

# winnipeg-group

## Sunday, Oct. 24 (AM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Sunday, Oct. 24, 9:00 AM – 10:00 AM	158.2	Poster	F36	<u>D.R.Smith</u> <sup>1,3*</sup> ; R.P.Van Der Ploeg <sup>3</sup> ; J.S.Schapansky <sup>3</sup> ; P.F.Gardiner <sup>2</sup> ; G.Glazner <sup>1,3</sup>	Pharm & Therapeut, U. of Manitoba	<b>ELECTRICAL CONDUCTION REGULATES AXOTOMY-INDUCED NF-<math>\kappa</math>B BINDING IN ADULT RAT SENSORY NEURONS.</b>
Sunday, Oct. 24, 10:00 AM – 11:00 AM	158.3	Poster	F37	<u>C.W.Tweed</u> <sup>1*</sup> ; D.R.Tomlinson <sup>1</sup> ; J.Schapansky <sup>2</sup> ; G.W.Glazner <sup>2</sup> ; P.Fernyhough <sup>2</sup>	Sch. of Biological Sci., Univ. of Manchester	<b>CHARACTERIZATION OF NUCLEAR FACTOR KAPPA B SUBUNITS REGULATING SURVIVAL OF ADULT SENSORY NEURONS</b>
Sunday, Oct. 24, 10:00 AM – 11:00 AM	164.11	Poster	J7	<u>K.L.Olson</u> <sup>1,2*</sup> ; K.Binns <sup>3,4</sup> ; X.Mao <sup>2</sup> ; J.S.Schapansky <sup>2</sup> ; R.P.Van Der Ploeg <sup>2</sup> ; A.Pawson <sup>3,4</sup> ; G.W.Glazner <sup>1,2</sup>	Pharm & Therapeut, U of Manitoba	<b>RELEASE OF CALCIUM FROM RAT BRAIN MICROSOMES REGULATES A NOVEL PROTEOLYTIC ACTIVITY</b>
Sunday, Oct. 24, 11:00 AM – 12:00 PM	166.8	Poster	K15	<u>C.E.Flores</u> <sup>1*</sup> ; X.Li <sup>2</sup> ; C.Castillo <sup>1</sup> ; J.I.Nagy <sup>2</sup> ; A.E.Pereda <sup>1</sup>	Neurosci., Albert Einstein Col. of Med.	<b>EXTENSIVE CO-LOCALIZATION OF CONNEXIN35 (CX35) WITH ZONULA OCCLUDENS-1 (ZO-1) AT MIXED SYNAPSES ON MAUTHNER CELLS</b>
Sunday, Oct. 24, 10:00 AM – 11:00 AM	171.11	Poster	O8	<u>B.Fedirchuk</u> *; Y.Dai	Dept Physiol, Univ Manitoba	<b>ACTIVATION OF PROTEIN KINASE C (PKC) DEPOLARIZES THE VOLTAGE THRESHOLD FOR ACTIVATION OF SPINAL NEURONS IN THE NEONATAL RAT.</b>
Sunday, Oct. 24, 9:00 AM – 10:00 AM	230.2	Poster	AAA19	<u>J.Clark</u> <sup>1*</sup> ; G.Herzberg <sup>2</sup> ; J.Peeling <sup>3,4</sup> ; R.Buist <sup>3</sup> ; D.Corbett <sup>1</sup>	Basic Med. Sci., Fac. of Med., Mem. Univ.	<b>DIETARY SUPPLEMENTATION OF OMEGA-3 POLYUNSATURATED FATTY ACIDS WORSENS FORELIMB MOTOR FUNCTION AFTER INTRACEREBRAL HEMORRHAGE IN RATS</b>

## Sunday, Oct. 24 (PM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Sunday, Oct. 24, 2:00 PM – 3:00 PM	278.14	Poster	G24	<u>G.W.Glazner</u> <sup>1,2*</sup> ; A.Buchting <sup>1</sup>	Fac. Med, U Manitoba	<b>NF-<math>\kappa</math>B BINDING ACTIVITY REDUCES CALCIUM RELEASE FROM INTRACELLULAR STORES BY REGULATING ENDOPLASMIC RETICULUM-RESIDENT IP<sub>3</sub>-MEDIATED CALCIUM CHANNELS</b>
Sunday, Oct. 24, 1:00 PM	299.1	Poster	R22	<u>J.E.Rash</u> <sup>1*</sup> ; N.Kamasawa <sup>1</sup> ;	Dept Biomed Sci, Colorado	<b>SIX TYPES OF GAP JUNCTIONS IN ADULT RAT AND MOUSE RETINA:</b>

- 2:00 PM				T.Yasumura <sup>1</sup> ; K.G.V.Davidson <sup>1</sup> ; M.Morita <sup>1</sup> ; J.I.Nagy <sup>2</sup> ; C.S.Furman <sup>1,3</sup>	State Univ	<b>DIFFERENTIAL DISTRIBUTION OF CONNEXIN-36 (CX36) AND CONNEXIN-45 (CX45)</b>
Sunday, Oct. 24, 1:00 PM - 2:00 PM	359.17	Poster	GGG12	<u>O.H.Khan</u> <sup>1,2</sup> ; M.Del Bigio <sup>1,2*</sup>	Pathology, Univ. of Manitoba	<b>EFFECTS OF WHITE MATTER HYPOXIA IN KAOLIN-INDUCED NEONATAL RAT HYDROCEPHALUS</b>

### Monday, Oct. 25 (AM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Oct. 25, 8:00 AM - 9:00 AM	417.17	Poster	Z1	<u>K.Stecina</u> <sup>1*</sup> ; S.Chakrabarty <sup>1</sup> ; J.S.Riddell <sup>2</sup> ; D.A.McCrea <sup>1</sup>	Dept of Physiology, Univ of Manitoba	<b>CANDIDATE NEURONS MEDIATING GROUP II AFFERENT REFLEXES DURING FICTIVE LOCOMOTION</b>

### Monday, Oct. 25 (PM) – Platform Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Oct. 25, 1:30 PM - 4:00 PM	470	Symposium	San Diego Convention Center – Room 6C	<u>D.A.McCrea</u> <sup>4</sup> ; S.Arber <sup>3</sup> ; E.Jankowska <sup>5</sup> ; R.M.Brownstone <sup>1,2*</sup>	Physiol., Univ. of Manitoba	<b>FUNCTIONAL ORGANIZATION OF MAMMALIAN SPINAL MOTOR SYSTEMS</b>

### Monday, Oct. 25 (PM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Oct. 25, 2:00 PM - 3:00 PM	516.6	Poster	N19	<u>D.Derjean</u> ; S.J.Shefchyk*	U of Manitoba	<b>RAT SACRAL SPINAL PARASYMPATHETIC NEURONS; L TYPE CALCIUM CHANNELS, CALCIUM ACTIVATED NON-SPECIFIC CATIONIC CURRENTS (ICAN) AND MULTIPLE FIRING PATTERNS</b>
Monday, Oct. 25, 3:00 PM - 4:00 PM	518.7	Poster	P1	<u>P.Miao</u> ; M.Melanson; M.P.Namaka*	Fac. of Pharm., Univ. of Manitoba	<b>INJURY-INDUCED EXPRESSION OF INFLAMMATORY CYTOKINES WITHIN RAT DORSAL ROOT GANGLIA</b>

### Tuesday, Oct. 26 (AM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Tuesday, Oct. 26, 8:00 AM – 9:00 AM	610.1	Poster	D19	<u>N.L.Ward</u> <sup>1,2,3</sup> ; T.Putoczki <sup>3</sup> ; K.Mearow <sup>4</sup> ; D.J.Dumont <sup>3</sup> ; T.L.Ivanco <sup>2</sup>	Anat., Case Western Reserve Univ.	<b>THE VASCULAR SPECIFIC GROWTH FACTOR ANGIOPOIETIN 1 IS INVOLVED IN THE ORGANIZATION OF NEURONAL PROCESSES</b>
Tuesday, Oct. 26, 8:00 AM – 9:00	631.9	Poster	O28	<u>F.E.Parkinson</u> *; W.Xiong	Dept Pharmacol, Univ	<b>DIFFERENTIAL EXPRESSION OF ADENOSINE REGULATING GENES IN CULTURED RAT FOREBRAIN</b>

## Tuesday, Oct. 26 (PM) – Platform Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Tuesday, Oct. 26, 5:30 PM – 6:30 PM	N/A	Workshop	San Diego Convention Center – Room 17A			SFN BUSINESS/MEMBERS MEETING

## Tuesday, Oct. 26 (PM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Tuesday, Oct. 26, 2:00 PM – 3:00 PM	761.10	Poster	BB10	B.J.MacNeil <sup>1</sup> , D.M.Nance <sup>2*</sup>	Physical Therapy, Univ of Manitoba	THE EFFECTS OF STRESS ON THE IN VIVO CYTOKINE RESPONSE TO ENDOTOXIN

## Wednesday, Oct. 27 (AM) – Platform Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Wednesday, Oct. 27, 9:45 AM – 10:00 AM	820.8	Slide	San Diego Convention Center – Room 2	M.Xue <sup>1,2,4*</sup> , Balasubramaniam <sup>1,2,4</sup> , K.Parsons <sup>1,2,4</sup> , I.McIntyre <sup>4</sup> , J.Peeling <sup>3</sup> , D.R.Marc <sup>1,2,4</sup>	Human Anat & Cell Sci, Univ. of Manitoba	INHIBITION OF THROMBIN ACTIVATION BY HIRUDIN REDUCES BRAIN DAMAGE, INFLAMMATION, AND IMPROVES NEUROLOGICAL IMPAIRMENT FOLLOWING INTRACEREBRAL HEMORRHAGE IN NEONATAL MICE

