical bacterial isolates produce and release cytotoxic beta-amyloid and tau that are reminiscent of neuronal species. In rodents, these lung-derived EC-amyloids self-replicate, propagate among lung ECs with prion-like characteristics, are transmissible between animals, cause endothelial cytotoxicity, hinder vascular repair following injury, impair learning, and damage the brain. Importantly, these cytotoxic EC-amyloids can also be recovered from bronchoalveolar lavage fluid, plasma and cerebrospinal fluid during bacterial pneumonia in humans.

Based on the results of our mechanistic studies in rodents, this project tests the central hypothesis that neurotoxic EC-amyloids released from the lung endothelium following bacterial pneumonia in ICU patients will be detected in the bloodstream of these patients for weeks after recovery from bacterial pneumonia and may be one of the mechanisms that explain the high incidence of delirium and long-term cognitive impairment in these patients.

in patients with postoperative delirium (POD) and melatonin

Stéphanie Sigaut, MD, PhD

Praticien Hospitalier, service d'Anesthésie

Réanimation. Hôpital Beaujon - Hôpitaux Universitaires

Paris Nord Val de Seine



Collaborators:

Pierre Gressens, MD, PhD (Hopital Robert Debre)

Philippe Montravers, MD, PhD (Assistance Publique Hopitaux de Paris)

Pauline Glasman, MD (Assistance Publique Hopitaux de Paris)

Raphaël Desal, MD (Assistance Publique Hopitaux de Paris)

Patients with postoperative delirium (POD) may exhibit perturbations of inflammatory response that may be prevented by melatonin. To answer this hypothesis we plan an ancillary study of DELIRLESS randomized controlled trial (NCT04335968). In this RCT, patients above 70 years old with fractures of a lower limb are randomized into 2 groups: melatonin 4mg or placebo every night from anesthetist preoperative visit until d5 after surgery.

At postoperative d1, blood withdrawal is performed and the following analysis will be performed for deep phenotyping of the inflammatory response: 1/ Flow cytometry for phenotypical and functional characterization of peripheral blood mononuclear cells (PBMC) populations; 2/ RNA-Seq for analysis of PBMC transcriptome; 3/ Luminex immunoassay for detection and quantification of cytokines in plasma; 4/Reactive Oxygen Species measurement in peripheral blood by luminometry.

Association of these results with POD diagnosed by the CAM score during the first 10 days after surgery will be analyzed and the effect of melatonin perioperative administration will be evaluated.

Effects of postoperative delirium on older surgical patients

Brian O'Gara, MD, MPH

BIDMC Anesthesia Critical Care

Collaborators:

Kimberly Rengel, MD (Vanderbilt)

Christopher Hughes, MD (Vanderbilt)

Alvaro Pascual Leone, MD, PhD (Harvard)

Edward Marcantonio, MD (Harvard)



Postoperative delirium affects 15-50% of older surgical patients and increases the risk of postoperative complications, hospital mortality and long-term cognitive dysfunction including dementia. There remains a critical need for interventions to prevent postoperative delirium. Increasing preoperative cognitive reserve via computerized cognitive prehabilitation is an innovative yet unproven patient-led intervention with the potential to prevent PD.

We believe that a future clinical trial of computerized cognitive prehabilitation to prevent postoperative delirium is warranted but faces significant threats to feasibility, implementation, and validity. To resolve these challenges, we will form a multidisciplinary collaboration of anesthesiologists, geriatricians, and cognitive neurologists to refine and enhance a computerized cognitive prehabilitation intervention for a future clinical trial and test whether these improvements can increase adherence.

A multi-method study to adapt existing DSD (delirium superimposed on dementia) contents

Shih-Yin Lin, MM, MPH, PhD

Senior Research Scientist/Project Director

NYU Rory Meyers College of Nursing

**Collaborators:**

Abraham A. Brody, PhD, RN, FAAN (NYU)

Donna M. Fick, PhD, RN, GCNS-BC (Penn State)

Dena Schulman-Green, PhD (NYU)

Jason Fletcher, PhD (NYU)

Shih-Yin Lin's research interests include dementia-friendly communities, non-

She currently provides scientific and operational leadership on the NIH-funded, 25-site Hospice Advanced Dementia Symptom Management and Quality of Life Trial (PI: Brody) that tests the effectiveness of an agency-wide quality improvement program, Aliviado Dementia Care, on dementia symptom management, including behavioral and psychological symptoms of dementia, pain, and delirium.

