

# WINNIPEG\_GROUP

## Sunday, Nov. 5 AM – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Sunday, Nov. 5, 8:00 AM – 9:00 AM	35.5	Poster	N-6	<u>P.N. Shepel*</u> ; C.P. Holden; J.D. Geiger	Department of Pharmacology and Therapeutics Faculty of Medicine, University of Manitoba	<b>RYANODINE RECEPTORS ASSOCIATED WITH RAT BRAIN SYNAPTIC VESICLES ARE MODULATED BY DIADENOSINE POLYPHOSPHATES.</b>
Sunday, Nov. 5, 8:00 AM – 9:00 AM	59.1	Poster	II-80	<u>S. Gosgnach*</u> ; J. Quevedo; K. Stecina; D.A. McCrea	Dept. of Physiology, University of Manitoba	<b>A COMPARISON OF MONOSYNAPTIC IA EPSP AND FIELD POTENTIAL DEPRESSION DURING FICTIVE LOCOMOTION AND FICTIVE SCRATCH.</b>
Sunday, Nov. 5, 9:00 AM – 10:00 AM	59.2	Poster	II-81	<u>L.M. Jordan*</u> ; D.M. Nance; K. Madec	Dept. of Physiology, University of Manitoba	<b>5-HT7 RECEPTOR IMMUNOREACTIVITY IS FOUND IN SOME SPINAL NEURONS THAT EXPRESS C-FOS FOLLOWING TREADMILL LOCOMOTION IN THE ADULT RAT.</b>
Sunday, Nov. 5, 10:00 AM – 11:00 AM	59.3	Poster	II-82	<u>D.M. Fyda*</u> ; B. Fedirchuk; L.M. Jordan	Dept. of Physiol., Univ. of Manitoba	<b>THE ABILITY OF SEROTONERGIC RECEPTORS TO ALTER LOCOMOTOR PERFORMANCE IN ADULT ANIMALS.</b>
Sunday, Nov. 5, 9:00 AM – 10:00 AM	60.2	Poster	JJ-4	<u>K.C. Cowley</u> ; B.J. Schmidt*	Medicine and Physiology, University of Manitoba	<b>CHARACTERIZATION OF PROPRIOSPINAL COUPLING BETWEEN THE CERVICAL AND LUMBAR REGIONS DURING RHYTHMIC MOTOR ACTIVITY IN THE <i>IN VITRO</i> NEONATAL RAT SPINAL CORD.</b>
Sunday, Nov. 5, 10:00 AM – 11:00 AM	64.15	Poster	JJ-83	<u>D.J. Kriellaars*</u> ; S. Webber; C. Lewis	Sch Med Rehab, Univ Manitoba	<b>NEUROMECHANICAL BASIS OF TRUNK STABILIZATION.</b>
Sunday, Nov. 5, 8:00 AM – 9:00 AM	73.1	Poster	LL-49	<u>J.D. Churchill</u> <sup>1,3*</sup> ; T.L. Ivanc <sup>1,3</sup> ; S. Patel <sup>3</sup> ; D. Norr <sup>3</sup> ; M. DeRidder <sup>3</sup> ;	Beckman Institute	<b>LEARNING INDUCED NEUROPHYSIOLOGICAL MODIFICATIONS IN THE RAT CORTEX: ARE THEY LTP-LIKE?</b>

				W.T. Greenough <sup>1,2,3</sup>		
Sunday, Nov. 5, 11:00 AM – 12:00 PM	80.12	Poster	NN-59	T.L. Ivanco <sup>1*</sup> ; W.T. Greenough <sup>1,2,3</sup>	Beckman Institute, University of Illinois	<b>FRAGILE X KNOCKOUT MICE SHOW AN INCREASE IN MOSSY FIBER SPROUTING IN THE HIPPOCAMPUS COMPARED TO WILDTYPE MICE.</b>
Sunday, Nov. 5, 8:00 AM – 9:00 AM	89.5	Poster	PP-53	M. Mayne <sup>1*</sup> ; C.P. Holden <sup>1</sup> ; A. Nath <sup>2</sup> ; J.D. Geiger <sup>1</sup>	Department of Pharmacology and Therapeutics, University of Manitoba	<b>RELEASE OF CALCIUM FROM IP<sub>3</sub> RECEPTOR-REGULATED STORES BY HIV-1 TAT REGULATES TNF-<math>\alpha</math> PRODUCTION IN HUMAN MACROPHAGES.</b>
Sunday, Nov. 5, 9:00 AM – 10:00 AM	89.6	Poster	PP-54	J.J. Kort <sup>*</sup> ; J.D. Geiger	Department of Pharmacology and Therapeutics, University of Manitoba	<b>HIV INFECTION ALTERS EXPRESSION AND ACTIVITY OF HUMAN NUCLEOSIDE TRANSPORTERS.</b>

**Sunday, Nov. 5 PM – Poster Presentations**

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Sunday, Nov. 5, 3:00 PM – 4:00 PM	132.15	Poster	U-1	A.C.W. Weeks <sup>1</sup> ; T.L. Ivanco <sup>2</sup> ; J.C. LeBoutillier <sup>1</sup> ; R.J. Racine <sup>2</sup> ; T.L. Petit <sup>1*</sup>	Psychology Department, University of Toronto	<b>SYNAPTIC MORPHOLOGY DURING THE LONG-TERM MAINTENANCE OF LTP: STRUCTURAL CHANGES 5 DAYS POST-LTP INDUCTION.</b>
Sunday, Nov. 5, 1:00 PM – 2:00 PM	149.5	Poster	II-48	J.D. Geiger <sup>*</sup> ; J.A. Fotheringham <sup>1</sup> ; M.B. Mayne <sup>1</sup> ; G.W. Glazner	Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Manitoba Fac Med	<b>ADENOSINE A<sub>2A</sub> RECEPTOR ACTIVATION INHIBITS TNF-<math>\alpha</math> PRODUCTION IN A CAMP INDEPENDENT MANNER.</b>

