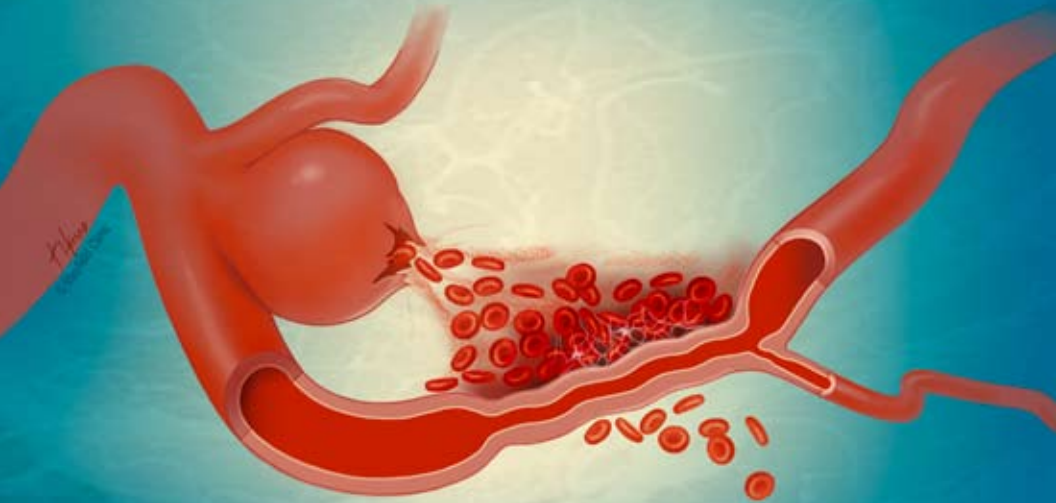


Program Guide



VASOSPASM 2011

11th International Conference on Neurovascular Events after SAH

July 21-23, 2011

www.vasospasm11.com

Cincinnati, Ohio, USA

Hosted by

UNIVERSITY OF
Cincinnati

UC Neuroscience Institute

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Welcome

We would like to welcome you to Vasospasm 2011: The 11th International Conference on Neurovascular Events after Subarachnoid Hemorrhage!

Vasospasm 2011 will engender a true translational and international ethos. Continuing the excellent tradition of previous meetings, we aim to address both clinical management strategies and basic science studies on cerebral vasospasm and neuronal damage occurring after SAH. This meeting format includes plenary sessions, workshops, and platform and poster presentations based on abstract submissions.

Despite intensive research effort, there is still no optimal clinical management strategy for SAH patients. This conference will focus on the neurovascular events following SAH, and how we can use this information to further clinical management strategies via translational and clinical research efforts. In order to maximize this effort, there is a special White Paper session to formulate an International Consensus Document regarding the clinical management of SAH patients in a Neurocritical Care setting.

We are delighted to welcome both COSBID investigators and Neuro Nurses to this meeting for the first time. The Co-Operative Study on Brain Injury Depolarizations facilitates collaborative international research on cortical spreading depression, which complements our conference focus. We are pleased to announce their joint participation throughout the program.

Young investigators and early career practitioners and scientists have been encouraged to participate with novel research ideas and compete for a range of awards, including Young Investigator, Bench to Bedside and Back Again, and The Next Big Idea.

Cincinnati is located on the banks of the river Ohio, and was founded in 1788, making it the first major inland city in America. Cincinnati boasts several fine restaurants, historic architecture and many opportunities for sightseeing. Cincinnati is a great family destination, with professional athletics, beautiful parks and attractions such as Coney Island Amusement Park and King's Island Theme Park, world-class performing arts, and a vibrant nightlife.

We believe that this conference will build on previous meetings, and lead to a greater understanding of the multidisciplinary nature of SAH research and management, from molecular events to clinical trials and treatment.

We hope you enjoy the meeting!



Mario Zuccarello, MD
Conference Chairman



Joseph Clark, PhD
Conference Co-Chairman

Committees

Local Organizing Committee

Mario Zuccarello, Chair
Joseph Clark, Co-Chair
Todd Abruzzo
Opeolu Adeoye
Norberto Andaluz
Krissy Atchley
Pat Bell
Jed Hartings
Tonya Hines
Christa McAlpin
Joanie Pope
Gail Pyne-Geithman
Andrew Ringer
Tom Rosenberger
Faye Smith

International Organizing Committee

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Chul-Jin Kim Korea
Talat Kiris Turkey
Aij-Lie Kwan Taiwan
Shigeru Nishizawa Japan
Hans-Jakob Steiger Germany
Claudius Thome Austria
Peter Vajkoczy Germany
John Zhang USA

Local Scientific Committee

Joseph Clark, Chair
Opeolu Adeoye
Norberto Andaluz
Jed Hartings
Gail Pyne-Geithman
Mario Zuccarello

International Scientific Committee

Isao Date Japan
Michael Diringer USA
Jens Dreier Germany
Javier Fandino Switzerland
Hua Feng PR China
Jennifer Frontera USA
Giovanni Grasso Italy
Daniel Hanggi Germany
Carla Jung Germany
Kenji Kanamaru Japan
Hidetoshi Kasuya Japan
Emanuela Keller Switzerland
Chul-Jin Kim South Korea
Talat Kiris Turkey
Peter Kirkpatrick UK
Giuseppe Lanzino USA
Kwan-Sung Lee South Korea
R. Loch Macdonald Canada
David Mendelow UK
Tadayoshi Nakagomi Japan
Shigeru Nishizawa Japan
Audrey Quinn UK
Alejandro Rabinstein USA
Tatsuya Sasaki Japan
Lothar Schilling Germany
Fatima Sehba USA
Seung Hun Sheen South Korea
Lori Shutter USA
Hans-Jakob Steiger Germany
Jose Suarez USA
Rafael Tamargo USA
Claudius Thome Austria
Francesco Tomasello Italy
Peter Vajkoczy Germany
George Wellman USA
Christine Wijman USA
George KC Wong PR China
Howard Yonas USA
John Zhang USA

Session Co-Chairs

Session 1a: Clinical Trials and Dilemmas

Co-Chairs: Hidetoshi Kasuya (Tokyo, Japan), Ferdinand Miteff (New South Wales, Australia)

Session 1b: Clinical Trials and Dilemmas

Co-Chairs: R. Loch Macdonald (Toronto, Ontario, Canada), Javier Fandino (Aarau, Switzerland)

Session 2a: Neurocritical Care: Monitoring

Co-Chairs: Emanuela Keller (Zurich, Switzerland), Jennifer Frontera (New York, New York, USA)

Session 2b: Neurocritical Care: Management

Co-Chairs: Michael Diringer (St. Louis, Missouri, USA), Paulo Henrique Pires de Aguiar and Renata Simm (Sao Paulo, Brazil)

Award Finalist Presentations

Co-Chairs: John Zhang (Loma Linda, California), Ryszard Pluta (Bethesda, Maryland, USA), Daniel Hänggi (Dusseldorf, Germany)

COSBID Social/Workshop

Co-Chairs: Jed Hartings (Cincinnati, Ohio, USA), Martin Fabricius (Copenhagen, Denmark)

Session 3a: Spreading Depolarizations: Clinical Studies

Co-Chairs: Ryszard Pluta (Bethesda, Maryland, USA), Anthony Strong (London, England)

Session 3b: Spreading Depolarizations and Neurovascular Coupling: Animal Studies

Co-Chairs: R. Loch Macdonald (Toronto, Ontario, Canada), Cenk Ayata (Boston, Massachusetts, USA)

White Paper Discussion

Co-Chairs: Emanuela Keller (Zurich, Switzerland), Jose Suarez (Houston, Texas, USA)

Session 4: Inflammation and Blood-Brain Barrier

Co-Chairs: Javier Provencio (Cleveland, Ohio, USA), Gail Pyne-Geithman (Cincinnati, Ohio, USA)

Neurosurgery Breakfast Seminar

Co-Chairs: Kenji Kanamaru (Suzuka, Japan), Talat Kiris (Istanbul, Turkey)

Session 5a: Early Brain Injury

Co-Chairs: George Wellman (Burlington, Vermont, USA), Shigeru Nishizawa (Fukuoka, Japan)

Session 5b: Vascular and Microvessel

Co-Chairs: John Zhang (Loma Linda, California, USA), Fatima Sehba (New York, New York, USA)

Session 6: Genetic and Environmental Factors

Co-Chairs: Joseph Broderick (Cincinnati, Ohio, USA), Paul Nyquist (Baltimore, Maryland, USA)

Breakout: COSBID

Session A & B Co-Chairs: Oliver Sakowitz (Heidelberg, Germany), Martin Fabricius (Copenhagen, Denmark)

Breakout: COSBID

Session C & D Co-Chairs: Johannes Woitzik (Berlin, Germany) Rudolf Graf (Cologne, Germany)

A Cincinnati Gift — limited edition Rookwood tile

Rookwood Pottery was founded in 1880 by Marie Longworth Nichols. Rookwood pottery's initial work demonstrated an Oriental and European influence. Throughout Rookwood's years they mastered such diverse styles as Victorian, art nouveau, arts and crafts, and art deco.

Rookwood Pottery of Cincinnati was the first to gain artistic recognition and respect for the United States on an international level. In 1889, Rookwood was awarded the First Prize Gold Medal at the Paris Exposition Universelle. This was a shock to the international artistic community who had never really paid much attention to American ceramics. In less than a decade after starting as a hobby pottery shop, Rookwood had grown to become a company with an international reputation for ceramic excellence.

We selected three tiles for attendees to remember the Cincinnati Vasospasm 2011 conference. The tiles depict venerable icons of Cincinnati:

Carew Tower-Netherland Plaza Hotel:

Built during the Great Depression, this complex is one of the finest examples of skyscraper modernism in America. A national historic landmark, it is beautifully adorned in French Art Deco and Rookwood tile.

Roebling Suspension Bridge:

The John A. Roebling Suspension Bridge spans the Ohio River between Cincinnati, Ohio and Covington, Kentucky. Completed in 1866, it was the longest suspension bridge in the world. The Cincinnati Roebling bridge became the model for the famous Brooklyn Bridge in New York City.

Tyler Davidson Fountain:

The fountain was a gift to Cincinnati in 1871 by Henry Probasco in honor of his brother-in-law Tyler Davidson. The 9-foot central figure, "The Genius of Water," stands with arms outstretched over groupings of figures representing the uses of water. Probasco gave the fountain to Cincinnati on the condition that it be placed in the city's center - today known as Fountain Square.



Carew Tower-Netherland Plaza Hotel



Roebling Suspension Bridge



Tyler Davidson Fountain

Schedule at a Glance & Hotel Map

Wednesday, July 20, 2011

16:00-18:00	Registration	Desk in Hotel Lobby
18:00-20:00	Welcome Reception	Continental Ballroom

Thursday, July 21, 2011

7:00-8:00	Breakfast	Pavillion Ballroom
8:00-8:20	Welcome	Pavillion Ballroom
8:20-9:40	Session 1a: Clinical trials and dilemmas	Pavillion Ballroom
9:40-10:00	Break	
10:00-12:00	Session 1b: Clinical trials and dilemmas	
10:00-12:00	Concurrent Session: Neuro Nurses Breakout	Rosewood
12:00-13:00	Lunch	Pavillion Ballroom
13:00-13:30	Keynote Lecturer, Tomio Sasaki	Pavillion Ballroom
13:30-14:45	Session 2a: Neurocritical care: monitoring	Pavillion Ballroom
14:45-15:15	Break	
15:15-17:00	Session 2b: Neurocritical care: management	
17:00-18:00	Poster Session	Pavillion Ballroom & Rookwood
18:00-20:00	Award Finalist Presentations & Reception	Pavillion Ballroom

Friday, July 22, 2011

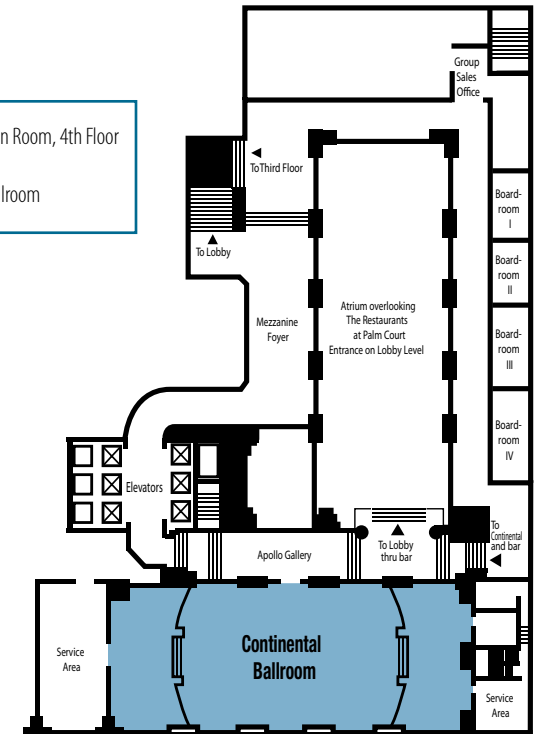
7:00-8:00	Breakfast	Pavillion Ballroom
	Breakout: COSBID Social/Workshop	Salon BC
8:00-10:00	Session 3a: Spreading depolarizations	Pavillion Ballroom
9:50-10:20	Break	
10:20-12:00	Session 3b: Spreading depolarizations	
12:00-14:00	Lunch, Breakout White Paper Discussion Lunch, Poster Session	Pavillion Ballroom Pavillion Ballroom & Rookwood
14:00-14:30	Guest Lecturer, David Mendelow	Pavillion Ballroom
14:30-16:30	Session 4: Inflammation and blood-brain barrier	Pavillion Ballroom
16:30-17:30	Bid Presentations: Vasospasm 2013	Pavillion Ballroom
17:00-18:00	COSBID business meeting	Salon BC
18:00-21:00	Dinner	Celebrations Riverboat

Saturday, July 23, 2011

7:00-8:15	Breakfast	Pavillion Ballroom
	Breakout: Neurosurgery Breakfast Seminar	Salon BC
8:15-8:30	Announcement of Award Winners	Pavillion Ballroom
8:30-9:30	Session 5a: Early brain injury	Pavillion Ballroom
9:30-10:00	Break	
10:00-12:00	Session 5b: Vascular and microvessel	
12:00-13:00	Lunch	Pavillion Ballroom
13:00-13:30	Keynote Lecturer, Costantino Iadecola	Pavillion Ballroom
13:30-17:00	Session 6: Genetic and environmental factors	Pavillion Ballroom
13:30-17:00	Concurrent Session: COSBID Breakout	Rosewood
17:00-17:30	2013 Venue Announcement & Closing Remarks	Rosewood

Registration: Pavillion Foyer Registration Room, 4th Floor
Exhibits: Pavillion Foyer & Caprice
Posters: Rookwood & Pavillion Ballroom

Mezzanine Level



4th Floor



Hotel Information

Hilton Cincinnati Netherland Plaza
35 West Fifth Street
Cincinnati, Ohio 45202
Phone: 1-513-421-9100
www.cincinnatietherlandplaza.hilton.com

The AAA Four-Diamond Hilton Cincinnati Netherland Plaza is Cincinnati's unique meeting place. The hotel has been designated a National Historic Landmark by the U.S. Department of the Interior, and continues to receive acclaim as one of the finest examples of French Art Deco architecture in existence.

Social Events

Wednesday, July 20
Welcome Reception, 18:00-20:00
Continental Ballroom

Thursday, July 21
Poster Session & Reception, 17:00-20:00
Pavillion Ballroom

Friday, July 22
Dinner, 18:00-21:00
Celebrations Riverboat
* Important note: Meet in hotel lobby at 18:00 to board buses.

Clothing

Informal for all occasions. The dinner on Friday evening will take place on a riverboat, so please feel free to dress in a casual and comfortable manner if the temperature is warm.

Internet Station

If you are interested to check your email during conference hours, there will be a free internet station for this purpose located in the Caprice Room.

Guest Room Internet Availability

If you are interested in internet access in your guest room, as a conference registrant, you will only be charged a one-time fee of \$9.95 USD for the duration of your stay (instead of the per day charge.) Note that the guest room internet is wired. Wireless internet is not available in the guest rooms. Cords are provided in the top drawer of the desk in each room.

Fitness Center

The Gym at Carew Tower, located on the Hilton's lower level, is open to all registered guests. This 13,000 square-foot complex is the largest downtown and features the latest in fitness equipment, a lap pool, aerobics studio, sauna, steam room, and a whirlpool. For joggers, there are several scenic routes around downtown.

Airport Service

The Cincinnati/Northern Kentucky International Airport is located 12 miles from downtown Cincinnati and the Hilton – just a short 15 minute drive! Shuttle service to the Hilton Cincinnati Netherland Plaza is provided by Executive Transportation. Please call 1-800-990-8841 the day prior to your arrival or departure to guarantee your reservation. Same day reservations can be accommodated based upon availability. Taxi cabs run 24 hours a day from the airport to downtown Cincinnati.

Speaker Information

Speaker preparation

Two laptop computers and technical support will be available for any speaker needing last-minute assistance with their presentation. Visit the conference registration desk on the 4th Floor of the hotel for more information.

Pre-loading presentations

All general session speakers must report to the tech table in the back of the Pavilion Ballroom **at least 30 minutes** prior to the start of the session in which you

are speaking. You will need to bring your presentation on a flash drive or CD to pre-load on to the presentation laptop.

All breakout session speakers must report to the room in which you are speaking **at least 30 minutes prior** to the start of your session to pre-load your presentation to the breakout session laptop. If no one is in the breakout session room, visit the conference registration desk for assistance.

Poster Information

Location & Time

The Vasospasm 2011 Poster Session will be held from 17:00-20:00 on Thursday, July 21 at the Hilton Cincinnati Netherland Plaza in the Rookwood Room & Pavillion Ballroom on the 4th Floor of the hotel. There will be additional time to view the posters from 12:00-14:00 on Friday, July 22.

Set-up

Posters may be set-up Wednesday, July 20 from 19:00 – 21:30 or Thursday, July 21 from 7:00 – 17:00 in the Rookwood Room & Pavillion Ballroom on the 4th Floor of the hotel. Set-up should be completed by 17:00 on Thursday, July 21, when the Poster Session begins. Award Finalist Presentations will take place from 18:00-19:00. The Reception will end at 20:00.

Posters can be posted for the remainder of the meeting. Tear-down of posters should take place before 17:00 on Saturday, July 23.

You will be provided one 8 ft. (width) x 4 ft. (height), maximum size, fabric poster board. Pins will be available to affix your poster. The boards are double-sided so there will be another poster displayed on the back of your board.

Thank you for your participation in the Poster Session of the Vasospasm 2011 Conference!

Awards

Award Categories

Bench to Bedside and Back
Next Big Idea
Young Investigator

Announcement of Award Winners

First and Second Place award winners will be announced Saturday, July 23 from 8:15 – 8:30 during the General Session in the Pavillion Ballroom on the 4th Floor.

Detailed Program

Thursday, July 21, 2011

7:00 - 9:40

Pavillion Ballroom

7:00-8:00 Breakfast

8:00-8:20 Welcome, Mario Zuccarello and Joseph Clark

Session 1a:	CLINICAL TRIALS AND DILEMMAS	<u>Abstract #</u>
	Co-Chairs: Hidetoshi Kasuya, Ferdinand Miteff	
8:20-8:50	History and Definition of Delayed Cerebral Ischemia <i>R. Loch Macdonald, Toronto, Ontario, Canada</i>	invited
8:50-9:05	Development of Nicardipine Prolonged Release Implants after Clipping for Preventing Cerebral Vasospasm: From Laboratory to Clinical Trial <i>Hidetoshi Kasuya, Tokyo, Japan</i>	39
9:05-9:20	Intracisternal magnesium injection therapy (experimental data for its clinical application) <i>Kentaro Mori, Shizuoka, Japan</i>	12
9:20-9:40	A Prospective, Randomized and Controlled Trial Investigating the Use of Lumbar Cerebrospinal Fluid Drainage Following Aneurysmal Subarachnoid Hemorrhage <i>Yahia Al-Tamimi, West Yorkshire, United Kingdom</i>	33

9:40-10:00	Break	
Session 1b:	CLINICAL TRIALS AND DILEMMAS	Abstract #
Co-Chairs:	R. Loch Macdonald, Javier Fandino	
10:00-10:15	Effect of Clazosentan on Clinical Outcome after Aneurysmal Subarachnoid Hemorrhage and Surgical Clipping: Results of the CONSCIOUS-2 Study <i>R. Loch Macdonald, Toronto, Ontario, Canada</i>	31
10:15-10:30	Recent Developments on Nitric Oxide Research <i>Ali Reza Fathi, Aarau, Switzerland</i>	73
10:30-10:45	Safety and Feasibility of Long Term Intravenous Sodium Nitrate Infusion in Healthy Volunteers <i>Ryszard Pluta, Bethesda, Maryland, USA</i>	34
10:45-11:00	Magnesium Sulphate for Aneurysmal Subarachnoid Hemorrhage: Why, How, and Current Controversy <i>George Wong, Hong Kong, China</i>	30
11:00-11:20	Interim Analysis of Prospective Randomized Controlled Trial to Investigate the Efficacy of Endovascular Treatment in Cerebral Vasospasm after Subarachnoid Hemorrhage <i>Johannes Platz, Frankfurt, Germany</i>	38
11:20-11:35	Identifying Patient Report Outcomes (PRO's) Relevant to Aneurysmal Subarachnoid Hemorrhage Follow-up <i>Stuart Ross, West Yorkshire, United Kingdom</i>	106
11:35-12:00	Q&A	

Concurrent Session: NEURO NURSE BREAKOUT

Rosewood

10:00-11:15	GUEST LECTURER: MARY KAY BADER Avoiding Collateral Damage in Aneurysmal Subarachnoid Hemorrhage
11:15-11:30	Break
11:30-12:00	Continuous EEG in the NSICU: Improving the Quality of Bedside Monitoring <i>Jennifer Fields and Lisa Seiler, Cincinnati, Ohio, USA</i>

12:00-13:00	Lunch	
13:00-13:30	KEYNOTE LECTURER: TOMIO SASAKI Proposed Mechanism of Cerebral Vasospasm: Our Hypothesis and Current Topics	
Session 2a:	NEUROCRITICAL CARE: MONITORING	Abstract #
Co-Chairs:	Emanuela Keller, Jennifer Frontera	
13:30-13:45	Monitoring of Cerebral Hemodynamics and Oxygenation to Detect DIND <i>Emanuela Keller, Zurich, Switzerland</i>	invited
13:45-14:00	The Dilemmas Surrounding Vasospasm Screening: Pro's and Con's of CTP and Its Foreseeable Place in Assessing Vasospasm Management Strategies <i>Ferdinand Miteff, New South Wales, Australia</i>	invited
14:00-14:15	Cerebral Hemodynamic Changes after Wartime Traumatic Brain Injury <i>Alexander Razumovsky, Hunt Valley, Maryland, USA</i>	65
14:15-14:30	Control of Vasospasm after Subarachnoid Hemorrhage by Means of Transcranial Doppler and Simultaneous Clinical Management <i>Renata Simm, Sao Paulo, Brazil</i>	invited
14:30-14:45	A Platform for Multimodal Data Collection and Research in Neurocritical Care <i>Adam Wilson, Cincinnati, Ohio, USA</i>	68
14:45-15:15	Break	

Thursday, July 21, 2011

15:15 - 20:00

Pavillion Ballroom

Session 2b:	NEUROCRITICAL CARE: MANAGEMENT	Abstract #
Co-Chairs:	Michael Diringer, Paulo Henrique Pires de Aguiar, Renata Simm	
15:15-15:45	Report on the 1st International Consensus Conference on Critical Care Management of Subarachnoid Hemorrhage <i>Michael Diringer, St. Louis, Missouri, USA</i>	invited
15:45-16:00	Removal of Clots in Subarachnoid Space Could Reduce the Vasospasm after Subarachnoid Hemorrhage <i>Paulo Henrique Pires de Aguiar, Sao Paulo, Brazil</i>	invited
16:00-16:15	Neurogenic Pulmonary Edema - A Complication of Aneurysmal Subarachnoid Hemorrhage: A Single Center Experience <i>Carl Muroi, Zurich, Switzerland</i>	74
16:15-16:30	Quantification of Subarachnoid Hemorrhage by 3D-CT Part 2: Correlation Between Hematoma Volume and Symptomatic Vasospasm <i>Tatsuya Sasaki, Aomori, Japan</i>	55
16:30-16:45	Early Brain Injury Linearly Correlates with Reduction in Cerebral Perfusion Pressure During the Hyperacute Phase after Subarachnoid Hemorrhage <i>Serge Marbacher, Aarau, Switzerland</i>	108
16:45-17:00	Q&A	
17:00-18:00	Poster Sessions	Rookwood & Pavillion Ballroom
18:00-19:00	Award Finalist Presentations	Pavillion Ballroom
Co-Chairs:	John Zhang, Ryszard Pluta, Daniel Hänggi	
18:00-20:00	Reception	Pavillion Ballroom

Friday, July 22, 2011

7:00 - 10:20

Pavillion Ballroom

7:00-8:00	Breakfast	
7:00-8:00	COSBID SOCIAL/WORKSHOP	Salon BC
Co-Chairs:	Jed Hartings, Martin Fabricius	
Session 3a:	SPREADING DEPOLARIZATIONS: CLINICAL STUDIES	Abstract #
Co-Chairs:	Ryszard Pluta, Anthony Strong	
8:00-8:25	Lower Incidence of Cerebral Infarction Correlates with Improved Functional Outcome after Aneurysmal Subarachnoid Hemorrhage <i>Nima Etminan, Dusseldorf, Germany</i>	36
8:25-8:50	The Role of Spreading Depolarization, Spreading Depression and Spreading Ischemia in Patients with Aneurysmal Subarachnoid Hemorrhage <i>Jens Dreier, Berlin, Germany</i>	87
8:50-9:05	Delayed Cerebral Ischemia Associated with Spreading Depolarization Can Occur Despite Absence of Proximal Vasospasm after Aneurysmal Subarachnoid Hemorrhage <i>Johannes Woitzik, Berlin, Germany</i>	82
9:05-9:20	Full-Band Electrooculography Study of Spreading Depolarizations in Patients with Aneurysmal Subarachnoid Hemorrhage <i>Jed Hartings, Cincinnati, Ohio, USA</i>	99
9:20-9:35	Impact of Body Temperature on Occurrence of Cortical Spreading Depolarizations in Subarachnoid Hemorrhage <i>Christoph Drenckhahn, Berlin, Germany</i>	89
9:35-9:50	Analgesics and Sedative Drugs Have an Impact on Frequency of Spreading Depolarizations in the Injured Human Brain <i>Daniel Hertle, Heidelberg, Germany</i>	98
9:50-10:20	Break	

Friday, July 22, 2011

10:20 - 14:00

Pavillion Ballroom

Session 3b: SPREADING DEPOLARIZATIONS AND NEURO-VASCULAR COUPLING: ANIMAL STUDIES [Abstract #](#)
Co-Chairs: R. Loch Macdonald, Cenk Ayata

10:20-10:45 Spreading Depolarizations: Modulation by Systemic Physiology and Drugs [invited](#)
Cenk Ayata, Boston, Massachusetts, USA

10:45-11:00 Coupling of Cerebral Blood Flow and Glucose Metabolism During Spreading Depolarizations - A Multimodal Study [101](#)
Delphine Feuerstein, Cologne, Germany

11:00-11:15 Spatia Temporal Patterns of Cerebral Blood Flow and Hemoglobin Oxygenation During the Propagation of Spreading Depolarizations Following Middle Cerebral Artery Occlusion [100](#)
Rudolf Graf, Cologne, Germany

11:15-11:30 Subarachnoid Blood Converts Neurally Evoked Vasodilation to Vasoconstriction in Rat Brain Cortex [70](#)
Masayo Koide, Burlington, Vermont, USA

11:30-11:45 Matrix Metalloproteinase and Epidermal Growth Factor Receptor Activation Cause Suppression of Voltage Gated Potassium (KV) Channels to Enhance Constriction of Rat Parenchymal Arterioles after Subarachnoid Hemorrhage [83](#)
George Wellman, Burlington, Vermont, USA

11:45-12:00 Q&A

12:00-14:00 Lunch [Pavillion Ballroom](#)

12:00-14:00 Poster Sessions [Pavillion Ballroom Rookwood](#)

12:00-14:00 **Breakout - WHITE PAPER DISCUSSION** [Pavillion Ballroom](#)
Co-Chairs: Emanuela Keller, Jose Suarez

Friday, July 22, 2011

14:00 - 21:00

Pavillion Ballroom

14:00-14:30 **GUEST LECTURER: DAVID MENDELOW**
Progress with the STICH II Trial

Session 4: INFLAMMATION AND BLOOD-BRAIN BARRIER [Abstract #](#)
Co-Chairs: Javier Provencio, Gail Pyne-Geithman

14:30-14:50 Introduction [invited](#)
Javier Provencio, Cleveland, Ohio, USA

14:50-15:05 Statin Induced T- Lymphocyte Modulation and Neuroprotection Following Experimental Subarachnoid Hemorrhage [119](#)
Robert Ayer, Loma Linda, California, USA

15:05-15:20 Microglia (MG) Activation after Acute Subarachnoid Hemorrhage (aSAH): An Intraparenchymal Reaction to an Extraparenchymal Disease [40](#)
Ulf Schneider, Berlin, Germany

15:20-15:35 L-Citrulline Therapy Prevents Basilar Artery Vasospasm in Haptoglobin 2-2 Transgenic Mice after Induced Subarachnoid Hemorrhage [24](#)
Rafael Tamargo, Baltimore, Maryland, USA

15:35-15:50 Intracranial Pressure Controlled Rabbit Subarachnoid Hemorrhage Model for the Study of Early Brain Injury [21](#)
Serge Marbacher, Aarau, Switzerland

15:50-16:05 The Effect of Variation in Low Dose LPS Injection on Mouse Delayed Cerebral Vasospasm (DCV) after Subarachnoid Hemorrhage [22](#)
Saksith Smithason, Cleveland, Ohio USA

16:05-16:30 Q&A

16:30-17:30 Bid Presentations: Vasospasm 2013
Co-Chairs: Joseph Clark, Mario Zuccarello

17:00-18:00 **COSBID Business Meeting** [Salon BC](#)

18:00-21:00 Dinner; Meet in hotel lobby at 18:00 to board buses. [Celebrations Riverboat](#)

Breakout: Co-Chairs:	NEUROSURGERY BREAKFAST SEMINAR Kenji Kanamaru, Talat Kiris	<u>Abstract #</u>
7:05-7:15	Neck Clipping of Paraclinoid Small Aneurysms <i>Kenji Kanamaru, Suzuka, Japan</i>	102
7:15-7:25	Comparison of Surgical or Endovascular Treated Aneurysmal Subarachnoid Hemorrhage Patients with a Special Emphasis on Cerebral Vasospasm <i>Talat Kiris, Ibrahim Akinci, Istanbul, Turkey</i>	2
7:25-7:35	Effect of Aneurysm Treatment Modalities on Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage <i>Hidenori Suzuki, Tsu, Mie, Japan</i>	104
7:35-7:45	Proposed New Grading System for Delayed Vasospasm Following Aneurysmal Subarachnoid Hemorrhage: Value of Cisternal Irrigation with Ascorbic Acid and Mg++ <i>Takeshi Ogura, Saitama, Japan</i>	78
7:45-7:55	Technological Innovations in Aneurysm Surgery <i>Norberto Andaluz, Cincinnati, Ohio, USA</i>	invited
7:55-8:05	The Effect of Surgical Treatment on Delayed Ischemic Neurological Deficit (DIND) in Patients with Aneurysmal Subarachnoid Hemorrhage <i>Muhammad Chohan, Albuquerque, New Mexico, USA</i>	81

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8:50-9:10	Impact of Subarachnoid Hemorrhage on Parenchymal Arteriolar Function <i>George Wellman, Burlington, Vermont, USA</i>	invited
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14:00-14:30	Haptoglobin Genotype and Risk of Vasospasm <i>Rafael Tamargo, Baltimore, Maryland, USA</i>	invited
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16:00-16:15	Addition of New Criteria to the SOFA (Sequential Organ Failure Assessment) for Patients with SAH <i>Henrique Nuss Teixeira de Oliveira, Itaperuna, Brazil</i>	109
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B. Factors Influencing Depolarizations

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14:45-15:00	Influence of Parenchymal Damage and Hemorrhage on Cortical Spreading Depression in Patients with Subarachnoid Hemorrhage <i>Nina Eriksen, Copenhagen, Denmark</i>	42
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15:30-15:45	Subarachnoid Hemorrhage Increases the Susceptibility to Ischemic Stroke but not to Peri-Infarct Depolarizations after Middle Cerebral Artery Occlusion <i>Ulrike Hoffmann, Boston, Massachusetts, USA</i>	88
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Acute care of SAH patients

1. Repeated intra-arterial infusions of fasudil hydrochloride (IAF) and a single intra-arterial infusion of nicardipine (IAN) for cerebral vasospasm: A Case Report

Okuma, Yu (Presenting); Ono, Shigeki; Itami, Hisakazu; Hishikawa, Tomohito; Tokunaga, Koji; Sugiu, Kenji; Date, Isao
Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

We report a case of repeated intra-arterial infusions of fasudil hydrochloride (IAF) and a single intra-arterial infusion of nicardipine (IAN) for cerebral vasospasm. A 67-year-old woman suffered from ruptured aneurysm was admitted to our hospital on day 12 from its onset of subarachnoid hemorrhage (SAH). Computed tomography (CT) showed minimal subarachnoid hemorrhage with subacute hydrocephalus. Cerebral angiography showed an aneurysm on the right internal carotid-anterior choroidal artery (IC-AchA), and severe and diffuse cerebral vasospasm were observed in the bilateral MCA area. We diagnosed her condition as SAH (Hunt & Kosnik grade 2, Fisher group 1), on day 12. Cerebral vasospasm was so severe to perform coil embolization that firstly IAN (1 milligram) was performed in the right M1 to dilate the proximal artery. By using IAN, we expected as not only therapeutic effect for prolonged vasospasm but also preventive effect for mechanical vasospasm. And then the aneurysm was successfully embolized with platinum coils. Spastic vessels were partially dilated by IAN, and angiography showed improvement of their blood flow to some extent after IAN and embolization. Because the vasodilative effects of IAN was mild and temporary, an additional treatment, 25 milligrams of fasudil hydrochloride was injected into the bilateral spastic M1 artery selectively. Cerebral vasospasm was almost recovered after IAF. However, on the next day after embolization, the patient suddenly developed severe left motor weakness. Repeated angiography revealed recurrence of moderate cerebral vasospasm in the right M1, M2 segments. IAF was performed and left motor weakness improved gradually. She had no neurological deficits on the day of discharge. Nicardipine is a calcium channel antagonist and fasudil is a protein kinase inhibitor. Because of the different mechanism of vasodilative effects, IAF and IAN may be good combination therapy for treatment of vasospasm following SAH.

