2015

Book of Abstracts

2015

Nobel Day Festivities

10th of December 2015

Traditionally, on 10th of December, the anniversary of Alfred Nobel's death, is awarded the Nobel Prize in Physiology or Medicine. School of Health and Medical Sciences shows attention to this day by organizing own research activities and festivities.

School of Health & Medical Sciences
School of Medicine
Örebro University
10th of December 2015

Program Committee:
Professors; Nikolaos Venizelos (chair), Allan Sirsjö, Magnus Grenegård and Mats G Karlsson

Book of abstracts, Nobel Day's Festivities 10th of December 2015

Preface

The"**Nobel Day Festivities"** were established 2009 by Biomedicine, Department of Clinical Medicine, School of Health and Medical Sciences at Örebro University, and is organized traditionally every year in order to notice the anniversary of Alfred Nobel's death (10th of December) with scientific activities including poster presentations and selected oral presentations by doctoral students, Postdocs/Researchers, which are documented in this *"Book of abstracts".* Nobel day's activities are open and scheduled so that all students and personnel can attend the scientific activities.

We warmly welcome you to enjoy all the good science that will be presented at Nobel Day 2015

The Organizers

Nikolaos Venizelos, Professor em. (Chair)
Allan Sirsjö, Professor (Biomedicine)
Magnus Grenegård, Professor (Medicine)
Mats G Karlsson, Professor adj. (Medicine)

Digital Rectal Examination for Initial Assessment of the Multi-injured Patient: What's the Point?

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Objective: Digital rectal examination (DRE) is carried out as part of the initial assessment of trauma patients in accordance with the Advanced Trauma Life Support (ATLS®) concept [1]. The theory is to aid early diagnosis of potential lower intestinal, urethral and spinal cord injuries. Previous studies suggest that test characteristics of DRE are unreliable. This study examines the correlation between DRE findings and diagnosis and effects on subsequent trauma management.

Methods: Patients with ICD-10 codes for spinal cord, urethral and lower intestinal injuries were identified from the trauma registry at an urban university hospital between 2007-2011. A retrospective review of electronic medical records was performed to analyse DRE findings and subsequent management.

Results: 253 patients met the inclusion criteria. The mean age was 44 ± 20 years, 75% were male and 90% of injuries were caused from blunt trauma with mean ISS of 26 ± 16. A total of 160 patients had detailed DRE documentation with abnormal findings in 48%. The sensitivity rate was 0.47. Correlational analysis between examination and diagnosis produced a *kappa* value of 0.12. Only 5% of patients were taken directly to the operating theatre, selected exclusively based on clinical deterioration due to hypotension.

Conclusions: DRE in trauma settings has low sensitivity and does not change subsequent management. We therefore suggest it is deferred from the initial assessment of trauma patients. DRE can be performed when the patient has been stabilised at a stage when it does not risk increasing patient agitation and delaying immediate life-saving care.

References:

American College of Surgeons Committee on Trauma Initial Assessment and Management. Advanced Trauma Life Support for Doctors. 7th ed. Chicago: American College of Surgeons, 2004. p. 18–19.

Influence of pre-stroke characteristics in adolescence on stroke severity after first stroke in middle-aged men

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Objective: Stress resilience and other characteristics from late adolescence are associated with subsequent stroke risk[1] but associations with stroke severity among survivors are incompletely described. We investigated this by using hospital admission duration and occurrence of second stroke.

Methods: Some 237 835 males born between 1952 and 1956 were followed from 1987 to 2010 using information from Swedish registers. Cox regression estimated associations with hospital admission duration and second stroke. More severe non-fatal stroke was defined as eight days or more as a hospital inpatient, or a second stroke after 28 days.

Results: A total of 3010 diagnoses of non-fatal stroke between ages 31-58 years were identified. Low stress resilience was statistically significantly associated with longer duration of hospital stay, and with greater risk of second stroke. Adjusted hazard ratios (and 95% confidence intervals) associated with low stress resilience are 1.27(1.01–1.60) for longer hospital admission in ischemic stroke; 1.75(1.20–2.55) in haemorrhagic stroke; and 1.24 (0.97–1.57) for second stroke irrespective of subtype. High BMI, low cognitive function, low physical fitness and elevated blood pressure were also statistically significantly associated with duration of stay and second stroke.

Conclusions: Risks for a more severe stroke prognosis among stroke survivors are already present in adolescence, including low stress resilience. This highlights the potential value of lifestyle interventions even before adulthood. This is relevant to both stroke prevention and also reduction of severity among those who have a stroke.

Reference

Bergh C, Udumyan R, Fall K, Appelros P, Montgomery S. ***(2014).*** *Stress resilience in adolescence and subsequent stroke risk: Cohort study****. J Neurol Neurosurg Psychiatry. 85(12):1331-6.***

Maternal and Neonatal Death Review System to Improve Maternal and Neonatal Health Care Services in Bangladesh

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Objectives: To look at the development of the system, implementation and evaluate the Maternal and Neonatal Death Review (MNDR) system in Bangladesh.

Methods: Both qualitative and quantitative methods. Quantitative data was collected from the MNDR database. Whereas, qualitative data was collected used different data collection techniques included In-depth interviews, focus group discussions, group discussions, participant's observations and document reviews.

Results: Using existing government infrastructure and resources, Maternal and Neonatal Death Review (MNDR) was found to be feasible/implementable in Bangladesh. The system was found to be well accepted by the health managers and health workers of the Directorate General of Health Services (DGHS) and Directorate General of Family Planning (DGFP). The system enables an excellent partnership between government and development partners, including non-government organizations. Death mapping in MNDR, has been utilized in the study for improvement of overall health services in the community in one of the sub-district, thus helped to reduce the maternal and neonatal deaths. Verbal and social autopsy of maternal, neonatal deaths and stillbirths helps to identify medical and social causes. Facility death review in MNDR explores causes, gaps and challenges in the facilities to improve quality of care.

Conclusions: MNDR in Bangladesh has created evidence for the establishment of a comprehensive MNDR package for Bangladesh that reflects vital death registration, identifies under-reported deaths, and covers a wide spectrum of deaths, including maternal and neonatal deaths and stillbirths, at both community and facility level. MNDR research in Bangladesh has every scope for use in countries with similar settings to meet the sustainable developmental goal by 2030.

Translation and linguistic validation of self-administered Swedish version of WHODAS 2.0

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Objective: To translate the self-administered 36-item version of WHODAS 2.0 into Swedish and examine the understanding and interpretation of the instruments´ content and response processes.

Methods: Translation process was made following WHO guidelines (1) and the WHODAS 2.0 translation package (version 1.0) including; forward-translation, expert panel discussion, back-translation, pre-test of preliminary version, and final version. Pre-test was conducted through cognitive and structured interviews in a purposeful sample of 13 Swedish speaking adults. Interview protocols were analyzed item by item in comparison with the original manual of WHODAS 2.0 (2).

Results: Forward-translation, expert panel discussion, and back-translation resulted in a preliminary Swedish version of WHODAS 2.0. Pre-test revealed some issues related to items in the Participation in society domain, and in the overall lay-out. This resulted in minor changes in selection of words in the final version and suggestions for further revision of the instrument.

Conclusions: The self-administered, 36-item Swedish version of WHODAS 2.0 is easy to understand and respond to, in general. Further linguistic validation of the final version in people with disability remains to be completed before it can be recommended for use in patients. Studies are also needed to provide evidence for other aspects of validity.

