Join Us for the

3rd Annual Meeting of the American Delirium Society

June 2–4, 2013
Omni Severin Hotel
40 West Jackson Place
Indianapolis, Indiana

Learn from colleagues and contribute to scientific ideas regarding delirium etiology, state of the art clinical practice and groundbreaking research presentations. Meet like-minded clinicians and scientists from many different disciplines and specialties; develop friendships and research partnerships. This is a great networking opportunity!

IMPORTANT DATES

- January 7, 2013 - Submission deadline for abstracts for oral presentations and symposia/workshop
- March 3, 2013 - Submission deadline for abstracts for posters
- April 28, 2013 - Early registration ends

http://www.americandeliriumsociety.org/Call_for_Proposals.html

www.americandeliriumsociety.org

This issue

P2  2013 Conference Schedule, Keynote Speakers
P3  Research Committee Update
P4  New and (frequently) used tools and resources on our website
P5-6  ADS Member Activity
P7  ADS members participate in the European Delirium Association 2012 meeting
P8-10 Animal Model of Delirium
The American Delirium Society consists of a broad array of health care professionals from diverse subspecialties and healthcare disciplines. Our goals are: to improve recognition, treatment, and prevention of delirium among patients everywhere within the healthcare system.

A PRECONFERENCE COURSE IS OFFERED FOR CLINICIANS OF ALL BACKGROUNDS
- 6/2/13 13:00 – 17:00
Approach to the Delirious Patient
This course includes a hands-on, practical approach to the recognition, treatment and prevention of delirium in the hospitalized patient.

THE CONFERENCE SCHEDULE
- 6/2/13, 18:30 – 22:00 Welcome Reception and Presidential Keynote Address
- 6/3/13, 08:00 – 18:00 Scientific Program including Oral Presentations and Symposia
- 6/3/13, 18:00 – 21:00 Poster Session
- 6/4/13, 08:00 – 18:00 Scientific Program including Oral Presentations and Symposia

Keynotes
Dr. Kenneth Rockwood and Dr. Donna Fick will be the keynote speakers this year.

“We are delighted and honored to have these two leaders in the field speak at the upcoming ADS meeting. Their participation is a testament to the importance of delirium and the growth of the Society.”
- Dr. Karin Neufeld, Chair of 2013 Meeting

Kenneth Rockwood, MD, FRCPC, FRCP
Professor of Medicine (Geriatric Medicine & Neurology) Dalhousie University, Kathryn Allen Weldon Professor of Alzheimer’s Research University, Department of Medicine, QEII Health Sciences Centre, Halifax, Nova Scotia Canada

Donna Fick, PhD, GCNS-BC, FGSA, FAAN
Professor of Nursing; Professor of Medicine, Department of Psychiatry; Co-director, Hartford Center of Geriatric Nursing Excellence at Penn State; Editor, Journal of Gerontological Nursing

GET INVOLVED: Join a committee
The ADS would like to invite you to be part of its exciting growth. We hope that the benefits of working with your peers in this burgeoning area will far outweigh the time commitment necessary to make the ADS a success. Please join this cadre of current and future leaders in delirium, while helping the ADS!
American Delirium Society
Research Committee
Update

The American Delirium Society includes in its mission statement (http://www.americandeliriumsociety.org/About_ADS.html) the responsibility of fostering delirium research and implementation into clinical practice.

To facilitate this objective, the ADS leadership created the Research Committee with the goal of establishing the home of delirium research and collaboration within the organization. The research committee hopes to foster collaboration among researchers across the organization, promote the innovation of research tools, and maximize the impact of clinical trials in delirium.

