



# Hydrocephalus Association RESEARCH UPDATE

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### IN ATTENDANCE

**NINDS Advisory Council Meeting**, January 31, 2013, Bethesda, MD. Attended by Paul Gross, Dawn Mancuso, and Ashly Westrick.

**Rare Disease Day**, February 28, 2013, Bethesda, MD. Attended by Dawn Mancuso and Ashly Westrick.

**Health Research Alliance**, March 21-22, 2013, Chevy Chase, MD. Attended by Dawn Mancuso and Ashly Westrick.

**American Association of Neurological Surgeons (AANS) Annual Conference**, April 28-May 1, 2013, New Orleans, LA. Attended by Ashly Westrick, Aisha Heath, and Karima Roumila.

**HCRN Meeting**, May 6-7, 2013, Vancouver, British Columbia, Canada. Attended by Ashly Westrick.

**International Society for Hydrocephalus and CSF Disorders**, June 29-July 2, 2013, Athens, Greece. Attended by Ashly Westrick.

## RSRI AND HA PARTNERSHIP

### Research Grant in Cerebrospinal Fluid Production, Flow, and Regulation Therapeutics and Diagnostics

In June 2012, the Hydrocephalus Association announced a research partnership with the Rudi Schulte Research Institute (RSRI) to find significant advances in the treatment of hydrocephalus. RSRI has long been the sponsor of our research-focused keynote speaker at our biennial education conference. This past year, we expanded our partnership in two ways. First, RSRI co-sponsored our hydrocephalus research conference, "Opportunities in Hydrocephalus Research: Pathways to Better Outcomes," which took place in Seattle in July 2012. That sponsorship was intended to help RSRI develop a picture of promising hydrocephalus research for the Institute to tackle. Having completed the consensus conference, we partnered with RSRI to launch a major new Request for Applications (RFA) targeted at gaining a better understanding of the dynamics of cerebrospinal fluid (CSF). This RFA expands on the work that we funded starting in 2011 to not only consider therapeutic targets but to also consider discovery of new pathways or diagnostic biomarkers.

RSRI plans to commit a significant effort to the most promising research in this area. At the conclusion of our review process, they expect to select one or two researchers and invest a minimum \$600,000 in advancing this research over three years. HA will consider further augmenting the investment in these applications to bring the total investment up to \$1M over the next three years. These research areas were described in our five-year Research Initiative plan and represent significant potential to alter the course of diagnosis and treatment for those who suffer from hydrocephalus.

The grant applications have been reviewed and ranked by our 2013 Scientific and Medical Review Committee (SMRC) chaired by Donna Ferriero, M.D., a Pediatric Neurologist from the University of California San Francisco Benioff Children's Hospital and a member of the NINDS Advisory Council since 2010.

The Committee reviewers include a number of highly talented and accomplished hydrocephalus researchers: William G. Bradley, Jr., M.D., Ph.D., FACR, Professor and Chairman of the Department of Radiology at University of California, San Diego; David Frim, M.D., Ph.D., Professor and Chief of Neurosurgery at the University of Chicago; John Kestle, M.D., M.Sc., FRCSC, FACS, Head of the Department of Surgery at the University of British Columbia in Vancouver; Miles Johnston, B.Sc., Ph.D., of SunnyBrook Research Institute in Toronto; Jill Morris, Ph.D., Program Director at the National Institute of Neurological Disorders and Stroke (NIH's NINDS); and Jan-Marino (Nino) Ramirez, Ph.D., Professor of Neurological Surgery and Director of the Center for Integrative Brain Research at the Seattle Children's Research Institute.

Rudi Schulte was one of the two founders of PS Medical, which developed the Delta and Strata valves used in the treatment of hydrocephalus. The company was later sold to Medtronic, which has continued to advance those shunt technologies. Rudi Schulte founded the Rudi Schulte Research Institute in 1974 to continue research into hydrocephalus. The Hydrocephalus Association is pleased to have expanded our partnership to help RSRI target research that is meaningful to our members.

# HA GRANT RECIPIENTS

As of 2013, HA has funded nine grantees: 7 Mentored Young Investigators (MYI) and 2 Established Investigator awards.

## Mentored Young Investigator Grants

Three MYI grants have been clinical/patient based research, two have focused on CSF dynamics and two have been basic science studies.

Just recently, two of our MYIs have completed their funding cycles. Sonia Podvin, Ph.D., a post-doctorate from the University of California, San Diego, finished her MYI funding for her study, “Augurin is a novel choroid plexus-derived peptide,” which investigated the role of augurin in the development of hydrocephalus. The goal of Dr. Podvin’s study was to (1) develop an augurin animal genetic model in mice and to determine the phenotype of the augurin knock out and (2) to identify the unknown cell surface receptor of augurin. The ultimate aim, if the hypothesis is correct, is to pharmacologically manipulate augurin to treat hydrocephalus. Dr. Podvin and her colleagues concluded their study and are anticipating submitting the results for publication.