Poster Only, Rookwood Room

2. Comparison of surgical or endovascular treated aneurismal SAH patients with a special emphasis on cerebral vasospasm

Kamar, Ceren; Guresti, Ece; Sencer, Altay; Sencer, Serra; Aydin, Kubilay; Basel, Ahmet; Aras, Yavuz; Kiris, Talat; Akinci, Ibrahim Ozkan (Presenting)

I.U. Istanbul Medical School, Fatih, Istanbul, Turkey

Introduction: We want to evaluate the incidence of delayed cerebral ischemia (DCI) and outcome in 139 consecutive SAH patients with a special reference to the treatment modality who were admitted to our hospital in the past three years for surgical or endovascular procedures to treat cerebral aneurysm.

Material and Methods: Patients were evaluated according to demographic data, severity of illness on admission with Fisher and WFNS grade, incidence of DCI, outcome and choice of treatment. Statistical evaluations were made by t-test for parametric and Fisher's exact test for non-parametric values.

Results: All patients' demographic data were as shown in table 1. Clinical vasospasm diagnose was made by the existence of three signs which are headache, neurological deficit, and worsening at Glasgow coma score (GCS). Due to this evaluation 42 of the 139 patients demonstrated DCI. While 26 of them were in clipping group, other 16 were in coiling group. But HH therapy and CSF drainage with lumbar puncture started more liberally, to 88/ and 57 patients respectively, due to at least the two of the following findings or clinicians decision: headache, agitation, elevated leukocyte level (without infection), new motor deficit and worsening in GCS. The severity of cases on admission in clipping and coiling groups were similar for both (APACHE-II: 3.8 ± 2.8 to 6.3 ± 5.8). Although mortality and morbidity rates were higher in coiling group there was no statistical difference in both groups (Table).

Conclusion: This study demonstrated that although mortality, morbidity rates and DCI incidence were lower in the surgical group, there was no statistical significance.

Oral Presentation

3. Magnesium use on prophylaxis of Vasoospasm Morbidity and Mortality Rate in Sub Arachnoid Hemorrhage(SAH)

Macedo, Sergio Kiffer (Presenting); Siqueira, Carlos Mauricio; Siqueira, Savio; Nuss, Rodrigo; Carvalho, Robson; Dias, Joana; Guarãoni, Angelo; Fiorot, Jessica

Sao Jose Do Avai Hospital, Itaperuna, Rio De Janeiro, Brazil

INTRODUCTION: Cerebral aneurysms are an important cause of morbidity and mortality. We propose this study in order to reach 2 end points: (a) its clinical incidence, confirmed by CT; and (b) the mortality of this patients in 28 days. It shows a comparison of a group of patients which used Mg(Intervention Group-1) from those that didn't use (Control Group-2).

METHOD: After institutional approval and informed consent, a prospective, randomized, single blind study was occurred between February 2008 to March 2009. The study evaluated the Mg use on patients from the 1 to 4 Beds and control group from 5 to 8 beds. The serum measure of Mg was made by colorimetric method in order to reach the measurement between 2,5 to 3,5mg/dl, using a solution of Mg 2%(SG 5% - 400ml + MgSO4 10% - 100ml / 24h), during the first 14 days of event (aneurysm rupture). Admission Criteria: Patients diagnosed with SAH confirmed by CT or cerebral angiography and $\text{I}^{\text{t}} < 96\text{h}$. Exclusion Criteria: Patients with SAH and $\text{I}^{\text{T}} > 96\text{h}$; Patients who presented a vasospasm episode in less than 24 hrs of Mg Solution Infusion; SDMOS \hat{a} €" multiple organic failure; Previous Hepatic Failure documented or TB $\geq 1,2$.

RESULTS: In a previous study evaluation were analysed a total of 94 patients with n = 46 on Group 1 and n = 48 on Group 2 (table 1 and 2). The main results refer: Group 1 \hat{a} €" Vasospasm Frequency 19,6% confidence interval(CI) = 9,4% - 33,9%; and Mortality 17,4% in 28 days CI = 7,8% - 31,4% ; Group 2 \hat{a} €" Vasospasm Frequency 54,2 % CI = 39,2% - 68,6%; and Mortality 22,9% in 28 days CI = 12,0% - 37,3%. The analysis for the vasospasm showed Odds Ratio (OR) = 0,20 CI = 0,08% - 0,51% and pvalue = 0,0011 and the mortality has OR = 0,70 CI = 0,25% - 1,95% and p-value = 0,6818.

CONCLUSION: The Group 1 obtained a greater protection on the vasospasm incidence in comparison to Group 2 but showed no difference in mortality. The p-value was significant for vasospasm but still not significant for mortality.

Poster Only, Rookwood Room

4. Nitroprusside Sodium intrathecal for prophylaxis and treatment of cerebral vasospasm associated to Subarachnoid Hemorrhage

Macedo, Sergio Kiffer (Presenting); Siqueira, Savio; Gonçalves, Ivete; Guarçoni, Angelo; Colodetti, Thais; Silva, Luciana
Sao Jose Do Avai Hospital, Itaperuna, Rio De Janeiro, Brazil

Introduction: Therapy using sodium nitroprussid intrathecal aims for a more effective approach for prophylaxis and treatment of cerebral vasospasm associated to a subarachnoid hemorrhage.

Results: Two patients ,first one female with 62 years old with aneurysm rupture of the left posterior communicating artery, SAH Fisher: III, Hunt Hess: 2. The second one male with 46 years old with artery rupture of the Middle Cerebral artery, SAH Fisher: III, Hunt Hess:2, both submitted to embolization, leading to with acute hydrocephalus, in which external ventricular drainage (EVD) was established. Through the EVD, a prophylactic intrathecal protocol was instituted (solution 2ml SNP with 10,5 ml of normal saline 0,9% applying 2ml NPS through the EVD each 12 hours for 1hour by infusion pump). Patients evolved well with no neurologic or motor sequelae, with removing of the EVD and insertion of a ventricle-peritoneal shunt, patients were sent to a ward, then discharged without complications with a modified Rankin scale = 0. The third patient was male with 37 years old with aneurysm rupture anterior communicating artery, SAH Fisher III, Hunt Hess 4,severe vasospasm per operative in the left middle cerebral artery ,treated by angioplasty with balloon. Starting by lombar catheter the treatment protocol of cerebral vasospasm: Dosage 50 mg(2ml) SNP, solution with 4ml SNP at 6 ml of normal saline 0,9% applying 4ml through the lombar catheter each 12 hours for 1hour by infusion pump.the patient progressed without complications with modified Rankin scale = 1.

Conclusion: The use of intraventricular SNP may be a viable therapeutic option in preventing and treatment cerebral vasospasms and cerebral ischemia. We noted that the cost for prophylactic therapy for 14 days was of U\$627,86; in case the patient developed clinical vasospasm, the cost for a 14 day treatment would be an average of U\$15.287,80, having a great impact in the reduction of morbidity, mortality and cost of hospital stay.

Poster Only, Rookwood Room

5. Simvastatin improves outcomes in subarachnoid haemorrhage with heavy blood load: Results from a single centre audit

Chakraborti, Santo (Presenting); Ling, John; Tolia, Christos; Walsh, Daniel
King's College Hospital, London, UK

Introduction: Do statins reduce the risk of vasospasm, delayed cerebral ischemia, and death after aneurysmal subarachnoid hemorrhage (SAH)? Two recent meta-analyses (1,2) reach opposite conclusions. The current analysis looks at outcomes associated with different prescribing practices by two neurovascular surgeons within our neurosurgical department.

Materials and Methods: 150 patients were analysed. 80 patients received simvastatin and 70 patients did not. Primary outcome measures were: modified Rankin score (mRS) and extended Glasgow Outcome Score (EGOS). Secondary outcome measure was infarction on CT. The interaction between Fisher grade and outcome was also assessed.

Results: In the statin group at 8 months follow up, the mRS was better (1.1 vs 2.5) as was the EGOS (6.8 vs 5.5). The incidence of infarction was also less in the statin group (5% vs 7%). Fisher's exact test was used to assess the interaction between functional outcome and Fisher grade. Patients were dichotomised into those with Fisher grade 3 (F3) or those who fulfilled both Fisher 3 criteria and also had intraparenchymal/intraventricular blood (F3+F4). In these subsets, the improvement in functional outcome was magnified (MRS 1.0 vs 3.0 and EGOS 7.0 vs 5.3, $p < 0.05$). Incidence of infarction was also significantly reduced in patients who had Fisher 3 or Fisher 3+4 haemorrhages (3% vs 9% for Fisher 3 and 3% vs 8% for Fisher 3+4, $p < 0.05$).

Conclusions: There is a trend towards better outcomes in patients who received simvastatin. The trend towards better functional outcomes and reduced incidence of infarction is magnified in those patients with Fisher 3 and Fisher 3+4 subarachnoid haemorrhages. The results of the ongoing STASH trial and other large randomised controlled trials will provide further insight into this potentially important therapeutic intervention.

Poster Only, Rookwood Room

Aneurysm formation, characterization, treatment

6. Anatomical classification of posterior communicating artery aneurysms

Pierobon, Marcel (Presenting); Zicarelli, Carlos; Santiago, Natali; Maudaun, Marcos; Simm, Renata; Aguiar, Paulo H P
Universidade Federal do Rio Grande do Sul, Dourados, Mato Grosso do Sul, Brazil

This article aims to review literature on the classification of aneurysms own posterior communicating artery. Scientific research aneurysms own posterior communicating artery is a practical necessity in the clinical neurological and neurosurgery, as represent 0,1 to 2.8% of all aneurysms. The classification of aneurysms of the posterior communicating artery is important in that it favors a firm diagnosis in surgical technique. The results show that there are marked differences in the results of surveys conducted among the authors studied, yet all believe that the classification of aneurysms of the posterior communicating artery facilitates the surgical technique and can eliminate possible complications during surgery.

Poster Only, not attending

7. Lenticulostriate brain aneurysms

Santiago, Nataly; Pires De Aguiar, Paulo Henrique (Presenting)
Santa Paula Hospital, São Paulo, Brazil

Objective: Lenticulostriate artery aneurysms are rare. We present two cases of lenticulostriate artery aneurysm, their clinical presentation, diagnosis, surgical treatment and postoperative follow-up, with a review about the topic.

Case Report: We report twocases of lenticulostriate artery aneurysms among 194 surgically treated aneurysms in Santa Paula and São Camilo Hospital. The first one is a 48-year-oldwhose aneurysms were detected incidentally in an angiographic study performed due to a cavernous sinus thrombosis. Both cerebral angiogram and magnetic angioresonance were performed and demonstrated a left lenticulostriate aneurysm and two parassylvian aneurysms. The other one is a 62-year-old, Japanese, hypertensive patient who presented with subarachnoid hemorrhage (SAH), Fisher scale 2 and Hunt-Hess classification 2. Her angiogram demonstrated a right LSA, left middle cerebral artery and anterior communicating artery aneurysms. No other pathology or infectious etiology was noted. Both patients were treated by opening of the sylvian fissure, allowing the visualization of lenticulostriate vessels and aneurysm clipping. Postoperative angiographies were performed in both cases. During two year follow-up the younger patient remained with distal right arm paresis and Rankin scale score 1; the older patient developed normal pressure hydrocephalus, needing peritoneal ventricular drainage.

Conclusion: Lenticulostriate artery aneurysms are uncommon. The most common clinical presentation is intraparenchymal hemorrhage. Microsurgical treatment is often the chosen modality of intervention Elderly people are more likely to develop postoperative complications before and after hospital discharge. They are under higher risk of more severe vasospasm and risk of hydrocephalus development in cases of ruptured aneurysms.

Oral Presentation

8. Intraoperative angiography within the concept of a hybrid operation room: Applications in cerebrovascular surgery

Fandino, Javier (Presenting); Marbacher, Serge; Muroi, Carl; Tausky, Philipp; Fathi, Ali-Reza; Remonda, Luca
Kantonsspital Aarau, Aarau, Switzerland

Introduction: The use of intraoperative digital subtraction angiography (iDSA) is a tool in cerebrovascular surgery. According to recent studies, iDSA has been shown to alter surgical treatment in approximately 12% of cases. Moreover, it has been demonstrated that even experienced cerebrovascular surgeons might not accurately predict the need for an iDSA. iDSA prevents unnecessary surgical manipulations after aneurysm occlusion and accurately demonstrate occlusion rates. We present our preliminary experience using routinely iDSA within the concept of a hybrid operation room (OR) for cerebrovascular surgery.

Methods and Results: Since the introduction of iDSA in our center in August 2006, a total of 95 patients underwent iDSA. Indications included intraoperative evaluation of occlusion rate of clipped aneurysms (85), dural arteriovenous fistulas (3), arteriovenous malformation (2), chemical angioplasty with papaverin (n=4), and balloon angioplasty (n=1). In two patients clip reposition was needed due to neck remnant and perfusion of the aneurysm sack after clipping. In one case the clip was repositioned due to occlusion of a vicinity vessel to the aneurysm. In one case a suboptimal occlusion of an aneurysm could be documented. In this case clip reposition was unsuccessful in reaching total aneurysm occlusion and the remnant aneurysm was coiled. A total of 5 cases underwent combined microsurgical and endovascular treatment of ruptured aneurysms and AVMs.

Conclusions: The concept of a hybrid OR must be considered in the planning and design of OR's dedicated to cerebrovascular surgery. Hybrid procedures combining endovascular with microsurgical strategies within the same surgical session are feasible and save. iDSA within the hybride OR enhances the quality in identifying cases of vessel occlusion or aneurysm remnant after clipping and facilitated the definitive treatment of cerebrovascular pathologies. These procedures are associated with cost benefit advantages.

Poster Only, Rookwood Room

9. Computerized Occlusion Rating in Embolized Ruptured Intracranial Aneurysms and the Relation to Intra- and Postinterventional Aneurysm Rehemorrhage

Milavec, Helena Maria (Presenting); Gruber, Andreas; Schuster, Ernst; Lahnsteiner, Eva; Dorfer, Christian; Krawagna, Maximilian; Knosp, Engelbert; Sherif, Camillo
Medical University of Vienna, Vienna, Austria

Introduction: A major drawback of endovascular occlusion of ruptured aneurysms is the higher rebleeding rate as compared to surgical treatment. Aneurysm coil occlusion rate (OR) is a strong predictor of aneurysm rebleeding. Computerized occlusion rating (COR) is considered an objective method to measure ORs compared to individual evaluation. We studied the OR based on COR as a risk factor for the occurrence of intraprocedural ruptures (IPR) and postprocedural ruptures (PPR).

Material & Methods: This retrospective single center study included 14 out of 249 consecutive patients treated in our institution between 1998 and 2005 who presented with IPR or PPR. Computerized DSA-Evaluation was performed by use of the new custom-made software Coil Control® which was developed in cooperation with the Institute of Medical Informatics and Biometry of the Medical University of Vienna. We used the binary logistic regression model to evaluate influences on IPR and PPR.

Results: Among 14 patients (9 female/5 male) there were 7 cases (50%) of IPR and 7 cases (50%) of PPR. Mean COR value was 85% ranging from 71% to 96%. 6 out of 7 PPRs (85.7%) had a COR of less than 90%. There was no PPR in aneurysms with a COR of 95% or higher. All patients with IPR harbored multiple aneurysms. There was a trend for females to present with PPR (P= 0.094) rather than do males. Aneurysm location, total aneurysm area, and initial Hunt and Hess Grade did not influence the occurrence of IPR or PPR in this series.

Conclusions: According to the results of this study, COR measurements reveal that the initial coil ORs achieved are lower than currently assumed and that IPR is associated with multiple aneurysms. An objectively assessed COR of 100% might reduce the risk of rebleeding and lead to aneurysm occlusion.

Poster Only, Rookwood Room

10. Biological mechanisms of adaptive remodeling in flow loaded cerebral arteries: potential significance to the pathogenesis of cerebral aneurysms in a rat model.

Pyne-Geithman (Presenting), Gail; Kurosawa, Yuko; DiNapoli, Vincent; Choutka, Ondrej; Smith, Shawn; Martini, Sharyl; El-Badewi, Yasmine; Abruzzo, Todd

University of Cincinnati, Cincinnati, OH, USA

Cerebral aneurysms (CA) are the product of an interaction between hemodynamic factors in a permissive biological and anatomical milieu; in animal models, flow loading is a necessary hemodynamic factor. The spectrum of promotional biological factors likely includes variant forms of the adaptive response to flow loading. Using a rat model, this study characterizes the molecular and anatomical events comprising the cerebral arterial response to flow loading and reveals their significance in relation to the CA phenotype. Rats were subjected to bilateral common carotid artery ligation or sham carotid surgery. Tail cuff blood pressure was monitored at baseline and post-operatively. Nineteen days after surgery the vertebrobasilar arterial complex was harvested from each rat and processed for analysis of mRNA and protein expression. Each basilar artery terminus was preserved and processed for histological examination. Flow induced changes in mRNA expression; protein expression and mural structure/histology were determined by comparing carotid ligated to sham surgery rats. Flow induced changes in mRNA and protein expression were assessed. Blood pressure was not significantly different between sham and carotid ligated animals. Over 1500 significantly ($P < 0.05$) altered gene expressions (more than 2-fold) were identified. These included: Cbp/p300 – interacting transactivator, a VEGF –responsive element active during vascular remodeling; Interferon-gamma receptor-1, known to be activated in vascular/endothelial repair after injury; abselon helper integration site 1, involved in actin filament generation; alpha-2 laminin, a blood brain barrier component, and ectonucleotide pyrophosphatase/phosphodiesterase, which has been shown to be upregulated in vascular calcification and plaque formation. Thus, our preliminary findings suggest several interconnected processes implicated in the pathogenesis of CA.

Oral Presentation

11. Association of morphological and demographic features of intracranial aneurysms with their rupture: A retrospective analysis

Dey, Saugat (Presenting); Ghosh, Sayantani; Maltenfort, Mitchell; Tjoumakaris, Stavropoula; Gonzalez, L. Fernando; Jabbour, Pascal; Rosenwasser, Robert; Jallo, Jack

Thomas Jefferson University Hospital, Philadelphia, PA, USA

Introduction: To evaluate the association of different morphological and demographic features with the rupture of intracranial aneurysms (IA), by comparing the same with the unruptured ones. The features studied include age, sex, smoking habits, alcohol consumption, hypertension, family history of ruptured intracranial aneurysms, aneurysmal size, multiplicity, neck type, aspect ratio, location and right or left sidedness.

Methods: Retrospective review of 5138 intracranial aneurysms, both ruptured and unruptured, from 2347 patients. Parameters were analyzed individually for significance via contingency tables and significant parameters ($p < 0.05$) were further examined by multivariate regression analysis.

Results: Size of the aneurysm seemed to have the strongest correlation with rupture with an odds ratio (OR) of 4.68 (95% confidence interval CI, 4.07-5.39) followed by the history of IAs in first degree relatives (OR 3.52, 95% CI 2.81-4.41), multiplicity (OR 3.53, 95% CI 2.96-4.21), smoking (OR 2.81, 95% CI 2.25-3.54), aspect ratio (OR 2.75, 95% CI 2.39-3.16), hypertension (OR 1.96, 95% CI 1.61-2.38), deviated neck (OR 1.40, 95% CI 1.16-1.69) and right sidedness (OR 1.32, 95% CI 1.17-1.49). Males had a slightly higher chances of rupture compared to females, however not significant on a multivariate model ($p = 0.08$). Although anterior circulation harbored more number of aneurysms, those in the posterior circulation ruptured more ($p = 0.012$).

Conclusion: The knowledge regarding the role of different morphological and demographic features in the process of rupture can facilitate early detection of cases 'at risk' and their subsequent surgical interventions. Intensive lifestyle modification and extensive screening from an early age should be warranted for those with a positive family history.

Oral Presentation

Animal models of SAH/Vasospasm

12. Intracisternal magnesium injection therapy (Experimental data for its clinical application)

Mori, Kentaro (Presenting); Yamamoto, Takuji; Hasegawa, Hiroshi; Nakao, Yasuaki; Esaki, Takanori
Juntendo University Shizuoka Hospital, Izunokuni, Shizuoka, Japan

Introduction: The temporal profile of the vasodilatory effect and optimal CSF Mg²⁺ concentration after intracisternal magnesium sulfate (MgSO₄) solution were investigated in the canine SAH model (Part 1). We also evaluated MgSO₄ therapy via a microcatheter for the treatment of cerebral vasospasm in the clinical setting of endovascular treatment of ruptured aneurysm (Part 2).

Material & Methods: Cerebral vasospasm was induced in 33 dogs. Part 1: In 26 dogs, on Day 7, 0.5 ml/kg of 15, 10, 5, or 0 mmol/l MgSO₄ in Ringer was injected into the cisterna magna. Angiography was performed on Day 1, and before and 1, 3, and 6 hours after the intracisternal injection on Day 7 to measure arterial diameters. Part 2: In 7 dogs, angiography was repeated on Day 1, and on Day 7 before and 1.5 hours after injection of 0.5 ml/kg of 15 mmol/l MgSO₄ via the tip of a microcatheter placed in the cisterna magna from the lumbar spine.

Results: Part 1: The arterial diameter ratios (ratio of arterial diameter after MgSO₄ injection to diameter before injection on Day 7) at 1 and 3 hours after intracisternal injection were positively correlated with CSF Mg²⁺ concentration. Arterial diameter ratios exceeded one if the CSF Mg²⁺ concentration was more than 3 mEq/l. Animals with CSF Mg²⁺ concentration more than 3 mEq/l showed significantly increased arterial diameters 3 to 6 hours after injection compared with before injection. Part 2: After intracisternal injection of MgSO₄ via a microcatheter, the spastic arterial diameters significantly increased (Fig.1).

Conclusions: The reversible effect of intracisternal MgSO₄ therapy requires CSF Mg²⁺ concentration of more than 3 mEq/l. The vasodilatory effect continues for 3 to 6 hours after injection, therefore continuous or intermittent injection is needed to constantly ameliorate vasospasm. Intracisternal MgSO₄ therapy using a microcatheter can be effective against vasospasm in the clinical setting of endovascular treatment of ruptured aneurysm.

Oral Presentation

13. Pharmaceutical prevention of cerebral vasospasm in subarachnoid hemorrhage animal models: systematic review and meta-analysis

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INTRODUCTION: Since angiographic vasospasm and delayed cerebral ischemia are potentially treatable causes of poor outcome after SAH, animal models have been developed to simulate angiographic vasospasm and test preventive drugs. The goal of this work was to determine the effect of pharmaceutical preventive treatments (tested in SAH clinical trials) on angiographic vasospasm in preclinical studies in order to determine if any model most accurately reflects results reported in humans.

MATERIALS/METHODS: A systematic review of preclinical SAH studies for prevention of angiographic vasospasm was performed. Data on treatment, species and method of induction of SAH were extracted. For the meta-analysis, data on number of animals and degree of vasospasm in treatment and control groups were extracted.

RESULTS: 74 studies were included. Overall pharmaceutical prevention of vasospasm was effective in the studies. Heterogeneity was detected. Using multivariate meta-regression, calcium antagonists were significantly associated with effect size. Subgroup analysis by drug and species, respectively, showed that all drugs except magnesium were effective and that pharmaceutical prevention was effective in all species. Meta-regression of subgroups by drug showed that the effect of erythropoietin and statins were associated with the method of induction of SAH, while calcium antagonist effect was related to the species. Meta-regression of subgroups by species showed that the effect in rats was associated with the method of induction, in dogs with plasminogen activator, and in monkeys with tirilazad and severity of vasospasm. The presence of publication bias was confirmed.

CONCLUSION: In experimental studies pharmaceutical prevention of angiographic vasospasm is effective. However, this effect is related not only to the drug but also to species and model. Further analyses need to assess the relationship between animal and human studies to determine if a most appropriate model can be suggested.

Poster Only, Pavillion Ballroom
Award Finalist

14. Dissociation of Vasospasm and Secondary Effects of Experimental Subarachnoid Hemorrhage by Clazosentan

Ai, Jinglu (Presenting); Sabri, Mohammed; Tariq, Asma; Jeon, Hyo-jin; Chen, Gang; Lakovic, Katarina; Elaine, Tang; Macdonald, R. Loch

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Introduction: A common complication of subarachnoid hemorrhage (SAH) is cerebral vasospasm of the large arteries at the base of the brain. However, a recent clinical trial clazosentan demonstrated a 65% relative risk reduction in angiographic vasospasm but had no effect on clinical outcome. We used clazosentan to gain insight into the pathophysiology of SAH by determining if decreasing vasospasm is associated with alleviation of other secondary complications of SAH such as oxidative stress, endothelial nitric oxide synthase (eNOS) dysfunction, microthromboembolism, loss of long-term potentiation (LTP) and neuronal injury.

Materials and Methods: Mice or rats were subjected to SAH by injection of blood into the chiasmatic cistern. For rats, 10 mg/kg clazosentan bolus was administered intravenously 1 hour after SAH, followed by a continuous infusion of 1 mg/kg through an osmotic pump with a catheter inserted into the jugular vein. For mice, 1 mg/kg bolus was given intraperitoneally 1 hour after SAH, and infused through an osmotic pump implanted into the peritoneum. Infusions were for 48 hours (mice) or 7 days (rats). Middle cerebral artery vasospasm, microthromboemboli, cerebral blood flow, neuronal injury and mortality were assessed for both mice and rats. Mice were also assessed for eNOS uncoupling, superoxide anion radical and peroxynitrite in the brain. Rats were also tested for LTP presence.

Results: Clazosentan preserved cerebral blood flow, alleviated vasospasm and decreased mortality but did not affect superoxide anion radical, peroxynitrite and microthromboemboli, or prevent endothelial NOS uncoupling and neuronal injury in mice. In rats, clazosentan reduced vasospasm and mortality but did not reverse the loss of LTP, microthromboemboli or neuronal cell death.

Conclusions: This study suggests that large-artery vasospasm is pathophysiologically independent of some other effects of SAH. The findings have implications for development of treatments for this disease.

Poster Only, Pavillion Ballroom
Award Finalist

15. Predeterminative Effect of Pterygopalatine Ganglion Neuron Density on Choroid Plexus Degeneration in Subarachnoid Hemorrhage Induced Choroidal Artery Vasospasm: Experimental Study.

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Introduction: The choroid plexuses (CP) have important roles in cerebral nutrition, detoxification, immunity, endocrine, secretory, repository and regulation of cerebrospinal fluid pH (1). CPs degeneration may be possible due to anterior choroidal artery (AChA) vasospasm induced by subarachnoid hemorrhage (SAH) (2). We examined whether there is a relationship among the CP degeneration, severity of AChA vasospasm and vasodilatory pterygopalatine ganglion (PPG) (3) neuron density in SAH.

Materials & Methods: This study was conducted on 24 rabbits which they had been used in formerly experiments. Five of them were normal, five of them from SHAM and fourteen of them from SAH created animals by injecting autologous blood into their cisterna magna and followed up twenty days. Their CPs, AChAs stained with TUNNEL and PPGs stained with MTC and examined stereologically. Wall ring surface/lumen surface values ($R2-r2/r2$) were accepted as vasospasm index (VSI). Densities of CPs cells and PPGs neurons were estimated stereologically. Densities of apoptotic CPs cells and VSI values compared with PPGs neurons density. The data analysis consisted of the Kruskal-Wallis and Mann-Whitney U test.

Results: The mean VSI was 0.375 ± 0.032 , the mean CPs cells density was $10320 \pm 1890 / \text{mm}^3$, and the mean apoptotic CPs cells numbers was $110 \pm 14 / \text{mm}^3$ and the mean neuronal density of the PPGs was $12310 \pm 1590 / \text{mm}^3$ in all animals ($n=24$). There was no important differences in the SHAM ($n=5$; $p < 0.5$) and less vasospasm developed animals ($n=6$; $p < 0.05$). But the mean VSI were estimated as 1.380 ± 0.150 , apoptotic CPs cells density was $6342 \pm 957 / \text{mm}^3$ and the mean neuronal density of the PPGs was $8960 \pm 990 / \text{mm}^3$ in severe vasospasm developed animals ($n=8$; $p < 0.005$) (Figure-1: A,B: PPG, C:ChA, D: CP).

Conclusion: High neuron density of PPGs may play significant roles on the prevention of AChA vasospasm. Ischemic CPs degeneration may play significant roles on the development of various neurodegenerative diseases.

Oral Presentation

16. Role of platelet-derived growth factor in cerebral vasospasm after subarachnoid hemorrhage in rats

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Introduction: Role of platelet-derived growth factor (PDGF) in cerebral vasospasm after subarachnoid hemorrhage (SAH) remains controversial. We examined that whether imatinib mesylate (imatinib), an inhibitor of specific protein tyrosine kinases of PDGF receptor (PDGFR), prevents cerebral vasospasm after SAH.

Materials & Methods: Imatinib was administered intraperitoneally to rats undergoing SAH by the endovascular perforation, and its effects were evaluated at 24-72 hours post-SAH by measuring the diameter of cerebral arteries on india-ink angiograms and neurobehavioral testing. Western blotting was performed to explore the underlying mechanisms using cerebral arteries at 24 hours post-SAH. Recombinant tenascin-C (TNC), an extracellular matrix glycoprotein, was also administered intracisternally to imatinib-treated SAH rats, and those effects were evaluated.

Results: Administration of imatinib prevented vasospasm and neurological impairments at 24-72 hours post-SAH. Western blot analyses revealed that PDGFR- α were upregulated and activated after SAH. Imatinib prevented the activation of PDGFR and p38, and an increase of PDGFR- α and TNC in the spastic cerebral arteries. Intracisternal administration of recombinant TNC prevented anti-vasospastic effects by imatinib.

Conclusions: These findings suggest that PDGF is involved in pathogenesis of vasospasm after SAH at least partially via TNC-mediated signaling pathways.

Poster Only, Pavillion Ballroom

17. Microthrombosis and Microcirculatory Spasm: A Potential Mechanism of Neurological Deterioration after Subarachnoid Hemorrhage (SAH)

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Introduction: Increasing evidence suggests the involvement of microcirculatory dysfunction in the development of delayed cerebral ischemia and neurological deficits after SAH. The goal of the study is to investigate the structural changes of microvessels and its relationship to DCI in a mouse model of SAH.

Material & Methods: 15 mice were divided into three groups; sham (n = 5), saline (n = 5) and SAH (n = 5). Experimental SAH was induced by the injection of 100 μ l autologous blood into the prechiasmatic cistern. Saline mice were injected the same volume of saline. Sham mice were subjected to needle insertion without injection. Mouse brains were then prepared for scanning (SEM) and transmission electron microscopy (TEM) for the analysis of microcirculatory spasm and microthromboembolism using standard procedures. Effects of microthrombosis and microcirculatory spasm was assessed by colocalization of fibrinogen, P-selectin and cell apoptosis.

