The present results demonstrate that the insertion of APS is safe. Nevertheless, our APS insertion technique has the error range of approximately 10 degree (2SD) of the insertion angle. For improving the accuracy of APS insertion, wider corpectomy is recommended, which shortens the distance between the APS insertion point and the pedicle entrance zone.

Conclusion: Insertion of APS is feasible and safe. APS could become a useful tool for obtaining rigid construct anteriorly in cervical spinal fusion.

Images:

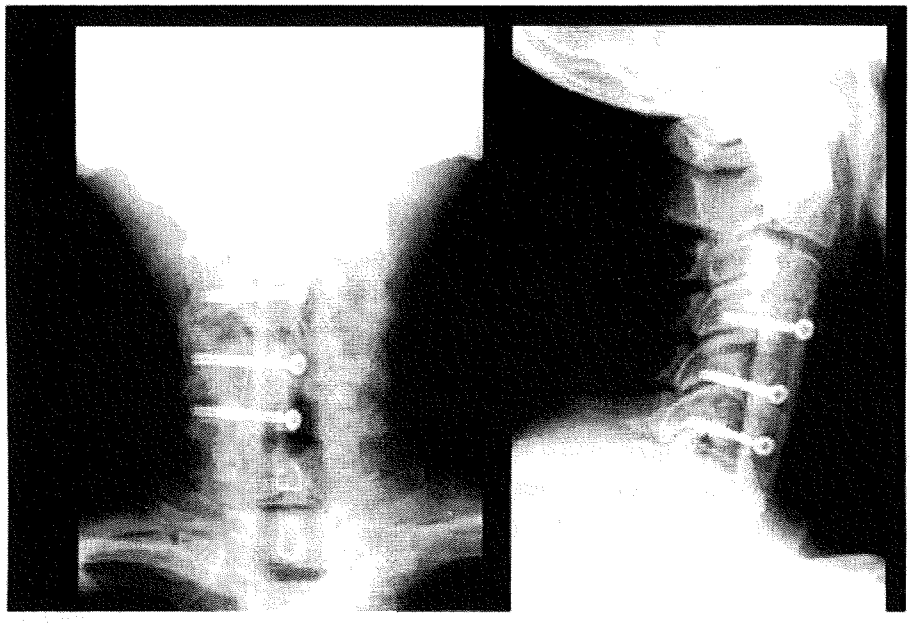


Figure 1.

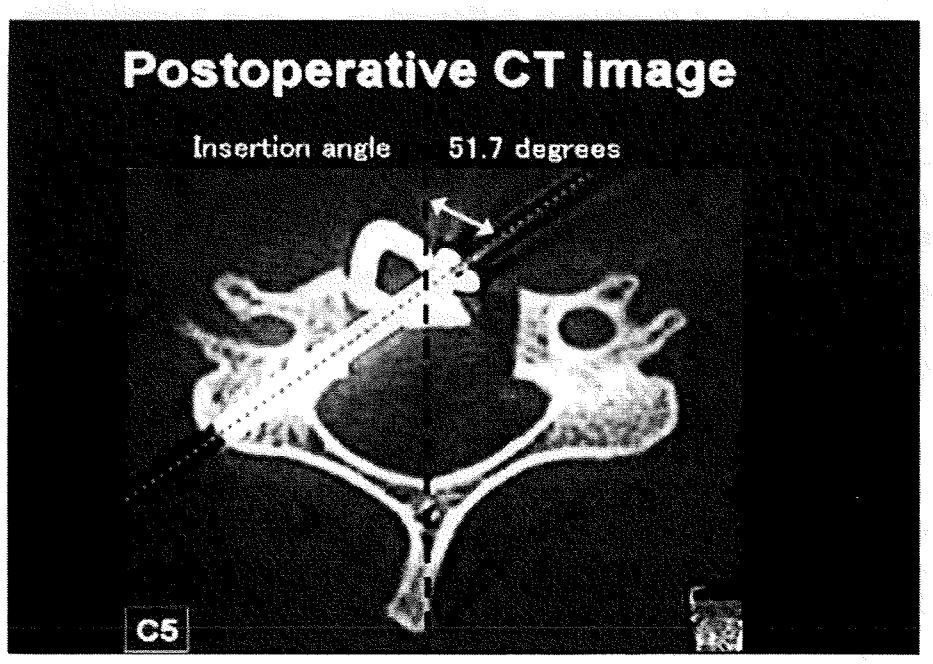


Figure 2.

- The FDA has not cleared this drug and/or medical device for the use described in this presentation (i.e., the drug or medical device is being discussed for an "off label" use). See inside back cover for full information.

Neuroprotective Effects of Granulocyte Colony-Stimulating Factor (G-CSF) on the Injured Spinal Cord: Experimental Studies and its Early Clinical Trial

Masashi Yamazaki, MD, *PhD, Chiba, Japan (n);*
Masao Koda, MD, PhD, Chiba, Japan (n);
Junko Kawabe, MD, PhD, Chiba, Japan (n);
Koichi Hayashi, MD, Chiba, Japan (n);
Tsuyoshi Sakuma, MD, Chiba, Japan (n);
Hiroshi Takahashi, MD, Chiba, Japan (n);
Akihiko Okawa, MD, PhD, Chiba, Japan (n)

Introduction: Recent reports have shown that G-CSF, one of hematopoietic growth factors, has neuroprotective effects on experimental spinal cord injury (SCI), though the detailed mechanisms remain to be elucidated. Because the process of angiogenesis correlates with neural regeneration after SCI, we hypothesized that G-CSF displays the neuroprotective effects via enhancement of angiogenesis. In the present study, we analyzed the effects of G-CSF on vascular system after experimental SCI. Based on the results, we started its early clinical trial.

Methods: (Study 1) We produced contusive SCI model in rats, and divided them to G-CSF treated group (15□g/kg i.v. for 5days after SCI) and control group. For the 2 groups, we evaluated (1) integrity of blood spinal cord barrier, (2) histology of revascularization, (3) RT-PCR for angiogenic cytokine, and (4) recovery of motor function.
(Study 2) We performed a Phase I/II clinical trial of G-CSF administration (5□g/kg i.v. for 5days) in 5 patients with acute SCI and 5 patients with severe compression myelopathy. To address the safety and feasibility, we assessed general conditions and neurological condition of patients by blood data, CT, MRI, and neurological examination.

Results: (Study 1) In the G-CSF group, the number of vessels was larger than that in the control group ($p<0.01$). Expression of angiogenic cytokines in the G-CSF group was significantly higher than that in the control group ($p<0.01$), and the G-CSF group showed significant recovery of hind limb function compared to that of the control group ($p<0.01$).
(Study 2) All 10 patients showed a certain degree of neurological recovery without any serious side effects.

Discussion/Conclusion: In the present study, G-CSF exerts neuroprotective effects via promoting angiogenesis after experimental SCI, suggesting that G-CSF is an attractive candidate for therapeutic drug for acute SCI. Prior to the clinical trail of G-CSF, we planned to start the trial with the administration of low-dose G-CSF (5□g/kg) to confirm the safety of this drug. In the early clinical trial, no serious side effect occurred, indicating that this low-dose G-CSF administration is principally safe. In addition, a certain neurological recovery was obtained in all the patients even after the low-dose administration. Further clinical trials with high-dose administration of G-CSF (15□g/kg) will be required to establish the G-CSF therapy for patients with damaged spinal cord.

- **Evaluation of Upper Extremity Function Recovery Using the Hand Function Test (STEF) After Laminoplast**

Fumitake Nakajima, MD, *Ichihara, Japan (n);*
Yoshikazu Ikeda, MD, Ichihara, Japan (n);
Yasuchika Aoki, MD, Ichihara, Japan (n);
Masatsune Yamagata, MD, Ichihara, Japan (n);
Masashi Yamazaki, MD, Chiba, Japan (n)

Introduction: Clumsy hand is one of the common symptoms in cervical myelopathy. The purpose of this study is to show postoperative recovery of upper extremity function after laminoplasty by evaluating clumsiness using a simple test for evaluating hand functions (STEF) and to show which patients attain high STEF scores after surgery.

