



ZIHP *News*

Zurich Center for Integrative Human Physiology

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Sound asleep for research

During deep sleep our brains remain active, generating distinct signals that can be detected by electroencephalography (EEG). Sleep researchers who joined forces in ZIHP cooperative projects relied on this method to examine the influence of genetic variations and intelligence on sleep and to obtain novel insights into brain development.

Christina Giger

Are our individual sleep characteristics genetically predetermined? Is our brain able to perform better if we sleep more? Does an intelligent brain need more or less sleep? Can sleep even provide information about the current level of maturity of a child's brain?

To answer such questions of enormous social relevance an interdisciplinary research approach is needed, involving a team of experts in both basic and clinical research. The ZIHP promotes this research approach by granting cooperative projects in which at least three ZIHP members collaborate to generate a synergistic value. The results of ZIHP-funded projects in sleep research confirm the benefit of this approach.



Gene variant causes sleepiness and reduced vigilance

To find out how genes determine sleep features, ZIHP researchers studied a gene variant of an enzyme that metabolizes adenosine. Adenosine is important for cellular energy production, and induces sleepiness by triggering sleep-promoting brain regions. This gene variant is present in around ten percent of the Caucasian population, rendering the enzyme less effective so that adenosine is only partly metabolized.

To test whether this small genetic modification affects sleep, ZIHP researchers kept volunteers awake for forty hours in a sleep laboratory. Interestingly, the volunteers carrying the mutation slept deeper before and

after the sleep deprivation than the volunteers with the normally functioning enzyme.

To quantify sleep depth, researchers employed electroencephalography (EEG). This method allows to examine various features of sleep with the use of electrodes that record potential differences on the scalp. These differences result from electrical signals of brain cells and reflect the transmission and processing of information in the brain. Thus, they are a robust, large-scale measure of neocortical dynamics and closely related to the state of the brain.

During deep non-rapid-eye-movement (NREM) sleep the reduced brain activity is represented by waves with low frequency ("slow waves") in the EEG. It is assumed that deep sleep contributes to the storage and formation of new memories. Moreover, deep sleep is believed to be an important recovery phase for the brain. A shortage of sleep one night will be compensated by a deeper and longer sleep the following night.

The fact that the volunteers with the gene variant sleep deeper and have

longer periods of “slow wave sleep” suggests that they may suffer more during sleep deprivation. This suggestion was supported by additional tests during prolonged wakefulness. The activity of α -amylase – a proposed biomarker for sleepiness – was determined in saliva. The volunteers also had to rate their sleepiness and mental state on questionnaires. All tests led to the same result: The subjects with the mutation were sleepier and less attentive than the persons with a normally functioning adenosine-degrading enzyme. These observations show that genetic factors indeed have an impact on sleep characteristics. For a publication evolving from this ZIHP cooperative project, the ZIHP award was given last summer.

Intelligent kids need less sleep

Apart from such distinct genetic differences, sleep demand also changes during human development and aging. Children need more sleep because their brains are still developing. Nevertheless, not all kids need the same amount of sleep. ZIHP researchers were interested to investigate whether children’s sleep duration influences their cognitive performance. They studied eight to twelve year old school kids who had to fill in questionnaires, keep a sleep diary together with their parents and

wore activity monitors to measure their rest/activity patterns. Additionally the children were performing an intelligence test.

Counter-intuitively, the results showed that children who needed less sleep had a higher IQ. Particularly, they had a higher ability to solve new problems independently of acquired knowledge. Does this mean that we should keep our children awake in order for them to become more intelligent? The researchers clearly oppose such a suggestion. Children with a higher IQ might need less sleep because their brains not only work more efficiently but also regenerate faster. If kids who need more sleep are forced to sleep less, this could even have negative consequences on their cognitive performance and development.

EEG-imaging of brain development

ZIHP researchers also estimated brain development in children and adolescents by measuring the EEG during deep sleep. Changes in brain activity in specific regions are observed during maturation or structural reorganisation. A topographical map of the active brain regions can therefore give a picture of the current state of maturity of the brain.

Employing this method, researchers found that the brain development of children and adolescents born pre-term might be altered compared to term born peers. Thirteen year old children born prior to the 32nd week of gestation and with a birth weight of less than 1500 grams performed slightly worse in tests for planning and working memory than their term born peers. Also their average IQ was lower, however still within normal limits.

EEG for ADHD classification

EEG is also used in other fields of research, for example to improve the understanding of the brain changes seen in attention-deficit/hyperactivity disorder (ADHD). ZIHP researchers reported that several characteristics in the EEG of ADHD-children differ from those of healthy peers. In a follow-up project it will be determined to what extent the EEG together with other measurements can be used as diagnostic markers for ADHD.