Results: TEM and SEM demonstrated that SAH animals had significantly more microthrombi, and severe vasospasm of cortical and hippocampal arterioles. In agreement with previous work, NO levels were depleted in SAH animals in comparison to saline and sham mice. The presence of thrombosis also correlated with the degree of apoptosis in cortical sections. Additionally, membrane levels of P-selectin expression were up-regulated in the endothelial layer of arterioles in the SAH mice. This was correlated with decreased NO in the brain parenchyma.

Conclusions: In this anterior circulation mouse model, SAH results in microthrombosis and microspasm, which are correlated with neuronal cell death. This suggests that microcirculatory dysfunction may play a role in DCI after SAH. The up-regulation of P-selectin after SAH was correlated with NO depletion suggesting they may contribute to microthrombosis and microspasm.

Oral Presentation

18. Preconditioning Atrovastatins Attenuate Endothelins in Chronic Vasospasm

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Statins have been reported owing beneficial effect in cardiovascular disease as well as neurodegenerative disease. Evidence of clinical and experimental study also reveals this compound has the potential to induce apoptosis in neurons and astroglia. Thus, it was of interest to examine the effect of statins on the endothelin(ET-1), which is generated partly from glia cells, and vasospasm in the experimental subarachnoid hemorrhage(SAH). A rodent SAH model was employed. Animals were assigned to four groups (sham, vehicle, 10mg/day atrovastatin preconditioning, 10mg/day atrovastatin). Basilar artery cross sectional area was measured to evaluate vasospasm. Cerebrospinal fluid Enothelin-1 was measured using ELISA. Significant vasospasm was noted in the vehicle group (lumen potency 63.4%, compared with the sham group, $p < 0.01$), but neither in the atrovastatin preconditioning and treatment group (lumen potency, 87.3%; 70.2%). Additionally, preconditioning atrovastatin effectively decreased release of ET-1 in cerebrospinal fluid ($p = 0.204$) when compared with the sham group, and avoided experimental vasospasm, while the same condition was not found in atrovastatin treatment group. This study supports preconditioning atrovastatin attenuates endothelins production in vasospasm and suggests that astroglia might play a role in chronic vasospasm.

Oral Presentation

19. Thalidomide, a Glutamic Acid Derivative, Attenuates TNF- α - mediated Adhesive Molecules in Experimental Vasospasm

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Increased adhesion molecules, including intercellular adhesion molecule₁ (ICAM-1), vascular cell adhesion molecule₁ (VCAM-1), and E-selectin, are observed in the serum of patients following aneurysmal subarachnoid hemorrhage (SAH). Thalidomide was proved to be effective in halting arterial narrowing in a rodent SAH model. This present study is of interest to examine the effect of thalidomide on adhesion molecules/tumor necrotic factor- α (TNF- α) in this animal model.

Methods: A rodent SAH model was employed. Animals were each injected with autologous blood into the cisterna magna, and oral administration with thalidomide (1 mg/kg) was initiated 1 hr before (prevention) or later (reversal). The compound was subsequently administered at 24hr interval post-SAH. Serum samples were gathered at 72 hr post-SAH to determine TNF- α , ICAM-1, VCAM-1, and E-selectin levels (ELISA). The basilar arteries (BAs) were harvested and sliced to measure their cross-sectional areas. Furthermore, TNF- α (1ng/ml) was administered to test the down-regulation of thalidomide on TNF- α mediated adhesion molecules.

Results: Morphologically, convoluted internal elastic lamina, deformed endothelial wall, and necrotic smooth muscle were well perceived in the SAH groups, which was not in the thalidomide plus SAH groups or the healthy controls. The levels of ICAM-1, VCAM-1, and E-selectin were increased in all animals subject to SAH (SAH only and SAH plus vehicle groups) compared with the healthy controls (no SAH), but not in the thalidomide group (SAH plus thalidomide reversal and prevention). Likewise, the levels of TNF- α in the SAH only and SAH plus vehicle groups were significantly elevated ($p < 0.01$), and pretreatment and treatment with thalidomide reduced TNF- α to control levels.

Conclusion: These results show that TNF- α may play a role in mediating SAH-induced vasospasm and a reduction of both adhesive molecules and TNF- α after SAH may contribute to the antispastic effect of thalidomide.

Poster Only, Pavillion Ballroom

20. KMUP-3 attenuates cerebral vasospasm after experimental subarachnoid hemorrhage

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KMUP-3 (7-[2-[4-(4-nitrobenzene)piperazinyl]ethyl]-1, 3-dimethylxanthine) has been shown to induce aortic relaxations through both endothelium-dependent and -independent mechanisms. Mechanisms of vaso-relaxation induced by both compounds involve multiple processes, such as accumulation of cyclic nucleotides partly as a result of PDE inhibition, K-channel activation, and indomethacin-sensitive endothelium function. Therefore, we investigate the possibility of KMUP-3 protects against vasospasm after subarachnoid hemorrhage (SAH). Sprague-Dawley rats were divided into five groups (n=6/group): (1) normal control, (2) SAH only, (3) SAH + vehicle, (4) SAH + KMUP-3 (prevention), and (5) SAH + KMUP-3 (reversal). SAH was induced by double injecting autologous blood into cisterna magna. A capsular mini-pump filled with KMUP-3 was subcutaneously implanted at 72hr and 1 hr before the initiation of first SAH in the prevention and reversal protocols, respectively. The release rate is 5ml/ hour and the dose is 0.3mg/kg/day. Behavioral changes were assessed at 48 hr after second SAH. Blood pressure was monitor during procedure of SAH and before sacrifice. The degree of vasospasm was determined by averaging the cross-sectional areas of the basilar artery (BA) 7 days after the first SAH. Deficits in motor function were obvious in the SAH rats, significantly decreased of the cross-sectional in the basilar artery of SAH rats. Treatment with KMUP-3 significantly reduced these effects. There were no significant different blood pressures between these groups. In conclusion, these results demonstrate that KMUP-3 play pivotal roles in cerebral vasospasm after SAH. It shows that KMUP-3 is an effective strategy for the treatment of this disease. Further investigation for the possible treatment mechanism of KMUP-3 is considered in the future study.

Oral Presentation

21. Intracranial-Pressure-Controlled Rabbit Subarachnoid Hemorrhage Model for the Study of Early Brain Injury

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Introduction: Cerebral vasospasm is no longer believed to be solely responsible for unfavorable outcome following subarachnoid haemorrhage (SAH). Pathophysiological derangements at the time of bleeding and within the first few days are made responsible for significant brain damage. This phenomenon of early brain injury (EBI) after SAH moved into the center of current research activities. To this day, a rabbit model that reflects early events after SAH is missing.

Methods: Experimental SAH was initiated by opening of an extra-intracranial (EC/IC) shunt from the subclavian artery into the cerebromedullar cistern in 8 rabbits. Standard cardiovascular monitoring (arterial blood pressure, heart rate, ECG, end-tidal carbon dioxide partial pressure), intracranial pressure (ICP), cerebral perfusion pressure (CPP), and bilateral regional cerebral blood flow (rCBF) were continuously measured. Apoptosis was detected 24 hours post SAH using terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL). Neurodegeneration secondary to ischemia was determined using Fluoro-jade B (FJB) in bilateral basal cortex and hippocampal regions (CA1 and CA3).

Results: After initiation of the EC/IC blood shunt ICP rose to diastolic blood pressure within 1–2 minutes and returned to a steady state in 3–5 minutes. Increase of ICP caused decrease of CPP to almost zero (8.2 ± 4.9 mmHg) and drop of left and right rCBF to $23 \pm 8\%$ and $19 \pm 9\%$ of its baseline value. TUNEL- and FJB-stained sections revealed significant apoptosis and neurodegeneration in both cortex and hippocampal regions when compared to sham operated animals ($p < 0.05$).

Conclusion: The presented experimental bleeding technique closely simulates human pathophysiological sequelae of aneurysm rupture and reflects early pathophysiological derangements after SAH. The detection of marked neuronal cell death and neurodegeneration warrants the study of EBI in the EC/IC blood shunt-induced SAH model in rabbits.

Oral Presentation

22. The effect of variation in low dose LPS injection on mouse delayed cerebral vasospasm (DCV) after subarachnoid hemorrhage (SAH).

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Introduction: High dose LPS administration in the CSF causes delayed cerebral vasospasm (DCV) in rabbits (1). Low dose LPS delivered systemically in specific regimens induces tolerance to ischemic brain injury in stroke models (2). Small doses of LPS given systemically likely lead to down-regulation of inflammatory mechanisms in the brain and vascular endothelium. This has not been tested in DCV. We explored whether low-dose LPS affects delayed cerebral vasospasm (DCV) after experimental SAH in mice.

Materials and Methods: To test the development of DCV after low dose systemic LPS injection, two treatment paradigms were studied: (1) a single intraperitoneal (ip) dose of 20 µg LPS was injected 24 hours prior to experimental SAH, and (2) four 20 µg ip LPS doses were administered at 96, 72, 48 and 24 hours prior to experimental SAH. DCV was determined by India ink angiography at day 6 after SAH. Behavioral testing with a Barnes maze test (from day 5 through 10) and semiquantitative analysis of chemokines was done in a separate group of animals.

Results: The effect of low dose LPS on DCV was different in these two regimens. Vessel caliber was unchanged from control in the single LPS injection regimen ($0.113\text{mm} \pm 0.005$ vs. 0.120 ± 0.007 , $p=0.51$) but significantly different from control in the multiple LPS injection regimen ($0.113\text{mm} \pm 0.005$ vs. 0.098 ± 0.002 , $p=0.04$). By cognitive testing, the single LPS injection again protects from cognitive deficit whereas the multiple LPS injection worsen cognitive deficit after SAH (2 way ANOVA, $p<0.001$). The brain inflammatory chemokine KC was up-regulated with multiple LPS doses and down regulation in the single LPS dose.

Conclusions: Single dose LPS preconditioning is protective for DCV and the associated behavioral deficits whereas multiple dose LPS preconditioning exacerbate DCV and contribute to worse cognitive outcome. This strongly suggests an inflammatory etiology of DCV and suggests a role for the endothelium.

[Oral Presentation](#)

23. Effect of intrathecal injection of lipocalin-type prostaglandin D synthase on cerebral vasospasm after subarachnoid hemorrhage and outcome in primates

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Lipocalin-type prostaglandin (PG) D synthase (L-PGDS) is one of the major proteins in human cerebrospinal fluid (CSF), and acts as both a PGD₂-producing enzyme and as an extracellular transporter for lipophilic ligands. We have already reported that the L-PGDS concentration increased in the CSF of patients with aneurysmal subarachnoid hemorrhage (SAH) and combined with biliverdin which was one of vasoconstrictors (1,2). In this paper, we present a newly developed less-invasive SAH model with delayed cerebral vasospasm using primate, and investigated effect of intrathecal administration of L-PGDS on cerebral vasospasm and cognitive outcome. Under general anesthesia, A polyethylene tube was inserted into the subarachnoid space by a lumbar puncture and the tip of the tube was placed in the prepotine cistern of a Cynomolgus monkey. SAH was induced by 2ml of arterial blood injection through the tube twice with a two-day interval. L-PGDS (2mg/kg/day) (L-PGDS group, n=5) or artificial CSF (control group: n=6) was administrated through the tube for 7 days after SAH. Serial cerebral angiography, MRI (perfusion study), and food retrieval test (3) (to estimate spatial memory) were performed for one month. All monkeys showed cerebral vasospasm on angiogram 7 days after SAH. Diameter of basilar artery of the control group (68.82 ± 5.03 %) was smaller than that of L-PGDS group (79.00 ± 8.07 %), but there was no statistical significance. MRI perfusion study showed that mean transit time (MTT) tended to be prolonged in both group on day 7-14. Spatial memory function of L-PGDS group in the chronic state is significantly better than that of control group. We developed a less invasive and reproducible SAH model with delayed cerebral vasospasm using primate. Intrathecal administration of L-PGDS improves chronic cognitive outcome after SAH and would become a new treatment for SAH sequelae.

[Poster Only, Pavillion Ballroom](#)

24. L-CITRULLINE THERAPY PREVENTS BASILAR ARTERY VASOSPASM IN HAPTOGLOBIN 2-2 TRANSGENIC MICE AFTER INDUCED SUBARACHNOID HEMORRHAGE

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INTRODUCTION: Depletion of nitric oxide (NO) and periadventitial inflammation contribute to the pathophysiology of posthemorrhagic cerebral vasospasm. L-citrulline is an amino acid that participates in the urea cycle and increases L-arginine levels, resulting in elevated NO synthesis. Transgenic C57Bl6 mice with a haptoglobin (Hp) 2-2 genotype appear to develop more severe vasospasm, with higher concomitant inflammatory cell penetration than wild type (Hp1-1) mice after subarachnoid hemorrhage (SAH). In the present study the toxicity of systemic L-citrulline, its effect on basilar artery (BA) vasospasm, neurobehavioral scores, and iNOS/eNOS expression after SAH were evaluated in Hp2-2 mice.

MATERIALS & METHODS: Hp2-2 genotypes were confirmed by RT-PCR. L-citrulline toxicity was assessed with escalating doses. To test efficacy, Hp1-1 and Hp2-2 mice (n=64) were divided into four groups (n=32/genotype): sham surgery (n=8), SAH-no-treatment (n=8), SAH+vehicle (n=8), and SAH+L-citrulline (200-mg/kg q8h i.p., n=8). Post-SAH neurobehavioral scores were recorded at 24 hours, animals were perfused, and BAs were processed for analysis. Expression of iNOS and eNOS was determined by RT-PCR.

RESULTS: The administration of L-citrulline resulted in higher BA lumen patencies in both genotypes (Hp1-1: SAH+vehicle 77.8±3.2% vs. SAH+L-citrulline 91.8±5.9% (mean±SEM, p<0.05); Hp2-2, AH+vehicle 67.1±2.0% vs. SAH+L-citrulline 86.9±2.2%, p<0.0001). Neurobehavioral scores were higher in Hp2-2 mice treated with L-citrulline (SAH+vehicle 1.2±0.2 vs. SAH+L-citrulline 2.4±0.2, p<0.01). Expression of iNOS and eNOS increased in Hp2-2 mice after L-citrulline treatment, but limited sample sizes prevented further statistical analysis. L-citrulline was not toxic even at the highest dose.

CONCLUSIONS: L-citrulline is safe, increases BA patency, neurobehavioral scores, and NOS expression in Hp 2-2 mice post-SAH, and is a potential agent for treatment of vasospasm after SAH.

Oral Presentation

25. Administration of S-4-CPG (S-4-carboxyphenylglycine) decreases vasospasm in haptoglobin 2-2 mice by inhibition of metabotropic glutamate receptors.

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Introduction: Cerebral vasospasm is an important cause of stroke after aneurysmal subarachnoid hemorrhage (SAH)(1,2). Infiltrating immune cells such as neutrophils secrete glutamate (3). S-4-CPG is a selective antagonist of metabotropic glutamate receptors (mGluR) 1 and 5, which are expressed in endothelial cells. Vasodilator-stimulated phosphoprotein (VASP) is a protein that regulates endothelial function by modulating actin polymerization and tight junctions and nitric oxide/cGMP pathway effects. Hp2-2 genotype in humans predicts a higher risk of presenting vasospasm after SAH. We tested the efficacy of S-4-CPG in the treatment of vasospasm after induction of SAH in Hp2-2 and Hp1-1 mice.

Methods: The penetration of S-4-CPG through the blood brain barrier (BBB) in vivo after systemic injection was studied. Hp 1-1 and Hp 2-2 mice were randomized to four groups to measure basilar artery lumen patency: 1) Sham surgery (Sham, n=5), 2) SAH only (n=5) 3) SAH + vehicle (n=8), and 4) SAH + S-4-CPG (n=8). We evaluated the presence of neutrophils surrounding the basilar artery after experimental SAH. VASP phosphorylation status in response to S-4-CPG and glutamate was assessed through immunoblotting.

Results: S-4-CPG is able to cross the BBB with a concentration of 4.02±0.7 µg/mL at 1.5 hours (t_{1/2}=2.76±1.8 hr). S-4-CPG is not toxic to wild-type mice. Treatment of mice with S-4-CPG after SAH significantly decreases vasospasm after 24 h. Exposure of human brain microvascular endothelial cells to glutamate decreases the phospho-VASP. S-4-CPG maintains phospho-VASP in the presence of glutamate.

Conclusions: S-4-CPG is a potential therapeutic agent to prevent vasospasm after aneurysmal SAH. It crosses the BBB and prevents vasospasm after SAH. Maintenance of phospho-VASP suggests a possible mechanism for this effect through the maintenance of the integrity of the BBB and possibly maintaining the nitric oxide/cGMP signaling pathway.

Poster Only, Pavillion Ballroom

26. Continuous intravenous sodium nitrite can maintain reversal of cerebral vasospasm after subarachnoid hemorrhage in primates

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Introduction: Subarachnoid hemorrhage (SAH)-induced vasospasm is a significant cause of morbidity and mortality. While longterm intravenous sodium nitrite (NaNO₂) infusion has been shown to prevent cerebral vasospasm after SAH in primates, the purpose of this study was to determine if intravenous NaNO₂ can reverse established SAH-induced vasospasm in primates and whether this effect can be maintained with continuous infusion.

Methods: SAH-induced vasospasm was created in 14 cynomolgus macaques. Animals were randomized to either control (saline infusion; n=5) or treatment groups (intravenous NaNO₂ infusion for 3 hours [n=7] or 8 hours [n=2] at 300 µg/kg/hr). Arteriographic vessel diameter was blindly analyzed to determine the degree of vasospasm. Nitric oxide metabolites (NO₂, NO₃ and S-Nitrosothiols) were measured in whole blood and cerebrospinal fluid (CSF).

Results: Moderate-to-severe vasospasm was present in all animals before treatment (control, 36% ±8.3 [SD]; treatment, 45%±12.5; p=0.9). While saline infusion did not reduce vasospasm, NaNO₂ infusion significantly reduced the degree of vasospasm (27%±7.6; p=0.008). Two hours after cessation of NaNO₂ infusion, the reduction in vasospasm persisted (mean increase vessel diameter, 17.8%±10.9; p<0.05). The NaNO₂-induced vasodilation lasted 4 hours after infusion cessation. At 6 and 8 hours after infusion cessation vessels returned to spasm (mean reduction artery diameter, 38.4%±8.3). Continuous NaNO₂ infusion over 8 hours maintained a significantly reduced degree of vasospasm (32.3%±5.3 compared to 56.8%±23.1 after SAH; mean increase vessel diameter, 24.5%±17.8). Nitrite (peak value, 3.7±2.1 µmol/L), nitrate (18.2±5.3 µmol/L) and S-nitrosothiols (33.4±11.4 nmol/L) increased significantly in whole blood and nitrite increased significantly in CSF.

Conclusion: These findings suggest that intravenous infusion of NaNO₂ can reverse SAH-induced vasospasm in primates and that this effect can be maintained with prolonged infusions.

Poster Only, Pavillion Ballroom

Blood and CSF biomarkers

27. The Value of Serial Plasma/CSF Nuclear and Mitochondrial DNA Levels in Aneurysmal Subarachnoid Hemorrhage

Wang, Hung-Chen (Presenting); Kwan, Aij-Lie
Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Introduction: Increased levels of plasma nuclear and mitochondrial DNA have been reported in critically ill patients and extracellular DNA may originate from damaged tissues to peripheral blood. We tested the hypothesis that nuclear and mitochondrial DNA levels in CSF and plasma are substantially increased in acute spontaneous aneurysmal SAH patients and decrease thereafter, and that nuclear and mitochondrial DNA levels can predict treatment outcomes.

Material & Methods : We examined serial nuclear and mitochondrial DNA levels in CSF and plasma from 21 adult spontaneous aneurysmal SAH patients. The nuclear and mitochondrial DNA levels in CSF and plasma were also evaluated from 39 volunteer subjects who received myelography examinations during the study period.

Results: Our data showed that circulating plasma nuclear DNA concentrations and both nuclear and mitochondrial DNA level in CSF significant increased in aneurysmal SAH patients at admission compared with volunteers group. The levels of nuclear and mitochondrial DNA levels in both CSF and plasma were significantly increased initially and substantially decreased thereafter. Both CSF nuclear DNA and CSF mitochondrial DNA levels on admission are significantly negative correlate with Barthel Index (average) at 6 months after discharge (average) ($r=-0.668$, $P=0.013$ and $r=-0.713$, $P=0.006$), respectively, in this study. Both higher CSF nuclear (cut-off value of >85.1 ng/ml) and mitochondrial DNA levels (cut-off value of >31.4 ng/ml) at presentation were associated with worse outcome in aneurysmal SAH patients.

Conclusions: Based on our results, the higher CSF DNA levels, rather than plasma DNA levels at presentation, were associated with a worse outcome. Therefore, we look forward to more prospective multicenter investigations specifically confirm the predictive value of CSF and plasma DNA levels in outcome prediction.

Poster Only, not attending

28. Serial expression of SOCS3 in CSF after subarachnoid hemorrhage

Osuka, Koji (Presenting); Takayasu, Masakazu
Aichi Medical University, Nagakute, Aichi, Japan

Introduction: We have previously reported that elevation of inflammatory cytokine, interleukin-6 (IL-6), activates janus kinasesignal transducer and activator of transcription 3 (JAK-STAT3) signaling pathway in rat single subarachnoid hemorrhage (SAH) model (Fig. 1).¹ This pathway might play an important role in cerebral vasospasm. In this study we have explored the expression of suppressor of cytokine signaling 3 (SOCS3), which regulates JAK-STAT3 signaling pathway in CSF after SAH.

Material & Methods: Eight patients who underwent clipping surgery within 24 hour after the onset of SAH (Fisher Group 2~3) are included in this study. CSFs were collected during surgery (Day 0) and on day 1, 3, 5, 7, 10 after surgery through the cisternal drainage tube. CSF samples from unruptured aneurysm were used as control. Concentrations of IL-6 were measured using ELISA kits. SOCS3 immunoprecipitated from CSF with a SOCS3 antibody. The resulting immunocomplexes were subjected to Western blot analysis with SOCS3 antibody.

Results: Concentrations of IL-6 in CSF were increased transiently on Day 1 compared with Day 0. Those of IL-6 decreased gradually thereafter. Expressions of SOCS3 were detected on Day 1 and 3, which decreased thereafter.

Conclusions: JAK-STAT3 signaling pathway activated by IL-6 is strictly regulated by multiple factors. SOCS3 is well known inhibitor of JAK-STAT3 signaling pathway, which attaches to JAK molecules and inhibit the activity of JAK kinase. From our data expression of SOCS3 is immediately induced in CSF and might regulate the signaling pathway of JAKSTAT3 after SAH.

[Poster Only, Rookwood Room](#)

29. Do NSE and S100 in serum as well as excitatory and inhibitory amino acids in CSF indicate cerebral vasospasm or ischemia after subarachnoid hemorrhage

Jung, Carla (Presenting)
University of Heidelberg, Heidelberg, Germany

Delayed cerebral vasospasm after aneurysmal subarachnoid hemorrhage (SAH) and delayed ischemic neurological deficits are still feared complications after subarachnoid hemorrhage (SAH). Although, microdialysis has been demonstrated to be a useful method for detection of brain ischemia, it remains a local indicator for intracerebral events. Therefore, we sought to determine, if alterations in NSE and S100 in serum or CSF levels of free amino acids (AA) including inhibitory and excitatory AA may be associated with cerebral vasospasm or ischemic lesions in patients after SAH. Levels of free AA (including glutamate, aspartate, glycine and GABA) in CSF were analysed by HPLC in patients after SAH. Cerebral arteriograms were performed to assess cerebral vasospasm and follow-up CCT scans were performed to assess ischemic brain lesions. Glutamate increased after SAH. S100 in serum indicated ischemic events and glycine was associated with arteriographic cerebral vasospasm. Further studies with larger number of cases are needed to validate these results.

[Poster Only, Rookwood Room](#)

Clinical trials (ongoing, challenges, design)

30. Magnesium sulphate for aneurysmal subarachnoid hemorrhage: Why, how, and current controversy.

Wong, George (Presenting)

The Chinese University of Hong Kong, Hong Kong, China

The neuroprotective effect of magnesium sulphate infusion has been confirmed in experimental models. Pilot clinical trials using magnesium sulphate in patients with acute aneurysmal SAH have reported a trend toward a reduction in clinical deterioration due to delayed cerebral ischemia (DCI) and an improvement in clinical outcomes. Our recent multi-center trials and systemic review failed to confirm benefit in neurological outcome. In post-hoc analysis, data also did not support that a higher dose of magnesium sulphate infusion might improve clinical outcome. We here review the current literature and highlighted these discrepancies.

[Oral Presentation](#)

31. Effect of Clazosentan on Clinical Outcome After Aneurysmal Subarachnoid Hemorrhage and Surgical Clipping: Results of the CONSCIOUS-2 Study

Macdonald, R. Loch (Presenting); Higashida, Randall; Keller, Emanuela; Mayer, Stephan; Molyneux, Andrew; Raabe, Andreas; Vajkoczy, Peter; Wanke, Isabel; Bach, Doris; Frey, Aline; Marr, Angelina; Roux, Sebastien; Kassell, Neal
St. Michael's Hospital, Toronto, Ontario, Canada

Introduction: CONSCIOUS-2 assessed whether clazosentan improves vasospasm (VSP)-related morbidity/all cause mortality after aneurysmal subarachnoid hemorrhage (aSAH).

Methods: CONSCIOUS-2 was a randomized, double-blind, placebocontrolled trial. Inclusion criteria were: age 18-75 years; SAH due to ruptured saccular aneurysm secured by surgical clipping; diffuse subarachnoid clot; and WFNS grades I-IV. Patients were randomized 2:1 to intravenous clazosentan (5mg/h) or placebo. The primary composite endpoint at week 6 was: all-cause mortality; VSP-related new cerebral infarcts; delayed ischemic neurological deficit due to VSP; rescue therapy in the presence of angiographic VSP. The main secondary endpoint was clinical outcome by extended Glasgow Outcome Scale (GOSE) at week 12.

Results: There were 1147 patients (clazosentan n = 764, placebo n = 383). The primary endpoint occurred in 21% of clazosentan- and 25% of placebo-treated patients (relative risk reduction [RRR] 17%, 95% CI, -4 to 33%; p = 0.10). Poor outcome (GOSE score ≤4) occurred in 29% of clazosentan- and 25% of placebo-treated patients (RRR -18%, 95% CI, -45 to 4%, p = 0.10). In subgroup analyses, clazosentan reduced mortality/VSP-related morbidity in patients with poor WFNS grade (I-III) (RRR 33%; 95% CI, 8 to 51%) and diffuse thick SAH (RRR 25%; 95% CI, 5 to 41%); however, no effect was observed on GOSE. Rescue therapy was used in 11% of clazosentan and 16% of placebo patients. Mortality was 6% with clazosentan and 6% with placebo. Lung complications, anemia, and hypotension occurred in 34%, 22% and 12% of clazosentan-treated patients, respectively. Equivalent values for placebo were 18%, 15%, and 4%.

Conclusions: Clazosentan led to a non-significant 17% reduction in mortality/VSP-related morbidity that was not associated with an improvement in GOSE. Pulmonary complications, anemia, and hypotension were more common in patients treated with clazosentan.

[Oral Presentation](#)

32. Effect of intrathecal urokinase, intravenous fasudil and additional intraarterial fasudil for prevention of cerebral vasospasm - Comparison between clipping and coiling

Takazawa, Hiroki (Presenting); Sasaki, Tatsuya; Morita, Takahiro; Narisawa, Ayumi; Saito, Atsushi; Arai, Masayuki; Koide, Kenichiro; Harada, Jun; Hasegawa, Takeshi; Nishijima, Michiharu
Koseiren Takaoka Hospital, Takaoka, Toyama, Japan

Object: In order to prevent symptomatic vasospasm (SVS), intrathecal urokinase (UK), intravenous fasudil chrolide (FC) and additional intraarterial FC has been performed in patients who underwent acute surgery for aneurysmal subarachnoid hemorrhage (SAH). The effect of our protocol in preventing SVS was evaluated separately in clipping and coiling groups.

Materials and Methods: From January 2008 to January 2011, we have had 132 patients with aneurysmal SAH (Hunt and Kosnic grade I-IV). These patients were divided into two 2 groups: clipping group (77 patients) and coiling group (55 patients). In clipping group, intraoperative cisternal irrigation of UK and intrathecal UK via cisternal drainage was performed for 3 days after clipping. In coiling group, intrathecal UK via spinal drainage was performed for 3 days after coiling. Intravenous administration of FC (90 mg) was combined in all cases for 14 days after surgery. DSA was performed at Day 5-7 and intraarterial administration of FC (30 mg) was added if the arterial narrowing was observed.

Results: Intraarterial FC was performed in 58 in clipping group (75.3%) and 34 patients in coiling group (61.8%). Symptom due to VS remained in 3 of clipping group (3.9%, MD 1, SD 2) and in 5 patients of coiling group (9.1%, MD 1, SD 2, VS 1, D 1). Adverse effect of these therapies was not observed at all.

Conclusion: Intrathecal UK and intravenous FC and additional intaraarterial FC may be safe and effective for prevention of SVS after aneurysmal SAH. SVS was fewer in clipping group than in coiling group. This result might reflect the effect of intraoperative UK irrigation.

Poster Only, Rookwood Room

33. A prospective, randomised and controlled trial investigating the use of lumbar cerebrospinal fluid drainage following aneurysmal subarachnoid haemorrhage

Al-Tamimi, Yahia (Presenting); Bhargava, Deepti; Hall, Greg; Feltbower, Richard; Goddard, Anthony; Quinn, Audrey; Ross, Stuart
Leeds Teaching Hospital NHS Trust, Leeds, West Yorkshire, UK

Introduction: A single-centre prospective randomised and controlled trial has been conducted in order to test the hypothesis that lumbar drainage of cerebrospinal fluid (CSF) following aneurysmal subarachnoid haemorrhage (aSAH) reduces the prevalence of delayed ischaemic neurological deficit (DIND) and improves outcome.

Materials & Method: Patients with World Federation of Neurosurgeons Grade (WFNS) 1-3 aSAH and Fisher grade 2-4 were randomised to either the study group of standard therapy plus insertion of a lumbar drain or the control group of standard therapy alone. The primary outcome measure was the prevalence of delayed ischaemic neurological deficit.

Results: 210 patients with aSAH (166 f, 44 m; median age 54 years, interquartile range 45-62 years) were recruited between October 2006 and July 2010 into the control (n=105) and study (n=105) groups of the trial. WFNS grade was: 1 (n=139), 2 (n=60) and 3 (n=11); Fisher grade was: 2 (n=87), 3 (n=85) and 4 (n=38). There was no significant difference in patient characteristics between the two groups. The prevalence of DIND was 35.2% in the control group and 21.0% in the study group. This was statistically significant (p=0.021). The prevalence of a Modified Rankin Score of 4, 5 or 6 at day 10 post ictus was 62.5% in the control group and 44.8% in the study group (p=0.009). At six months this was 18.6% in the control group and 19.8% in the study group (NS). There were 22 and 15 patients with a radiologically proven infarct at discharge in the control and study groups respectively (NS). The prevalence of permanent CSF shunting was 7.6% in the control group and 5.7% in the study group (NS). There were two cases of meningitis associated with lumbar drain use and one case of a superficial lumbar drain exit site infection. All treated successfully with antibiotics.

Conclusions: There is a significant reduction in the prevalence of DIND and improvement in early outcome with the use of lumbar CSF drainage following aSAH.

Oral Presentation
Award Finalist

34. Safety and Feasibility of Long-term Intravenous Sodium Nitrite Infusion in Healthy Volunteers

Pluta, Ryszard (Presenting)
NIH/JAMA, Bethesda, MD, USA

Introduction: Infusion of sodium nitrite could provide sustained therapeutic concentrations of nitric oxide (NO) for the treatment of a variety of vascular disorders. The study was developed to determine the safety and feasibility of prolonged sodium nitrite infusion.

Material & Methods: Healthy volunteers, aged 21 to 60 years old, were candidates for the study performed at the National Institutes of Health (NIH; protocol 05-N-0075) between July 2007 and August 2008. All subjects provided written consent to participate. Twelve subjects (5 males, 7 females; mean age, 38.8±9.2 years (range, 27-56 years)) were intravenously infused with increasing doses of sodium nitrite for 48 hours (starting dose at 4.2 µg/kg/hr; maximal dose of 533.8 µg/kg/hr). Clinical, physiologic and laboratory data before, during and after infusion were analyzed.