The activities of the committee are generated within one of the above goals, with capabilities expected to grow along with the organization as a whole. Current members of the research committee include the following ADS members:

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tr>
<td>Noll Campbell, Chair</td>
<td>Purdue University</td>
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<tr>
<td>Jim Rudolph</td>
<td>Harvard University/Boston VAMC</td>
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<tr>
<td>Malaz Boustani</td>
<td>Indiana University</td>
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<td>Babar Khan</td>
<td>Indiana University</td>
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<tr>
<td>Michael LaMantia</td>
<td>Indiana University</td>
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<tr>
<td>Jin Han</td>
<td>Indiana University</td>
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<td>Michelle Weckman</td>
<td>Vanderbilt University</td>
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<td>Sapna Kudchadkar</td>
<td>Iowa University</td>
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<tr>
<td>Ann Gruber-Baldini</td>
<td>Johns Hopkins University</td>
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<tr>
<td>Nathan Brummel</td>
<td>University of Maryland/Baltimore</td>
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<td>Rakesh Arora</td>
<td>Vanderbilt University</td>
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<tr>
<td>Charlie Brown</td>
<td>University of Manitoba</td>
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<td>Eduard Vasilevskis</td>
<td>Johns Hopkins University</td>
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In its early activity a subset of the committee has accepted the responsibility of creating a statement that identifies the need for improved coding practices within the existing diagnostic and reimbursement criteria. The need arises from the variability in screening and coding practices that currently exist in the clinical environment, limiting the progress of clinical care, research and education.

The research committee plans to present the draft at the annual meeting in Indianapolis in 2013, subsequently publishing this work as a white paper on behalf of the ADS.

Any existing member of the ADS who wishes to engage with the research committee should contact the committee chair, Noll Campbell, at campbeln@iupui.edu. Several opportunities exist to participate in the current activity and generate new capabilities of the committee and the organization.
Helpful Online Resources and Links on the ADS website:
http://www.americandeliriumsociety.org/ResearchandResources.html

Tools

**Anticholinergic Burden Scale**

Confusion Assessment Method- ICU Form & Instructions [www.icudelirium.org](http://www.icudelirium.org)

Delirium Rating Scale DRS-R-09 (Please email Paula Trzepacz for access to this scale: TRZEPACZ_PAULA_T@lilly.com)

**eCHAMP Delirium Protocol- Physician**

**eCHAMP Delirium Protocol- Nurse**

Resources

University of Iowa Carver College of Medicine, James Amos, MD Delirium: The Skinny [http://medicine.uicapture.uiowa.edu/Panopto/Pages/Viewer/Default.aspx?id=486ea41c-ad76-42da-a26a-0087a957019d](http://medicine.uicapture.uiowa.edu/Panopto/Pages/Viewer/Default.aspx?id=486ea41c-ad76-42da-a26a-0087a957019d)

Clinical Trials Search [http://clinicaltrials.gov](http://clinicaltrials.gov)

Indianapolis Discovery Network for Dementia [www.indydiscoverynetwork.org](http://www.indydiscoverynetwork.org)

Vanderbilt University Delirium Website [www.icudelirium.org](http://www.icudelirium.org)

**Delirium education module** from the Geri-Ed Programs at the University of Maryland, Baltimore

Videos on Delirium: Quiet and Excited

*Agitated Behaviors Among Older Hospitalized Patients,* and

*Agitated Behaviors Among Older Nursing Home Residents*

*(photos below are from this video)*
Several ADS members presented a preconference course at this year’s

ACADEMY OF PSYCHOSOMATIC MEDICINE • 59th Annual Meeting

Bioethics at the Interface of Psychiatry & Medicine

The preconference, which was in Atlanta, Georgia (November, 2012), was titled,

“Delirium: Novel Perspectives on Etiology, Diagnosis, Prevention, Treatment, and Long-Term Outcomes”

Faculty included

José R. Maldonado, MD, FAPM, FACFE (Stanford University School of Medicine, Stanford, CA)

J.J. Rasimas, MD, PhD (Penn State College of Medicine; NIMH, Bethesda, MD)

Karin J. Neufeld, MD, MPH (Johns Hopkins University School of Medicine)