References:

1. *World Health Organization (2006). Process of translation and adaptation of instruments. [cited Available from: http://wwwwhoint/substance_abuse/research_tools/translation/en/printhtml.]*
2. *Üstün TB, Kostanjsek N, Chatterji S, Rehm J (2010). Measuring health and disability: manual for WHO Disability Assessment Schedule WHODAS 2.0. Geneva: World Health Organization.*

The Cure rate in first line treatment of Graves' disease in Sweden 7-9 years after diagnosis

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Introduction: The incidence of hyperthyroidism was 27.1/100000 inhabitants (children included) / year in a prospective study 2003-2005 with a catch up area of 40% of the Swedish population of 9 million inhabitants. 2916 patients were included and this cohort has been studied 7 – 9 years after the diagnosis with the intent to evaluate the long-term outcome. Sweden is considered iodine sufficient.

Methods: 2916 patients were included in the original cohort (see figure 1:1). After 7-9 years from diagnosis 2451 were contacted for follow-up by questionnaires, Fifty-nine percent (1466 patients) agreed to participate.
Patients answered three questionnaires at home and returned them by mail. There were two quality of life questionnaires (SF-36 and Thy-Pro) and one which gave information about recurrence of hyperthyroidism, final treatment regime, symptoms and treatment of TAO, smoking habits and comorbidity.

Results: 1437/1466 patients have been evaluated where 75.3% had Graves' disease and 24.7% had Toxic Multinodular Goitre. The cure rate in first line treatment among Graves´patients were 44.5% with antithyroid drugs, 68.4% with radio iodine and 96.2% with operation.

Conclusion: In this prospective study 615/1173 (52%) patients with Graves' disease were cured with one initial treatment period, ranging from 43% for ATD in smokers to 96% with surgery in non-smokers. The 629 individuals that did not respond the questionnaires will be studied to exclude recruitment bias.

Work and health in persons with Usher syndrome type 2

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Endothelial function and physical activity in young adults

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Objective: Impairment of vascular endothelial function is an early sign of atherosclerosis. An active lifestyle is suggested to be positively associated with favorable endothelial function as opposed to a sedentary lifestyle.
The aim of this ongoing study (*Lifestyle, Biomarkers and Atherosclerosis Study*) is to investigate associations between vascular endothelial function and physical activity level in 1000 non-smokers without know disease aged 18-25 years. Preliminary data from the 317 first subjects with complete data will be reported here.

Methods: Flow-mediated dilation was assessed in *a. brachialis* by high-resolution ultrasound (Vivid e9) before and after 5-minutes occlusion, and time spent active (at moderate or vigorous intensity level) or sedentary was assessed by accelerometry (ActiGraph wGT3X-BT).

Results:

	Females n=226	Males n=91	Gender differences (*P*-value)
Age	21,8	21,8	1,00
BMI	22,4	22,9	0,14
Body fat (%)	27,8	15,0	<0,001
Time spent active (min/day)	45	45	0,99
Time spent sedentary (min/day)	514	524	0,32
Flow Mediated Dilatation measures			
Diameter, pre-stas (mm)	3,16	3,74	<0,001
Increase, post-stas (mm)	0,28	0,28	0,96
Increase, post-stas (%)	8,9	7,5	<0,001

Multiple regression analyses show that time spent active is statistically associated with diameter increase (mm) and percentage increase (adjusted for pre-stas diameter) in females (beta coefficient = 0,144; p=0,032 and beta-coefficient=0,135; p= 0,041, respectively) but not in males. Time spent sedentary did not show any associations with the flow-mediated dilatation variables in neither females nor males.

Conclusion: Already in young adulthood, an active lifestyle is associated with higher flow-mediated dilatation as a measure of endothelial function.

Live with your body - Acceptance and Commitment Therapy to increase body acceptance in patients with eating disorders

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Objective: A poor body image is common in eating disorder (ED) patients, often complicates treatment, and is associated with ED relapse. This poster presents data from an RCT conducted at a specialized ED clinic in Sweden. The trial compares a group intervention based on Acceptance and Commitment Therapy (ACT) focusing on improving body image to treatment as usual (TAU) in ED patients. The intervention is based on a manual following an ACT self-help book (Ghaderi & Parling, 2009), containing 12 group sessions following the steps in the book. The present poster present participants' view on whether their body image changed due to treatment, and if so how.

Methods: 100 patients were randomized, of whom 53 to ACT. Data in this poster is based on written evaluations from 43 participants after completion of the ACT intervention. Their answers were analyzed through content analysis.

Results: Results will be presented as quotes from the participants evaluations
Conclusions: Many of the participants described a change in their relationship with their bodies after treatment. They did not necessarily like their bodies better, but they had more acceptance of negative thoughts and feelings and would act in presence of them. They tended to describe how other areas in life were more important than preoccupation with thoughts and feelings regarding their body image. We interpret the results as the core principles in ACT seem to be a potent treatment for body image problems, and further studies are needed.

References:

Ghaderi, A. & Parling, T. (2009) Lev med din kropp: Om acceptans och självkänsla. Natur & Kultur, Stockholm.

Understanding avoidance and non-attendance among adolescents in dental care - an integrative review

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Objective: The aim of this study was to review articles exploring manifestations of avoidance of dental care, or non-attendance to dental appointments, to identify background and concomitant factors specifically associated with dental avoidance among adolescents (13–19 years old).

Methods: PubMed, CINAHL and PsychINFO were searched using MeSH terms and keywords covering dental avoidance, non-attendance and non-utilization. Searches were limited to peer-reviewed studies in English, published in 1994–2014, in populations aged 13-19 years. Twenty-one research articles were included. Data were extracted, ordered, coded, categorized, and summarized according to the integrative review method.

Results: Outcomes were classified as either dental avoidance or dental non-attendance/non-utilization. Identified background and concomitant factors associated with dental avoidance and/or non-attendance/non-utilization formed three common major themes: *Environmental*, *Individual* and *Situational factors*. Only seven studies, all from Sweden or Norway, where dental care is free for children and adolescents, investigated factors associated with dental avoidance. For the remaining 14 studies, the geographic spread was wide. Regarding avoidance, the main focus was found to be on individual and situational factors, while environmental factors were more investigated for the outcome non-attendance/non-utilization.

Conclusions: To understand avoidance or non-attendance of dental care among adolescents, attention must be paid to a wide variety of circumstances. In a context of free dental care, there is a need for further research on the possible impact of modern life-styles, as well as psycho-social and cultural factors.

**This paper is submitted in Community Dental Health*

Specific non-digestible polysaccharides attenuate mast cell induced hyperpermeability in colonic biopsies mounted in Ussing chambers

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Objective: It is widely known that diseases such as inflammatory bowel disease and celiac disease are associated with a leaky gut, highlighting the importance of a healthy barrier function. Prebiotic substances such as non-digestible polysaccharides (NPS) have been shown to be able to improve immune function but their effect on the barrier function remains unknown. Our aim is to investigate the efficacy of specific NPS to counteract barrier disruption mediated through mast cell degranulation in colonic biopsies.

Method: The effect of NPS on intestinal hyperpermeability was investigated in colonic biopsies obtained from 10-14 healthy volunteers and in on going experiments with elderly seniors (65 years above, N=7) suffering from constipation and/or diarrhoea. Twelve colonic biopsies per participant were mounted in Ussing chambers. The biopsies were pre-treated with NPS, either 0.5 mg/ml β-glucan derived from yeast or 0.1 mg/ml Arabinoxylan derived from wheat for 20 minutes prior to addition of the mast cell degranulating compound 48/80 (10 ng/ml). All substances were present throughout the whole experiment (90 min). Non-treated biopsies were used as control. FITC-dextran 4000 was used to measure paracellular permeability while horseradish peroxidase (HRP) was used as a transcellular marker.