Results: The maximal tolerated dose for intravenous infusion of sodium nitrite was 267 µg/kg/hr. Dose limiting toxicity occurred at 446 µg/kg/hr. Toxicity included a transient asymptomatic decrease of mean arterial blood pressure (more than 15 mmHg) and/or an asymptomatic increase of methemoglobin level above 5%. Nitrite, nitrate, S-nitrosothiols concentrations in plasma and whole blood increased in all subjects and returned to preinfusion baseline values within 12 hours after cessation of the infusion. The mean half-life of nitrite estimated at maximal tolerated dose was 45.3 minutes for plasma and 51.4 minutes for whole blood.

Conclusions: Sodium nitrite can be safely infused intravenously at defined concentrations for prolonged intervals. These results should be valuable for developing studies to investigate new NO treatment paradigms for a variety of clinical disorders, including cerebral vasospasm after subarachnoid hemorrhage, and ischemia of the heart, liver, kidney and brain, as well as organ transplants, blood-brain barrier modulation and pulmonary hypertension.

[Oral Presentation](#)

35. Erythropoietin for the treatment of vasospasm: a new age may be close

Grasso, Giovanni (Presenting)
University of Palermo, Palermo, Italy

Subarachnoid hemorrhage (SAH) associated with ruptured cerebral aneurysm is a devastating clinical syndrome constituting 3% of all stroke. Although several drugs have been developed with the aim to prevent the arterial narrowing and limit the delayed ischemic neurological deficit (DNID) following the initial hemorrhage, no pharmacological agent has been shown conclusively to improve the outcome in the clinical practice. Neuroprotection has been advocated as the ultimate goal in the treatment of acute neurological conditions, maintaining the highest possible integrity of cellular interactions in the brain and protection of neural function. Among all the neuroprotective agents so far proposed, a large body of preclinical and clinical studies has pointed out the high beneficial effect of the human recombinant erythropoietin (rHuEPO) in reducing neuronal injury. Systemic EPO therapy acts via EPO receptors on cerebrovascular endothelia and ischemic neurons, inhibiting neuronal apoptosis, favoring production of antioxidant enzymes in neurons and neoangiogenesis, with the ultimate effect of reversing impaired autoregulation, reducing vasospasm and DNID. Beside the encouraging results provided by the use of rHuEPO in the experimental SAH, the recent clinical trials have not been conclusively on EPO efficacy in this setting. The clinical side effects related to rHuEPO administration such as hypertension, hypertensive encephalopathy, atherosclerosis, seizures and thrombotic events, may be overcome using the new-EPO deriving drugs, which have been demonstrated to present the same neuroprotective effect without erythropoietic action. Further clinical investigations which considering the optimal tolerated dosage, therapeutic time window and duration of therapy are encouraged in order to assess safety and efficacy of this promising therapeutic agent.

[Poster Only, Rookwood Room](#)

36. Lower incidence of cerebral infarction correlates with improved functional outcome after aneurysmal subarachnoid hemorrhage

Etminan, Nima (Presenting); Vergouwen, Mervyn; Ilodigwe, Don; Macdonald, R. Loch
Heinrich-Heine University, Düsseldorf, NRW, Germany

Despite an undisputed association between vasospasm and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage (SAH), there is debate if this association implies causality. It has been suggested that cerebral infarction is a better outcome measure than vasospasm in clinical trials and observational studies. To further investigate the relationship between infarction and outcome, we performed a systematic review and meta-analysis of all randomized, double-blind, placebocontrolled trials that studied the efficacy of pharmaceutical preventive strategies in SAH patients, and had both cerebral infarction and clinical outcome as outcome events. Effect sizes were expressed in (pooled) risk ratio (RR) estimates with corresponding 95% confidence intervals (CI). Sensitivity analyses were performed for studies with a low risk of bias and for those who reported outcome at three months after SAH. Twenty-four studies including 8552 patients were included. Pharmaceutical treatments decreased the incidence of both cerebral infarction (RR 0.83 [95% CI 0.74-0.93]) and of poor functional outcome (RR 0.92 [95% CI 0.86-0.98]). The sensitivity analyses did not change the results essentially. These data suggest that the previously observed association between cerebral infarction and functional outcome implies causality, and that cerebral infarction is a better outcome measure than vasospasm in clinical trials and observational studies.

Oral Presentation
Award Finalist

37. Prospective randomized phase II trial on concomitant intraventricular thrombolysis and low-frequency head-motion after severe subarachnoid hemorrhage: Analysis of effect on clot clearance rate, radiological vasospasm, delayed cerebral ischemia and functional outcome

Etminan, Nima (Presenting); Eicker, Sven; Beseoglu, Kerim; Perrin, Jason; Steiger, Hans-Jakob; Haenggig, Daniel
Heinrich-Heine University, Düsseldorf, NRW, Germany

Previous pilot studies demonstrated a positive effect on delayed cerebral ischemia (DCI) and functional outcome in patients suffering from aneurysmal subarachnoid hemorrhage (SAH) using a combination of intracerebral thrombolysis and kinetic therapy. The goal of this prospective, randomized Phase II study was to investigate the effect of concomitant low-frequency head-motion therapy and intraventricular thrombolysis on clot clearance rate, radiological vasospasm, clinical features of DCI and clinical outcome in patients suffering from severe SAH. 50 patients suffering from severe SAH (WFNS III-V) were included in the study. Experimental therapy in the study group consisted of intraventricular application of rt-PA and lateral rotational therapy (RotoRest®) for 48 hours after admission and aneurysm treatment, was compared to best medical treatment (control group). Clot clearance rate was evaluated based on computerized tomography (CT). For these patients, radiological vasospasm, clinical features of DCI and functional outcome, as measured by modified Rankin Scale (mRS), were observed during the course of treatment. There were no severe adverse events in the study group. Clot clearance rate was higher in the study group than in the control group ($p=0.003$). The incidence of radiological vasospasm did not differ between the two groups ($p=0.713$). The incidence of clinical features of DCI in awake patients was significantly decreased in the study group ($p=0.016$). A distinct trend of mRS improvement ($p=0.06$) was noted in the study group at 1 month follow-up. The preliminary data of our Phase II study suggests a beneficial effect of concomitant intraventricular thrombolysis and lateral rotational therapy regarding clot clearance rate and clinical features of DCI, in the absence of severe adverse events. The effect on cerebral perfusion, cerebral infarction and functional outcome at 3 months remains to be analyzed.

Poster Only, Rookwood Room

38. Interim analysis of a prospective randomized controlled trial to investigate the efficacy of endovascular treatment in cerebral vasospasm after subarachnoid hemorrhage.

Platz, Johannes (Presenting); Berkefeld, Joachim; Güresir, Erdem; du Mesnil de Rochemont, Richard; Mayer, Thomas E.; König, Ralph W.; Seifert, Volker; Vatter, Hartmut

Johann Wolfgang Goethe-University, Frankfurt am Main, Germany

Introduction: Endovascular treatment (EVT) like transluminal balloon angioplasty (TBA) or intra-arterial nimodipine (IAN) represent rescue therapy for cerebral vasospasm (CVS) after subarachnoid hemorrhage (SAH). Even though improvement of vessel diameter and cerebral blood flow was shown, its efficacy to prevent delayed cerebral infarction (DCI) is missing. The aim of the present study was, therefore, to investigate if delayed cerebral infarction can be reduced by repeated EVT.

Methods: The design of the trial is prospective, controlled, and multicentric. Patients with CVS proven by MR based perfusion (PWI)- /diffusion weighted imaging (DWI) mismatch (baseline MR) are randomized into an invasive or conventional treatment arm. All patients are treated with induced hypertension. In the invasive arm, an additional digital subtraction angiography (DSA) is performed after the MRI. CVS is then treated by TBA and/or IAN. 48±12 hours after treatment, follow-up MRI is acquired to assess the treatment success. If CVS persists, DSA and EVT is repeated. Primary endpoint is the development of DCI defined as new DWI-lesions on a final MRI. For analysis the brain was partitioned into 19 segments of comparable volume. Major infarct (MI) was defined as a lesion ≥ 50% of one segment.

Results: This interim analysis is based on the first 18 (of 92 scheduled) patients of the trial. 7 were randomized into the invasive and 11 into the conventional arm. In the interventional arm, one patient died before the final MRI. DCI was observed in 7 (64%) patients in the conventional and in 3 (50%) in the interventional arm. MI occurred in 4 (36%) and in 2 patients (33%), respectively.

Conclusion: This interim analysis suggests that there are patients who may benefit from EVT. However, DCI was also observed in spite of supposed successful EVT. It remains, therefore, to be seen if the efficacy of endovascular therapy is significantly higher than the periprocedural risk including transport of these patients.

Oral Presentation

39. Development of nicardipine prolonged-release implants after clipping for preventing cerebral vasospasm: From laboratory to clinical trial

Kasuya, Hidetoshi (Presenting)

Tokyo Women's Medical University Medical Center East, Tokyo, Japan

Currently, there are no drugs supported by sufficient evidence of efficacy for cerebral vasospasm, despite abundant evidence of anti-vasospasm drugs at an experimental level. We have developed a drug-delivery system that can be implanted intracranially at the time of surgery for aneurysm clipping. We started our project on 1994 for making slowly-releasing drug-delivery system in vitro. We presented the efficacy and safety of this drug delivery system using both canine double hemorrhage and clot placement model. Since October 1999, nicardipine pellets (NPs) have been used to prevent vasospasm in patients with SAH. NPs were placed in the cistern of the cerebral arteries, where thick clots existed, and, therefore, vasospasm related to delayed ischemic neurological deficits (DIND) was highly probable. Vasospasm was completely prevented in the arteries in cisterns with thick clots by placing NPs. In the first 100 patients treated with NPs, the ratio of DIND, severe angiographical vasospasm, cerebral infarctions and independent rate were 7%, 11%, 5% and 82%, respectively. No complications were experienced. The incidence of cerebral vasospasm in the multicenter cooperative trial of 136 patients between Jan 1, 2007 and Dec 31, 2008 is similar to that of our first trial. The randomized, double-blind trial of 32 patients with severe SAH was done in Germany. The incidence of angiographic vasospasm was significantly reduced (73% control versus 7% NPs). The NPs group demonstrated more favorable outcome as well as a lower incidence of deaths (38% control versus 6% NPs). In conclusion, we found that vasospasm is completely prevented in arteries in cisterns with thick clots by placing NPs. Implantation of NPs improves clinical outcome of SAH patients. We consider that this could not be achieved by developing new drugs but by developing methods to maintain an appropriate concentration of the drug in the target cerebral artery and its surrounding environment.

Oral Presentation

CNS pathology: acute and delayed deficits

40. Microglia (MG) Activation after Acute Subarachnoid Hemorrhage (aSAH) – An Intraparenchymal Reaction to an Extraparenchymal Disease

Schneider, Ulf (Presenting); Radon, Anja-Maria; Brandenburg, Susan; Brück, Wolfgang; Heppner, Frank; Vajkoczy, Peter
Charité - Universitätsmedizin Berlin, Berlin, Germany

Objective: Recently, inflammatory reactions have been discussed as contributor to brain damage after aSAH. To characterize the intraparenchymal reaction to the extraparenchymal noxa of aSAH, we evaluated time-course and cytokine expression of MG activation after experimental and clinical aSAH.

Methods: 1.) Experimental aSAH was induced in mice. On days 4, 14 and 28 brain slices were stained for ionized calcium binding adaptor molecule 1 (Iba-1) and amyloid precursor protein (APP). 2.) CD11b-positive MG cells were isolated from murine brains after aSAH on days 4, 14 and 28. PCR was performed for TNF α , IL 1a, b, 6 and their corresponding receptors. 3.) Human brain sections of patients who had died from aSAH were stained for Iba-1 and APP.

Results: In murine as well as in human brain sections after aSAH an intraparenchymal accumulation of Iba-1 positive cells was documented which started around day 4 and peaked around day 14. Furthermore, axonal damage could be recorded in murine and human brain slices according to intense APP expression, following the same time course and expression pattern. (humand4/d14/d28: Iba-1 (cells/hpf): 13.5 \pm 8.7 / 73.4 \pm 36.8 / 15.7 \pm 4.6; APP-activation(arbitrary scale): 0.3 / 1.8 / 1.0; murined4/d14/d28: Iba-1 (area in sqmm): 0.23 \pm 0.04 / 4.13 \pm 1.22 / 3.15 \pm 2.77; APP (area in sqmm): 0.19 \pm 0.01 / 3.36 \pm 1.01 / 0.27 \pm 0.02). Cytokine levels of IL1 a, b, 6 and TNF as well as the corresponding receptors in the isolated CD11bpositive cells were significantly increased on day 14. (IL1a 2.5, IL1b 5.2, TNF 4.1, IL1R2 3.2, TNFR1 2.4, TNFR2 4.1 –fold vs. control)

Conclusion: A significant intraparenchymal accumulation of MG cells was documented after aSAH. Time course, expression pattern and upregulated transcription of inflammatory cytokines corresponded well with signs of axonal damage. For the first time MG activation as intraparenchymal inflammatory reaction to aSAH was characterized and a hint on the underlying mechanisms could be achieved

Oral Presentation
Award Finalist

41. Global Cerebral Atrophy After Subarachnoid Hemorrhage: A Marker of Acute Brain Injury and Impact on Outcome

Tam, Alan KH; Ilodigwe, Don; Li, Zeyu; Schweizer, Tom; Macdonald, R Loch (Presenting)
St. Michael's Hospital, Toronto, Ontario, Canada

Background: Atrophy in specific brain areas correlates with poor neuropsychological outcome after subarachnoid hemorrhage (SAH). Infarct volume in SAH patients has been studied as a surrogate to predict outcome but no study has compared global atrophy in SAH with outcome. Global atrophy might reflect diffuse early brain injury from SAH. This analysis of the CONSCIOUS-1 data examines the relationship between global brain atrophy after SAH and clinical factors and outcomes.

Methods: CONSCIOUS-1 was a randomized double-blind, placebo-controlled trial involving 413 patients with aneurysmal SAH. Of the 413 patients in the CONSCIOUS-1 study, we excluded patients with focal infarctions. 97 remaining patients had baseline and week 6 CT images that were analyzed quantitatively to derive a total brain volume at each time. Percentage difference in volume between time points was compared against clinical variables.

Results: Greater age (OR 0.95 CI 0.89-0.997), female gender (OR 3.32 CI 1.06-10.47) and higher body temperature (OR 0.22 CI 0.07-0.68) were significantly correlated with brain atrophy. There was increased incidence of angiographic and delayed neurological deterioration in patients with greater brain atrophy, but these factors were not independently predictive. Greater brain atrophy was significantly correlated with poor functional outcome as defined by the modified Rankin scale (mRS, OR 0.084 CI 0.01-0.72), severity of the stroke defined by NIHSS score (OR 0.22 CI 0.07-0.76), worse executive functioning rating (OR 0.34 CI 0.12-0.99) and lower EQ-5D score (OR 3.18 CI 1.06-9.56).

Conclusions: In patients with SAH, worse mRS, NIHSS, executive functioning rating and EQ-5D scores correlate with greater brain atrophy. Several clinical factors were independently predictive of brain atrophy, including age, female gender and ICU body temperature. There was no independent association with radiological or clinical vasospasm.

Oral Presentation

42. The influence of parenchymal damage and hemorrhage on cortical spreading depression in patients with subarachnoid hemorrhage

Eriksen, Nina (Presenting); Pakkenberg, Bente; Rostrup, Egill; Lauritzen, Martin J; Fabricius, Martin E; Woitzik, Johannes; Scheel, Michael; Strong, Anthony J; Dreier, Jens P

Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark

Introduction: Acute brain injury is often followed by serious complications. The initial brain damage is the most important factor for outcome; hence, we are focusing on the early phase after subarachnoid hemorrhage. In ischemic brain injury, a phase of delayed deterioration sometimes develops between 2 - 5 days post ictus, and is associated with severe and refractory brain swelling and poor outcome. Experimental investigations have shown that spreading depolarization of grey matter may lead to progressive deterioration in border zones of ischemic foci. This project is a part of COSBID – CoOperative Study on Brain Injury Depolarizations, and the aim is to focus on volume estimation of injured regions as a prognostic tool.

Materials & Methods: Quantitative measurements, such as regional volumes under various conditions are essential for understanding both structural and functional changes in the brain, and assessing prognosis. The affected brain tissue in patients suffering from acute brain injury is very inhomogeneous; hence traditional methods are not always applicable, and automatic methods may not be able to match the individual observer. Stereological techniques are alternative tools for quantification of damage to the human brain. In the current project, we used the Cavalieri method, to obtain the volume of injured regions and hemorrhage in patients during the acute and sub-acute stage on CT scans. The volumes were correlated to events of spreading depolarizations.

Results: Our preliminary data in 20 patients showed a positive correlation between the number of spreading depolarization, versus volume of parenchymal damage and hemorrhage.

Conclusion: This may suggest that increased parenchymal damage and blood in the subarachnoid space favor the occurrence of spreading depolarization in acute brain injury. However, we will need to analyze more patients to fully understand the relationship between and parenchymal damage, hemorrhage and spreading depolarization.

[Oral Presentation](#)

43. Clinical, transcranial Doppler ultrasound, radiological features and, prognostic significance of delayed cerebral ischemia

Wong, George (Presenting); Poon, Wai Sang

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Objective: We aimed to investigate the profiles and prognostic values of delayed cerebral ischemia (DCI) and delayed cerebral infarction.

Methods: IMASH was registered at www.strokecenter.org/trials, and www.ClinicalTrials.gov (NCT00124150). Data of 327 patients were retrieved for logistic regression analyses. Data of the published randomized controlled clinical trials were retrieved, reviewed and analyzed.

Results: Seventy-one (22%) patients developed DCI and 35(11%) patients developed delayed cerebral infarction. Permanent focal neurological deficits occurred in 17/71(24%) patients, and there were 7/71(10%) death directly related to DCI. Only 18(25%) patients with DCI and 7/35(20%) patients with delayed cerebral infarction had mean middle cerebral artery velocities (transcranial Doppler ultrasound) over 120 cm per second. Regarding the prognostic significance of the components of DCI, delayed cerebral infarction predicted favorable outcome in terms of GOSE (OR 3.1, 95% CI 1.3 to 7.8), good outcome in terms of mRS (OR 3.0, 95%CI 1.2 to 7.7), and independent activity of daily living in terms of BI (OR 3.6, 95%CI 1.4 to 9.2) at six months, after adjustments for other prognostic factors. On the other hand, clinical deterioration predicted in-patient mortality (OR 8.8, 95%CI 1.6 to 48.8) after adjustments for other prognostic factors.

Conclusions: Delayed cerebral ischemia and delayed cerebral infarction carried different prognostic values in aneurysmal subarachnoid hemorrhage.

[Poster Only, Rookwood Room](#)

44. Early CT perfusion measurement in 50 patients with aneurysmal subarachnoid hemorrhage – a tool to detect primary damage determining clinical course and outcome

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Introduction: The clinical outcome of patients suffering from aneurysmal subarachnoid hemorrhage (SAH) seems to be influenced by the primary perfusion damage as well as by delayed cerebral ischemia. The goal of the present study was to investigate the predictive impact of early CT-perfusion measurement in SAH patients on the clinical course and outcome.

Materials & Methods: 50 patients with aneurysmal SAH were included in the prospective setting of this study. An early CT based perfusion measurement within the first 12 hours after initial bleeding was performed. The mean transit time (MTT) and the time to peak (TTP) were recorded. The results were correlated with the WFNS score and the Glasgow Outcome Scale (GOS).

Results: The initial TTP correlated significantly with the WFNS scale ($P = 0.004$; correlation coefficient $r = 0.405$; Spearman correlation (Sc) with significance level (sl) of 0.01), i.e. the higher TTP, the higher the WFNS-score. The initial MTT correlated negatively with the GOS ($P = 0.016$; $r = -0.339$; Sc , sl : 0.05) as did the initial TTP ($P = 0.018$; $r = -0.333$; Sc , sl : 0.05), i.e. the higher MTT or TTP the lower the GOS. 36 patients, i.e. 72 % required an EVD. Patients with EVD showed a significantly higher MTT than those without EVD ($P = 0.001$; $r = 0.472$; Sc , sl : 0.01). The occurrence of vasospasm in the clinical course correlated highly with initial TTP ($P = 0.008$; $r = 0.370$; Sc , sl : 0.01), i.e. the higher the initial TTP the more likely was the occurrence of vasospasm in the clinical course.

Conclusion: The results of the present study reveal that 1) early CT-perfusion measurement correlates highly significantly with the initial clinical grade and 2) contains a highly predictive impact to determine the clinical course and outcome in patients suffering from aneurysmal SAH. Based on the present results delayed cerebral ischemia as the major secondary morbidity after SAH could be esteemed as a sequel of the primary decreases in perfusion status.

Poster Only, Rookwood Room
Award Finalist

45. Early activation of cell death after subarachnoid hemorrhage

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Introduction: Cell death in brain by apoptosis and necrosis is present at 24 hrs after experimental subarachnoid hemorrhage (SAH). It is not known how soon after SAH does cell death begins. We studied apoptosis and necrosis in brain during the first 24 hr after SAH.

Methods: Animals (rats) were sacrificed at 10 min to 24 hrs after SAH, or sham surgery ($n = 5$ per group per time studied). Apoptosis in brain sections was studied by cleaved caspase-3 immunostaining and necrosis by fluoro-jade staining. Vascular and parenchymal origin of caspase-3 positive cells was studied by rat endothelial cell antigen (RECA-1; endothelial marker) and DAPI staining. Brains sections were photographed and the number of caspase-3 and fluoro-jade positive cells was determined (IP lab). Brain areas examined included cerebral cortex, caudate putamen and hippocampus.

Results: Caspase-3 staining was present in endothelial and parenchymal cells at 10 minutes after SAH and was significantly greater than time matched shams ($P < 0.05$). Caspase-3 staining increased further at 24hr after SAH and was similar in all brain regions and across hemisphere. Fluoro-jade positive neurons were present in caudate putamen at 6 hrs after SAH. By 24 hrs fluoro-jade staining had spread to cortex, hippocampus, and caudate putamen and was significantly greater in right compared to left hemisphere. No fluoro-jade staining was present in sham animals.

Conclusion: Our data establishes an early activation of endothelial and parenchymal cell apoptosis and neuronal necrosis after SAH and identifies end points that can be targeted to reduce early brain injury after SAH.

[Oral Presentation](#)

Definition and diagnosis of vasospasm

46. Evaluation of cerebral vasospasm with CT angiography and perfusion CT

Kasuya, Hidetoshi (Presenting); Tanaka, Noriko; Hagiwara, Shinji; Tani, Shigeru; Akiyama, Mami; Koseki, Hirokazu; Hana, Taijun; Yoshimura, Chika

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Introduction: We investigated the usefulness of three-dimensional CT angiography (CTA) and perfusion CT (pCT) for the diagnosis and management of cerebral vasospasm (CV).

Material and Methods: 41 consecutive patients suffering from aneurysmal SAH were retrospectively evaluated. CTA and pCT were performed on the day of admission (day 0) and at least once between days 5-14. Data were analyzed by comparing clinical characteristics and findings with conventional CT and digital subtraction angiography (DSA).

Results: Eighteen patients were >60yo in age; 24 were female; 22 were WFNS grade 4 and 5; 32 were in Fisher group 3; 35 of the ruptured aneurysms were located in the anterior circulation; 18 were treated by craniotomy. Sensitivity and specificity for detecting severe CV on DSA was 100% and 76%, respectively. 4 patients received intra-arterial vasodilator treatment according to the results found in CTA and pCT. False positive findings was caused by coil artifacts, parenchymal hematoma and effects related to the surgical and endovascular procedures. CV was well characterized with combination of mean transit time, cerebral blood flow and cerebral blood volume.

Conclusions: CTA/pCT can detect critical vasospasm and be used as an indicator for invasive treatment.

Poster Only, Rookwood Room

47. Application of non-invasive continuous monitoring system, INVOS® for detecting cerebral vasospasm

Ono, Shigeki (Presenting)

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Introduction: Detection of cerebral vasospasm after subarachnoid hemorrhage is somehow difficult because, so far, there are no absolute tools detecting it timely and accurately. Although transcranial Doppler monitor, SPECT, 3DCT or angiography are all excellent monitoring tools for vasospasm, these are not continuous non-invasive monitoring systems. The INVOS monitor shows continuous regional saturation data in the brain cortex through the skin and skull and it reveals site-specific insights on perfusion of brain cortex. Also, it is not only non-invasive detachable monitor but also small and portable one. We here report whether or not it can be useful for detection of cerebral vasospasm and analyze its advantages and disadvantages for vasospasm detection.

Methods and results: Patients showing Hunt and Kosnik grade between 2 and 4 were included from 2005 to 2011 in Okayama University Hospital. The INVOS monitoring system is used for detecting vasospasm from day 3 to day 14. Monitoring probes were usually attached to the regions predicted for vasospasm. When INVOS values decreased, immediate angiography was routinely performed, and we checked a degree of vascular narrowing and then intraarterial Fasudil infusion was carried out if necessary. In 38 patients the INVOS was applied and saturation was analyzed for detecting vasospasm. Except 2 patients, vasospasm was well detected timely and accurately. Vasospasm could be treated very well by intraarterial Fasudil injection in the early time of vasospastic period. However, local vasospasm or vasospasm in the very peripheral lesions could not be detected very well in 2 patients.

Discussion and conclusions: The INVOS monitor can detect cerebral vasospasm timely and accurately. It may be a good monitoring system for detecting vasospasm. In the meantime, we need some ingenuity for detecting local vasospasm or vasospasm in the very peripheral regions.

Poster Only, Rookwood Room

48. Detection of Delayed Ischemic Neurological Deficits by Combined Transcutaneous and Intraparenchymal Near Infrared Spectroscopy

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University Hospital Zurich, Zurich, Switzerland

Introduction: The benefits of monitoring cerebral blood flow (CBF) in patients after aneurismal subarachnoid hemorrhage are apparent. New techniques combining near infrared spectroscopy (NIRS) and indocyanine green (ICG) dye dilution to estimate CBF are available. However, transcutaneous NIRS with optodes applied over the skin is controversially discussed, because the signal is contaminated by extracerebral tissues. Recently a new brain tissue probe for combined monitoring of intracranial pressure (ICP), CBF and oximetry with NIRS has been developed.

Methods: For NIRS measurements two approaches are applied: 1. A conventional intraparenchymal probe for ICP monitoring is supplied with optical fibers (NeMo Probe®). The light is coupled out into the brain tissue and collected after absorption and scattering with a light detector. 2. A plaster based patch carrying optodes is placed over the skin (NeMo Patch®). Central venous injections of 0.2mg/kgbw ICG are performed. Measurement values are collected in parallel, with the NeMo Probe® and NeMo Patch® (NeMo System®, NeMoDevices, Zurich, Switzerland). Regional values for the mean transit time of ICG, CBF and cerebral blood volume are calculated.

Results: In patients with high-grade subarachnoid hemorrhage pairs of repetitive measurements with the transcutaneous approach and NIRS-ICP tissue probe are performed. Measurement values obtained with the two approaches are compared and allow estimating the amount of extracerebral signal contaminating the patch values.

Conclusions: NIRS allows for synchronous determination of multiple parameters of cerebral oxygenation and hemodynamics with two approaches. The strictly non-invasive approach allows monitoring over different vascular territories in patients being awake, whereas the minimal-invasive NIRS-ICP probe might be the ideal device in comatose/sedated patients. Algorithms to eliminate the extracerebral contamination of the signal obtained with optodes over the skin will be developed.

Poster Only, Rookwood Room

Endovascular approaches

49. Beneficial effect of selective, better than non-selective, intra-arterial infusion of fasudil hydrochloride for symptomatic vasospasm following subarachnoid hemorrhage

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Introduction: Recently, intra-arterial infusion of fasudil hydrochloride (IAF) for symptomatic vasospasm (SVS) following subarachnoid hemorrhage (SAH) has become popular. However, the optimal method of IAF is uncertain.

Material & Methods: Over 2 years, 103 patients with aneurismal SAH were treated with clipping or coiling. Among them, 30 patients (29.1%) developed SVS. We performed IAF in 19 patients, 9 patients with selective method and 10 patients with non-selective. Functional outcome was evaluated by final Glasgow outcome scale (GOS). We referred GR as 1, MD as 2, SD as 3, PVS as 4 and dead as 5. We analyzed the extent of cerebral infarction due to delayed vasospasm by original grading scale. We referred computed tomography (CT) scores as follows: no definite infarction due to vasospasm as 1, less than 1cm in major axis as 2, limited in the territory of one cortical branch as 3, extending to the territory of 2 or more cortical branches but unilateral as 4, extending to bilateral hemispheres as 5. We retrospectively compared the group that underwent selective IAF into the intracranial arteries such as the middle or anterior cerebral arteries (group1) with the group that underwent IAF into the extracranial carotid or vertebral arteries (group2) and the group without IAF (group3). This retrospective study does not require an approval of IRB in our institute.

Results: Mean GOS of the group1, group2 and group3 were 2.3, 3.6 and 3.5, respectively. Mean GOS of the group1 was less than that with group2 ($p < 0.01$: statistical method; student t-test) and with group3 ($p < 0.01$). Mean CT scores of the group1, group2 and group3 were 2.1 3.2, and 3.8, respectively. Mean CT score with group1 was less than that with group2 ($p < 0.05$) and that with group 3 ($p < 0.01$).

Conclusions: This study may show that selective IAF is more effective than non-selective IAF. Thus, it is strongly suggested that, in the cases of SVS, we should try to perform selective IAF rather than non-selective IAF.

Poster Only, Rookwood Room

50. Intraarterial verapamil-induced seizures: an underrecognized side effect or the result of rapid reperfusion?

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Introduction: Seizures induced by intraarterial infusion of vasodilators in patients with post-hemorrhagic vasospasm are exceptionally reported and thought to result from a direct effect of the drug on metabolically challenged neurons. We present evidence that challenges this concept.

Materials and Methods: A 27-year old female patient suffered rupture of a left posterior communicating artery aneurysm resulting in massive subarachnoid hemorrhage. Despite stent-assisted coiling, the aneurysm exhibited early recanalization and rerupture within a few weeks, necessitating additional coiling. Five days later, the patient became obtunded with a dense left hemiparesis. Cerebral angiography demonstrated severe vasospasm of the right internal carotid and middle cerebral arteries. The patient was treated by direct intraarterial infusion of verapamil (20 mg) into the right internal carotid artery.

Results: Immediately after verapamil infusion, the patient complained of severe headache and became agitated. This was quickly followed by left hemibody clonic convulsions and a self-limited secondary generalized tonic-clonic seizure. Repeat angiography documented immediate resolution of vasospasm and enhanced right hemispheric perfusion. Following a transient postictal state, the patient regained normal consciousness and left hemibody motor strength. Over the next few days, the patient had recurrence of severe symptomatic vasospasm twice. She was treated with intraarterial verapamil and exhibited each time headache, agitation, and a secondarily generalized tonic-clonic seizure followed by neurological improvement.

Conclusion: Intraarterial verapamil-induced seizures do not necessarily represent an adverse event. In the absence of an angiographically demonstrable complication such as intraprocedural aneurysm rupture, seizures may be caused by rapid drug-induced reperfusion of the ischemic brain and may be followed by neurological improvement.

Poster Only, Rookwood Room

51. Continuous Intra-Arterial Nimodipine Infusion for the Treatment of Cerebral Vasospasm

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BACKGROUND To treat cerebral vasospasm balloon angioplasty has shown to be effective and permanent in selected cases. But since it is technically challenging and insufficient, if more distal segments are involved, it has not proven to be clinically effective. I.a. infusion of vasodilators is known to reverse vasospasm. There is indication that calcium channel blockers have longer lasting effects, including the also systemically applied nimodipine, which has been used i.a. by neurointerventional groups for subarachnoid hemorrhage but also catheter induced vasospasm. Nevertheless infarctions occurs in patients treated by i.a. short time infusion in up to 3 sessions with nimodipine. Therefore we investigated long-term i.a. infusion.

METHODS In case of clinical, TCD, CBF or angiographic signs of vasospasm patients were included in the study protocol. Patients were treated by 1 - 4 microcatheters implanted for 12 to 288 hours in the ICAs or VAs. Nimodipine was infused through the microcatheters with a dosage of 0.5 to 3 mg/h per vessel. All patients received at least single antiplatelet therapy.

RESULTS So far in the first 25 patients there were two major complication with one internal carotid artery dissection and one embolism. In the first patient, the guiding catheter was left in place, not exchanged for a microcatheter. The other patient did only receive heparin for anticoagulation, but no antiplatelet therapy. Only one patient did not respond to an i.a. dosage of 1 mg/h, but the following day, the dosage was increased to 2 mg/h nimodipine in one ICA and this led to normalization of the vessel diameters. In all other patients complete or almost complete recanalization occurred. Clinical evaluation at that time is not completed.

CONCLUSION Continuous intra-arterial nimodipine infusion for the treatment of cerebral vasospasm has the potential to recanalize all patients until the end of the vasospastic phase. Randomized clinical studies are demanded.