## Wednesday, Oct. 27 (AM) – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Wednesday, Oct. 27, 8:00 AM – 9:00 AM	840.5	Poster	F21	J.de Melo; G.Du; D.D.Eisenstat*	Human Anat. and Cell Sci., Univ. of Manitoba	DLX1 AND DLX2 FUNCTION IS NECESSARY FOR TERMINAL DIFFERENTIATION AND SURVIVAL OF LATE-BORN RETINAL GANGLION CELLS IN THE DEVELOPING MOUSE RETINA
Wednesday, Oct. 27, 8:00 AM – 9:00 AM	849.17	Poster	L11	J.S.Schapansky <sup>2*</sup> , R.Van Der Ploeg <sup>2</sup> , M.Morissette <sup>2</sup> , G.W.Glazner <sup>1</sup>	Div. of Neurovirology and Neurodegenerative Disorders, St. Boniface Res. Centre	NEUREGULIN $\beta$ -1 REGULATES INTERCELLULAR CALCIUM INFLUX IN CULTURED RAT HIPPOCAMPAL NEURONS VIA NMDA RECEPTORS
Wednesday, Oct. 27, 9:00 AM – 10:00 AM	882.14	Poster	GG12	Y.Dai <sup>1*</sup> , L.M.Jordan <sup>1</sup> , R.M.Brownstone <sup>2</sup>	Dept Physiol, Univ Manitoba	CHARACTERIZATION OF ELECTROPHYSIOLOGICAL AND PHARMACOLOGICAL PROPERTIES OF LOCOMOTOR ACTIVITY RELATED NEURONS IN CFOS-EGFP MICE
Wednesday, Oct. 27, 8:00 AM – 9:00 AM	883.1	Poster	GG20	M.Lafreniere-Roula <sup>*</sup> , D.A.McCrea	Univ of Manitoba, Spinal Cord Res. Centre	DELETIONS OF ENG ACTIVITY DURING FICTIVE LOCOMOTION AND SCRATCH SHOW MAINTAINED

AM						<b>CYCLE PERIOD TIMING DESPITE FAILURES OF RHYTHMIC MOTONEURON EXCITATION AND INHIBITION</b>
Wednesday, Oct. 27, 9:00 AM – 10:00 AM	883.2	Poster	HH1	<u>S.Chakrabarty</u> <sup>1*</sup> ; I.A.Rybak <sup>2</sup> ; D.A.McCrea <sup>1</sup>	Spinal Cord Res. Centre, Univ Manitoba	<b>MODELLING THE VARIETY OF ACTIVATION PATTERNS OF BIFUNCTIONAL HINDLIMB MOTONEURONS DURING FICTIVE LOCOMOTION</b>
Wednesday, Oct. 27, 10:00 AM – 11:00 AM	883.3	Poster	HH2	<u>I.A.Rybak</u> <sup>1*</sup> ; M.Lafreniere-Roula <sup>2</sup> ; N.A.Shevtsova <sup>1</sup> ; D.A.McCrea <sup>2</sup>	Sch Biomed Engin., Drexel Univ	<b>A TWO LAYER MODEL OF THE SPINAL LOCOMOTOR CPG: INSIGHTS FROM DELETIONS OF ACTIVITY DURING FICTIVE LOCOMOTION</b>
Wednesday, Oct. 27, 11:00 AM – 12:00 PM	883.4	Poster	HH3	<u>D.A.McCrea</u> <sup>1*</sup> ; N.A.Shevtsova <sup>2</sup> ; K.Stecina <sup>1</sup> ; I.A.Rybak <sup>2</sup>	Dept Physiology, Univ Manitoba Fac Med	<b>MODELLING PROPRIOCEPTIVE SENSORY CONTROL OF THE MAMMALIAN LOCOMOTOR CPG</b>
Wednesday, Oct. 27, 11:00 AM – 12:00 PM	883.8	Poster	HH7	<u>L.M.Jordan</u> *; J.R.McVagh	Dept Physiology, Univ Manitoba	<b>WELL-COORDINATED LOCOMOTOR ACTIVITY CAN BE PRODUCED IN THE ISOLATED NEONATAL RAT SPINAL CORD BY ACTIVATION OF THE ENDOGENOUS CHOLINERGIC PROPRIOSPINAL SYSTEM</b>
Wednesday, Oct. 27, 9:00 AM – 10:00 AM	883.18	Poster	HH17	<u>J.Liu</u> *; L.M.Jordan	The Univ Manitoba	<b>THE ROLES OF SPINAL 5-HT2A AND 5-HT7 RECEPTORS IN BRAINSTEM EVOKED LOCOMOTION</b>

**Program Number:** 158.2

**Day / time:** Sunday, Oct. 24, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # F36

**ELECTRICAL CONDUCTION REGULATES AXOTOMY-INDUCED NF- $\kappa$ B BINDING IN ADULT RAT SENSORY NEURONS.**

D.R. Smith<sup>1,3\*</sup>; R.P. Van Der Ploeg<sup>3</sup>; J.S. Schapansky<sup>3</sup>; P.F. Gardiner<sup>2</sup>; G. Glazner<sup>1,3</sup>

*1. Pharm & Therapeut, 2. Physiology, U. of Manitoba, Winnipeg, MB, Canada3. Div of Neurodegenerative Disorders, St. Boniface Res Ctr, Winnipeg, MB, Canada*

The transcription factor, nuclear factor kappa B (NF- $\kappa$ B) is required for survival in many neurons, including rat embryonic sensory neurons from dorsal root ganglia (DRG). These cells die following axotomy in vivo, and cannot survive in vitro without exogenous neurotrophic factors. Adult sensory neurons can survive axotomy in vivo or in defined media lacking neurotrophins in vitro. We have observed that cultured adult DRGs still require NF- $\kappa$ B activity, but can generate the signalling cascade endogenously (See abstract #3155). Previous studies in adult rats have reported that NF- $\kappa$ B levels increase in the L4 and L5 DRG 14 days after axotomy. In the present study, we observed that NF- $\kappa$ B binding activity increased in ipsilateral DRG within 2 hours of nerve injury in adult rats. In contrast, NF- $\kappa$ B binding activity did not increase significantly at the site of injury until 6 hrs post-crush. We hypothesized that the initial signal stimulating this rise in NF- $\kappa$ B activity in DRG might be a change in electrical conduction. To test this lidocaine was applied to an otherwise undamaged sciatic nerve, of anesthetised rats. As in the crush model, NF- $\kappa$ B binding activity increased in the ipsilateral DRG within 2 hrs of lidocaine application. In a further test, both sciatic nerves underwent crush injury in anesthetized rats, however, on one side an electrode was placed proximal to the axotomy site. This electrode delivered a small current (0.1 v, 5 Hz) to the nerve. In agreement with our hypothesis, electrical stimulation attenuated the increase in NF- $\kappa$ B binding activity in ipsilateral DRG. These data indicate that the conduction of electrical impulses along the nerve may be part of the control mechanism for the activation of NF- $\kappa$ B in the DRG neurons after sciatic nerve injury.

*Support Contributed By: CIHR – Canadian Institute of Health Research*

Citation:

D.R. Smith, R.P. Van Der Ploeg, J.S. Schapansky, P.F. Gardiner, G. Glazner. ELECTRICAL CONDUCTION REGULATES AXOTOMY-INDUCED NF- $\kappa$ B BINDING IN ADULT RAT SENSORY NEURONS. Program No. 158.2. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 164.11

**Day / time:** Sunday, Oct. 24, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # J7

**RELEASE OF CALCIUM FROM RAT BRAIN MICROSOMES REGULATES A NOVEL PROTEOLYTIC ACTIVITY**

K.L. Olson<sup>1,2\*</sup>; K. Binns<sup>3,4</sup>; X. Mao<sup>2</sup>; J.S. Schapansky<sup>2</sup>; R.P. Van Der Ploeg<sup>2</sup>; A. Pawson<sup>3,4</sup>; G.W. Glazner<sup>1,2</sup>

*1. Pharm & Therapeut, U of Manitoba, Winnipeg, MB, Canada2. Div. of Neurodegenerative Disorders, St. Boniface Res. Centre, Winnipeg, MB, Canada3. Programme in Mol. Biol. and Cancer, Samuel Lunenfeld Res. Inst., Mt Sinai Hosp., Toronto, ON, Canada4. Med. Genet. and Microbiology, Univ. of Toronto, Toronto, ON, Canada*

Many neuropathological conditions have intracellular calcium (Ca<sup>2+</sup>) release as a feature of both protective and apoptotic signal generation. In vitro, inhibition of intracellular Ca<sup>2+</sup> release, primarily from stores in endoplasmic reticulum (ER), protects neurons from apoptosis induced by treatments such as amyloid beta peptide and glutamate. ER Ca<sup>2+</sup> release also appears to play an important role in the generation of reactive oxygen species, and may signal mitochondrial stimulation of apoptosis. A handful of proteins residing in the ER membrane have been identified as being intracellular signal mediators, regulated by cleavage and release from intracellular membranes. We suspect however, that many mediators remain to be discovered. Using a cell-free system of adult rat microsomes rich in ER membrane, treated with either activators or inhibitors of Ca<sup>2+</sup> release, we have identified a number of proteins whose degradation appears to be regulated by Ca<sup>2+</sup> flux through microsomal membrane. These proteins include  $\alpha$  and  $\beta$  tubulin, annexin III, cyclophilin A,

and ERp57. All but annexin III appear to be cleaved upon activation of Ca<sup>2+</sup> efflux from microsomes, whereas annexin III is cleaved in the absence of Ca<sup>2+</sup> flux. Subsequently, we have observed similar cleavage patterns in annexin III and cyclophilin A in cultured neurons, namely that the induction of ER Ca<sup>2+</sup> release by thapsigargin decreased cyclophilin A protein levels, while inhibition of ER Ca<sup>2+</sup> release had a similar effect on annexin III levels.