Results: Intervention with C48/80 showed a significant increase of 2-3 times higher para - and transcellular permeability compared to controls. Pre-treatment with 0.1 mg/ml Arabinoxylan (N=13-14) resulted in a significant reduction of C48/80's effect on paracellular – and transcellular permeability ($p=0.04$ and $p=0.03$ respectively), in healthy volunteers. Pre-treatment with 0.5 mg/ml β-glucan (N=10-11) showed no statistical difference compared to C48/80 treated biopsies in healthy volunteers. Experiments performed on senior participants (N=7) showed a significant increase in both para – and transcellular permeability induced by C48/80 but none of the NPS showed a statistical significant reduction of the increased permeability.

Conclusion: Our results demonstrate that Arabinoxylan (0.1 mg/ml) can reduce C48/80 induced hyperpermeability in healthy volunteers. More experiments with senior participants are needed and underway to demonstrate whether any of the NPS can reduce C48/80 induced hyperpermeability.

An International Expert Survey on Functioning, Disability and Contextual Factors of Adults with Hearing Loss using the International Classification of Functioning, Disability and Health (ICF)

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Background: The World Health Organization (WHO) classification *International Classification of functioning, disability and health (ICF)* have gained considerable attention since its adoption in 2001. To facilitate the clinical use of the ICF, the WHO has initiated Core Sets projects targeting specific health conditions. Core sets aims at determine the most relevant ICF categories for a specific health condition based on scientific evidence. The ICF Core Sets for Hearing Loss project aims at developing core sets targeting adults with hearing loss. The present study concerns one study in the project, the expert perspective.

Objectives: to identify relevant aspects of functioning, disability and contextual factors of adults with hearing loss from the perspective of hearing health professionals (experts) and to link these aspects to the International Classification of functioning, disability and health (ICF) classification.

Method: An internet- based cross sectional survey was conducted using a stratified sampling procedure among hearing health professionals worldwide. By a simplified content analysis the results were linked to ICF categories.

Results and conclusions: 106 ICF categories were mentioned by 5% or more of the respondents. The experts emphasized interaction dimensions, the physical environment and certain internal factors such as confidence as highly influential functioning.

References:

Granberg, S., Swanepoel, DW., Englund, U., Möller, C., & Danermark, B. (2014).The ICF Core sets for hearing loss project: International expert survey on functioning and disability of adults with hearing loss using the international classification of functioning, disability, and health (ICF). International Journal of Audiology, 53, 497-506.

Impact of IL-37 on Regulation of Chemokine Expression in Colon Epithelial Cells Using the CRISPR/Cas9 System

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Microscopic colitis (MC), comprising collagenous colitis (CC) and lymphocytic colitis (LC), is characterized clinically by chronic watery diarrhea, abdominal pain, and weight loss. IL-37 (IL-1F7) is a newly described anti-inflammatory cytokine of the IL-1 family. Previously, reduced gene expression of IL-37 has been observed by our group in the colonic mucosa of MC patients, which was suggested as one of the reasons for the chronicity of the colonic inflammation.
We here investigated the role of IL-37 on pro-inflammatory cytokine responses mediated by TLR5 signaling pathways in the T84 cell line upon stimulation with flagellin following reduction of IL-37 with the CRISPR/Cas9 system.

Gene and protein expressions of IL-37, CCL2, 3, 4, 5, 20, 22, CXCL8, 11 and CX_3CL1 were detected using qRT-PCR and ELISA or Luminex. Reduced IL-37 levels led to increased gene and protein expressions of CCL2, CCL5, and CXCL11 upon TLR5 stimulation. We also detected highly increased CCL3, CCL20, and CX3CL1 in the presence of reduced amounts of IL-37 upon TLR5 stimulation. On the other hand, reduced IL-37 protein levels led to decreased gene and protein expressions of CCL4, CCL22, and CXCL8 after TLR5 stimulation.

Altogether, these results may help to highlight the immunopathogenesis of MC, and explain the consequences of reduced gene expression of anti-inflammatory IL-37 in colonic biopsies from MC patients as previously reported by us.

T cell receptor Beta (TCR-β) Repertoire in Colon of Patients with Microscopic and Ulcerative Colitis Patients Analyzed by Next Generation Sequencing

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Microscopic colitis (MC), comprising collagenous colitis (CC) and lymphocytic colitis (LC), is characterized clinically by chronic watery diarrhea, abdominal pain, and weight loss. The ability of the adaptive immune system to respond to a variety of foreign antigens is dependent on the repertoire of the T cell receptors (TCRs) consisting of either an αβ or a γδ heterodimer.

The TCR antigen specificity and diversity are mainly determined by the third complementarity-determining region (CDR3) of the TCR-β chain formed by rearrangement of the variable (V), diversity (D), and joining (J) gene segments during early lymphoid differentiation in the thymus. In response to an antigenic challenge T cells undergo extensive clonal expansion that results in a highly efficient antigen-specific immune responses.

Analysis of the TCR diversity was performed using next generation sequencing from whole biopsies of patients with MC, ulcerative colitis (UC) and non-inflamed controls. The data were analyzed using sparse partial least squares regression (sPLS) to find clones discriminating disease groups from controls or remission patients.

The most important TRBV-J combinations in which CC patients were significantly different from CC patients histopathologically in remission (CC-HR) were TRBV10-2-J2-6 and TRBV12-5-J1-1. UC patients can be significantly discriminated from controls by TRBV24-J1-2, TRBV4-3-J2-2, and TRBV10-2-J1-4, whereas UC-R patients revealed TRBV28-J1-4, TRBV10-3-J1-1, and TRBV10-2-J1-4.

These results are important to understand TCR-β clone specific response in MC patients, in which T cell infiltrations play an important role. Moreover, these TCR-β clones could be possible therapeutic candidates to investigate T cell filtration.

Faecal microbiota transplantation in patients with Irritable Bowel Syndrome – a methodology poster

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Disaster radio; a tool to promote recovery among survivors after a natural disaster

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Objectives: The context of a natural disaster includes a severely damaged infrastructure and a large number affected people. After the Haiyan typhoon that hit the Philippines in November 2013, disaster radio was used to disseminate information and music to the affected population[1]. This study[2] describes survivors' experiences of the immediate aftermath of a natural disaster and the impact disaster radio made on recovery from the perspectives of the individuals affected.

Method: A qualitative design using phenomenological hermeneutical method was used. Twenty-eight survivors between 19-84 years old were interviewed in focus groups and individual interviews, five months after the disaster.

Results: *Being in survival mode* included several experienced needs. Disaster radio supported recovery by providing information that created a sense of control and helped the survivors to adapt to the situation. Also, the music played contributed to emotional endurance and instilled hope.

Conclusion: Disaster radio contributed positively to recovery among disaster survivors. Both information and music was important for the experienced recovery. Other interventions are needed to re-establish social relations. Further studies on the use and effects of disaster radio in a health perspective are suggested.

References:

1. *Hugelius K, Gifford, M, Örtenwall, P, Adolfsson, A (2015). Disaster Radio for Communication of Vital messages and Health-related Information; analysis from the Haiyan typhoon, The Philippines. (Accepted July 2015).*
2. *Hugelius K, Gifford, M, Örtenwall, P, Adolfsson, A (2015). "To silence the deafening silence"; survivors´ needs and experiences of the impact of disaster radio for their recovery after a natural disaster. (Under review)*

LOS-dependent *Neisseria meningitidis*-induced activation of inflammasome in human neutrophils

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Lipooligosaccharide (LOS) of *Neisseria meningitidis* is an endotoxin that is responsible for activation of immune cells and the release of pro-inflammatory cytokines. Inflammasomes are intracellular multi-protein complexes that trigger caspase-1 mediated maturation of interleukin-1β. The NLRP3 inflammasome; the best characterized of all inflammasomes, is activated by a number of microbial factors as well as danger molecules, but there are no data available regarding a role for inflammasome activation in meningococcal disease.
The aim of this study was to investigate if *N. meningitidis* activates the inflammasome and if so, the role of bacterial LOS in this activation.
Neutrophils were subjected to LOS-deficient *N. meningitidis* (*lpxA* mutant) and wild-type FAM20 bacteria.