The main components of Aliviado Dementia Care include interdisciplinary dementia care training, symptom management algorithms, assessments, care plans, caregiver education materials, and an mHealth app that provides remote access to the program.

In her NIDUS II 2022 pilot award application, Dr. Lin proposes a multi-method study to adapt the existing DSD contents in the currently clinician-led Aliviado Dementia Care program into a family-centered, caregiver-administered behavioral intervention to improve DSD knowledge, detection, and prevention in the community.

Delirium as a modifiable risk factor for dementia – a large, population based cohort study

Bjørn Erik Neerland, MD, PhD

Overlege, postdoktor forsker

Geriatrisk avdeling, Oslo Universitetssykehus



Collaborators:

Christian Myrstad (Vestfold Hospital Trust)

Geir Selbæk (Vestfold Hospital Trust)

Bjørn Heine Strand (Norwegian Institute of Public Health)

Torgeir Bruun Wyller (Oslo University Hospital)

The aim of this study is to extensively study inter-relations between delirium and dementia. The Health Study in Trøndelag (HUNT) is a population-based cohort study with four assessments (HUNT1-HUNT4) over up to 40 years follow-up (1984 to 2023). In HUNT4 (2017-2019), participants ≥ 70 years

dementia (also subtyped).

The Ageing in Trøndelag (AiT) study is an ongoing four-year follow-up of the entire HUNT4-70+ cohort. It applies the same protocol and will be completed in 2023. Virtually all established risk factors for dementia were assessed at HUNT1-HUNT4.

There are two hospitals in the HUNT catchment area, and specially trained researchers will identify delirium, number of episodes, severity and duration of delirium by scrutinizing the electronic health records, for all participant admissions from the period 2005-2023, applying a validated method. We will also record precipitating causes, reasons for admission, and acute illness severity.

We will merge these data with the data in HUNT1-4, HUNT4-70+, AiT and relevant health registers, and comprehensively study possible interactions between delirium and dementia. Long follow-up will reduce reverse causation bias. Plasma, serum and microbiota are available and genotyping has been done, making it possible to include biomarkers in the analyses.

Randomized placebo-controlled trial of perioperative fluvoxamine

Ben Palanca, MD, PhD

Washington University School of Medicine, St. Louis

Collaborators:

Robert D. Sanders, MBBS, PhD (University of Sydney)

Angela Reiersen, MD, MPE (Washington University)

Sarah Kendall Smith, MD, PhD (Washington University)



Dr. Ben Palanca at Washington University School of Medicine in St. Louis proposes a safety and feasibility study of a randomized placebo-controlled trial of perioperative fluvoxamine. In collaboration with Dr. Robert Sanders at University of Sydney, the transcontinental collaborative investigation will establish the infrastructure for a larger investigation to probe whether the



Circadian rhythms, acute inflammation, and neurological disease in postoperative delirium

S. Kendall Smith, MD, PhD

Assistant Professor of Anesthesiology & Critical Care Medicine

Washington University School of Medicine, St. Louis

Collaborators:

Rosemary Braun, MD, MPH (Northwestern)

Robert Sanders, MBBS, PhD (University of Sydney)

Ben Palanca, MD, PhD, MSCI (Washington University)

Dr. Kendall Smith aims to probe the temporal interplay between disrupted circadian rhythms, acute inflammation, and neurological disease in the development of postoperative delirium.

Her proposal brings together a multidisciplinary team including Dr. Rosemary Braun at Northwestern University, Dr. Robert Sanders at the University of Sydney, and Dr. Ben Palanca at Washington University and adds a molecular arm to an ongoing NIH-funded investigation of relationships among delirium and electroencephalographic markers of sleep and wakefulness.

Her proposal will lay the groundwork for elucidating the pathophysiology of delirium at a molecular level and for identifying novel therapeutic targets regulating circadian rhythms.

Do Polygenic Risk Scores of Alzheimer's Disease and Related Dementias Identify the Delirium-Vulnerable Brain?

Sarinnapha Vasunilashorn, PhD



Collaborators:

Miles Berger, MD (Duke)

Yi-Hsiang Hsu, ScD (Harvard)

Long Ngo, PhD (Harvard)

This clinical and translational project uses four unique datasets of older adults undergoing major elective surgery to advance our understanding of the potential shared pathophysiology underlying the delirium-AD/ADRD relationship.

The goal of this proposal is to test the hypothesis that polygenic risk for Alzheimer's Disease and Alzheimer's Disease-Related Dementias (AD/ADRD) identifies individuals with a "vulnerable brain," who may be predisposed to bad outcomes, including delirium, cognitive decline, and AD/ADRD, in the presence of an inflammatory insult (e.g., surgery or infection).