As a center of competence generously funded by a University Research Priority Program of the UZH, the ZIHP is proud of these projects that have contributed new insights and understanding in the fields of sleep research and human physiology, and of their translation to the clinics.

→ Sleep and cognition in children and adults in health and disease: a cooperative and integrative approach

Consortium members: Landolt Hans-Peter, Achermann Peter, Huber Reto, Brugger Peter, Jenni Oskar

Project duration: January 2007 – December 2009

Two PhD students (within the → [imMed PhD Program](#)) were supported.

→ Executive function in preterm born children: an integrative approach from genetics to brain function

Consortium members: Haggmann Cornelia, Huber Reto, O’Gorman Tuura Ruth, Latal Beatrice, Rauch Anita

Project duration: January 2012 – December 2013

One PhD student (within the → [imMed PhD Program](#)) was supported.

→ Linking the major system markers for typical and atypical brain development

Consortium members: O’Gorman Tuura Ruth, Brandeis Daniel, Klaver Peter, Boesiger Peter, Martin Ernst, Henning Anke

Project duration: January 2011 – December 2013

Two PhD students (within the → [imMed PhD Program](#)) and one Post-Doc were supported.

The 10th imMed retreat: Science, Sports and Socializing in Solothurn

Marta Bombardó and Gladys Filliat

Any Monday morning in Zurich looks the same - but June 1, 2015 was an exception. Around 65 students from the imMed PhD Program met at Zurich Hauptbahnhof. We all had the same objective: enjoying the long-awaited two days of the → 10th annual retreat of our PhD program.

This year our destination was Solothurn, Switzerland's finest baroque town. At the Youth Hostel in Solothurn we were warmly welcomed with coffee and croissants. The beautiful location at the river Aare and the wonderful weather were ideal for first interactions between the PhD students. After getting to know each other the scientific part of the retreat was opened by the members of the Commission of the imMed PhD Program and Peter Achermann from the Steering Committee of the ZIHP.

The first presentation session where some of us presented their exciting PhD projects covered a broad variety of topics from *in-vitro* experiments to *in-vivo* applications.

A delicious lunch lifted our glucose level and reboosted our energy to discuss our fellow students' posters and discover more about Solothurn's picturesque old town before we met



again in the conference room for the second part of the scientific presentations.

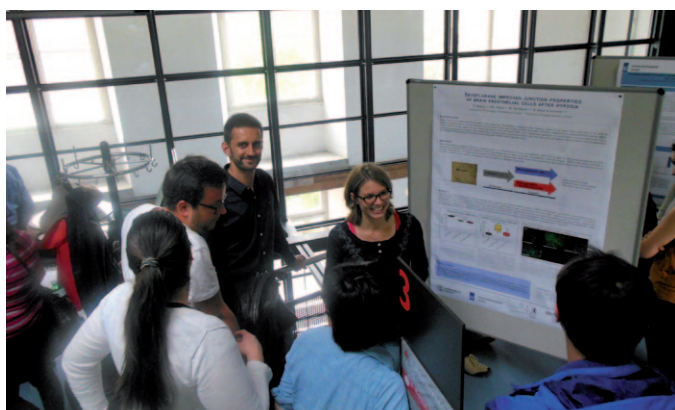
Later in the afternoon Roger Gförer from the Career Services UZH gave an inspiring talk on ways and strategies on how to “push luck” to find an exciting job after our PhD.

To close off the first day of the retreat, we were invited to an outdoor aperitif and award ceremony. The prizes went to Esther Gottwald for the best presentation «The iron chelator deferasirox induces kidney toxicity via mitochondrial dysfunction or how to make mitochondria flash» and Fabrizio Lucchini for the best poster «The role of apoptosis signal-regulating kinase 1 (ASK1) in the development of obesity-associated insulin resistance». Congratulations to both of them! The evening con-

tinued with a dinner and we were all in a social mood for further scientific and non-scientific exchanges! We had a lot of fun.

Now, we were looking forward to the adventure on Tuesday at Seilpark Balmberg. The second day was fully dedicated to increase our networking. After all the safety instructions and rules such as how to put on our harness and carabineers, we were ready to play like monkeys! All of us had a great time testing our limits on the different routes and memorizing our ancestral origins. The intense morning full of fun and adrenaline ended with an amazing barbecue and a well-deserved rest.

It was a wonderful experience! It is not easy to get to know PhD students from other labs located all over Zurich, personally and professionally. Since all of us have different projects, the exchange of ideas, points of view and experiences was the most valuable point of this imMed retreat. The time away from the lab and the daily PhD schedule was very well invested! One more time, many thanks to all the organizers for these two great days!