Dana Moore, Ph.D., of Cornell University, completed her two years of MYI funding for her study, “Quantitative measurement of ventricular volume and cortical atrophy to improve diagnosis of normal pressure hydrocephalus,” which investigated the role of imaging in differentiating normal pressure hydrocephalus (NPH) patients from normal controls and Alzheimer’s disease (AD) patients. The study compared normal controls and AD patients with NPH patients in terms of average cortical thickness and lateral ventricular volume. In August 2011, the pilot study data was published in the journal *Neurology Research International*. Published results indicated that NPH patients had larger ventricular volume than AD patients, and a statistical model using ventricular volume and cortical thickness could distinguish

between the groups. The study was completed in 2012, and the researchers are expected to submit the results for publication.

## Established Investigator Grants

In addition to our MYIs, we also funded two Established Investigator grants for research on cerebrospinal fluid (CSF) during the 2012 funding cycle to experienced researchers, Drs. James P. McAllister and Miles Johnston.

Dr. McAllister received two years of funding for his study, “Novel neurobiological interventions for the treatment of hydrocephalus.” Dr. McAllister’s study investigates the abnormal blockage of CSF flow. The study uses animal models and patient CSF to increase our understanding of the damage that occurs in the hydrocephalic brain. Using this information can help advance the development of novel transplantation therapies. Results from the first year of funding were published in the journal *Cell Tissue Research*. This current study provides evidence that maldevelopment of the subcommissural organ precedes hydrocephalus indicating that it is possible the maldevelopment is causing the hydrocephalus.

Dr. Johnston received a one-year grant for his study, “Hydrocephalus and lymphatic cerebrospinal fluid absorption,” which investigated the role that the lymphatic vessels of the brain play in relation to CSF clearance. He was specifically testing how these lymphatic vessels respond to pharmaceutical interventions. The preliminary results have shown that the application of certain drugs can cause the lymphatic vessels to contract, which can affect CSF outflow.

We are very encouraged and proud to support our grantees’ research. These studies have provided significant insight into the root causes of hydrocephalus and the dynamics of CSF.

## HA’s Research Mission

The Hydrocephalus Association is dedicated to the advancement of promising research that will promote the understanding, diagnosis, treatment, and, ultimately, prevention of and cure for hydrocephalus. Since the first National Institutes of Health (NIH)-sponsored workshop on hydrocephalus in 2005 (in which HA played an instrumental role), the increase in research on hydrocephalus has been a cause for hope for the hydrocephalus community. With the launch of HA’s Research Initiative in 2009, the association has directly funded both basic and clinical research, thereby advancing the knowledge base on hydrocephalus leading to improvements in diagnosis and treatment. HA remains committed to stimulating and funding research which improves the quality of life for people living with hydrocephalus, while encouraging more investigators – both new and experienced – to focus on this condition, so we may better understand, diagnose, treat and eventually cure it.

In 2011, the HA board of directors established three priorities for the use of research dollars. The programs HA organizes and executes are all meant to directly address our established research priority areas.

## HA Research Priorities



## HCRN UPDATE

We continue to pursue and encourage strategic partnerships, which will further advance the research ecosystem. In the summer of 2012, we signed a 3-year partnership agreement with the Hydrocephalus Clinical Research Network (HCRN) to accelerate the delivery of value from HA research initiatives, unify significant philanthropic fundraising activities for the hydrocephalus community, and solidify the fundamental requirement for clinical trials to bring translational research to market. HCRN is a network of nine children's hospitals that conduct clinical research on hydrocephalus. Their mission is to dramatically improve the lives of kids suffering from hydrocephalus by conducting important and field-changing, multi-center clinical research. The research agenda includes reducing the incidence of shunt infection, improving the treatment

of shunt infection, compiling a comprehensive patient registry, and enhancing the management of hydrocephalus in premature children.

It was announced in June that, with the move of two of the investigators, Dr. John Wellons to Vanderbilt and Dr. John Kestle to the University of British Columbia, HCRN decided to expand the network from seven to nine centers. Each center will begin its trial period immediately, which involves adding patients to the HCRN registry as well as participating in the HCRN Quality Improvement Study for post-surgical infections. More information about HCRN and the studies being conducted can be found on their website at [www.hcrn.org](http://www.hcrn.org).

Current/Active HCRN Studies	Principal Investigator
Quality improvement: shunt infection protocol	John Kestle, M.D., M.Sc., FRCSC, FACS
Shunting outcomes in post hemorrhagic hydrocephalus	John Wellons, M.D., M.S.P.H.
Shunt registry	Jay Riva-Cambrin, M.D., FRCSC, M.Sc.
ETV registry	Abhaya Kulkarni, M.D., Ph.D., FRCSC
Infection registry	Tamara Simon, M.D., M.S.P.H.
Biomarkers in post hemorrhagic hydrocephalus	David Limbrick, M.D., Ph.D.
Ventricular size involvement in neuropsychological outcomes in pediatric hydrocephalus	Jay Riva-Cambrin, M.D., FRCSC, M.Sc.