*Support Contributed By: Canadian Institutes for Health Research and the Manitoba Health Research Council*

Citation:

K.L. Olson, K. Binns, X. Mao, J.S. Schapansky, R.P. Van Der Ploeg, A. Pawson, G.W. Glazner. RELEASE OF CALCIUM FROM RAT BRAIN MICROSOMES REGULATES A NOVEL PROTEOLYTIC ACTIVITY Program No. 164.11. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 158.3

**Day / time:** Sunday, Oct. 24, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # F37

**CHARACTERIZATION OF NUCLEAR FACTOR KAPPA B SUBUNITS REGULATING SURVIVAL OF ADULT SENSORY NEURONS**

C.W. Tweed<sup>1\*</sup>; D.R. Tomlinson<sup>1</sup>; J. Schapansky<sup>2</sup>; G.W. Glazner<sup>2</sup>; P. Fernyhough<sup>2</sup>

*1. Sch. of Biological Sci., Univ. of Manchester, Manchester, United Kingdom2. St. Boniface Res. Centre, Univ. of Manitoba, Winnipeg, MB, Canada*

The nuclear translocation of the transcription factor nuclear factor kappa B (NF- $\kappa$ B) has been shown to have opposing roles promoting both cell death and survival in neurons dependant on cell type and environmental factors. Unlike CNS neurons, axotomized adult sensory neurons have the unique property of being able to survive in vivo following peripheral axon damage. Furthermore, in culture these neurons survive independently of neurotrophic factors and serum. We, therefore, tested the hypothesis that survival of axotomized adult sensory neurons, following peripheral axon damage, was dependent upon activation of NF- $\kappa$ B. In cultured adult rat sensory neurons, an in vitro model of axotomized sensory neurons, there was significant activation of NF- $\kappa$ B as measured using an NF- $\kappa$ B binding assay (EMSA) and revealed the activated transcriptional complex to contain the p50 subunit. Immunocytochemical analysis of these cultures revealed p65 NF- $\kappa$ B subunit staining to be absent from nuclei, whereas the p50 subunit was found localized within the nucleus of all sub-populations of neurons. There was positive staining for p65 and p50 within the cytoplasm of all neurons. Neurons were then subjected to inhibition of NF- $\kappa$ B by using the peptide SN50, which blocks entry of activated NF- $\kappa$ B subunits into the nucleus. SN50 caused a dose-dependent induction of neuronal cell death within 6hrs. The medium-large sub-population of sensory neurons were particularly sensitive to SN50 and died by a necrotic, not apoptotic, process. These results suggest a role for p50, but not p65, in protecting neurons from necrotic cell death following peripheral axon damage.

*Support Contributed By: BBSRC, UK and CIHR, Canada*

Citation:

C.W. Tweed, D.R. Tomlinson, J. Schapansky, G.W. Glazner, P. Fernyhough. CHARACTERIZATION OF NUCLEAR FACTOR KAPPA B SUBUNITS REGULATING SURVIVAL OF ADULT SENSORY NEURONS Program No. 158.3. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 166.8

**Day / time:** Sunday, Oct. 24, 11:00 AM – 12:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # K15

**EXTENSIVE CO-LOCALIZATION OF CONNEXIN35 (CX35) WITH ZONULA OCCLUDENS-1 (ZO-1) AT MIXED SYNAPSES ON MAUTHNER CELLS**

C.E. Flores<sup>1\*</sup>; X. Li<sup>2</sup>; C. Castillo<sup>1</sup>; J.I. Nagy<sup>2</sup>; A.E. Pereda<sup>1</sup>

*1. Neurosci., Albert Einstein Col. of Med., Bronx, NY, USA2. Physiology, Univ. of Manitoba, Fac. of Med., Winnipeg, MB, Canada*

ZO-1, a protein found at tight junctions and adherens junctions, has been identified to interact with several connexins. Recent studies have revealed co-localization of Cx36 and ZO-1 in mouse brain (Li et al., 2004). We asked whether at identifiable goldfish electrical synapses this pattern of co-localization with ZO-1 also occurs with Cx35 (fish ortholog of Cx36). Auditory afferents terminating as <sup>2\*</sup> Large Myelinated Club Endings<sup>3\*</sup> (Club Endings) on the distal portion of the lateral dendrite of the Mauthner cells are identifiable <sup>4\*</sup> mixed<sup>5\*</sup> (electrical and chemical) synaptic terminals that offer the unique opportunity to correlate physiological properties with biochemical composition of individual synapses. Gap junctions at these endings contain Cx35 (Pereda et al., 2003). In double-immunolabeling experiments, confocal microscopy revealed that Cx35 extensively co-localizes with ZO-1 at these terminals. This pattern of co-localization was not restricted to Club Endings; intense punctuate staining was also observed at the proximal portion of Mauthner cell lateral dendrite, soma and ventral dendrites. Similarly, co-localization of Cx35 and ZO-1 was found between neurons in other brain regions, suggesting that this association is common in goldfish brain. Biochemical studies showed that Cx35 and ZO-1 co-immunoprecipitate in goldfish brain. The functions of connexin/ZO-1 association are not yet known. Their co-localization in these identifiable neuronal gap junctions provides the opportunity to explore possible functional roles in regulating electrical transmission, which is dynamically modulated at these endings by a variety of mechanisms.

*Support Contributed By: NIH (DC03186 to A.P.) and CIHR (to J.N.)*

Citation:

C.E. Flores, X. Li, C. Castillo, J.I. Nagy, A.E. Pereda. EXTENSIVE CO-LOCALIZATION OF CONNEXIN35 (CX35) WITH ZONULA OCCLUDENS-1 (ZO-1) AT MIXED SYNAPSES ON MAUTHNER CELLS Program No. 166.8. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 171.11

**Day / time:** Sunday, Oct. 24, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # O8

**ACTIVATION OF PROTEIN KINASE C (PKC) DEPOLARIZES THE VOLTAGE THRESHOLD FOR ACTIVATION OF SPINAL NEURONS IN THE NEONATAL RAT.**

**B.Fedirchuk\***; Y.Dai

*Dept Physiol, Univ Manitoba, Winnipeg, MB, Canada*

We have previously shown that the voltage threshold (V<sub>th</sub>) for action potential initiation is lowered (i.e. hyperpolarized) for lumbar motoneurons during fictive locomotion in the decerebrate cat (Krawitz et al., 2001). Lowering of V<sub>th</sub> can also be seen in spinal neurons of the neonatal rat during bath application of serotonin (5-HT) or noradrenaline (Fedirchuk and Dai, 2004) and during electrical stimulation of the brainstem (Gilmore and Fedirchuk, 2004). Computer modeling has suggested that facilitation of the fast sodium current (I<sub>Na</sub>) underlying spiking might mediate the lowering of V<sub>th</sub> (Dai et al., 2002). Others have shown that PKC-induced phosphorylation of sodium channels can modulate the peak I<sub>Na</sub> in rat brain neurons (Numann et al., 1991). The aim of this study is to assess the effect of PKC activity on the V<sub>th</sub> of spinal neurons and the possible interaction of PKC activity and the 5-HT induced lowering of V<sub>th</sub>. Spinal cords from postnatal day 1–5 rats were isolated and placed in a recording chamber. Whole-cell patch clamp recordings were made from ventral horn neurons in the lower lumbar segments and V<sub>th</sub> assessed. With the bath application of the PKC activator 1-oleoyl-2-acetyl-sn-glycerol (OAG; 15–40  $\mu$ M), ~50% of recorded neurons (n=23) showed a depolarization

of V<sub>th</sub> of about 4 mV, in ~30% V<sub>th</sub> was unchanged, and in ~20% V<sub>th</sub> hyperpolarized by about 4 mV. With inclusion of the PKC inhibitor PKC119-36 in the microelectrode (10–20  $\mu$ M), the effect of OAG on V<sub>th</sub> was

either entirely or partially blocked. Bath application of 5-HT could still induce a lowering of V<sub>th</sub>, even following blockade of PKC activity. It appears therefore, that the PKC pathway does not mediate the 5-HT induced lowering of V<sub>th</sub>. These results show that increasing PKC activity can induce a depolarization of V<sub>th</sub> in spinal neurons, and that multiple mechanisms for modulating the V<sub>th</sub> of spinal neurons exist.

*Support Contributed By: Canadian Institutes of Health Research / CNRP*

**Citation:**

B. Fedirchuk, Y. Dai. ACTIVATION OF PROTEIN KINASE C (PKC) DEPOLARIZES THE VOLTAGE THRESHOLD FOR ACTIVATION OF SPINAL NEURONS IN THE NEONATAL RAT. Program No. 171.11. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 278.14

**Day / time:** Sunday, Oct. 24, 2:00 PM – 3:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # G24

**NF- $\kappa$ B BINDING ACTIVITY REDUCES CALCIUM RELEASE FROM INTRACELLULAR STORES BY REGULATING ENDOPLASMIC RETICULUM-RESIDENT IP3-MEDIATED CALCIUM CHANNELS**

**G.W.Glazner<sup>1,2\*</sup>**; A.Buchting<sup>1</sup>

*1. Fac. Med, U Manitoba, Winnipeg, MB, Canada. 2. Div. of Neurodegenerative Disorders, St. Boniface Res. Centre, Winnipeg, MB, Canada*

Release of intracellular calcium from endoplasmic reticulum (ER), is a critical component of neuronal calcium homeostasis, and under normal conditions regulates numerous intracellular pathways important for neuronal function. However, excess stress-induced calcium release from ER is strongly associated with neuronal cell death in vitro. Stimulation of ER-resident IP<sub>3</sub>-mediated calcium channels in particular leads to mitochondrial reactive oxygen species generation, release of cytochrome C, and initiation of the cell death program, while inhibition of IP<sub>3</sub>-mediated calcium release provides significant protection to cultured neuron from A $\beta$  toxicity and glutamate-mediated excitotoxicity. Paradoxically, ER-mediated calcium release also enhances stress-induced activation of the transcription factor NF- $\kappa$ B, which inhibits apoptosis. Augmented NF- $\kappa$ B DNA binding results in decreased intracellular calcium accumulation and oxidative stress. We wished to determine if NF- $\kappa$ B might regulate levels of IP<sub>3</sub>-mediated ER calcium channels. In cultured rat cortical neurons, activation of NF- $\kappa$ B by exposure to TNF $\alpha$  or I $\kappa$ B antisense resulted in decreased protein and mRNA levels of IP<sub>3</sub> receptor (IP<sub>3</sub>R), IP<sub>3</sub>-binding sites on microsomes isolated from neurons, and intracellular calcium release. Reduction of NF- $\kappa$ B binding activity using a peptide inhibitor of NF- $\kappa$ B nuclear translocation (SN50) had the opposite effect, resulting in increased levels of IP<sub>3</sub>R protein and mRNA, microsomal IP<sub>3</sub> binding sites, and intracellular calcium release. These results indicate that NF- $\kappa$ B and IP<sub>3</sub>R may exist in negative feedback loop, in which calcium release from ER stores stimulates NF- $\kappa$ B binding, which in turn reduces levels of IP<sub>3</sub>R, thus ameliorating stress-induced ER calcium release.