NLRP3 and *pro-IL-1β* expression was significantly increased in neutrophils stimulated with both wild-type strain and *lpxA* mutant indicating that LOS is not crucial for priming of the cells. Caspase-1 activity was significantly increased in neutrophils stimulated with wild-type strain, whereas the *lpxA* mutant was unable to induce any caspase-1 activity. To determine the involvement of TLR-mediated signalling, we utilised MyD88-/-THP1 cells. We found substantial increase in mRNA levels of *pro-IL-1β* and *NLRP3* in THP1 cells stimulated with wild-type strain and *lpxA* mutant, whereas MyD88-deficient cells were not activated by either strain.

We conclude that although non-LOS components of *N. meningitidis* contribute to the priming step of inflammasome via TLR2/MD2/MyD88-pathway resulting in the up-regulation of inflammasome components this study shows for the first time that it is LOS of *N. meningitidis* that adds the final touch to the decisive licensing steps of composition and activation of the inflammasome.

Plaque to Plaque: Innate responses in THP-1 cells induced by *Porphyromonas gingivalis*

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Objective: *Porphyromonas gingivalis (P. gingivalis)* is a gram negative anaerobe, indicated as the 'keystone pathogen' in dental plaque and chronic periodontitis (1). *P. gingvalis* DNA has been isolated from atherosclerotic plaques. Besides, periodontal pathogens have further been implicated to have a distal site impact, with the vasculature being the choice portal of systemic dissemination. Here in this study, we focus on *P. gingivalis* -induced vascular inflammation, elaborating on *P. gingivalis* interaction with THP-1 cells, a known monocyte surrogate widely used in *invitro* medical research.

Methods: We have analyzed the gene expression of surface and cytosolic pathogen sensors such as protease-activated receptors (PARs), toll-like receptors (TLRs) and NOD1/2, using quantitative real-time PCR (qPCR) at 6 and 24 hours. We also performed an in depth analysis of NF-kB and MAPKinase involvement in release of pro-inflammatory mediators such as IL-1β and CXCL8, using PKC, p38, ERK and NF-kB inhibitors. The results were validated using primary human monocytes.

Results: *P.gingivalis* up-regulated the receptor expression of PARs 1, 2, 3; TLRs 1, 2, 4, and NOD 2. Inhibition of PKC, p38 and ERK resulted in partial but significantly down-regulated release of IL-1β and CXCL8. However, inhibition of NF-kB completely suppressed the release of the cytokines to basal levels. *P. gingivalis* did not affect cell viability and also induced similar responses in primary monocytes.

Conclusions: *P. gingivalis* primarily signals via PKC, ERK and NF-kB in THP-1 cells. Results indicate that THP-1 cells are a good monocyte surrogate.

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IL6/IL6R induce slow and sustained tyrosine phosphorylation of STAT3 in human platelet mitochondria

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Introduction: Platelets are non-nucleated cells that play crucial roles in hemostasis and thrombosis. Platelets also contribute to acute inflammation by releasing a number of cytokines and chemokines. Conversely, several inflammation mediators act on surface receptors and modulate platelet functional responses. The transcription factor STAT3 is a key downstream signaling molecule of interleukin IL6-activated cells. Herein, we characterized the molecular and cellular effects of IL6 on human blood platelets with particular emphasis on STAT3. As platelets lack nucleus, they may represent an excellent cellular model to study non-genomic actions of STAT3.

Methods: Human platelets isolated from healthy volunteers were exposed to IL6 in the presence or absence of the soluble IL6 receptor (IL6R). Platelet aggregation and ATP secretion was monitored by using a lumino-aggregometer. Expression and release of IL6R were analyzed using a commercial ELISA kit. Phosphorylation of STAT3 at Tyr705 and Ser727 residues was analyzed using Western Blot and Ca^{2+}mobilization was analyzed by using the fura-2 technique. Mitochondria's were isolated using a commercial kit.

Results: Exposure of human platelet to IL6, soluble IL6R (sIL6R) and the combination of the two did not influence on platelet aggregation, dense granule secretion and Ca^{2+} mobilization. However, it was found that platelets expressed a releasable fraction of sIL6R. Furthermore, IL6 alone induced a minor phosphorylation of STAT3 at Tyr705 residue whereas sIL6R alone had no effect. Combined treatment of platelets with IL6/sIL6R induced a pronounced and long-lasting Tyr705 phosphorylation of STAT3. Finally, tyrosine phosphorylated STAT3 was detected within the mitochondria of platelets.

Conclusion: IL6/sIL6R-induced STAT3 phosphorylation was not accompanied by classical platelet functions like aggregation and secretion. Instead, STAT3 may participate in the regulation of platelet mitochondrial genome transcription, energy metabolism or other manifestations related to mitochondrial functions.

Activities of daily living, cognitive function, risk for pressure sores, malnutrition and falls in elderly patients readmitted to medical acute care.

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Objective: The aim is to describe activities of daily living (ADL), cognitive function but also the risk for pressure sores, malnutrition and falls. Furthermore, to compare ADL, risk for pressure sores, malnutrition and falls in this group of older people, readmitted to hospital.

Methods: This was a comparative study. Persons ≥75 years, who were readmitted to hospital, were assessed by an occupational therapist using the ADL-taxonomy and the Mini Mental State Examination. Risks for pressure sores, malnutrition and falls were assessed using Risk Assessment Pressure Sores, Short-Form Mini Nutritional Assessment, and Downton Fall Risk Index. Data for comparison for ADL was obtained from an earlier study and risk assessments from a national quality register.

Results: 60 persons were included, median age was 84 years. The patients had a median of 4 diagnoses. Mean hospital stay was 5 days. Most patients were independent in food intake. There was a high degree of dependency in other ADL activities. Nineteen of 48 patients had 24 point or lower in MMSE. Compared to an age-matched sample, these patients showed a higher risk for pressure sores, risk for falls and dependency in ADL.

Conclusion: There is a need for assessments of ADL, cognition, risk for falls, and pressure sores in older people who are readmitted to hospitals. Such assessments, and necessary interventions taken, may prevent unnecessary admissions.

Fucoidan mimetic glycopolymers induce full platelet aggregation

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Ancient musical schooling

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Objectives: How do schooling fish or flocks of birds manage to maintain appropriate distance and avoid collisions? In contrast with visual perception, the role of auditory perception in synchronizing movement is largely unknown. We present a hypothesis that acoustic perception contributes significantly to synchronized animal behavior, and moreover that acoustic benefits from this synchronization contributed to the evolution of social behavior in vertebrates, including human musicality.

Methods: Literature review and theoretical models.

Results: Song-learning birds and humans share independently evolved similarities in brain pathways for vocal learning. Similarities in multiple genes indicate that brain circuits for such complex traits may have been inherited from a common ancestor. Evolutionary links have been proposed between synchronized behavior (entrainment) and vocal learning, but putative mechanisms remain unclear. We hypothesize that acoustic perception related with locomotion and breathing in fish influenced the evolution of synchronized behavior in vertebrate descendants. Theoretical models suggest that fish' synchronized behavior results in predator confusion due to overlapping and complex *incidental sound of locomotion* (ISOL) and improved perception because of synchronized silence. Analogously at the individual level, an animal's locomotor-respiratory coupling synchronizes sound increases windows of silence and may communicate important spatial and temporal information to other school-members, possibly reinforcing synchronization.