Methods: A total of 88 patients who underwent laminoplasty were examined in this study. The hand function test (STEF) was performed according to Kaneko and Muraki's previously published method (Development and standardization of the hand function test. 1990). The battery consists of 10 subtests, and ten points (1 to 10) are awarded for each subtest, with the left and right hands evaluated separately. STEF scores indicate the sum of 10 subtests. Before surgery, all the patients had an estimated STEF score, i.e. STEF (before), JOA scoring systems, especially for the upper extremity motor function score (JOA (u/m)), grip and release test (10-second test), deltoid muscle weakness (estimated manual muscle test), and gasping power. STEF was readministered 6 months after surgery (STEF (f/u)). Patient history of traumatic tetra paresis (trauma) and diabetes mellitus (DM) was confirmed. Plausible predictors (age, trauma, DM, JOA (u/m), 10-second test, grasping power, and STEF (before)) were included in the original model. Best subset regression was performed and the final regression model was selected according to Akaike's Information Criterion.

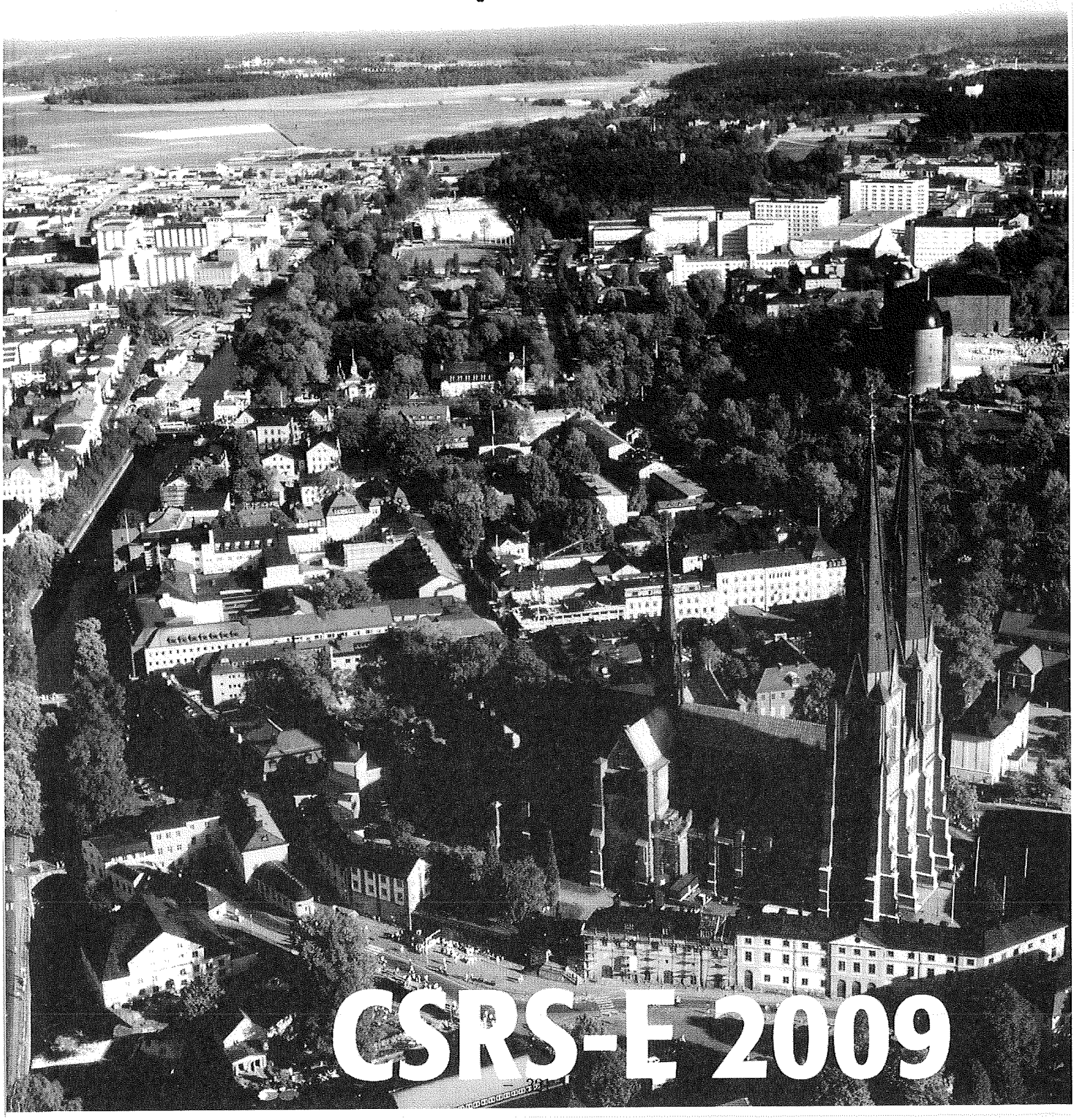
Results: As previously reported, there were correlations between STEF and the 10-second test. All the relative risks (RRs) are presented with 95% confidence intervals (CIs). The final linear regression model included age ($P = 0.08$), STEF (before) ($P < 0.01$), trauma ($P = 0.02$), DM ($P = 0.04$), 10-second test ($P < 0.01$), JOA (u/m) ($P = 0.06$) as significant variables influencing STEF (f/u). Compared with patients with no history of trauma, the RR for those who have a history of trauma was 14 (95% CI, 1.64–119.88). Also, compared with patients with no history of DM, the RR for those who have history of DM was 5.71 (95% CI, 1.06–30.65).

Conclusion: STEF scores in most myelopathy patients improved after surgery. However, some of them did not improve. This finding indicates that irreversible damage of the spinal cord before decompression surgery might affect the recovery process. STEF is a useful tool for monitoring upper extremity function in cervical myelopathy. A history of traumatic tetra paresis and diabetes mellitus in myelopathy patients may greatly influence their recovery after operation. This study provides an improved understanding of the recovery from myelopathy after decompression surgery.

The 25th Annual Meeting of the Cervical Spine Research Society – European Section, June 10–13th, 2009, Uppsala, Sweden

Final Programme

and Abstract Book



CSRS-E 2009

Anterior pedicle screw fixation for multilevel cervical corpectomy and fusion: cadaveric study and clinical case series

Masaaki Aramomi, Yutaka Masaki, Ryo Kadota, Akihiko Okawa, Masashi Yamazaki
Naruto General Hospital, Sanmu-shi, Japan

Introduction: Anterior Pedicle Screw (APS) fixation is a novel technique for multilevel cervical corpectomy and fusion (Acta Neurochir 2008; 150:575). In the present study, we analyzed the accuracy of APS insertion angle and reported its surgical outcome.

Methods: (1) Twelve human cadaveric cervical spines were used to assess the accuracy of APS placement. After corpectomy, APSs were inserted into 94 pedicles (C3-C7) under oblique and lateral fluoroscopy. Cortical integrity and insertion angle of APS were subsequently assessed with CT image.
(2) Case series of 19 patients were analyzed. All cases suffered from cervical myelopathy of varying causes including OPLL and multilevel disc herniation. Corpectomy of 2 vertebrae was performed in 8 cases, 3 vertebrae in 10 cases, and 4 vertebrae in 1 case. Fibula autograft was performed with APS fixation. APSs were inserted under oblique and lateral fluoroscopy into 50 pedicles at C4-C7. The placement of APS and the insertion angle were assessed with CT image.

Results: In the cadaveric study, two pedicles (2.1%) showed critical perforation. An average insertion angle of APS was 48.8 (SD=5.1) degrees.
In the clinical study, one APS (2.0%) was placed out of pedicle. An average insertion angle was 48.8 (SD=4.8) degrees. No vertebral artery injury or graft dislodgement occurred.

Discussion: The most severe complication of cervical pedicle screw fixation is injury of vertebral artery and spinal cord. In our method, vertebral artery is located at the lateral of the entrance point, and dura is visible in the surgical field. In addition, the ideal entrance point of APS can be identified using oblique fluoroscopy, which enables us to insert APS into the pedicle safely.

The present results demonstrate that the insertion of APS is safe. Nevertheless, our APS insertion technique has the error range of approximately 10 degree (2SD) of the insertion angle. For improving the accuracy of APS insertion, wider corpectomy is recommended, which shortens the distance between the APS insertion point and the pedicle entrance zone.

Conclusion: Insertion of APS is feasible and safe. APS could become a useful tool for obtaining rigid construct anteriorly in cervical spinal fusion.

