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WINNING ABSTRACTS

NERVE GUIDE WITH DOUBLE WALLED GDNF-CONTAINING MICROSPHERES IMPROVES RECOVERY AFTER FACIAL NERVE INJURY IN RODENTS

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The George Manstein, MD Award
Overall 1st Place

NERVE GUIDE WITH DOUBLE WALLED GDNF-CONTAINING MICROSPHERES IMPROVES RECOVERY AFTER FACIAL NERVE INJURY IN RODENTS

Background
Injury to the facial nerve and the resulting facial nerve palsy leads to devastating functional, psychological, and cosmetic challenges. Rapid functional recovery after facial nerve injury is critical to prevent muscle atrophy and restore expression. Bioengineering plays an important role to create artificial scaffolds that can enhance the recovery. This can be improved by addition of exogenous neuro-supportive agents such as glial-derived neurotrophic factor (GDNF). GDNF is a promoter of axonal elongation and branching and has been shown to promote Schwann cell proliferation and migration. In this study, we evaluated efficacy of a composite poly(caprolactone) nerve guide containing double-walled GDNF microspheres on functional, electrophysiological, and histological outcomes in a rat facial nerve injury model.

Methods
GDNF was encapsulated within double-walled poly(lactic-co-glycolic acid)/poly(lactide) microspheres and embedded in the walls biodegradable poly(caprolactone) nerve guides. This nerve guide capable of providing a sustained release of GDNF for >50 days was used to repair a facial nerve injury model in male Lewis rats. After transection and primary repair of the buccal branch of the facial nerve, the rats were divided as follows: a) transection and repair only, b) empty guide, c) GDNF-guide. Marginal mandibular branch of the facial nerve was also transected and ligated to prevent innervation of the whiskers. Weekly measurements of the whisking movements for protraction, retraction and amplitude angles were recorded. At the endpoint of 12-weeks, compound muscle action potentials at the whisker pad were assessed and nerve, muscle, and whisker pad were collected for histomorphometric analysis, including Schwann cell analysis.

Results
GDNF-guide treated rats displayed earliest peak and achieved the highest whisking amplitude with 36% recovery compared to the baseline. Weekly whisking amplitude measurements demonstrated both time and the treatment groups were independently associated with the recovery ($p<0.001$) and GDNF treatment had the highest impact versus all others ($p<0.05$). Compound muscle action potentials were significantly higher after GDNF-guide placement versus all others ($p<0.001$). Mean muscle fiber surface area at the levator labii superioris muscle was the highest ($p<0.01$). The axonal integrity loss was less prominent within the GDNF-guides. Gross morphology of the whisker pad was not different across the groups.

Conclusion
The novel tissue engineered nerve guide containing double-walled GDNF microspheres enhances recovery after facial nerve transection. Results support the clinical viability of these guides to enhance recovery after nerve injury and hold promise to facilitate recovery in defects with larger gaps.

ESTABLISHMENT OF PROTOCOL TO ENABLE ON-SITE CRYOPRESERVATION OF FAT FOR REPEAT PROCEDURES

Yusuf Surucu, MD
University of Pittsburgh

Winner

1st Place Basic Science

ESTABLISHMENT OF PROTOCOL TO ENABLE ON-SITE CRYOPRESERVATION OF FAT FOR REPEAT PROCEDURES

Introductions: Autologous fat transfer is an effective treatment for soft tissue reconstruction. The main challenge is that, on average, 63% of the graft volume takes, this necessitates repeat procedures. Therefore, preserving harvested tissue on-site for future injections is a clinical need. This study investigates different cryopreservation methods and applies the best results for a clinically usable device.

Methods: Different cryoprotectant combinations, freezing temperatures, and conditions were tested, and the outcome of the cryopreservation was assessed by measuring cell viability using trypan blue and Calcin-Am staining two days post freezing. In vitro validation of optimized conditions was tested for up to 3 months. For in-vivo testing, Nu/Nu athymic mice were used, and human fat cryopreserved for seven days, 21 days, three months, or 11 months was compared to fresh fat for graft weight and volume retention histology at nine weeks post graft. At +4 ◦C three months, stored combination compared to fresh.

