DEPARTMENT OF NEUROLOGY SERIES OF REPORTS SUPPLEMENT 6
UNIVERSITY OF KUOPIO

JUKKA JOLKKONEN (ed.) 2007

Kuopio Stroke Symposium 2007

Microteknia, Kuopio, Finland
June 6-8, 2007

Program and Abstracts

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KUOPION YLIOPISTO

KUOPIO 2007

Editor's address: Department of Neurology
University of Kuopio
P.O. Box 1627
FI-70211 KUOPIO
FINLAND
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Fax +358 17 162 048

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Kopijyvä
Kuopio 2007
Finland

Dear Participants of the Kuopio Stroke Symposium 2007

You are cordially welcome. I thank you on behalf of the organizing committee for the decision to direct your path to the city of Kuopio, one of the main cities in the lake-area of Finland. As always in Northern Europe, the weather is unpredictable. Three years ago at this symposium, it was mostly sunny and warm. We hope it will be the same this year!

The scientific community has already learned that stroke is the most common reason for disability during adulthood in the developed world. This fact has now been recognized generally, and in most countries the fight against stroke has really started. It is a common belief that the prevalence of stroke will increase as the population ages. This does not have to be the case, however, if we increase our efforts against it by means of prevention. We now have a very effective treatment tool for the acute phase of stroke – thrombolysis. The next step is to learn to use it effectively and enlarge the number of people who have access to it. Additionally, our understanding about the recovery of stroke is continuously increasing. We have realized that the human brain has plasticity, and is able to be re-modelled by physical and cognitive therapies. All of these aspects will be under discussion during these three days in Kuopio.

We hope you will find an opportunity to relax and enjoy the early summer and the atmosphere of Kuopio during your stay.

Juhani Sivenius
Chairman of the Organizing Committee

Boehringer Ingelheim Finland Ky:llä on kunnia olla tukemassa Kuopio Stroke Symposium 2007 tapahtumaa ja toivotamme kaikille osallistujille onnistunutta kokousta.

Kaj Linna
Boehringer Ingelheim Finland Ky:n puolesta

Kuopio Stroke Symposium 2007

Organized by Department of Neurology, University of Kuopio and
Brain Research and Rehabilitation Center, Neuron, Kuopio, Finland

Organizing Committee

Juhani Sivenius
Jukka Jolkkonen
Pekka Jäkälä
Markku Kaste
Ina M. Tarkka

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The Academy of Finland

Kuopio Stroke Symposium 2007

Wednesday, June 6, 2007

13.00-15.00 Registration and coffee

Opening ceremonies

15.00-15.15 Matti Uusitupa, University of Kuopio
Juhani Sivenius, The Organizing Committee

Prevention of stroke (chaired by Markku Kaste and Juhani Sivenius)

15.15-15.45 **Consequences of aging of population: Can we prevent the increasing burden of stroke?**
Juhani Sivenius, Department of Neurology, University of Kuopio, Kuopio, Finland

15.45-16.15 **Treatment of blood pressure and dyslipidemia in patients with TIA or stroke**
Timo Strandberg, Department of Public Health Science and General Practice, University of Oulu, Oulu, Finland

16.15-16.45 **Update on carotid stenting**
Werner Hacke, Department of Neurology, University Hospital of Heidelberg, Heidelberg, Germany

16.45-17.15 **Benefits and risks of antiplatelet therapy in secondary prevention of stroke**
Hans-Christoph Diener, Department of Neurology, University of Essen, Essen, Germany

19.00- Get-together party at the Lumberjack's Cabin (Jätkänkämppä, Rauhalahti). Bus transportation from and to hotels will be provided.

Thursday, June 7, 2007

Present state of management of stroke (chaired by Risto Roine and Pekka Jäkälä)

9.00-9.30 **Emerging therapies of stroke**
Markku Kaste, Department of Neurology, Helsinki University Hospital, Helsinki, Finland

9.30-10.00 **Why is an acute ischemic attack an emergency?**
Perttu Lindsberg, Emergency Neurological Services, Helsinki University Hospital, Helsinki, Finland

10.00-10.30 Coffee and exhibition

10.30-10.40 **Scandinavian Candesartan Acute Stroke Trial (SCAST)**
Dag Aarhus, Department of Internal Medicine, Ullevål University Hospital, Oslo, Norway

10.40-11.15 **Modern practice of thrombolysis**
Risto Roine, Department of Neurology, Turku University Central Hospital, Turku, Finland

11.15-12.00 **Biology of saccular intracranial aneurysm (SIA) wall and subarachnoid hemorrhage (ASAH)**
Juha E. Jääskeläinen, Neurosurgery, Kuopio University Hospital, Kuopio, Finland

12.00-13.15 Lunch, poster presentations and exhibition

Brain plasticity and functional reorganization after brain injury (chaired by Ina M. Tarkka and Jukka Jolkkonen)

13.15-14.00 **Rehabilitation of gait in stroke patients**
Stefan Hesse, Klinik Berlin, Neurological Rehabilitation, Charité - University Medicine Berlin, Berlin, Germany

14.00-14.45 **Strategies to enhance motor training effects in neurorehabilitation**
Leonardo G. Cohen
Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic; National Institute of Neurological Disorders and Stroke; National Institutes of Health, Bethesda, MD, USA

14.45-15.15 Coffee break and exhibition

15.15-16.00 **Cellular and molecular mechanisms of stroke recovery**
S. Thomas Carmichael, Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

16.00-16.45 **Plasticity in cortex after stroke**
Randolph Nudo, University Kansas Medical Center, Kansas City, KS, USA

16.45- **Award ceremonies**
The Kuopio Stroke Symposium 2007 Poster
Kuopio University Neuroscience Center Awards for Best NEUROSCIENCE Papers of the Year 2006, Heikki Tanila

19.00-21.00 Reception at Kuopio Art Museum (Kauppakatu 35) hosted by the City of Kuopio
Snack and viewing the exhibition. Bus transportation from and to hotels will be provided.

Perjantai, 8.6.2007

Aivohalvauskuntoutus 2007 (puheenjohtaja Juhani Sivenius)

9.00-9.30 **Onko kuntoutuksen ajoituksella ja intensiteetillä vaikutusta ennusteen kannalta?**
Sinikka Peurala, Suomen gerontologian tutkimuskeskus, liikunta- ja terveystieteiden laitos, Jyväskylän yliopisto

9.30-10.00 **Upper limb rehabilitation in stroke**
Jane Burridge, School of Health Professions and Rehabilitation Sciences, University of Southampton, Southampton, UK

10.00-10.30 Kahvitauko ja näyttely

10.30-11.00 **Kantasoluterapian mahdollisuudet aivohalvauksen hoidossa**
Jukka Jolkkonen, Neurologian yksikkö, Kuopion yliopisto, Kuopio

11.00-11.30 **Neglect-ilmiö ja sen kuntoutus**
Riitta Luukkainen-Markkula, Suomen aivotutkimus- ja kuntoutuskeskus Neuron, Kuopio

11.30-12.00 **Puheterapian uudet menetelmät ja niiden aivoperäiset mekanismit**
Matti Lehtihalmes, Logopedian laitos, Oulun yliopisto, Oulu

12.00-13.15 Lounas ja näyttely

13.15-13.45 **Lyhyitä puheenvuoroja**
Aivohalvaus- ja dysfasialiiton esittely
Aivohalvaus- ja dysfasialiiton kuntoutusprojekti
Boehringer Ingelheim Finland

13.45-14.15 **Aivoverenkiertohäiriöt ja epilepsia**
Reetta Kälviäinen, Kuopion Epilepsiakeskus, Kuopion yliopistollinen sairaala, Kuopio

14.15-14.45 Kahvi ja näyttely

14.45-15.15 **Voiko kuntoutumista kuvantaa?**
Ritva Vanninen, Radiologian klinikka, Kuopion yliopistollinen sairaala, Kuopio

15.15-15.45 **Hoitotyön merkitys aivohalvauskuntoutuksessa**
Katri Vehviläinen-Julkunen, Hoitotieteen laitos, Kuopion yliopisto, Kuopion yliopistollinen sairaala, Kuopio

15.45- Keskustelu ja tilaisuuden päätös

Kuopio Stroke Symposium 2007

Wednesday, June 6, 2007

CONSEQUENCES OF AGING OF POPULATION: CAN WE PREVENT THE INCREASING BURDEN OF STROKE?

Juhani Sivenius

Department of Neurology, University of Kuopio, Kuopio, Finland

It is well known that increasing age is the strongest risk factor of stroke. Therefore, it has been a common belief that the numbers of stroke patients will certainly surge high during the next two decades in Finland because the population gets older. The FINMONICA and FINSTROKE registers operated in Kuopio are and city of Turku from 1983 to 1997. Their results showed that incidence and mortality of stroke events declined significantly. Furthermore, it was stated that stroke mortality and incidence among the elderly (> 74 years) was declining in Finland, too. Afterwards, a model for whole country was created. This model was based on the trends of these registers from Turku and Kuopio area, and Statistics Finland produced the aging trends of population until year 2030.At year 2000, the annual number of new stroke cases is assumed to be 11,500. If favourable trend of risk reduction would totally stop after year 2000, the number of new strokes would be 20,100 at year 2030, instead of 12,100 if the good trend continues like during the previous years 1983-97. The numbers of patients over 64 years old would increase dramatically from 8,600 annual patients at year 2000 to 17,200 patients at year 2030, if the good trend seizes. Conclusion: Aging of population in Finland does not remarkably increase the burden of stroke if the level of risk reduction remains high, but increases nearly two-fold if risk reduction remains on the level it was at year 2000.

Sivenius J, Tuomilehto J , Immonen-Räihä P, Kaarisalo M, Sarti C, Torppa J, Kuulasmaa K, Mähönen M, Lehtonen A, Salomaa V. Continuous 15-year decrease in incidence and mortality of stroke in Finland. The Finstroke Study. Stroke 2004;35:420-5

Lehtonen A, Salomaa V, Immonen-Räihä P, Sarti C. Mähönen M, Tuomilehto J, Torppa J, Sivenius J. Declining incidence and mortality in patients aged >75 years in Finland; the FINSTROKE Study. Eur J Cardiovasc Prev Rehabil 2004;11:466-70

TREATMENT OF BLOOD PRESSURE AND DYSLIPIDEMIA IN PATIENTS WITH TIA OR STROKE

Timo Strandberg

Department of Public Health Science and General Practice, University of Oulu and Oulu University Hospital, Unit of General Practice, Oulu, Finland

Treatment of hypertension and dyslipidemia (especially with statins) are now established treatments to prevent ischemic stroke. They are also important in secondary prevention. In treatment trials the combination an ACE inhibitor (perindopril) + diuretic (indapamide) was effective in the secondary prevention of stroke (the PROGRESS study). In the MOSES study, an angiotensin receptor blocker (eprosartan) was more effective than a calcium channel blocker despite similar blood pressure lowering among patients with previous stroke or TIA. Although blood pressure lowering is important, drugs affecting the renin-angiotensin-aldosterone system seem to have benefits beyond blood pressure lowering. More effective reduction of the central blood pressure, prevention of diabetes and atrial fibrillation are intriguing properties of these drugs. In the SPARCL trial, high dose atorvastatin (80 mg) was more effective than placebo in the secondary prevention of ischemic stroke. Atorvastatin also reduced other major cardiovascular events among these patients without prior coronary disease. Actually, it is essential to remember that atherosclerotic vascular disease is a systemic disease, the treatment of which should be performed multifactorially. A recent modeling study (Hackam & Spence, Stroke, April 2007) suggested a dramatic effect of prevention: the combination of five proven strategies (dietary treatment, exercise, acetosalisylic acid, statin and an antihypertensive agent) was calculated to reduce cumulatively the relative risk of recurrent stroke by 80%.

UPDATE ON CAROTID STENTING

Werner Hacke

Department of Neurology, University Hospital of Heidelberg, Heidelberg, Germany

During the last 12 months, new results have enriched our knowledge about the usefulness and efficacy of carotid artery stenting in symptomatic carotid stenoses.

While carotid endarterectomy is the gold standard for stenting, until recently, only underpowered and methodologically disputable results of registries and smaller sized randomized clinical trials have been available. A metaanalysis from 2004 did not reveal any signal superiority of carotid artery stenting. In addition, the question whether protection devices should be used or not, was also not scientifically answered.

In 2006, two large scale clinical randomized trials, SPACE and EVA 3S, have been published. While EVA 3S was finalized prematurely due to a significantly elevated risk for perioperative morbidity and mortality in the transvascular arm, SPACE reported the results of 1.200 randomized patients and just missed the primary endpoint, which was non inferiority, by a small margin.

The updated metaanalysis of all available trials currently suggest a slight superiority of carotid artery stenting; however, the trials underlying this metaanalysis are significantly heterogeneous. If those trials, contributing to heterogeneity, are excluded, there is no obvious difference between the two methods. In addition, at the present time, although no randomized trial has tested the use of protection devices, there is no hint whatsoever, that protection devices really offer additional safety in if stenting.