Conclusions: Since vocalization is largely associated with breathing, acoustical benefits due to locomotor-respiratory coupling in fish may have stimulated an evolutionary link between locomotion and vocal communication. Species that travel in highly synchronized groups in homogenous substrates will be regularly exposed to oscillating, predictable ISOL. In theory that sound could serve a signaling function improving motor or vocal synch. It may be a process of mutual reinforcement, with increasingly distinct ISOL improving synchronization and vice versa. Acoustic benefits due to synchronized movements may have stimulated the evolution of entrainment to external auditory cues, paving the way for the development of vocal learning.

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The evolution of right handedness – the heart protection hypothesis

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Objective: Almost 90% of humans are right handed. Similar hand-preferences are not present in other primates. The hypothesis here is asymmetry of the torso resulted in selective advantage for right-handers. In combat, handedness may influence the level of exposure of the left hemi-thorax, as holding a weapon in a unilateral grip will determine which area of the thorax is most exposed to an enemy's attack. The use of the left hand will rotate the left side towards the opponent, increasing the exposure of the left hemi-thorax.

Methods: The human heart location was investigated by computer tomography (CT). Thirty-seven CT-scans of men 45-65 y, who had been examined for clinical reasons, were randomly selected. The area of the heart was calculated at the level of the visually widest point, *the widest heart area* was subdivided into the *right thorax heart area* (RTHA) and the *left thorax heart area (LTHA)* and the ratio *RTHA:RTLA* was calculated.
Nineteen physicians estimated the likely outcome of a wound penetrating the trunk at a random point in a society without modern medical care.

Results: A larger fraction of the heart was situated left of midline; mean *RTHA:RTLA*=0.38 (SD 0.14). Early ancestors with a preference for using the right forelimb in combat may therefore have had reduced risk wounding the heart. This increase in risk of left handers might be counteracted if abdominal injuries to the right resulted in increased mortality compared to injuries of the left abdomen. Therefore, the differential risk of injury from a sharp implement attack to the left and the right human *trunk* was estimated: One physician suggested right trunk injury, ten estimated left side injury to cause higher mortality, while eight estimated equal mortality (p=0.008). The mean estimated mortality for trunk injuries was 72% for the left side and 66% for the right side.

Conclusions: Increased vulnerability in combat among left handers may have been sufficient to confer a selective advantage to right handedness and have contributed to the development of right-forelimb preference.

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Steps in the origins of music

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Objectives: Walking side-by-side, people often subconsciously synchronize steps. Why? Walking typically creates noise, which may mask sound signals from the surroundings. Three hypotheses are raised: (1) Human locomotion and ventilation can mask critical sounds in the environment. (2) Synchronization of locomotion reduces that problem. (3) Bipedal gait and the associated sounds of locomotion influenced the evolution of human rhythmic abilities.

Methods: We investigated the potential of sound created by walking to mask perception of speech and compared masking produced by walking in step with that produced by unsynchronized walking. The masking sound (footsteps on gravel) and the target sound (speech) were presented to fifteen normal-hearing subjects. The walking sound was modified to mimic the sound of two individuals walking in pace or walking out of synchrony. The participants were instructed to adjust the sound level of the target sound until they could just comprehend the speech signal (JFC) when presented simultaneously with synchronized or unsynchronized walking sound.

Results: Synchronized walking sounds produced slightly less masking of speech than unsynchronized sound. The median JFC threshold in the synchronized condition was 38.5 dBA, while the corresponding value for the unsynchronized condition was 41.2 dBA.

Conclusions: Synchronized walking reduces masking, and may improve perception by providing periods of relative silence and by facilitating auditory processing. The adaptive value of early ancestors may have been keener detection of prey or stalkers. A sense of rhythm could aid the brain in distinguishing among sounds arising from discrete sources and also help individuals to synchronize their movements with one another. Human locomotion is likely to produce more predictable sounds than those of non-human primates. Predictable locomotion sounds may have improved our capacity of entrainment to external rhythms and to feel the beat in music. Bipedal walking may have influenced the development of entrainment in humans and thereby the evolution of rhythmic abilities.

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The evolution of vertebrate visual systems - the *eye-forelimb hypothesis* is more parsimonious than the traditional *stereopsis hypothesis*

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Objective: Ipsilateral retinal projections (IRP) in the optic chiasm (OC) vary considerably. Most animal groups possess laterally situated eyes and no or few IRP, while e.g. cats and primates have frontal eyes and high proportions of IRP. The traditional hypothesis is that bifocal vision and IRP developed to allow *Stereopsis*. In contrast, *the eye-forelimb (EF)-hypothesis* suggests that the reception of visual feedback of limb movements in the limb-steering hemisphere was the fundamental mechanism; i.e. evolutionary change in the OC was necessary to preserve hemispheric autonomy.

Methods: Comparative analyses of mammalian and non-mammalian associations among IRP, eye convergence, and visual guidance of the limbs.

Results: Motor processing, and inflow of tactile, proprioceptive, and visual information involved in steering of the hand/limb/paw/fin primarily engage the contralateral hemisphere; multisensory information from the ipsilateral limb is minimal. Since the involved motor nuclei, somatosensory areas, and vision neurons are situated in same hemisphere, the neuronal pathways involved will be relatively short, optimizing the size of the brain. That would not have been possible without, evolutionary modifications of IRP. Multiple axon-guidance genes, which determine whether axons will cross the midline or not, have shaped the OC anatomy.

Conclusions: Evolutionary change in the OC seems to be key to preserving hemispheric autonomy when the body and eye evolve to fit new ecological niches. The EF hypothesis may explain the low proportion of IRP in birds, reptiles, and most fishes; the relatively high proportions of IRP in limbless vertebrates; high proportions of IRP in arboreal, in contrast to ground-dwelling, marsupials; the lack of IRP in dolphins; abundant IRP in primates and most predatory mammals, and why IRP emanate exclusively from the temporal retina. *The EF hypothesis* is applicable to vertebrates in general and considerably more parsimonious than the traditional *Stereopsis*-hypothesis.

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Basic body awareness therapy in stroke rehabilitation: effect and experiences among patients and physiotherapists

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Background: After stroke a decreased balance and limitations in mobility is common. Basic body awareness therapy (BBAT) is method that challenge the individual`s stability limits. The purposes of the two parallel studies were, 1) to investigate the effect of physiotherapist (PT)-led BBAT for patients with stroke and, - 2) to describe the experiences from the perspective of both patients and PT.

Methods: A RCT was conducted with the intervention BBAT in group for 8 weeks. Outcome measures were tests of walking and balance. Follow-up tests were conducted at week 9 and week 14. At week 9, qualitative interviews were also conducted with the PT´s and the patients in the intervention group. The interviews were analyzed using qualitative content analysis.

Results: Forty-six patients were included; 24 randomized to intervention and 22 to control (27 men and 19 women, mean age 64 years). Between groups there was no significant difference over time. Significant differences within the intervention group were found for the measures Berg Balance Scale, Timed up and Go cognitive and 6-minute walk test, and within the control group for Timed Up and Go cognitive and Timed-stands test. The analysis of the interviews revealed one overall theme, "Simple, yet challenging" which illustrates that the basic body awareness therapy in many aspects was regarded as challenging, although the exercises in themselves were small and simple. **Conclusion**: The results suggest that BBAT with simple repetitive movements could be a complementary method in stroke-rehabilitation. Most patients appreciated the simplicity and accepted the challenge with BBAT.