*Support Contributed By: Manitoba Medical Science Foundation*

**Citation:**

G.W. Glazner, A. Buchting. NF- $\kappa$ B BINDING ACTIVITY REDUCES CALCIUM RELEASE FROM INTRACELLULAR STORES BY REGULATING ENDOPLASMIC RETICULUM-RESIDENT IP<sub>3</sub>-MEDIATED CALCIUM CHANNELS Program No. 278.14. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 230.2

**Day / time:** Sunday, Oct. 24, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # AAA19

**DIETARY SUPPLEMENTATION OF OMEGA-3 POLYUNSATURATED FATTY ACIDS WORSENS FORELIMB MOTOR FUNCTION AFTER INTRACEREBRAL HEMORRHAGE IN RATS**

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Recently, there have been widespread recommendations for increased dietary intake of omega-3 polyunsaturated fatty acids (PUFA) due to their known protective effects against cardiovascular disease and ischemic stroke. However, high intakes of these fatty acids lead to reduced clotting ability and increased risk of hemorrhagic stroke. The aim of the current study was to assess the effect of dietary supplementation of omega-3 PUFA on functional outcome after hemorrhagic stroke. Male Sprague-Dawley rats (n=57) were maintained on a diet containing ~30% of energy as either fish oil (rich in omega-3 PUFA) or safflower oil (rich in omega-6 PUFA) and subjected to either intracerebral hemorrhage or sham surgery. Behavioral tests, infarct measurement, and magnetic resonance imaging techniques were used to assess outcome. While there was no significant difference in infarct volume between rats on different diets, animals maintained on a diet enriched with fish oil exhibited increased cerebral blood flow after surgery. These animals were significantly more impaired than rats fed the safflower oil-enriched diet in tests of forelimb dexterity and fine motor control. These results suggest that high intake of omega-3 PUFA may not only increase the risk of hemorrhagic stroke as shown in previous studies, but most importantly may lead to a more severe motor impairment and a poorer functional outcome after such an event.

*Support Contributed By: Natural Sciences and Engineering Research Council of Canada (NSERC), Canadian Institute for Health Research (CIHR) and the Canadian Stroke Network.*

**Citation:**

J. Clarke, G. Herzberg, J. Peeling, R. Buist, D. Corbett. DIETARY SUPPLEMENTATION OF OMEGA-3 POLYUNSATURATED FATTY ACIDS WORSENS FORELIMB MOTOR FUNCTION AFTER INTRACEREBRAL HEMORRHAGE IN RATS Program No. 230.2. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 299.1

**Day / time:** Sunday, Oct. 24, 1:00 PM – 2:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # R22

**SIX TYPES OF GAP JUNCTIONS IN ADULT RAT AND MOUSE RETINA: DIFFERENTIAL DISTRIBUTION OF CONNEXIN-36 (CX36) AND CONNEXIN-45 (CX45)**

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Gap junctions are abundant between neurons in inner plexiform (IPL) and ganglion cell layers (GCL), and are less abundant in the outer plexiform layer (OPL). We used antibodies to Cx36 and Cx45 with freeze-fracture replica immunogold labeling (FRIL) to find gap junctions between neurons, identify their connexins, characterize their size and morphology, and map them to retinal layers. Neuronal gap junctions (n>500) were categorized as: 1) "regular plaques" (smooth margins; hexagonal arrays of connexons), 2) "irregular plaques" (smooth margins; connexons not in hexagonal arrays), 3) "reticular plaques" (clear areas within irregular connexon clusters), 4) "ribbons" (simple vs. complex; each strand uniformly two or three connexons wide), 5) "strings" (simple, complex or compound; each strand usually one connexon wide), and 6) "meandering" (irregular and wavy elongate clusters of connexons; usually as single aggregate, but occasionally in multiples). Neuronal gap junctions containing Cx36 were present in all morphological types of gap junctions in all layers of neuropil. However, in OPL, Cx36 was primarily in relatively rare "meandering" gap junctions. In the outer (or "off") sub-lamina of the IPL, Cx36 was in abundant "string" gap junctions. In both the "on" sub-lamina of the IPL and in the GCL, Cx36 was in abundant plaque gap junctions (large, medium and small, regular and irregular). In contrast, Cx45 was present primarily in small to medium-diameter "plaque-type" gap junctions in the IPL and GCL, but was rarely detected in large plaque gap junctions, or in string, ribbon, or meandering gap junctions. The functional significance and possible inter-conversion of the several types of gap junctions is being investigated.

*Support Contributed By: NIH and CIHR*

**Citation:**

J.E. Rash, N. Kamasawa, T. Yasumura, K.G.V. Davidson, M. Morita, J.I. Nagy, C.S. Furman. SIX TYPES OF GAP JUNCTIONS IN ADULT RAT AND MOUSE RETINA: DIFFERENTIAL DISTRIBUTION OF CONNEXIN-36 (CX36) AND CONNEXIN-45 (CX45) Program No. 299.1. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 359.17

**Day / time:** Sunday, Oct. 24, 1:00 PM – 2:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # GGG12

**EFFECTS OF WHITE MATTER HYPOXIA IN KAOLIN-INDUCED NEONATAL RAT HYDROCEPHALUS**

**O.H.Khan**1,2; M.Del Bigio1,2\*

*1. Pathology, Univ. of Manitoba, Winnipeg, MB, Canada2. Manitoba Inst. of Child Hlth., Winnipeg, MB, Canada*

Hydrocephalus is a common neurological condition characterized by obstruction of cerebrospinal fluid (CSF) flow leading to enlargement of CSF-containing ventricular cavities in the brain. Our first goal was to characterize the structural changes and behavioral outcomes of a neonatal model of kaolin-induced hydrocephalus in rat. Our second goal was to demonstrate in situ evidence of tissue hypoxia in hydrocephalic rat by administration of pimonidazole hydrochloride. The third goal was to compare vascular endothelial growth factor (VEGF) expression in hydrocephalic and control rat brains by immunohistochemistry and ELISA. Decrease in tissue oxygen saturation should lead to production of VEGF whose main effect is to cause production of new blood vessels. VEGF expression can have an influence on vascular permeability and could play a role in water dysregulation in the hydrocephalic brain. Sprague–Dawley rats injected with kaolin at postnatal day 1 had enlarged ventricles by one week and severe dilatation by 3 weeks as assessed by magnetic resonance imaging (MRI) and histology. Hydrocephalic rats had decreased weight gain, reduced time for geotactic orientation, and rotorod (endurance and accelerating). Enzyme assays and western blots revealed decreased expression of myelin associated proteins including myelin basic protein (MBP). Following pimonidazole administration, immunohistochemistry demonstrated hypoxia-associated pimonidazole adducts in periventricular glial cells. VEGF immunohistochemistry in normal rats revealed positive cortical neurons that diminished with age. The pattern of expression shifted to more white matter glial cells in hydrocephalic rats. VEGF expression determined by ELISA supports those findings. We conclude that hypoxia in brain white matter might contribute to vascular changes in hydrocephalus.

*Support Contributed By: University of Manitoba and Manitoba Institute of Child Health*

**Citation:**

O.H. Khan, M. Del Bigio. EFFECTS OF WHITE MATTER HYPOXIA IN KAOLIN-INDUCED NEONATAL RAT HYDROCEPHALUS Program No. 359.17. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 470

**Day / time:** Monday, Oct. 25, 1:30 PM – 4:00 PM

**Presentation Type:** Symposium

**Presentation Location:** San Diego Convention Center – Room 6C

**FUNCTIONAL ORGANIZATION OF MAMMALIAN SPINAL MOTOR SYSTEMS**

**D.A.McCrea**4; S.Arber3; E.Jankowska5; R.M.Brownstone1,2\*

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The neural organization of the spinal cord, and the way in which proprioceptive and descending neural activity is integrated to produce movements have challenged neuroscientists for over 100 years. The moment-by-moment control of limb position can be described in terms of discharge rates of motoneurons that control the muscles around each joint. Despite the fact that excitation and inhibition of motoneurons is largely controlled by spinal interneurons, little is known about the role of these neurons in motor activity. Recent advances offer new possibilities for gaining insight into the integration of interneurons into spinal motor networks. Silvia Arber will address genetic strategies through which connectivity between proprioceptive sensory neurons and motoneurons is achieved during development, and show the importance of hierarchical activation of transcription factor cascades towards functional organization of sensory-motor connectivity. Rob Brownstone will show how the combination of molecular biological and electrophysiological techniques can lead to the identification of functional classes of ventral interneurons. Elzbieta Jankowska will describe a high degree of functional specialization in a network of multifunctional commissural interneurons which play a key role in coordinating limb movements. Dave McCrea will demonstrate that modeling and electrophysiological experiments can be used as complementary tools to explain function at the network level. This symposium will show that the combination of many techniques – molecular biological, anatomical, physiological, and modeling – is now leading to the understanding of this

mammalian CNS network from ion channels to behaviour. This will facilitate new approaches towards spinal cord repair.

1:30 470.1 The Mammalian Locomotor CPG: Insights from Fictive Locomotion and Modeling Studies. D.A. MCCREA, Univ. of Manitoba.

2:10 470.2 Genetic Control of Sensory-Motor Connectivity. S. ARBER, Biozentrum & Friedrich Miescher Inst.

2:45 470.3 Functional Specialization in a Network of Spinal Commissural Interneurons. E. JANKOWSKA, Goteborg Univ.

3:20 470.4 Characterization of Genetically Defined Spinal Interneurons. R.M. BROWNSTONE, Dalhousie Univ.