BENEFITS AND RISKS OF ANTIPLATELET THERAPY IN SECONDARY PREVENTION OF STROKE

Hans-Christoph Diener

Department of Neurology, University of Essen, Essen, Germany

Patients with a TIA or a stroke have a high risk to suffer a first or recurrent stroke. Immediate implementation of secondary prevention based on the pathophysiology of the ischaemic event is of major importance. Patients with cardiac source of embolism, most of them with atrial fibrillation benefit from oral anticoagulation. The relative risk reduction for first (primary prevention) or recurrent events (secondary prevention) of warfarin versus placebo is 60-70%. Aspirin reduces stroke risk by 15-18%. The combination of aspirin and warfarin carries a higher bleeding risk than each drug alone and offers no additional benefit in patients with AF.Patients with thrombo-embolic stroke are treated with antiplatelet agents. Aspirin monotherapy leads to a 13% relative risk reduction compared to placebo for the combined endpoint ischemic stroke (IS), myocardial infarction (MI) or vascular death (VD). In the CAPRIE trial clopidogrel 75 mg was superior to aspirin 325 mg in patients with MI, IS or peripheral arterial disease (PAD). The combination of aspirin plus clopidogrel offered no benefit over clopidogrel monotherapy in stroke patients as shown by the MATCH trial. The combination of clopidogrel plus aspirin was inferior to aspirin monotherapy in patients with vascular risk factors and showed a trend for superiority in patients with established arterial disease for the prevention of ischaemic stroke (CHARISAM). In both trials the combination resulted in a higher number of bleeding complications than aspirin or clopidogrel alone. The combination of aspirin and modified release dipyridamole is superior to aspirin monotherapy (ESPS2, ESPRIT) without a significant increase in bleeding complications. Therefore patients with a low recurrence risk should be treated with aspirin montherapy. Patients with a high recurrence risk should receive the combination of aspirin plus dipyridamole. Patients who do not tolerate aspirin or stroke patients with PAD should receive clopidogrel.

Kuopio Stroke Symposium 2007

Thursday, June 7, 2007

EMERGING THERAPIES OF STROKE

Markku Kaste

Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland

Background: The only approved treatment for acute ischemic stroke (AIS) is limited to a 3-hour time window, a period in which most AIS patients do not arrive at the hospital. Furthermore, not all patients with AIS are eligible for thrombolysis. There is a great need for new therapies for the vast majority of AIS patients. What may soon be available? DIAS1, DEDAS2 and DIAS-2 trials have revealed that desmoteplase can safely extend the treatment window from 3 hours up to 9 hours when diffusion-perfusion MRI and perfusion CT are used to select patients with an ischemic penumbra (perfusion mismatch). Intra-arterial (I.A.) thrombolysis is also able to extend the time window for thrombolysis[3] and may be effective when intra-venous (I.V.) thrombolysis has failed. The rate-limiting step of I.A. thrombolysis is shortage of neurointerventionists but an alternative is to start the treatment I.V. and continue it I.A.4 when the Cat Lab and the interventionalist are ready for it. Mechanical thrombolysis with a MERCI retriever[5] is also a possible alternative to recanalize a brain artery resistant to thrombolytic drugs if an interventionalist is available. A promising treatment for the most severe AIS patients is early decompressive surgery, which in a meta-analysis has been shown to improve the outcome of patients with malignant MCA occlusion[6]. What is under investigation? Reperfusion may increase oxidative stress and production of free radicals. Thrombolysis can be combined with neuroprotectants to prevent the damage induced by free radicals. Preliminary data supports the idea that free radical scavengers combined with rt-PA is effective in experimental stroke[7] but the hypothesis waits for verification in clinical randomized trials. The combination therapies could also involve hypothermia. Mild hypothermia as a stand-alone treatment needs also to be studied while deeper hypothermia has not fulfilled the expectations placed on it[8]. What is waiting to be investigated? Experimental research has verified that it is possible to facilitate recovery from a MCA occlusion with stem cells and drug treatments that induce neurogenesis from animals' own stem cells[9,10]. The time window for experimental neurogenesis has been days instead of hours as is the case with thrombolysis and neuroprotective agents[11]. If the induction of neurogenesis can be translated to clinical patient care it would be a major breakthrough and a highway not only in neuronal recovery and reorganization after AIS but also for spinal cord and head injuries, Alzheimer and Huntington diseases and many other neurological disorders that are desperately waiting for breakthroughs. Conclusions: Despite of history of failures of translating therapies effective in experimental research into clinical practice the endurance and enthusiasm of clinical stroke scientists ensure that there will be breakthroughs in AIS also after rt-PA[12]. It is also most likely that there will be new stroke therapies, which benefit much larger stroke population than I.V. rt-PA with a 3-hour time window.

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WHY IS AN ACUTE ISCHEMIC ATTACK AN EMERGENCY?

Perttu J. Lindsberg

Emergency Neurological Services, Helsinki University Central Hospital, Helsinki, Finland

When prevention of cerebrovascular disease fails, there are two effective therapies for acute stroke: care in a specialized stroke unit and thrombolysis of the occluded vessel with r-TPA. In a typical infarct, occlusion of the middle cerebral artery, permanent ischemic necrosis ensues already after 30 minutes in the territory of basal ganglia. If critical ischemia prevails with blood flow reduced more than 50 %, depending on the patency of the leptomeningeal collateral perfusion, the rest of the largely cortical MCA territory will be lost during the subsequent few hours. Sadly, most patients with are not even hospitalized at this time. Recent estimates indicate that during that perilous period, 120 million neurons, 830 billion synapses and 714 km of myelinated neuron fibers are lost per one hour (Saver 2006). Unfortunately, also the hospitals responsible for immediate evaluation of stroke patients were not initially designed to for fast diagnostic and therapeutic procedures. For example, CT scanning needs to be started immediately and in many hospitals it sits far from the ER and the just arrived patient. In Helsinki, before moving the CT inside the ER, it took more than 1 hour to start CT while it now takes only 7 minutes and patients can be treated with r-TPA within 30 minutes of arrival (Lindsberg et al. 2006). Similar steps and imperatives could be implemented also elsewhere to expedite recanalization therapy and reperfusion of the quickly diminishing portion of salvageable brain tissue in order to prevent permanent disability.

Saver JL. Time is brain - quantified. Stroke 2006;37:263-266.

Lindsberg PJ, Häppölä O, Kallela M, Valanne L, Kuisma M, Kaste M. Door to thrombolysis: ER reorganization and reduced delays to acute stroke treatment. Neurology 2006;67:334-336.

MODERN PRACTICE OF THROMBOLYSIS

Risto O. Roine

Department of Neurology, Turku University Central Hospital, Turku, Finland

The Safety Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST), was a major condition of the European Union (EU) for granting a licence for the use of alteplase for the treatment of acute ischaemic stroke and to assess the safety profile of alteplase in clinical practice through a comparison with results from randomised controlled trials.[1] A total of 6,483 patients were recruited from 285 centres (50% with little previous experience in stroke thrombolysis) in 14 countries between 2002 and 2006 for this prospective, open, monitored, observational study. Finland recruited 590 patients from 17 centers. In the entire SITS registry, there are now 1.175 finnish patients entered, which makes Finland the fourth overall and number one by per capita enrollment. Treatment delays are, on the average, shorter (onset to needle 129 vs 143 min) and the outcome results better in Finland (independence at 3 months 57% vs 50%) than in the entire registry.

In SITS-MOST, patient baseline characteristics were comparable with those in the pooled randomised controlled trials. The primary outcome measures were symptomatic intracerebral haemorrhage (type 2) and death within 3 months. Functional independence at 3 months was a secondary outcome. At 24 h, the proportion of patients with symptomatic intracerebral haemorrhage per protocol was 1.7% (107/6,444; 95% CI 1.4–2.0); at 7 days, the proportion with the same condition as per the Cochrane definition was 7·3% (468/6,438; 6.7–7.9) compared with 8.6% (40/465; 6.3–11.6) in the pooled randomised controlled trials. The proportion of independent patients at 3 months in SITS-MOST was 54.8% (3,362/6,136; 53.5–56.0) compared with 49.0% (227/463; 44.4–53.6) in the pooled randomised controlled trials. The mortality rate at 3 months in SITS-MOST was 11.3% (701/6,218; 10.5–12.1) compared with 17.3% (83/479; 14.1–21.1) in the pooled randomised controlled trials. The mortality was lower in experienced than in inexperienced centers.

The results from SITS-MOST confirm that intravenous alteplase, when used in routine clinical practice, has a safety profile at least as good as that seen in randomised controlled trials and is an effective treatment when used within 3 h of stroke onset, even in stroke centres with little previous experience of thrombolytic therapy for acute stroke. Although mortality was higher in less experienced centres than in those with previous experience, it was lower than in randomised controlled trials, and the difference was not caused by haemorrhagic complications.

The Finnish guidelines for the management of acute ischemic stroke, prepared by a working group set up by the Finnish Medical Society Duodecim and the Finnish Neurological Society, were published in 2006. They conform to the newest American Stroke Association treatment guidelines except for the extension of treatment window to 4.5 hours in case a perfusion deficit can still be demonstrated in noninfarcted brain tissue and if a large infarct is not visible on CT. According to the US guidelines, a patient with a seizure at the time of onset of stroke may be eligible for treatment as long as the physician is convinced that residual impairments are secondary to stroke and not a postictal phenomenon. Furthermore, i.a. thrombolysis is an option for treatment of selected patients who have major stroke of <6 hours' duration due to occlusions of the MCA and who are

not otherwise candidates for intravenous rtPA. Intra-arterial thrombolysis is also reasonable in patients who have contraindications to use of intravenous thrombolysis, such as recent surgery. According to the US guidelines, i.a. treatment requires the patient to be at an experienced stroke center with immediate access to cerebral angiography and qualified interventionalists, and that i.a. thrombolysis should not preclude the i.v. administration of rtPA in otherwise eligible patients. The utility of mechanical thrombectomy devices in improving outcomes after stroke is unclear, and additional clinical trials are recommended. In Finland, the use of i.a. thrombolysis or mechanical thrombectomy have generally not been advocated, but endovascular therapies are likely to be an option in the future.

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BIOLOGY OF SACCULAR INTRACRANIAL ANEURYSM (SIA) WALL AND SUBARACHNOID HEMORRHAGE (ASAH)

Juha E. Jääskeläinen

Neurosurgery, Kuopio University Hospital, Kuopio, Finland; Finnish Intracranial Aneurysm Research Concortium (FIARC)

Primary subarachnoid hemorrhage (SAH) – a devastating form of stroke - is mostly caused by the rupture of the wall of saccular aneurysms (sIAs) at the bifurcations of the main cerebral arteries in the CSF space. The age-adjusted incidence is generally 6-7 / 100 000 / year. aSAH mainly affects working-age population – median age of 51 years in Finland. There is a 50% mortality, and only 20% of aSAH patients return to work.

Unruptured sIAs develop after birth in as much as 2% of population but most will go unnoticed during life. Unruptured sIAs are rarely diagnosed before 30 years of age, may increase in size during life, and rarely occlude spontaneously. It is not exactly known why a small proportion of unruptured sIAS eventually rupture, but inflammation and degradation of the sIA wall plays a role (Frösen 2004, 2006).

Familial sIA disease occurs in 10% of aSAH patients. aSAH is obviously a multifactorial disease with different loci behind sIA families in different populations. Acquired risk factors of sIA / aSAH include age, smoking, hypertension and alcohol. The interplay of sIA loci and acquired risk factors in the sIA wall remains to be elucidated.

Challenges – how to prevent
1. formation of sIA in general population?
2. rupture of sIA wall in sIA carriers, in general or in defined risk groups?
3. re-repture of ruptured sIA wall in acute aSAH?
4. delayed ischemic neurological injury (DIND) that may develop after aSAH?

REHABILITATION OF GAIT IN STROKE PATIENTS

Stefan Hesse

Klinik Berlin, Neurological Rehabilitation, Charité – University Medicine Berlin, Campus BF, Germany

Stroke affects 180 persons per 100.000 inhabitants in the EC each year. Three months after stroke, 25% of the surviving patients remain wheelchairbound, and 50% have a reduced walking velocity and endurance. Modern concepts favour a task-specific repetitive approach, i.e. “who wants to relearn walking, has to walk”.

1. The non-ambulatory patient

Treadmill training with partial body weight support was a first step enabling the harness-secured patients to practise several hundred steps during one session. However, controlled trials, comparing the intensive gait practice on the treadmill vs. on the floor, failed to show any superiority. Most likely, the workload for the therapists was too big, e.g. placing the paretic limb, limiting the step frequency due to fatigue. A solution to this problem are gait machines, as the Lokomat, a powered exoskeleton, or the electromechanical gait trainer GT I. On the latter, the harness-secured patient is positioned on two foot plates, whose movements simulate stance and swing. Ropes control the vertical and horizontal movement of the centre of mass. FES of up to 8 channels is optional. Several controlled trails (Germany, Finland, Hong Kong, Korea, Portugal, France) have shown a superior effect, the largest is the Deutsche Gangtrainerstudie, DEGAS [1]. Four centres included 155 first time non-ambulatory stroke patients in the acute phase. Patients had been wheelchair mobilised and could sustain 10 min verticalisation in the standing frame. Group A patients had 20 min GT I + 25 min individual physiotherapy and group B patients 45 min physiotherapy every workday for 4 weeks. At study end, significantly more patients of group A, 42 vs. 17, had become ambulatory. Six months later, the favourable outcome persisted. A higher gait intensity, at least 800 steps per session on the GT I, was the most likely explanation. A Cochrane report is being prepared.

2. The ambulatory patient

To improve gait velocity and endurance, both highly relevant for daily life, aerobic treadmill training is applied. Cardiovascular stable patients try to reach a target heart rate (THR) by gradually increasing speed and inclination of the belt. They wear a harness, their body weight is not reduced. THR is either set following bicycle ergometry or, if not possible, according to the formula 180 – age, the intake of beta blocker reduces the THR for 15 to 20 beats. A controlled trial in 50 patients revealed that six weks of daily aerobic treadmill training resulted in a significant and persistent imrpovement of gait velocity and endurance, gait quality did not differ [2]. Another pole of interest of our group is the effect of orthoses on the gait of hemiparetic subjects and the optimisation of the neurolytic treatment of focal lower limb spasticity.