O. Joseph Bienvenu, MD, PhD (Johns Hopkins University School of Medicine, Baltimore, MD)

Yesne Alici, MD (Memorial Sloan-Kettering Cancer Center, New York, NY)

Special thanks to the Conference Planning Committee for all their hard work and time so far, and the efforts they are continuing to put out to make the 2013 conference a success.
Brainstorming Delirium Team

Karen Reynolds, DNP, CNS-BC, Advanced Practice Nurse at Sarasota Memorial Health Care System, is one of 11 Fellows nationwide selected to participate in the Geriatric Nurse Leadership Academy (GNLA), an 18-month mentored leadership development experience presented by the Honor Society of Nursing, Sigma Theta Tau International (STTI).

At Sarasota Memorial, Reynolds is leading the hospital’s newly formed Brainstorming Delirium Team to develop innovative ways to manage vulnerable older patients who are affected by delirium while being treated in the hospital for acute medical needs. The team’s goals include the prevention, early identification, best practice and evidence-based treatment and interventions for delirium. Desired outcomes include: decreased length of stay, lower hospital readmission rates and overall improvement in the potential long-term effects of delirium on their quality of life.

Delirium Project at Summa Health System is a finalist for ASHP Foundation’s Award for Excellence in Medication Safety

A delirium project performed at Summa Health System in Akron, Ohio was awarded one of the American Society of Health System Pharmacy Foundation’s finalist awards for Excellence in Medication Safety. An interdisciplinary health care team developed a protocol to identify patients at risk for delirium, implement methods to prevent delirium, guide prescribers to the appropriate assessment when delirium occurs and use appropriate medication for behavioral management if necessary. A pharmacist led the group to improve the medication-use component of the program. Medication initiatives included development of evidence-based interventions, use of technology to efficiently support 24-hour care collaboration between physicians and all pharmacists, and administration of an education program for pharmacists. Additionally, pharmacists were involved in the education of nurses, physicians and other support personnel.

ADS member Susan M. Fosnight, B.S.Pharm, RPh, BCPS, CGP, led the multidisciplinary group that performed the study.

For full details of the study, see Allen KR, Fosnight SM, Wilford R, et.al. Implementation of a system-wide quality improvement project to prevent delirium in hospitalized patients. JCOM 2011; 18: 253-258. fosnighs@summahealth.org
ADS Represented at EDA (European Delirium Association)

Across the Atlantic, the European Delirium Association held its Annual Congress in Bielefeld, Germany. Two ADS board members attended the meeting as delirium ambassadors from the United States. Both Dr. Karin Neufeld and Dr. Jim Rudolph presented at the EDA. Future collaboration with the EDA is likely.

October in Germany is known for many things...Oktoberfest, crop harvest, beer... and now delirium. The EDA Congress was hosted in Bielefeld by Christine Thomas and Stefan Kiesel. The EDA was sponsored by Bethel, a religious foundation devoted to improving the lives of those with disabilities and a world renown center for epilepsy research. In the auditorium of Bethel, our ADS members spread tidings of goodwill across the divide.

Karin Neufeld, ADS president elect, presented original data in her talk entitled "Delirium Diagnosis Standards in Research Settings." Jim Rudolph presented "Delirium Diagnosis in the United States". Both representatives called for increased collaboration to improve the standardization of delirium diagnosis in research studies.

The reception for such a collaboration was well received. Dr. Alasdair MacLullich stated, "As our societies are so focused on improving delirium science, collaboration on such an important topic just makes sense." Dr. Neufeld was also pleased with the reception, "Our EDA colleagues have a genuine interest in advancing delirium science and we have much to learn from each other." In the coming months, the ADS hopes to establish a working group to outline the key elements that should be requisite in all future delirium research. Interested parties should contact Jim Rudolph at jrudolph@partners.org.