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Gene expression profile of fibroblasts from patients with bipolar disorders reveals alterations in genes and pathways related to amino acid transport.

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Introduction: Bipolar Disorder is a severe, lifelong psychiatric disease characterized by abnormally elevated mood (mania) that cycle with abnormally low mood (depression). Studying such diseases with gene expression microarray experiments we emphasize on broad, biological themes, rather than on specific genes. In this direction comparative transcriptomic profiling to characterize skin fibroblasts gene expression of bipolar disorder patients compared to healthy controls has been performed.

Methods: Skin fibroblast cells from bipolar disorder patients (n=10) and healthy controls (n=5) have been cultured. RNA was extracted and then hybridized onto Illumina Human HT-12 v4 Expression BeadChips.
Differentially expressed genes between disease and control groups were identified by performing t-test. Fold change values were calculated for each gene. The resulting gene list was obtained by setting the p-value threshold to 0.05 and by removing genes that presented a fold change below |0.5| (in log2 scale). A subset of the differentially expressed transcripts that occurred was validated by quantitative real-time PCR. The lists of significant genes were subjected to pathway analysis and target prioritization.

Results: We concluded to 457 differentially expressed genes. Various genes and pathways have been found to be involved in amino acid transport mechanisms such as taurine and alanine transporter SLC6A6, the cationic amino acid transporter SLC7A1 the phospholipase A2 receptor PLAR2, the tyrosine and tryptophan metabolic pathways, ATPase activity and fatty acid metabolism.

Conclusion: These findings may explain the alterations observed in tyrosine transport mechanisms observed in bipolar type-1 disorder at the membrane level, implying further a limited access of tyrosine in the brain that could lead to alterations in neurotransmitter systems.

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Patients experiences of opportunities and barriers for successful return to work after acquired brain injury

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Objective: The aim of this study was to describe opportunities and barriers for successful return to work (RTW) among individuals with acquired brain injury (ABI).

Method: Five females and five males with ABI between 41 and 54 were interviewed in regard to their experiences of the work rehabilitation process. They had completed the rehabilitation and had successfully returned to work. All of them had worked at least 20 hours a week in at least one year after the injury. The interviews were transcribed, structured and analyzed by latent content analysis.

Result: Three main themes that influenced RTW after ABI were identified: (i) individually adapted rehabilitation process, (ii) motivation for RTW and (iii) cognitive abilities and inabilities.
The findings indicated that an individually adapted vocational rehabilitation (VR) process was important because the individuals with ABI could be involved in their own rehabilitation process and they required continuous individual support from the society, the specialists, their employers and colleagues. A moderate level of motivation for RTW was necessary to achieve the best result for RTW and the balance between too high and too low motivation was important. Finally, a comprehensive knowledge about the cognitive abilities and inabilities of the individual after ABI helped the individuals and their employers to find compensatory strategies to handle their work tasks. One implication of the findings was the necessity of a good support system and a good VR that functions well then it could last for a long time.

Conclusion: Consequently the support built for a person individually, with a balanced motivation, a high knowledge about the cognitive abilities and awareness of how to proceed further in the process will help to build a successful and sustainable RTW.

IL-17A and IL-6 synergies to induce GRO-α secretion in human endothelial cells

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IL-17 cytokines, a family of six structurally related isoforms (IL-17A through IL-17F, IL-17A/F heterodimer), have been linked to chronic inflammatory diseases including atherosclerosis. Previous animal and clinical studies showed associations between IL-17 cytokines and release of pro-inflammatory chemokines. Animal studies have also shown an amplification of inflammatory response after simultaneous exposure to IL-17 and IL-6. However, most previous studies focused on IL-17A thus little is known about functions of the other isoforms. In addition, impact of these cytokines on endothelial cells is not well characterized. Since all the isoforms have significant degree of amino acid homology (up to 50%) to IL-17A, we hypothesize that the other isoforms could have similar pro-inflammatory roles as well. Hence, we treated HUVECs with IL-17 isoforms, IL-6 and its soluble receptor (IL-6R) and investigate pro-inflammatory changes both at gene and protein level using qPCR and ELISA respectively.

We show that IL-17A and IL-17A/F induces release of GRO-α in a dose dependent manner though IL-17A is more potent than IL-17A/F. The remaining isoforms fail to induce GRO-α release and, all isoforms fail to induce release of IL-8 and IL-6. We detect an amplified effect in GRO-α induction both at gene and protein levels when IL-17A is combined with IL-6 and IL-6R. Further, knockdown of the IL-6 gene reduces induction of GRO-α release by IL-17A. We also find out that stimulation of endothelial cells with IL-17A combined with IL-6R alone tends to increase release of GRO-α.

Taken together, our data suggest that IL-17A and IL-17A/F induce release of the pro-inflammatory chemokine GRO-α. This effect seems to be partly mediated by IL-6. IL-6R also amplifies the IL-17-induced release of GRO-α.

Positive Serum Ethanol in severe Traumatic Brain Injury is Associated with Better Long-term Functional outcome

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Objective: Several retrospective clinical studies have noted an association between positive blood alcohol level (BAL) and improved survival in patients suffering from moderate to severe traumatic brain injury (TBI). However, the data comparing functional outcome in these settings is scarce. The purpose of this study was to investigate the functional outcome in TBI patients with positive (+) BAL.

Study Design: Brain trauma registry of an academic trauma center was queried for patients admitted between 1/2007 and 12/2011. All adult patients (age ≥18 years) with a neurosurgical intensive care (NICU) length of stay beyond 2 days were included. Patient demographics, clinical characteristics on admission, injury profile, Abbreviated Injury Scale Score, Marshall grading, Rotterdam score, S100B levels, Charlson Comorbidity Index, in-hospital and one year mortality, and serum ethanol levels on admission were abstracted for analysis. Glasgow Outcome Score (GOS), at discharge and between 3-12 months after discharge, was used for functional assessment. Primary outcome was unfavorable functional outcome defined as GOS ≤3. Secondary outcomes included were NICU and hospital LOS, in-hospital and first year post-trauma mortality. Multivariable regression models were used for analysis to compare outcomes between patients exposed and those not exposed to ethanol.

Results: A total of 352 patients met inclusion criteria. Of these, 39% tested positive for BAL at admission. The BAL (+) patients were significantly younger (47 ±17 years vs. 52 ±18, p=0.005) with less comorbidities (Charlson Comorbidity Index: 1.7 ±1.8 vs. 2.8 ±2.6, p=0.001). There was no significant difference in the severity of the intracranial injury and the use of intra-cranial monitoring or surgical interventions between the cohorts. Further, there was no difference in in-hospital mortality (p=0.1) or one-year mortality (p=0.5) between the groups.
There was a better long-term functional outcome in BAL (+) patients compared to their BAL (–) counterparts after adjustment for confounders (unfavorable GOS: AOR 2.0, 95% CI 1.1-3.5, p=0.02).

Conclusion: Positive BAL on admission is associated with a better long-term functional outcome in patients suffering severe traumatic brain injury. The potential therapeutic implication of this association warrants further investigation.

Prognostic impact of Wnt proteins in cervical carcinoma

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Objective: Wnt signaling was assessed in patients with primary cervical carcinomas who received chemoradiation. Because nuclear expression of Wnt proteins has been suggested to be an independent prognostic marker in a variety of carcinomas, we examined associations between Wnt and prognosis in cervical carcinoma.

Methods: 131 cases of invasive cervical carcinoma were immunohistochemically analyzed for the expression of Wnt pathway proteins: APC, Axin and β-catenin. Possible associations between Wnt expression, clinico-pathological parameters and the clinical outcome data were studied.