Poster Only, Rookwood Room

52. Transluminal balloon angioplasty for symptomatic distal vasospasm refractory to medical therapy in patients with aneurysmal subarachnoid hemorrhage.

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Introduction: Cerebral vasospasm (VSP) is a major cause of morbidity and mortality associated with subarachnoid hemorrhage (SAH). The current endovascular paradigm for vasospasm refractory to medical therapy is to perform angioplasty for proximal vessel VSP, and vasodilator infusion for distal vessel VSP. The authors report their experience of a large series of balloon angioplasty for distal VSP refractory to medical therapy in patients with aneurysmal SAH.

Material and Methods: Retrospective series of 32 patients with SAH and symptomatic VSP refractory to medical therapy who were treated with balloon angioplasty for distal vessel VSP. Immediate angiographic results, procedure related complications, and clinical outcomes were assessed.

Results: From September 2001 to January 2010, 32 patients with symptomatic vasospasm refractory to medical therapy underwent angioplasty for distal arterial vasospasm. There were 26 women (81.3%), aged from 29 to 67 years. A total of 175 vessels were angioplastied (95 proximal and 80 distal). The only complication was due to rupture of an incompletely clipped aneurysm that was treated by immediate coiling and did not result in any clinical worsening. Repeated treatment was needed for 6 arteries (6/80=7.5%). There was no procedure related symptomatic complication. Good outcomes (mRS <2) were observed in 23/28 (82.1%) patients with follow-up.

Conclusion: Balloon angioplasty for distal VSP is safe, effective, and decreases the need for repeated intra-arterial treatments seen with infusion of vasodilator.

Poster Only, Rookwood Room
Award Finalist

53. Comparison of the clinical outcome of cerebral vasospasm post aneurysmal subarachnoid hemorrhage in patients undergoing to two types of angioplasty: mechanical and chemical.

Aburto-Murrieta, Yolanda (Presenting); Marquez, Juan Manuel; López-de-Santiago Iván, Iván Tomás; Hernández-Curiel, Bernardo; Bonifacio-Delgadillo, Dulce
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Introduction. Cerebral vasospasm (CV) causes significant morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (aSAH). Angiographic vasospasm (AV) is seen in 30%-70% of patients post aSAH and delayed ischemic neurologic deficit (DIND) has been associated with this. Prevention of rebleeding with exclusion of ruptured aneurysm is followed by a combination of interventional procedures, such as mechanical and chemical angioplasty and medical therapy.

Methods. Retrospective clinical trial of 30 patients post aSAH (anterior circulation) with AV were treated with intrarterial nimodipine therapy or mechanical angioplasty for CV and fulfilled Eskridge criteria. At admission Hunt-Hess (HH) and Fisher Scale was registered. Doppler Transcranial was done before and after. Clinical follow up was recorded every 3 months for 1 year. AV was classified as none/mild, moderate or severe, (0%-33, 34%-66%, >67%) and infarctions were categorized as secondary to AV, other or unknown causes.

Results. We performed 22-intrarterial nimodipine and 8 mechanical angioplasty in 30 patients (18 female) aged 18-74 year. At admission the patient were HH scale I:20%, II:30%, III:37%, IV:13% and Fisher III:33%, IV:20%. No differences in both scales were found. Intracranial Doppler velocities post procedure diminished at least 45%. Clinical outcome was defined as good when a modified Rankin (mRs) scale 0-2 was present at 12 months. Good outcome was present in 37% of patients. Good outcome between the 2 groups was similar, p=0.36. Mortality was 20%.

Conclusions. We did not find differences in the clinical outcome despite the modality of endovascular strategy and adequate angiographic and ultrasound response.

Poster Only, Rookwood Room

54. Treatment of RCVS with intraarterial verapamil: a novel treatment paradigm?

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Introduction: RCVS is a poorly understood clinical entity and the precise underlying pathophysiology is unknown. Both primary or idiopathic and secondary types have been described. The diagnosis is usually made clinically with sparse angiographic evaluation depending upon institutional preference and the index of suspicion for underlying vasculitis. Other than avoiding the triggers and withdrawal of secondary causes, no treatment has gained therapeutic currency.

Methods: Four patients at this institution were treated with intraarterial (IA) verapamil after an angiographic diagnosis of RCVS was made. All patients had a clinical history suggestive of the diagnosis, prompting the angiographic evaluation. Three patients were females and one was male. Age range was 19-58 years. Clinical presentation encompassed thunderclap headache in 3 patients, subarachnoid hemorrhage in 1 patient, cerebral ischemia/infarction in 2 patients, and reversible parieto-occipital T2 signal hyperintensities in 1 patient. None of the patients had disabling neurological deficits. The mean dose of IA verapamil used was 10- 20 mg per vessel.

Results: Complete resolution of angiographic abnormalities with dramatic improvement in arterial luminal caliber was demonstrated 15 minutes after verapamil infusion in all cases. There were no adverse neurological sequelae. The improvement in vascular luminal caliber was the same in anterior and posterior circulations. There were no procedure-related complications in any of these cases. No angiographic follow up was done as there was no recurrence of symptoms.

Conclusion: IA verapamil may have a role in proving the angiographic confirmation of the RCVS diagnosis and could be a therapeutic modality available in the acute phase of the disease to prevent symptomatic ischemia in severely affected patients.

Poster Only, Rookwood Room

Human imaging studies

55. Quantification of subarachnoid hemorrhage by 3D-CT Part 2: Correlation between hematoma volume and symptomatic vasospasm

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Object: We developed a new method to quantify hematoma volume of subarachnoid hemorrhage (SAH) by three-dimensional computed tomography (3D-CT) (Sato T, et al: *Neurol Med Chir (Tokyo)*, 2011). We analyzed correlation between hematoma volume and symptomatic vasospasm (SVS) using our method.

Methods: The study population consists of consecutive 50 patients with aneurysmal SAH. These 50 patients were divided into 3 groups: patients without SVS, with SVS and transient symptoms, and with SVS and persistent symptoms. The appearance of a newly developed low density area on CT was also evaluated. With respect to reference findings regarding the occurrence of SVS, we evaluated the presence of a new low density area on CT. 3D-CT angiography was performed if SVS was suspected, but not in all cases.

Results: SVS occurred in 4 of the 50 patients. SVS was transient in 2 patients and persistent in 2 patients who manifested a newly-developed low density area. The chronological changes in the SAH volume in the 4 patients with SVS are shown in Figure. At all time points examined, the SAH volume was significantly smaller in patients without SVS than in those with SVS ($p < 0.01$ on days 0, 1, 4, 7, and 14). The minimum SAH volume in patients with SVS was 92, 76, 42, 24, and 12 ml on days 0, 1, 4, 7, and 14, respectively.

Conclusions: This method allows the quantitative determination of SAH volume based on 3D-CT, and may be useful in clinical studies of cerebral vasospasm.

Oral Presentation

56. Quantification of subarachnoid hemorrhage by 3D-CT Part 1: Comparison of hematoma volume between 3D-CT and 2D-CT

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Object: Estimation of hematoma volume of subarachnoid hemorrhage (SAH) on computed tomography (CT) has been subjective and not quantitative, although relation between hematoma volume and development of delayed ischemic neurological deficit has been confirmed. Attempts to quantify the SAH with a novel software-based technique and twodimensional CT (2D-CT) encountered problems posed by the partial volume effect and the absence of SAH in the convexity or posterior fossa. We compared hematoma volume between our new method by 3D-CT and conventional one by 2D-CT.

Methods: We used the width of CT number 40-80 Hounsfield units (HU), which was the reported CT number of SAH ranges. We examined correlation of hematoma volume by actual measurement and by 3D-CT using experimental hematomas and compared SAH volumes by 3D-CT with those by 2D-CT. Experimental hematomas were made with blood obtained from 10 volunteers. Clinical materials were 50 patients with aneurysmal SAH.

Results: The experimental hematoma volume was determined by actual measurements and by 3D-CT on days 1, 4, 7, 11, and 14. The coefficients on days 1 and 4 were relatively high and the correlation between measured and estimated volumes was significant on days 7, 11, and 14. These results suggest that CT number of 40-80 may be reliable to estimate the hematoma volume by 3D-CT. The SAH volume including the volume of normal structures was automatically calculated (V1). The volume of normal structures (V2) was calculated in another 50 patients without intracranial lesions as 12 ml. The total SAH volume was defined as V1 minus mean V2. The mean SAH volumes by 3DCT and by 2D-CT were 44 ml and 34 ml on days 0. The SAH volume was significantly larger by 3D-CT than by 2D-CT ($p<0.05$).

Conclusion: The SAH volume by 3D-CT may be reliable to estimate the hematoma volume. This method can rapidly measure SAH volume based on 3D-CT and chronological changes in the SAH volume can be monitored easily.

Poster Only, Rookwood Room

Markers, monitoring and point of care

57. Paradoxical Increases in Near Infrared (NIR) Cerebral Oximetry in Subarachnoid Hemorrhage Suggest Vasospasm.

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Henry Ford Hospital, Detroit, MI, USA

Introduction: The combination of hypertensive and vasodilatory (HVD) therapy via IV nicardipine demonstrated faster reductions in mean MCA velocities following SAH. Recently we reported reductions in brain oxygenation, measured by nearinfrared spectrophotometry (NIRS)-determined regional cerebral oxygen saturation, with this therapy. We report findings in a patient that potentially explain this finding.

Methods: A report of a patient treated with HVD. Data included daily TCD mean velocities of the middle cerebral and basilar arteries and NIRS oximetry. NIRS is a noninvasive, optically-based technique to monitor brain oxygenation by determining the cerebral tissue oxygen saturation. Light from the NIRS forehead sensor passes through extracerebral and brain tissues, the latter containing oxy- and deoxyhemoglobin within cerebral arterioles, capillaries and venules. NIRS oximetry is a mixed-vascular oxygen saturation parameter.

Results: 5 of 7 patients demonstrated reduced TCD velocities correlating to nicardipine administration. Six had NIRS performed. These values significantly ($p<0.05$) fell 8-10% in 5 of 6 patients correlating with nicardipine administration. NIRS reductions correlated to neurologic exam improvements. One patient required intra-arterial therapy for vasospasm. The patient's TCD velocities and NIRS readings increased in the days before angiography. Angiography demonstrated ECA to ICA collateral flow via branches of the internal maxillary artery. After angioplasty and intra-arterial nicardipine, the NIRS values decreased 4-8%, continue to decrease 5-8% over 8 hours, then rose to pre-angiography levels.

Conclusions: In this small series of HVD therapy, we found reductions in both TCD velocities and NIRS values in the majority of patients treated. This patient's findings suggest reductions in NIRS values the result of reduced ECA arterial contribution. Increases in NIRS values may suggest increased ECA to ICA cross-flow in vasospasm.

Poster Only, Rookwood Room

58. Systemic Interleukin-6 Levels Reflect Illness-course and Prognosis of Patients with Spontaneous Nonaneurysmal Subarachnoid Hemorrhage

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Introduction: Patients with spontaneous non-aneurysmal subarachnoid hemorrhage (SAH) show either perimesencephal (pm) SAH, with blood strictly located around the midbrain, or non-perimesencephalic (non-pm)SAH, with hemorrhage extending into adjacent cisterns. Patients with non-pmSAH have a higher risk for a complicated clinical course with development of cerebral vasospasm (CVS) and subsequent worse outcome. Systemic inflammatory response syndrome has been linked to CVS occurrence and worse outcome in patients with aneurysmal (a)SAH. We analyzed whether levels of systemic interleukin (IL)-6, a proinflammatory cytokine, differ in patients with pmSAH from those with non-pmSAH reflecting a different clinical course.

Methods: The clinical course with attention to symptomatic CVS-occurrence and clinical outcome was assessed during a oneyear period. Daily systemic IL-6 levels and leukocyte (Lc) counts were measured in the acute phase in 11 patients with pmSAH and in 9 patients with non-pmSAH.

Results: Patients with non-pmSAH had statistically significant higher IL-6 levels during the illness-course compared to patients with pmSAH (14.7 ± 3.2 vs. 3.0 ± 0.6 pg/ml, $p=0.001$), while the Lc counts did not differ (11.5 ± 0.5 vs. $11.2 \pm 0.6 \times 10^3/\text{ul}$, $p=0.485$). Patients with non-pmSAH had a statistically significant longer stay in the neurocritical care unit (16.4 ± 2.1 vs. 10.2 ± 1.1 days, $p=0.012$). In 2 of 9 patients with non-pmSAH symptomatic CVS occurred in the illness-course. However, the dichotomized outcome did not differ between the groups.

Conclusions: Higher IL-6 levels in patients with non-pmSAH supports the common observation of more complicated illness-course with higher incidence of CVS compared to patients with pmSAH.

Poster Only, Rookwood Room

59. Early Platelet Activation after Subarachnoid Hemorrhage is related to Poor Admission Hunt Hess Grade

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Introduction: Brain injury that occurs at the time of aneurysm rupture is the most important predictor of long term outcome, yet little is known about the mechanism of injury. Animal models of subarachnoid hemorrhage (SAH) suggest that early platelet activation and microthrombosis may play a role.

Methods: Spontaneous SAH patients were prospectively enrolled within 72 hours of ictus, excluding those with baseline coagulation abnormalities. Jugular and peripheral venous blood was sampled at admission prior to angiography or aneurysm repair and then every 12 hours for 72 hours and assessed by thromboelastography (TEG) and standard measures of coagulation. TEG studies were compared between good and poor grade patients (Hunt-Hess [HH] 1-3 versus 4-5) using repeated measures analysis. Logistic regression analysis was used to compare TEG and standard coagulation values with admission demographic features, and neurological status.

Results: A total of 15 SAH patients were studied. The median HH score was 3 (range 1-5) and 27% of patients were HH 4-5. Abnormally high TEG measures of platelet activation occurred in 88% of patients. Jugular venous TEG markers of platelet activation were significantly higher in poor grade compared to good grade patients. This difference in platelet activation was evident earlier in venous jugular blood (beginning at 24 hours) and was more pronounced ($P=0.008$) as compared to peripheral venous blood (36 hours; $P=0.033$). There was a trend towards increasing TEG measures of platelet activation with each increase in HH grade (OR 4.6, 95% CI 0.8-26.0, $P=0.083$). D-Dimer levels were elevated in 90% of patients (median 2.0, range 0.3-18.5) as were fibrinogen levels (median 523, range 264-617), but neither were related to clinical status.

Conclusions: Platelet activation, as measured by TEG, is increased acutely in poor grade SAH patients compared to good grade patients and may play a role in the mechanism of early brain injury.

Oral Presentation

60. Is routine renal screening in aneurysmal subarachnoid hemorrhage patients rational?

Ghosh, Sayantani; Dey, Saugat (Presenting); Maltenfort, Mitchell; Tjoumakaris, Stavropoula; Gonzalez, L. Fernando; Jabbour, Pascal; Rosenwasser, Robert; Jallo, Jack
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Introduction: Acute kidney injury is a problem of paramount importance in majority of critically ill patients and hence a routine renal screening is warranted. But there is very little known regarding the burden of acute kidney injury in aneurysmal subarachnoid hemorrhage (aSAH), therefore we have studied the effects of levels of serum BUN (Blood Urea Nitrogen), creatinine and bun:creatinine ratio in such patients to investigate the extent of kidney damage.

Material & Methods: 1000 cases of aSAH with no prior history of kidney disease were retrospectively reviewed for their levels of serum BUN, creatinine and their ratio, on the day of admission and on the 4th day of hospitalization, from the records of Thomas Jefferson University Hospital. Outcome of the patients on discharge was measured via extended Glasgow Outcome Score (GOS-E). Parameters were initially analyzed by student's t test and were further scrutinized by multivariate regression analysis.

Results: Kruskal-Wallis (non-parametric) comparisons across outcomes came significant for BUN, creatinine and BUN: creatinine ratio ($p < 0.0001$); however in a multivariate regression model, serum creatinine was not found to have any effect on the outcome. Odds ratio for a poor outcome with per unit increase of the BUN: creatinine ratio, in a multivariate regression, was 1.39 (95% CI, 1.22- 1.68) for the 4th day and 1.22 (95% CI, 1.14- 1.31); while a ratio of $< 10:1$ on the day of admission was also related with poor prognosis ($p < 0.0001$). Inverse prediction provided 50% chance of good outcome at the maximum BUN:creatinine ratio of 22.2: 1 (95% CI, 21.2: 1- 23.5: 1).

Conclusions: It was concluded that serum BUN imbalances affecting the short term prognosis of aSAH patients are mainly following the cardiovascular or neurologic damage and are less likely as a result of direct kidney injury, hence routine renal screening in all such patients is questionable.

Poster Only, Rookwood Room

61. Copeptin as possible prognostic biomarker for disease severity and detector for cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage

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Introduction: Aneurysmal subarachnoid hemorrhage (SAH) is known to be a severe disease with high morbidity and mortality rates. Early prediction of possible outcome is consequential for optimized care and treatment decision. Copeptin, a stable and sensitive surrogate for vasopressin release, has recently emerged as a valid prognostic biomarker in a variety of severe diseases. Its prognostic value for spontaneous SAH is yet unknown.

Material & Methods: Copeptin levels were measured with a line immuno assay in 10 consecutive SAH patients on day of admission. Further measurements were conducted in synchronization with performed CT-perfusion scans to also evaluate a possible correlation between copeptin levels and changes if the mean transit time. Initial disease severity was assessed by Glasgow Coma Scale (GCS) and WFNS Grade on admission, recovery by Glasgow Outcome Score (GOS) on discharge. GCS smaller than 10 and WFNS larger than 3 was considered as severe; a favorable outcome was defined as a Glasgow Outcome Score of 4 and above.

Results: Preliminary results demonstrated that there is a positive correlation between copeptin level on admission and disease severity. Higher copeptin levels were detectable in patients with GCS 10 or lower. Copeptin levels also correlated positively with changes of the mean transit time measured by repeated CT-perfusion scans ($r \approx 0.6$). Copeptin levels were notably higher in patients during presence of cerebral vasospasm. Statistical significance could not yet be reached due the present low number of patients

Conclusion: Copeptin is a promising prognostic biomarker for mortality and outcome in a variety of diseases associated with cerebral damage. Its predictive value for the disease severity of aneurysmal SAH patients seems promising. Furthermore copeptin could be considered as a possible supportive detector of cerebral vasospasm. Larger studies with close consideration of comorbidities have to be conducted for further evaluation.

Poster Only, Rookwood Room

Neurocritical care monitoring

62. Multicenter controlled trial about the reexamination of triple H therapy after subarachnoid hemorrhage-preliminary report

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Introduction: Volume management is crucial in intensive care, however, in some patients it is very hard to achieve optimal water balance. Subarachnoid hemorrhage (SAH) patient is a representative example. Cardiopulmonary complications are common after SAH: neurogenic pulmonary edema, cardiac failure, and so on. Triple H therapy is a standard management after SAH, but it also has adverse effects; pulmonary edema, increased intracranial pressure, hyponatremia, sepsis and so on. We have started the multicenter controlled trial about cardiopulmonary function after SAH. We describe herein a trial of minimally invasive PiCCO Plus monitoring of cardiopulmonary function to reexamine the effect of triple H therapy after SAH.

Material & Methods: This multicenter controlled trial analyzed the cardiopulmonary functions of 87 patients after SAH by PiCCO Plus monitoring over a period of two weeks.

Results: Output, contractility and afterload were essentially normal after SAH. However, slightly elevated intrathoracic blood volume led to fluid redistribution that caused hydrostatic fluid retention in the lung tissues. Triple H therapy had no additional cardiopulmonary features except for the elevated plasma BNP levels. Persistent catecholamine release and altered sensitivity of blood vessels to catecholamines caused the blood volume redistribution and hydrostatic pulmonary edema. Cardiac preload due to catecholamine release led to brain natriuretic polypeptide (BNP) release, resulting in natriuresis. This appeared to be the underlying mechanism of cerebral salt wasting syndrome.

Conclusions: We found that hydrostatic pulmonary fluid retention occurred after SAH. Triple H therapy gave no additional benefits on the systemic circulation after SAH.

Poster Only, Rookwood Room

63. Continuous Regional Cerebral Oxygenation Monitoring by Multi-Channel Near-Infrared Spectroscopy to Assist Intra-Arterial Fasudil Therapy for Vasospasm after Subarachnoid Hemorrhage

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Introduction: Cerebral vasospasm following aneurysmal subarachnoid hemorrhage (SAH) that has refractory to maximal medical management can be treated with intra-arterial administration of vasodilators. However, it remains unclear regarding the effectiveness on regional cerebral circulation to assume the treatment response of distal/diffuse vasospasm.

Methods: We describe a 63-year-old male with SAH and intracerebral hematoma due to ruptured right middle cerebral artery aneurysm, and developed aphasia and right-side weakness on day 9 after SAH onset, which were highly suspected of delayed cerebral ischemia attributable to diffuse vasospasm in the distal territory of left anterior and middle cerebral arteries. The patient was refractory to hyperdynamic therapy but successfully treated with intra-arterial infusions of fasudil hydrochloride assisted by continuous monitoring with regional cerebral oxygen saturation (rSO₂) with 4-channel flexible near-infrared spectroscopy sensors and cardiac output.

Results: Decreased and fluctuating rSO₂ in angiographically documented vasospasm territories elevated immediately after intra-arterial fasudil infusion in accordance with the relief of vasospasm that correlated with neurological improvements. The procedure was repeated on day 11 since the effect was transient and vasospasm-related neurological deterioration recurred. The symptoms gradually resolved accompanied by maintenance of stable rSO₂ values, resulting in favorable functional outcome.

Conclusions: Our clinical experience suggests that rSO₂ with multi-channel near-infrared spectroscopy may provide noninvasive, real-time, and clinically relevant information to assist intra-arterial fasudil therapy for detecting and treating distal/diffuse vasospasm.

Poster Only, not attending

64. Mechanism for Dobutamine-Induced Hyperdynamic Therapy for Reversing Focal Cerebral Ischemia Affected by Vasospasm after Subarachnoid Hemorrhage

Mutoh, Tatsushi (Presenting); Ishikawa, Tatsuya; Kobayashi, Shinya; Yasui, Nobuyuki; Suzuki, Akifumi
Research Institute for Brain and Blood Vessels-Akita, Akita, Japan

Introduction. Therapeutic hemodynamic augmentation by increasing cardiac output (CO) with dobutamine (DOB) is a valuable method of maintaining rCBF and oxygenation in the dysautoregulated vascular territories by vasospasm following aneurysmal subarachnoid hemorrhage (SAH). We aimed to determine the effect of DOB-induced hyperdynamic therapy on CO and regional cerebral oxygenation (rSO₂) for reversing clinical deterioration attributable to vasospasm.

Materials & Methods. Fifty-five consecutive patients with SAH treated surgically within 24 h of ictus and diagnosed to have symptomatic vasospasm between days 4 and 14 were investigated. For medical treatment, DOB was administered at an initial dose of 3 µg/kg/min and then increased in 3 µg/kg/min increments until resolution of the symptoms. CO and rSO₂ changes during the therapy in conjunction with the assessment of neurological improvements were analyzed.

Results. A total of 225 DOB challenges were performed with a maximum dose of 11±3 µg/kg/min. In spasm-affected territories, decreased and/or fluctuating rSO₂ was detected compared with recordings in other brain regions. Patients who exhibited rapid elevation of CO by DOB challenges had subsequent uptake and stabilization of rSO₂ followed by improvement of the symptoms. A fairly strong relationship was found between peak CO slope and rSO₂ elevation during each DOB challenge ($r = .79, P < 0.0001$), while a poor correlation was found between peak CO change and rSO₂ ($r = .33, P = 0.09$). Area under the ROC curve to discriminate neurological responders to DOB was higher for peak CO slope (0.86 ± 0.08) than for peak CO (0.65 ± 0.12) ($P < 0.05$). Values of average peak CO slope of 0.007 predicted neurological improvement with DOB therapy, with 83% specificity and 70% sensitivity.

Conclusion. Maximal hemodynamic acceleration rather than the peak CO values plays a key role of DOB hyperdynamic therapy in relieving focal cerebral ischemia in patients suffering from vasospasm after SAH.

Poster Only, not attending

65. Cerebral Hemodynamic Changes After Wartime Traumatic Brain Injury

Razumovsky, Alexander (Presenting); Tigno, Teodoro; Hochheimer, Sven; Stephens, Frederick; Bell, Randy; Vo, Alexander; Severson, Meryl; Ecker, Robert; Armonda, Rocco
Sentient NeuroCare Services, Inc., Hunt Valley, MD, USA

Introduction: Traumatic brain injury (TBI) is associated with the severest casualties from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). From Oct. 1, 2008 AMEDD TBI program initiated transcranial Doppler (TCD) ultrasound service for TBI patients who were presented for care at the National Naval Medical Center and at the Walter Reed Army Medical Center.

Material & Methods: Seventy-seven patients (3 females) aged 18 to 40 years (mean 25.9 years) who had suffered wartime TBI injuries (with Glasgow Coma Scale scores ranging from 3 to 15) were investigated with daily TCD studies. A total of 483 TCD recordings (mean 6.5 tests per patient, ranged from 1 to 30) were made after admission. There were 28 (36.4%) patients after explosive blast injury, 18 patients (23.4%) after GSW and 31 (40.2%) after other causes of TBI (closed, penetrating, MVA, falls, etc). Comprehensive TCD protocol and well published diagnostic criteria for vasospasm and abnormally high intracranial pressure (ICP) applied in all cases.

Results: The TCD signs of mild, moderate and severe vasospasm were observed in 28 (36.4%), 16 (20.7%) and 9 (11.6%) of patients, respectively. The TCD signs of intracranial hypertension were recorded in 51 (66.2%) patients. Abnormally high CBFV's without TCD signs of vasospasm and abnormally low CBFV's were recorded in 7 (9%) and 12 (15.5%) of all patients, respectively. Four patients (5.1%) underwent transluminal angioplasty for post-traumatic vasospasm treatment.

Conclusions: These findings demonstrate that delayed cerebral arterial spasm is a frequent complication of combat TBI and that the severity of spasm is comparable to that seen in aneurysmal SAH. In addition, TCD provided valuable information about the presence of abnormally high ICP. Because vasospasm and intracranial hypertension represent significant events in a high proportion of patients after wartime TBI, close daily TCD monitoring is recommended for the management of such patients.

Oral Presentation

66. Illustrative Case: Failure to detect severe cerebral vasospasm following subarachnoid hemorrhage despite multiparameter neuromonitoring

Sikorski, Christopher (Presenting); Dent, Wolfgang; Wyss, Sabine; Farokhzad, Faraneh; Keller, Emanuela
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Introduction: The detection of delayed ischemic neurological deficits (DIND) in sedated or comatose patients after aneurysmal subarachnoid hemorrhage (SAH) remains an unsolved challenge in neurocritical care.

Methods: An illustrative case of a patient is presented with multiple delayed ischemic infarctions with late onset at day 16, not detected by multimodality neuromonitoring. Specific limitations of actual available neuromonitoring modalities are discussed.

Results: A 43 year-old patient was admitted to the neurointensive care unit, University Hospital of Zurich, suffering from poor grade SAH (H&H grade 4, WFNS grade 5, Fisher grade 3). Ruptured aneurysm of the basilar artery was successfully coiled within 24 hours after admission. Further treatment included insertion of an external ventricular drainage, intravenous administered nimodipin, high-dose magnesium-sulfate and pravastatine. As the patient remained comatose, a multiparameter neuromonitoring was established, including bilateral probes for brain tissue oxygenation and cerebral microdialysis supplemented by oxymetry from the right-sided jugular bulb and daily transcranial Doppler (TCD) blood flow measurements. TCD showed increased mean blood flow velocities in both middle cerebral arteries (MCA) in the early stage after SAH onset up to a maximum of 198 cm/sec, however without corresponding pathological findings in repeated CT perfusion scans. No clear signs for ischemia or impaired cerebral metabolism were detected by invasive neuromonitoring until a routine CT scan on day 16 demonstrated bihemispheric MCA infarction due to angiographically confirmed diffuse vasospasm.

Conclusion: In this case, brain-specific neuromonitoring failed to indicate severe vasospasm underlining the limitations of the various techniques. Neuromonitoring data should be carefully interpreted and additional strategies in vasospasm screening are needed, focussing on real-time, global parameters.

Poster Only, Rookwood Room

67. Prognostic role of basic csf analysis in aneurysmal subarachnoid hemorrhage patients.

Dey, Saugat (Presenting); Ghosh, Sayantani; Maltenfort, Mitchell; Tjoumakaris, Stavropoula; Gonzalez, L. Fernando; Jabbour, Pascal; Rosenwasser, Robert; Jallo, Jack
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Introduction: The basic cerebrospinal fluid (csf) analysis is routinely performed in aneurysmal subarachnoid hemorrhage (aSAH) patients but is seldom studied. We have considered the effect of the csf picture on the patient outcome and whether it can serve as a prognostic indicator for such patients.

Material & Methods: A retrospective review of 661 cases of aSAH with no preexisting systemic infection was done from the records of Thomas Jefferson University Hospital. The levels of csf glucose, protein, leukocyte (wbc) count and culture, on the day of the admission and 10th day post admission, was compared with the patient outcome at discharge, as measured via extended Glasgow Outcome Score (GOS-E). Parameters were analyzed by student's t test.

Results: Csf glucose > 80 mg/dl ($p < 0.0001$) and csf protein > 90 mg/dl ($p < 0.0001$) on admission and csf glucose > 75 mg/dl ($p = 0.0013$) and csf protein > 85 mg/dl ($p < 0.0001$) on the 10th day worsened the chances of a good outcome; although csf glucose < 40mg/dl ($p < 0.0001$) and csf protein < 15mg/dl ($p < 0.0001$) at admission were also associated with higher mortality. Per 1 mg/dl rise of csf glucose had an odds ratio of 1.087 (95% CI, 1.078-1.096) for a poor outcome and 1.048 (95% CI, 1.041-1.055) for death; while per 1mg/dl rise in csf protein had an odds ratio of 1.93 (95% CI, 1.84-2.1) for a poor outcome and 1.55 (95% CI, 1.37-1.73) for death. Csf wbc count of 3-5/dl was associated with the best outcome ($p = 0.0014$), more so on the 10th post admission day ($p < 0.0001$). Culture negative cases had a better prognosis than culture positive ones on both the days.

Conclusion: All the csf parameters, both on admission and follow up, gave their best prognostic results in their median values. Hence basic csf analysis can give an insight to the prognosis of aneurysmal subarachnoid hemorrhage patients, however more elaborate and prospective studies could offer us a clearer picture.

Poster Only, Rookwood Room

68. A Platform for Multimodal Data Collection and Research in Neurocritical Care

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Neuromonitoring in patients with severe brain trauma and stroke is often limited to intracranial pressure (ICP), while advanced Neuroscience Intensive Care Units may also monitor brain oxygenation (PtiO₂), electroencephalogram (EEG), cerebral blood flow (CBF), or neurochemistry. For example, cortical spreading depolarizations (CSDs) recorded by electrocorticography (ECoG) are associated with delayed cerebral ischemia after subarachnoid hemorrhage and are an attractive target for novel therapeutic approaches. However, to better understand pathophysiologic relations and realize the potential of multimodal monitoring, a common platform for data collection and integration is needed. We have developed a multimodal system that integrates clinical, research, and imaging data into a single R&D platform. Our system is adapted from the widely-used BCI2000, a brain-computer interface tool which is written in C++ language and supports over 20 data acquisition systems. It is optimized for real-time analysis of multimodal data using advanced time and frequency domain analyses and is extensible for research development using a combination of C++, Matlab, and Python languages. Continuous streams of raw and processed data, including BP, ICP, PtiO₂, CBF, ECoG, EEG, and patient video are stored in an open binary data format. Selected events identified in raw (e.g. ICP) or processed (e.g. CSD) measures are displayed graphically, can trigger alarms, or can be sent to researchers or clinicians via text message. For instance, algorithms for automated detection of CSD have been incorporated, and processed ECoG signals are projected onto 3D brain models based on patient MRI and CT scans, allowing real-time correlation of pathoanatomy and cortical function. This platform will provide clinicians and researchers with an advanced tool to investigate pathophysiologic relationships and novel measures of cerebral status, as well as implement treatment algorithms based on such multimodal measures.

[Oral Presentation](#)
[Award Finalist](#)

69. Improved Cerebral Oxygenation after Intrathecal Nicardipine for Vasospasm: Case Report

Freeman, William; Taussky, Philipp (Presenting); Daugherty, Wilson; Tawk, Rabih, MD; Hanel, Ricardo; Miller, David; Barrett, Kevin; Richie, Alexa
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Introduction: The effects of intrathecal nicardipine are described by pre- and post-transcranial Doppler ultrasound (TCD). We describe a patient with improvement in multimodal monitoring variables of alpha delta ratio (ADR) monitoring by EEG, non-invasive near-infrared spectroscopy (NIRS) cerebral oximetry, and ICP/ CPP values after IT-nicardipine for vasospasm.