The authors have disclosed no conflict of interest

O-C2 Angle Has a Major Impact on the Sleep Apnea Syndrome in Patients with Rheumatoid Arthritis and Upper Cervical Lesions

Ataka Hiromi, Takaaki Tanno, MD, PhD, Tomohiro Miyashita, MD, Masashi Yamazaki, MD, PhD
Matsudo City Hospital, Matsudo-shi, Chiba, Japan

Introduction: We have reported high incidence of sleep apnea syndrome (SAS) in patients with rheumatoid arthritis (RA) and upper cervical lesions. In the present study, we analyzed morphological factors of upper cervical spine that contributed to the development of SAS in RA patients.

Methods: We analyzed 32 consecutive RA patients with upper cervical lesions who underwent orthopaedic surgeries since September 2006. Their mean age at operation was 65.9 years, and all were females. The patients were examined with all-night polysomnography. Patients who had apnea-hypopnea index values greater than 5 were diagnosed as SAS. Abnormal respiratory events were analyzed to determine the type of SAS: obstructive apnea (OSAS), or central apnea (CSAS). O-C2 angle and Redlund-Johnell distance were measured on cervical radiographs. O-C7 distance was measured as the vertical distance between the McRae line and the lower endplate of C7 on the midsagittal plane of 3DCT images.

Results: SAS was observed in 27 patients (84.4%). Twenty-two of them (81.5%) showed OSAS and five showed CSAS. The compression of medulla was found on MR images in 27.3% in patients with OSAS and 20% in patients with CSAS, showing no significant difference between OSAS and CSAS. In patients with OSAS, the mean O-C2 angle and Redlund-Johnell distance were 1.8 degrees and 27.5mm, both of which were significantly smaller compared with 8.8 degrees and 31.7mm in patients without OSAS. The mean O-C7 distance showed no significant difference between patients with OSAS and those without OSAS. Seven patients with OSAS underwent occipitocervical fixation, and 6 of them showed postoperative improvement of SAS. In the 6 patients, their O-C2 angle was significantly increased after surgery, although their Redlund-Johnell and O-C7 distances were not changed.

Conclusions: The present results demonstrate that O-C2 angle has a major impact on development and postoperative improvement of OSAS, rather than the length of cervical spine, in patients with RA and upper cervical lesions. Decreased O-C2 angle seems to increase upper cervical flexure, which might result in the narrowing of upper airway and cause OSAS. Thus, occipitocervical fixation with correction of kyphosis may have a potential to improve OSAS in RA patients.

The authors have disclosed no conflict of interest

P42

Neuroprotective effects of Granulocyte colony stimulating factor (G-CSF) on acute spinal cord injury: experimental study and early clinical experience

Junko Kawabe, Masao Koda, Masayuki Hashimoto, Takayuki Fujiyoshi, Takeo Furuya, Tomonori Endo, Koichi Hayashi, Akihiko Okawa, Masashi Yamazaki
Chiba University Graduate School of Medicine, Chiba, Japan

Background: G-CSF is a hematopoietic growth factor. Recent reports have shown the neuroprotective effects of G-CSF on experimental spinal cord injury (SCI), though its mechanism remains to be elucidated. Because the process of angiogenesis at sub-acute phase after SCI correlates with regenerative responses, there is a possibility that G-CSF displays the neuroprotective effects after SCI via enhancement of angiogenesis. In this study, we demonstrated the detailed effects of G-CSF on vascular system after experimental SCI and started its early clinical trial.

Material/Method(s): (Study 1) We made contusive SCI model in rat; G-CSF treated group (15μg/kg i.v. for 5days after SCI) and control group. We evaluated (1) integrity of blood spinal cord barrier, (2) histology of revascularization, (3) RT-PCR for angiogenic cytokine, and (4) recovery of motor function.
(Study 2) We performed a Phase I/II clinical trial of G-CSF administration (5μg/kg i.v. for 5days after SCI) in 3 SCI patients. To address safety and feasibility concerns, we assessed general conditions and neurological condition of patients by blood data, CT, MRI, and neurological examination.

Results: (Study 1) In the G-CSF group, the number of vessels was larger than that in the control group ($p<0.01$). Expression of angiogenic cytokines in the G-CSF group was significantly higher than that in the control group ($p<0.01$), and the G-CSF group showed significant recovery of hind limb function compared to that of the control group ($p<0.01$).
(Study 2) All patients recovered motor and sensory function without any serious side effects.

Discussion: In the present study, G-CSF exerts neuroprotective effects via promoting angiogenesis after experimental SCI, suggesting that G-CSF is an attractive candidate for therapeutic drug for acute SCI. Based on these data, we planned to start the clinical trial of G-CSF administration for patients with acute SCI, and obtained an approval from our hospital ethical committee. In the early clinical trial, no serious side effect occurred. The preliminary study shows that this low-dose G-CSF administration is principally safe for patients with acute SCI. Further clinical trials with high-dose administration of G-CSF will be required to establish the G-CSF therapy for acute SCI patients.

The authors have neglected to disclose any conflict of interest

P53

Clinical outcome of anterior decompression and arthrodesis with a dynamic cervical plate for cervical spondylotic myelopathy in elderly patients

Macondo Mochizuki, Atuomi Aiba, Ryou Kadota, Masashi Yamazaki
Numazu City Hospital, Numazu, Japan

(Introduction) The pathology of CSM in elderly patients is thought to be focal involvement at C3/4 and/or C4/5, the spinal cord attenuation, however, are usually found at multilevel segments. From 2002 we have performed anterior decompression and arthrodesis using a dynamic plate exclusively between C3/4 and /or C4/5 in elderly patients. The purpose of this study is to discuss the validity and the efficacy of our anterior surgery with a dynamic plate for elderly patients.

(Materials) Thirty-five cases, ACDF in 15 cases and ACF of C4 in 20 cases, were studied and the mean age at surgery was 77 y/o with 30 months F/U periods on an average (group E). Control group (group Y) consisted of 58 CSM cases under 70 y/o, treated with ACDF in 25 cases and one level ACF in 33 cases at same periods.

(Methods) OR time, blood loss, JOA score, perioperative complications, changes of the fusion angle, bone union and construct failure were surveyed and compared between two groups. Mann-Whitney test and Fisher Exact test were used for statistical analysis.

(Results) Mean OR time (ACDF/ACF) was 84±13 min. / 114±21 min. in group E and 86±14 min. /124±29 min. in group Y. Mean blood loss (ACDF /ACF) was 23±6 g / 28±9 g in group E, and 22±8 g /38±18 g in group Y. JOA score (ACDF/ACF) of group E improved from 8.7±3.2 to 12.8±2.5 / from 8.7±2.7 to 12.1±2.5 and its score (ACDF/ACF) of group Y improved from 7.6±1.9 to 12.6±1.9 / from 11.6±2.5 to 15.9±1.7 ($p<0.05$). There were two revision cases in group E and one case in group Y. Fusion angle of group E increased in 10% cases, 40% of group Y cases increased its angle. Solid fusion (ACDF/ACF) was obtained in 100% /95 % cases in group E, and in 95% / 90% in group Y.

(Conclusion) Our anterior surgery of the selective lesions for CSM in elderly patients was safe and less invasive procedures with acceptable recovery and little complications. A dynamic plate facilitated earlier Rehabilitation with little concern even in elderly patients.

The authors have disclosed no conflict of interest

P61

The outcome of posterior decompression surgery for patients with cervical myelopathy due to the K-line(-)-type OPLL: laminoplasty versus posterior decompression with instrumented fusion

Takayuki Fujiyoshi, Masashi Yamazaki, Akihiko Okawa, Junko Kawabe, Koichi Hayashi, Takeo Furuya, Tomonori Yamauchi, Hiroshi Takahashi, Atushi Sakuma, Hiroaki Konishi, Kazuhisa Takahashi
Graduate school of medicine, Chiba university, Chiba, Japan

Introduction: We previously reported a concept for making decisions regarding surgical approach for cervical OPLL: the K-line (the line that connects the midpoints of the spinal canal at C2 and C7). When OPLL exceeds the K-line, the patient is classified into the K-line(-) group. In the K-line(-) group, sufficient posterior shift of the spinal cord and neurologic improvement was not obtained after posterior decompression surgery (Spine 2008; 33: E990). In addition, our analyzes on asymptomatic OPLL showed that patients with massive OPLL hardly developed myelopathy if the mobility of the cervical spine was highly restricted (E-CSRS 2008; paper #AB15). In the present study, we analyzed the efficacy of posterior decompression with instrumented fusion for patients with cervical myelopathy due to the K-line(-)-type OPLL.