Results: Positive immunohistochemical staining (percentage) for the Wnt proteins (cell-membranes, cytoplasm and nuclei) was recorded. The staining intensity distribution was also analyzed.

Tumors with a nuclear β-catenin staining of > 5% was associated with a worse prognosis and a significantly inferior cancer-specific survival (CSS) rate compared with no nuclear staining. The presence of any staining intensity of the cell-membranes was a highly significant favorable prognostic factor for CSS. The overall recurrence rate was significantly higher in the group with increased nuclear staining (66.7%) compared with the group with no staining (32.7%) and higher in tumors with weak cell-membrane staining (41.3%) than in tumors with strong cell-membrane staining (10.3%).

Nuclear APC staining was associated with a significantly worse CSS compared to tumors with weak staining. The overall recurrence rate was also significantly associated with the intensity of the nuclear staining. Distant recurrences were recorded in 29.2% of cases with intense nuclear APC and in 14.0% of cases with low staining.

The Axin staining, neither percentage nor intensity, was of any statistical significance.

Conclusions: The Wnt signaling pathway seems to be of importance in the multistep process of cervical oncogenesis. A predictive and prognostic value was found for β-catenin, where strong cell-membrane staining was favorable, and > 5% positive nuclear staining was associated with poorer CSS and overall recurrence rate. Nuclear APC staining was also associated with (including distant recurrences) with a less favorable prognosis. A blockage of this pathway may be a potential treatment option in the future

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Haptic technical aids for improvement of Time perception, Environmental perception and Mobility (in a riding arena) and Music perception for persons with deafblindness

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Persons with deafblindness (DB) have frequently difficulties in environmental perception, spatial awareness, time perception, social participation and music experience are examples of frequent problems [1]. To experience independence, participation and control, adequate processing of sensory information is important.
Purpose of this project is to develop and evaluate aids using haptic as information channel for persons with DB to improve their time perception, environmental perception and also mobility of riders in a riding arena and music perception.
Four prototypes, Distime, Monitor, Ready-ride and Good vibrations are developed [2].
Distime, an application in a smart phone which informs the person with DB about the planed activity auditive, visually, tactually or combined depending on the sense that works and the person's ability.
Monitor, a vibratory aid that informs the person with DB about ongoing events in their environment which produce sound. It is as a bracelet consisting of a microphone, processor and vibrator with the microphone and processor placed on the wrist and the vibrator placed under the wrist.
Ready-Ride, a vibratory aid consisting of two smart phones and up to 11 vibrators, which helps the rider with DB, communicate with the instructor from distance via vibrations. The instructors sends commands to the riders smart phone which interprets the command and activates the corresponding vibrator.
Good vibration, a vibratory aid that informs the person with DB about music. It consists of a microphone, processor and four vibrators.
Preliminary pilot laboratory tests and field tests by persons with deafblindness have shown optimal results.

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Beta-blocker use and cancer-specific survival in patients with exocrine pancreatic cancer: a national Swedish study

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Objective: Pre-clinical studies suggest that β-adrenergic receptor signalling is involved in pancreatic cancer (PanCa) progression. In this first general population-based cohort study we aimed to investigate whether β-blocker use is associated with improved pancreatic cancer-specific survival.

Methods: We identified all individuals diagnosed with primary malignant exocrine PanCa in Sweden between 2006 and 2009 (n=2,396) using the Cancer Register, and followed them using the Cause of Death and Total Population registers. We used multivariable Cox regression to estimate hazard ratios (HR) and 95% confidence intervals (CIs) for the association of β-blocker use with cancer-specific mortality. Exposure to β-blockers was analysed overall, as well as by receptor selectivity and lipid solubility.

Results: β-blocker use before diagnosis compared with non-use (HR, 0.66; 95% CI, 0.49 to 0.89) and compared with the use of other anti-hypertensive monotherapies (HR, 0.54; 95% CI, 0.33 to 0.89) was associated with a reduced PanCa mortality risk among patients without metastases. Associations were similar for β-blockers defined by receptor selectivity and lipid solubility. Use of β-blockers after diagnosis was also associated with a reduced PanCa mortality risk compared with that of non-users (HR, 0.57; 95% CI, 0.36 to 0.90). The magnitude of the association was greater among patients who also used β-blockers before diagnosis (HR, 0.23; 95% CI, 0.10 to 0.53).

Conclusions: The use of β-blockers among patients diagnosed with non-metastasized PanCa was associated with a reduced disease-specific mortality risk. These results add further support to the hypothesis that inhibition of β-adrenergic receptor signaling may impede pancreatic tumour progression.

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Live music therapy with lullaby singing as affective support during venepuncture. A case study with microanalysis of two premature born infants.

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Introduction: Acute and repeated pain has long-term negative impact on infants' development and future behaviour. The use of analgesic drugs has negative side-effects, which emphasizes the need for complementary approaches to pain management.

Objective: The objectives were to analyze the live lullaby singing for two premature infants during venepuncture in comparison to standard care only, and the infants' physiological and affective responses emerging before, during and after this procedure.

Methods: Preterm and ill term infants (n=38) were subjected to venepuncture with and without live infant-directed lullaby singing, in a randomised order with a cross over design. Physiological data were collected and the procedures were videotaped. Two premature infants' behavioural and physiological responses as well as the live-performed lullaby, were analysed in-depth with microanalysis and with the pain assessment tool Behavioral Indicators of Infant Pain (BIIP).

Results: Live singing with premature infants is a social communicative interaction. If the vocal performance is predictable and regular from start, it may optimize homeostasis during painful procedures.

Conclusion: Since emotional regulation is a central feature of music therapy this case study brings important clinical implications for how the affective interaction between the music therapist or the parent and the infant should be composed during painful procedures. Pain involves the interaction of biopsychosocial and situational factors, therefore more research is needed to explore the potential benefits of music therapy including the role of the parents.

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Health and People with Usher syndrome

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Objective: The aim was to describe health for people with Usher syndrome (USH). People with USH have a congenital hearing loss of various degrees and an eye disease with a progressive course; for some, the balance is also affected. Three clinical groups have been identified 1, 2 and 3, and 13 genes have currently been identified. USH is the most common cause of deafblindness. Clinical knowledge and the limited research that exists have shown that people with deafblindness experience difficulties in everyday life. Depression, anxiety and social withdrawal have been described.

Methods: The empirical material was based on an extensive survey in which people with USH answered two questionnaires concerning health, anxiety, depression, social trust, work, health-care, financial situation, and alcohol and drug use. Four studies have been conducted; three studies focus on USH1, 2 and 3, respectively; the fourth study provides an in-group comparison of people with USH. In two of the studies the results are compared with a cross-section of the Swedish population.
Results: The results revealed poor physical and psychological health, a lack of social trust and a strained financial situation regardless of clinical group.

Conclusion: Major problems with health, social trust and financial situation were described, such as headache, shoulder and neck pain, fatigue, suicide ideation, general mistrust and strained financial situation. This needs to be addressed from a biopsychosocial perspective, to reveal mechanisms that affect people with USH and their health.

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Thyroid cancer surgery and how accurate presurgery diagnostic

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Objective: It is estimate that five to seven percent of the population has a lump in the thyroid gland. Most of these are benign and harmless. However, some are malignant and can be treated by radical surgery. It is important to know in advance that it is a malignant tumor when surgery is performed on thyroid tumors. Preoperatively known thyroid cancer give us the opportunity to plan for a cancer operation with excision of surrounding lymph nodules and thus perform radical surgery. In the opposite way it is also important to know that a nodule is true benign and a cancer operation is not needed.