Methods/Results: Case report of a 60 year old Asian female with a modified Fisher 4 subarachnoid hemorrhage with right frontal intraparenchymal hematoma from rupture of an right anterior cerebral artery pericallosal aneurysm. The patient arrived comatose, Glasgow Coma Scale 7 (E1M5V1T), with intact brainstem reflexes. She underwent right frontal craniotomy and clipping of her aneurysm along with placement of external ventricular drain (EVD). Thick temporal bone revented TCD vasospasm monitoring. The patient developed severe vasospasm of the bilateral ACA-A1, MCA-M1s and mild bilateral PCA-P1 and basilar arteries on CT angiogram on day #13. Intrathecal nicardipine 4mg was administered and transiently elevated EEG ADR from 0.4 over the left hemisphere to 0.6 and from 0.6 on the right to 0.8 about 15min after procedure lasting up to 1 hour before returning to baseline values. NIRS oximetry rose from a baseline of 82 over the right frontal head region to a peak of 99, whereas the left rose from 78 to 84, and CPP rose from 87 to 122 before returning to baseline. ICP went from 14 to 11 mmHg during the same timeframe. The patient did not sustain cerebral infarction as measured clinically or by noncontrast CT scan by hospital discharge.

Conclusion: Intrathecal nicardipine elevated cerebral oximetry by NIRS, increased CPP, and elevated alpha delta ratio transiently but was short lived. Larger studies are needed for intrathecal nicardipine, optimal dosing, frequency, and its effects on vasospasm, cerebral blood flow, CPP, and delayed cerebral infarction.

[Poster Only, Rookwood Room](#)

Neurovascular coupling/blood brain barrier

70. Subarachnoid blood converts neurally-evoked vasodilation to vasoconstriction in rat brain cortex

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Background: Neurovascular coupling is the basis of functional hyperemia in the brain. This matching of blood flow to regional brain function involves the coordinated activity of neurons, astrocytes and parenchymal arterioles. Under physiological conditions, localized neuronal activation leads to elevated astrocyte endfoot Ca²⁺ and vasodilation. Currently, the impact of subarachnoid hemorrhage (SAH) on neurovascular coupling is unknown.

Methods: Using a combination of two-photon and infrared-differential interference contrast microscopy, arteriolar diameter and astrocyte endfoot Ca²⁺ were simultaneously measured in cortical brain slices from un-operated (control), sham-operated and SAH model rats.

Results: Increased neuronal activity caused by electrical field stimulation (EFS) elicited the predicted elevation in endfoot Ca²⁺ and vasodilation in brain slices from control animals. In brain slices from SAH model animals; 1) EFS induced a similar increase in endfoot Ca²⁺, but in marked contrast, caused arteriolar constriction. 2) Bypassing neurons by directly elevating endfoot Ca²⁺ via photolysis of caged Ca²⁺ also caused arteriolar constriction. 3) Paxilline (1 μM), a blocker of large-conductance calcium-activated potassium (BK) channels, greatly reduced EFS-induced vasoconstriction. The action of paxilline likely reflects block of BK channels on astrocyte endfeet, as this compound did not influence the ability of neuronal activation to increase endfoot Ca²⁺ and did not directly alter arteriolar diameter.

Conclusions: These data demonstrate a fundamental switch from vasodilation to constriction in response to neuronal activation in cortical brain slices from SAH model rats. This pathological vasoconstriction involving elevation of astrocyte endfoot Ca²⁺ and K⁺ efflux via endfoot BK channels may play role in the development of neurological deficits following SAH. (Supported by NIH P01 HL095488, R01 HL078983, R01 HL44455 & Totman Medical Research Trust).

Oral Presentation
Award Finalist

Nitric oxide and oxidative stress

71. Simvastatin Re-Couples Dysfunctional Endothelial Nitric Oxide Synthase in Experimental Subarachnoid Hemorrhage

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Introduction: Reduced endothelial nitric oxide synthase (eNOS) function has been linked to secondary complications of subarachnoid hemorrhage (SAH). We previously found that there is increased eNOS function after SAH but that it is uncoupled, leading to secondary complications such as vasospasm, microthromboembolism and neuronal apoptosis. Here we test the hypothesis that recoupling eNOS with simvastatin can prevent these complications.

Materials & Methods: Anterior circulation SAH was created in mice that were treated with vehicle or simvastatin starting 2 weeks before or 30 minutes after SAH. Animals were then divided into multiple groups for either immunohistochemical detection of nitrotyrosine (oxidative stress), Caspase-3/TUNEL (apoptosis) and Fibrinogen (Microthromboemboli), or for western blot detection of eNOS-P^{Ser1177} and TeNOS, iNOS and nNOS. Furthermore, fresh homogenates were used for the biochemical detection of superoxide radicals and NO using chemiluminescent and fluorescence detection methods respectively.

Results: SAH increased phosphorylated eNOS which was prevented by pre- or post-treatment with simvastatin. Simvastatin pre-treatment also prevented the increase in eNOS monomer formation that was associated with SAH, decreased superoxide anion radical production and increased NO. These changes were associated with decreased vasospasm, microthromboemboli and neuronal injury.

Conclusions: The data suggest that simvastatin re-couples eNOS after SAH, leading to decreased secondary complications such as vasospasm, microthromboemboli and neuronal injury.

Poster Only, Rookwood Room

72. Hydroperoxides (R-OOH) in the Cerebrospinal Fluid of Patients with Subarachnoid hemorrhage

Kimura, Hitoshi (Presenting); Saito, Norihiko; Nakano, Hiroyasu; Akahata, Masaki; Nakayama, Haruo; Hayashi, Morito; Harashina, Junichi; Aoki, Kazuya; Ishii, Masashi; Ito, Keisuke; Izukura, Hideaki; Iwabuchi, Satoshi
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Introduction: Recently, it has become clear that various diseases are associated with oxidative damage caused by reactive oxygen species (ROS) and free radicals. It has been reported on the relevance of free radicals and subarachnoid hemorrhage, especially vasospasm. Here we examined the relationship between ROS/free radicals and subarachnoid hemorrhage by measuring total hydroperoxides (R-OOH) in the cerebrospinal fluid (CSF) of patients with subarachnoid hemorrhage. The quantity of R-OOH is considered to be directly proportional to the quantity of reactive oxygen metabolites (ROMs), which are affected by ROS and free radicals.

Material & Methods: R-OOH levels in the CSF were measured in 13 patients with aneurysmal SAH. The patients' CSF samples were collected from the spinal drainage or the cisternal drainage, from Day 0 to Day 8. On Day 7, angiography was performed to verify the vasospasm. The relationship between the patients' clinical profiles and the levels of R-OOH in patients' CSF were investigated. Rather than measuring the ROS and free radicals directly, the free radical automatic analyzer (FRAS 4) that we used for this study measures the R-OOH concentration in the CSF using the colorimetric method (d-ROMs test).

Results: In all patients, R-OOH levels in the CSF showed an increase immediately after the onset of SAH. This trend was observed until Day 8. In the time-dependent change, R-OOH levels showed no significant change. R-OOH levels were higher in patients of Grade \neq W- \neq X (H&K grade) than in patients of Grade \neq U- \neq V. There were no significant differences in R-OOH levels between symptomatic vasospasm and asymptomatic vasospasm.

Conclusions: In Grade \neq W- \neq X, ROOH levels were higher. In this study, R-OOH levels in the CSF are assumed to reflect the damage caused by subarachnoid hemorrhage. In the future, cases should be increased and a more detailed examination is required.

Poster Only, Rookwood Room

73. Estrogen induces nitric oxide production via nitric oxide synthase activation in endothelial cells

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Introduction: 17 β -estradiol (E2) has been found to induce vasodilation in the cardiovascular system, and at physiological levels, to prevent cerebral vasospasm following SAH in animal models. The goal of this study was to analyze the cellular mechanism of nitric oxide (NO) production in vitro and specifically compare its effects on brain endothelial cells with those of peripheral endothelial cells.

Methods: In order to evaluate the impact of E2 on endothelial nitric oxide synthase (eNOS) activity and consequently NO production, human umbilical endothelial cells (HUVEC) as well as brain endothelial cells (bEND) were treated with 3 different concentrations of E2 (0.1, 10 and 1000 nM), and supernatant was collected after 2 hours for nitrite (NO₂) measurements. Cells were also treated for 2 hours with E2 in the presence of 1400W, a potent eNOS inhibitor. To evaluate whether the E2-induced NO release is mediated via estradiol receptors (ERs), we used ICI, an antagonist of ERs. Western blot analyses were performed to verify the presence of eNOS in the cells and to assess the effects of E2 on eNOS expression.

Results: E2 significantly increased NO₂ levels irrespective of its concentration in both cell lines by 35% and 42% ($p < 0.05$). The addition of an E2 antagonist, ICI (10 μ M) prevented the E2-induced increases in NO₂ levels (11% $p > 0.05$). The combination of E2 (10 nM) and a NOS inhibitor (1400W, 5 μ M) inhibited NO₂ increase also (4%, $p > 0.05$). E2 additionally induced increases in eNOS protein levels at concentrations of 10 and 1000 nM.

Conclusions: This study indicates that E2 induces increased NO levels in cerebral and peripheral endothelial cells in vitro via eNOS activation and through E2-receptor mediated mechanisms. Further in vivo studies are warranted to evaluate the therapeutic value of estrogen for the treatment of SAH-induced vasospasm.

Oral Presentation

NSICU care of SAH patients

74. Neurogenic Pulmonary Edema, a Complication of Aneurysmal Subarachnoid Hemorrhage: A single Center Experience

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Introduction: Neurogenic pulmonary edema (NPE) can lead to an acute cardiopulmonary failure with global hypoperfusion and hypoxia. These circumstances might cause severe secondary ischemic brain damage in patients with subarachnoid hemorrhage (SAH), their brain being especially vulnerable. We aimed to assess clinical presentation and risk factor for the development of NPE and to report on our experience. Patients/

Methods: The database contained prospectively collected data from 477 patients in an 8 years period. Baseline characteristics, clinical and radiologic severity of the bleeding, localization of the ruptured aneurysm, and clinical outcome of patients with NPE were compared with those of patients without NPE. Further, in patients with NPE, intracranial pressure, serum cardiac biomarkers, and hemodynamic parameters during the acute phase were evaluated retrospectively.

Results: The incidence of NPE was 8% (39 of 477 patients). Most patients with NPE were severely impaired and all of them presented with radiologically severe hemorrhage. The incidence of NPE was significantly higher in patients with ruptured aneurysm in the posterior circulation. Elevated intracranial pressure was found in 67%, pathologically high cardiac biomarkers in up to 83% of patients with NPE. However, no patient suffered from persistent cardiac dysfunction. Compared with patients without NPE, patients with NPE showed poor neurologic outcome.

Conclusion: Patients with clinically and radiologically severe SAH, ruptured aneurysm in the posterior region, and elevated intracranial pressure during the acute phase have a higher risk for developing NPE. Morbidity and mortality due to cardiopulmonary failure might be reduced by appropriate recognition and treatment. However, patients with NPE have a high mortality rate more likely due to their severity grade of the bleeding.

[Oral Presentation](#)

Prevention of DIND, including neuroprotection

75. Cerebral vasospasm after aneurysmal subarachnoid hemorrhage in elderly patients.

Ooigawa, Hidetoshi (Presenting); Satoh, Akira; Sugiyama, Tatsuya; Ogura, Takeshi; Takeda, Ririko; Fusihara, Goji; Suzuki, Kaima; Ishihara, Shoichiro; Tanahashi, Norio; Nishikawa, Ryo; Kurita, Hiroki
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Introduction: Cerebral vasospasm is known to occur in 20% to 30% of patients with aneurysmal subarachnoid hemorrhage (SAH) and contribute to morbidity and mortality. The cause of the vasospasm is multi-factorial and age is reported to be one of the risk factors. However, it is unclear whether treatment modality (clipping or coiling) affects the occurrence. We compared the incidence of vasospasm after surgical clipping and endovascular coiling in elderly patients with SAH.

Methods: Medical chart was retrospective reviewed in consecutive 64 elderly (>75y.o.) patients with aneurysmal SAH who underwent surgical repair (clipping 34, coiling 30) during a 36-month period (April 2007- March 2010) in our stroke center. Treatment modality was mainly decided on the basis of aneurysmal topography, independent from age or patient status. Cisternal irrigation was performed in clipping group, while spinal drainage was placed in coiling group after surgical repair.

Results: Of 34 patients treated by surgical clipping (mean age 79.9, mean Hunt and Kosnik grade 3.29), 3 (8.8%) were found to have vasospasm followed by cerebral infarction. On the other hand, 6 patients (20%) were found to have vasospasm in coiling group (mean age 82.6, mean Hunt and Kosnik grade 2.8). A modified Rankin scale on discharge was 4.12 and 3.4 respectively.

Conclusions: No statistical significance was found regarding occurrence of vasospasm between surgical clipping and endovascular coiling. Clipping group tend to be low incidence of vasospasm. Clot removal by cisternal irrigation may contribute to the results.

[Poster Only, Rookwood Room](#)

76. Effectiveness of continuous cisternal irrigation with mock-CSF containing ascorbic acid and Mg++ for prevention of symptomatic vasospasm

Satoh, Akira (Presenting); Sugiyama, Tatsuya; Ooigawa, Hidetoshi; Ogura, Takeshi; Takeda, Ririko; Fushihara, Goji; Kurita, Hiroki

International Medical Center, Saitama Medical University, Hidaka City, Saitama, Japan

Introduction. Symptomatic vasospasm (SVS) is still a major cause of unfavorable outcome in patients suffering subarachnoid hemorrhage. By using postoperative continuous cisternal irrigation with mock-CSF containing ascorbic acid (ASA) and Mg++, we could have achieved an excellent result regarding prevention of SVS in patients who underwent surgical intervention for ruptured intracranial aneurysm at acute stage. The result was better with Mg++ concentration of 4mEq/L than with that of 3mEq/L.

Methods. Mock-CSF comprises 500ml of lactate-Ringer solution, 4mg/L of ASA and 3 or 4mEq/L of Mg++ and is adjusted to pH 7.4 with sodium bicarbonate. One hundred and seven consecutive cases were treated with mock-CSF containing 3mEq/L of Mg++ (3M), and 35 cases with 4mEq/L. Statistical analysis was done by Student's t, chi-square or Mann-Whitney test.

Results. In 3M and 4M groups, age (62 vs 59), male to female ratio(0.52 vs 0.33) and incidence of Fisher group3 (78% vs 78%) were not different. There was no difference as to grade at admission (Gr.1+2: 34 vs 42%, Gr.3: 39 vs 36%, Gr.4: 19 vs 11%, Gr.5: 8 vs 11%), too. Incidence of SVS in which permanent neurological deficits or low density areas on CT remained was 7.5% in 3M group and 0% in 4M group. Overall outcome was significantly better in 4M group than in 3M group ($P < 0.02$).

Conclusions. Continuous cisternal irrigation with ASA and Mg++ is exceedingly effective in preventing postoperative SVS, especially when Mg++ concentration is 4mEq/L.

[Poster Only, Rookwood Room](#)

77. Magnesium therapy to prevent delayed ischemic neurological deficits (DIND) in aSAH patients- Pharmacokinetic considerations

Dent, Wolfgang (Presenting); Sikorski, Christopher; Wyss, Sabine; Farokhzad, Faraneh; Keller, Emanuela

University Hospital Zurich, Zurich, Switzerland

Introduction: Several clinical trials showed promising results for high dose MgSO₄ therapy as a prophylactic treatment option in aSAH. However, a recent phase-III study has questioned the favorable effect of MgSO₄ (1). As some investigators used MgSO₄ regimens with fixed dosages, the aim of the present study was to establish a clue about the pharmacokinetics of applied MgSO₄, and furthermore, if a fixed Mg-regimen can guarantee the drugs assigned properties.

Material and Methods: Plasma Mg profiles of forty-seven aSAH patients treated with a standardized intravenous MgSO₄ schedule (target plasma Mg-level: 1.5 to 2.0 mmol/l) were retrospectively analyzed. Plasma Mg-levels were measured six-hourly and Mg-dosage was adapted according to the protocol. Special attention was given to A) the affordable Mg doses and duration till therapeutic mg levels have been reached, B) the Mg-rate that was necessary to maintain therapeutic Mg-levels, and C) the changes of Mg-dosage needed over time.

Results: The mean Mg-application period to reach therapeutic plasma levels was 37 hours [h] and 50 minutes [min](SD ± 21.5; range: 12 to 104 h). Therefore, a mean amount of 89.7 mmol/L Mg (area under the curve; SD ± 60.1; range: 27.0 to 296.5 mmol/L) was necessary. While Mg reached therapeutic plasma levels current Mg-dose was 66.8 mmol/24h on average (SD ± 21.4; range: 44 to 124 mmol/24h). To hold therapeutic Mg levels a subsequent steady elevation of Mg-dosage was necessary.

Conclusions: To keep Mg in the aspired therapeutic range, we found considerable differences of Mg dosages required for our aSAH patients. Moreover, to maintain constant therapeutic plasma Mg levels, a steady increase of the Mg was necessary. This means that Mg-regimens without adaption of Mg to plasma levels might inevitably result in a significant Mg over and under dosage, respectively. In turn, the real capability of Mg-therapy in preventing DIND can't be estimated based on the phase-III study recently published.

[Poster Only, Rookwood Room](#)

78. Proposed new grading system for delayed vasospasm following aneurysmal subarachnoid hemorrhage: value of cisternal irrigation with ascorbic acid and Mg⁺⁺

Ogura, Takeshi (Presenting); Akira, Satoh; Hidetoshi, Ooigawa; Tatsuya, Sugiyama; Ririko, Takeda; Goji, Hushihara; Kaima, Suzuki; Hiroki, Kurita

Saitama International Medical Center, Hidaka City, Saitama Prefecture, Japan

Introduction: application of multimodal therapies, symptomatic vasospasm (SVS) continues to result in morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage (SAH). The authors propose new grading system for SVS with investigation of effectiveness of cisternal irrigation with mock CSF containing ascorbic acid and Mg⁺⁺ (CCI) for prophylaxis.

Material & Methods: Medical chart of consecutive 173 patients with aneurysmal SAH who underwent surgical repair during 5-year period was retrospectively reviewed to assess the incidence of SVS. 133 patients (76.9%) were treated with CCI for SVS prophylaxis. Severity of SVS was graded as follows; grade 1: without any SVS symptom, grade 2: transient symptom requiring no treatment, grade 3: transient symptom required additional treatment such as hyperdynamic and/or interventional therapy, grade 4: permanent ischemic symptom or development of cerebral infarction.

Results: The occurrence of SVS was significantly lower ($p < 0.01$) in the CCI group (15%) than in the non-CCI group (25%). SVS in CCI group is found to be more mild form (grade 3&4; 5.6%), compared to non-CCI group (20%)

Conclusions: Analysis of the results suggests that cisternal irrigation with ascorbic acid and Mg⁺⁺ have a role in cerebral vasospasm prophylaxis.

[Oral Presentation](#)

79. Combined Intravenous Magnesium and Nimodipine injection for prevention of symptomatic Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage: A Prospective Study

Sheen, SeungHun (Presenting); Hwang, Gyojun; Sukh Que, Park

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Objective: Symptomatic cerebral vasospasm is a still major problem after aneurysmal subarachnoid hemorrhage. Intravenous magnesium injection is a controversial for prevention of symptomatic cerebral vasospasm after aneurysmal subarachnoid hemorrhage. Several drugs were used for prevention of vasospasm, but the rate of cerebral vasospasm is still significantly high. The purpose of this pilot study is to evaluate the efficacy and safety of combined intravenous magnesium and nimodipine to prevent symptomatic cerebral vasospasm after aneurysmal subarachnoid hemorrhage.

Methods: One hundred and forty eight patients were treated in our hospital from March 2007 to December 2010. Early ninety two patients were treated with only intravenous magnesium until November 2009. Late fifty six patients were treated with combined with magnesium and nimodipine. There was no complication using intravenous treatment.

Results: Fifty six patients were enrolled in this prospective study. In combined group (n=56), eight patients (14%) experienced symptomatic vasospasm which confirmed with cerebral angiography. In nimodipine only group (n=92), 28 patients (30%) experienced symptomatic vasospasm.

Conclusion: Combined intravenous magnesium and nimodipine injection is an effective and safe method for prevention of symptomatic cerebral vasospasm after aneurysmal subarachnoid hemorrhage.

[Poster Only, Rookwood Room](#)

80. Evaluation of endovascular treatment of cerebral vasospasm after subarachnoid hemorrhage. Establishment of inclusion criteria and assessment of its efficacy by MR perfusion/diffusion-mismatch.

Platz, Johannes, MD (Presenting); Güresir, Erdem; Berkefeld, Joachim; Raabe, Andreas; Beck, Jürgen; du Mesnil de Rochemont, Richard; Seifert, Volker; Weidauer, Stefan; Vatter, Hartmut
Johann Wolfgang Goethe-University, Frankfurt am Main, Germany

Introduction. Endovascular treatment like transluminal balloon angioplasty or intra-arterial nimodipine represents a rescue therapy for cerebral vasospasm (CVS) after aneurysmal subarachnoid hemorrhage (SAH). However, the selection of patients who might benefit from this treatment is difficult and the efficacy of the therapy is inconsistent. We, therefore, evaluated (1) the usefulness of MRI perfusion (PWI)-/diffusion weighted imaging (DWI) for patient selection and (2) the efficacy of the endovascular therapy based on MR PWI/DWI-mismatch.

Material & Methods. In case of suspected CVS MRI was performed. For quantitative evaluation the brain was partitioned into 19 arbitrary segments of comparable volume. A segment was defined "at risk" (SAR) when a significant PWI/DWI mismatch was detected. In these cases, MRI was followed by a digital subtraction angiography (DSA) including endovascular treatment. Follow-up MR-imaging was acquired 48±12 hours after treatment in case of new or persisting SAR, endovascular treatment was repeated. Treatment efficacy was classified by the improvement of the proximal vessel diameter in DSA after the treatment.

Results. In 25 patients, 48 treatment cycles, each consisting of MRI, DSA and follow-up MRI were completed. Overall, 95 SAR were identified. Delayed infarction was significantly higher in SAR (37%) compared to segments without risk (4%). The risk of infarction in SAR was significantly reduced if endovascular treatment could improve severe or moderate CVS to mild proximal CVS only. In case of persisting severe CVS infarcts occurred in all SAR.

Conclusions. Our results suggest that the development of delayed infarction can be predicted by a PWI/DWI mismatch. The risk of infarction was lower if proximal CVS was sufficiently reduced by endovascular treatment.

Poster Only, Rookwood Room

81. The effect of surgical treatment on delayed ischemic neurological deficit (DIND) in patients with aneurysmal subarachnoid hemorrhage

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INTRODUCTION: The role of aggressive surgical manipulation with clot evacuation, arachnoid dissection and papaverine guided adventitial dissection during aneurysm surgery after subarachnoid hemorrhage (aSAH) in reducing clinically significant vasospasm is controversial. Here we describe a single institution experience with and without aggressive surgical manipulation and compare to patients undergoing coil embolization.

MATERIALS AND METHODS: Retrospective analysis of all patients >18yo that presented with aSAH of anterior circulation aneurysms between 1996-2010 at University of New Mexico Hospital. Vasospasm was characterized on day 3-14 post SAH based on 1. angiographic evidence of vascular narrowing, 2. whether vasospasm required intervention during angiography and 3. development of a delayed ischemic neurological deficit.

RESULTS: A total of 188 patients were included. Of those, 33 (17.5%) underwent coiling, 154 (82%) were clipped. Of the surgical group, 111 (72%) had aggressive vascular manipulation and 43 (28%) had limited manipulation. Over 60% of all patients presented with a Hunt and Hess score of ≥ 3 and Fisher grade of 4. All patients were similar in their demographic characteristics. There was a statistically significant decrease in the incidence of DIND in all surgical patients (23.4%) compared to non-surgical group (42.4%, $p=0.02$). Similar data was observed with aggressive surgery (18.9%) when compared with limited surgery (34.9%, $p 0.04$). There was a nonsignificant ($p=0.09$) reduction of 14% of ipsilateral radiographic vasospasm (30.6% vs. 44.2% for aggressive vs limited surgery). A nonsignificant trend was observed in the need for angiographic intervention (12.6% vs. 16.3% for aggressive vs. limited surgery $p=0.6$)

CONCLUSIONS: We conclude that 1. surgical manipulation results in a lower incidence of clinically significant vasospasm in patients treated for aSAH. 2. the more aggressive this surgical manipulation is, the lower this incidence becomes.

Oral Presentation

Resistance vessel pathology after SAH

82. Delayed cerebral ischemia associated with spreading depolarization can occur despite absence of proximal vasospasm after aneurysmal subarachnoid hemorrhage.

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It has been hypothesized that proximal vasospasm is the prime mechanism of delayed cerebral ischemia (DCI) after subarachnoid hemorrhage (aSAH). Recently, it was found that clusters of spreading depolarizations are associated with DCI. Spreading depolarizations could mediate lesion progression or be involved in repair mechanisms under the ischemic condition induced by proximal vasospasm. Surgical placement of nicardipine prolonged-release implants (NPRIs) was shown previously to strongly attenuate proximal vasospasm. In the present study, we tested in 13 patients with major aSAH whether DCI and SDs are abolished when proximal vasospasm is reduced or abolished by NPRIs. After clipping of the ruptured aneurysm, 10 NPRIs were placed next to the proximal intracranial vessels. SDs were recorded using a subdural 6-contact electrode strip. The degree of proximal vasospasm was assessed by digital subtraction angiography (DSA). DCI was assessed by repeated neurological exams and serial CT and/or MRI scans. 534 SDs were recorded in 10 of 13 patients (77%). DSA revealed no vasospasm in 8 of 13 patients (62%) and only mild or moderate vasospasm in the remaining patients. Five patients developed DCI associated with clusters of SD while proximal vasospasm was absent in three of those patients. There was no correlation between the degree of proximal vasospasm and the occurrence of DCI. In contrast, the number of SDs and the total duration of the electrocorticographic depression periods correlated significantly with the development of DCI. In conclusion, SDs occurred abundantly after aSAH although proximal vasospasm was strongly attenuated. Occurrence of SDs must have been the consequence of other mechanisms that may explain why reduction of proximal vasospasm alone has not been sufficient to improve outcome in clinical studies.

Oral Presentation
Award Finalist

83. Matrix metalloproteinase and epidermal growth factor receptor activation cause suppression of voltage-gated potassium (KV) channels to enhance constriction of rat parenchymal arterioles after subarachnoid hemorrhage.

Koide, Masayo; O'Connor, Kevin P.; Smith, Gregory J.; Pappas, Anthony C.; Wellman, George C. (Presenting)
University of Vermont, Burlington, VT, USA

Introduction: Constriction of the cerebral microcirculation may contribute to neuronal deficits in subarachnoid hemorrhage (SAH) patients. We have previously shown that oxyhemoglobin can acutely suppress KV currents in pial artery myocytes via activation of matrix metalloproteinases (MMPs) and epidermal growth factor receptors (EGFR) (1). Here, our goal was to determine the role of MMPs, EGFRs, and KV channels in the enhanced constriction of parenchymal arterioles following SAH.

Methods: The conventional whole-cell patch clamp technique was used to measure KV currents of parenchymal arteriolar myocytes from control and SAH model rats. To assess arteriolar function, diameter measurements were obtained from isolated parenchymal arterioles. RT-PCR was used to examine KV subtype expression.

Results: Parenchymal arteriolar tone was elevated and KV current density was decreased by > 40% in myocytes from SAH model animals. Although SAH decreased KV currents, mRNA levels of KV subunits were similar between groups. Consistent with SAH-induced suppression of KV currents, 4-aminopyridine-induced constriction was reduced in parenchymal arterioles from SAH animals. The EGF receptor ligand, HB-EGF, suppressed KV currents in myocytes from control, but not SAH animals, suggesting EGFR activity may be up-regulated following SAH. Compounds that specifically interfere with either HB-EGF signaling (CRM197) or MMP activity (GM6001) increased KV current density in myocytes isolated from SAH, but not control animals. Further, vasodilation induced by CRM197 and GM6001 were significantly enhanced after SAH.

Conclusions: These data suggest increased MMP activity causing HB-EGF shedding and enhanced EGFR activity leads to KV channel suppression in parenchymal arterioles from SAH animals. We propose that EGFR-mediated KV suppression contributes to enhanced parenchymal arteriolar constriction after SAH. Supported by NIH P01HL095488, R01HL078983 & Totman Medical Research Trust.

Oral Presentation

Smooth muscle signaling

84. The combination of argatroban and vitamin C normalizes the increased vascular contractile response after subarachnoid hemorrhage (SAH)

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Introduction: Increased vascular reactivity plays a key role in the pathogenesis of cerebral vasospasm in SAH. We investigated the role of thrombin and its receptor PAR1 in the increased vascular contractile response in SAH, and examined the preventive effects of the thrombin inhibitor, argatroban and vitamin C on contractility.

Material & Methods: We investigated the role of thrombin and its receptor PAR1 in the increased vascular contractility utilizing a rabbit double SAH model. The contractile response of the isolated basilar artery and the level of oxidative stress of brain tissues were evaluated.

Results: In the control basilar arteries, 1 U ml⁻¹ thrombin and 100 μM PAR1-activating peptide (PAR1-AP) induced a small and transient contractile response, while they induced an enhanced and sustained contractile response in SAH. When the arteries were consecutively stimulated with PAR1-AP, the reactivity to the second stimulation was markedly attenuated in the control, while it was maintained in SAH. Intrathecal treatment with 1 μg argatroban kg weight⁻¹ per injection (ARG) attenuated the response to thrombin and PAR1-AP in SAH. However, the contraction still sustained and the tachyphylactic attenuation of the contraction was impaired. The combination of ARG and 0.6 mg vitamin C kg weight⁻¹ per injection (VC) normalized the vascular contractility to PAR1 agonists. Oxidative stress was increased in SAH. Treatment with ARG, VC or their combination normalized the level of oxidative stress.

Conclusions: The contractility of the basilar artery to thrombin was enhanced and prolonged after SAH. The combination of ARG and VC is suggested to normalize the increased vascular contractility in SAH.

Poster Only, Rookwood Room

85. Matricellular protein: a new player in cerebral vasospasm following subarachnoid hemorrhage

Suzuki, Hidenori (Presenting); Shiba, Masato; Kawamura, Kengo; Fujimoto, Masashi; Matsushima, Satoshi; Kanamaru, Kenji; Imanaka-Yoshida, Kyoko; Yoshida, Toshimichi; Taki, Waro
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Introduction: Matricellular protein (MCP) is a class of non-structural and secreted extracellular matrix proteins that exert diverse functions. Recently, we showed that osteopontin (OPN), one of MCPs, is protective against cerebral vasospasm after subarachnoid hemorrhage (SAH). However, the role of tenascin-C (TNC), another MCP, has not been sufficiently investigated in vasospasm.

Material & Methods: First, TNC was measured in cerebrospinal fluid (CSF) and serum from 33 aneurysmal SAH patients of Fisher computed tomography Group III, and compared between those with and without vasospasm. Second, 2 kinds of rat SAH models, endovascular perforation and single cisternal injection models, were produced to examine if TNC was induced in vasospastic cerebral arteries using Western blotting and immunostaining. Third, recombinant TNC (r-TNC) with or without a toll-like receptor (TLR) 4 antagonist was injected into a cisterna magna in rats, and the diameter of basilar arteries was measured.

Results: CSF TNC levels peaked immediately after SAH, and were significantly higher in patients with than without vasospasm on days 4-9. Serum TNC levels were not significantly different between patients with and without vasospasm, but the levels increased transiently on days 4-6, the extent being significantly greater in patients with subsequent vasospasm. In rats, Western blot analyses showed that TNC significantly increased in vasospastic arteries. TNC immunoreactivity was induced from the adventitia to the smooth muscle cell layers with the occurrence of vasospasm. r-TNC injections caused prolonged arterial contractions, which were reversed by a TLR4 antagonist.

Conclusions: TNC may cause cerebral vasospasm via activation of TLR4-dependent signaling pathways. Considering the multifaceted functions of MCPs, further investigations may prove that MCPs, including TNC and OPN, contribute to the pathophysiology of cerebral vasospasm, and provide a novel therapeutic approach against it.

Poster Only, Rookwood Room
Award Finalist

86. Potentiation of endothelin-1-induced myofilament Ca²⁺ sensitization following subarachnoid hemorrhage

Kikkawa, Yuichiro (Presenting); Matsuo, Satoshi; Kameda, Katsuharu; Nakamizo, Akira; Sasaki, Tomio
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Introduction: Increased vascular contractility in response to endothelin-1 (ET-1) plays an important role in the development of cerebral vasospasm. We elucidated some mechanisms of the increased vascular contractility to ET-1 using the basilar artery in a rabbit subarachnoid hemorrhage (SAH) model.