Methods: Since January 2000 through March 2007, 11 patients with the K-line(-)-type OPLL underwent posterior decompression surgery in our institute. Laminoplasty was performed in 4 patients (LMP group) and posterior decompression (laminoplasty/laminectomy) with instrumented fusion in 7 patients (PDF group). We investigated age at surgery, follow-up period, pre-/post-op. JOA score, recovery rate, OPLL occupation ratio and segmental range of motion at the maximum spinal cord compression level (SRM).

Results: Pre-/post-op. JOA score was 7.6/6.8 points in LMP group and 6.7/10.8 points in PDF group. The recovery ratio was -14.2% in LMP group and 41.3% in PDF group ($p<0.05$). No significant difference was found in the age at surgery, follow-up period, occupation ratio and SRM between LMP group and PDF group.

Conclusions: We previously reported that larger segmental ROM at the maximum cord compression level was a risk factor leading to poor surgical outcome after laminoplasty for cervical OPLL patients (J Spinal Disord Tech 2007; 20: 7). The present results demonstrate that the addition of posterior instrumented fusion can knock-out the dynamic factor and obtain better surgical outcome even in the K-line(-) group. We believe that complete excision of the ossified mass using an anterior approach is theoretically the best procedure. However, when laminoplasty is selected for such cases, the addition of posterior instrumented fusion is desirable for stabilizing the spine and decreasing damage to the cord.

The authors have disclosed no conflict of interest

P74

Insertion angle of anterior pedicle screw fixation for multilevel cervical corpectomy and fusion: an anatomical study

Ryo Kadota, Masaaki Aramomi2), Yutaka Masaki2), Macondo Mochizuki1), Atsuomi Aiba1), Akihiko Okawa3), Masashi Yamazaki3)
1) Department of Orthopedic Surgery, Numazu City Hospital, 2) Department of Orthopedic Surgery, Naruto General Hospital, 3) Department of Ortho Numadu City Hospital, 550 Higasisiiji-azaharunoki, Numadu-City, SHIZUOKA, Japan

Introduction: We have developed a new technique of anterior pedicle screw (APS) fixation for multilevel cervical corpectomy and spinal fusion, and reported its early clinical experience (Acta Neurochir 2008;157:575). Especially, the APS technique is useful for anterior surgery for patients with cervical OPLL. In the present study, we analyzed appropriate insertion angle of APS for the cervical vertebrae of OPLL patients using CT images, and discussed the safety of the APS insertion.

Methods: We analyzed CT images of cervical vertebrae of 33 OPLL patients who underwent myelography in our institute (26 male, 7 female, mean age 61.2 yo). The CT images were reconstructed to the pedicle axis plane (C4-6). On the CT images, we performed 3 styles of simulation of pedicle screw insertion; (1) APS15: APS insertion after the corpectomy of 15mm width, (2) APS20: APS insertion after the corpectomy of 20mm width, and (3) PPS: posterior pedicle screw insertion using the Abumi's technique. In each simulation, we measured (A) anatomical pedicle angle, (B) maximum angle of PS insertion and (C) minimum angle of PS insertion.

Results: (A) the anatomical pedicle angles were C4: 47.2+0.5°, C5: 46.2+0.4°, C6: 43.8+0.5°. (B) the maximum angles were C4: 65.1+0.6°, C5: 63.4+0.5°, C6: 62.1+0.5° in APS15, C4: 74.8+0.9°, C5: 72.0+0.7°, C6: 68.9+0.8° in APS20, and C4: 60.3+0.4°, C5: 60.2+0.4°, C6: 59.4+0.7° in PPS. (C) the minimum angles were C4: 31.3+0.6°, C5: 31.2+0.6°, C6: 31.3+0.6° in APS15, C4: 22.6+1.0°, C5: 24.1+1.0°, C6: 24.4+1.0° in APS20, and C4: 40.7+0.4°, C5: 40.5+0.4°, C6: 39.7+0.6° in PPS. The maximum angles and the minimum angles of APS20 were greater than those of PPS, respectively ($p<0.01$).

Discussion: When we compare the procedure for the placement of APS with that of posterior pedicle screw, the entrance point of APS is closer to the pedicle if we perform corpectomy of 20mm width. Thus, the safety area at the insertion of APSs after appropriate corpectomy was larger than that of posterior pedicle screws.

Conclusion: After appropriate corpectomy and extirpation of OPLL from anterior direction, the insertion of APSs is feasible and safe.

The authors have disclosed no conflict of interest

P77

Effects of cilostazol on an acute or chronic experimental spinal cord injury model of rats

Koichi Hayashi, Masayuki Hashimoto,Masashi Yamazaki, Akihiko Okawa, Masao Koda, Junko Kawabe, Takayuki Fujiyoshi, Tomonori Endo, Takeo Furuya, Tsuyoshi Sakuma, Hiroshi Takahashi, Kazuhisa, Takahashi.
Graduate School of Medicine, Chiba University, Chiba City, Japan

Introduction: Phosphodiesterase 3 inhibitor (cilostazol) inhibits hydrolysis of cAMP and has neuroprotective effects through phosphorylating cAMP response element-binding protein (p-CREB). In cerebral infarction models, cilostazol attenuates neuronal death through above pathways. We administered cilostazol just after or 3 days before spinal cord injury (SCI) in rats, or on chronic phase of SCI rats and assessed locomotor recovery for 8-10 weeks.

Materials and methods: (Just after ad.) 8 weeks old, female SD rats were subjected to be spinal cord injury at T9/10 level with IH impactor (200 Kdyn). After operation, animals were received gavage administration of cilostazol (6 mg/day) for 1 week, and later they were provided laboratory food mixed 0.3 % cilostazol for 7 weeks (cilostazol group). The same numbers of rats were received gavage administration of vehicle as a same way (control group). We examined BBB score every week and examined other 3 behavior tests at 8 weeks. In the histological studies, we performed luxol fast blue staining and p-CREB staining.
(3days before ad.) Animals were received gavage administration of cilostazol or vehicle 3 days before SCI. After operation, they were treated with the same procedure as described above. We examined BBB score for 8 weeks, and measured cavity area in histological studies.

(Chronic ad.) After operation, all animals were provided vihicle for 5 weeks, and later they were provided laboratory food mixed 0.3 % cilostazol (cilostazol group) or vehicle (control group) for 5 weeks. We examined BBB score for 10 weeks, and compared bleeding time by Modified Duke's method at the point of 6-7 weeks.

Results: (Just after ad.) There was no statistical significant difference in BBB score and all other behaviour tests and histological examinations.
(3days before ad.) Cilostazol group showed significantly worse BBB score at 4 ,7 and 8 weeks after SCI. There was no statistical significant difference in cavity area measurement.
(Chronic ad.) There was no statistical significant difference in BBB score and bleeding time.

Conclusion: Preoperative administration of cilostazol significantly exacerbated locomotor recovery after SCI. We speculated that microbleeding caused by cilostazol exacerbated locomotor recovery.

The authors have neglected to disclose any conflict of interest

NEUROTRAUMA
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P83

TRANSPLANTATION OF ASTROCYTES DERIVED FROM INDUCED PLURIPOTENT STEM CELL ON AN EXPERIMENTAL SPINAL CORD INJURY IN RATS

Koichi Hayashi, Masayuki Hashimoto, Masashi Yamazaki, Akihiko Okawa, Masao Koda, Tsuyoshi Sakuma, Hiroshi Takahashi
Graduate School of Medicine, Chiba University, Chiba City, Japan

Induced pluripotent stem (iPS) cell can be a potent alternative in case of autograft cell transplantation, because it can be made from somatic cells without breaking fertilized egg. Neural Stem Sphere (NSS) method is one of ES-cell differentiation methods, which migrates neural stem cell (NSC) peripherally around ES-cell colony. In the present study, we applied NSS method to iPS cell differentiation. In CNS injury, the glial scar has bright side, because it prevents survival tissue from inflammation spreading. The purpose of this study is to investigate effectiveness of iPS cell-derived astrocytes transplantation into injured spinal cord.
Mouse iPS cell colonies were cultured in astrocyte-conditioned medium (ACM) and bFGF under free-floating conditions for four days. Mouse iPS cell colonies give rise to floating spheres of concentric stratiform structure with a periphery of NSCs. NSCs were immunoreactive for Nestin, and could be differentiated into β-III-positive neurons GFAP or S100-positive astrocytes, and O4 or GalC-positive oligodendrocytes. NSCs were cryopreserved and could be differentiated into GFAP-positive astrocytes when bFGF was replaced with 10% FBS.
Adult female SD rats were subjected to moderate spinal cord contusion injury (200 kdyn, IH impactor) at T9/10 level. We transplanted iPS cell-derived astrocytes (100,000/5μl) labeled with PKH-26 into injury site three days after spinal cord injury. We injected DMEM into injury site as a control. We are planning to assess BBB locomotor score for eight weeks, then do immunohistological studies.