Results: A combination of 10% DMSO and 2% human serum albumin at -80◦C provided optimum cryopreservation. We observed no significant differences in cell viability of cryopreserved fat for up to 3 months compared to the fresh fat. Cryopreserved fat grafts showed weight and volume retention and histological morphology comparable to fresh fat grafts. The cryopreservation solution was stable during storage..

Conclusion: The result of this study will enable the development of devices with clinically compatible appendages and a defined protocol for clinical use for long cryopreservation of fat tissue at -80◦C within a closed system.

TOLL-LIKE RECEPTOR AGONISM WITH THYMOSIN ALPHA 1 IMPROVED CHRONIC WOUND RESILIENCE TO BIOFILM ADHERENCE AND HEALING OF COLONIZED WOUNDS

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Winner

2nd Place Basic Science

TOLL-LIKE RECEPTOR AGONISM WITH THYMOSIN ALPHA 1 IMPROVED CHRONIC WOUND RESILIENCE TO BIOFILM ADHERENCE AND HEALING OF COLONIZED WOUNDS

Background/Purpose: Biofilm formation is a critical barrier to chronic wound healing. Macrophage activation by toll-like receptors (TLRs) is critical to control and clearance of biofilms. Thymosin alpha-1 is an activator of the innate immune response in part via TLR2/4/9 stimulation. Here we sought to determine if Thymosin alpha-1 modulation of TLR signaling reduces biofilms and improves closure in infected diabetic wounds.

Methods: Male obese diabetic (B6.Cg-Lep^{ob}) mice received bilateral edge-inverted wounds. After 1-week intraperitoneal thymosin alpha-1 daily was initiated. Concurrently, Lubbock-type pre-made polymicrobial biofilms were generated transferred murine wounds. After 72-hours wounds were photographed for biofilm adherence and sacrificed for flow cytometry of granulation tissue. Samples were gated to determine CD11b(null), (low), (med), and (high) populations. Relative fraction of macrophages (CD11b+Ly6G-F4/80+) and neutrophils (CD11b+Ly6G+F4/80-) were assessed.

Results: Thymosin alpha-1 treated animals demonstrated 46.6% reduction in biofilm adherence. Granulation tissue collected from infected chronic wounds demonstrated significantly increased macrophage enrichment after treatment for CD11b(low; 1.11+/-0.07% [vehicle control] vs 2.99+/-0.12% [Thymosin alpha-1]; $p<0.05$); (mid; 0.71+/-0.03 [vehicle control] vs 2.05+/-0.09% [Thymosin alpha-1]; $p<0.05$); and (hi; 0.35+/-0.03% [vehicle control] vs 0.91+/-0.04% [Thymosin alpha-1]; $p<0.05$) populations. 1-week post-infection, no further evidence of healing was noted in infected wounds from vehicle-treated mice (107.98+/-13.30% pre-treatment) vs. decrease by 69.63+/- 8.69% ($p=0.013$) in treated samples.

Discussion/Conclusion: Thymosin alpha-1 improved the resilience of diabetic wound against biofilm adherence and colonization and generated a more robust macrophage-dependent response to biofilm presence. This resulted in enhanced wound healing vs. untreated infected samples.

MANAGEMENT AND OUTCOMES OF PATIENTS WHO PRESENT WITH SAGITTAL CRANIOSYNOSTOSIS AFTER THE AGE OF ONE YEAR

Casey Zhang
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Winner

1st Place Clinical

MANAGEMENT AND OUTCOMES OF PATIENTS WHO PRESENT WITH SAGITTAL CRANIOSYNOSTOSIS AFTER THE AGE OF ONE YEAR

Introduction

While early diagnosis and management are the hallmarks of successful craniosynostosis treatment, some patients present after the age of one year with new-onset or previously undiagnosed sagittal craniosynostosis. Potential long-term sequelae of untreated craniosynostosis include elevated ICP, vision loss, neurologic deficits, and developmental delay. We previously published our protocol to treat this complex group of patients. Here we present a follow-up and update of this cohort to evaluate intermediate-term outcomes of our treatment protocol.