**Monday, Nov. 6 AM – Poster Presentations**



Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Nov. 6, 11:00 AM – 12:00 PM	234.16	Poster	Y-6	S. Camandola <sup>1</sup> ; G.W. Glazner <sup>2</sup> ; J.D. Geiger <sup>2</sup> ; M.P. Mattson <sup>1</sup>	Laboratory of Neuroscience, National Institute on Aging	<b>REGULATION OF IP3 CALCIUM CHANNELS BY NUCLEAR FACTOR-<math>\kappa</math>B.</b>
Monday, Nov. 6, 9:00 AM – 10:00 AM	257.10	Poster	KK-11	K.P. Carlin*; K.E. Jones; Z. Jiang; R.M. Brownstone	Dept Physiology, Univ Manitoba	<b>SEQUENTIAL ACTIVATION OF DENDRITES IN THE GENERATION OF CALCIUM CURRENTS IN MAMMALIAN MOTONEURONES.</b>
Monday, Nov. 6, 9:00 AM – 10:00 AM	289.2	Poster	QQ-52	J. Peeling <sup>1</sup> ; M.R. Del Bigio <sup>2</sup> ; D. Corbett <sup>3</sup> ; A.R. Green <sup>4</sup> ; D. Jackson <sup>5</sup> *	Depts of Radiology, University of Manitoba	<b>EFFICACY OF DISODIUM 4-[(<i>TERT</i>-BUTYLIMINO) METHYL] BENZENE-1,3-DISULFONATE N-OXIDE, A WATER SOLUBLE SPIN TRAP, IN A RAT MODEL OF HEMORRHAGIC STROKE.</b>

### Monday, Nov. 6 AM – Platform Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Nov. 6, 10:00 AM – 10:15 AM	204.9	Slide	Conference Auditorium A	T. Szturm; T. Bhatt; J. Paterson*	Faculty of Medicine, University of Manitoba	<b>LIMITS OF BALANCE RECOVERY IN HEMIPARETIC STROKE INDIVIDUALS DURING CORRECTIVE INPLACE AND STEPPING RESPONSES.</b>

### Monday, Nov. 6 PM – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Monday, Nov. 6, 1:00 PM – 2:00 PM	384.5	Poster	QQ-17	M. Qiao <sup>1</sup> ; K.L. Malisza <sup>1</sup> ; S. Bascaramurti; T. Foniok <sup>1</sup> ; M. Del Bigio <sup>2</sup> ; U.I. Tuor <sup>1</sup> *	Institute for Biodiagnostics, National Research Council of Canada	<b>CORRELATION OF CEREBRAL HYPOXIC/ISCHEMIC CHANGES IN T2 WITH ALTERATIONS IN WATER CONTENT AND VASCULAR PERMEABILITY.</b>

## Tuesday, Nov. 7 AM – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Tuesday, Nov. 7, 10:00 AM – 11:00 AM	423.15	Poster	O-4	<u>Y. Dai</u> *; R.M. Brownstone; B. Fedirchuk; L.M. Jordan	Dept of Physiology, University of Manitoba	<b>COMPUTER SIMULATION OF NMDA-MEDIATED VOLTAGE-DEPENDENT EXCITATION OF CAT LUMBAR MOTONEURONS DURING FICTIVE LOCOMOTION.</b>
Tuesday, Nov. 7, 9:00 AM – 10:00 AM	460.2	Poster	LL-57	<u>D.A. McCrea</u> *; K. Stecina; J. Quevedo; S. Gosgnach	Dept. Physiology, University of Manitoba	<b>FLEXOR GROUP II MUSCLE AFFERENTS CAN ENHANCE FLEXOR ACTIVITY DURING FICTIVE LOCOMOTION.</b>

## Tuesday, Nov. 7 AM – Platform Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Tuesday, Nov. 7, 8:15 AM – 8:30 AM	406.2	Slide	Room 388	<u>J. de Melo</u> <sup>1</sup> ; X. Qiu <sup>1</sup> ; J.L. Rubenstein <sup>2</sup> ; D.D. Eisenstat <sup>1*</sup>	Manitoba Institute of Cell Biology, University of Manitoba	<b>EXPRESSION OF DLX HOMEBOX GENES IN THE EMBRYONIC AND POSTNATAL VERTEBRATE RETINA.</b>

## Wednesday, Nov. 8 AM – Poster Presentations

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Wednesday, Nov. 8, 10:00 AM – 11:00 AM	625.19	Poster	GG-10	<u>T. Othman</u> ; C.J.D. Sinclair; L. Mazur; N. Haughey; J.D. Geiger; F.E. Parkinson*	Dept. of Pharmacology and Therapeutics Univ. of Manitoba	<b>HYDROGEN PEROXIDE-MEDIATED OXIDATIVE STRESS INHIBITS GLUTAMATE AND ADENOSINE TRANSPORT IN RAT ASTROCYTES AND C6 CELLS.</b>
Wednesday,	629.5	Poster	HH-28	<u>K.L.</u>	Dept.	<b>CHOLINERGIC NEURONS AND</b>

Nov. 8, 8:00 AM – 9:00 AM				<u>Paroschy*</u> ; S.J. Shefchyk	Physiology, University of Manitoba	<b>TERMINALS WITHIN THE L6 AND S1 VENTRAL HORN OF THE ADULT AND NEONATAL RAT SPINAL CORD.</b>
Wednesday, Nov. 8, 10:00 AM – 11:00 AM	655.11	Poster	MM-44	<u>C.P. Holden</u> 1; P.N. Shepel1; M. Mackiewicz2; A.I. Pack2*; J.D. Geiger1	Dept. of Pharmacology and Therapeutics Univ. of Manitoba	<b>BRAIN GLYCOGEN LEVELS ARE DECREASED WITH INCREASED WAKEFULNESS AND MAY REPRESENT A HOMEOSTATIC DRIVE FOR SLEEP.</b>

**Wednesday, Nov. 8 PM – Poster Presentations**

Day / Time	Prog #	Presentation Type	Location	Authors	1st Author 1st Affiliation	Title
Wednesday, Nov. 8, 2:00 PM – 3:00 PM	747.6	Poster	LL-50	<u>J.N. Quevedo</u> *; K. Stecina; S. Gosgnach; D.A. McCrea	Department of Physiology, Faculty of Medicine, University of Manitoba	<b>ACTIVITY OF HIP FLEXORS PRECEDES THAT OF ANKLE FLEXORS DURING FICTIVE LOCOMOTION AND SCRATCHING.</b>