Poster session at the Youth Hostel Solothurn

→ Photo album of the 10th imMed Retreat

Saltin Award for Christoph Siebenmann

Christoph Siebenmann, → **alumnus of the imMed PhD program**, received the → **Saltin Award** «for his unique ability to design and execute complicated studies on human physiology, often outside a laboratory setting.» His capability to address important questions on the impact of exercise in human physiology and to interpret observations from an integrated perspective was considered to reflect a cornerstone of the heritage from Bengt Saltin, one of the big names in exercise and integrative physiology who passed away in September 2014.

After his PhD Christoph continued his research in the group of ZIHP assistant professor Carsten Lundby. Currently he holds a postdoc fellowship at the Royal Institute of Technology in Stockholm, Sweden.

ZIHP News: Congratulations on this prestigious award, Christoph! What are your plans?

Christoph Siebenmann: The prize money is dedicated to scientific travelling. I am planning to spend some time in a laboratory abroad and to travel to international conferences. But even more important is that I received encouraging feedback from several established phy-



Crown Prince Frederik of Denmark hands over the Saltin Award to Christoph Siebenmann.

siologists and some inquiries for collaborations. I feel confident that the award will push my career.

Do you see any differences in research culture in physiology between Denmark and Switzerland?

Yes. Denmark has a long tradition in human integrative physiology. This «classic physiology» is more popular there and receives more recognition. In Switzerland, research primarily focuses on molecular and animal experiments. But distinguished mechanistic insights can also be gained in studies with healthy human subjects. However, some invasiveness is necessary. In the ZIHP research group of Carsten Lundby we did this for example by taking muscle biopsies or administering drugs to block a single receptor type. This allows deep insights

into the complex functions of the organism. However, in Switzerland we frequently have to make a higher effort to obtain the permission from the ethic committees.

The prize was awarded by Crown Prince Frederik of Denmark? What was the ceremony like?

Danish royals are quite down-to-earth. Nevertheless, the audience had to stand up when Prince Frederik entered the auditorium and I was instructed how to act. For example I had to address my scientific presentation to «His Royal Highness Crown Prince Frederik». It was an interesting experience to meet a royal - and I really enjoyed it.

All the best for you, Christoph, and for integrative human physiology!

Congratulations!

Elena Osto has received the → **Swiss Cardiovascular Biology Prize** for the scientific work published in *Circulation* in March 2015 «Rapid and body weight-independent improvement of endothelial function and HDL properties after Roux-en-Y gastric bypass: role of glucagon-like peptide-1». This paper evolved from a → **ZIHP cooperative project**.

Die Entwicklungspädiaterin und ZIHP-Forscherin Bea Latal vom Universitäts-Kinderspital Zürich hat den renommierten → **Georg-Friedrich-Götz-Preis 2014** erhalten. Der Preis wird jährlich für besondere Leistungen in der medizinischen Forschung vergeben.

ZIHP-Forscherin Susanne Walitza wurde zur → **Prodekanin Klinische Lehre an der Medizinischen Fakultät gewählt**. Damit ist sie die erste Frau in der Geschichte der UZH, die dieses Amt an der Medizinischen Fakultät übernimmt.

WISSEN-SCHAFT WISSEN

Präzisionsarbeit am Nervenzentrum



Die Neurochirurgie in Zürich genießt Weltruf. Professor Luca Regli, Professor für Neurochirurgie an der UZH, erklärte in der Veranstaltungsreihe «Wissen-schaf(f)t Wissen», welche Rolle die Technologie bei Hirnoperationen spielt.

→ [Zum UZH News Artikel](#)

Griff in die Schöpfungskammer



Die Operation eines ungeborenen Kindes im Mutterleib ist ein anspruchsvolles Unterfangen. Über die Voraussetzungen und Risiken des Eingriffs gab der Kinderchirurg Professor Martin Meuli in der Reihe «Wissen-schaf(f)t Wissen» Auskunft.

→ [Zum UZH News Artikel](#)

→ Gebrochene Herzen

Eine Herzkammer, die aussieht wie eine japanische Tintenfischfalle, und Symptome wie bei einem Herzinfarkt: Kardiologen um das ZIHP-Mitglied Thomas Lüscher erforschen das rätselhafte und gefährliche «Broken Heart»-Syndrom.

magazin. Die Zeitschrift der Universität Zürich, 15. Mai 2015

→ Narkotisierte Krebszellen

Eine Krebsoperation ist eine grosse Belastung für den Körper, auch das Immunsystem gerät unter Stress. In der Gruppe von ZIHP-Forscherin Beatrice Beck Schimmer wird untersucht, ob Narkosemittel, die während einer OP eingesetzt werden, das Immunsystem unterstützen können.