Material & Methods: The contractile response and the expression of regulatory protein of the isolated basilar artery were evaluated.

Results: ET-1 induced greater contraction than other agonists or high K⁺ depolarization for the extent of [Ca²⁺]_i elevation, suggesting that myofilament Ca²⁺ sensitivity is a greater contributor to ET-1-induced contraction than other contractions. ET-1-induced contraction of α -toxin-permeabilized strips was significantly enhanced and sustained in SAH compared to control, suggesting that the ET-1-induced myofilament Ca²⁺ sensitization was enhanced after SAH. Therefore, we investigated the intracellular signaling pathway involving Rho-kinase (ROCK) and protein kinase C (PKC), which are two major signaling molecules that contribute to Ca²⁺ sensitization. ET-1-induced contraction of α -toxin-permeabilized control strips was blocked by inhibitors to ROCK and PKC in a concentration-dependent manner, whereas the concentration-response curve shifted to the right in SAH, suggesting that ROCK and PKC signaling was activated in SAH. Immunoblotting showed that the expression of PKC α , ROCK2, CPI-17, and MYPT-1 was significantly upregulated after SAH. Phosphorylation of MYPT-1 at T853 and CPI-17 at T38 was significantly increased in SAH, but the phosphorylation of MYPT-1 at T696 remained unchanged. However, in response to ET-1 stimulation, the phosphorylation of T696 was significantly increased in SAH, whereas the phosphorylation of T853 and T38 was increased both in control and SAH.

Conclusion: ET-1-induced myofilament Ca²⁺ sensitization is potentiated after SAH, leading to enhancement of vascular contractility in response to ET-1.

Poster Only, Rookwood Room

Spreading depolarizations

87. The role of spreading depolarization, spreading depression and spreading ischemia in patients with aneurismal subarachnoid hemorrhage.

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Charité University Medicine Berlin, Berlin, Germany

The term spreading depolarization describes a wave in the brain's gray matter characterized by near-complete breakdown of ion homeostasis, a large change of the slow electrical (or direct current (DC)) potential, swelling of neurons and distortion of dendritic spines. The DC change is a direct extracellular index of spreading depolarization (Canals et al. *J Neurophysiol* 2005 94:943-51), and it shows a wide spectrum in the human brain ranging from short- to very long-lasting events (Dreier *Nat Med* 2011 in press). Spreading depolarization can be associated with three different depression patterns of brain activity: (i) nonspreading depression, (ii) spreading depression and (iii) persistent depression of activity. The depression pattern is observed in a higher frequency range of the electrocorticogram than the DC change. Hence, spreading depolarization and the depression pattern are observed as two clearly distinct signals. The near-complete breakdown of the electrochemical gradients leads to a dramatic loss of Gibbs free energy. Based on the intra-/extracellular cation changes and the resulting changes in mixing entropy, we here calculated that the loss in Gibbs free energy during spreading depolarization exceeds that during epileptic seizure activity seven times. To restore ion homeostasis and the normal tissue level of Gibbs free energy, additional chemical energy (ATP) is required to fuel the sodium pump. Therefore, resistance vessels respond to spreading depolarization with tone alterations, causing transient hyperperfusion (physiological hemodynamic response) in healthy tissue. After aneurismal subarachnoid hemorrhage (aSAH), this neurovascular coupling can be disturbed in such a way that spreading depolarization induces severe vasoconstriction and hypoperfusion (inverse hemodynamic response or spreading ischemia). Hence, in a moment of maximal metabolic demand, energy supply is reduced, a mechanism that may be involved in delayed ischemic stroke after aSAH.

Oral Presentation

88. Subarachnoid hemorrhage increases the susceptibility to ischemic stroke but not to peri-infarct depolarizations after middle cerebral artery occlusion

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Introduction: Peri-infarct depolarizations (PID) akin to spreading depression (SD) occur frequently after ischemic stroke and subarachnoid hemorrhage (SAH), and worsen the outcome of compromised tissue by exacerbating the blood flow-metabolism mismatch. SAH is often associated with ischemic brain injury presumed to be due to vasospasm. We tested whether SAH increases the sensitivity of brain tissue to focal arterial occlusion, and whether the mechanism involves increased susceptibility to SD or PIDs.

Materials and Methods: Mice (C57BL/6, male) and rats (Sprague-Dawley, male) were subjected to single or double intracisternal autologous blood or saline injection. Twelve or 24h later, middle cerebral artery was occluded (MCAO) for 1h using an intraluminal filament to assess infarct volume, neurological deficits and PIDs. SD susceptibility was assessed in a separate group using KCl or electrical stimulation. To investigate vascular mechanisms, vasoreactivity was assessed using isolated pressurized posterior cerebral arteries (PCA), and cerebral blood flow (CBF) deficit was mapped using laser speckle flowmetry with high spatiotemporal resolution during distal MCAO. In all applicable experiments physiological parameters were monitored continuously.

Results: SAH increased infarct volumes by approximately 30% after both filament and distal MCAO, when ischemia was induced 12 but not 24 hours after SAH. Contrary to our hypothesis, however, both SD susceptibility and PID frequency were decreased after SAH. Isolated PCAs showed smaller resting diameters and higher myogenic tone, suggesting vasospasm. Consistent with this, resting CBF was lower and CBF deficits during dMCAO were worse in SAH group to explain the larger infarct volumes.

Conclusion: Our data suggest that SAH worsens the outcome of focal ischemia by causing vascular dysfunction and worsening the perfusion deficit, and that cortical susceptibility to SD or PIDs is not increased after SAH.

Oral Presentation

89. Impact of body temperature on occurrence of cortical spreading depolarizations in subarachnoid hemorrhage.

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From animal models it is known that elevated temperature can abet or trigger the generation of cortical spreading depolarizations (CSD). CSD were demonstrated to occur in patients suffering from aneurysmal subarachnoid hemorrhage (aSAH) and it is assumed that they are a negative prognostic factor for outcome of these patients. To investigate the impact of normothermia and hyperthermia on the occurrence of CSD, 21 patients with acute aSAH were monitored for 38 to 266 hours after onset of the initial SAH. Temperature was determined every 30 min leading to a total of 9739 episodes of temperature measurement in all patients. A cortical electrode strip to record the electrocorticogramme (ECoG) was implanted within 24h after SAH onset in the course of the aneurysm clipping. The post-hoc analysis of the ECoG showed a total of 460 CSD in 17 patients. 4 patients did not show evidence for CSD. For every CSD the temperature at the time point of occurrence was determined and divided into 3 temperature ranges (normothermia: 36.0-36.9°C, mild hyperthermia: 37.0-37.9°C, moderate hyperthermia: 38.0-38.9°C). 1580 (= 790 hours) of the 9739 monitored temperature episodes showed normothermia and 16 CSD were recorded within this temperature range, resulting in an average of 0.02 CSD per hour. During 6037 (= 3018.5 hours) temperature episodes with mild hyperthermia 120 CSD occurred (0.04 CSD per hour in average) and during 1678 (= 839 hours) temperature episodes of moderate hyperthermia 92 CSD were recorded (0.11 CSD per hour in average). For the comparison of body temperature and the occurrence of CSD within a temperature range from 36.0 to 38.9°C, we calculated a correlation coefficient of 0.76. During moderate hyperthermia the probability for a CSD was more than fivefold higher than during normothermia. Our data suggest an association between higher temperature and CSD. It would be interesting to investigate whether reduction of temperature would decrease the incidence of CSD.

Oral Presentation

90. Spreading depolarization-induced injury to neurons and astrocytes

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Introduction. 2-photon laser scanning microscopy (2PLSM) enables real-time visualization of cells expressing GFP deep within living neocortex in vivo. Using 2PLSM we have previously shown that SDs cause acute damage to neurons in the ischemic penumbra. We also have evidence that cardiac arrest-induced global ischemia elicits astroglial swelling, indicating acute damage.

Materials & Methods. 2PLSM was used to monitor astroglial changes concurrently with neuronal injury in two different models of ischemic stroke and mild TBI. The 1st method was transient bilateral common carotid artery occlusion, which allowed for the induction of global ischemia and subsequent reperfusion. The 2nd method was modified photothrombotic occlusion, in which a square-shaped ischemic lesion was made to surround a penumbra-like "area at risk" with SDs recurring for several hours following photothrombosis. TBI was induced by a non-penetrating localized deformation of the cortex with a controlled cortical impact device.

Results. In stroke models, SD wave coincides with astroglial swelling alongside dendritic beading. Though rapid neuronal recovery was seen in both models, astroglial swelling persisted long after the occurrence of SD, with no structural recovery seen for the duration of the acute imaging period. In TBI model without spontaneous SDs dendritic injury in peri-contusional area was developing relatively slow but injury was greatly facilitated by SDs evoked by injecting KCl with a micropipette. Astroglial swelling persisted in the peri-contusional area for the duration of acute imaging.

Conclusions. Dendrites rapidly bead in concert with propagating SDs, recovering when there is sufficient local capillary flow. The accumulating stress of repeated SDs eventually results in "terminal" injury. Astrocytes swell during recurring spontaneous SDs, with no recovery seen in acute experiments. Early astroglial swelling may exacerbate functional outcome as astrocytes fail to provide neuronal support.

[Oral Presentation](#)

91. Trauma trumps stroke: Why is our higher brain inept at dealing with blocked blood flow?

Andrew, David (Presenting); Brisson, Devin
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While poorly documented, at the moment of traumatic brain injury (TBI), neurons in the impacted cortex completely depolarize as a consequence of mechanical sheer/stretch. Within seconds this `traumatic depolarization` (TD) propagates to adjacent gray matter, driving neurons beyond the point of discharge, thereby silencing the contused region while also inducing regional vasoconstriction. TD promotes a `lie-low` survival strategy that immobilizes the subject for minutes or more, as well as counteracting hemorrhage. We propose that evolutionary pressure to develop this trauma defense has created a deadly catch-22: our higher brain is inept at dealing with the TD-like ischemic depolarization (ID) triggered by global ischemia or occlusive stroke. Head trauma was a common way to die throughout our brutal vertebrate evolution so there was strong selective pressure to cope with it. At the same time our ancestors' lives were usually brief, rigorous and nutrient-inadequate so few died from clogged brain arteries. Without evolutionary selection for mechanisms to deal with occlusive stroke, sudden loss of blood flow in cortical gray evokes ID and vasoconstriction (inverse neurovascular coupling) as though the region is hemorrhaging from TBI. In support of ID being a rapid, but inappropriate, shut-down defense we also contend: a) To maintain vital functions, internal brain structures (hypothalamus, brainstem) do not generate potent ID with resultant rapid shut down as do more exposed gray regions in telencephalon, cerebellum & spinal cord^{1,2}. This helps explain why brainstem better survives global ischemia. b) Cortical ID is generated by all vertebrates despite their not naturally suffering stroke. c) Migraine CSD is a residual ID response to a mis-perceived loss of blood flow, evoking headache as part of the lie-low strategy of dealing with TBI. d) Anoxia induces ID & immobilization in insects³ which lack arterioles/capillaries. Neuronal type dictates if a region shuts down.

[Poster Only, Rookwood Room](#)

92. Intracortical electroencephalography monitoring for detection of cortical spreading depolarisations in three patients after traumatic brain injury

Zakrzewska, Agnieszka (Presenting); Walsh, Daniel; Tolia, Christos; Strong, Anthony John
King's College Hospital, London, UK

Introduction: Cortical spreading depolarisations (CSD) occur in 50 to 60% of patients after traumatic brain injury (TBI) in areas of cortex adjacent to contusions in the injured human brain, in 70-90% of SAH WFNS 3-5, and in all patients with malignant hemisphere stroke. These events are believed to be an important pathophysiological mechanism of secondary brain injury, but currently can only be detected with a subdural strip inserted when craniotomy has been required. **Aims:** To test CSD-detection sensitivity of a Spencer depth electrode as an alternative to subdural strip.

Methods: EEG was recorded continuously in 3 patients undergoing craniotomy for TBI: a subdural strip electrode was placed on cortex exposed by the craniotomy and a depth electrode was implanted intraparenchymally close to the strip.

Results: In the first patient a CSD event was recorded on the depth electrode and on the subdural strip simultaneously. In first two patients several (3 in patient 1 and 12 in patient 2) slow potential change (SPC) events occurring synchronously across channels were detected on both strip and depth electrodes. In the third patient no CSDs and SPCs were observed on both strip and depth electrodes.

Conclusions: There is preliminary evidence that the depth electrode can record SPCs that also appear on the surface electrode. On the basis of these observations we propose that continuous monitoring from a depth electrode inserted into cortex via an access bolt will allow less invasive monitoring for depolarisations.

[Oral Presentation](#)

93. Vascular, electrophysiologic, and metabolic consequences of cortical spreading depression in a mouse model of simulated neurosurgical conditions.

Carlson, Andrew (Presenting); Carter, Russell; Shuttleworth, C. William
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Introduction: Cortical spreading depression (CSD) is a metabolically taxing wave of cellular depolarization. CSD occurs frequently in humans after brain injury, and is associated with worse outcomes¹. Less is known about possible contributions of CSD to injury following standard neurosurgical procedures. The current work evaluated CSD in a mouse model of simulated intra-operative conditions.

Materials and Methods: Mice were intubated and ventilated; arterial line was placed. Normothermia and normocapnia were maintained and neuroanesthesia simulated with fentanyl, propofol and isoflurane. Craniotomies were made to record responses to cortical coagulation with bipolar cautery. Separate sets of experiments (3 animals each) examined electrocorticographic activity (ECoG), optical measures of blood volume and vascular diameters (540nm absorbance), or autofluorescence attributed to NADH (750nm, 2 photon excitation).

Results: Ipsilateral cauterizations invariably resulted in a robust propagating CSD wave, identified by slow DC potential shifts (2.8 ± 0.2 mm/min, n=6) and suppression of ECoG activity (range 0.5-7.3min, n=10). Each evoked CSD was associated with an initial pronounced arteriolar constriction, followed by a longer-lasting vasodilation. These changes led to similar tissue blood volume responses. Tissue oxygenation, assessed indirectly by NADH imaging, was consistent with sustained demand on oxidative metabolism. Furthermore, repetitive SDs resulted in progressive loss of tissue autofluorescence, suggestive of tissue compromise.

Conclusions: CSD is consistently elicited by simulated neurosurgical stimuli under simulated intra-operative conditions in mice. These events caused prolonged ECoG depression, transient vasoconstriction, and significant metabolic demand that propagated from the manipulation site. It is possible that CSD events contribute to metabolic challenge at locations distant from sites of surgical manipulation.

[Oral Presentation](#)

94. Detection of spreading depression by surface EEG

Fabricsius, Martin (Presenting); Lauritzen, Martin
Glostrup University Hospital, Glostrup, Denmark

Introduction. Cortical spreading depression/depolarization (CSD) of the acutely injured human brain may be readily detected by electrocorticogram (ECoG) (Ref). CSD, supposedly the mechanism of migraine aura, spreads at a speed of 2-3 mm/min and recovers within 6 minutes in the normal brain, thus depression of the EEG occurs in a narrow strip of cortex, around 2 cm wide. Non-invasive surface EEG recordings have failed to demonstrate EEG depressions during migraine aura. In brain injury, CSD duration may be prolonged, thus expanding the strip of depressed activity. This might increase the likelihood of detecting changes in surface EEG.

Material & Methods. Six patients suffering from aSAH (n=4) or intracerebral haematoma (n=2) underwent craniotomy on clinical indication, and a 6-electrode platinum strip was placed subdurally. Postoperatively intradermal EEG electrodes were placed. EEG and ECoG was recorded on two separate recording systems. Surface EEG trends, e.g. Brain Symmetry Index (BSI) were inspected for episodes suggesting transient (10-30 minutes) periods of regional loss of EEG power. The ECoG was scored independently for episodes of CSD (Ref).

Results. During 250 hours of recording, 51 CSDs were recorded on ECoG. On surface EEG, 17 transient reductions in BSI occurred in the same period as a CSD. 34 CSDs occurred without any obvious changes in EEG trends. 18 transient changes in EEG trends occurred without any CSD being recorded simultaneously.

Conclusions Episodes of CSD may be reflected in surface EEG trends, particularly BSI. In this limited material sensitivity was 33 % and specificity ~50 %. Some false positive changes in surface EEG may in fact represent episodes of CSD occurring in regions remote from the subdural strip, and some CSDs recorded from a dural strip placed below the frontal lobe may never reach the convexity of the brain. Further refinement of the EEG analysis may lead to increased sensitivity and pave the way for non-invasive detection of CSD.

[Oral Presentation](#)

95. Cerebral glucose and spreading depression in patients with aneurysmal subarachnoid hemorrhage

Sarrafazadeh, Asita; Oehmchen, Marcel; Santos, Edgar (Presenting); Wiesenthal, Dirk; Martus, Peter; Vajkoczy, Peter; Unterberg, Andreas; Dreier, Jens; Sakowitz, Oliver
University Hospital Geneva, Geneva, Switzerland

Introduction: The pathogenesis of delayed cerebral ischemia (DCI) is multi-factorial and not completely elucidated. The objective of this study was to determine if episodes of spreading depolarization (SD) are reflected in compromised levels of extracellular glucose monitored by bedside microdialysis (MD) in aneurysmal subarachnoid hemorrhage (SAH) patients.

Methods: SAH patients, prospectively included in the COSBID protocol of Berlin and Heidelberg, had hourly monitoring of cerebral glucose by MD and in parallel electrocorticographical monitoring (ECoG) for SD detection on day of admission until day 10-14 after SAH. Cerebral MD probes were placed intraoperatively in the vascular territory at risk for DCI. The two-sample sign test was performed to compare lower / higher levels of glucose. Number of SDs determined by applying local regression (LOESS).

Results: In 21 SAH patients (53.3±9.1 yrs; mean±SD, 12F/9M), combined MD/ECoG monitoring was performed. Patients were classified as according to the WFNS in low (I-III, 11) and high grade (IV-V, 10). 13 patients (62%) presenting with DCI. Median glucose was 1.48 [0.00 - 8.79]. Median occurrence of SD was 7 [0 - 66]/patients, 3 patients had no SD within the intensive care stay. Patients with high WFNS grade have more SDs ($p=0.027$, t-test), while the overall glucose level did not differ significantly ($p=0.844$, t-test). During and 1 hour after SD, the levels of cerebral glucose in the interstitial brain fluid of SAH patients were slightly but not significantly lower ($p=0.210$).

Conclusions: The occurrence of spreading ischemia is associated with the WFNS grade in SAH patients. In high grade SAH patients, SDs were more frequent while MD-glucose levels remained stable. Rapid sampling MD techniques and analyses of SD clusters may elucidate more detail of the relationship between SD and brain energy metabolism.

[Oral Presentation](#)

96. On the role of external patient movements that can trigger spreading depolarizations in subarachnoid hemorrhage patients

Santos, Edgar (Presenting); Schöll, Michael; Hertle, Daniel; Sanchez-Porras, Renan; Unterberg, Andreas; Sakowitz, Oliver W.

University of Heidelberg, Heidelberg, Baden Württemberg, Germany

Introduction. It has recently been reported that spreading depolarizations (SD) are spontaneously produced in patients suffering from brain injury. In animals, SDs can be induced even in healthy brains using electrical, mechanical and K⁺ stimuli. Since patients in the neurocritical care environment undergo various nursing maneuvers and are rarely kept in one position, we hypothesized that even these minute movements could trigger SD “mechanically”.

Methods. In order to study the relationship between SDs and movement, we retrospectively analyzed 18 SAH patients, enrolled in the COSBID study, who presented SDs. We compared the overall occurrence of SDs to those time periods, when usually less nursing maneuvers occur (i.e. changes of the shift). In 4 consecutive patients a movement sensor was placed on the skin of the frontal or parietal area of the head to study these events prospectively. The time relationship between SDs and movement was assessed.

Results. A total of 435 SDs were summed up in a histogram according to the hours of the day. There were a mean of 18.1 ± 6.7 SDs per hour. Occurrence of SD was not evenly distributed. During the first scheduled brake during the morning report there were 11 SDs per hour. During the second scheduled brake at noon, there were 6 SDs per hour. From the prospectively analyzed patients, one presented 36 SDs from which 24 were associated with previous movement (3-7 min before the SDs). The second patient presented 3 SDs that were preceded by movement in all the cases (7-10 min). The third patient presented 2 SDs, but they were not preceded by movement. The fourth patient did not show SDs.

Conclusions. SDs that are associated with external patient movements may be found in SAH patients. The triggering mechanism remains speculative. Movement of the patients should be documented in the studies, because it could be a confounding factor for the occurrence of SDs and it might have a negative effect on outcome.

Oral Presentation

97. Towards Use Of Near-Infrared Spectroscopy (NIRS) To Detect Cortical Spreading Depolarisations (CSDs) Non-Invasively

Zakrzewska, Agnieszka (Presenting); Blasi, Anna; Everdell, Nick; Mifsud, Victoria; Walsh, Daniel; Pahl, Clemens; Strong, Anthony John

King's College Hospital, London, UK

Introduction: NIRS detects changes in the concentration of oxygenated, deoxygenated and total hemoglobin by measuring changes in the absorbance of light in the NIR region of the spectrum over the illuminated tissue. Brain activity is closely related to regional changes in blood flow (CBF) and oxygenation. The method is based on the assumption that change in neuronal activity is reflected by a change in CBF and blood volume which affects the mean local oxygenation. Previous experimental studies have shown that CSDs produce hyperaemia in healthy brain; in the injured human or experimental brain peri-lesion depolarisations often induce vasoconstriction and spreading ischemia, all of which may result in tissue oxygenation changes measurable with NIRS.

Aims: To develop a non-invasive method for detection of CSDs in acutely brain injured patients.

Methods: 23 sessions of Continuous Wave (CW) NIRS of mean duration of 2hr 04min 47s, were recorded in 17 patients after head injury, subarachnoid or intracerebral haemorrhage, or stroke. Monitoring was performed using a model of the UCL NIRS system with an array of 6 sources and 4 detectors, providing a total of 10 channels placed over the brain area of interest in patients either after surgery or treated conservatively.

Results: A total of 47hr 50min 19s of data were recorded. 8 subjects showed transient changes in the concentrations of the three chromophores which could potentially be related to CBF alterations caused by CSDs. A further validation against electrocorticography monitoring will enable distinction between local oxygenation variations induced by CSD and those caused by systemic hemodynamic changes such as transient hypotension.

Conclusions: Relative changes in the concentrations of oxy-, deoxy-, and total-hemoglobin measured by CW-type instruments may be sufficient to detect CSD, constituting a less invasive method than currently, with the advantage that it can be used on both unconscious and conscious individuals.

Poster Only, Rookwood Room

98. Analgesics and sedative drugs have an impact on frequency of spreading depolarizations in the injured human brain.

Hertle, Daniel (Presenting); Hartings, Jed A.; Woitzik, Johannes; Dreier, Jens P.; Vidjeon, Steven; Strong, Anthony J.; Kowoll, Christina; Dohmen, Christian; Diedler, Jennifer; Veltkamp, Roland; Unterberg, Andreas W.; Sakowitz, Oliver W.
University of Heidelberg, Heidelberg, Germany

Spreading depolarizations (SDs) are known to occur in humans after brain injury. These patients are in critical medical condition, and therefore often treated with analgesics and sedatives. Such drugs influence brain activity and are possible modulators for the frequency of spreading depressions. We therefore undertook a study to analyze drug effects on SDs, Peri-Infarct Depolarizations (PIDs) and clusters of SDs. 115 patients with acute brain injury (subarachnoid hemorrhage, trauma, ischemic stroke) from the "Cooperative Study on Brain Injury Depolarizations" (COSBID) were included. Midazolam, flunitrazepam, thiopental, fentanyl, sufentanil, remifentanil, ketamine, propofol, gamma-hydroxybutyric acid (GHB), morphine and clonidine were included in our analysis. Recorded hours with and without SDs under influence of each drug were counted. Combined data of several drugs as indicated was used to calculate odds ratio. In this preliminary analysis we found marked effects of midazolam, fentanyl increasing the probability for occurrence of SDs with an odds ratio (OR) of 1.2, 95% confidence interval (95% CI) 1.1/1.4. In contrast propofol, sufentanil, ketamine and morphine seemed to reduce the number of hours with SDs in the combined analysis (OR 0.76 95% CI 0.7/0.8). The result of this preliminary report suggests a possible impact of anesthetic drugs on the occurrence of SDs. A careful evaluation of potential modulators is necessary. This might affect the choice and use of anesthetic drugs after acute brain injury.

Oral Presentation

99. Full-band electrocorticography study of spreading depolarizations in patients with aneurysmal subarachnoid hemorrhage

Hartings, Jed (Presenting); Wilson, J. Adam; Look, Andrew; Shutter, Lori; Ringer, Andrew; Zuccarello, Mario
University of Cincinnati, Cincinnati, OH, USA

Cortical spreading depolarizations (CSD) are a novel pathologic mechanism occurring in patients with aneurysmal subarachnoid hemorrhage (aSAH) and may contribute to delayed cerebral ischemia and infarction^{1,2}. Here we conducted a pilot observational study of CSD using full-band electrocorticography (ECoG) to measure depolarization durations, which reflect the pathogenic effect of CSD. Six patients (5 female) aged 35-63 years were surgically treated by clip ligation for ruptured saccular aneurysms. All patients had Fisher grade 3-4 SAH and WFNS clinical grade 3-4. Electrode strips were placed on cortex in the territory of the affected vessel at the conclusion of surgery. Full-band ECoG was performed [by direct-current amplifier (g.USBamp, Guger Tec, Graz, Austria) with +/- 250 mV range, 24-bit digitization, and recording/display with customized BCI2000 platform] through days 13 and 15 in two patients, but were terminated by day 5 in the others. Electrode impedances ranged 6-110 K Ω , with the majority (68%) in the 20-40 range, and offset potentials were typically <100 mV. 191 CSDs were recorded in 4 patients, with 3/6 patients exhibiting 148 CSDs through day 5, and 2/2 with 43 CSDs on days 6-13. Two patients had focal electrographic status epilepticus (17 and 8 hr) based on the ECoG, with scalp EEG findings negative in one and positive in the other. CSD direct-current (DC) shifts (n=403) were measured at 20 electrodes and had amplitudes of 7.2 mV (quartiles: 6.2, 7.9). DC shift durations were 2 min 10 sec (median, quartiles: 1:46, 2:47), similar to values reported previously in brain trauma patients (2:22, quartiles: 1:56, 3:04)³. However, 10 DC shifts in 2 patients were longer than 10 min, ranging up to 28 min. All patients had new onset neurologic deficits on days 6-15. These results demonstrate the clinical feasibility of DC recordings to measure the pathologic duration of cortical depolarizations, which may contribute to delayed ischemic complications after aSAH.

Oral Presentation

100. Spatia-temporal patterns of cerebral blood flow and hemoglobin oxygenation during the propagation of spreading depolarisations following middle cerebral artery occlusion

Takagaki, Masatoshi; Gramer, Markus; Feuerstein, Delphine; Backes, Heiko; Kohl-Bareis, Matthias; Graf, Rudolf (Presenting)

MPI for Neurological Research, NRW, Germany

Objectives: In the surrounding of focal ischemia, spreading depolarisations (SDs) are thought to cause secondary tissue damage. However, the underlying mechanisms are obscure. We combined here Laser Speckle Flowmetry (LSF) to track the SD waves and hemodynamic responses to them with RGB Reflectometry (RGRB) to measure tissue concentrations in oxyhaemoglobin (HbO₂) and deoxy-haemoglobin (HHb).

Methods: The temporo-parietal cortex of Wistar rats was exposed to laser illumination (for LSF) and high power white light LEDs (for RGRB) through thinned skull. Reflected signals were spectrally separated and acquired by two CCD chips within a single camera [1]. After baseline measurement, the middle cerebral artery was occluded (MCAo) by slow intracarotid injection of TiO₂ microspheres [2]. Simultaneous LSF and RGRB imaging was continued for 3 hours.

Results: Immediately following MCAo, a gradient of CBF levels developed, differentiating ischemic core from border zones [3]. Subsequently, a primary, concentric wave of CBF, HbO₂ and HHb changes originated from the primary ischemic territory. CBF and oxygenation waves were almost synchronous and congruent in space. Subsequently, multiple waves appeared over the observation period. They mostly propagated circumferentially around the ischemic core. A first analysis suggests a very close synchronization and congruence of these LSF and RGRB waves as well. CBF declines were typically accompanied by HbO₂ decrease and HHb increase. First observations also suggest a gradual and steady decrease in HbO₂ and increase in HHb as the SD waves repeat.

Conclusions: SD waves were tracked as concomitant and congruent waves of both CBF and O₂ alteration. Our results suggest that the fast, almost immediate change in CBF after MCAo is accompanied by a slower gradual aggravation of tissue oxygenation with time and with repeating SDs.

Oral Presentation

101. Coupling of cerebral blood flow and glucose metabolism during spreading depolarisations - A multimodal study

Feuerstein, Delphine (Presenting); Takagaki, Masatoshi; Gramer, Markus; Kumagai, Tetsuya; Vollmar, Stefan; Sué, Michael; Backes, Heiko; Graf, Rudolf

MPI for Neurological Research, Cologne, Germany

Objectives: Recent clinical studies suggest that multiple spreading depolarisations (SDs) in human injured brain cause failure of metabolic coupling [1-2]. We have characterized this “uncoupling” using an in vivo multimodal approach. Laser speckle flowmetry (LSF) tracked SDs and corresponding blood flow responses, positron emission tomography (PET) of 18F-2-fluoro-2-deoxy-D-glucose (FDG) measured glucose metabolism, and rapid-sampling microdialysis (rsMD) glucose and lactate.

Methods: In Wistar rats, the temporo-parietal cortex was exposed to laser illumination through thinned skull. A microdialysis probe was inserted to assess glucose and lactate using rsMD [3]. Within the PET scanner, baseline of rsMD and LSF was measured, and subsequently, FDG was injected and PET images acquired for 90 min. SDs were induced 20 min after FDG injection by either a needle prick (single SD group) or by epidural potassium chloride (multiple SD group).

Results. The passage of a single SD wave (n=10) caused a moderate fall in glucose and a sharp increase in lactate by -15% and +35%, respectively. FDG uptake increased compared to the contra-lateral hemisphere. Both rsMD levels and FDG uptake returned to normal by 20 minutes post-SD. Following multiple SDs (n=10), FDG preferentially accumulated in regions with a high occurrence of SDs. The amplitude of increased FDG uptake correlated with the frequency of SDs ($r=0.729$, $p=0.002$). rsMD glucose steadily decreased while lactate remained elevated.

Conclusions. The passage of a SD wave causes a local transient increase in energy utilization. Normalization of FDG uptake and rsMD levels at 20 min post-SD suggests a resting phase of reduced energy consumption. However, when SDs repeat frequently, the increased energy demand leads to irreversible changes in FDG uptake, depletion of glucose and elevation of lactate. This energy “crisis” during multiple SDs would be amplified in already compromised tissue after brain injury.

Oral Presentation

Surgical, management and intervention

102. Neck clipping of paraclinoid small aneurysms

Kanamaru, Kenji (Presenting)

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Introduction: The International Study of Unruptured Intracranial Aneurysms reported that, in the absence of a history of previous rupture, the risk of rupture for small (< 7mm) anterior circulation aneurysms was low, at only 0.1% per year (1). However, many experienced neurosurgeons and endovascular therapists report that, in practice, most ruptured aneurysms encountered are small (2,3). According to other reports, the extent of SAH after the rupture of small aneurysms is often greater than after the rupture of larger aneurysms (3,4). Despite the advent of sophisticated endovascular materials, embolization of very small aneurysms is associated with relatively high rates of intraprocedural rupture, especially intraoperative rupture (5). From surgical point of view, blood blisterlike aneurysms arising from the anterior wall of internal carotid artery (ICA) may be devastating once it ruptures (6). In the present study we demonstrate 10 cases with small aneurysms in the paraclinoid segment of ICA and all of those were successfully clipped.

Materials and Methods: The patients included 6 women and 4 men, 41-66 years of age (mean 56 years). Key points of surgical procedures were as follows: 1) frontotemporal craniotomy with removal of sphenoid ridge; 2) open the Sylvian fissure as much as possible; 3) removal of anterior clinoid process and falciforme ligament to create sufficient space for clip application; 4) dural adherence to aneurysm left intact for protection of thin aneurysm dome; 5) avoid to touch the dome of aneurysm before neck clipping; 6) angled clip is suitable for anterior wall aneurysms and straight one is for ophthalmic artery aneurysms; 7) additional wrapping and coating may be necessary for anterior wall aneurysms if parent artery is affected entirely.

Results: There were no perioperative complications. Glasgow outcome scale after 3 months demonstrated excellent results in all patients.