**Program Number:** 35.5

**Day / time:** Sunday, Nov. 5, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**RYANODINE RECEPTORS ASSOCIATED WITH RAT BRAIN SYNAPTIC VESICLES ARE MODULATED BY DIADENOSINE POLYPHOSPHATES.**

P.N. Shepel\*; C.P. Holden; J.D. Geiger

*Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Canada*

Calcium-sensitive release of intracellular calcium ( $Ca^{2+}_i$ ) from endoplasmic reticulum is regulated by the ryanodine receptor-regulated  $Ca^{2+}_i$  release channel (RyR) and  $Ca^{2+}_i$ -induced  $Ca^{2+}_i$  release (CICR) processes are mediated by this receptor complex. In this work, we tested the hypothesis that RyRs could be modulated by an endogenous group of purinergic compounds termed diadenosine polyphosphates (ApnAs) which are formed during protein synthesis reactions. In addition, we investigated the subcellular origin of ryanodine binding activity previously found in synaptosomal fractions. Western blot analysis was used to determine the presence of RyR subtypes in subcellular fractions as well as the relative abundance of synaptic vesicle (synaptophysin) and endoplasmic reticulum (GRP 78) proteins in synaptosomal subfractions separated by sucrose gradient centrifugation. [ $^3H$ ]Ryanodine binding assays were used to determine the extent of RyR modulation by ApnAs. The increase in [ $^3H$ ]ryanodine binding by ApnAs in both microsomal and synaptosomal fractions suggested that these compounds were acting to potentiate the open state of the channel complex. The lightest synaptosomal subfractions, that contained the highest abundance of synaptophysin and only traces of GRP 78, showed the highest levels of [ $^3H$ ]ryanodine binding and most robust effects by ApnAs compared to heavier subfractions containing higher levels of the ER protein. These data suggest that ApnAs can alter the activity of RyRs and that RyRs associated with synaptic vesicles may play a role in  $Ca^{2+}_i$ -mediated neurotransmitter release. (This research was supported by grants and salary awards from the Medical Research Council of Canada.)

**Program Number:** 59.2

**Day / time:** Sunday, Nov. 5, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**5-HT<sub>7</sub> RECEPTOR IMMUNOREACTIVITY IS FOUND IN SOME SPINAL NEURONS THAT EXPRESS C-FOS FOLLOWING TREADMILL LOCOMOTION IN THE ADULT RAT.**

L.M. Jordan\*; D.M. Nance; K. Madec

*Dept. of Physiology, University of Manitoba, Winnipeg, MB, Canada*

5-HT agonists enhance locomotion in chronic spinal cats (Rossignol et al, *Ann. N.Y. Acad. Sci.*, 860:346, 1998) and in adult spinal rats (Feraboli-Lohnherr et al, *J. Neurosci. Res.*, 55:87, 1999; Kim et al, *J. Neurosci.*, 19:6213, 1999), and 5-HT is sufficient for evoking locomotion in the isolated neonatal rat spinal cord (Cowley & Schmidt, *Neurosci. Lett.* 171:147–150). 5-HT<sub>7</sub> receptors appear to be required for 5-HT and brainstem-evoked locomotion in the neonatal rat (Cina & Hochman, *Soc. Neurosci. Abstr.* 24:654.24, 1998; Fyda & Jordan, *Soc. Neurosci. Abstr.* 25:762.2, 1999). Here we use double-labeling with an anti-5-HT<sub>7</sub> receptor antibody in combination with an anti-*c-fos* antibody to detect spinal neurons which are activated during a treadmill locomotor task and possess 5-HT<sub>7</sub> receptors. Nuclear *c-fos* labeling, co-localized with dense cytoplasmic 5-HT<sub>7</sub> receptor labeling, was most commonly observed in neurons of laminae VI–VIII and lamina X in the thoracic and lumbar segments of the spinal cord, and to a lesser degree in laminae IV and V. Double-labeled neurons were found throughout the thoracic (T11 – T13) and lumbar (L1–L3) segments. The incidence of double-labeled neurons diminished in more caudal lumbar segments (L4–L6). No cytoplasmic 5-HT<sub>7</sub> receptor labeling was observed in the motoneurons of the ventral horn, although motoneurons were surrounded by bouton-like profiles that were stained with the 5-HT<sub>7</sub> receptor antibody. Confocal microscopy revealed no evidence for membrane labeling of motoneurons with the 5-HT<sub>7</sub> receptor antibody; rather, the labeling in the vicinity of motoneurons appeared to be confined to presynaptic elements. Dense cytoplasmic 5-HT<sub>7</sub> receptor labeling was also observed in many neurons in the superficial dorsal horn, but cells in this region did not express *c-fos* following the treadmill locomotor task. The double-labeled neurons described here are likely responsible for the 5-HT<sub>7</sub> receptor-mediated effects on the initiation of locomotion  
Supported by: The M.R.C.

**Program Number:** 59.1

**Day / time:** Sunday, Nov. 5, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**A COMPARISON OF MONOSYNAPTIC IA EPSP AND FIELD POTENTIAL DEPRESSION DURING FICTIVE LOCOMOTION AND FICTIVE SCRATCH.**