P84

PHASE I CLINICAL RESULTS OF THE ECE/NEP INHIBITOR SLV334, A NEW THERAPEUTIC CLASS TO BE INVESTIGATED IN TRAUMATIC BRAIN INJURY (TBI)

Hanka De Voogd[1], Edu Zondag[1], Pieter Van den Broeck[1], Koos Drooger[1], Tinka Tuinstra[1], Eric Sondag[1], Elizabeth Allen[2], Michiel De Vries[1]
[1]Solvay Pharmaceuticals, Weesp, Netherlands, [2]Guy's Drug Research Unit, London, United Kingdom

Introduction: SLV334, a metalloprotease inhibitor, is in clinical development for TBI. It inhibits endothelin converting enzyme (ECE), preventing formation of the vasoconstrictor endothelin-1 (ET-1) from its precursor Big endothelin (Big-ET-1). SLV334 also inhibits neutral endopeptidase (NEP), preventing the breakdown of natriuretic peptides, i.e. atrial natriuretic peptide (ANP). In animal models, SLV334 was neuroprotective at the site of impact, prevented secondary damage in the hippocampus and improved motor and cognitive function dose-dependently up to 24 h after experimental injury. SLV334 had a favorable ADME and toxicology profile after iv dosing.
Purpose: Assess safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) related to mode of action after single (SD) and multiple (MD) doses of iv SLV334, in healthy male subjects.
Methods: SLV334 was given in a randomized, double-blind, placebo-controlled manner. SD: 0.25–1 h increasing dose infusions (cross-over design); MD: 1 h infusions (parallel design) twice daily. A 6 h infusion was given open label. Assessments: safety lab, blood pressure (BP), heart rate (HR), ECG (Holter), adverse events, plasma drug levels, plasma levels of ANP, cyclic guanosine monophosphate (cGMP), Big-ET-1 and ET-1.
Results: 60 subjects received SLV334. SD doses (n = 40) of 50–1650 mg and/or 3000 mg as 6-h infusion; MD (n = 20) 2000 and 4000 mg (as 1000 and 2000 mg b.i.d. for 8 days).
Safety: BP, HR, lab and ECG gave no cause for concern; SLV334 was well tolerated with occasional (postural) dizziness and irritation at the infusion site. PK: C_{max} and AUC increased with dose, with a $t_{1/2}$ of 1–3 h, no accumulation during MD. PD: Big-ET-1 levels increased dose dependently for 12–24 h after dosing; all doses were significantly different from placebo, with maximal effect (E_{max}) at 2–4 h, being 5-8x higher than placebo. ET-1 levels were below LOQ. ANP levels rose dose dependently for 4–8 h, statistically significant at doses $\geq$ 100 mg, with an E_{max} 2–7x higher than placebo; cGMP increase was statistically significant at doses $\geq$ 400 mg.
Conclusion: SLV334 in healthy subjects was safe and well tolerated. The marked increase in Big-ET-1 and ANP levels observed confirmed the mode of action of SLV334 as an ECE/NEP inhibitor; the duration of action suggests a b.i.d. dosing schedule.
The results support further development of SLV334 in TBI patients in early Phase II studies.

P85

RESPONSE TO METHYLPHENIDATE ADMINISTRATION AND DOPAMINERGIC FUNCTION IN PERSONS WITH TBI AND HEALTHY CONTROLS

Joelle Scanlon, Julie Price, Joseph Ricker, Yvette Conley, Carl Becker, Joshua Burkhardt, Edward Dixon, Amy Wagner
University of Pittsburgh, Pittsburgh, PA, United States

Genetic variants affecting dopamine transporter (DAT) and D2 receptor (DRD2) function may impact responsiveness to treatment with the DAT inhibitor methylphenidate (MPH) after TBI. The differential impact of DAergic genotype on baseline DAT/DRD2 binding may moderate this effect. This hypothesis was examined in persons with moderate to severe TBI (N = 9) 1 year post-injury and in healthy controls (N = 10). DAT and DRD2 binding was measured, respectively, using [C-11] βCFT and [C-11] raclopride via PET imaging. Cognitive function was measured following a one-time treatment with placebo and with 20 mg/kg MPH within 4 weeks of imaging. Subjects were evaluated for the candidate genes, DAT1 3′ VNTR and DRD2 receptor Taq 1 promoter RFLP. Results showed imaging and cognitive function were influenced by injury group and DA genotype. TBI subjects had a significant reduction in DAT receptor binding in striatal regions and in cognitive performance during both treatment conditions as compared to controls. DAT binding in TBI, but not controls, for carriers of the DAT 9 allele was significantly lower compared to homozygotes for the DAT 10 allele. Carriers of the DAT 9 allele in the TBI group displayed poorer cognitive performance during both treatment conditions. MPH administration did result in a significant improvement in executive function for both TBI and controls as measured by Trail-Making Test Part B (TMT-B) that was not attributable to differences in processing speed. Treatment response was influenced by DAT and DRD2 genetic variants. Better TMT-B performance under the placebo condition was related to higher DAT binding in the right putamen ($p < 0.001$) for TBI but not controls. Additionally, there was a trend for better cognitive performance during the MPH condition and higher DRD2 binding in TBI. PET imaging may help elucidate the neurobiological basis for cognitive deficits and pharmacological treatment response following TBI. This research helps determine the role of DAergic genetic variability in moderating DA neurotransmission, treatment effects, and outcome after TBI.

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P86

THE ANXIETY ASSESSMENT AND NURSING OF PATIENTS WITH HEAD INJURY DURING THE 2008 WENCHUAN EARTHQUAKE

Li Pengcheng, Chen Maojun
West China Hospital of Sichuan University, Chengdu, China

Objective: To investigate the anxiety state of patients with head injury during the Wenchuan earthquake and the effects of psychological nursing.
Methods: 95 patients with mild head injuries suffered from Wenchuan earthquake were enrolled in the study, among these 59 were male and 36 were female, aging from 20 years to 67 years with a mean age of 37 years. Each patient was assessed anxiety state by self-rating anxiety scale after admission, then accepted a unified psychological counseling. 3 days later self-rating anxiety scale was performed again and the data were analyzed by SPSS.
Results: 75 patients(accounted for 78.9%) had anxiety, fear and somatization, cognitive change. After accepted a unified psychological counseling, 49 patients (accounted for 51.6%) had anxiety, fear and somatization. After intervention, the rate of anxiety was significantly decreased ($P = 0.006$).
Conclusions: After earthquake, many wounded may have anxiety, fear and somatization, cognitive change. Psychological nursing can greatly ease the psychological anxiety of the wounded and reduce the physical symptoms.