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STRATEGIES TO ENHANCE MOTOR TRAINING EFFECTS IN NEURO-REHABILITATION

Leonardo G. Cohen

Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic; National Institute of Neurological Disorders and Stroke; National Institutes of Health, Bethesda, MD, USA

Stroke is the leading cause of long-term disability worldwide and a condition for which there is no well accepted treatment. The development of new effective therapeutic strategies relies on a better understanding of the mechanisms underlying recovery of function. Noninvasive techniques to study brain function, including functional magnetic resonance imaging, positron emission tomography, transcranial magnetic stimulation, electroencephalography, and magnetoencephalography, led to recent studies that identified some of these operating mechanisms, resulting in the formulation of novel approaches to motor rehabilitation. Overall, interventions using transcranial magnetic or electrical stimulation that enhance activity in the ipsilesional motor cortex or that downregulate activity in the intact motor cortex appear to play beneficial roles when appropriately combined with customarily used neurorehabilitation treatments. Another approach to accomplish a comparable result in some trials is somatosensory stimulation of the paretic hand and anaesthesia of the intact hand.

CELLULAR AND MOLECULAR MECHANISMS OF STROKE RECOVERY

S. Thomas Carmichael

Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Stroke produces an initial region of cell death, but also adjacent areas of tissue reorganization and repair. Two mechanisms of neural repair after stroke include axonal sprouting and neurogenesis. In axonal sprouting neurons in peri-infarct cortex adjacent to the stroke produce new patterns of connections with partially damaged areas. In post-stroke neurogenesis newly born, immature neurons migrate from the subventricular zone into peri-infarct cortex. Post-stroke axonal sprouting means that a fully differentiated neuron must elaborate a growth program. By using a novel labeling method we have selectively isolated sprouting neurons after stroke, probed their gene expression with whole genome arrays, and determined the transcriptional profile of this sprouting response. Post-stroke neurogenesis involves a novel neurovascular niche, in which neuroblasts associate with angiogenic blood vessels in peri-infarct cortex and interact through specific vascular growth factors. We have used selective isolation and gene expression profiling of both blood vessels and neuroblasts to identify the conjoint signaling systems shared by these two cell types after stroke. Together, this selective genomics analysis of axonal sprouting and neurogenesis provides a comprehensive profile of the transcription control of neural repair after stroke, or the “regeneration transcriptome”, and highlights important signaling cascades that may form the framework for novel drug therapies to improve functional recovery in this disease.

PLASTICITY IN CORTEX AFTER STROKE

Randolph J. Nudo

University of Kansas Medical Center, Kansas City, KS, USA

Numerous studies have shown that the cerebral cortex undergoes functional and structural plasticity after injury. While most of this work has focused on the peri-infarct cortex, recent studies from our laboratory and others have now demonstrated that a focal injury results in widespread changes throughout the ipsilesional and contralesional hemisphere. Our studies have utilized a non-human primate model of focal ischemic injury, since primates possess multiple motor representations that might potentially play a role in recovery. After damage to the distal forelimb representation in the primary motor cortex (M1), hand representations in remaining premotor areas (dorsal and ventral premotor cortex, supplementary motor area) are substantially altered. Remaining distal forelimb representations expand in a size-dependent manner: the larger the injury in M1, the larger the expansion in the premotor area. Reorganization of premotor areas is correlated with functional recovery in hand use. Furthermore, these remote motor areas in the ipsilesional cortex sprout new connections after M1 injury. In primates, the ventral premotor area sends novel intracortical fibers to terminate in the somatosensory cortex. In rats, the spared forelimb representation (rostral forelimb area) sends new fibers to the contralesional striatum. In summary, it would appear that the remaining cortical motor network can sustain recovered functions by altering its anatomical connections and functional organization.

Kuopio Stroke Symposium 2007

AIVOHALVAUSKUNTOUTUS 2007

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ONKO KUNTOUTUKSEN AJOITUKSELLA JA INTENSITEETILLÄ VAIKUTUSTA ENNUSTEEN KANNALTA?

Sinikka H. Peurala

Suomen gerontologian tutkimuskeskus, liikunta- ja terveystieteiden laitos, Jyväskylän yliopisto, Jyväskylä

Pitkittäistutkimusta, jossa olisi verrattu eri sairastumisen ajankohtina aloitettua ja toisaalta yhtäaikaisesti aloitettuja, mutta intensiteetiltään erilaisia kuntoutusinterventioita kontrolliryhmineen ei toistaiseksi ole. Tällaiselle tutkimukselle olisi kuitenkin tarvetta, vaikka se tulisi olemaan haasteellinen toteutettava niin käytännöiltään kuin eettisiltä näkökohdiltaan. Koko tutkimuksen aikainen kuntoutus tulisi kirjata suunnitellun mukaisten ryhmien todentamiseksi ja tutkimusinterventioiden ulkopuolinen fyysinen aktiivisuus/kuntoutuksen toteutuminen tulisi suunnitella, rajata ja kirjata huolellisesti.
Tässä esitelmässä tyydymme tarkastelemaan kuntoutuksen ajoitusta ja intensiteettiä olemassa olevien kuntoutusinterventioiden näkökulmista sekä katsomaan minkälaiselle toimintakyvyn tasolle niissä on päästy missäkin kuntoutuksen vaiheessa. Aluksi käyn läpi 2004 julkaistun systemaattisen kirjallisuuskatsauksen avulla löydettyjen terapeuttisen harjoittelun interventioiden sisältöjä ja intensiteettejä, jonka jälkeen tarkastelen esimerkinomaisesti uudempien tutkimusten ajoitusta, intensiteettiä ja tuloksia erilaisista harjoitusinterventioista.

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UPPER LIMB REHABILITATION IN STROKE

Jane Burridge

School of Health Professions and Rehabilitation Sciences, University of Southampton, Southampton, UK

Background

Approximately 75% of middle cerebral artery infarcts result in motor deficit, particularly the upper limb [Feys 1998] and 24% of patients have residual motor loss of the upper limb at three months post-stroke [Parker 1986] Various longitudinal studies have investigated the long-term outcome following stroke. Kwakkel estimated that between 30 and 60% of patients eventually regain functional arm movement [Kwakkel 1999] and Wade that half of all acute stroke patients starting rehabilitation will have a marked impairment of function of one arm and only about 14 % of these will regain useful upper limb function and argued that arm and hand function was more important than mobility in achieving independence following stroke [Wade 1983].

Conventional treatment

Half of all stroke patients receiving conventional rehabilitation fail to regain upper limb function (Broeks 1999). Although there is now overwhelming evidence that patients treated in specialist stroke units have a better outcome than those treated in general hospitals there is no conclusive evidence that one conventional physical or occupational therapy is more effective than another, and there has been no conclusive evidence to support the effectiveness of conventional therapy in the treatment of upper limb impairment following stroke [Hummelsheim 1999].

Measurement

While great advances have been made in most branches of medicine similar improvements have not occurred in rehabilitation. Rates and levels of recovery have changed little over the last decade and new treatments are slow to be accepted or robustly evaluated.

We need valid, reliable and objective measurement tools to:

- Improve understanding of the mechanisms underlying the functional problems
- Provide differential diagnosis enabling targeted treatment
- Measure the effect of treatment and evaluate new treatments.

New interventions

Constraint Induced Movement Therapy (CIMT) has shown promising results in clinical trials that are supported by neurophysiology and animal studies [Nudo]. CIMT however is extremely demanding on therapy time and therefore if it is to be widely used ways of providing independent intensive exercise that is interesting and motivating need to be found. Much attention has recently been focused on *Forced Use Therapy (FUT)* - the constraint without the shaping - and we have recently completed a small study using a low-cost hand mitten that was found to be safe, acceptable and effective [Burns 2007].

Robot therapy, popular in the US, has been slower to be accepted in Europe. Robot therapy may be an effective way to enable patients to practice independently and, with the addition of computer games or reality settings may be more motivating than conventional therapy activities.

Electrical Stimulation (ES) has been used for many years without gaining wide acceptance by therapists. Finding correct electrode positions and the hassle of applying surface

electrodes may explain the reluctance of therapists to us ES routinely. Small studies have shown modest but significant improvement in function with reduction in impairment. De Kroon, in her recent review of electrical stimulation for the upper limb, showed that stimulation triggered by voluntary activity was more likely to be effective. In a study in Southampton we have implanted seven patients with between 5 and 7 microstimulators in a minimally invasive procedure and developed a triggered open loop control system to provide functional movement that is responsive to the patients' demands. Results have been very varied, but in some cases dramatic improvement in function has been seen.
Combined therapies: In Southampton we are also currently investigating the potential of combining electrical stimulation and robot therapy. The motivation for this is to provide independent highly repetitive functionally based activities for people with little control of movement. ES is controlled by an Iterative Learning Control algorithm and preliminary experiments with unimpaired subjects have demonstrated the feasibility of the concept.

A concerted effort is now needed to improve upper limb rehabilitation following stroke. New interventions must be robustly evaluated using valid and reliable objective measurement tools.

KANTASOLUTERAPIAN MAHDOLLISUUDET AIVOHALVAUKSEN HOIDOSSA

Jukka Jolkkonen

Neurologian yksikkö, Kuopion yliopisto, Kuopio

Kantasolut ovat soluja, jotka pystyvät sekä uusiutumaan että tuottamaan erilaistuneita soluja. Kantasoluja on löytynyt lähes kaikista elimistä, myös keskushermostosta aivokammioiden reunalta. On kokeellista näyttöä, että kantasoluilla voitaisiin auttaa kudosvaurion korjautumista ja siksi kantasolut ovat erittäin kiinnostava ja lupaava tutkimusalue AVH-potilaiden hoidossa. Kantasolujen hyödyntämiseen liittyy kuitenkin vielä paljon käytännön ongelmia kuten siirrettävän solukon saatavuus, tehokkain antotapa ja ajoitus. Samoin eettiset kysymykset ovat olleet esillä.

Yksi potentiaalinen ja eettisesti ongelmaton kantasolujen lähde on istukkaveri. Istukkaveren kantasolujen siirto on jo vakiintunut vaihtoehto pahanlaatuisten veritautien hoidossa. Suonensisäisesti annettuna istukkaveren solut näyttäisivät nopeuttavan kuntoutumista kokeellisissa malleissa. Yhteistyössä SPR Veripalvelun kanssa olemme testanneet erilaisia istukkaveren fraktioita (mm. lin^-, $CD34^+$), mutta emme ole pystyneet osoittamaan niillä merkittävää tehoa. Soluja ei myöskään löydetty aivokudoksesta histologisilla värjäyksillä. Tarkemmissa tutkimuksissa, joissa seurattiin radioaktiivisesti leimattujen solujen kulkeutumista elimistössä (SPECT) havaittiin, että suuri soluista päätyi sisäelimiin (mm. keuhkot, maksa, perna). Näin systeeminen annostelu ei todennäköisesti toimi vaikka se AVH-potilaiden kannalta olisi helppo ja turvallinen antoreitti.

Kantasoluja voidaan istuttaa myös suoraan aivokudokseen. Valitettavasti suuri osa istutetuista soluista kuolee 1-2 kk sisällä. Ei ole myöskään vakuuttavaa näyttöä siitä, että istutetut solut erilaistuisivat neuronaaliseen suuntaan tai että ne muodostaisivat toiminnan kannalta relevantteja yhteyksiä. On viitteitä, että kantasolujen käyttäytymistä voitaisiin ohjata kuntoutuksen avulla. Olemme osoittaneet, että esimerkiksi tehokuntoutusta mallintava rikastettu ympäristö lisää aivokuorelle istutettujen hiiren kantasolujen (SVZ) hengissäsäilymistä ja kulkeutumista infarktin suuntaan. Osa soluista ilmensi myös neuronaalisia proteiineja. Mielenkiintoista oli, että sensorimotorinen toipuminen oli näillä eläimillä kontrolleja nopeampaa.

Olemme testanneet myös ihmisen alkion kantasoluja. Solut ovat kasvatettu GMP standardien mukaisesti ilman eläinperäisiä proteiineja (Solu- ja kudosteknologiakeskus Regea), mikä mahdollistaa siirtymisen alkuvaiheen potilaskokeisiin heti kun tarvittava kokeellinen näyttö solusiirtojen tehosta ja turvallisuudesta on käytettävissä. Myös näillä soluilla saatiin eläinten sensorimotorista kuntoutumista tehostettua.

Kantasoluhoitojen tehosta alkaa siis olla yhä enemmän kokeellista näyttöä. Onko kyse todellisesta menetettyjen solujen korvautumisesta vai aivojen omien korjausmekanismien aktivoitumisesta on vielä epäselvää. Tarvitaankin vielä lisätutkimuksia ja saatujen tulosten kriittistä arviointia ennen siirtymistä potilaskokeisiin.