UZH News, 11. Mai 2015

Press review

→ Seltene Krankheiten – gar nicht so selten

Verbesserte Behandlungsmethoden für Patienten mit einer seltenen Krankheit zu entwickeln, steht im Zentrum des Programms «radiz – Rare Disease Initiative Zürich». Es ist eines von elf Klinischen Forschungsschwerpunkten der Universität Zürich. Geleitet wird es von ZIHP-Mitglied Matthias Baumgartner.

UZH News, 24. Juni 2015

→ Erster Preis für «Cutiss»

Anfang dieser Woche fand der schweizweite Startup-Wettbewerb «venture» statt. Den ersten Preis erhielt «Cutiss», ein Neuunternehmen, das individuell angepasste Hauttransplantate auf den Markt bringen will. Entwickelt wurde die laborgezüchtete Haut in der Gruppe von ZIHP-Forscher Ernst Reichmann am Kinderspital der Universität Zürich.

UZH News, 18. Juni 2015

→ Die Vielfalt der Multiplen Sklerose

Multiple Sklerose ist eine Krankheit, die in vielfältigen Formen auftritt. Im Klinischen Forschungsschwerpunkt «Multiple Sklerose» der Universität Zürich wird versucht, verschiedene Typen der Krankheit zu identifizieren und daraus neue Behandlungsformen abzuleiten. Geleitet wird er von ZIHP-Mitglied Roland Martin.

UZH News, 8. Juni 2015

→ Catch me if you can

BBC reporter Mark Daly investigates serious allegations of doping in athletics, spanning more than 30 years and involving some of the biggest stars in the sport. In order to understand how erythropoietin and the Athlete Biological Passport work he came to Zurich to interview ZIHP assistant professor Carsten Lundby.

BBC, June 3, 2015

→ Einfluss der Schwerkraft auf Zellen mit drei Weltraumexperimenten erforscht

Gleich drei Raketen beförderte die Universität Zürich im April 2015 ins All, um Weltraumexperimente durchzuführen. Alle drei Missionen sollen den Wissenschaftlern um ZIHP-Mitglied Oliver Ullrich Erkenntnisse über den Zusammenhang von Schwerkraft und verschiedenen Zellfunktionen liefern.

Medienmitteilung UZH, 7. Mai 2015

→ Mit Nanomagneten Tumore bekämpfen

Kohlenstoff beschichtete Eisenpartikel im Körper einzusetzen, verspricht grosse Hoffnungen in der Krebstherapie. Noch arbeitet die Forschung daran, dass Tumore eines Tages damit entfernt werden können. Doch ZIHP-Forscherin Beatrice Beck Schimmer vom Universitätsspital Zürich sieht darin Potenzial.

Chancen und Risiken von Nanomaterialien, NFP 64, 27. April 2015

11th ZIHP Symposium: August 21, 2015

Basic researchers and clinical scientists get together to present and discuss their research in fields related to human physiology. In particular, young researchers will have the opportunity to present their cutting-edge results in oral and poster presentations.

A major part of the presentations is given by students of the → **imMed PhD Program** and originates from ZIHP funded → **cooperative projects**. Cash prizes will be awarded for the best presentation and the best posters.

Don't miss the opportunity for an intensive scientific exchange in a relaxed atmosphere!

→ **Website and program of the symposium**

Deadline for → **registration** is Friday, August 17, 2015.

Events

July 9, 2015 - PhD Thesis Defense
→ **Keep dementia in mind, but forget memory formation: Plasticity of the N-methyl-D-aspartate receptor in erythroid cells and its potential for the treatment of sickle cell anemia**
Pascal Hänggi, Institute of Veterinary Physiology, UZH

July 9, 2015
→ **Nanobodies, versatile tools for research diagnostics and therapy**
Sasa Stefanic, Institute of Parasitology, UZH and Raimund Dutzler, Department of Biochemistry, UZH

July 10, 2015
→ **Is the luminal amino acid transporter BOAT1 regulated by amino acids?**
Julia Jando, Institute of Physiology, UZH

Keynote speakers:
→ **Prof. Sir Peter Ratcliffe, Nuffield Department of Medicine, University of Oxford, U.K.**

Elucidation of oxygen sensing pathways: Implications for physiology and medicine

→ **Prof. Dr. Dr. Thomas Thum, Institute of Molecular and Translational Therapeutic Strategies (IMTTS), Hannover Medical School, Germany**
NoncodingRNAs in cardiac (patho)-physiology

→ **Prof. Dr. Fabrizio Benedetti, National Institute of Neuroscience, University of Turin, Italy**
Drugs and placebos: what's the difference?