P115

TRANSPLANTATION OF ACTIVATED MACROPHAGE FOR CHRONIC SPINAL CORD INJURY IN RATS

Masao Koda[1], Koichi Hayashi[2], Masayuki Hashimoto[3], Takeshi Sakuma[2], Hiroshi Takahashi[2], Akihiko Okawa[2], Masashi Yamazaki[2]
[1]Chiba Aoba Municipal Hospital, Chiba, Japan, [2]Chiba University Graduate School of Medicine, Chiba, Japan, [3]Chiba Kaihin Municipal Hospital, Chiba, Japan

Objective: Chronic spinal cord injury (SCI) is the most challenging area in the field of SCI research. Glial scar is one the main obstacles for spinal cord regeneration in chronic phase of SCI. Thus the elimination or modulation of glial scar might be main component of therapeutic strategy for chronic SCI. Macrophage may have potential to eliminate or modulate the glial scar via the phagocytosis or secretion of various kinds of enzymes (e.g. MMPs). It has been reported that transplantation of activated macrophage for spinal cord injury (SC) in acute phase is effective. However, it is still unknown that transplantation of activated macrophage is also effective for chronic SCI. The aim of the present study was to assess therapeutic effects of activated macrophage for chronic SCI.
Methods: Adult male SD rats were laminectomized and spinal cords were contused using Infinite Horizon Impactor. Macrophage was cultured from green fluorescent protein (GFP) transgenic rat bone marrow. Four weeks after injury, 5×10^5 inteferon-gamma-stimulated macrophage was directly injected into injured spinal cord. In control rats, same volume of medium was injected. After transplantation, hind limb functional recovery was assessed using BBB locomotor scale. Hsitological and immunohistochemical assessment was performed.
Results and Discussion: Transplantation of activated macrophage promotes hind limb functional recovery. We will explore the precise mechanisms underlying therapeutic effects of activated macrophage for chronic SCI.

P116 — STUDENT COMPETITION FINALIST

DELAYED INSULIN-LIKE GROWTH FACTOR-1 OVEREXPRESSION PROVIDES REGIONAL NEUROPROTECTION DEPENDENT ON INJURY SEVERITY

Sindhu Kizhakke Madathil, Kathryn Saatman
University of Kentucky, Lexington, KY, United States

Insulin-like growth factor 1 (IGF-1) is a potent neurotrophic factor that is essential for cell survival, synaptogenesis, and myelination. In traumatic brain injury (TBI) clinical trials, patients receiving IGF-1 showed improved metabolic status. We have previously shown that administration of IGF-1 improved neurobehavioural function following TBI in rats. However, the neuroprotective potential of IGF-1 treatment in brain injury has not been determined. In this study we investigated the histological effects of astrocytic overexpression of IGF-1 after moderate and severe TBI using transgenic mice (IGF-1Tg) which conditionally express IGF-1 under the control of the GFAP promoter regulated by a 'tet-off' system. Both C57BL/6 wildtype (WT) and IGF-1Tg mice received a controlled cortical impact (CCI) injury of either 0.5mm or 1.0mm depth or sham injury. Augmented astrocytosis concomitant with IGF-1 expression was observed in the cortex and hippocampus of IGF-1Tg mice 72h after both moderate and severe injuries. However, cortical neuroprotection was observed only for the moderate injury whereas hippocampal neuroprotection was observed following both injury severities. Interestingly, at 24h after severe CCI, astrocytosis accompanied by increased IGF-1 was observed in the hippocampus but not in the cortex of IGF-1Tg mice. More rapid astrocytosis in the hippocampus compared to the cortex provided an earlier upregulation of IGF-1 which may have contributed to effective neuroprotection in the hippocampus. The current findings suggest that non-neuronal IGF-1 overexpression promotes neuronal survival following TBI and endorses the usefulness of IGF-1 as a therapeutic agent in brain-injured patients.

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P117 — STUDENT COMPETITION FINALIST

CREATING GROWTH SUPPORTIVE PATHWAYS TO ENHANCE DOPAMINERGIC AXON GROWTH

Chen Zhang, George Smith
University of Kentucky, Lexington, KY, United States

Different experimental and clinic strategies have been used to promote axon growth from transplanted embryonic ventral mesencephalic (VM) neurons. However, very few studies have focused on long-distance growth of dopaminergic fibers from VM transplants. The aim of this study is to examine whether creating a growth supportive pathway can direct long-distance growth of dopaminergic fibers from VM transplants. Using our corpus callosum model, several growth supportive pathways were made along the corpus callosum using lentivirus encoding the growth factors GDNF, and Netrin-1. Lentivirus encoding GFP was used as a control group. Lentiviruses encoding a single factor or a combination of multiple growth factors were injected along the entire corpus callosum at 0.5mm, 1.5mm and 2.5mm from the midline of both hemispheres. Two weeks later, a piece of E14 VM tissue was transplanted into the right side of the corpus callosum, 2.5mm from the midline. Chondroitinase ABC was injected at the transplant site prior to VM transplantation (2ul at 10U/ml). Four weeks after transplantation, the rats were perfused and brains were dissected. Coronal sections with the graft were cut and stained with antibody against tyrosine hydroxylase (TH). TH+ fibres were counted at 0.5mm, 1.5mm in both sides and 2.5mm on the left side of the corpus callosum. In sham and GFP control groups, TH+ fibres grew very short distance from VM transplants, very few reached the midline. However, in GDNF and Netrin-1 expressing groups, more TH+ fibres grew out of transplants and reach to the midline. Some of these fibres grew across the midline entering the contralateral side. Combined pathway expressing both GNDF and Netrin-1 showed significant increase in the number of TH+ fibres at all counting points compared to other groups. These data suggest that combining growth factors along a pathway can support long-distance growth of dopaminergic fibres from VM transplants. Future studies will test whether creating this combined pathway from the substantia nigra to the striatum can reconstruct the nigrostriatal pathway and direct the growth of dopaminergic axons from VM transplant at the substantia nigra along the pathway to their target in the striatum and improve motor function for Parkinson's disease.

P118

GALECTIN-3 AND MICROGLIAL-RELATED INFLAMMATION AFTER SPINAL CORD INJURY

Kimberly Byrnes, Qing Shu, Kyni Jones, Alan Faden
Georgetown University, Washington, DC, United States

Following spinal cord injury (SCI), expression of microglial-related inflammatory genes and proteins is strongly up-regulated. This up-regulation is related to the delayed tissue damage and cell death that may expand away from the primary injury and is commonly termed 'secondary injury'. Galectin-3 is a member of the delayed-expression genes found after SCI, with a peak in expression at 7 days post-injury, and up-regulation that lasts through at least 28 days. Galectin-3 is involved in chemotaxis of monocytes, activation of NADPH oxidase, phagocytosis, and phosphorylation of p38, resulting in further inflammatory cell activation and cytokine/chemokine production. The aim of this study was to determine the chronic expression of Galectin-3 in the spinal cord after injury, as well as determine the effects of Galectin-3 inhibition on functional and histological markers of recovery. Mice were subjected to moderately-severe contusion SCI at T9, with and without administration of the Galectin-3 inhibitor, modified citrus pectin (MCP, 1%, in the drinking water). Immunohistochemistry and Western blotting demonstrated that Galectin-3 was significantly up-regulated in injured mouse spinal cord from 7 days through 4 months post-injury. Functional assessment of the mice that received MCP administration revealed a significant improvement in BMS motor scores at 21 and 28 days post-injury, in comparison to vehicle-treated mice. To further investigate the role of Galectin-3 in SCI and inflammation, primary microglia cultures were used to assess the effects of MCP administration. MCP pre-treatment resulted in significant reductions in nitric oxide production, reactive oxygen species production and proliferation in response to stimulation with lipopolysaccharide (LPS). These studies support the role of Galectin-3 as a pro-inflammatory and potentially neurotoxic protein in the injured spinal cord, and suggest that inhibition of Galectin-3 activity may improve functional recovery after injury.

P376

EFFECTS OF BFGF INCORPORATED GELATIN HYDROGEL AND BONE MARROW STROMAL CELL- DERIVED NEURAL PROGENITOR CELL TRANSPLANTATION IN A RAT SPINAL CORD CONTUSION MODEL

Masayuki Hashimoto[1], Takeo Furuya[1], Masao Koda[1], Koichi Hayashi[1], Atsushi Murata[1], Akihiko Okawa[1], Mari Dezawa[2], Yasuhiko Tabata[3], Kazuhisa Takahashi[1], Masashi Yamazaki[1]

[1]Chiba University, Graduate School of Medicine, Chiba, Japan, [2]Tohoku University, Graduate School of Medicine, Sendai, Japan, [3]Kyoto University, Institute for Frontier Medical Sciences, Kyoto, Japan

In the previous meeting, we presented "Effects of bFGF incorporated gelatin hydrogel transplantation in a rat spinal cord contusion model." In that presentation, we compared locomotor score and histological difference among bFGF incorporated gelatin hydrogel, gelatin hydrogel and saline injection. Although BBB score was better in bFGF group and Gel group than Saline control, it did not reach statistical significance. bFGF group showed significantly less neuropathic pain or sensory abnormality than saline group at 7 weeks.