S. Gosgnach\*; J. Quevedo; K. Stecina; D.A. McCrea

*Dept. of Physiology, University of Manitoba, Winnipeg, MB, Canada*

During fictive locomotion evoked by electrical stimulation of the brainstem (MLR) in decerebrate cats, there is a substantial reduction in the amplitude of monosynaptic EPSPs recorded in motoneurons and extracellular field potentials evoked by stimulation of hindlimb group Ia muscle spindle afferents (Gosgnach et al., *J. Physiol.* in press). This depression of afferent transmission is presynaptic in origin and persists for several minutes after fictive locomotion. We now report the depression of Ia transmission during another rhythmic motor behaviour, fictive scratch. Fictive scratch was evoked in paralysed decerebrate preparations following topical application of curare to the cervical spinal roots and gentle manual stimulation of the pinna. The depression of monosynaptic Ia actions is similar in the two behaviours. The mean depression of extracellular field potentials during fictive scratch and fictive locomotion was 25% and 28% and EPSPs recorded in motoneurons were reduced by 43% and 30% respectively. During both scratch and locomotion, fields and EPSPs recorded during either the flexion and extension phases were smaller than during control conditions (i.e. a tonic depression). The depression during one of the phases was more pronounced in some cases but there was no consistency in which phase the maximum depression occurred. Recovery of field and EPSP amplitude was delayed following both fictive scratch and locomotion. Recovery following fictive scratch, however, occurred more rapidly (mean 30s, n=12) than after locomotion (mean 120s n=32). The depression of monosynaptic Ia transmission and the delayed recovery is further support for the suggestion that such depression is a feature of the central generation of these two fictive behaviours and not a consequence of brainstem stimulation per se (Perreault et al. *J. Physiol* 521:691–703, 1999).  
Supported by: Canadian MRC.

**Program Number:** 59.3

**Day / time:** Sunday, Nov. 5, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**THE ABILITY OF SEROTONERGIC RECEPTORS TO ALTER LOCOMOTOR PERFORMANCE IN ADULT ANIMALS.**

D.M. Fyda\*; B. Fedirchuk; L.M. Jordan

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

A variety of evidence contends that spinal 5-HT is involved in the initiation of locomotion. 5-HT agonists enhance locomotion in chronic spinal cats (Rossignol et al., *Ann. N.Y. Acad. Sci.*, 860:346, 1998), both 5-HT and a 5-HT<sub>2</sub>-receptor agonist enhance weight-supported stepping in adult spinal rats (Feraboli-Lohnherr et al. *J. Neurosci. Res.*, 55:87, 1999, Kim et al. *J. Neurosci.*, 19:6213, 1999), and 5-HT receptor antagonists abolish locomotion in the neonatal rat (Fyda Jordan, *Soc. Neurosci. Abstr.*, 1999). In the current study, we examine the role of various 5-HT receptor antagonists, when applied to either upper thoracic or lower lumbar regions of the spinal cord, on both treadmill locomotion in the adult rat and fictive locomotion in the adult cat. Treadmill-trained adult rats had an intrathecal catheter chronically implanted with the tip ending at either T10 or L3. Following recovery, the rats' ability to perform treadmill locomotion during the administration of the 5-HT antagonists was assessed. The application of a 5-HT<sub>7</sub>-receptor antagonist, clozapine (50µM), completely abolished the ability of rats to locomote on a treadmill. However, the 5-HT<sub>2A</sub>-receptor antagonist, ketanserin (100µM), only mildly disrupted the ability of adult rats to co-ordinate fore- and hind-limb locomotor activity. Adult decerebrate cats produced fictive locomotion in response to electrical stimulation of the brainstem. An intrathecal catheter was inserted beneath the dura with the tip ending at T7 and clozapine (1mM) completely blocked fictive locomotion. This data supports a differential role for 5-HT-receptor subtypes in the generation of locomotion in the adult rat and cat and suggests that 5-HT<sub>7</sub> receptors may be important for the initiation of locomotion in adult as well as neonatal animals.  
Supported by: The [\*]M.R.C.[\*].

**Program Number:** 60.2

**Day / time:** Sunday, Nov. 5, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**CHARACTERIZATION OF PROPRIOSPINAL COUPLING BETWEEN THE CERVICAL AND LUMBAR REGIONS DURING RHYTHMIC MOTOR ACTIVITY IN THE *IN VITRO* NEONATAL RAT SPINAL CORD.**

K.C. Cowley; B.J. Schmidt\*

*Medicine and Physiology, University of Manitoba, Winnipeg, MB, Canada*

In this series, we examine propriospinal connections responsible for coupling rhythmic forelimb and hindlimb activity. Cervical and lumbar motor output was monitored via recordings of multiple ventral roots within each region. The cervical and lumbar rhythms induced by whole cord application of 5-HT/NMDA, with or without bicuculline (BIC), were coupled. Bath partitions were then established at the T1 and T12 cord levels, isolating the cervical, thoracic and lumbosacral (LS) regions. Application of 5-HT/NMDA/BIC to either the cervical or LS cord alone was capable of inducing synchronous rhythmic activity within both the cervical and LS region, and the activity of these two regions was in-phase. Subsequent addition of 5-HT/NMDA (without BIC) to whichever cord enlargement was not previously exposed to 5-HT/NMDA/BIC resulted in desynchronization of left–right discharge in that region only, suggesting local activation of the rhythmogenic network can dominate over its propriospinal inputs. When 5-HT/NMDA/BIC was added to both the LS and cervical (but not thoracic) baths, synchronous rhythmic activity on the LS and cervical roots was coupled; subsequent suppression of synaptic transmission in the thoracic region, using calcium-free ACSF, produced a partial, but definite, uncoupling of the cervical and LS rhythms. This effect was mimicked by addition of CNQX or atropine, but not AP5, to the thoracic bath. These preliminary results suggest that coupling of rhythmic activity between the LS and cervical regions depends, at least in part, on propriospinal neurons with synaptic relays in the thoracic cord.

Supported by: M.R.C. (Canada)

**Program Number:** 73.1

**Day / time:** Sunday, Nov. 5, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**LEARNING INDUCED NEUROPHYSIOLOGICAL MODIFICATIONS IN THE RAT CORTEX: ARE THEY LTP-LIKE?**

I.D. Churchill 1,3\*; T.L. Ivanco 1,3; S. Patel 3; D. Norr 3; M. DeRidder 3; W.T.