Photo submitted by EDA member Daniel Davis, Department of Public Health and Primary Care, University of Cambridge. He will be using this on the EDA website. “Although it looks like a sunset (which is usually associated with ageing) it’s actually a sunrise (which represents new beginnings. And the clouds are like the clouding of consciousness, which is a reminder of the task we have as a research and advocacy organization.”
As a young organization, we depend on the help and support of members to help us maintain and grow our financial strength so that our mission can be achieved. To become a member, go to www.americandeliriumsociety.org

Existing memory impairment is a significant predisposing factor for delirium but how this prior impairment interacts with acute triggers to induce delirium is unknown. A lack of relevant animal models has left many key questions in delirium pathophysiology unanswered. We have recently developed mouse models to interrogate interactions between prior degenerative pathology and superimposed systemic inflammation, demonstrating that mild systemic inflammation induces acute and transient working memory deficits, but only in animals with prior pathology (Murray et al., 2012). This ‘prior pathology’ consists of robust synaptic loss in the hippocampus and thalamus, induced by the ME7 model of prion disease, and microglia (brain macrophages) that are primed by the primary pathology to produce exaggerated responses to subsequent inflammatory insults (Cunningham et al., 2005).

Caution about the use of this prion disease model has perhaps distracted from what these data unequivocally show: that where there is existing pathology or ‘vulnerability’ in particular regions of the brain, systemic inflammation can selectively disrupt function in those regions more easily than it can in normal animals, recapitulating the observation that systemic infection can produce profound CNS effects in some patients while leaving others unaffected. Nonetheless, there are good reasons to try to take this observation out of the prion disease setting and replicate it in a neuroanatomical and neurochemical setting more relevant to clinical delirium.

There are both hypocholinergic and neuroinflammatory hypotheses of delirium but whether these are parallel and/or interacting is largely unknown. We recently published findings in *The Journal of Neuroscience* (Field et al., 2012) showing that systemic inflammation induced by bacterial endotoxin (LPS) induces acute working memory deficits, but only in animals with prior pathology in the basal forebrain cholinergic nuclei (BFCN). The BFCN, which comprises the medial septum, the diagonal bands and the nucleus basalis (see Figure 1), is the source of most acetylcholine in the forebrain and this area degenerates markedly during Alzheimer’s disease. We used an immunotargeted ribosomal toxin (p75NTR-saporin) to specifically lesion approximately 20% of the BFCN. This had no effect on working memory function, but 40 days post-lesioning systemic LPS then induced working memory deficits, only those animals with prior lesions.

Despite our prior implication of primed microglia in LPS-induced cognitive impairments, 40 days after p75NTR-saporin lesions, microglia showed equally robust responses to systemic inflammation in lesioned and normal animals. Thus the acute cognitive deficits occur independently of microglial priming.

In the absence of microglial priming the ‘vulnerability’ in these animals probably represents a neuronal susceptibility to disruption of function. We showed, using the acetylcholine muscarinic receptor antagonist scopolamine, that the T-maze task used in these studies was dependent on cholinergic function. This demonstrates that acute cholinergic failure induces the same deficits as systemic inflammation superimposed on prior cholinergic pathology and thus also shows parallels to the original atropine rodent cholinergic model of delirium (Trzepacz et al., 1992). More importantly, we demonstrated that treatment with the acetylcholinesterase inhibitor donepezil, 1 hour after LPS, protected against the acute cognitive deficits.

Collectively these data show that the loss of 20% of cholinergic neurons of the BFCN does not robustly affect cognitive function, but leaves these animals vulnerable to significant cognitive impairments upon acute systemic inflammatory insult. The data also show that preserving acetylcholine levels using an acetylcholinesterase inhibitor is protective in

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**A novel animal model to interrogate cholinergic and neuroinflammatory interactions in delirium**

(Trzepacz et al., 1992)
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This setting. (see figure)

We believe that these findings have significant implications for delirium, particularly in the setting of existing cognitive impairment/dementia and that this limited cholinergic lesion model will be a useful tool in delineating molecular pathways to dysfunction that are relevant to delirium.

However, many researchers are hesitant about applying these data to clinical delirium and this raises a number of questions:

Q Can we really say that these mice are delirious or is this just a hippocampal memory deficit?