Our findings will inform targeted strategies to identify older adults vulnerable to adverse brain-related outcomes under stress and high inflammation, thereby potentially leading to new interventions to prevent delirium and reduce AD/ADRD.

Measures of pre-surgical electroencephalography (EEG) combined with cognitive function***Mouhsin Shafi, MD, PhD***

Associate Professor of Neurology, Harvard Medical School; Director, Berenson-Allen Center for Noninvasive Brain Stimulation

**Collaborators:**

Miles Berger, MD (Duke)

Alvaro Pascual-Leone, MD (Harvard)

M. Brandon Westover, MD (Harvard)

Delirium is common in hospitalized individuals, and is associated with cognitive

reliable mechanistic biomarkers are sorely needed. Recently, our group found that simple measures of the pre-surgical electroencephalography (EEG), in combination with simple tests of cognitive function, might help predict which patients develop post-operative delirium.

In the proposed project, we will further evaluate the relationship between baseline EEG / cognitive function and post-operative delirium, and validate these findings in an independent cohort of older surgical patients recruited from another center. The proposed project will thus provide evidence that simple, easy-to-obtain baseline measures of cerebral electrophysiology and cognitive function can predict post-operative delirium with high accuracy.

This work will provide key data for subsequent multi-site studies prospectively assessing the utility of this approach as an individualized predictive biomarker of delirium risk, as well as studies evaluating whether these measures can predict long-term cognitive decline and risk of developing dementia.

Visit the NIDUS Blog

[The NIDUS Blog](#) features posts on a variety of topics related to delirium research with a focus on the core NIDUS II aims. Most blogs are authored by NIDUS Bootcamp alumni and Pilot Grant Awardees. The latest blog post by Brian O’Gara, MD is on “[Cognitive Prehabilitation to Prevent Postoperative Delirium](#)”

NIDUS posts new Blogs at least monthly. We encourage you to regularly check out new NIDUS Blog posts.



Welcome to the NIDUS Blog

Monthly posts on new topics in delirium research

[Back to NIDUS Home](#)

Delirium Research Hub Spotlight: Colm Cunningham, PhD

Posted on November 4, 2021 by nidus_delirium

Every few months, the Delirium Research Hub selects an investigator and research study included in the Delirium Research Hub to feature as a Spotlight Investigator. This month, we are featuring Dr. Colm Cunningham for his study "Brain Vulnerability, Inflammation, and Energy Metabolism in Animal Models". His research focuses on the role of systemic inflammation on [...]

Subscribe to our mailing list

* indicates required

Email Address *

First Name *

[Privacy](#) [Terms](#)

Other NIDUS Communications

In addition to the NIDUS Blog, we offer regular updates on delirium-related news, events and research through social media, our email listserve, and newsletters.

- [Announcements](#) - Visit this page for News and Announcements
- [Email Listserve](#) - Subscribe to our email list for regular updates delivered straight to your inbox
- [Newsletters](#) - Find previous editions of NIDUS newsletters on our website
- [Social Media](#) – For all the latest updates, follow NIDUS on Twitter ([@nidus_delirium](#))

If you're interested in contributing to NIDUS communications with a blog post, newsletter item, or social media post, [contact us](#).



Follow us on Twitter



Visit our Website



Thanks to all who have [signed up](#) to become a NIDUS member
or to receive our [announcements and newsletters](#).

NIDUS is always looking to reach new audiences –
please forward this newsletter to a colleague or mentee!

Please visit our [website](#) for more information on NIDUS.

Follow NIDUS on [Twitter: @NIDUS_delirium](#).

About NIDUS

NIDUS is a collaborative research network dedicated to spurring innovation and new advances in delirium research through development of new research and measurement resources, training opportunities, pilot funding and dissemination of information. It is funded through an award from the National Institutes of Health/National Institute on Aging (grant no. R33AG071744).

Find Out More

NIDUS © 2017. NIDUS is funded through grant no. NIA R33AG071744 (Inouye), *All rights reserved.*

Want to change how you receive these emails?
You can update your preferences or unsubscribe from this list.

Subscribe

Past Issues

Translate ▼

This email was sent to <<Email Address>>

[why did I get this?](#) [unsubscribe from this list](#) [update subscription preferences](#)

NIDUS · Aging Brain Center, Institute for Aging Research · 1200 Centre St · Boston, MA 02131 · USA