Greenough 1,2,3

1. Beckman Institute, Urbana/Champaign, IL, USA

2. Departments of Psychology, Psychiatry, and Cell and Structural Biology, University of Illinois, Urbana/Champaign, IL, USA

3. University of Illinois, Urbana/Champaign, IL, USA

Considerable evidence indicates that growth or change in existing neuronal structure, particularly alterations in dendritic morphology and synapse number and structure, are associated with learning. If morphological changes are involved in learning and memory, this should be reflected in the physiology of the pathways that they mediate. Evidence indicates that some of the mechanisms that are associated with the structural modifications following long-term potentiation (LTP) in the motor cortex may be the same as those associated with the morphological plasticity seen with learning. These findings suggest that 1) measurable changes in synaptic efficacy and 2) alterations in capacity for LTP induction may accompany learning. We investigated this within cortical areas using electrophysiological techniques following exposure to different learning paradigms that are known to induce structural changes within the cortex, including locomotor skill learning on an obstacle course, housing in a complex environment, and learning to reach into a chamber for food. One of our key findings was that obstacle course training (a series of difficult elevated pathways previously shown to result in synaptic reorganization) produced significant increases in evoked response amplitudes within motor cortex, above those seen in inactive animals maintained in standard housing. Furthermore, this training appeared to inhibit the ability to induce LTP. The apparent occlusion of LTP following training indicates that learning and LTP induction may rely on shared mechanisms. The results from multiple experiments are summarized and discussed in relation to task specific effects and changes in excitation and inhibition levels.

Supported by: (MH35321, NICH07333, Kiwanis Foundation, Beckman Institute).

**Program Number:** 64.15

**Day / time:** Sunday, Nov. 5, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**NEUROMECHANICAL BASIS OF TRUNK STABILIZATION.**

D.J. Kriellaars\*; S. Webber; C. Lewis

*Sch Med Rehab, Univ Manitoba, Winnipeg, MB, Canada*

The control of trunk stability is an important factor in the etiology of low back injury. During upper and lower limb tasks, the motion of the limbs mechanically impacts upon the trunk requiring precise control of neuromuscular activation patterns to minimize communication of mechanical events to the trunk by the interposed segments or by generating suitable activation strategies of the trunk musculature to compensate for the limb motion. We employed accelerometry as a measure of trunk stability during repetitive upper and lower limb tasks to 1) assess the use of accelerometry as a measure of trunk stability, and 2) to investigate the impact of short term instruction on trunk acceleration and control strategies. A calibrated accelerometer was placed on the L4 vertebral process or on the upper or lower limbs during standardized repetitive tasks on 10 subjects. In some trials surface electromyography was recorded of the prime movers. A stereotypical trunk acceleration pattern was observed consisting of four phases (P1, P2, P3, P4) which related to the EMG activation patterns and the upper and lower limb accelerations patterns. The magnitude of acceleration during each phase was determined. The effect of short term (5 minutes) instruction, commonly used in therapeutic and preventative interventions, was to decrease the peak magnitudes by over 50% ( $p < 0.05$ ). In the upper limb task, we observed a strategy shift where the complex trunk acceleration pattern was simplified to the stereotypical four phase pattern. Trunk accelerations can be used to assess trunk stability and reflect neuromuscular activation patterns used to control trunk motion in response to upper and lower limb motion.

Supported by: Workers Compensation Board of Manitoba

**Program Number:** 80.12

**Day / time:** Sunday, Nov. 5, 11:00 AM – 12:00 PM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**FRAGILE X KNOCKOUT MICE SHOW AN INCREASE IN MOSSY FIBER SPROUTING IN THE HIPPOCAMPUS COMPARED TO WILDTYPE MICE.**

T.L. Ivanco 1\*; W.T. Greenough 1,2

1. Beckman Institute, University of Illinois,

2. Department of Psychology, Psychiatry, and Cell and Structural Biology, University of Illinois, Urbana/Champaign, IL, United States of America

The Fragile Mental Retardation Protein (FMRP) is absent in individuals with Fragile X Syndrome. This protein appears to function in synapse development and neuronal plasticity. The most common neurologic abnormality in Fragile X afflicted children is seizures. Approximately 20% of Fragile X children exhibit seizures. The type of seizure may include absence episodes, partial motor, generalized or partial complex seizures. Children with Fragile X tend to have a developmental onset of seizures at about 2–5 years of age, although some show a later onset. Whereas most outgrow the seizure problem by 5–15, an occasional case persists into adulthood. The cause of epilepsy in Fragile X syndrome is not known. There is some possibility that there is excessive neuronal excitation within the brains of Fragile X afflicted children. In tissue collected from epilepsy patients and from animals in the experimental epilepsy model *kindling*, in which repeated electrical stimulation of forebrain structures triggers more intense electroencephalographic and behavioral seizure activity, there is a permanent sprouting of the mossy fiber pathway from the dentate gyrus. This sprouting may be triggered by enhanced neuronal activation. Thus, an animal model of Fragile X Syndrome may provide some insight into the epilepsy seen in children. We sought to examine mossy fiber sprouting in the FMR1 knockout mouse hippocampus. Knockout and wildtype mouse brains were processed for Timm's staining, which reveals the zinc rich terminals of the dentate gyrus. We found that FMR1 knockout animals showed a pattern of Timm granules within the stratum oriens of subfield CA3 that was significantly different from wildtype animals, indicating mossy fiber sprouting into CA3. The consequences of this sprouting are unclear, but the sprouting could explain the development of seizures in Fragile X afflicted children.

Supported by: (The FRAXA Research Foundation).

**Program Number:** 89.5

**Day / time:** Sunday, Nov. 5, 8:00 AM – 9:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**RELEASE OF CALCIUM FROM IP<sub>3</sub> RECEPTOR–REGULATED STORES BY HIV–1 TAT REGULATES TNF– $\alpha$  PRODUCTION IN HUMAN MACROPHAGES.**

**M. Mayne** [\*]; C.P. Holden [ ]; A. Nath [ ]; J.D. Geiger [ ]

1. Department of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, MB, Canada

2. Department of Neurology, University of Kentucky, Lexington, KY, USA

HIV–1 protein Tat is neurotoxic and increases macrophage and microglia production of TNF– $\alpha$  a cytopathic cytokine linked to the neuropathogenesis of HIV dementia. Others have shown that intracellular calcium regulates TNF– $\alpha$  production in macrophages and we have shown that Tat releases calcium from IP<sub>3</sub> receptor–regulated stores in neurons and astrocytes. Accordingly, we tested the hypothesis that Tat–induced TNF– $\alpha$  production was dependent on the release of intracellular calcium from

IP<sub>3</sub>–regulated calcium stores in primary macrophages. We found that Tat transiently and dose–dependently increased levels of intracellular calcium and that this increase was blocked by xestospongin C, pertussis toxin, and by inhibitors of phospholipase C and type 1 protein kinase C but not by inhibitors of protein kinase A or phospholipase A<sub>2</sub>. Xestospongin C, BAPTA–AM, U73122, and bisindolylmaleimide significantly inhibited Tat–induced TNF– $\alpha$  production. These results demonstrate that in macrophages, Tat–induced release of calcium from IP<sub>3</sub>–sensitive intracellular stores and activation of non–conventional PKC isoforms play an important role in Tat–induced TNF– $\alpha$  production.