Oral Presentation

103. Comparison of clearance of clots in patients with subarachnoid hemorrhage between surgical clipping and GDC embolization

Shirao, Satoshi (Presenting); Yoneda, Hiroshi; Yoshino, Hiroko; Ishihara, Hideyuki; Ueda, Katsuhiko; Nakano, Kaori; Nomura, Sadahiro; Fujii, Masami; Suzuki, Michiyasu

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Objective: Subarachnoid clot play an important role in the development of delayed vasospasm after subarachnoid hemorrhage (SAH). The purpose of this study is to compare clearance of subarachnoid clot and the incidence of symptomatic vasospasm between surgical clipping and Guglielmi detachable coils (GDC) embolization for aneurysmal SAH.

Methods: The subjects were 115 patients with Fisher group 3 aneurysmal SAH on a computerized tomography (CT) scan at admission, in whom the aneurysm was treated by surgical clipping (Clip group, n=86) or GDC embolization (Coil group, n=29) within 72 hours of ictus. Software-based volumetric quantification of the subarachnoid clot was performed. The amount of hemoglobin (Hb) in drained cerebrospinal fluid was also measured by biochemical assay.

Results: Clearance of the subarachnoid clot on the CT scan was rapid in the Clip group until the day after the operation, but slow in the Coil group (58.9% removed vs. 27.8% removed, P=0.008). However, postoperative clearance of the clot occurred more rapidly in the Coil group. Difference in the reduction of clot until Day 3-5 was not significant between two groups (72.9% removed vs. 75.2% removed). The amount of Hb in the Clip group was >0.8g/day until Day 3 and then gradually decreased (n=15), but Hb in the Coil group remained at >0.8 g/day until Day 5 (n=17). The incidence of symptomatic vasospasm did not differ between both groups.

Conclusion: Subarachnoid clot can be directly removed during surgical clipping, which is not possible for endovascular treatment. However, the percentage reduction of the clot on Days 3-5 did not differ between the two groups.

Poster Only, Rookwood Room

104. Effect of aneurysm treatment modalities on cerebral vasospasm after aneurysmal subarachnoid hemorrhage

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Introduction: The effect of aneurysm treatment modalities on cerebral vasospasm remains controversial. The aim of this study was to examine if the selection of treatment modality (clip or coil) affects cerebral vasospasm following aneurysmal subarachnoid hemorrhage (SAH).

Material & Methods: 579 SAH patients were enrolled in the Prospective Registry of Subarachnoid Aneurysms Treatment project, and were treated either microsurgically or endovascularly within 12 days of onset. The incidence of vasospasm was compared between patients treated with clipping and coiling.

Results: Clipping (282 patients) was preferably performed for small aneurysms with a wide neck and for middle cerebral artery aneurysms, while coiling (297 patients) was preferred for higher-aged patients, larger, internal carotid artery and posterior circulation aneurysms or treatment during a non-acute stage. Admission World Federation of Neurosurgical Societies (WFNS) grade and SAH severity on CT scans were similar between the treatment modalities. After aneurysmal obliteration, cerebrospinal fluid drainage was performed more in clipped patients, and antithrombotic treatment was performed more in coiled patients. Although the incidence of symptomatic vasospasm and endovascular therapy for vasospasm was not significantly different, vasospasm-induced cerebral infarct occurred more frequently in clipped patients than in coiled patients. However, this difference disappeared after multivariate analyses, which showed that younger age and admission WFNS grade IV-V were significant factors for vasospasm-induced cerebral infarct occurrence. Higher incidence of vasospasm-induced cerebral infarct after clipping was explained by the fact that clipping was selected more for the ruptured middle cerebral artery aneurysm with massive SAH or hematoma, in which vasospasm more frequently occurred.

Conclusions: The incidence of vasospasm may be not significantly different between clipping and coiling.

Oral Presentation

105. Symptomatic vasospasm in elderly patients with aneurysmal subarachnoid hemorrhage: Comparison with non-elderly patients

Inoue, Mizuho (Presenting); Sasaki, Tatsuya; Takazawa, Hiroki; Morita, Takahiro; Narisawa, Ayumi; Saito, Atsushi; Midorikawa, Hiroshi; Nishijima, Michiharu
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Object: In order to clarify the effect of age in symptomatic vasospasm (SVS), we analyzed SVS in elderly and non-elderly patients with aneurysmal subarachnoid hemorrhage (SAH).

Materials and Methods: From 2008 to 2010, we have had 119 patients with aneurysmal SAH (Hunt and Kosnic grade I-IV). These patients were divided into 4 groups: elderly (>70 years old) clipping 22 patients (group A), elderly coiling 14 (group B), non-elderly (<69 years old) clipping 49 (group C) and non-elderly coiling 34 (group D), respectively. In clipping group, intraoperative cisternal irrigation of urokinase (UK) was performed and intrathecal UK via cisternal drainage was added for 3 days after clipping. In coiling group, intrathecal UK via spinal drainage was performed for 3 days after coiling, as well. Intravenous administration of fasdil chrolide (FC, 90 mg) was combined in all cases for 14 days after surgery. DSA was performed at Day 5-7 and intraarterial administration of FC (30 mg) was added if the arterial narrowing was observed.

Results: Ratio of grade IV in each group was 23%, 28%, 10% and 9% (alphabetical order), respectively. Symptom due to SVS remained in 5%, 7%, 4% and 5%, respectively. Ventriculo-peritoneal shunt was performed in 41%, 43%, 13%, and 5%, respectively. Favorable outcome (GR and MD) was obtained in 73%, 50%, 92% and 88%, respectively. Mean value of days in hospital was 51, 40, 36 and 36 days, respectively.

Conclusion: Since there was a lot of selection bias, we have to be careful to interpret data of this study. Ratio of Grade IV, coiling and VP shunt patients was higher in elderly patients. Ratios of SVS were not significantly different among all groups. Favorable outcome was fewer in elderly patients, especially in coiling group. Duration in hospital was longer in elderly clipping patients. Our protocol may be effective for prevention of SVS after aneurysmal SAH regardless age.

Poster Only, Rookwood Room

Other

106. Identifying Patient Report Outcomes (PRO's) relevant to Aneurysmal Subarachnoid Haemorrhage follow-up

Bhargava, Deepti; Al-Tamimi, Yahia; Goddard, Tony; Tennant, Alan; Ross, Stuart (Presenting); Quinn, Audrey
Leeds General Infirmary, Leeds, West Yorkshire, UK

Introduction: Up to 50% of ASAH patients are left with significant cognitive deficits. Up to 50% of survivors, who were in employment pre-haemorrhage, do not return to the same level of work. Many studies report on the Modified Rankin score at discharge, and while it is a useful classification of outcome, it masks the underlying impairments which contribute to that rank. Any therapeutic intervention to offset the sequelae need appropriate Patient Reported Outcomes for these sequelae.

Method: A self-completed questionnaire was sent to two cohorts of patients with ASAH treated in a tertiary neurosurgical centre between 1998-2008. Standardised scales included: AKC Short Sentences Test, Barthel Index, Self-Report Dysexecutive Questionnaire, Everyday Memory Questionnaire, Stroke Symptom Checklist, Wimbledon Self-Report Scale, and the Modified Rankin Score.

Results: Of 214 patients who returned questionnaires, 76% had a WFNS grade of 1 & 2. The mean age was 56.6 years (SD 10.7) and 68.2% were female. The most frequent aneurysm type was that of the anterior communicating artery with approximately 70% of aneurysms of the anterior circulation. 82.6% were 0-2 on the self reported MRS. Of those previously in full or part-time employment, 48.9% were unemployed at follow-up. 28% were noted to have a significant mood disorder. Two in five patients reported impairments of everyday memory, including of speech and reading and writing, and various behavioural difficulties associated with executive functioning, such as impulsivity.

Conclusion: A range of self-reported cognitive and physical deficit measures have been shown to provide important information for the continuing clinical management of the effects of ASAH. Memory and various behavioural difficulties are common in a substantial minority and all are significantly associated with return to work. Thus these PRO's provide useful data to assess recovery and inform therapeutic interventions.

[Oral Presentation](#)

107. Supply or Demand?

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Introduction: There is an evolving understanding that Delayed Ischaemic Neurological Deficit (DIND) is a result of various interdependent pathologic processes like vasospasm, microthrombosis, inflammation, Cortical Spreading Ischaemia and effects of Early Brain Injury. All these processes are believed to reduce cerebral blood flow (CBF) i.e. the supply and cause cellular ischaemia. However, clinical features of DIND have been observed above the ischaemic threshold of CBF. With real-time neuromonitoring we explored cerebral pathophysiology in Aneurysmal Subarachnoid Haemorrhage patients before and during DIND and with institution of triple-H therapy.

Methods: Patients with Fisher grade 3/4 were recruited. Probes to monitor tissue oxygenation, regional CBF and microdialysis were placed at the time of Clipping/Coiling. Normoxia and normovolaemia was maintained afterwards, no prophylactic triple-H therapy was used. If the patient developed symptoms of DIND, they were treated with standardised triple-H therapy.

Results: 16 patients were recruited. 2 patients died early and 2 were sedated throughout monitoring. Of the remaining 12, 7 developed DIND. 6/14 had reduced cerebral blood flow, of these 2 were symptomatic (DIND). Interestingly, 6/7 patients with DIND had parallel elevation of Lactate and Pyruvate at time of symptoms, 4/5 asymptomatic patients did not (OR=24:1). CBF and metabolism did not seem to bear any direct association. Triple H therapy increased CBF, symptoms improved.

Conclusion: We present evidence that DIND might be an issue of demand as well as supply. Triple H therapy may restore balance.

[Poster Only, Pavillion Ballroom](#)

108. Early Brain Injury Linearly Correlates with Reduction in Cerebral Perfusion Pressure During the Hyperacute Phase after Subarachnoid Hemorrhage

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Introduction: Early brain injury (EBI) after aneurysmal subarachnoid haemorrhage (SAH) emerged as a recent concept which embraces complex pathophysiological mechanisms that are linked to the initial bleed. The triggers and consequences of EBI are still poorly understood. The aim of the present study was to investigate whether hyperacute depletion of cerebral perfusion pressure is correlated with an increase in neuronal injury following experimental SAH.

Methods: Various degrees of SAH in terms of ICP increase were initiated and controlled using a shunt from the subclavian artery to the cerebromedullary cistern in 14 rabbits. Standard cardiovascular monitoring, intracranial pressure (ICP), cerebral perfusion pressure (CPP), and bilateral regional cerebral blood flow (rCBF) were continuously measured. Apoptosis was detected using the terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL). Neurodegeneration secondary to ischemia was determined 24 hours after SAH using Fluoro-jade B (FJB) in bilateral basal cortex and hippocampal regions (CA1 and CA3).

Results: rCBF was significantly correlated to reduction in CPP during the initial 15 minutes after SAH in a linear regression pattern (reg coeff $r=0.82$, $r^2=0.68$, $p<0.001$). The mean amount of TUNEL and FJB labeled cells were linearly correlated to reduction in CPP during the first 3 minutes of hemorrhage in the hippocampal regions CA1 and CA3 (reg coeff $r=0.71$, $r^2=0.50$, $p<0.01$) and the basal cortex (reg coeff $r=0.76$, $r^2=0.54$, $p<0.01$).

Conclusion: The degree of early brain injury in terms of neuronal cell degeneration in both, basal cortex and hippocampal regions linearly correlates with the first few minutes of reduced CPP and impeded CBF following SAH. However, it remains unknown whether global ischemia itself or subsequent events are responsible for the detected cell death and neurodegeneration.

Oral Presentation
Award Finalist

109. Addition of new criteria to the sofa (sequential organ failure assesment) for the patients with subarachnoid hemorrhage

Macedo, Sergio Kiffer; Silva, Andre; Bastos, Nathalia; Paz, Juliano; Pessamilio, Thiago; Castro, Rodolfo; Lacerda, Mauricio; Teixeira De Oliveira, Henrique Nuss (Presenting)

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INTRODUCTION:The SOFA was originally created to sepsis, but their quality is now used in others medical conditions. Therefore, we add some criteria to the index to assess the patients with subarachnoid hemorrhage. **PURPOSE:**New criteria to the SOFA: glycemia, arterial lactate, magnesium, calcium, sodium, hourly diuresis and axillary temperature for predictions (death or survival) in patients with subarachnoid hemorrhage; in view of the importance of these criteria in the clinical course of that group of patients.

METHOD: Informed consent for each patient/family; APACHE II (criteria for admission) and SOFA weekly, serum glucose, lactate, calcium, sodium and magnesium; and measurement of axillary temperature and hourly diuresis as the additional prognostic index SOFA. The study enrolled 103 patients diagnosed with SAH. The conduct in relation to the approach these new criteria was the same in all patients evaluated. These patients were divided into two groups according to their development in the ICU: Group I – patients who had good evolution (out of ICU) and Group II – patients who progressed to death in the ICU.

RESULTS: Among 103 patients, 74 (71,84%) were female and 29 (28,16%) were male. The APACHE II for admission varied from 2 to 34, with an average of 15,5. The spent time maximum in ICU was of 49 days (two patients). The group I had 64 patients (62,14%) and the 39 remaining patients (37,86%) were classified as a Group II.

CONCLUSION: The group of patients with SAH are predominance of female (74:29). The APACHE II: Group I was 10,9, while group II was 17,9. The only criteria which showed statistical significance in the prediction of death was the serum sodium ($p=0,002$). It is necessary a new complementary study to standardize these additional criteria to SOFA as an assessing method of prognosis of patients with SAH, but we can conclude that the change in serum sodium has fundamental importance in the evolution of this group of patients.

Oral Presentation

110. CSD-Monitor: Concept and demonstration of a software for online bedside analysis and simultaneous visualization of ECoG-data from brain-injured patients for care and research

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Introduction: Spreading depolarizations (SD) are a potential cause of secondary brain injury following traumatic, hemorrhagic and/or ischemic incidents to the cerebrum. Although SDs can be quite easily discerned in electrocorticographic recordings (ECoG) by an experienced investigator, this has to be carried out off-line and involves large datasets which are cumbersome to handle. A bedside monitoring tool could provide additional data not only during off-line analysis but also in realtime and thereby help to improve the outcome of brain-injured patients. **Features:** Implemented features include those for routine inspection of ECoG-data and filtering algorithms to emphasize SD specific signal parts. Fast automatic detection of artifacts are implemented to inform about problems in the recording setup. Specific modules for the analysis of SDs include the projection of ECoG-data onto a 3D-model of the electrodes on the cortex. Furthermore automatic detection and visualization of clusters of SDs with similar patterns will also be implemented. Automatically inserted events like SDs or artifacts can be approved manually in a comfortable user interface to ensure data quality for off-line analysis.

Methods: Our implementation (C++, GCC-compiler, Qt 4.7) ensures platform independence. A modular plugin concept allows for easy extension of functionality with plugins written even in different programming languages like Matlab or Java. An advanced user interface enables authorized users with different qualifications to adjust configurations and parameter settings.

Conclusions: Off-line analysis and annotation functionality has been tested with ECoG-data from different patients of the large dataset acquired within the COSBID study. Results of the analysis algorithms will be discussed and compared with the already established signal analysis in the COSBID group. Interested members of the COSBID group can contact us to work together in use and development of the software.

Oral Presentation

111. Epidemiological analysis of patients with cerebral aneurysms submitted an embolization at Sao José do Avai Hospital

Macedo, Sergio Kiffer (Presenting); Siqueira, Carlos Mauricio; Siqueira, Savio; Oliveira, Dias, Lucas; Da Matta, Nayara; Almeida, Erica; Brito, Lara; Bastos, Nathalia; A.S, Carvalho
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INTRODUCTION: The treatment of intracranial aneurysms evolved since the introduction of endovascular neurosurgery by Guglielmi Detachable Coils (GDC), because of the safety and feasibility of this method.

METHOD: It was conducted from the database of patients submitted an ablation in the neurosurgery department, in the period of 2006 to 2009.

RESULTS: We studied 1504 patients submitted to ablation. These, 1120 were females (74,46%) and 384, males (25,84%). The average age was 52 years (variable:10-91). patients that required hospitalization in ICU was 176 (34,4%), staying on average of 6,1 days (Odds ratio: 5,0). Hunt-Hess scale prevalence: 1 – 68,48%, 2 – 16,35%, 3 – 8,04%, 4 – 4,78%, 5 – 2,32%, and Fisher (tomography scale): 1 – 62,58%, 2 – 7,91%, 3 – 23,5%, 4 – 7,58% and incidental – 4,85%. The main risk factors involved into cerebral vascular accident were: Systemic arterial hypertension (n = 608 – 40,4%) and smoking (n = 463 – 30,8%). The arteries more commonly involved were: posterior communicant = 725 (25,33%), median cerebral = 562 (19,62%), anterior communicant = 469 (19,38%), ophthalmic = 124 (4,34%), PICA = 52(1,81%) and pericallosa = 82 (2,6%). Among the 218 events that occurred, there were coil into the vascular lumen in 96 cases (6,38%), bleeding in 58 (3,85%) and others. The material used were: 334 balloons (71,06%) and 136 stents (28,94%). Angiographic vasospasm occurred in 178 patients.

CONCLUSIONS: We note in the occurrence of cerebral vascular aneurysmatic accident: the predominance of females, the average age:52 years and systemic hypertension and smoking are associated. The arteries of the previous segment were those that had higher incidence of aneurysms. More than half of the patients did not had complication during the procedure, however, when had, coil in the lumen and angiographic vasospasm were most frequent. embolization of cerebral aneurysms revealed to be low lethality method.

Poster Only, Pavillion Ballroom

112. Frequency/prevalence analysis of risk factors on aneurysmal subarachnoid hemorrhage

Macedo, Sergio Kiffer (Presenting); Siqueira, Carlos Mauricio; Siqueira, Savio; Nuss, Rodrigo; Dias, Joana; Carvalho, Robson; Guarçoni, Angelo; Fiorot, Jessica
Sao Jose Do Avai Hospital, Itaperuna, Rio De Janeiro, Brazil

Introduction: Subarachnoid hemorrhage (SAH) is a catastrophic clinical event in which 2/3 of spontaneous SAH are characterized by rupture and bleeding of cerebral aneurysm.

Methods: After institutional approval and informed consent, this prospective observational study took place from April 2008 to November 2009, involving all adult patients with spontaneous SAH admitted on ICU, evaluating the frequency/prevalence of some factors as: Gender, Age, Skin Color, Arterial Hypertension (AH), Smoking Habit, Diabetes Mellitus (DM), Alcoholism, Dyslipidemia, Sedentary and Use of Oral Contraceptive Method.

Results: There were observed a total of 128 patients (n), average age of 55,3 y-old, and obtained as main results of frequency with respective confidence intervals (CI): Gender F 73,4% (94)–(IC) 64,9–80,9 M 26,6% (34)–(IC) 19,1–35,1; Skin Color: White 46,2% (54)–(IC) 36,9–55,6 Black 24,8% (29)–(IC) 17,3–33,6 Brown 29,1% (34)–(IC) 21,0–38,2; AH Yes 72,7% (93)–(IC) 64,1–80,5 No 27,3% (35)–(IC) 19,8–35,9; Smoking Habit Yes 44,5% (57)–(IC) 35,7–53,6 No 55,5% (71)–(IC) 46,4–64,3; Diabetes Mellitus: Yes 14,8% (19)–(IC) 9,2–22,2 No 85,2% (109)–(IC) 77,8–90,8; Alcoholism Yes 12,6% (16)–(IC) 7,4–19,7 No 87,4% (111)–(IC) 87,4–92,6; Dyslipidemia Yes 10,9% (14)–(IC) 6,1–17,7 No 89,1% (114)–(IC) 82,3–93,9; Sedentary Yes 25,8% (33)–(IC) 18,5–34,3 No 74,2% (95)–(IC) 65,6–81,5; Obesity Yes 11,7% (15)–(IC) 6,7–18,6 No 88,3% (113)–(IC) 81,4–93,3; Oral Contraceptive Method* Yes 5,3% (5)–(IC) 1,7–12,0 No 94,7% (89)–(IC) 88,0–98,3. * Analysis obtained only for female gender population.

Conclusions: We can show that among all RF, F Gender, AH and Smoking Habit had greatest prevalence index; the factor Skin Color had wide distribution from its variants; other RF as DM, Alcoholism, Dyslipidemia, Sedentary, and Use of Oral Contraceptives had not obtained significant prevalence on patients with aneurysmal SAH.

Poster Only, Pavillion Ballroom

113. Effects of Sinvastatin in prevention of vasospasm in non-traumatic subarachnoid hemorrhage (preliminary data)

Macedo, Sergio Kiffer (Presenting); Siqueira, Carlos Mauricio; Siqueira, Savio; Campeao, Andre; Dias, Lucas
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Introduction: Vasospasm is the main cause of death and cognitive deficits in patients with subarachnoid hemorrhage after rupture of the aneurysm (aSAH). Some trials have shown that statins in the acute phase of aSAH reduces the incidence, morbidity and mortality of cerebral vasospasm.

Methods: Was realized a prospective study, randomized, non-blind, with the use of 80mg of SVT (at night) in the first 72h of the beginning of bleeding, and the control group that didn't use SVT, for 21 days, between January to December 2008. Informed consent for all patients. CT scans was performed as control and another CT scan in patients with altered neurological signals. In the presence of changes suggestive of vasospasm or correlation in clinical and CT scans the patients were taken to cerebral arteriography exam followed by angioplasty procedure if necessary. Liver and renal function, LDL cholesterol evaluated weekly, and CK Total evaluated every 3 days. Exclusion criteria: liver and renal disease, pregnant elevation of serum transaminases (3 times the value of normality), creatinine $\geq 2,5$, rhabdomyolysis or CK Total ≥ 1000 U/L.

Results: Were excluded 2 patients with bleeding more than 72hs. There was no significant change in the levels of CK total, renal or liver function. We included 21 patients, 11 in the SVT group and 9 in the control group. The mortality was 8 patients (38%), 6 patients in the control group and 2 of the SVT group. Vasospasm was confirmed by cerebral arteriography exam in 4 patients in the control group and 1 patient in the SVT group. All the patients who died had scale Fisher IV.

Conclusions: The SVT at a dose of 80mg was effective in reducing the mortality (18,1% against 66%) compared to the group that did not use SVT, and also decrease the incidence of cerebral vasospasm despite the APACHE II higher in the group that used SVT (14,3 vs 10,7). Less morbidity in the SVT group with an average of scale of Glasgow 3,25 vs 2,1.

Poster Only, Pavillion Ballroom

114. Outer Skull Landmark Based Coordinates for Measurement of Cerebral Blood Flow and Intracranial Pressure in Rabbits.

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Objectives. Despite the increased use of intracranial neuromonitoring for the evaluation of acute pathophysiological derangements during experimental subarachnoid hemorrhage (SAH) reliable stereotactic coordinates for the placement of monitoring probes in rabbits are missing. The aim of the presented study was to determine and evaluate the safety and reliability of various locations of intraparenchymal intracranial pressure (ICP) and cerebral blood flow (CBF) probes according to outer skull landmarks.

Methods. Experimental SAH was performed in 22 rabbits using an arterial shunt cisterna magna model. Intraparenchymal recordings from ICP probes placed in the frontal lobe were compared to measurements recorded from the olfactory bulb. CBF probes were placed on various locations in the frontal cortex anterior to the coronary suture. Insertion depth, relation to the ventricular system, and ideal placement location were determined on postmortem gross total dissections and histological examination.

Results. There were no significant differences in ICP recordings obtained from the right frontal lobe (8.8 ± 1.9 mm anterior to the bregma and 1.5 ± 0.5 parasagittal) compared to the right olfactory bulb (midpupillary line anterior to the bregma and 2 mm parasagittal). Ideal coordinates for intraparenchymal CBF probes in the left and right frontal lobe were found to be located 4.6 ± 0.9 and 4.5 ± 1.2 anterior to the bregma, 4.7 ± 0.7 mm and 4.7 ± 0.5 mm parasagittal, and in a depth of 4 ± 0.5 mm and 3.9 ± 0.5 mm, respectively.

Conclusions. The results of this study demonstrates that coordinates in relation to cranial landmarks allow feasible and fast hitting of intraparenchymal locations for ICP and CBF probes. Practical accuracy of these coordinates can be warranted for safe and reproducible neuromonitoring in the rabbits' brain without the use of a stereotactic frame.

Poster Only, Pavillion Ballroom

115. Angiotensin-1 is associated with cerebral vasospasm and delayed cerebral ischemia in subarachnoid hemorrhage

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Background: Angiotensin-1 (Ang-1) and -2 (Ang-2) are keyplayers in the regulation of endothelial homeostasis and vascular proliferation. Angiotensins may play an important role in the pathophysiology of cerebral vasospasm (CVS). Ang-1 and Ang-2 have not been investigated in this regard so far.

Methods: 20 patients with subarachnoid hemorrhage (SAH) and 20 healthy controls (HC) were included in this prospective study. Blood samples were collected from days 1 to 7 and every other day thereafter. Ang-1 and Ang-2 were measured in serum samples using commercially available enzyme-linked immunosorbent assay. Transcranial Doppler sonography was performed to monitor the occurrence of cerebral vasospasm.

Results: SAH patients showed a significant drop of Ang-1 levels on day 2 and 3 post SAH compared to baseline and HC. Patients, who developed Doppler sonographic CVS, showed significantly lower levels of Ang-1 with a sustained decrease in contrast to patients without Doppler sonographic CVS, whose Ang-1 levels recovered in the later course of the disease. In patients developing cerebral ischemia attributable to vasospasm significantly lower Ang-1 levels have already been observed on the day of admission. Differences of Ang-2 between SAH patients and HC or patients with and without Doppler sonographic CVS were not statistically significant.

Conclusions: Ang-1, but not Ang-2, is significantly altered in patients suffering from SAH and especially in those experiencing CVS and cerebral ischemia. The loss of vascular integrity, regulated by Ang-1, might be in part responsible for the development of cerebral vasospasm and subsequent cerebral ischemia.

Poster Only, Pavillion Ballroom

116. Cellular microparticles as a marker for cerebral vasospasm in spontaneous subarachnoid hemorrhage

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Innsbruck Medical University, Austria

Background: Spontaneous subarachnoid hemorrhage (SAH) still carries a high risk for poor outcome frequently attributable to symptomatic cerebral vasospasm (CVS). We hypothesize that cellular microparticles (MP) play a role in the pathogenesis of CVS and may serve as biomarkers for CVS.

Methods: In 20 consecutive SAH-patients endothelial, leukocyte, platelet and erythrocyte MP were measured during 15 days after ictus. CVS was detected by Transcranial Doppler sonography (TCD). 20 matched volunteers served as healthy controls (HC).

Results: Endothelial, leukocyte and erythrocyte MP were elevated in SAH patients compared to HC. CD105+ and CD62e+ endothelial MP (EMP) were significantly higher in SAH patients with Doppler sonographic CVS (dCVS). Especially CD105+ EMP were increased on the days of dCVS onset. In patients experiencing cerebral infarction due to vasospasm (CIV), CD41+ platelet MP (PMP) were elevated in addition to EMP. CD41+ PMP were significantly higher in patients with any level of disability (mRS \geq 1) compared to those who made a full recovery (mRS = 0) on discharge from hospital.

Conclusion: EMP were elevated in patients with SAH. This elevation coincided with the occurrence of dCVS and could therefore be a novel biomarker for CVS. PMP might be involved in the pathogenesis of CIV resulting in neurological morbidity.

Poster Only, Pavillion Ballroom

117. Screening for vasospasm significant biomarkers in cerebral spinal fluid using multidimensional separation techniques with MALDI-TOF/TOF-MS and ESI-LTQ-MS

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Worldwide, SAH and its sequela, CV, kill or seriously debilitate an estimated 1.2 million people annually. One of the barriers to research progress in prevention or reversal of CV after SAH is the ability to predict which SAH patients will develop vasospasm, and elucidation of the signaling pathways that contribute to cerebral vasospasm. Approximately half of all people who survive SAH suffer from CV 3-10 days following the initial stroke. Currently transcranial Doppler flow determinations performed every 24-48 hours can help screen for the onset of vasospasm.¹ This delayed onset gives researchers and clinicians a window to treat SAH patients in order to prevent vasospasm. Investigations involving traditional biological techniques into the etiology of CV have led to promising advances.²⁻⁵ These studies have found that excessive oxidative environments², platelets³, glutathione peroxidase⁵ and even bilirubin⁴ could contribute to the onset of CV. This study focuses on using multidimensional separation techniques by combining isoelectric focusing and strong cation exchange chromatography with liquid chromatography matrix assisted laser desorption ionization-time of flight/time of flight mass spectrometry (MALDI-TOF/TOF-MS) and liquid chromatography electrospray ionization-linear trap quadrupole mass spectrometry (LC-ESI-LTQ-MS) to explore three different cerebral spinal fluid (CSF) samples, control (normal, healthy, CSF control), SAH stroke patients (no vasospasm, CSF C) and SAH CV patients (CSF V), for potential biomarkers. A number of potentially significant proteins were identified and continuing studies are currently underway for further investigations of these proteins.

Poster Only, Pavillion Ballroom

118. Complications Associated with the Endovascular Management of Vasospasm with Unsecured Intracranial Vascular Lesions

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Introduction. The management of cerebral ischemia due to vasospasm involves increasing cerebral perfusion with hypervolemic hemodilutional hypertensive (HHH) therapy, intra-arterial vasodilators, or angioplasty. All therapies are usually undertaken with secured vascular lesions. Patients may rarely present with vasospasm with unidentifiable pathology or a lesion that cannot be secured prior to treating vasospasm. This unique circumstance requires cautious application of medical and endovascular treatment to balance the risk of stroke from vasospasm with re-rupture of the vascular lesion.

Methods. We retrospectively reviewed our endovascular database of patients treated from 2002-2011. We searched the database for keywords of vasospasm, verapamil, papaverine, and angioplasty to identify SAH patients with ruptured unsecured intracranial vascular lesions receiving intra-arterial vasodilators or angioplasty. We excluded patients with secured lesions or those who only had diagnostic studies. Charts were reviewed for complications associated with endovascular management.

Results Our search yielded 100 possible patients that met our initial search terms. Of these, 70 had secured lesions, 12 had missing records, and 9 had only diagnostic studies leaving 9 patients with SAH with unsecured pathology receiving endovascular therapy. Of 13 treatments in these 9 patients, 2 (15%) resulted in brain death within 24 hours treatment. One patient had a giant vertebrobasilar aneurysm and had a brainstem stroke after angioplasty of a vertebral artery and the other patient had intra-operative re-rupture of a vertebral artery dissection during verapamil administration and coil occlusion.

Conclusion. Patients with unsecured intracranial aneurysms and dissections have a high major complication rate when using endovascular means to treat vasospasm and should be approached cautiously. Angiogram-negative SAH patients may be safer to treat with endovascular means than patients with known pathology.

Poster Only, Pavillion Ballroom

119. Statin induced T-lymphocyte modulation and neuroprotection following experimental subarachnoid hemorrhage.

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Introduction: Statins influence immune system activities through mechanisms independent of their lipid lowering properties. They are potent inducers of a Th2 switch in immune cell response. T-cells can be subdivided on the basis of cytokine secretion patterns into two subsets, T-helper cell type 1 (Th1) and type 2 (Th2). Independent laboratory studies have also shown statins to be neuroprotective in several models of CNS disease including neuroregeneration, MS, stroke, spinal cord injury and traumatic brain injury. This study is the first to evaluate the immune modulating effects of statins in subarachnoid hemorrhage (SAH). We hypothesize that statins will induce a Th2 immune switch that results in neuroprotection against the early brain injury following SAH.

Methods: Simvastatin was administered to rats intraperitoneally in two dosages (1 mg/kg and 20 mg/kg), 30 minutes after the induction of SAH using endovascular perforation. Neurological scores were assessed 24 hours later. Animals were then sacrificed and sampled of cortex and brain stem were tested for expression of the T-regulatory cell cytokine TGF-B1, as well as IL-1B, proinflammatory cytokine associated with Th1 immune responses. The presence of TGF-B1 secreting T-cells was evaluated with the use of brain slices.

Results: SAH significantly impaired neurological function in all SAH groups (treated and untreated) vs. Sham. High-dose treated simvastatin animals had less neurological impairment than both untreated and low dose groups. Cortical and brainstem levels of TGF-B1 were significantly elevated following SAH in the high-dose group. IL-1B was significantly elevated following the induction of SAH, but was inhibited by high-dose simvastatin. Double-labeled fluorescent immunohistochemical data demonstrated the presence of lymphocytes in the subarachnoid and perivascular spaces following SAH. Expression of TGF-B1 by lymphocytes was markedly increased following treatment with high dose simvastatin.

Conclusion: The present study elucidates the potential role of a Th2 immune switch in statin provided neuroprotection following SAH.

Oral Presentation

COSBID

Co-Operative Study on Brain Injury Depolarizations