*Support Contributed By: CIHR, HFSP, NIH, and SNSF*

**Citation:**

D.A. McCrea, S. Arber, E. Jankowska, R.M. Brownstone. FUNCTIONAL ORGANIZATION OF MAMMALIAN SPINAL MOTOR SYSTEMS Program No. 470. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 417.17

**Day / time:** Monday, Oct. 25, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center –

Hall A–H, Board # Z1

**CANDIDATE NEURONS MEDIATING GROUP II AFFERENT REFLEXES DURING FICTIVE LOCOMOTION**

**K.Stecina**1\*; S.Chakrabarty1; J.S.Riddell2;

D.A.McCrea1

*1. Dept of Physiology, Univ of Manitoba, Winnipeg, MB, Canada2. Inst. of Biomed. and Life Sci., Univ. of Glasgow, Glasgow, United Kingdom*

Although group II afferent information is strongly suppressed at some spinal locations during fictive locomotion evoked by electrical stimulation in the midbrain of decerebrate cats, flexor muscle group II afferents continue to have strong actions on the step cycle. Depending on the nerve stimulated, trains of stimuli at group II intensity (5 times threshold) either prolong flexion or terminate flexion and evoke a premature extensor phase.

Here we report on extracellular recordings from interneurons and propriospinal neurons located throughout the 4th and 7th lumbar segments and activated by flexor muscle group II afferents (often from several flexor muscles) as well as cutaneous nerves.

Propriospinal neurons were antidromically activated by spinal cord stimulation above the lumbar cord.

Complete or partial suppression of group II afferent evoked activity during locomotion was present in the majority (57/74) of neurons. Some of this depression is likely to be presynaptic since cutaneous afferent-evoked activation was relatively unaffected in some cells.

Eleven cells (6 propriospinal) in the mid to caudal lumbar segments (depth 1.4 to 2.5 mm) were able to follow muscle group II afferent stimulation during perturbations of the step cycle. Six of these (5 propriospinal) were also rhythmically active during locomotion: 2 in flexion, 2 in extension and 2 fired tonically.

Rhythmically active group II neurons that can also follow sensory inputs during perturbations of the step cycle could play an important role in co-ordinating the output of the central pattern generator circuitry with sensory input. Furthermore, propriospinal neurons activated by lumbar group II afferents may also serve to regulate locomotor activity at cervical levels.

*Support Contributed By: the NIH and CIHR*

**Citation:**

K. Stecina, S. Chakrabarty, J.S. Riddell, D.A. McCrea. CANDIDATE NEURONS MEDIATING GROUP II AFFERENT REFLEXES DURING FICTIVE LOCOMOTION Program No. 417.17. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 516.6

**Day / time:** Monday, Oct. 25, 2:00 PM – 3:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # N19

**RAT SACRAL SPINAL PARASYMPATHETIC NEURONS: L TYPE CALCIUM CHANNELS, CALCIUM ACTIVATED NON-SPECIFIC CATIONIC CURRENTS (ICAN) AND MULTIPLE FIRING PATTERNS**

**D.Derjean**; S.J.Shefchyk\*

*U of Manitoba, Winnipeg, MB, Canada*

Pelvic reflexes are regulated by interneurons and parasympathetic preganglionic neurons (PGNs) within the intermediolateral (IML) region of the L6–S2 spinal cord segments. We studied the intrinsic electrophysiological properties of biocytin filled PGNs (n=29) and presumed interneurons (n=63), and particularly, their ability to express plateau and oscillatory properties using whole-cell patch-clamp recording in transverse slices from rat postnatal days 14 to 21.

47% (n=43/93) of PGNs and interneurons expressed long-lasting afterdischarges and 9% (n=8/93) displayed slow oscillatory bursts in the presence of 25  $\mu$ M DHPG, a specific agonist of group I metabotropic glutamate receptors. The plateaus were voltage-dependent and abolished by the mGluR1 antagonist, 4-CPG (500  $\mu$ M, n=4/4).

Similar to other observations in rat spinal cord and hippocampus, plateau potentials examined in this study were sustained by 2 cationic currents : – a L-type calcium current that was activated by S-BayK8644, 1  $\mu$ M (n=8) and blocked by nifedipine 10  $\mu$ M (n=10/10).

– and a calcium activated non-specific cationic current (ICAN) blocked by Flufenamic acid (500  $\mu$ M, n=5/5).

We have begun to address the role of TRPC1 channel activation in plateau expression. Using the TRPC1 antagonist, 2-APB (25  $\mu$ M), we have shown that inhibiting the IP3 receptors-TRPC1 pathway could drastically reduce the plateau potential activation (n=3/3).

This suggests a role of TRPC1 channels as modulators of plateau expression. The link between TRPC1 activation and plateau conductances expression remains to be investigated.

Our results demonstrate that neurons within the sacral IML area, including PGNs, may produce different firing patterns due to mechanisms described as responsible of cellular and central sensitization in other systems (motor, memory, and pain pathways). This ability could involve plasticity of autonomic nervous system at spinal cord level. (Funded by the Canadian Institutes for Health Research)

Citation:

D. Derjean, S.J. Shefchyk. RAT SACRAL SPINAL PARASYMPATHETIC NEURONS; L TYPE CALCIUM CHANNELS, CALCIUM ACTIVATED NON-SPECIFIC CATIONIC CURRENTS (ICAN) AND MULTIPLE FIRING PATTERNS Program No. 516.6. 2004 *Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 518.7

**Day / time:** Monday, Oct. 25, 3:00 PM – 4:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # P1

**INJURY–INDUCED EXPRESSION OF INFLAMMATORY CYTOKINES WITHIN RAT DORSAL ROOT GANGLIA**

**P.Miao;** M.Melanson; M.P.Namaka\*

*Fac. of Pharm., Univ. of Manitoba, Winnipeg, MB, Canada*

The general objective of this research was to determine the involvement of the dorsal root ganglia (DRG) in the underlying pathogenesis of chronic pain. The specific objective of this research was to determine if peripheral nerve axotomy induces the expression of inflammatory cytokines such as: tumor necrosis factor alpha (TNF- $\alpha$ ), interferon gamma (IFN- $\gamma$ ) and interleukin–12 (IL–12) within the DRG.

**Background:** Neuropathic pain is a chronic pain syndrome caused by drug, disease or injury induced damage or destruction of sensory neurons housed within the DRG. Neuronal hyperexcitability represents the hallmark cellular mechanism involved in the underlying pathophysiology of neuropathic pain. Injury–induced expression of inflammatory cytokines are thought to be associated with the development of this type of hyperexcitability that is linked to chronic pain syndromes such as neuropathic pain. **Methods:** Juvenile (postnatal day 11), sprague–dawley rats were divided into three experimental groups: naïve control, sham control and peripheral nerve axotomy (PNA). Naïve control animals had no surgical manipulation while sham controls had the sciatic nerve exposed without manipulation or damage. Animals in the PNA group underwent unilateral transection of sciatic nerve. In addition a marker of cell proliferation: 5–Bromo–2–Deoxyuridine (BrdU), was injected intraperitoneal (50  $\mu$ g/g) in all experimental groups. Immunohistochemical analysis was conducted on DRG cryostat sections (10  $\mu$ m) using antibodies directed against TNF- $\alpha$ , IFN- $\gamma$ , IL–12, and BrdU in conjunction with neuronal

markers NSE or glial markers such as GFAP. **Results:** PNA induces the up–regulation of inflammatory cytokine(s) within the DRG.

**Conclusion:** The injury–induced production of inflammatory cytokines within the DRG represents a plausible alternative target for attenuating the development of chronic pain syndromes.

**Citation:**

P. Miao, M. Melanson, M.P. Namaka. INJURY–INDUCED EXPRESSION OF INFLAMMATORY CYTOKINES WITHIN RAT DORSAL ROOT GANGLIA Program No. 518.7. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 631.9

**Day / time:** Tuesday, Oct. 26, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # O28

**DIFFERENTIAL EXPRESSION OF ADENOSINE REGULATING GENES IN CULTURED RAT FOREBRAIN NEURONS, ASTROCYTES AND C6 GLIOMA CELLS**

**F.E.Parkinson\***; W.Xiong

*Dept Pharmacol, Univ Manitoba, Winnipeg, MB, Canada*

In previous studies, we demonstrated that cultured astrocytes and neurons release adenosine and inosine, while C6 glioma cells released only inosine, upon treatment with in vitro ischemia–like conditions. Interestingly, while astrocytes, neurons and C6 cells appeared to release inosine via equilibrative nucleoside transporters, adenosine release appeared to be transporter–dependent in neurons and transporter–independent in astrocytes. The present study was performed to test the hypothesis that the differences in release of adenosine and inosine from cultured astrocytes, neurons and C6 cells is due to differences in expression of adenosine regulating enzymes. We isolated total RNA from cultured neurons, astrocytes, C6 cells and whole brain and performed RT–PCR analysis using oligonucleotide primers for cytosolic 5–nucleotidase type IA, IB and II (cNIA, cNIB, cNII), adenosine monophosphate deaminase types 1, 2 and 3 (AMPD1, AMPD2, AMPD3), equilibrative nucleoside transporter subtype 2 (ENT2), concentrative nucleoside transporter subtype 2 (CNT2), and glyceraldehyde–3–phosphate dehydrogenase (GAPDH). Expression of adenosine regulating genes was normalized to expression of GAPDH. Our results indicate cell type differences in expression of these genes. No expression of cNIB or AMPD1 was detected. C6 cells did not express cNIA, which may explain the lack of adenosine release from these cells. Neurons did not express AMPD3; however, as these cells did express AMPD2 this metabolic pathway in conjunction with cNII may still mediate inosine formation and release. The functional importance of ENT2 in these cells has been well established; however the additional expression of CNT2 indicates that this transporter may be important under some conditions. In conclusion, cell type differences in adenosine and inosine formation and release correspond to some of the differences in gene expression.