While we cannot say that these mice are definitely delirious, it is also difficult, in a non-verbal animal, to assert that they are not. According to DSM-IV, one should demonstrate acute onset impairments in attention and some other cognitive domain, that can’t be better explained by existing dementia and that are triggered by physiological disturbances resulting from some general medical condition. Our model fulfills these criteria rather well. There is room for debate only on the nature of the dysfunction. We have shown that the T-maze task is hippocampal-dependent but this oversimplifies matters and thus requires some clarification: in order to successfully solve the T-maze task, animals must attend to the maze exit on first entry, be attentive to the body-turn they made to escape the maze and recall this choice just 30 seconds later to find the new location of the exit on re-exposure to the maze. Whether the deficit is one of attention or short-term memory is difficult to dissect, but it is undeniably distinct from long-term memory: we have shown that mice are not impaired on retention of hippocampal-dependent reference memory after LPS treatment (Cunningham et al., 2009). Consistent with this, patients with delirium could access previously learned information but showed impairments on tasks involving online processing of novel, trial specific, information (Brown et al., 2011). Thus there are important parallels between the type of cognitive impairments seen in delirium and those in animals with cholinergic “vulnerability”. We are not simply describing a generalised hippocampal
deficit and we do not imply that delirium is a hippocampal phenomenon.

Q Can these findings be reconciled with the failure of acetylcholinesterase inhibition in ICU delirium?

No protective effect of rivastigmine against delirium was found in the ICU (van Eijk et al., 2010). However, our data are most relevant to patients with existing cholinergic vulnerability, such as occurs in Alzheimer’s disease. We propose, based on our murine studies, that individuals with neurodegeneration in the cholinergic system, who then suffer moderate systemic inflammatory insults (infection or surgery), might benefit from boosting of cholinergic function. However, in ICU patients who have suffered severe trauma/sepsis, we believe that it is highly unlikely that bolstering a single neurotransmitter system will be able to correct the marked divergence from homeostasis in multiple systems, including severe inflammation, impaired tissue perfusion and hypoxia, blood brain barrier breakdown and multi organ dysfunction. Divergent routes to delirium will influence correct treatment strategies. Just as it is too simplistic to assume that hypocholinergic function is the final common pathway to delirium simply because robust cholinergic inhibition can produce a delirious state, so is it unwise to reject the importance of cholinergic function just because cholinesterase inhibition did not protect against delirium in one profoundly sick population. The hypocholinergic animal model allows us to ask simple questions in this domain and to provide empirical evidence that can contribute to supporting or rejecting clinical hypotheses.

Concluding remarks

In considering the value of this and other animal models, purportedly relevant to delirium, clinical researchers must be measured in their expectations. It is worth noting that widely used animal models of depression, schizophrenia and even Alzheimer’s and Parkinson’s diseases lack some features of the conditions they model. This is a reality of using animal models. We must now focus on what these models do provide rather than on what they do not provide. Whether or not these animals fit all the criteria for delirium, in as much as anyone can definitively say what these criteria should be in a mouse, they offer a unique tool to investigate the interaction between cholinergic and neuroinflammatory routes to acute neuropsychological dysfunction and this represents a significant advance on previous knowledge in this field. Our recent study shows, unequivocally, that systemic inflammation induces acute and transient attentional/working memory deficits, which are relevant to delirium, in animals with prior cholinergic pathology in the basal forebrain. The data arising from such models should form part of the discussion on delirium pathophysiology.

Full reference for citation

Field RH, Gossen A, Cunningham C. Prior Pathology in the Basal Forebrain Cholinergic System Predisposes to Inflammation-Induced Working Memory Deficits: Reconciling Inflammatory and Cholinergic Hypotheses of Delirium. The Journal of Neuroscience, May 2, 2012 • 32(18):6288 – 6294 (This article is freely available (open access) through The Journal of Neuroscience)

References