Supported by: MRC/AstraZeneca.

**Program Number:** 132.15

**Day / time:** Sunday, Nov. 5, 3:00 PM – 4:00 PM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**SYNAPTIC MORPHOLOGY DURING THE LONG–TERM MAINTENANCE OF LTP: STRUCTURAL CHANGES 5 DAYS POST–LTP INDUCTION.**

**A.C.W. Weeks** [ ]; T.L. Ivanco [ ]; J.C. LeBoutillier [ ]; R.J. Racine [ ]; T.L. Petit [ ] \*

1. Psychology Department, University of Toronto, Scarborough, ON, Canada

2. Psychology Department, McMaster University, Hamilton, ON, Canada

LTP has been associated with changes in synaptic morphology but the nature of these changes over the time course of the enhanced electrophysiological response has not been fully determined. Synapses were examined in the middle third of the molecular layer (MML) of the rat dentate gyrus following repeated high frequency tetanization of the perforant path. Synapses from both the ipsilateral inner third of the dentate molecular layer (IML), which was not directly stimulated during the induction of LTP, as well as implanted, non–stimulated animals, served as controls. LTP was induced over a 4 h period, and the animals were sacrificed 5 days after the final stimulation of the LTP group. Ultrastructural quantification included the total number of synapses per neuron, synaptic curvature, the presence of synaptic perforations, and the maximum length of the synapses. No overall changes in the number of synapses per neuron, shape, or synaptic perforations were observed. There was, however, a significant increase in the length of synapses in the directly stimulated LTP tissue. This increase in synaptic length was particularly evident in the concave shaped synapses. Further, a larger proportion of these concave synapses exhibited perforations. These results, together with previous findings, describe a sequence of changes in synaptic morphology that accompany LTP in a brain structure that is associated with learning and memory.

Supported by: grants from the Natural Sciences and Engineering Research Council of Canada to T.L.P. and R.J.R.

**Program Number:** 89.6

**Day / time:** Sunday, Nov. 5, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**HIV INFECTION ALTERS EXPRESSION AND ACTIVITY OF HUMAN NUCLEOSIDE TRANSPORTERS.**

**J.J. Kort** [\*]; J.D. Geiger

1. Department of Pharmacology and Therapeutics, University of Manitoba, Winnipeg, MB, Canada

2. Center for Immunology and Microbial Disease, Albany Medical College, Albany, NY, USA

Nucleoside analog reverse transcriptase inhibitors (NRTIs) are an important component of current highly active anti–retroviral therapy (HAART) against HIV infection. Little is known about the transport and metabolism of these pro–drugs in target cells of HIV infection in the brain, including T cells, macrophages, and astrocytes. The hypothesis that HIV infection may alter nucleoside transport and potentially affect NRTI effectiveness was tested in the presence and absence of HIV infection of human fetal astrocytes (HFA), Jurkat CD4<sub>+</sub> T cells, and the macrophage–type THP–1 cell line. Equilibrative nucleoside transporters (ENT1 and ENT2) were expressed in all cells tested. RNA for pyrimidine–selective, concentrative nucleoside transporters (CNT1) was detected in HFA and Jurkat cells, but not in THP–1 cells. Purine–selective CNT2 RNA was expressed in HFA and Jurkat cells, but not in HIV–infected Jurkat cells. The sensitivity of nucleoside transport to inhibition by S–(p–nitrobenzyl)–6–thioinosine and dipyridamole was significantly reduced in HIV–infected Jurkat cells (3–fold reduction) and THP–1 cells (6–fold reduction) when compared to respective mock–infected cells, suggesting inhibition of the ENT1 nucleoside transporter in HIV–infected cells. Uptake of the NRTI zidovudine (AZT), a weak substrate for CNT1, was not different between mock–infected cell types and HIV infected cells. In summary, restricted HIV infection of HFA did not affect nucleoside transport and AZT uptake. In contrast, productive HIV infection of CD4<sub>+</sub> T cells and macrophage–type cells significantly alters the expression and/or activity of nucleoside transporters in these cells. Further studies are underway to determine the effect of HIV infection on intracellular metabolism of NRTIs. Supported by: NIH grants NS39184 (J.D.G.) and AI36668 (J.J.K.).

**Program Number:** 149.5

**Day / time:** Sunday, Nov. 5, 1:00 PM – 2:00 PM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**ADENOSINE A<sub>2A</sub> RECEPTOR ACTIVATION INHIBITS TNF– $\alpha$  PRODUCTION IN A CAMP INDEPENDENT MANNER.**

**J.D. Geiger** [\*]; J.A. Fotheringham; M.B. Mayne; G.W. Glazner

Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Manitoba Faculty of Medicine, Winnipeg, MB, Canada