**Support Contributed By:** CIHR

**Citation:**

F.E. Parkinson, W. Xiong. DIFFERENTIAL EXPRESSION OF ADENOSINE REGULATING GENES IN CULTURED RAT FOREBRAIN NEURONS, ASTROCYTES AND C6 GLIOMA CELLS Program No. 631.9. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 610.1

**Day / time:** Tuesday, Oct. 26, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # D19

**THE VASCULAR SPECIFIC GROWTH FACTOR ANGIOPOIETIN 1 IS INVOLVED IN THE ORGANIZATION OF NEURONAL PROCESSES**

**N.L.Ward**1,2,3; T.Putoczki3; K.Mearow4; D.J.Dumont3; T.L.Ivanco2\*

*1. Anat., Case Western Reserve Univ., Cleveland, OH, USA2. Psychology, Univ. of Manitoba, Winnipeg, MB, Canada3. Div. of Mol. and Cell. Biol. Res., Sunnybrook and Women's Col. Res. Inst., Toronto, ON, Canada4. Div. of Basic Med. Sci., Mem. Univ. of Newfoundland, St. Johns, NF, Canada*

Neuronal processes and vessels have similar anatomical patterning in the adult body and appear to use many of the same molecules during their development. In order to determine whether the endothelial growth factor, angiopoietin (Ang) plays a unique role in the nervous system in addition to its angiogenic role, we utilized a conditional tetracycline based mouse molecular genetics approach to express the secreted growth factor, Ang1 in mouse forebrain neurons. Increases in overall vascularization, consistent with prior reports describing the role of Ang1 were found. In addition, nonvascular events, involving alterations in the dendritic organization of layer II motor cortex neurons, dentate granule cells, and the pyramidal cells of CA1 were seen, suggesting Ang1 was able to influence the growth of these processes. The angiopoietin tyrosine kinase receptor Tie2 was not found on neurons or their processes, but  $\alpha$ 1 integrin was and has previously been found to act as an Angiopoietin receptor. These findings provide some of the first data evaluating the effects of angiopoietins on the development of the nervous system. Understanding interactions between the developing nervous and vascular systems will lead to novel insight into how the two systems interact during development and in disease.

**Support Contributed By:** CIHR, NCI, NSERC, CFI, Carsen Group, MicroBrightField, and Optical Imaging.

**Citation:**

N.L. Ward, T. Putoczki, K. Mearow, D.J. Dumont, T.L. Ivanco. THE VASCULAR SPECIFIC GROWTH FACTOR ANGIOPOIETIN 1 IS INVOLVED IN THE ORGANIZATION OF NEURONAL PROCESSES Program No. 610.1. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** N/A

**Day / time:** Tuesday, Oct. 26, 5:30 PM – 6:30 PM

**Presentation Type:** Workshop

**Presentation Location:** San Diego Convention Center – Room 17A

**SFN BUSINESS/MEMBERS MEETING**

Information will be posted on the SFN Web site as it becomes available. CONTACT: Bridget Faraci Executive Department Society for Neuroscience 11 Dupont Circle, NW Suite 500 Washington, DC 20036 Phone: (202) 462–6688 [bridget@sfn.org](mailto:bridget@sfn.org)

**Citation:**

. SFN BUSINESS/MEMBERS MEETING Program No. N/A. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 761.10

**Day / time:** Tuesday, Oct. 26, 2:00 PM – 3:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # BB10  
**THE EFFECTS OF STRESS ON THE *IN VIVO* CYTOKINE RESPONSE TO ENDOTOXIN**

**B.J. MacNeil<sup>1</sup>; D.M. Nance<sup>2\*</sup>**

*1. Physical Therapy, Univ of Manitoba, Winnipeg, MB, Canada*; *2. Susan Samueli Ctr. for Integrative Med., Univ of California, Irvine, Orange, CA, USA*

Previously, we reported that rats injected with lipopolysaccharide (LPS, 0.1 μg iv) and

immediately exposed to 15 minutes of intermittent footshock displayed a marked suppression of tumor necrosis factor-α (TNF) production when measured 60 minutes after LPS injection. In

the present experiments a higher dose of LPS was used to expand the range of detectable cytokines. Further, we assessed whether the order of exposure to stress and LPS injection altered *in vivo* cytokine responses. Male Sprague Dawley rats were injected iv with 10 μg LPS and

subjected immediately to 15 minutes of intermittent footshock and sacrificed 45 minutes later for assay of splenic cytokine mRNA and protein. Footshock suppressed LPS-induced *in vivo* TNF mRNA production (p=0.01) but enhanced IL-6 mRNA synthesis (p=0.007) while IL-1β and MCP-1 mRNA production were not altered. These effects were consistent for splenic and plasma cytokine proteins; footshock reduced splenic (p=0.001) and plasma (p=0.004) TNF protein concentrations and increased splenic (p=0.017) and plasma (p=0.014) IL-6 levels. The effects of stress were not altered when footshock preceded LPS injection; stress inhibited *in vivo* TNF mRNA production (p<0.001), enhanced IL-6 synthesis (p=0.0014), and had no effect on IL-1β or MCP-1. Extending the duration between footshock and LPS injection to 4 or 24 hours eliminated all stress effects. Lastly, stress by itself was not able to enhance IL-6 mRNA production in saline-injected rats. In conclusion, footshock stress produces distinct effects on LPS-induced cytokine responses in that TNF production is markedly inhibited while IL-6 mRNA expression is enhanced. In contrast, production of IL-1 and MCP-1 was not altered by stress. Footshock alone did not stimulate IL-6 production indicating that stress enhanced the LPS-induced IL-6 response rather than providing an independent IL-6 stimulus.

*Support Contributed By: NIH (MH43778) and CIHR (38088)*

**Citation:**

B.J. MacNeil, D.M. Nance. THE EFFECTS OF STRESS ON THE *IN VIVO* CYTOKINE RESPONSE TO ENDOTOXIN Program No. 761.10. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 840.5

**Day / time:** Wednesday, Oct. 27, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # F21

**DLX1 AND DLX2 FUNCTION IS NECESSARY FOR TERMINAL DIFFERENTIATION AND SURVIVAL OF LATE-BORN RETINAL GANGLION CELLS IN THE DEVELOPING MOUSE RETINA**

**J.de Melo; G.Du; D.D.Eisenstat\***

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Dlx homeobox genes, vertebrate homologs of Distal-less, play important roles in development of the vertebrate forebrain and craniofacial structures. Members of the Dlx gene family are also expressed in retinal ganglion cells (RGC), amacrine and horizontal cells of the developing and postnatal retina. Expression begins at E12.5 and is maintained until late embryogenesis for Dlx1, while Dlx2 expression extends to adulthood (de Melo et al., 2003). The Dlx1/Dlx2 double knockout mouse dies at birth with cleft palate and abnormalities in differentiation of several cell types in the CNS. We have determined the retinal phenotype of the Dlx1/Dlx2 double knockout mouse by quantifying the expression of differentiation markers for specific retinal cell-types, transcription factors, proliferation indices and cell death. We have also assessed differentiation of retinal explant cultures derived from late embryonic wild-type and mutant mice, since retinal development proceeds postnatally in the mouse. Phenotypic analysis of the Dlx1/2 mutant demonstrates a reduced ganglion cell layer (GCL), with loss of differentiated RGCs due to significantly increased apoptosis of committed RGC progenitors, and corresponding thinning of the optic nerve. Proliferation indices are unaffected. Ectopic expression of Crx, the cone and rod photoreceptor homeobox gene, in the neuroblastic layer of the Dlx1/Dlx2 mutants may signify altered cell fate of uncommitted RGC progenitors. However, amacrine and horizontal cell differentiation is relatively unaffected in the Dlx1/2 null retina. Dlx1 and Dlx2 play an important role in retinal development by regulating terminal differentiation of RGC. We propose a model whereby Dlx1 and Dlx2 function is necessary for terminal differentiation of late-born RGC progenitors, whereas the transcription factor Brn3b is required for specification of early RGC progenitors.

*Support Contributed By: March of Dimes*

**Citation:**

J. de Melo, G. Du, D.D. Eisenstat. DLX1 AND DLX2 FUNCTION IS NECESSARY FOR TERMINAL DIFFERENTIATION AND SURVIVAL OF LATE-BORN RETINAL GANGLION CELLS IN THE DEVELOPING MOUSE RETINA Program No. 840.5. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 820.8

**Day / time:** Wednesday, Oct. 27, 9:45 AM – 10:00 AM

**Presentation Type:** Slide

**Presentation Location:** San Diego Convention Center – Room 2

**INHIBITION OF THROMBIN ACTIVATION BY HIRUDIN REDUCES BRAIN DAMAGE, INFLAMMATION, AND IMPROVES NEUROLOGICAL IMPAIRMENT FOLLOWING INTRACEREBRAL HEMORRHAGE IN NEONATAL MICE**

**M.Xue<sup>1,2,4\*</sup>; J.Balasubramaniam<sup>1,2,4</sup>; K.Parsons<sup>1,2,4</sup>; I.McIntyre<sup>4</sup>; J.Peeling<sup>3</sup>; D.R.Marc<sup>1,2,4</sup>**

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The mechanisms of brain cell injury following intracerebral hemorrhage (ICH) may be in part related to proteolytic activities in the brain, some of which are also functional in the developing brain. We hypothesized that activities of thrombin and plasmin (serine proteases) are responsible for brain damage following neonatal ICH and that inhibition of thrombin or plasmin activation would reduce brain damage and improve the neurological impairment following ICH in the neonatal mice. Neonatal rats (n=38) or mice at 2-day (n=85) and 10-day (n=40) ages were used. Rat brain cells were cultured for MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H tetrazolium bromide] colorimetric viability assay. Rats received injection of autologous blood into the striatum and brain slices were tested with enzyme overlay (EOM, thrombin and plasmin fluorogenic substrates). The two ages of mice in the short-term study were used to select which inhibitor we should use for the long-term study. Hematoxylin & eosin (H&E), Fluoro-Jade, lectin histochemistry, TUNEL staining were performed at 48 hours. The long-term study used low and high doses of hirudin mixed with blood to inhibit the thrombin activity. MRI, H&E, solochrome cyanine staining, ELISA for MBP, and behavioural testing were done. Whole blood decreased cell viability more than thrombin or plasmin. EOM showed increased serine protease activity around hematoma immediately after the blood injection. Hirudin significantly reduced brain inflammation, cell death, and brain damage 48 hours following ICH. Ten weeks after neonatal ICH, high dose hirudin exhibited a trend to mild brain protection. These results suggest that thrombin plays a role in neonatal brain damage following ICH.