We hypothesized that bFGF incorporated gelatin hydrogel is not enough to show significant locomotor recovery than controls. In the present study, we transplanted bFGF incorporated gelatin hydrogel and Bone marrow stromal cell- derived neural progenitor cells (BMSC-N) on rat injured spinal cords.

Adult female Sprague-Dawley rats were subjected to be a spinal cord contusion injury at T10 vertebral level using IH impactor (200Kdyn). One week after contusion, gelatin hydrogel containing bFGF (20μg) and BMSC-N was injected into the lesion center (BMSC-N group). Only gelatin hydrogel containing bFGF (bFGF group) was designated as a control. Locomotor recovery was assessed using BBB score for 11 weeks. Neuropathic pain or sensory abnormality of rat hind paws were evaluated with thermal nociceptive thresholds and mechanical withdrawal thresholds at 11 weeks. At 11 weeks after spinal cord injury, BMSC-N was survived around the cavity of the injured spinal cords. BBB score and sensory tests showed no statistical significant difference between BMSC-N and bFGF groups.

P377

FUNCTIONAL TESTING OF CANDIDATE NEUROPROTECTIVE GENES IN VITRO

Deborah Watson, Saafan Malik,

University of Pennsylvania, Center for Brain Injury and Repair, Philadelphia, PA, United States

Neurotrophin-4/5 (NT-4/5) is a potent neuroprotective agent for hippocampal CA3 pyramidal neurons after experimental traumatic brain injury (TBI). To characterize the mechanism of neuroprotection, we have identified a set of genes which may contribute to hippocampal neuroprotection after TBI. Area CA3 neurons were isolated by laser capture microdissection from brain sections of rats that had received a sham or lateral fluid percussion (LFP) injury followed by infusion of vehicle or NT-4/5 for 30 hr. Genes that were specifically upregulated by neurotrophin infusion after injury were identified by microarray analysis. Validation of the microarray data by PCR was not feasible, since none of six "housekeeping" genes needed for normalization was unchanged by injury (GUSB, GAPDH, RNR, PPIA, ACTB and TBP). Therefore, we developed a method for functional screening of candidate genes in vitro, which can be extended to later in vivo experiments. Recombinant adeno-associated viral vectors are used to deliver the gene of interest to primary cultures of hippocampal neurons. Transduction levels are typically over 90% and expression is stable for weeks in vitro. We measure the protection conferred by each gene against an excitotoxic concentration of glutamate (see Royo et al, Brain Research 1190:15–22, 2008). In this assay, NT-4/5 and one of the downstream effectors identified by our assay, thyrotropin releasing hormone, were potently neuroprotective. We will present the results from testing of additional candidate neuroprotective genes in this ongoing study. Genes that are protective individually or in combination will be evaluated in a later in vivo study using the same viral vector to transduce hippocampal pyramidal neurons. Our overall goal is to identify downstream factors that could be delivered at delayed times (hours to days) after the injury.

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P378

DIFFERENCES IN RESPONSIVENESS TO EXERCISE AFTER TBI IN IMMATURE AND ADULT RATS

David Garfinkel, Grace Griesbach, S., Yan Cai, Christopher Giza, C., David Hovda, A.

UCLA, Los Angeles, CA, United States

Voluntary exercise, when appropriately timed after traumatic brain injury (TBI), has proven to restore hippocampal brain-derived neurotrophic factor (BDNF) levels in adult rats and shift cognitive performance toward baseline. It is known that expression of BDNF and experience-dependent neuroplasticity show changes across development. The present study seeks to determine if the developing brain will respond similarly to post-injury exercise, or if different neural mechanisms are present in the rat pup. Adult rats and postnatal day 19 (P19) pups were housed without (sedentary — SED) or with access to a running wheel (RW) for 14 days. At the end of this period, hippocampal BDNF was quantified using an enzyme-linked immunoabsorbent assay. A significant increase (63.3%) in BDNF was found in adult RW rats, as compared to SED rats ($p = .045$), but no RW effect was present in pups ($p = .36$). To evaluate the ramifications of these results in a pediatric TBI model, P19 rats were subject to lateral fluid percussion (FP) or sham injury and housed in RW or SED conditions during post-injury days 1–7. No significant difference in duration of apnea (mean $\pm$ SEM; FP-RW 92 ± 40 sec, FP-SED $= 91 \pm 26$ sec) or loss of toe pinch response (FP-RW 128 ± 37 sec, FP-SED 154 ± 51 sec) was observed between FP groups. Rats were then cognitively assessed utilizing the novel object recognition (NOR) task, a behavioral measure of hippocampal-based working memory. Brain regions were harvested immediately following NOR in order to determine BDNF levels. Exercise did not prove to have a significant effect on NOR performance among either the LFP ($p = .71$) or sham ($p = .28$) injured pups in comparison to their sedentary counterparts. No significant correlation was found between time exercised, measured in nightly wheel revolutions per hour, and cognitive (NOR) performance ($R^2 = .074$). Thus, while voluntary exercise may be a viable tool for treatment of TBI in adults it does not appear to have the same therapeutic effect in the rat pup model.

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EXAMINATION OF THE USE OF A BIOENGINEERED HYDROGEL CONTAINING HYALURONAN TO IMPROVE THE OUTCOME OF POST TRAUMATIC SYRINGOMYELIA IN RATS

James Austin[1], Catherine Kang[3], Lisa DiDiodato[4], Douglas Baumann[3], Greg Stanisz[4], Molly Shoichet[3], Michael Fehlings[2]

[1]University of Toronto, Toronto, ON, Canada, [2]Toronto Western Research Institute, Toronto, ON, Canada, [3]Institute of Biomaterials and Biomedical Engineering, Toronto, ON, Canada, [4]Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Rationale and Overall Objective: Post traumatic syringomyelia (PTS) occurs in approximately 25% of spinal cord injury cases and is characterized by the formation of a syrinx causing segmental pain, weakness, and spasticity. PTS is thought to occur due to scarring of the subarachnoid space leading to increased CSF flow into the injured spinal cord cavity. We hypothesize that an injectable blend of hyaluronan (HA) and methyl cellulose (MC; HAMC) will reduce the development of PTS in rats. The proposed therapeutic use of HAMC to treat PTS is based on the extensive tissue remodelling and immune modulating properties of HA.

Methods: PTS was induced by subjecting female Wistar rats to a 35 g clip compression injury at T7 followed by an intrathecal injection of kaolin to cause arachnoiditis and scarring. The HAMC hydrogel, or aCSF control, was injected intrathecally 24 hours after injury. Neurobehavioural outcome was assessed by examining hindlimb locomotion, motor function, and the incidence of neuropathic pain. Acute cell survival and inflammation were assessed by immunohistochemistry, immunoblotting, and qPCR. Syrinx size was measured with MRI and immunohistochemical methods.

Results: HAMC injection resulted in an improvement in hindlimb locomotor recovery, decreased incidence of neuropathic pain, and reduced size of syrinxes compared to aCSF controls. In acute studies up to a week following injury, HAMC treatment contributed to increased axonal preservation as demonstrated by increased NF200 immunoblot densities 2 days following injury. HAMC did not decrease the proliferation/infiltration of microglia/macrophages or neutrophils but did alter cytokine and growth factor expression. PCR studies demonstrated that HAMC significantly increased gene expression of TGF-beta and MMP-9 2 days following injury.

Conclusions: Intrathecal HAMC injection has therapeutic potential to treat PTS. Our data suggest that HAMC modulates immune responses and preserves axons acutely following injury. These results further suggest that HAMC has the potential to treat cases associated with arachnoid scarring and, thus, lead to a reduction in the development of post traumatic syringomyelia.