Inflammation is a key factor in the pathology of many neurodegenerative diseases. The pro–inflammatory cytokine tumor necrosis factor– $\alpha$  (TNF– $\alpha$ ) is an important mediator of neuroinflammation and is produced primarily by activated macrophages and microglia. TNF– $\alpha$  production is inhibited by activation of cell surface adenosine receptors. Because we and others have reported that activation of the adenosine A<sub>2A</sub> receptors potentially inhibits TNF– $\alpha$  production in primary macrophages, we performed experiments to map the signaling events regulated by this receptor. Human promonocytic U937 cells were treated with phorbol–12–myristate–13–acetate (PMA) and phytohemagglutinin (PHA) for 4 hours to stimulate TNF– $\alpha$  production. The specific adenosine A<sub>2A</sub> receptor agonist, CGS21680, produced 85  $\pm$  2% inhibition of TNF– $\alpha$  production stimulated by PMA/PHA. Pre–treatment of U937 cells with either the adenylate cyclase inhibitor SQ22536 or the cAMP–dependent kinase inhibitor H89 did not significantly alter the inhibition of TNF– $\alpha$  production produced by CGS21680. Stimulation of TNF– $\alpha$  production by PMA/PHA is dependent on protein kinase C and MAP kinase activation, but western blot analysis showed that MAP kinase was not a target of A<sub>2A</sub> receptor activation. The inhibitory effect of CGS21680 on TNF– $\alpha$  production was blocked by pre–treatment of cell cultures with the protein phosphatase 1 and 2A inhibitor, okadaic acid. These data suggest that activation of adenosine A<sub>2A</sub> receptors inhibits PMA/PHA–induced TNF– $\alpha$  production in a manner that involves activation of a protein phosphatase independent of cAMP. Supported by: the Medical Research Council of Canada and the Alzheimer Society of Canada.

**Program Number:** 234.16

**Day / time:** Monday, Nov. 6, 11:00 AM – 12:00 PM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**REGULATION OF IP3 CALCIUM CHANNELS BY NUCLEAR FACTOR- $\kappa$ B.**

S. Camandola<sup>1</sup>\*; G.W. Glazner<sup>2</sup>; J.D. Geiger<sup>2</sup>; M.P. Mattson<sup>1</sup>

1. *Laboratory of Neurosciences, National Institute on Aging, Baltimore, MD, USA*

2. *University of Manitoba Faculty of Medicine, Winnipeg, MB, Canada*

Activation of nuclear factor  $\kappa$ B (NF- $\kappa$ B) is known to represent a highly protective response in neurons by modulating the expression of pro-survival genes as well as by stabilization of calcium homeostasis. One of the most important and metabolically relevant sources of cellular calcium is endoplasmic reticulum (ER), and IP3 receptors have been shown to play a role in apoptosis. We recently showed that a factor/s able to activate NF- $\kappa$ B is released from ER in response to calcium efflux (Glazner et al., this meeting). The present study was conducted in order to investigate if changes in NF- $\kappa$ B activation may affect IP3-dependent calcium release. Our results demonstrate that inhibition of NF- $\kappa$ B causes an enhanced increase of intracellular calcium following exposure to ATP in intact neurons as well as of intramitochondrial calcium following IP3 treatment in permeabilized neurons. Conversely, when NF- $\kappa$ B was induced by TNF $\alpha$  or I $\kappa$ B $\alpha$  antisense there was a significantly reduced elevation of intracellular calcium levels following ATP and mitochondrial calcium uptake following IP3. These differences seem to be related with changes in receptor levels. In fact, IP3 receptor 1 immunoreactivity was decreased after NF- $\kappa$ B activation, while inactivation of the transcription factor causes an up regulation of IP3 receptor 1. Studies are under way to determine the mechanism responsible for this inverse correlation and its importance in the protection afforded by NF- $\kappa$ B.

**Program Number:** 289.2

**Day / time:** Monday, Nov. 6, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**EFFICACY OF DISODIUM 4-[(*tert*-BUTYLIMINO) METHYL] BENZENE-1,3-DISULFONATE N-OXIDE, A WATER SOLUBLE SPIN TRAP, IN A RAT MODEL OF HEMORRHAGIC STROKE.**

J. Peeling<sup>1</sup>; M.R. Del Bigio<sup>2</sup>; D. Corbett<sup>3</sup>; A.R. Green<sup>4</sup>; D. Jackson<sup>5</sup>\*

1. *Depts of Radiology, 2. Pathology, University of Manitoba, Winnipeg, MB, Canada*

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4. *AstraZeneca RDCharmwood, Loughborough, UK*

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Because free radical mechanisms may contribute to brain injury in hemorrhagic stroke, the effect of the spin trapping nitron, NXY-059, was investigated on outcome following intracerebral hemorrhage (ICH) in rat. ICH was induced in 20 adult rats by infusion of collagenase into the caudate-putamen. Thirty min later rats were treated with NXY-059 (50 mg/kg sc plus 8.8 mg/kg/hr for 3 days sc delivered via implanted osmotic pumps) or saline. Magnetic resonance imaging 24 h after ICH confirmed that the hemorrhage was uniform in the 2 groups, and subsequent imaging at 7 and 42 days post-ICH showed that the hematoma resolved similarly in the two groups. Behavioral testing on days 1, 3, 7, 14, and 21 after ICH showed that rats treated with NXY-059 had significantly decreased neurological impairment at all times. Deficits on other tests including skilled forelimb use (staircase test) carried out 4–5 weeks post-ICH, and tests of striatal function (rotometer test) carried out 6 weeks post-ICH, were not reduced by treatment with NXY-059. Treatment with NXY-059 significantly reduced the neutrophil infiltrate observed 48 hours post-hemorrhage in the vicinity of the hematoma. Furthermore, NXY-059 treatment reduced the number of TUNEL-positive cells 48 hours post-hemorrhage at the hematoma margin, although by 6 weeks there were no differences in neuronal densities in treated and control rats.

**Program Number:** 257.10

**Day / time:** Monday, Nov. 6, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**SEQUENTIAL ACTIVATION OF DENDRITES IN THE GENERATION OF CALCIUM CURRENTS IN MAMMALIAN MOTONEURONES.**