*Support Contributed By: MHRC, CIHR*

**Citation:**

M. Xue, J. Balasubramaniam, K. Parsons, I. McIntyre, J. Peeling, D.R. Marc. INHIBITION OF THROMBIN ACTIVATION BY HIRUDIN REDUCES BRAIN DAMAGE, INFLAMMATION, AND IMPROVES NEUROLOGICAL IMPAIRMENT FOLLOWING INTRACEREBRAL HEMORRHAGE IN NEONATAL MICE Program No. 820.8. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 849.17

**Day / time:** Wednesday, Oct. 27, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # L11

**NEUREGULIN β<sub>1</sub> REGULATES INTERCELLULAR CALCIUM INFLUX IN CULTURED RAT HIPPOCAMPAL NEURONS VIA NMDA RECEPTORS**

**J.S.Schapansky<sup>2\*</sup>; R.Van Der Ploeg<sup>2</sup>; M.Morissette<sup>2</sup>; G.W.Glazner<sup>1</sup>**

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Neuregulin (NRG) is an important signaling protein necessary for neural development, functioning of neuromuscular junctions and synaptic plasticity. It has been implicated in glial cell-neuronal interaction, and has been shown to be a potential marker/target for schizophrenia. A great deal of study has focused on post-synaptic densities, where neuregulin seems to interact with its primary neuronal receptor, ErbB4 and in turn other synaptic proteins such as the NMDA receptor. In our studies, we have observed that 24h neuregulin β<sub>1</sub> pretreatment modulated glutamate response in cultured rat hippocampal neurons. Cells treated with neuregulin showed an increased initial glutamate-induced spike in intracellular calcium, followed by a more rapid drop in calcium levels compared to control neurons. Though neuregulin increased NMDA response, there was no increased glutamate-induced excitotoxicity. Indeed, neuregulin treatment afforded a small but significant protection from the excitotoxic effects of glutamate. Preliminary western blot analysis of cells treated with neuregulin show an increase in NR1 subunit expression, as well as phosphorylation of NR1 at S896. This phosphorylation was repressed by the P13 kinase inhibitor LY294002, indicating the AKT pathway may be involved. These initial results point to an ability of neuregulin to modulate intercellular calcium levels and simultaneously prevent the cell death often associated with increased activation of NMDA.

*Support Contributed By: Alzheimer's Society of Canada*

**Citation:**

J.S. Schapansky, R. Van Der Ploeg, M. Morissette, G.W. Glazner. NEUREGULIN β<sub>1</sub> REGULATES INTERCELLULAR CALCIUM INFLUX IN CULTURED RAT HIPPOCAMPAL NEURONS VIA NMDA RECEPTORS Program No. 849.17. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 882.14

**Day / time:** Wednesday, Oct. 27, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # GG12

**CHARACTERIZATION OF ELECTROPHYSIOLOGICAL AND PHARMACOLOGICAL PROPERTIES OF LOCOMOTOR ACTIVITY RELATED NEURONS IN CFOS–EGFP MICE**

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*1. Dept Physiol, Univ Manitoba, Winnipeg, MB, Canada. 2. Depts Surgery, Anat & Neurobiol, Dalhousie Univ, Halifax, NS, Canada*

Although it is well accepted that the spinal cord contains a system of interneurons (INs) capable of producing the locomotor rhythm, little is known about their electrophysiological properties. Here we investigate the properties of these neurons and the modulation of their properties by 5-HT and ACh, transmitter substances known to induce locomotor activity. Fluorescent INs were studied using whole cell patch clamp techniques in spinal cord slices from P4–P8 Cfos–EGFP mice (Brownstone et al. SFN Abs 65.8, 2002) following locomotor activity (walking or swimming 60–90 min). The target areas of study included laminae VII, VIII&X from segment T11–L6. The main properties measured from these neurons include input resistance(Ri), time constant, whole cell capacitance, current(Ith) and voltage threshold(Vth), and the frequency–current(f/I) relation. The EGFP labeled cells could be classified into three types based on firing induced by current injection(n=34): single spike (type 1, n=6), brief firing (type 2, n=7), and repetitive firing (type 3, n=21). The type 1 cells are mainly located in lamina VII&VIII, the type 2 in X, and the type 3 in VII,VIII&X. The type 1 cells show a higher Ith and lower Vth & Ri than those measured from the type 2&3 cells. Bath application (10–40 uM) of 5-HT and/or ACh modulated the firing properties, usually producing a hyperpolarization of Vth, left–shift of the f/I curve, depolarization of the membrane potential(Em), and changes in Ri. Some cells, however, showed hyperpolarization of Em and/or depolarization of Vth. The Em oscillations with peak–to–peak amplitude of ~8 mV and frequency of ~9 Hz are observed in type 3 cells (n=4) after application of 5-HT. Investigation of the locations and axonal projections of the various cell types revealed in this study should allow delineation of functional classes of locomotor INs.

*Support Contributed By: NIH391313520*

**Citation:**

Y. Dai, L.M. Jordan, R.M. Brownstone. CHARACTERIZATION OF ELECTROPHYSIOLOGICAL AND PHARMACOLOGICAL PROPERTIES OF LOCOMOTOR ACTIVITY RELATED NEURONS IN CFOS–EGFP MICE Program No. 882.14. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.2

**Day / time:** Wednesday, Oct. 27, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # HH1

**MODELLING THE VARIETY OF ACTIVATION PATTERNS OF BIFUNCTIONAL HINDLIMB MOTONEURONS DURING FICTIVE LOCOMOTION**

**S.Chakrabarty**<sup>1</sup>\*; I.A.Rybak<sup>2</sup>; D.A.McCrea<sup>1</sup>

*1. Spinal Cord Res. Centre, Univ Manitoba, Winnipeg, Manitoba, MB, Canada. 2. Sch Biomed Eng, Drexel Univ, Philadelphia, PA, USA*

During real locomotion the activity of the bifunctional hip extensor and knee flexor muscles, posterior biceps semitendinosus (PBST), varies according to the gait or posture of the animal and sensory feedback may be one of the components shaping bifunctional activity patterns (e.g., Carlson–Kuhta et al. J Neurophysiol, 1998). This report describes the variety of PBST activities observed during fictive locomotion in the absence of proprioceptive sensory feedback. During fictive locomotion evoked by midbrain stimulation, four different patterns of PBST activity have been observed in 30 pre–collicular, post–mamillary decerebrate cats. (1) a short burst of activity at the onset of each flexion phase (37%); (2) firing throughout the flexion phase (15%); (3) firing throughout the extension phase (22%); (4) activity during both the flexion and extension phases (26%). Intracellular recordings from PBST motoneurons show that these patterns result from distinct profiles of rhythmic depolarization and hyperpolarization produced at a pre–motoneuronal level and not just alterations in the amplitude of a biphasic depolarizing drive to PBST motoneurons during the step cycle.

A model of PBST motoneurons was incorporated into our computational model of the locomotor CPG in which rhythm generator (RG) and pattern formation networks (PF) are separated (Rybak et al this meeting). We show that it is possible to reproduce all 4 PBST patterns by changing the balance between inhibition from RG level and excitation from flexor and extensor parts of PF network. The model also predicts that afferent feedback can control the expression of each particular pattern type, which is consistent with data on real locomotion. This prediction may be tested experimentally in fictive locomotion preparations.

*Support Contributed By: Supported by the CIHR*

**Citation:**

S. Chakrabarty, I.A. Rybak, D.A. McCrea. MODELLING THE VARIETY OF ACTIVATION PATTERNS OF BIFUNCTIONAL HINDLIMB MOTONEURONS DURING FICTIVE LOCOMOTION Program No. 883.2. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.1

**Day / time:** Wednesday, Oct. 27, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # GG20  
**DELETIONS OF ENG ACTIVITY DURING FICTIVE LOCOMOTION AND SCRATCH SHOW MAINTAINED CYCLE PERIOD TIMING DESPITE FAILURES OF RHYTHMIC MOTONEURON EXCITATION AND INHIBITION**

**M.Lafreniere–Roula**<sup>\*</sup>; D.A.McCrea

*Univ of Manitoba, Spinal Cord Res. Centre, Winnipeg, MB, Canada*

Central pattern generator (CPG) circuits exist in the mammalian spinal cord that can produce rhythmic activity in the absence of both rhythmic sensory feedback and cortical input. In order to better understand the possible organization of the CPG we have been analysing errors (deletions) in rhythmic pattern generation that occur spontaneously during electrically–evoked fictive locomotion and drug–evoked fictive scratch in paralysed, decerebrate cats.

Deletions consist of missing bursts of motoneuron firing recorded in peripheral nerve electroencephalograms (ENGs). During both behaviours, deletions are accompanied by sustained activity in antagonist ENGs. Intracellular recordings show that the amplitude of the locomotor and scratch drive potentials in motoneurons is reduced during deletions: the depolarizing phase is reduced in motoneurons belonging to agonist pools (those with deletions) and the hyperpolarizing phase is most often reduced in motoneurons of the antagonist pools (those with sustained activity).

Although the rhythmic drive to motoneurons is reduced during spontaneously occurring deletions, the timing of the cycle period is often unaffected. A comparison of the interval between successive bursts of activity during deletions and normal cycles shows that the reappearance of activity following a deletion comes at an integer multiple of the average period during normal cycles. Thus, the timing of the rhythmic activity can be maintained despite a failure in the drive to motoneuron pools. This is not a feature expected from a simple half–centre organization of the mammalian CPG.

A more realistic model of the CPG should allow for a dissociation of the generation of cycle timing and the distribution of the rhythmic excitation and inhibition to motoneuron pools. This concept is implemented in a model of the CPG presented at this meeting (Rybak et al. SFN 2004).