Methods

This study includes patients with isolated sagittal craniosynostosis who presented to UPMC Children's Hospital between July 2013 and April 2021 for an initial consultation after the age of one year. All patients underwent a detailed physical exam, a dilated fundoscopic exam and visual evoked potential testing. Reconstructive surgical intervention was recommended for patients with abnormal ophthalmic examinations, elevated intracranial pressure or severe head shape anomalies.

Results

108 patients met inclusion criteria. The average age at presentation was 5.2 ± 3.4 years. Seventy-nine (73.1%) were male, and 15 (13.9%) were syndromic. The indications for imaging were head shape (54.6%), headache (14.8%), trauma (9.3%), seizure (4.6%), papilledema (2.8%), and other (13.9%). Of the 108 patients, 12 (11.1%) underwent surgery following their initial consultation: 5 for papilledema, 4 for elevated ICP, 2 for severely scaphocephalic head shapes, and 1 for abnormal fundoscopic findings. Two of these patients underwent additional reconstructive surgery, one for the recurrence of papilledema and headache and the other for forehead contour irregularities. The average length of time between surgeries was 4.9 years. Of the 96 patients who were initially conservatively managed, 4 (4.2%) underwent surgery at an average of 1.2 ± 0.5 years later (average age 4.4 ± 1.5 years) for aesthetic concerns (n=1), persistent, refractory headaches (n=1), Chiari malformation with syrinx (n=1), and shunt-dependent hydrocephalus (n=1). The average follow-up was 23.9 ± 24.5 months.

Conclusion

We present our protocol for the management of late-presenting sagittal synostosis, involving symptomatic evaluation, objective testing, and morphologic assessment to recommend treatment. Patients who present with single-suture sagittal craniosynostosis after the age of one year require surgical correction less often than patients who present earlier in life, likely due to decreased severity of phenotype. The most common indications for operation were related to increased ICP or morphology. Few patients placed in the conservative treatment arm based on our algorithm ultimately required surgery (4%). Cranioplasty remains safe in older patients.

BREAST FLAP NEUROTIZATION AFTER AUTOLOGOUS FREE FLAP BREAST RECONSTRUCTION: A PROSPECTIVE TRIAL

Abhishek Desai, MD
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Winner

2nd Place Clinical

BREAST FLAP NEUROTIZATION AFTER AUTOLOGOUS FREE FLAP BREAST RECONSTRUCTION: A PROSPECTIVE TRIAL

Purpose: Restoration of breast sensation is an important factor to consider following autologous breast reconstruction (ABR). Flap neurotization may result in improved sensation after ABR, but current literature regarding both patient-reported outcomes and quantitative sensation after neurotization is inadequate and heterogenous. We present a prospective trial investigating the long-term outcomes of flap neurotization regarding breast sensation.

Methods: 98 patients (n = 166 flaps) were prospectively evaluated for breast sensation and quality-of-life 1-5 years after ABR. This included 55 neurotized patients (n=97 neurotized breast flaps) and 44 non-neurotized patients (n=71 non-neurotized breast flaps). Evaluation consisted of the validated patient-reported questionnaire (BREAST-Q), a sensation-specific patient-reported questionnaire, and pressure-specified sensation testing at 9 locations on the breast using the AcroVal pressure-specified sensory device. Continuous variables were compared using independent *t*-tests. Categorical variables were compared using chi-squared analyses.

Results: Non-neurotized patients were significantly more likely to report breast sensation was affecting their daily lives due to pain or discomfort, while neurotized patients were more likely to report they did not notice a difference in breast sensation after ABR or that the change in sensation was not affecting their daily lives ($p= 0.035$). While there was no significant difference in quantitative sensation between neurotized and non-neurotized patients at 1 year after ABR, neurotized patients were significantly more sensate at 4 of 9 testing locations on the breast ($0.011<p<0.039$) when evaluated 2-5 years after ABR.

Conclusion: Breast sensation affects the daily lives of breast reconstruction patients and is an important long-term outcome to consider following ABR. Neurotization is associated with improved protective sensation as well as improved patient-reported outcomes such as reduced pain and discomfort in the long-term after ABR.