NEGLECT-ILMIÖ JA SEN KUNTOUTUS

Riitta Luukkainen-Markkula

Suomen aivotutkimus- ja kuntoutuskeskus Neuron, Kuopio

Neglect-oireisto esiintyy yleisimmin laajojen oikean aivopuoliskon vaurioiden jälkeen. AVH-potilaista 30%:lla esiintyy neglectiä heti sairastumisen jälkeen, pysyväksi oireisto jää vain 2% potilaista (Ringman et al., 2004). Varhaisimmissa teorioissa häiriötä pidettiin sensorisena, mutta kysymys ei ole näkemisen, kuulemisen, tuntemisen tai liikkeiden ensisijainen häiriö (Mesulam, 1994). Nykyisin uskotaan, että vasemmanpuoleisten ärsykkeiden huomiotta jättämisessä on kysymys vaurioituneen oikean aivopuoliskon puutteellisesta valmiustilasta käsitellä sisään tulevaa informaatiota (Berti & Rizzolatti, 1992). Vasemman puoleisen havaintoavaruuden huomiotta jättäminen voi ilmetä eriytyneesti oman kehoin tasolla (body space neglect), käden ulottuvuuden tilassa (peripersonal tai reaching space neglect) tai silmän kantaman ulottuvuudessa (far space tai extrapersonal space neglect). Huomioimattomuutta voi esiintyä myös muistissa ja mielikuvien tasolla (representational neglect). Motorinen neglect ilmenee vasensuuntaisten liikkeiden puuttumisena, viivästymisenä tai hidastumisena kehossa, pään ja silmien liikkeissä. Extinctiosta puhutaan, kun kilpailutilanteessa vasemmanpuoleiset ärsykkeet jäävät huomiotta (Robertson & Halligan, 1999). Neglectin visuospatiaalisia häiriöpiirteitä on 1960-luvulta saakka kuntoutettu opettamalla tahdonalaisesti huomioimaan vasemmalle. Harjoittelu edellyttää kompensatoristen strategioiden oppimista ja vakiinnuttamista suurella määrällä toistoja. Metodin ongelmana on ollut heikko yleistyvyys paperitehtävistä arkipäivän tilanteisiin (Manly, 2002). Viime vuosina on kehitelty menetelmiä, jotka vaikuttavat epäspesifisti oikean hemisfäärin toimintaa aktivoiden: on kokeiltu kalorista ja vestibulaarista stimulaatiota, optokineettistä metodia, niskalihasten sähköistä stimulaatiota, prismalasikuntoutusta ja käden aktivointia. Näiden menetelmien etuna on ei-tahdonalaisuus: ne korjaavat havaintovääristymää automaattisen reagoinnin tasolla. Ongelmana on kuitenkin se, että korjaava vaikutus jää useimmiten lyhytkestoiseksi. (Kerkhoff, 2003). Neuronissa on verrattu käden aktivoinnin metodia tavanomaiseen kuntoutukseen neglect-potilailla akuutti-, subakuutti- ja kroonisessa vaiheessa. Kolmen viikon kuntoutusjakson aikana akuutti- ja subakuuttivaiheen potilaat kuntoutuvat yleisimmillä mittareilla mitattuna molemmilla metodeilla: 20-30 tuntia käden aktivointia näyttäisi toimivan neglectin tiettyihin oirepiirteisiin yhtä hyvin kuin 10 tuntia perinteistä neuropsykologista kuntoutusta yhdessä toimintaterapian ja fysioterapian kanssa.

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PUHETERAPIAN UUDET MENETELMÄT JA NIIDEN AIVOPERÄISET MEKANISMIT

Matti Lehtihalmes

Suomen kielen, informaatiotutkimuksen ja logopedian laitos**,** Oulun yliopisto, Oulu

Akuuttivaiheen yli kestäviä neurokognitiivisia kielellisiä tai puhemotorisia ongelmia esiintyy noin 30 prosentilla aivoverenkiertohäiriön sairastaneilla tai aivovamman saaneilla potilailla. Varsinaisten afaattisten tai dysartristen häiriöiden lisäksi myös pragmaattisen kommunikoinnin häiriöt ovat yleisiä, joskin suurelta osin vielä vähän tunnettuja. Nämä erilaiset kommunikoinnin häiriöt aiheuttavat huomattavan psykososiaalisten ongelmien riskin. Lisäksi ne heikentävät sekä sairastuneen että hänen läheistensä elämänlaatua. Kommunikoinnin häiriöt muodostavat suuren kuntoutuksellisen haasteen, mikä lisää merkittävästi puheterapiatutkimuksen tarvetta.

Viimeisten kymmenen vuoden aikana on tapahtunut selvä paradigman muutos neurokognitiivisten kommunikointihäiriöiden kuntoutusajattelussa, jolle WHO:n vuosituhannen alussa julkistama uusi ICF-luokitus on antanut hyvän pohjan. Kielen käyttötaitojen ja yleensä pragmaattisten kommunikointitaitojen tutkimus ja kuntoutus on lisääntynyt selvästi. Yksinomaan potilaaseen kohdistuneet terapiatoimet ovat laajentuneet aiempaa selvemmin myös hänen läheistensä ohjaamiseen ja tukemiseen.

Puheterapian tarkempi kohdistaminen on selvästi lisääntynyt. Potilaan ”yleinen stimulointi ja aktivointi” ei johda niin hyviin tuloksiin kuin kuntoutuspolun eri vaiheissa sopivasti avainseikkoihin täsmennetty terapia. Lisäksi kuntoutuksen intensiivisyys on osoittautunut olennaisen keskeiseksi tuloksia parantavaksi tekijäksi. Kuntoutuksen intensiivisyyteen yhdistetyt erilaiset pakotetut menetelmät (esim. Constraint-induced aphasia therapy, CIAT) ovat antaneet hyvin lupaavia tuloksia. Näiden intensiivisten kuntoutusmenetelmien on myös osoitettu aiheuttavan aivojen kielellisessä verkostossa selviä plastisia terapiasidonnaisia muutoksia.

Lääkehoidon yhdistämistä puheterapiaan on myös enenevästi tutkittu viime vuosina. Toistaiseksi tulokset ovat olleet osin lupaavia, osin ristiriitaisia. Uusi teknologia, kuten transkraniaalinen magneettistimulaatio (TMS), on tullut käyttöön myös afasiaterapiassa, toistaiseksi kuitenkin vielä tutkimuksen tasolla. Lupaavia tuloksia ovat antaneet myös uudet neurokirurgiset tekniikat, kuten Parkinsonin tautiin liittyvän dysartrian hoidossa käytetty subtalaamisen tumakkeen stimulaatio (deep brain stimulation). Tämän on havaittu lieventävän motoristen oireiden ohella näillä potilailla usein vaikea-asteisina esiintyviä dysartrisia puheoireita.

AIVOHALVAUS- JA DYSFASIALIITTO RY

Heli Taskinen

Aivohalvaus- ja dysfasialiitto ry, Turku

Aivohalvaus- ja dysfasialiitto ry on kansanterveys-, vammais- ja potilasjärjestö, joka tukee edustamiensa ryhmien arjessa selviytymistä. Liiton toiminnan piirissä on aivohalvaus- ja afasiayhdistyksiä ja dysfasiayhdistyksiä sekä näiden alueellisia kerhoja yli 100 paikkakunnalla. Jäseniä yhdistyksissä on noin 11 000. Aivohalvaus- ja dysfasialiiton keskeiseen toimintaan kuuluvat muun muassa jäsenten tukeminen ja oikeuksien valvonta, oikean ja ajankohtaisen tiedon tarjoaminen, kuntoutuksen asiantuntijuus, kouluttaminen ja kotimainen sekä kansainvälinen yhteistyö. Liiton perustehtävä toteutuu konkreettisimmin alueellisessa työssä, jonka tavoitteena on tukea aivoverenkiertohäiriön sairastaneita ja heidän läheisiään sekä dysfaattisia lapsia ja heidän perheitään, välittää tietoa ja valvoa sosiaaliturvan palveluihin liittyvien oikeuksien toteutumista ja terveydenhuollon palvelujen saatavuutta.

Liitto viestii aktiivisesti ja kustantaa muun muassa AVH-aivoverenkiertohäiriöiden erikoislehteä sekä Dysfasia-puheen- ja kielenkehityksen erikoislehteä. Vuosittain järjestettävät valtakunnalliset AVH-päivät ja Dysfasiaseminaari ovat tärkeä osa viestintä- ja koulutustoimintaa.

Liitto järjestää edustamilleen ryhmille sopeutumisvalmennuskursseja ja muita kuntoutuspalveluja sekä virkistystoimintaa eri puolilla Suomea. Sopeutumisvalmennus on lakeihin perustuvaa lääkinnällistä kuntoutusta. Aivohalvaus- ja dysfasialiitto ry järjestää sopeutumisvalmennuskursseja kuntoutumisen eri vaiheissa oleville. Kurssit toteutetaan sekä Aivohalvaus- ja dysfasialiiton Erityisosaamiskeskus Suvituulessa Turussa että yhteistyökursseina kuntoutuskeskusten kanssa eri puolilla Suomea.

Puhevammaisten asioita ajetaan Aivohalvaus- ja dysfasialiitossa valtakunnallisesti, alueellisesti ja kansainvälisesti. Liiton Kommunikaatiokeskuksen tehtävänä on kehittää ja edistää puhetta tukevien ja korvaavien kommunikaatiokeinojen, tietokoneavusteisen kuntoutuksen sekä puhevammaisten tulkkipalvelun käyttöä afaattisten ja dysfaattisten henkilöiden kuntoutuksessa. Tavoitteena on osallisuus projekteissa, jotka tukevat afaattisten sosiaalista kuntoutusta sekä lisätä tietokoneavusteisen kuntoutuksen mahdollisuuksia dysfaattisilla ja afaattisilla asiakkailla.

Kansainvälisessä yhteistyössä liitto on mukana Association Internationale Aphasie:ssa (AIA), joka on kansainvälinen afaattisten sairastuneiden etujärjestö. Tarkoituksena on edistää kommunikaatiotietoutta ja tukee afaatikkojen terapeuttista, kuntoutuksellista ja sosiaalista palaamista yhteiskuntaan. Pohjoismainen afasianeuvoston (Nordic aphasia association) afasia-yhteistyö sisältää mm. puhevammaisten ja heidän perheidensä jatkuvaa oikeuksien valvontaa, kokemusten vaihtoa, tiedottamista sekä yhteisiä projekteja ja seminaareja. Euroopan tasolla toimiva yhteistyö SAFE (Stroke Alliance for Europe) panostaa tiedotuksessa erityisesti aivoverenkiertohäiriöiden ennaltaehkäisyyn, mutta myös hoitoketjun toimivuuteen kansainvälisen aivohalvauspäivän yhteydessä 10. toukokuuta. Liiton keskustoimisto sijaitsee Turussa, Erityisosaamiskeskus Suvituulessa, jossa työskentelee tiedotus-, hallinto- ja sopeutumisvalmennushenkilöstöä. Suvituulessa on monipuoliset tilat sopeutumisvalmennukseen, koulutukseen ja majoitukseen. Myös liiton Kommunikaatiokeskus sijaitsee Suvituulessa.

AIVOVERENKIERTOHÄIRIÖN SAIRASTANEIDEN KUNTOUTUKSEN TOTEUTUMINEN SUOMESSA (AVH-KUNTOUTUSPROJEKTI)

Teemu Takala

Aivohalvaus- ja dysfasialiitto ry, Turku

Tausta

Noin 14000 suomalaista sairastuu vuosittain aivoverenkiertohäiriöön (AVH). AVH on Suomessa kuten muuallakin länsimaissa kolmanneksi yleisin kuolinsyy. AVH on myös eniten sairaalahoitopäiviä ja pysyvää invaliditeettia aiheuttava sairausryhmä. Lokakuussa 2006 ilmestyneessä Aivoinfarktin käypä hoito –suosituksessa todetaan, että aivoinfarktipotilaiden tulisi saada hoitoa moniammatillisessa kuntoutusyksikössä, ja että aivoinfarktipotilaat hyötyvät tällaisesta kuntoutuksesta riippumatta iästä, sukupuolesta tai sairauden vaikeusasteesta. Moniammatillisesti toimivassa kuntoutusyksikössä sairastumisen alkuvaiheessa hoidettujen kuolleisuus ja pysyvään laitoshoitoon jäämisen riski on pienempi kuin tavallisella vuodeosastolla hoidettujen. Tehokas kuntoutus näkyy myös lyhentyneenä hoitoaikana, vähäisempänä vammaisuutena ja parempana elämänlaatuna

Aivoverenkiertohäiriöiden kuntoutuksesta ei ole Suomessa tehty systemaattista selvitystä. Aikaisempien raporttien perusteella voidaan arvella, että kuntoutuksen toteutumisessa on alueellisesti isoja eroja maassamme.

Tavoite

Tutkimusprojektin tavoitteena on selvittää AVH-kuntoutuksen nykytila ja resurssit perusteellisesti koko maassa. Selvitys luo pohjaa AVH-kuntoutuksen valtakunnalliselle kehittämiselle ja sen tulosten odotetaan johtavan hoitokäytäntöjen yhtenäistämiseen ja hoidon vaikuttavuuden parantumiseen lähivuosina.

Aineisto ja menetelmät

Tutkimuksen ensimmäisessä vaiheessa vuonna 2007 on tarkoitus haastatella henkilökohtaisesti Suomen kaikkien yliopistollisten ja keskussairaaloiden AVH-kuntoutuksesta vastaavat lääkärit ja tarvittaessa muutakin kuntoutukseen perehtynyttä henkilökuntaa. Tutkimuksen seuraavassa vaiheessa selvitetään kyselylomakkein AVH-kuntoutuksen resursseja Suomen terveyskeskuksissa ja AVH-kuntoutusta antavissa kuntoutuslaitoksissa. Tämä Aivohalvaus- ja dysfasialiiton kolmivuotinen projekti on Raha-automaattiyhdistyksen rahoittama.

Tulokset

Tutkimus on käynnistynyt vuoden 2007 alussa ja haastattelut ovat meneillään. Ensimmäisten tulosten analysointi on alkamassa ja loppuraportin on suunniteltu ilmestyvän 2008-2009.