1st Annual Meeting
of
Cervical Spine Research Society Asia Pacific Section

Venue : Kobe International Conference Center

Dates : April 24 (Sat.)-25 (Sun.), 2010

President : Kuniyoshi Abumi, MD

(Department of Spinal Reconstruction, Hokkaido University Graduate School of Medicine)

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Invited Lecture4

15:05~15:25

Moderator: Kyung-Jin Song (Department of Orthopedic Surgery, School of Medicine, Research Institute of Clinical Medicine, Chonbuk National University / Korea)

The spine surgeons perspective on ankylosing spondylitis

Claes Olerud (Department of Orthopedics Uppsala University Hospital / Sweden)

Invited Lecture5

15:25~15:45

Moderator: Thanh Van Vo (Spinal Surgery Department A, Hospital for Trauma-Orthopedics, HCMC / Viet Nam)

Tricks and pitfalls in anterior cervical approaches

Jose M. Casamitjana (Hospital Valle de Hebron University Orthopaedic Department Head of Cervical Pathorogy / Spain)

Symposium2

15:45~17:15

Moderator: Yoshiaki Toyama (Dept. of Orthopaedic Surgery, Keio University / Japan)

Surgical management for upper cervical spine lesions

S2-1 Anomalous vertebral artery at the extraosseous and intraosseous regions of the craniovertebral junction detected by 3-D CT angiography: analysis on the 100 consecutive operative cases

Masashi Yamazaki (Spine Section, Department of Orthopaedic Surgery, Chiba University Graduate School of Medicine / Japan)

S2-2 Intra-operative ISO-C navigation in complex upper cervical problems

S. Rajasekaran (Dept. of Orthopaedic & Spine Surgery Ganga Hospital / India)

S2-3 Surgical management of upper cervical spine disorders in severe rheumatoid patients

Takachika Shimizu (Gunma Spine Center / Japan)

S2-4 Surgical treatment for upper cervical lesions

Jin-Sup Yeom (Seoul National University Bundang Hospital / Korea)

S2-5 Atlantoaxial subluxation in ankylosing spondylitis

Jui-Teng Chien (Orthopedic Dept., Buddhist Dalin Tzuchi General Hospital / Taiwan)

Anomalous vertebral artery at the extraosseous and intraosseous regions of the craniovertebral junction detected by 3-D CT angiography: analysis on the 100 consecutive operative cases

Masashi Yamazaki, MD, PhD

Spine Section, Department of Orthopaedic Surgery, Chiba University Graduate School of Medicine, Chiba, Japan

Introduction:
To avoid intraoperative vertebral artery (VA) injury during instrumentation surgery at the craniovertebral junction (CVJ), we have preoperatively analyzed VA anomalies using 3-dimensional CT angiography (3DCTA).

Methods:
We analyzed 100 consecutive patients who underwent instrumentation surgery since July 1998. Fifty-nine patients had atlanto-axial subluxation, and cervical fixation including C2 was required in 41 patients. Among the 100 patients, 28 had congenital skeletal anomaly (CSA) at the CVJ (CSA-positive cases) and the other 72 had no CSA. Anomalous VAs at the extraosseous and intraosseous regions were evaluated by 3DCTA (Spine 30: 2452, 2005).

Results:
During operation, no neurovascular injury occurred. **(1) Anomaly of extraosseous VA**: Abnormal courses of the VA at the extraosseous region were detected in 11 cases (11.0%) out of the 100 cases: 2 had fenestration and 11 had persistent first intersegmental artery. In both anomalies, the VA entered the spinal canal at the caudal side of the C1 posterior. Intraoperatively, we determined the course of the abnormal branch of the VA using Doppler ultrasonography, and carefully exposed the operative site. Interestingly, all 11 cases with had CSA at the CVJ. When we focused on the 28 CSA-positive cases, 39.2% of them had such extraosseous VA anomalies. **(2) Anomaly of intraosseous VA**: In 29 cases (29.0% of 100 cases), the VA groove was located too medially, posteriorly, and cranially at the C2 isthmus (high-riding VA). Fourteen cases out of the 29 cases had CSA at the CVJ, indicating 50.0% of the 28 CSA-positive cases had high-riding VA.

Conclusions:
The present findings suggest that the frequency of abnormal VA at the extraosseous and intraosseous regions is increased when patients have CSA at the CVJ. With preoperative 3DCTA, we can precisely identify the anomalous VA, and reduce the risk of intraoperative injury to the VA, in advance.

Anomalous vertebral artery at the extraosseous and intraosseous regions of the craniovertebral junction visualized by 3-D CT angiography: analyses on the 100 consecutive operative cases

Neuroprotective therapy using granulocyte-colony stimulating factor for patients with acute spinal cord injury and rapidly aggravating compression myelopathy: phase I and IIa clinical trial

Masashi Yamazaki, MD, PhD, Tsuyoshi Sakuma, MD, Hiroshi Takahashi, MD, Koichi Hayashi, MD, Mitsuhiro Hashimoto, MD, Akihiko Okawa, MD, PhD, Masayuki Hashimoto, MD, PhD, Masao Koda, MD, PhD

Chiba Univ., Japan

Introduction:
In previous reports, we have shown that granulocyte-colony stimulating factor (G-CSF), one of hematopoietic growth factors, has neuroprotective effects on experimental spinal cord injury (SCI) [Brain Res 1149: 223-231, 2007, J Neuropathol Exp Neurol 66: 724-731, 2007]. Based on the results, we have started a phase I and IIa clinical trial that evaluates the safety of neuroprotective therapy using G-CSF for patients with acute SCI and rapidly aggravating compression myelopathy.

Methods:
The trial was performed in five patients with acute SCI and 5 patients with severe compression myelopathy. After obtaining informed consent from the patients, G-CSF (5 μg/kg/day) was intravenously administrated for five consecutive days. We evaluated the presence of diverse events that related to the G-CSF therapy. We also evaluated motor and sensory functions of the patients and their damaged spinal cord magnetic resonance imaging findings.

Results:
In all of the ten patients, neurological improvement of both motor and sensory functions was obtained, though the degree of the improvement differed depending on the patient. On the day following the start of G-CSF therapy, white blood cell count increased more than 15200. It was maintained from 15200 to 43200 during the administration, and returned to preadministration levels by the third day after the final administration. No adverse event occurred during or after the administration.

Conclusions:
In the present clinical trial, no serious side effect occurred, indicating that this low-dose G-CSF administration is principally safe. In addition, a certain neurological recovery was obtained in all the patients even after the low-dose administration. Further clinical trials with high-dose administration of G-CSF (10 μg/kg/day) will be required to establish the G-CSF therapy for patients with damaged spinal cord.

Clinical results of anterior pedicle screw fixation for multilevel cervical corpectomy and spinal fusion

Masaaki Aramomi, MD[1], Yutaka Masaki, MD[1], Akihiko Okawa, MD, PhD[2], Masashi Yamazaki, MD, PhD[2]

[1]*Naruto General Hospital, Japan* [2]*Chiba Univ. Japan*

Introduction:
We have developed a novel technique of anterior pedicle screw (APS) fixation for multilevel cervical corpectomy and spinal fusion [Acta Neurochir 150: 575-582, 2008]. In the present study, we have reported its surgical outcome.

Methods:
Twenty-five patients who underwent APS were analyzed. All cases were suffered from cervical myelopathy of varying causes including OPLL and multilevel disc herniation. Corpectomy of 2 vertebrae was performed in 9 cases, 3 vertebrae in 14 cases, and 4 vertebrae in 2 cases.
The accuracy of APS placement and the insertion angle were examined postoperatively using CT image. Screw malpositioning was classified either as screw exposure (<50% of the screw outside the pedicle) or pedicle perforation (>50% of the screw outside the pedicle boundaries).

Results:
No vertebral artery injury or graft dislodgement occurred. All patients improved neurologically. Spinal fusion was acquired in all 9 patients followed more than 2 years after operation. There was a surgery-related complication: one case of cerebrospinal fluid leakage. There were five postoperative complications: one case of deep wound infection, one case of C5 palsy, one case of airway occlusion by sputa, one case of radiculopathy caused from adjacent disc herniation at C7/Th1, and one case of axial pain. Sixty-six screws (97.1%) of a total of 68 APSs were placed precisely in the pedicles, whereas one APS (1.5%) was of screw-exposure type and another APS (1.5%) was of pedicle-perforation type. An average insertion angle was 47.9 (SD=4.9) degrees.

Conclusions:
The present results demonstrate that the insertion of APS is safe. Nevertheless, our APS insertion technique has the error range of approximately 10 degree (2SD) of the insertion angle. For improving the accuracy of APS insertion, wider corpectomy is recommended, which shortens the distance between the APS insertion point and the pedicle entrance zone.