Method: We have an ethical approvement to analyze patients included in the Swedish Quality Register for Thyroid, Parathyroid and Adrenal Surgery. There were 3033 operations included in this study. Patients were included because of either suspected malignancy or confirmed malignancy before surgery or postoperatively diagnosed malignancy in the specimen that was preoperatively unknown. We have also analyzed patients operated because of preoperatively confirmed malignancy were the postoperatively definitive macroscopic evaluation showed benign tissue. This material report also the number of patients who needed a second operation because of the preoperatively unknown malignant tumor. So far, in this study there is 520 included surgeries from seven different clinics around Sweden.

Results: In a pilot study, more than 25% of the thyroid malignant tumors were not diagnosed preoperatively. In this large material, we wish now to analyze the figures from the SQRTPA register.

Discussion: The results from this study is yet not available but there is still certain aspects that can be discussed. Thyroid surgery is performing all around Sweden. Is preoperatively investigation and then treatment equal comparing the different hospitals in Sweden?

Co-creation of communicative projects within the Swedish Video Relay Interpreting (VRI) Service

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Objective: The Swedish Video Relay Interpreting (VRI) Service is a facility that people who use signed language on a video phone can call in order to get in touch with people who use verbal language on a telephone, or vice versa. The interlocutors have different access to the visual arena and the auditive space, and are physically separated from each other. An interpreter enables the communication in this setting. Since the interaction in the VRI service follows several institutional principles, it is of interest to explicate what series of communicative projects occur, and the purposes they serve and how communicative projects are managed among all of the interlocutors.

Method: Analysis of authentic recordings of the service are based on Conversation Analytical (CA) methodology (Sidnell & Stivers 2013), in combination with dialogical theory (Linell 1998), and focuses on what is manifested in the calls, i.e. what actually happens among the interlocutors on a moment-by-moment basis.

Results: The interaction is systematically laminated by the interlocutors' establishment of global and local communicative projects that are dependent on the contingencies of the VRI service setting, e.g. the different media used, the modalities of interaction (Swedish, and Swedish Sign Language), and different manners of interacting in respective media.

Conclusion: The interlocutors co-create the call in reflexive, interactive, and dynamic ways on different levels. This structural organization of laminated systems of communicative projects is what manifests the institutionality of the interaction within the VRI Service.

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Flaviviruses; from virus to vaccine

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Objective: Reverse genetics has become an important technique to study different aspects of viral infections. Here we will present how we have generated an infectious clone of Tick-borne encephalitis virus (TBEV). We will also talk about the progress in developing TBEV vaccine in *Nicotiana benthamiana* (Tobacco) and *Tetragonia tetragonoides* (Spinach). A successful expression of the structural proteins (CPM) in the plant system generates virus like particles (VLPs) that can be used as vaccine candidate.

Methods: Reverse genetics approach was used to generate the infectious clone of TBEV. Sp6 promoter sequence was introduced at 5´end of TBEV genome by a PCR and cells were transfected with in-vitro transcribed RNA to generate the infectious clone. For developing the vaccine, 4-6 weeks plants will be infiltrated with *Agrobacterium tumefaciens* containing codon optimized TBEV-CME cloned into pEAQ.HT for expression.

Results: The rescued infectious clone replicated well in the cell culture and was virulent for the laboratory mice. Our reverse genetics method and recued clones are great tools to explore different aspects of virus infection. For vaccine project, we have successfully agroinfiltrated the tobacco plant with CME-pEAQ.HT and the control vector (GFP- pEAQ.HT). Next is to analyze the expression of CME and quantify the produced VLP.

Conclusions: We have generated an infectious clone of TBEV and we are further characterizing its replication and virulence in cell culture and mammalian models, respectively. We are in the start line of producing an edible TBEV vaccine by using two different plant platforms. The agroinfilteration with the control vector showed a successful GFP expression. The CME-pEAQ.HT infiltrated plants are under process of being analyzed for functional expression and quantification.

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Embodiment essential for reducing the influence of environmental barriers - experiences of users of myoelectric arm prosthesis

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Objective: Myoelectric prostheses are prescribed to people born with upper limb reduction deficiency or with acquired amputation in order to improve their everyday life. These prostheses are used in varying degrees. Why do some people abandon their prostheses and others continue to use them? This study describes experiences of how environmental factors influence myoelectric arm prosthesis use**.**

Method: Qualitative descriptive approach. Thirteen patients previously provided with a myoelectric prosthetic hand participated. Their age, sex, deficiency level, etiology, current prosthesis use, and length of experience varied. Semi-structured interviews were audiotaped, transcribed and analyzed through inductive content analysis.

Results: The overarching theme: Different degree of embodiment provides various experiences of influence from environment; illustrates the participants' adaptation to prosthesis, which in turn influence the ability to manage environmental barriers. Three categories and six subcategories emerged from the data. They describe the participants' experiences of the influence from environment, their different adaptations to this environment, and experiences of the prosthesis usability. Environmental facilitators, support from family and healthcare, good function and fit of the prosthesis, helped to make the prosthesis an embodied experience, leading to daily use. This embodiment reduces the influence of environmental barriers, e.g. climate, attitudes, and technical shortcomings. Myoelectric prosthesis use facilitates activity and participation among daily users.

Conclusions: The embodiment of the prosthesis reduces influence of environmental barriers and promotes myoelectric prosthesis use in both congenital and acquired upper limb deficiency. Support and training can facilitate the embodiment of myoelectric prosthesis.

Proinflammatory Cytokines and Oxidative Stress Reduces the Dopamine Precursor Tyrosine Uptake in Human Skin Fibroblasts: Role of Antioxidants as Adjuvants

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Objective: Disturbed transport of dopamine precursor amino acid, tyrosine is demonstrated in fibroblasts obtained from patients with schizophrenia and bipolar disorder. These neuropsychiatric disorders are indicated with disturbed dopaminergic, noradrenergic and serotonergic neurotransmission. The disturbed tyrosine transport could be one of the possible explanations for altered neurotransmission in these disorders. The reason for disturbed tyrosine transport in neuropsychiatric disorders is not completely understood. Over the last two decades, research and clinical studies have implicated the role of elevated proinflammatory responses and oxidative stress in the pathogenesis of many neuropsychiatric disorders. Moreover, recent evidences suggest that antioxidants as adjuvants can improve the symptoms of certain neuropsychiatric disorders, but the underlying molecular mechanism of action of antioxidants is not completely elucidated yet. The aims of the present study were to assess the role of proinflammatory cytokines, oxidative stress and antioxidants on tyrosine transportation by using the human skin derived fibroblasts as model cells. In addition, this study also examines the effects of pro-inflammatory cytokines and antioxidants on radical oxygen species (ROS) production in human fibroblasts.

Method: Fibroblasts obtained from a healthy control were used in this study. Fibroblasts were treated with proinflammatory cytokines or oxidative stress and/or antioxidants to analyze the uptake of ^{14}C-Tyrosine by using the cluster tray method. ROS was measured as fluorescent response after treatment with 2', 7'-dichlorodihydrofluorescein diacetate (H2DCFDA).

Results: The results of the present study indicate that pro-inflammatory cytokines, oxidative stress can decrease the uptake of tyrosine. Moreover, the results of this study indicate that proinflammatory cytokines stimulate the ROS production and is shown to be associated with the decreased amino acid transportation.

Conclusions: This study demonstrates that proinflammatory cytokines and oxidative stress can affect the functioning of tyrosine transporters. The proinflammatory cytokine affect is probably mediated by production of ROS. This study further demonstrates that, antioxidants can counteract the effects of both proinflammatory cytokines and oxidative stress on tyrosine transportation.

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Lovely, we don’t need to rent a frack for the Nobel Day Festivities