AIVOVERENKIERTOHÄIRIÖT JA EPILEPSIA

Reetta Kälviäinen

Kuopion Epilepsiakeskus, Kuopion yliopistollinen sairaala, Kuopio

Noin 1 % eli 53 000 suomalaista sairastaa epilepsiaa. Jatkuvaa epilepsialääkitystä tarvitsee 36 000 henkilöä (n. 0,7 % väestöstä) ja vaikeahoitoista epilepsiaa sairastaa 9000 henkilöä (n. 20 – 25% kaikista epilepsiaa sairastavista). Epilepsiaan voi sairastua missä iässä tahansa, yleisimmin varhaislapsuudessa tai ikääntyneenä. Iäkkäänä epilepsiaan sairastuvien osuus on noussut tasaisesti. Tällä hetkellä epilepsiaa sairastaa yli 65-vuotiaista noin 1,5 %, eli epilepsiaa esiintyy yli 65-vuotiailla kaksi kertaa enemmän kuin 25-65 -vuotiailla. Tämä johtuu eliniän noususta ja ikääntymiseen liittyvien sairauksien yleistymisestä. Ikääntymiseen liittyviä epilepsiaa aiheuttavia sairauksia ovat esim. aivoverenkierron häiriöt, dementoivat sairaudet kuten Alzheimerin tauti, aivovammat ja aivokasvaimet.

Äkilliseen aivoverenkiertohäiriöön liittyen noin 2% potilaista saa varhaisen tajuttomuuskouristuskohtauksen ensimmäisenä päivänä ja 4-6% potilaista ensimmäisen viikon sisällä aivoverenkiertohäiriöstä. Nämä varhaiset äkilliset kohtaukset eivät ole vielä epilepsiaa, vaan vielä aivoverenkiertohäiriön akuutteja oireita. Yli viikon kuluttua aivoverenkiertohäiriöstä ilmenevät epileptiset kohtaukset sen sijaan kuvastavat jo taipumusta saada jatkossakin epileptisiä kohtauksia aivoverenkiertohäiriön aivoihin synnyttäneen vaurion seurauksena eli ne ovat merkki epilepsian kehittymisestä. Suomessa tehdyssä tutkimuksessa todettiin, että epilepsia kehittyi 17 %:lle kuntoutusta tarvitsevista aivoverenkiertohäiriöpotilaista. Muissa tutkimuksissa riski on vaihdellut 5-20 % välillä. Riski on suurempi erilaisissa aivoverenvuodoissa kuin aivoinfarkteissa ja aivojen kuorikerroksen vaurioissa kuin aivojen syvien osien verenkiertohäiriöissä, samoin jos aivoverenkiertohäiriö uusiutuu. Kaiken kaikkiaan henkilö, jolla on ollut aivoverenkiertohäiriö, on 20-kertaa suuremmassa riskissä saada epilepsia kuin samanikäinen toinen henkilö, jolla ei ole ollut aivoverenkiertohäiriötä. Yleisimmin epilepsia kehittyy ensimmäisen vuoden kuluessa aivoverenkiertohäiriöstä. Epilepsian kehittyminen on 8 kertaa todennäköisempää, jos henkilöllä on esiintynyt varhaisvaiheen kohtauksia aivoverenkiertohäiriötä seuranneen ensimmäisen viikon aikana. Epilepsiakohtausten kehittyminen voi olla seurausta myös aivoverisuonen paikallisesta pullistumasta, kasvaimesta tai epämuodostumasta seuranneesta viereisen aivokudoksen vaurioitumisesta.

Aivoverenkiertohäiriön aiheuttamat epileptiset kohtaukset ovat paikallisalkuisia ja saavat alkunsa kyseisen aivoverenkiertöhäiriön aiheuttaman arven viereiseltä aivoalueelta. Aivoverenkiertohäiriön jälkeen sopivat kaikki paikallisalkuisen epilepsian lääkkeet. Hoidon tavoitteena on kohtauksettomuus. Valtaosalla (75-80%) epilepsiaa sairastavista kohtaukset saadaan hyvin hallintaan lääkkeillä. Lääkkeitä on käytettävä useita vuosia, joskus koko loppuelämän ajan. Jos kohtaukset eivät lopu ensimmäisellä lääkkeellä, kokeillaan vielä toista lääkettä ainoana lääkkeenä. Tämän jälkeen kohtauksien jatkuessa siirrytään yhdistelmälääkitykseen. Noin 20-25%:lla potilaista kohtaukset kuitenkin jatkuvat lääkehoidosta huolimatta. Osaa heistä voidaan auttaa leikkaushoidon avulla. Leikkaushoito ei käytännössä tule kyseeseen aivoinfarktin jälkeisessä epilepsiassa, mutta saattaa joskus tulla kyseeseen erilaisten aivoverisuonimuutosten tai niitä seuranneiden vuotojen aiheuttaman vaikean epilepsian hoidossa.

VOIKO KUNTOUTUMISTA KUVANTAA?

Ritva Vanninen

Radiologian klinikka, Kuopion yliopistollinen sairaala, Kuopio

Taustaa

Aivoverenkiertohäiriöt ovat maailmanlaajuisesti kolmanneksi tärkein kuolinsyy ja niihin kuolee Suomessa vuosittain noin 5500 ihmistä ja yli 4000 ihmistä jää vuosittain vaikeasti vammautuneeksi. Aivohalvauksen kuntoutuksessa on tarjolla useita lupaavia uusia menetelmiä sekä akuutissa että kroonisessa vaiheessa ja näiden menetelmien tutkimustyö on aktiivista. Useimmilla potilailla todetaan ainakin jonkin verran spontaania toiminnallista kuntoutumista ensimmäisinä infarktia seuraavina viikkoina ja kuukausina. Koska tuhoutuneiden neuronien ei oleteta merkitsevästi uusiutuvan aikuisen ihmisen aivokudoksessa, tapahtunee kuntoutuminen pääosin säästyneiden aivoalueiden reorganisaation pohjalta. Reorganisoitumisen mahdollisuudesta huolimatta useimmille potilaille jää huomattavia puutosoireita jotka vaikeuttavat selviytymistä jokapäiväisessä elämässä.

Parhaimmillaan moderni funktionaalinen neurokuvantaminen voi auttaa ymmärtämään kuntoutumisen taustalla olevia mekanismeja. Mikäli kuntoutumista kyettäisiin luotettavasti arvioimaan ja dokumentoimaan uusilla kuvantamismenetelmillä ja neurofysiologisilla tutkimusmenetelmillä, tällä olisi myös käytännön merkitystä ensinnäkin sen potilaiden alaryhmän valinnassa, joka todennäköisesti tulisi eniten hyötymään intensiivisestä kuntoutuksesta. Voitaisiinko kuntoutusmuodon valinta ja jakson ajoitus ja intensiivisyys tulevaisuudessa räätälöidä potilaskohtaisesti uusien funktionaalisten kuvantamis-menetelmien avulla?

Aivohalvauksen kuvantaminen

Akuutin vaiheen kuvantamisessa on päämääränä ensinnäkin iskeemisen ja vuodosta johtuvan infarktin erotusdiagnostiikka. Iskeemisissä aivohalvauksissa pyritään infarktin karakterisaatioon, sen koon, sijainnin ja iän määrittämiseen ja mahdollisen penumbran osoittamiseen. Lisäksi pyritään arvioimaan infarktin etiologiaa ja poissulkemaan erotusdiagnostiset vaihtoehdot.

Korkeatasoinen anatominen kuvantaminen on perusvaatimus tutkittaessa kuntoutumista, ja tähän tarvitaan korkeakenttämagneettikuvausta. Anatomisten perussekvenssien lisäksi voi olla hyötyä diffuusiokuvauksesta infarktialueen arvioinnissa, ja diffuusiotensorikuvaus ja traktografia voivat antaa lisätietoa valkean aineen ratayhteyksien säilymisestä. Suskeptibiliteettipainotteinen kuvaus näyttää herkästi veren hajoamistuotteet kroonisessakin intracerebraalivuodon tai hemorrhagisen infarktin vaiheessa, ja magneettiangiografia tuo lisätietoa aivovaltimoiden rekanalisaatiosta embolian jälkeen. Perfuusioreserviä voitaisiin arvioida MR-perfuusiokuvauksen avulla.

Funktionaalinen neurokuvantaminen

Funktionaalisen neurokuvantamisen tärkeimmät kuntoutumisen tutkimiseen sopivat metodit ovat funktionaalinen magneettikuvaus fMRI, PET, SPECT, ja TMS. Lepotilassa tehty aivoperfuusion gammakuvaus ennen ja jälkeen intensiivisen kuntoutuksen on osoittanut lisääntynyttä perfuusiota motorisilla alueilla. PETin avulla on tutkittu mm. harjoitteluun liittyvää plastisuutta ja tehtäväkohtaista motorista uudelleenoppimista. Tärkein kuvantamismenetelmä on kuitenkin fMRI ja BOLD-menetelmä. Lukuisia erilaisia aktiivisia, joskus passiivisiakin motorisia tehtäviä on käytetty kirjallisuudessa kuntoutumisen fMRI-tutkimuksissa.

Spontaanista aivojen kuntoutumisesta tiedetään, että parempi toipuminen liittyy säästyneeseen aktiivisuuteen primäärillä motorisella aivokuorella. Osa toipumisesta voi perustua reorganisaatioon, jolloin osa motorisesta aktivaatiosta siirtyy sekundaarisille kuorikerrosalueille, osa intaktiin hemisfääriin. Osa toimintakyvyn palautumisesta alkuvaiheessa selittyy iskeemisen, mutta vitaalina säilyneen penumbra-alueen toiminnallisella toipumisella ja osa diaschisiksesta palautumisella.
Kuntoutuksen vaikutuksesta on fMRI:n avulla todettu useimmiten lisääntynyttä aktivaatiota leesion puoleisella primäärisellä motorisella aivokuorella, dorsaalisella premotorisella alueella ja suplementaarisella motorisella alueella. Yksittäisissä tutkimuksissa on todettu myös kontralateraalisen hemisfäärin lisääntynyttä aktiivisuutta. Lisääntynyttä aktiivisuutta voidaan saavuttaa hoitotoimenpiteillä jopa vuosia primääritapahtuman jälkeen.

Lopuksi
Uusien kuntoutusmenetelmien tieteellisessä tutkimuksessa on tärkeää kyetä erottamaan toisistaan hoidosta johtuva reorganisaatio ja spontaani toipumisprosessi. Koska aivohalvauksen taustalla voi olla suuri kirjo leesioita joiden lokalisaatio, koko ja etiologia poikkeavat toisistaan, korkeatasoisissa tutkimuksissa tarvitaan riittävän suuri potilasjoukko ja verrokkipotilasjoukko, joille molemmille tehdään funktionaalinen neurokuvantaminen ennen ja jälkeen kuntoutusjakson. Tähän asti kuvantamistutkimuksissa on ollut mukana vain hyvin pieniä potilasaineistoja ja tutkimuksiin on valikoitunut potilaita joiden lähtötilanne ja ko-operaatiokyky on ollut poikkeuksellisen hyvä. Lisäksi on keskitytty motoriseen toipumiseen, ja vähemmän tutkimuksia on tehty puheen tai neglectin kuntoutumisesta. Funktionaalisen kuvantamisen nopea kehitys mahdollistaa entistä yksityiskohtaisemman informaation saamisen aivokudoksen regeneraatiokyvystä ja voi tulevaisuudessa olla apuna kuntoutusmenetelmien kehittämisessä ja räätälöimisessä yksityiselle potilaalle.

HOITOTYÖN MERKITYS AIVOHALVAUSKUNTOUTUKSESSA

Katri Vehviläinen-Julkunen

Hoitotieteen laitos, Kuopion yliopisto, Kuopion yliopistollinen sairaala, Kuopio

Aivohalvaus koskettaa sen yleisyyden vuoksi maassamme niin potilaiden kuin heidän omaistensa jokapäiväistä elämää. Kuntoutumisprosessien kehittymiseen on todettu vaikuttavan monia näyttöön perustuvia käytänteitä. Moniammatillisen kuntoutuksen hyöty on osoitettu myös tutkimuksissa. Hoitotyön merkitystä aivohalvauskuntoutuksessa korostaa aivoinfarktin Käypä hoito –suositukset, joissa kuntouttavalla hoitotyöllä on keskeinen merkitys. Hoitotyön merkitystä tällä alueella on tutkittu kansainvälisesti viime vuosikymmenen alusta alkaen. Keskeisenä on ollut keskustelu hoitajien toiminnan painotuksen ymmärtämisenä lähinnä perushoidon toteuttajina ja passiivisena kuntoutuksen mahdollistajana kuin aktiivisena potilaiden kuntoutumisen edistäjinä. Hoitajat ovat kokeneet oman roolinsa osin epäselväksi moniammatillisessa ryhmässä tutkimusten mukaan.

Tutkimustiedon analyysin perusteella voi todeta, että hoitajien osaamista ja tehtäviä aivohalvauspotilaiden kuntoutuksessa on selvitetty vähän maassamme ja myös kansainvälisesti. Tutkimuksissa hoitotyön tehtäväksi kuvataan mm. potilaiden sairastumisprosessin käsittelyn helpottaminen ja ylipäätänsä potilaiden kunnon huonontumisen estämistä. Hoitajien potilaslähtöinen toiminta ja yleensä myönteinen suhtautuminen vaikuttaa tutkimusten mukaan myönteisesti kuntoutumiseen. Näyttää kuitenkin siltä, että hoitotyön merkitystä aivohalvauskuntoutuksessa tulee tutkia interventiotutkimuksen asetelmin ja tarkastella laajasti myös hyvinvoinnin ja elämän laadun näkökulmista. Moniammatillinen yhteistyö edellyttää myös hoitotyön merkityksen tunnistamista ja tunnustamista aivohalvauskuntoutuksessa parhaan mahdollisen tuloksen saavuttamiseksi potilaiden hyväksi.