→ **Prof. Dr. Florian Lang, Institute of Physiology, University of Tübingen, Germany**
Klotho: Calcium-phosphate metabolism and aging

July 16, 2015 - Vision 2020
→ **Gut microbiota confers protection against malaria**
Miguel Soares, Instituto Gulberkian de Ciência Oeiras, Portugal

July 24, 2015 - PhD Thesis Defense
→ **Regulatory Functions of Sialylated Glycans and Gut Microbiota in Mucosal Immunity**
Yen-Lin Huang, Institute of Physiology, UZH

July 30 - August 1, 2015
→ **Evolutionary Medicine Conference: Interdisciplinary Perspectives on Human Health and Disease**
Institute of Evolutionary Medicine (IEM), UZH

New open PhD positions

→ **Control of metabolism by transporters of essential amino acids**
Institute of Physiology, UZH

→ **Can alpha calcitonin gene-related peptide-(alphaCGRP)-agonism inhibit pathological heart remodelling induced by chronic hypertension?**
Inst. of Veterinary Physiology, UZH

→ **Cardio-metabolic beneficial effects of bariatric surgery**
Inst. of Veterinary Physiology, UZH

→ **Targeting vascularized and hypoxic compartments in solid malignancies: from basic research to dogs with cancer**
Inst. of Veterinary Physiology, UZH

→ **Investigating novel aspects of mitochondrial function in the kidney**
Institute of Anatomy, UZH

→ **Novel oxygen sensing pathways in health and disease**
Institute of Physiology, UZH

→ **The effect of high altitude and erythropoietin on human and rodent red blood cell function and clearance**
Inst. of Veterinary Physiology, UZH

→ **Molecular characterization and investigation of pathomechanisms in methylmalonic aciduria**
Division of Metabolism, University Children's Hospital Zurich

→ **Transport of HDL through endothelial cells**
Institute of Clinical Chemistry, USZ

→ **Role of different aging and lipid metabolism genes in myocardial infarction**
Center for Mol. Cardiology, USZ/UZH

New imMed course

September 14-16, 2015
→ **Muscle plasticity: Molecular biological and cellular mechanisms and its impact in health regulation**
Deadline for registration: August 15, 2015

Recent publications

Brock M, Haider TJ, Vogel J, Gassmann M, Speich R, Trenkmann M, Ulrich S, Kohler M, Huber LC: → **The hypoxia-induced microRNA-130a controls pulmonary smooth muscle cell proliferation by directly targeting CDKN1A.** *Int J Biochem Cell Biol* 61: 129-37, 2015

Burda P, Kuster A, Hjalmarson O, Suormala T, Bürer C, Lutz S, Roussey G, Christa L, Asin-Cayuela J, Kollberg G, Andersson BA, Watkins D, Rosenblatt DS, Fowler B, Holme E, Froese DS, Baumgartner MR: → **Characterization and review of MTHFD1 deficiency: four new patients, cellular delineation and response to folic and folinic acid treatment.** *J Inher Metab Dis* [Epub ahead of print], 2015

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Ernst D, Murphy SM, Sathiyandan K, Wie Y, Othman A, Laurá M, Liu Y, Penno A, Blake J, Donaghy M, Houlden H, Reilly MM, Hornemann T: → **Novel HSN1 Mutation in Serine Palmitoyltransferase Resides at a Putative Phosphorylation Site That Is Involved in Regulating Substrate Specificity.** *Neuromolecular Med* 17(1): 47-57, 2015

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Mathes CM, Bohnenkamp RA, Blonde GD, Letourneau C, Corteville C, Bueter M, Lutz TA, le Roux CW, Spector AC: → **Gastric bypass in rats does not decrease appetitive behavior towards sweet or fatty fluids despite blunting preferential intake of sugar and fat.** *Physiol Behav* 142: 179-88, 2015

Montero D, Diaz-Cañestro C, Lundby C: → **Endurance Training and VO2max: Role of Maximal Cardiac Output and Oxygen Extraction.** *Med Sci Sports Exerc* [Epub ahead of print], 2015

Müller-Edenborn K, Léger K, Glaus Garzon JF, Oertli C, Mirsaidi A, Richards PJ, Rehauer H, Spielmann P, Hoogewijs D, Borsig L, Hottiger MO, Wenger RH: → **Hypoxia attenuates the proinflammatory response in colon cancer cells by regulating IκB.** *Oncotarget* [Epub ahead of print], 2015

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