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Spinal cord injury (SCI)-induced vascular disruption (VD) is a trigger for secondary injury. Thus, targeting VD may reduce tissue loss and impairment. Mesenchymal Stem Cells (MSCs), including those from the human umbilical cord matrix (HUCMCs), have pericytic attributes. They are well suited to addressing VD and the multi-factorial dynamic SCI pathophysiology. However, SCI treatment with live cells is severely hampered by logistical and practical considerations.

A novel, viable, safe and effective alternative to acute cell therapy for SCI.

R&D ELISA arrays were employed to profile serum-free media conditioned by age- and passage-matched cells cultured for 2 weeks in DMEM/F12 + 1% Glutamax. Concentrated HUCMC secretome (>9kDa) was systemically infused immediately after traumatic 1-minute C7 clip-compression SCI in 250–300g female Wistar rats, which were sacrificed 48 hours later. Vascular permeability was evaluated by spectrophotometric quantification of 2% Evans Blue dye infused 30 minutes pre-sacrifice in snap-frozen homogenates of lesional spinal cord tissue. Pre-sacrifice very-high-resolution ultrasound (VHRUS) measurements of haemorrhagic lesional volume were made.

HUCMCs secrete more and greater concentrations of pro-angiogenic factors (activin, angiogenin, angiopoietin-1, amphiregulin and coagulation factor III), anti-inflammatory cytokines (G-CSF, GM-CSF, IL-6, IL-8, ENA-78, MCP-3, midkine, MIP-1alpha/beta and MIP-3alpha) and neurotrophic factors (FGF2, FGF7 and GDNF) than adult bone marrow stromal cells (BMSCs) and (adult and newborn dermal) fibroblasts. At 48 hours post-SCI, lesion-induced vascular permeability ($p = 0.0067$, $n = 5$) and lesion volume size ($p = 0.001$, $n = 4$) were both reduced by concentrated HUCMC-CM relative to controls (concentrated Alpha-MEM). Inflammation (measured by MPO activity) and haemorrhage (measured using Drabkin's reagent) were only slightly reduced intra- and peri-lesionally.

HUCMCs have a more potent secretome than BMSCs and fibroblasts, and can reduce SCI-induced VD.

Key words
cervical, conditioned medium, Drabkin's, Evans blue, mesenchymal, secretome, spinal cord injury, ultrasound, umbilical cord matrix, vascular permeability

B2-10

FUNCTIONAL IMPROVEMENT WITH INTRANASALLY-DELIVERED HUMAN OLFACTORY STEM CELLS AND EXERCISE AND ENRICHMENT IN SPINAL CORD INJURY

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We hypothesized that exercise and environmental enrichment may produce greater functional improvement when combined with intranasally-delivered progenitor cells after spinal cord injury. Thirty male, athymic Nude rats (3 groups, 10 rats each) were injured at T9 spinal level using the MASCIS device. Two weeks later, Group 1 received intranasal saline, Groups 2 & 3 received intranasally-delivered human olfactory-derived progenitor cells and Group 3 additionally received enrichment and exercise. Exercise consisted of passive cycling, low- and high-level swimming, perturbation training and voluntary exercise in exercise balls. Environmental enrichment involved exposure to a social environment with novel objects. Outcome measures included the BBB, the Louisville Swim, Inclined Plane and Beam tests. A statistical difference ($p = 0.027$) using repeated measures ANOVA was obtained with the Beam test where the progenitor, exercise/enrichment group improved more than the progenitor cells alone group. Poor health in the Nude rats may be responsible for lack of even greater functional improvement. Immunohistochemistry using anti-human antibody revealed that the intranasally-delivered progenitor cells homed to the region of damage in the spinal cord. The greater functional improvement in rats receiving the olfactory progenitor cells, exercise and enrichment may suggest that progenitor cells require input in order to form appropriate circuitry necessary for functional improvement. This therapeutic approach has great potential for clinical translation because a person's own olfactory progenitor cells with a normal neural fate could be used. The cells are obtainable and deliverable with minimally invasive techniques. The recently discovered method of intranasal delivery (no injections) would mean that even patients with severe spinal injuries may be able to be treated subacutely.

Key words
enriched environment, exercise, intranasal delivery, progenitor cell

B3-01

ACUTE STRESS COMPLICATING MILD TRAUMATIC BRAIN INJURY IN RODENTS

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Mild traumatic brain injury (mTBI) in humans often occurs in the setting of acute stress (AS), especially with military injuries. It is not clear if AS significantly contributes to the chronic symptoms that occur after mTBI. Rodent models of mTBI do not share this characteristic because the animals are anesthetized at the time of injury. The purpose of this research was to study the effect of AS either immediately before or after a mild cortical impact injury (mCCI) on behavioral consequences of the injury.

Forty Long Evans rats, weighing 300–350 grams, were enrolled and randomly assigned to five groups: sham ($n = 8$), AS ($n = 8$), mCCI ($n = 8$), AS induced 1 hr after mCCI ($n = 8$), and mCCI induced 1 hr after AS ($n = 8$). To induce AS, rats were placed in a 1′ by 1′ enclosure with a cotton ball scented with trimethylthiazoline and subjected to white noise at random intervals for 15 minutes. Rats undergoing mCCI were anesthetized and subjected to a mCCI [3 m/sec, 2.5 mm deformation]. Outcome measures were beam walking and balance tests, novel object recognition test, open field test, and two Morris water maze variations for spatial navigation and working memory.

The mCCI animals had impaired performance on beam balance testing compared to sham ($p = .029$), and a trend for impaired working memory on the Morris water maze testing ($p = .086$). The AS animals had significant differences on the open field test, with greater distance traveled ($p < .001$) and greater velocity of movement ($p < .001$) compared to sham, but no impairments on the motor or cognitive tasks. When mCCI was complicated by AS, there was no greater impairment on the behavioral tasks than with mCCI alone. These animals with the combined injury did not have the increased activity on the open field testing as those with AS alone.