Kuopio Stroke Symposium 2007

POSTERS

Cafeteria, Microteknia

P1

LATENT HERPES INFECTION REACTIVATION CONTAMINATIONS AT THE ACUTE ISCHEMIC STROKE AND ITS PHARMACOCORRECTION

A.E. Kulchikov[1], A.N. Makarenko[2]

[1]Oryol Regional Hospital, Oryol, Russia; [2]Oryol State University, Oryol, Russia

The target: the study of possibility of reactivation of latent herpetic infection in patients with acute ischemic stroke (AIS) and its correction by Cerebrolysin (“Ebewe”, Austria).
Materials and methods: The patients of both sexes in the age from 55-85 years with primary AIS, in which the DNA of herpes simplex virus (HSV) was marked by means of polymerase chain reaction (PCR), were included in the study.
Results: PCR on HSV in blood was positive in 98 (27,7%) from 353 patients with acute ischemic stroke. Exactly these 98 patients were included in the study and divided in 2 groups: basic and control. Cerebrolysin was injected in the dose of 10 ml intravenously during 10 days, in the first 12 hours from the onset of the disease. To the 10th day of AIS in the basic group the accelerated restoration of neurologic dysfunctions was observed (according to NIH-NINDS scale, modified Rankin scale and Barthel index), the reduction of infectious syndrome level by SIRS scale, the reduction of quantity of positive PCR and EMIA on HSV, normalization of the disturbed indexes of immune system ($p<0,01$) were marked.
Conclusions: In AIS in patients in terms of immunodepression the reactivation of latent herpetic infection is marked in 27,7 %. Cerebrolysin is the effective drug in therapy of this complication of stroke due to neuroimmunoresolving action. These patients were divided in 2 groups: basic (receiving standard therapy and Cerebrolysin) and control (receiving standard therapy).

P2

WHY ARE STROKE PATIENTS PRONE TO DEVELOP DEMENTIA? (RISK FACTORS AND MECHANISMS OF POST-STROKE DEMENTIA)

Marjaneh Akbarzadeh[*1], Reza Akbarzadeh[2], Reyhaneh Akbarzadeh[1]

[1]Department of Psychology, Russian University of Economics and Culture, Moscow, Russia; [2]Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Dementia syndromes associated with cerebrovascular diseases were commonly recognized as an immediate consequence of stroke. Frequency of post stroke dementia (PSD) is high, and stroke considerably increases the risk of dementia.
Aims and Method: The aim of this review is to determine, mechanisms of dementia in stroke patients and identifies predictive factors for PSD. Especially those factors usually associated with cerebrovascular disease and degenerative dementia.
Results: Dementia is frequent after ischemic or hemorrhagic stroke. Dementia after stroke may be due to the cumulative effect of vascular and degenerative changes. Several factors, including type of stroke, recurrent episodes, the site and laterality of the lesion(s), volume of cerebral infarction, medial temporal lobe atrophy, and coexistent neurodegenerative pathology predict the degree of impairment. Aphasia, diabetes mellitus, atrial fibrillation, and depression are listed among other biologic factors that further exacerbate cognition and affect long-term survival. Besides sharing risk factors with stroke, dementia with multiple small or large brain infarcts is also associated with non-vascular risk factors such as high alcohol consumption, psychological stress in early life, lower formal education, and occupational exposures.
Conclusion: Prevention of stroke should reduce the morbidity and mortality associated with PSD. In addition, management of PSD with secondary prevention treatments could reduce occurrence of further strokes. Cholinesterase inhibitors may be beneficial not only in Alzheimer's disease associated with cerebrovascular lesions, but also for the treatment of cholinergic dysfunction arising from pure vascular dementia. Better knowledge of the risk factors for PSD, including environmental and genetic factors, should increase the effectiveness of preventive strategies in patients with this condition.

P3

IS POST STROKE DEPRESSION AN UNRESOLVED ISSUE? RESEARCH INTO THE SPECIFICITY OF DEPRESSION AFTER STROKE

Reyhaneh Akbarzadeh[*1], Reza Akbarzadeh[2], Marjaneh Akbarzadeh[1]

[1]Department of Psychology, Russian University of Economics and Culture, Moscow, Russia; [2]Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Post stroke depression (PSD) is one of the most frequent complications of stroke, affecting approximately 20% to 40% of all patients. In spite of the importance of this neuropsychiatric disorder, little attention has been given to the prevention of post stroke depression.
Aims and Method: This article provides an overview of depression diagnosis in stroke, reviews the epidemiology of post stroke depression and its associated morbidity and mortality, and reviews existing evidence on the treatment and prevention of post stroke depression.
Results: Depression after stroke is common and many people are not routinely assessed for depression after stroke, and only a minority are properly diagnosed and treated. In nearly a quarter of all PSD patients, depressive symptoms persist over at least 2 years. Several longitudinal studies have identified different factors which may increase the risk of PSD. Post stroke depression has been linked to higher mortality after stroke. The risk factors that have been associated with the occurrence of post stroke depression are: functional and cognitive impairment, previous history of depression and stroke, hypercortisolism, poor social support and stroke neuroanatomic correlates. Controversial risk factors are age, socioeconomic status (SES), prior social distress, dependency in regard to activities of daily living (ADL), and sex. Early diagnosis and adequate therapy are still necessary in stroke rehabilitation.
Conclusion: Post-stroke depression (PSD) is a very frequent and important consequence of stroke, but, in spite of the high number of papers aiming to clarify various aspects of this disorder, controversies about its incidence, its (biological or psychological) determinants, its consequences and its treatment still persist. The results suggest that identifying psychiatric history and preventing social deterioration and impairment should be part of multidisciplinary efforts to care for post stroke patients. We believe that a number of post stroke depressive disorders are likely to be the result of specific changes in brain pathology and neurophysiology. Nevertheless, there are relatively few hypotheses about the pathophysiology of post stroke depression.

P4

SCANDINAVIAN CANDESARTAN ACUTE STROKE TRIAL (SCAST)

Dag Aarhus, Ragnhild Iuell, Eivind Berge

Department of Internal Medicine, Ullevål University Hospital, Oslo, Norway

Background: It has long been a controversy whether high blood pressure should be lowered in the acute phase of stroke. ACCESS (Stroke 2003;34.1699) suggested a beneficial effect of the angiotensin receptor blocker candesartan in the acute phase of stroke, but these findings needs to be confirmed in new, larger trials.
Methods: SCAST is an international randomnised, placebo-controlled, double blind trial of candesartan threatment during acute stroke. Patients presenting within 30 hours of stroke (ischaemic or haemorrhagic) and with systolic blood pressure >140 mm Hg are randomly assigned to candesartan or matching placebo for 7 days (doses increasing from 4 to 16 mg once daily). The follow-up period is 6 months. Primary effect variables: i) Death or major disability; ii) Vascular events (Vascular death, myocardial infarction or stroke). Target recruitment; 2,500.
Status: Around 900 patients have been included during the first 23 months of the trial (centres in Sweden, Norway, Denmark and Belgium). Mean age 72 years; Blood pressure 172/89 mm Hg; Ischaemic stroke 85%, Haemorrhagic stroke 15%; Median SSS score 42 (IQR 31-51). The trial has now entered the main phase and we are expanding the trial to new centers in Finland, and other North-European countries. Preliminary, blinded results will be presented at the meeting. Funding: Basic funding from Norwegian health authorities. Trial drugs and unconditional grants from AstraZeneca. Participating centres receive a limited economical compensation.
Conclusion: The start-up phase is completed, and we are now seeking to expand to new centres and new countries. Interested centres are welcome to join the trial. Please visit us at www.scast.no.

ACCESS (Stroke 2003;34.1699)

P5

APPARENT DIFFUSION COEFFICIENT REFLECTS CROSSED CEREBELLAR DIASCHISIS IN PATIENTS WITH ISCHEMIC HEMISPHERIC STROKE

Yawu Liu, Jari O. Karonen, Juho Nuutinen, Mervi Könönen, Esko Vanninen, Jyrki T. Kuikka, Ritva L. Vanninen

Department of Clinical Radiology, Kuopio University Hospital; Kuopio University, Kuopio, Finland

Background and purpose: The crossed cerebellar diaschisis (CCD) refers to a matched hypoperfusion and hypometabolism in cerebellum due to remote effect of contralateral supratentorial lesion. The purpose of our study was to evaluate whether hemispheric ischemic lesions could cause apparent diffusion coefficient (ADC) change in the cerebellum.
Methods: Twenty-two stroke patients underwent diffusion-weighted MRI (DWI) and SPECT within first 48 hours and at day 8 after onset of stroke. SPECT interhemispheric asymmetry indexes (AIs) were calculated for medial, intermediate, and lateral zones in cerebellum. ADC of cerebellar white matter, cortex of medial, intermediate, and lateral zones were bilaterally measured from patients and 15 age-matched healthy volunteers.
Results: The ADC values within the first 48 hours and on day 8 were or tended to be significantly higher in patients than controls on both sides (>0.087) with one exception in the gray matter of the intermediate zone within 48 hours. Within the first 48 hours but not on day 8, the ADC ratio(ipsi/contra) of cerebellar white matter was significantly associated with the AIs of intermediate and lateral zones (>0.027); the ADC ratio(ipsi/contra) and AI of the intermediate zone was significantly associated with each other (p=0.044). The ADC ratio(ipsi/contra) of cerebellar white matter within the first 48 hours significantly associated with NIHSS within 48 hours, on day 8, and at 3-month (>0.028).
Conclusion: The ADC changes in cerebellum represent a complex physiological and pathological phenomenon in patients with supratentorial ischemic infarction. ADC measurements may afford additional information in investigating the CCD.

P6

RELATIONSHIP BETWEEN BALANCE AND FUNCTIONAL OUTCOMES IN STROKE SURVIVORS

R. Radžiuvien, N. Raškauskien, H. Kazlauskas, G. Varoneckas

Institute of Psychophysiology and Rehabilitation of Kaunas Medical University; Klaipeda Hospital, Lithuania

Objective: Balance dysfunction is commonly observed following stroke. This study determined the relationship between balance dysfunction and functional status in stroke survivors.
Materials and Methods: In prospective study 561 stroke survivors (66.1 (SN10.2) year, 51.1% women), using longitudinal data collected from consecutively admitted patients during 1995-2000 to the Klaipeda Hospital, were tested for functional independence by modified Rankin scale (MRS). The potential predictors (balance status, lesion side, function of limbs, mobility, age, and sex) were treated at discharge, at the 3, 6, and 12 mo follow-up after acute stroke.
Results: MRS revealed significant improvement in total functional outcome between discharge and 3 mo follow-up scores ($p<0.001$). Functional independence significantly improved at 6 ($p<0.001$) and 12 ($p<0.05$) mo follow-up relative to previous follow-up period. Between 1 and 2 years after stroke no significant change was noted in functional outcome by MRS. Statistically significant changes of all indices, reflecting person's function occurred between discharge and 3 mo follow-up: function of limbs ($p<0.001$), mobility ($p<0.001$), and balance status ($p<0.001$). Functional independence measured at 1 year was small correlated with balance at the time of discharge ($r=0.12$) and strong after 3 mo ($r=0.75$). Multiple regression analyses of functional independence at 1 year, controlling for earlier levels of functional independence, demonstrated that MRS at 3 mo and balance status at 3 mo were the most independent prognostic factors ($R^2=0.80$). Age effects persisted when controlling for MRS at discharge ($R^2=0.53$).
Conclusion: Assessment of balance forms an important part of early management of the stroke patient.

P7

PREHOSPITAL DELAY AFTER ACUTE STROKE IN KLAIPEDA, LITHUANIA

H. Kazlauskas, N. Raskauskien, G. Varoneckas, V. Janusonis

Institute of Psychophysiology and Rehabilitation of Kaunas Medical University; Klaipeda Hospital, Lithuania

Objective. This study was designed to analyse the variables that influence the time from symptom onset to hospital admission.
Methods. We prospectively examined acute stroke patients consecutively admitted to Stroke unit of Klaipeda Hospital in the period between January 1st 2004 and December 31st 2005. Demographic and neurological details, stroke syndromes, etiology, and time from symptom onset to the arrival at SU were recorded. A total of 823 patients were observed. For analysing the time variables, patients were dichotomised into those admitted within 3 hours (the current time window for thrombolytic therapy) and >3 hours. Logistic regression was used to analyse the factors associated with prehospital delay.
Results. A total of 43.3% of our patients arrived within 3 hours and an additional 10.1% within 3 to 6 hours, and 62.7% within 12 hours. Direct admission by EMS (73.1% of patients) was associated with earlier arrival at the SU compared with other ways of admission. Patients with carotid territory strokes, either of right or left hemisphere, arrived earlier than patients with vertebrobasilar ischemia (OR=1.3; 95% CI 1.2-2.1). The hemorrhagic stroke patients arrived earlier than ischemic stroke patients (OR=1.6;1.1-2.4). A history of TIA were associated with longer delays (OR=0.3;0.5-0.9). Age, sex did not appear to affect delay time. Severe neurological symptoms associated with shorter delay included presence of limb weakness (OR=2.5;1.8-3.3), consciousness disturbance (OR=1.6;1.2-2.1), and balance dysfunction (OR=2.6;1.9-3.5).
Conclusion. This study strongly suggests that the use of EMS is an important modifiable determinant of delay time for the treatment of acute stroke.