## ADULT STUDY EFFORTS

While the Hydrocephalus Clinical Research Network (HCRN) was founded initially to study pediatric hydrocephalus, HA is dedicated to improving the lives of patients with hydrocephalus at all life stages. Creation of an adult extension of HCRN is exciting because research is essential in improving the lives of patients. Hydrocephalus is not just a pediatric condition. It can strike at any age, and those children with hydrocephalus will be adults one day. It is important to address the whole age spectrum of hydrocephalus and HA believes that the development of an adult research network is essential.

To address the need to study hydrocephalus in adults - whether these adults developed hydrocephalus as a child or later in life - the association has worked in the past year with distinguished adult hydrocephalus researchers, including neurosurgeons, neurologists and neuropsychologists, to establish an adult hydrocephalus research network extension of the Hydrocephalus Clinical Research Network (HCRN). This group wants to improve the lives of adults with hydrocephalus, to raise awareness of the disease, and to cover issues related to transitional patients, congenital adults, and other adult-onset cases. Five sites were selected and progress was made throughout 2012 in developing essential data elements and protocols for the network. Participating in the network planning effort are Mark Hamilton, M.D., from the University of Calgary; Mark Luciano, M.D.,

Ph.D., from The Cleveland Clinic; Michael Williams, M.D., of The Sandra and Malcolm Berman Brain & Spine Institute in Baltimore; Norman Relkin, M.D., Ph.D., of the Weill Cornell Medical College in New York; Heather Katzen, Ph.D., of the University of Miami in Florida; and Petra Klinge, M.D., Ph.D., of Brown University in Rhode Island. Recently, Dr. John Kestle, co-founder of HCRN and advisor to this group, formally joined the group effort to study adult hydrocephalus, bringing the benefits of collaboration and Dr. Kestle's rich history in hydrocephalus research.

With funding from HA, the adult research group held an in-person meeting in February 2013, at the HA offices in Bethesda, Maryland, to review the data elements to be collected and to engage the data coordinating center (DCC) from the University of Utah. An additional in-person meeting is scheduled for November 2013 in Bethesda, Maryland. This work is on-going, and initial data collection and study is anticipated for the first quarter of 2014.

## COMMUNICATION INITIATIVE AROUND RESEARCH

HA has developed a strategic communication plan around research for 2013. The goal of this initiative is to inform our community, including patients, families, physicians, and researchers, about recent research findings and ongoing studies in hydrocephalus, updates on the current research initiatives being funded by HA, opportunities for research grants and/or collaborations, and HA's role in patient advocacy at research conferences and events.

### Website Blog Series

**Looking Back...Moving Forward** - Every six weeks, as a part of our 30th Anniversary interview series, we highlight one of our Medical Advisory Board members (MAB). To date we have highlighted Drs. Michael Williams, Harold Rekate, and John Kestle and their relationship with HA.

**Research UPDATE** - The Research UPDATE blogs can include written study summary articles, explanations and/or press releases about new research findings, and highlights of recent research conferences and events.

**HCRN Update** - A quarterly blog series that focuses on updates shared by HCRN and provides an overview of current HCRN research initiatives. To date, we have highlighted the work of Dr. John Wellons of Vanderbilt and Dr. David Limbrick of St. Louis Children's.

**MYI blog series** - A quarterly blog series that provides an overview and update of current MYI research initiatives. We have posted two Mentored Young Investigator blogs to date, featuring Dr. Sonia Podvin of the University of California, San Diego and Dr. Dana Moore from the Weill Cornell Medical College.

In addition to our standing blog series, HA attends a variety of scientific and non-profit conferences throughout the year. By attending these meetings, HA fosters our strong relationships with the preeminent hydrocephalus researchers and physicians in the field, at the same time educating them about the association. Keep an eye out for our HappeningNOW posts to see what event we are attending.

### Social Media Campaign

Along with our website blog posts and newsletter articles, we are conducting an aggressive social media campaign through various outlets to unify the hydrocephalus research community as well as patients. HA currently maintains an active Facebook page with over 11,500 individuals and a Twitter account with over 1,700 followers. In addition to individuals and organizations that have linked themselves with us through social media, we have also "liked" or "followed" relevant organizations, research institutions, medical facilities, and industry leaders. In this way, when we post through social media and mention or link to these organizations, our viewership increases exponentially to include the individuals who are associated with those organizations' social media accounts.

In order to maintain a steady stream of information around hydrocephalus research, every Thursday is dedicated to sharing a fact about hydrocephalus or hydrocephalus research, and often a blog that is posted to our website. Since implementing this strategy, these blogs, posts, and facts have had the highest views, shares, and click-throughs to our website than all other posts.

We always want to hear about important research and highlight our many hydrocephalus researchers. The HA community is eager to learn more about the research happenings. If you have a study, know of important hydrocephalus research, or would like to guest blog, **we want to hear from you!** Please email Ashly Westrick, Research Programs Manager, at [research@hydroassoc.org](mailto:research@hydroassoc.org).

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