*Support Contributed By: CIHR*

**Citation:**

M. Lafreniere–Roula, D.A. McCrea. DELETIONS OF ENG ACTIVITY DURING FICTIVE LOCOMOTION AND SCRATCH SHOW MAINTAINED CYCLE PERIOD TIMING DESPITE FAILURES OF RHYTHMIC MOTONEURON EXCITATION AND INHIBITION Program No. 883.1. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.3

**Day / time:** Wednesday, Oct. 27, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # HH2  
**A TWO LAYER MODEL OF THE SPINAL LOCOMOTOR CPG: INSIGHTS FROM DELETIONS OF ACTIVITY DURING FICTIVE LOCOMOTION**

**I.A.Rybak**<sup>1</sup>\*; M.Lafreniere–Roula<sup>2</sup>; N.A.Shevtsova<sup>1</sup>; D.A.McCrea<sup>2</sup>

*1. Sch Biomed Engin., Drexel Univ, Philadelphia, PA, USA. 2. Spinal Cord Res. Centre, Univ Manitoba, Winnipeg, MB, Canada*

A computational model of the locomotor central pattern generator (CPG) in the mammalian spinal cord has been developed on the basis of a comprehensive analysis of the patterns of motoneuron activity occurring during fictive locomotion evoked by midbrain stimulation in decerebrate cats. Specifically, our analysis focused on “deletions”, which are errors in the alternating rhythmic activity of flexor and extensor motoneurons that occur spontaneously during fictive locomotion. During deletions, the activity of agonist motoneurons (e.g., extensors) is missing for an integer number of cycles whereas the activity of antagonists becomes tonic or continues to be rhythmic. We concluded that the patterns of motoneuron activities observed during deletions could not be explained within the framework of existing CPG models, including the classical Brown–Lundberg “half–centre” model (HCM). Our model extends the HCM and is based on a two–level CPG consisting of a half–centre rhythm generator (RG) and a pattern formation circuitry (PF) with reciprocal inhibitory interactions between antagonistic groups of neurons at three levels (RG, PF and Ia interneurons). Each interneuron and motoneuron type in the model is represented by a population of 10–20 neurons modelled in the Hodgkin–Huxley style. The model realistically reproduces patterns of alternating rhythmic activity of flexor, extensor and bifunctional motoneuronal populations, as well as the dynamics of membrane potentials of individual motoneurons. In addition it can recreate the anomalous network behaviour seen during deletions in fictive locomotion including the maintenance of cycle period. The results of modelling provide a basis for functional identification of spinal cord interneurons involved in generation and control of the locomotor pattern in mammals.

*Support Contributed By: CIHR, NIH and NSF*

**Citation:**

I.A. Rybak, M. Lafreniere–Roula, N.A. Shevtsova, D.A. McCrea. A TWO LAYER MODEL OF THE SPINAL LOCOMOTOR CPG: INSIGHTS FROM DELETIONS OF ACTIVITY DURING FICTIVE LOCOMOTION Program No. 883.3. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.4

**Day / time:** Wednesday, Oct. 27, 11:00 AM – 12:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # HH3

**MODELLING PROPRIOCEPTIVE SENSORY CONTROL OF THE MAMMALIAN LOCOMOTOR CPG**

**D.A. McCrea**<sup>1</sup>; N.A. Shevtsova<sup>2</sup>; K. Stecina<sup>1</sup>; I.A. Rybak<sup>2</sup>

<sup>1</sup>. Dept Physiology, Univ Manitoba Fac Med, Winnipeg, MB, Canada<sup>2</sup>. Sch. of Biomed. Engin., Drexel Univ., Philadelphia, PA, USA

We have developed a computational model of the lumbar locomotor central pattern generator (CPG) in adult cats that contains a half-centre rhythm generator (RG) and a pattern formation network (PF) with reciprocal inhibitory interactions between antagonistic groups of neurons at several levels. Each functional type of neurons is represented by a population of 10–20 neurons modelled in the Hodgkin–Huxley style. Sensory feedback has been incorporated in the model using known neuronal connections and those suggested from our studies of fictive locomotion in decerebrate cats. The model accurately reproduces a series of experimentally observed phase-dependent effects of stimulation of group I and II flexor and extensor afferents upon patterns of motoneuron activities, timing of phase switching, and locomotor cycle period. Specifically and similar to our experimental findings, activation of extensor group I afferents during extension may prolong the extensor phase with or without resetting the step cycle, whereas their activation during flexion produces a temporary resetting to extension without changing the ongoing cycle period. The model shows that these phenomena may result from different effects of sensory input to the RG and PF layers of the CPG. The model also suggests that the different effects of flexor afferent stimulation during flexion observed experimentally (phase prolongation vs. resetting) may result from opposing influences of group I and II flexor afferents on the flexor and extensor parts of PF and RG. We show that the two-layered CPG can readily accommodate the effects of sensory regulation of stepping that have been observed during real and fictive locomotion. Modelling the effect of afferent stimulation provides insight into organization of mammalian CPG and allows us to postulate specific neuronal interactions in the spinal cord during locomotion that can be tested experimentally.

*Support Contributed By: the CIHR and NIH*

Citation:

D.A. McCrea, N.A. Shevtsova, K. Stecina, I.A. Rybak. MODELLING PROPRIOCEPTIVE SENSORY CONTROL OF THE MAMMALIAN LOCOMOTOR CPG Program No. 883.4. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.18

**Day / time:** Wednesday, Oct. 27, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # HH17

**THE ROLES OF SPINAL 5-HT<sub>2A</sub> AND 5-HT<sub>7</sub> RECEPTORS IN BRAINSTEM EVOKED LOCOMOTION**

**J.Liu**<sup>\*</sup>; L.M.Jordan

*The Univ Manitoba, Winnipeg, MB, Canada*

Experiments performed in *in vitro* and *in vivo* mammalian preparations demonstrated that 5-hydroxytryptamine (5-HT) plays a critical role in initiating locomotor activity. Thus, 5-HT must activate interneurons of the locomotor central pattern generator. In addition, motoneurons in the spinal cord receive serotonergic terminals originating from the medioventral medulla, and they are excited by 5-HT. To explore the contributions of 5-HT receptor subtypes to the generation and regulation of locomotion in the spinal cord, we used electrical stimulation of the ventromedial medulla to evoke locomotor-like activity in the brain-stem spinal cord preparation of the neonatal rat. The motor output was recorded with suction electrodes on ventral roots, and multiple bath partitions were set up to allow application of drugs to selected regions of the spinal cord. When 5-HT<sub>7</sub> antagonists clozapine (0.5–1 μM) and SB269970 (10–15 μM) were applied to the T10–L1 segments, locomotor activity was completely abolished. Both the rate of rhythmic activity and the amplitude of ventral root discharges were suppressed at low concentrations. In contrast, no effect was obtained when these drugs were applied caudal to the L1 level. The addition of the 5-HT<sub>2A</sub> receptor antagonist ketanserin caudal to the L1 level caused a considerable decrease in the amplitude of the ventral root activity. However, the rate of locomotion was little perturbed. Further increasing the concentration of ketanserin (20 μM) eliminated locomotion. The rhythmic activity as well as the amplitude of ventral root activity remained unchanged when the 5-HT<sub>2A</sub> antagonist was applied to the T10–T13 segments. We conclude that 5-HT<sub>7</sub> receptor antagonists influence the locomotor rhythm by acting directly on neurons of the locomotor CPG, whereas 5-HT<sub>2A</sub> receptor antagonists affect locomotion by reducing motoneuron output.

*Support Contributed By: Canadian Institutes of Health Research and National Institutes of Health*

Citation:

J. Liu, L.M. Jordan. THE ROLES OF SPINAL 5-HT<sub>2A</sub> AND 5-HT<sub>7</sub> RECEPTORS IN BRAINSTEM EVOKED LOCOMOTION Program No. 883.18. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.

**Program Number:** 883.8

**Day / time:** Wednesday, Oct. 27, 11:00 AM – 12:00 PM

**Presentation Type:** Poster

**Presentation Location:** San Diego Convention Center – Hall A–H, Board # HH7

**WELL-COORDINATED LOCOMOTOR ACTIVITY CAN BE PRODUCED IN THE ISOLATED NEONATAL RAT SPINAL CORD BY ACTIVATION OF THE ENDOGENOUS CHOLINERGIC PROPRIOSPINAL SYSTEM**

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Previous studies using the isolated neonatal rat spinal cord preparation showed that acetylcholine (ACh) can induce rhythmic activity, but only rarely does it produce sustained patterns of ventral root activity compatible with hindlimb stepping (Cowley and Schmidt, 1994). Instead, it most often produced alternating activity of the L and R sides, but synchronous activity of flexors and extensors of one side. ACh is known to have an action on spinal neural systems not related to locomotion; these effects may alter an underlying locomotor rhythm. We tested the notion that increasing the activity in the coupled cholinergic propriospinal network can produce well-coordinated locomotion. We enhanced the effects of endogenous ACh with edrophonium (25–100 μM, a cholinesterase inhibitor), and monitored the pattern of activity in the L2 and L5 ventral roots bilaterally. Rhythmic activity was produced in 87% of trials. Rhythm that was typical of hindlimb stepping was produced in 69% of these (L/R and flexor-extensor alternation bilaterally). Polar analysis of rhythmic activity in the ventral roots revealed that the onset of bursts in RL2 occurred out of phase with the bursts in RL5 (r=–.819, sd .089, n=27), indicating flexor extensor alternation. Comparisons between the bursts in RL2 and LL2 revealed l/r alternation (r=–.852, sd .092, n=26). RL2 and LL5 were in phase (r=–.888, sd .064, n=26), as were RL5 and LL2 (r=–.814, sd .183, n=26). Atropine (1 μM) blocked the edrophonium-induced rhythm, showing that muscarinic receptors are activated by the cholinergic propriospinal system. Low doses (3 nM) of 4DAMP (M3 antagonist) blocked the edrophonium-induced rhythm, while low doses of M1, M2 and M4 antagonists (telenzepine, 5 μM; methoctramine, 3 μM; MT3, 5 nM) were without effect. We conclude that M3 muscarinic receptors are involved in the activation of the cholinergic propriospinal system for the production of locomotion.

*Support Contributed By: CIHR and NIH*

Citation:

L.M. Jordan, J.R. McVagh. WELL-COORDINATED LOCOMOTOR ACTIVITY CAN BE PRODUCED IN THE ISOLATED NEONATAL RAT SPINAL CORD BY ACTIVATION OF THE ENDOGENOUS CHOLINERGIC PROPRIOSPINAL SYSTEM Program No. 883.8. 2004 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2004. Online.