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P8

CARDIAC COMPUTED TOMOGRAPHY FINDINGS IN 76 CONSECUTIVE PATIENTS WITH SUSPECTED CARDIOGENIC TRANSIENT ISCHEMIC ATTACK OR STROKE

Petri Sipola[1,4], Pekka Jäkälä[2], Marja Hedman[3], Keijo Peuhkurinen[3], Hannu Manninen[1,4], Ritva Vanninen[1,4]

Departments of [1]Clinical Radiology, [2]Neurology and [3]Medicine, Kuopio University Hospital and [4]Kuopio University, Kuopio, Finland

Purpose: To describe cardiac CT findings in patients with suspected cardiogenic embolization.
Methods: Seventy-six consecutive patients (51 M/25 F; age range, 32 - 84 years) with suspected cardiogenic brain embolization, based on clinical evaluation by neurologist, were evaluated by CT. First, imaging of heart, aorta and supra-aortic vessels was performed without ECG-gating. Second imaging, confined to heart only, was performed with ECG-gating. Images were interpreted by one experienced observer visually and with quantitative measurements, if needed. In image analysis, reconstruction images aligned along the short and long cardiac axes were used.
Results: Cardiac CT was abnormal in 43 patients (57%). The most common abnormalities were left atrial dilatation (44%) and pulmonary embolism (7%). The following abnormalities were found in left atrial appendix: impaired wash-in-wash-out kinetics (7%), thrombus (5%), dilatation without filling abnormality (2%), and blunted tip (2%). Left ventricular abnormalities were as follows: dilatation (5%), transmural infarct scar (2%), subendocardial thrombosis (2%), ventricular septal defect (2%), and aneurysm (2%). In addition, increased right heart size (5%), soft plaque in aortic valve (5%), and atrial septal aneurysm (2%) were found. Evaluation of atrial septal defects or open foramen ovale was not feasible.
Conclusion: Cardiac CT is a promising technique in the evaluation of patients with suspected cardiogenic embolization and can be combined to imaging of the brain and cervicocranial arteries.

P9

THREE WEEKS OF INTENSIVE GAIT-ORIENTED PHYSIOTHERAPY DURING EARLY ACUTE STAGE OF STROKE

Sinikka H Peurala[1], Olavi Airaksinen[3], Pekka Jäkälä[2], Ina M Tarkka[4], Juhani Sivenius[4]

[1]Finnish centre for interdisciplinary gerontology, University of Jyväskylä, Jyväskylä, Finland; [2]Department of Neurology, Kuopio University Hospital, Kuopio, Finland; [3]Department of Physical Medicine and Rehabilitation, Kuopio University Hospital, Kuopio, Finland; [4]Brain Research and Rehabilitation Center, Neuron, Kuopio, Finland

Introduction: The intensive exercise therapy is usually begun only about ten days after the stroke onset. In this study, the intensive gait-oriented physiotherapy was provided as early as possible and compared to conventional treatment.
Methods: The study was performed in an acute care hospital. Patients were randomly assigned to three groups: Patients in two groups received intensive walking exercises either in the gait trainer with body-weight support (GT) or on the floor (WALK). Each patient received also additional physiotherapy. On the third group, the patients received conventional treatment, and were transferred most often to the health centre after few days. 37 patients completed the intensive rehabilitation period and 10 patients were followed during conventional rehabilitation. The efficacy of rehabilitation programs were assessed in walking tests and other motor ability scales.
Results: The mean walking distance was 8 500 ± 1 700 meters in the GT group and 10 400 ± 5 700 meters in the WALK group (group difference NS). All walking tests and scores in motor scales improved ($p<0.0005$) and no differences in improvements were found between two walking groups ($p>0.05$).
Conclusions: Despite a very early stage of stroke, remarkable amount of repetitive task-specific walking exercises could be achieved. All patients in walking groups improved their motor performance. The improvement in gait parameters and motor tasks was not related to the type of exercise. Both walking training methods resulted in better gait after three weeks of rehabilitation, but exercising in the gait trainer demanded less effort from the therapists.

P10

WITHIN-DAY AND DAY-TO-DAY INTRA-RATER RELIABILITY OF DIAGNOSTIC ULTRASOUND IN THE MEASUREMENT OF ACROMIO-HUMERAL DISTANCE IN HEALTHY INDIVIDUALS

P. Kumar, M. Bradley, A. Swinkels

Department of Radiology, University of the West of England, Bristol, UK

Introduction: Shoulder subluxation is reported to affect up to 81% of stroke patients. Clinically, subluxation is regarded as a palpable increase in the gap between the inferior margin of the acromion and the head of the humerus (acromio-humeral distance (AHD)). The prevention and treatment of shoulder subluxation is hampered by the insensitivity of current clinical measurements. The aim of this study was to assess the intra-rater reliability of the portable diagnostic ultrasound in the measurement of AHD in healthy individuals prior to testing its application on stroke patients.
Method: Thirty-two healthy participants (13 male, 19 female) aged 51-85 years (mean 64.21±10.05) were recruited into the study. Seated participants were scanned using ultrasound by a single assessor who was blind to all measurements. Four measurements were recorded on day one, and then four on the same day one week later. Reliability was assessed by intra-class correlation coefficients (ICC) and standard error of measurement (SEM). Analysis of variance (ANOVA) was used to evaluate any measurement differences.
Results: The mean AHD was 1.67 cm±0.41 (range 0.92-2.52 cm) and 1.77 cm±0.40 (range 0.93-2.70 cm) for the left and right shoulders respectively. Within-day intra-rater reliability coefficients were 0.982 and 0.983 for the left and right shoulders respectively. Corresponding values for day-to-day reliability were 0.964 and 0.971.The SEM showed low values.ANOVA showed no significant differences in measurements either within ($p=0.524$) or between days ($p=0.497$).
Discussion: Portable diagnostic ultrasound is a quick and reliable method of assessing AHD in healthy individuals when measured by the same examiner.
Conclusion: Future study is needed to assess the inter-rater reliability of the portable diagnostic ultrasound on healthy individuals and on stroke patients.

P11

THE CORTICAL SILENT PERIOD ELICITED BY NAVIGATED BRAIN STIMULATION

Laura Säisänen

Departments of Clinical Neurophysiology, Kuopio University Hospital, Kuopio, Finland

Objective: Inhibitory silent period (SP) is a transient suppression of voluntary muscle activity caused by transcranial magnetic stimulation (TMS). Our aim was 1) to determine the impact of muscle activation level and stimulus strength on the duration of SP, 2) to study the relationship between motor evoked potential (MEP) and SP, and 3) to optimize the measurement of SP by on-line 3D-navigation of stimulus delivery.
Methods: The optimal cortical representation area of the thenar musculature was stimulated by single magnetic pulses in ten healthy adults. Real-time interactive 3D-positioning was used for precise stimulus targeting. The stimulation intensities varied from 80% to 120% of motor threshold (MT) at 10% increments. Muscle activation levels were 20, 40, 60 and 80% of the maximal voluntary contraction (MVC).
Results: Contralateral SP lengthened significantly with increasing SI independent of target muscle activation. The peak amplitude and area of the MEP increased linearly with SI and force up to 40% MVC and 60% MVC, respectively.
Conclusions: Neither MEP latency nor MEP duration alter significantly with SI or force. Therefore, SP including or excluding MEP can be used. SP excluding MEP describes just the inhibition, but SP including the MEP has better repeatability and is easier to define visually. Navigated brain stimulation allows a clinically potential and repeatable way of measuring SP.

P12

DOES LEFT VISUAL NEGLECT RECOVER BY LEFT ARM ACTIVATION?

Riitta Luukkainen-Markkula, Ina M. Tarkka, Kauko Pitkänen, Juhani Sivenius, Heikki Hämäläinen

Brain Research and Rehabilitation Center, Neuron, Kuopio, Finland

We had 24 right handed patients, who had large right hemisphere lesions and severe neglect after their first ever stroke. Six patients came to the three week rehabilitation session in acute phase (less than 12 weeks of the attack), seven patients in subacute phase (13 to 24 weeks of the attack) and 12 patients in chronic phase (more than one year after the stroke). The acute and subacute patients were randomized into arm-activation or traditional training groups, the chronic patients were taken first into the traditional training group and then into the arm activation group.Both trainings included physiotherapy, occupational therapy and group therapies. The traditional therapy of acute and subacute patients included ten hours of neuropsychological rehabilitation: videoscreen searching, visuoconstructive copying, reading and writing exercises. The arm activation group had twenty to thirty hours of arm activation: multi-channel FES-activated, mechanically induced, aided or independent movement of the left arm, instead of neuropsychological rehabilitation, part of occupational therapy and physiotherapy. All acute and subacute patients received about 45 hours of personal training during the three week rehabilitation. The chronic patients in the traditional training group had their individually planned therapies, whereas the chronic arm activation group received thirty hours of arm activation and physiotherapy. Neglect, some cognitive functions, left arm functions, walking, balance and ADL-functions were measured at baseline, after three week rehabilitation and 6 months after the training.

P13

STROKE REHABILITATION IN FINLAND

Teemu Takala, Tiina Viljanen, Juhani Sivenius

The Finnish Stroke and Dysphasia Association, Turku, Finland

Each year approximately 14000 people are hospitalized for stroke in Finland. Stroke is a leading cause of disability and about 40 % of stroke survivors are left with functional impairment. The costs related to stroke are high. The recently published guidelines for the treatment of ischemic stroke state that the stroke patients should get treatment and rehabilitation in a well-organized, multidisciplinary rehabilitation unit.

There are no earlier systematic studies of stroke rehabilitation resources in Finland. There are probably significant differences in rehabilitation practise inside the country. The Finnish stroke and dysphasia association has started to study the implementation of rehabilitation in Finland. The first phase of the study consists of interviews of hospital personnel working in the field of stroke rehabilitation in 45 Finnish central and regional hospitals. The first interviews have been done and the first phase of the study will be ready by the end of the year 2007. In the second phase (2008-2009), the written questionnaires will be send to local hospitals, health care centres, and private rehabilitation providers in Finland.

The aim of the study is to clarify the current state and resources of stroke rehabilitation in Finland. The results of this study will help to develop better and equal stroke rehabilitation for each patient in Finland. The analysis of preliminary data has shown some differences in rehabilitation practise in different parts of country, but it is too early to draw reliable conclusions on basis of these early results.

P14

TRENDS IN NEUROREHABILITATION OF THE STROKE HAND

Ina M Tarkka

Brain Research and Rehabilitation Center, Neuron, Kuopio, Finland

The ability to perform basic activities of daily living is initially reduced in three out of four patients with stroke. Patients with stroke may have difficulties in ambulation, unilateral upper limb movements and cognitive functions. Current neurorehabilitation strategies for stroke are based on increased knowledge of mammalian brain plasticity and reorganizational capacity of the cerebral networks of motor control. New knowledge in neurorehabilitation can effectively change the functional outcomes of the survivors. There is evidence that 1) early start of rehabilitation, 2) task-specific exercise and 3) appropriate medication are beneficial. Task-oriented therapies for paralysed upper limb include the constraint-induced movement therapy (CIMT), where 2 weeks of exercise is performed with the affected limb in order to relearn its use while the unaffected hand movements are restricted with casting. Controlled experiments have shown that CIMT is effective in improving limb use in real-world environments after stroke. CIMT results of 100 stroke patients is presented. Also techniques and results of two less common electrical stimulation techniques, cutaneous electrical stimulation and functional multi-channel electrical stimulation of the paralysed hand, will be presented. A number of hemodynamic neuroimaging and transcranial magnetic stimulation studies have shown that the massed practice of CIMT produces use-dependent reorganization in motor areas of the brain. Functional MRI studies have shown that electrical stimulation techniques of the paretic upper limb have an effect on the activation of sensorimotor cortex in humans. These findings provide the needed evidence to help in choosing the most appropriate rehabilitation strategy for an individual patient.

P15

SPECT IMAGING SHOWS ACCUMULATION OF STEM CELLS INTO INTERNAL ORGANS AFTER SYSTEMIC ADMINISTRATION

Riikka Lappalainen, Susanna Narkilahti, Tuulia Huhtala, Timo Liimatainen, Tiina Suuronen, Ale Närvänen, Riitta Suuronen, Outi Hovatta, Jukka Jolkkonen

REGEA Institute for Regenerative Medicine, University of Tampere and Tampere University Hospital, Tampere, Finland; Department of Biosciences, University of Kuopio, Kuopio, Finland; A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, Finland; Department of Neurology, University of Kuopio, Kuopio, Finland; Karolinska Institutet, CLINTEC, Karolinska University Hospital Huddinge, Stockholm, Sweden

The neuroregenerative therapeutic potential of human embryonic stem cell (hESC)-derived neuronal cells has been under intense investigation during the past few years. Before clinical trials hESC-derived neuronal cell grafts are preferably tested in experimental models of neurodegenerative diseases. To end up with a satisfactory therapeutic outcome it is crucial to get the cell transplants to the site of damage. Here, we tested the definite accumulation of In^{111} -labeled hESC-derived neural progenitors and rat hippocampal progenitors after intravenous administration (femoral vein vs. carotid artery) in sham-operated and middle cerebral artery occlusion (MCAO) rats. Cells were detected in vivo using SPECT/CT device designed for rodents. In comparison, a given number of In^{111}-labelled cells were injected stereotactically to the brain parenchyma to determine the sensitivity of the SPECT/CT device. Our results showed that after the intravenous injections, despite of the injection site, both cell types accumulated mostly into the internal organs instead of into the brain. Detection sensitivity of SPECT/CT device was approximately 1000 In^{111}-labelled cells in vitro. Thus, our results indicate that intravenous administration is not an optimal route to deliver cell transplants to the brain after MCAO.

P16

SIZE OF THE LESION DOES NOT PREDICT OCCURRENCE OF SEIZURES AFTER CORTICAL PHOTOTHROMBOSIS IN RATS

Heli Karhunen, Zinayida Bezvenyuk, Jari Nissinen, Juhani Sivenius, Jukka Jolkkonen, Asla Pitkänen

Department of Neurology, University of Kuopio, Kuopio, Finland; A.I. Virtanen Institute for Molecular Sciences, University of Kuopio, Kuopio, Finland

Stroke represents one major cause of symptomatic epilepsy. The underlying mechanisms of epileptogenesis, however, are not known. This study investigated whether lesion size and location or iron deposits are associated with occurrence of seizures in a rat model of stroke.A small vessel occlusion was induced with Rose Bengal model to two different cortical locations in male Sprague-Dawley rats. After lesioning the posterior frontoparietal cortex, occurrence of seizures was monitored with video-EEG at 2, 4, 6, 8, and 10 mo (24 h/d, for 7 or 14 d). Following the anterior frontoparietal lesion induction, video-EEG was recorded at 8 and 10 mo for 14 d. At the end, the brains were cut into 30-µm thick coronal sections and stained with Thionin and Perls' Prussian Blue for iron. Epilepsy developed in 7 out of 36 rats with experimental stroke in the posterior frontoparietal cortex. None of six rats with anterior coordinates had seizures. No clear association was found between the rostro-caudal extent or depth of the lesion or iron staining and the occurrence of spontaneous seizures. In conclusion, the location of the lesion, rather than the size of the lesion or accumulation of iron, seems to be important for the development of epilepsy in rats after an experimental stroke with thrombotic occlusion of small cortical vessels.

P17

INFLUENCE OF HOUSING CONDITIONS ON BEHAVIOR FOLLOWING FOCAL BRAIN INJURY

E. Gornicka, M. Janowski

NeuroRepair Department, Medical Research Institute, Warsaw, Poland

Housing conditions play an important role in quality of animal life influencing behavior as well as environment within the brain. Thus it is of critical importance for testing different neurorestorative strategies in rats after focal brain injury.
Aim: To compare spontaneous functional recovery following focal brain injury of rats housed in large groups in environmentaly enriched cages (EE) and singly in standard cages (IS).
Methods: Initially Wistar rats were housed in appropriate conditions for behavioral training for a couple days. Then focal brain injury was induced by stereotactic injection of ouabain (5nmol) into dorsolateral striatum and the animals returned to their housing conditions. Walking beam task, open field test, and apomorphin-induced rotations test were performed during 30 days.
Results: Performance of walking beam task revealed higher improvement in EE rats in comparison to IS animals. In contrast EE rats tended to turn more in contralateral direction to lesioned hemisphere in the open field and performed more apomorphin-induced rotations comparing to IS rats. So we obtained detectable deficits in EE rats which could be used to study functional recovery following neurorestorative therapies. Open field test revealed more exploratory behavior of IS than EE rats (lesioned and intact).
Conclusion: EE seems to be a good model for testing novel neurorestorative strategies due to possibilities for exercising functional impairments and obtaining measurable deficits.

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P18

EVALUATION OF THE NEUROPROTECTIVE POTENTIAL OF A LONG-LIFE PRODUCT OF COLLAGEN DEGRADATION – PEPTIDE PRO-GLY-PRO (PGP)

Denis N. Silachev, Stanislav I. Schramm, Jukka Jolkkonen

Department of Neurology, University of Kuopio, Kuopio, Finland; Department of Chemistry, Institute of Molecular Genetics, Moscow, Russia

Recent data suggest that some collagen- and ECM-derived small proteolytic products play an important role in inflammation (Weathington et al., 2006). On the other hand these peptides demonstrated various pharmacological activities in particular reduction of blood coagulation and protection of stomach mucous at the experimental ulcer (Ashmarin et al., 2005). However, the neurotropic effects of such peptides have not been investigated yet. The aim of our study is to evaluate the neuroprotective potential of one of the main long-life collagen-derived peptide PGP by using cellular and animal models of neuron degeneration and stroke. We studied an effect of PGP on viability of cultivated neuronal PC12 cells after H2O2-induced necrosis. It was shown that PGP prevent necrosis 4h after H2O2-treatment in a dose-dependent manner. At the concentration of 0.1 mM PGP reduced percent of necrotic cells 1.7 times ($p<0.001$) compared to control (H2O2/no peptide). Neuroprotective activity of PGP was investigated on the middle cerebral artery occlusion (MCAO) model. Chronic treatment of rats with 0.1 mg/kg (i.p.) but not 0.5 mg/kg PGP during 72h after MCAO lead to the 45% reduction of infarct volume in the cortex ($p=0.15$) in comparison to the sham-operated animals. At the same time we not revealed any differences between PGP-treated and sham-operated groups in neurologic status on 4 and 6 day after MCAO. In conclusion, this study demonstrated protective effects of PGP on in vitro and in vivo models of neuron damage. Thus, there is a reason for further research this peptide as a neuroprotectant.

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P19

IMPROVED FUNCTIONAL RECOVERY BY ROLIPRAM FOLLOWING FOCAL CEREBRAL ISCHEMIA IN RATS

Sonja Hätinen, Mikko Sairanen, Jouni Sirviö, Jukka Jolkkonen

Department of Neurology, University of Kuopio, Kuopio, Finland and Orion Pharma, Turku, Finland

Objective: Rolipram, a spesific phosphodiesterase 4 inhibitor (PDE4), was originally developed as an antidepressive agent but dose-limiting side-effects of emesis and nausea prevented its development for this indication. We examined the effect of rolipram on sensorimotor recovery in rats subjected to transient occlusion of the middle cerebral artery (MCAO).
Methods: Rat were subjected to transient occlusion of the middle cerebral artery for 2 h. Rolipram was administered at a dose of 0.1 or 1 mg/kg (i.p., twice a day, for 13 days) and administration was started on postoperative day 2. Sensorimotor outcome was assessed by using limb-placing, beam-walking and cylinder tests at baseline and 7, 14, and 21 days after MCAO.
Results: Analysis of hindlimb function by beam-walking test did show a significant overall group effect ($p<0.01$) and a significant day and treatment interaction ($p<0.01$). A more detailed analysis showed that performance of sham-operated, MCAO vehicle rats ($p<0.01$) and MCAO rats treated with rolipram at a dose of 0.1 mg/kg ($p<0.01$) was different. Interestingly, MCAO rats treated with rolipram at a dose of 0.1 mg/kg and 1.0 mg/kg were also different ($p<0.05$). More importantly, a higher rolipram dose was not different from sham-operated rats after cessation of drug treatment. Limb-placing performance was severely impaired in MCAO rats, but there were no statistically significant differences among MCAO rats. There was a significant group effect in use of left (impaired) forelimb ($p<0.001$) in the cylinder test, however, this was due to differences between sham-operated and MCAO rats. Although not statistically significant, MCAO rats treated with rolipram used impaired forelimb less compared to MCAO controls.
Conclusion: The present data suggest that rolipram provides some improvement in behavioral recovery in MCAO rats possibly by augmenting cAMP signalling through PDE4 inhibition, but this is masked by its acute side effect on sensorimotor function.

P20

NEUROTRANSMITTER SYNTHESIS IN THE CORTICAL NEUROGENESIS IN ADULT RATS AFTER PHOTOTHROMBOTIC RING STROKE WITH SPONTANEOUS REPERFUSION

Chao Gu[1], Per Wester[1], Wei Jiang[1], Weigang Gu[1, 2]

[1]Umea Stroke Center, University of Umea; [2]Department of Clinical Neuroscience and Neurology, University of Umea, Umea, Sweden

Neurons are not regenerated in the cerebral cortex and striatum in the adult brains in most mammalian species. However, cortical neurogenesis is induced in the adult rats exposed to photothrombotic ring stroke with spontaneous reperfusion and morphological recovery in the cortical region at risk (1). In the adult rats subjected to middle cerebral artery suture occlusion, neurons are regenerated in the ipsilateral striatum and the penumbral cortex (2). In the previous studies, we saw that neurite like structures exteneded from these neurons. Whether or not the newborn neurons may synthesize neurotransmitters was unknown. This study was aimed to study the possible neurotransmitter synthesis in the stroke-induced adult neurogenesis.

The adult male wistar rats, weighing 280-320g, were used for the induction of photothrombotic ring stroke (3). The DNA duplication marker BrdU was repeatedly injected (10 mg/kg body weight) intraperitoneally, which ended at day 7th post stroke. The rats were sacrificed at day 2nd, day 7th and day 30th post stroke. Coronal brain sections were processed for single/double immunohistochemistry and single/double immunofluorescent cell labeling. To identify the newborn cells, mouse anti-BrdU was used. To detect the neurotransmitters in cortical cells, rabbit anti-Ach, GABA and glutamate were chosen. To examine the acetylcholine synthesizing enzyme, rabbit anti-ChAT (choline acetyl transferase) was used. DAPI was used to counterstain the nuclear DNA. The double/triple immunofluorescently labeled brain sections were analyzed by 3-D confocal microscope. Numerous BrdU immunolabeled cells appeared in the cortical region at risk at day 2nd, day 7th and day 30th post-stroke. Under double immunohistochemistry, some of the cortical cells immunolabeled by BrdU in the nuclei were double labeled by Ach, GABA, glutamate or ChAT in the cytoplasm as examined under high magnification light microscope. The double labeled cells were randomly distributed in the cortical layer II to VI, more in the region at risk than in the adjacent cortex. Under 3-D confocal analysis, the BrdU immunolabeled cell nuclei were colocalized with Ach, GABA, glutamate or ChAT in the same cortical cells at various times post stroke.

This study suggests that newborn neurons in the post stroke cortex were capable of synthesizing Ach, GABA and glutamate, a process which is of fundamental importance for the new neurons to function in the post stroke adult brains.

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P21

RETINAL AND OPTIC NERVE EVALUATION IN RAT ISCHEMIA MODELS

Giedrius Kalesnykas[1], Timo Tuulos[1], Jukka Jolkkonen[2], Hannu Uusitalo[3]

[1]Department of Ophthalmology, Institute of Clinical Medicine, University of Kuopio, Kuopio, Finland; [2]Department of Neurology, Institute of Clinical Medicine, University of Kuopio, Kuopio, Finland; [3]Department of Ophthalmology, Institute of Clinical Medicine, University of Kuopio and Kuopio University Hospital, Kuopio, Finland

Purpose. To evaluate neurodegenerative changes in the retina and optic nerve following transient and permanent middle cerebral artery occlusions, cortical photothrombosis with Rose Bengal and bilateral common carotid artery occlusion (2VO) in rats.
Materials and methods. Male Wistar rats were used in the study. One week after induction of ischemia, rats were perfused, the eyes were enucleated and longitudinal cuts from the superior to inferior poles were made to divide the eye into two parts. Then, one part of the eye was taken and used for paraffin sectioning, while another was detached from sclera and used for immunohistochemistry as a whole-mount. Optic nerves of each eye were also collected. Histological, immunohistochemical and immunocytochemical methods were used to determine neurodegenerative changes in the retina and optic nerve. The total numbers of neurons in the retinal ganglion cell layer (RGCL) and retinal astrocytes were estimated using stereology.
Results. A decrease in the numbers of neurons in the RGCL and retinal astrocytes by approximately 50% was observed in the 2VO rats when compared to sham-operated animals. Similarly, severe neurodegenerative changes were observed in the optic nerve of those rats. However, other ischemic models did not show significant neurodegenerative changes in the retina and optic nerve.
Conclusion. Both retinal neurons and glial cells are affected in the rat model of bilateral carotid artery occlusion.

P22

RAT'S IMMUNOREACTIVITY UNDER THE EXPERIMENTAL MODELING OF ACUTE AUTOHEMORRHAGIC STROKE ON THE BACKGROUND CYCLOPHOSPHAN INDUCED IRNMUNOSUPRESSION WITH STAPHYLOCOCCUS INFECTION

A.N. Makarenko, Y.N. Mironyuk, S.O. Molozhavaya, V.K. Pozur, I.G. Vasilyeva, E.S. Galanta, A.E. Kulchikov

Institute of Neurosurgery, University of Kyiv, Kyiv, Ukraine; Oryol Regional Hospital, Oryol, Russia

Objectives. Hemorrhagic stroke affects a lot of people all over the world. Functional and biochemical disorders are often complicated by irnmunosupression and infection. Therefore we created a novel experimental model of hemorrhagic stroke on the background staphylococcus infections with cyclophosphan induced irnmunosupression and studied rat's immunoreactivity in these conditions.
Methods. Experimental modeling of hemorrhagic stroke (HS) was performed with using of conventional method (Makarenko A. at al., 2002). Cyclophosphan induced suppression has been created via single injection of cyclophosphane in amount 50 mg/ml/kg (Arkadiev V. at al., 2003). Intact animals, infected animals with cyclophosphan induced irnmunosupression and rats with modeled HS on the background of cyclophosphan induced irnmunosupression and Staphylococcus aureus infection where the groups of comparison.
Results. The investigation shows, that antibacterial activity of neutrophyles of peripheral blood was significantly higher in rats with Staphylococcus aureus infection and irnmunosupression without HS and reliably higher in rats with HS on the background Staphylococcus aureus infections with cyclophosphan induced irnmunosupression groups in comparison to intact animals. The level of immune complexes in serum of rats with HS on the background Staphylococcus aureus infections with cyclophosphan induced irnmunosupression was more lower than in group without HS and significantly lower than in intact animals. The level of antibrain antibodies was significantly elevated in both experimental groups in comparison to intact animals. Prolyferative activity of the main populations of lymphoid cells was strongly depressed in rats with and without HS on the background of infection and immune suppression, compared to control. Positive preliminary results were obtained by using drug "Cerebrolysin" ("Ebewe" (Austria)) for correction of experimental conditions.
Conclusion. These data exactly showed the development of second immunodeficiency state under conditions of modeling hemorrhagic stroke, complicated with cyclophosphan induced irnmunosupression and Staphylococcus aureus infection.