K.P. Carlin\*; K.E. Jones; Z. Jiang; R.M. Brownstone

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

We have previously demonstrated that mouse spinal motoneurons have dendritically located L-type calcium channels (Carlin KP, et al. (2000). Eur. J. Neurosci., in press). The dendritic location of these channels was demonstrated through the inability of a somatic electrode to voltage clamp these conductances: in response to voltage steps the distal calcium conductances were seen as late-onset persistent currents. Using whole cell recordings in spinal cord slice, a total of 9 motoneurons from mice ranging in age from P9–14 demonstrated multiple sequential late-onset calcium currents ("stair-case") in response to a single voltage step. As with the late-onset currents demonstrated previously, this waveform was only seen when the extracellular calcium concentration was raised from 1 mM to 1.5 – 2.5 mM. In these cells the number of late-onset currents ranged from 2 to 6 with the current density of each step in any given cell remaining relatively constant. From a holding potential of –60 mV the average activation voltage of the staircase waveform was  $-24.7 \pm 3.3$  mV (mean  $\pm$  SE). This "staircase" appearance of the current waveform is consistent with the sequential activation of voltage-gated calcium channels located on different dendrites (Oakley et al (1999). SFN Abstr p.1741). It has previously been demonstrated that individual dendrites of spinal motoneurons are capable of autonomous signal integration (Skydsgaard M, Hounsgaard J (1994). J Physiol (Lond) 479:233–46) and that only a fraction of the dendrites of a cell are necessary for plateau potential production (Hounsgaard J, Kiehn O (1993). J Physiol (Lond) 468:245–59). Furthermore, synaptic input shown to facilitate the production of plateau potentials may regionally be segregated to specific subpopulation of dendrites (Delgado-Lezama R, et al. (1999) J Physiol (Lond) 515: 203–7). These observations combined with the present observations lead to the suggestion that significant integration may occur in individual dendrites.

Supported by: MHRC and MRC of Canada

**Program Number:** 204.9

**Day / time:** Monday, Nov. 6, 10:00 AM – 10:15 AM

**Presentation Type:** Slide

**Presentation Location:** Conference Auditorium A

**LIMITS OF BALANCE RECOVERY IN HEMIPARETIC STROKE INDIVIDUALS DURING CORRECTIVE INPLACE AND STEPPING RESPONSES.**

T. Szturm; T. Bhatt; J. Paterson\*

*Faculty of Medicine, University of Manitoba, Winnipeg, MB, Canada*

The purpose of this study was to evaluate corrective balance reactions to unexpected disturbances of varying magnitudes during a leg lifting task, which places the subject in single limb support. This task is very similar to the task of gait initiation. Methods: Ten chronic hemiparetic stroke subjects with moderate residual motor deficits and ten healthy controls were subjected to sudden forward (FT) and backward (BT) support surface translations over three different velocities. Corrective balance reactions were elicited during lifting of the paretic and non-paretic legs. Responses from each subject were classified into an inplace or stepping strategy. Performance levels, based on kinematic analysis were graded as successful–good, successful–poor and falls. EMG recordings from bilateral Hamstrings (HA), Quadriceps (QU), Adductor Magnus (AD) and Gluteus Medius (GM) were analyzed for onset latencies. Linear and angular kinematics were obtained bilaterally using the PEAK 2D motion analysis system. Results: Healthy subjects showed a successful performance for all the trials for backward and forward translations. An in-place strategy predominated for the healthy subjects. 66% of the strokes showed a successful performance to BT whereas only 38% had a successful performance to FT. Corrective stepping responses predominated when the paretic side was in stance, and inplace responses were more common when non-paretic side was in stance. In general there were no significant delays in corrective muscle responses on the paretic side as compared to non-paretic side or healthy controls.

**Program Number:** 384.5

**Day / time:** Monday, Nov. 6, 1:00 PM – 2:00 PM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**CORRELATION OF CEREBRAL HYPOXIC/ISCHEMIC CHANGES IN T2 WITH ALTERATIONS IN WATER CONTENT AND VASCULAR PERMEABILITY.**

**M. Qiao** <sup>1</sup>; K.L. Malisza <sup>1</sup>; S. Bascaramurty <sup>1</sup>; T. Foniok <sup>1</sup>; M. Del Bigio <sup>2</sup>; U.I. Tuor <sup>1</sup> \*

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*2. Univ. Manitoba, Winnipeg, MB, Canada*

We have observed age-dependent cerebral hypoxic/ischemic (HI) changes on T2-weighted magnetic resonance images. We investigated whether the T2 changes following HI correspond to alterations in water content or vascular permeability. The right carotid artery was isolated surgically (sham control) or occluded in 1 and 4 week old Wistar rats. The rats were exposed to hypoxia (8% oxygen) for 2 hours (1 week old) or 30 minutes (4 week old). Multiecho T2-weighted images were obtained prior to, during, 1 or 24 hours post HI using a Bruker MSIX 9.4T spectrometer. Animals were decapitated either after the sham procedure, during the last minute of HI, 1 or 24 hours post HI. The rat brain was removed and samples (n=38 for 1 week old; n=33 for 4 week old) were analyzed immediately for water content by a dry/wet weight method. A block of the brain was also frozen for subsequent examination of alterations in vascular permeability by detection of IgG using immunohistochemistry. In 1-week-old brain, both the T2 relaxation time and water content in the hemisphere ipsilateral to the occlusion increased during HI, recovered within 1 hour of reperfusion, and increased again at 24 hours of reperfusion. In these animals, extravasation of IgG was observed during HI and this persisted at 1 and 24 hours of reperfusion. In 4-week-old brain, there were no changes in T2 or vascular permeability until 24 hours of reperfusion despite an elevation in water content during, 1 and 24 hours post HI. We conclude that there is a good correspondence between the incidence of vasogenic edema and the age-dependent differences in T2-weighted imaging. Thus, T2-weighted imaging is a reliable technique for the detection of vasogenic edema but increases in brain water without protein extravasation can go undetected with this method. Supported by: MRC Canada.

**Program Number:** 460.2

**Day / time:** Tuesday, Nov. 7, 9:00 AM – 10:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**FLEXOR GROUP II MUSCLE AFFERENTS CAN ENHANCE FLEXOR ACTIVITY DURING FICTIVE LOCOMOTION.**

**D.A. McCrea** <sup>\*</sup>; K. Stecina; J. Quevedo; S. Gosgnach

*Dept. Physiology, University of Manitoba, Winnipeg, MB, Canada*

The critical role of hindlimb extensor muscle afferents in augmenting extensor motoneuron output during both real and fictive locomotion in the cat is now well established. There is much less information available, however, on how afferent feedback from flexor muscle afferents may regulate stepping. It has previously been reported that during fictive locomotion activation of group II muscle afferents from tibialis anterior (TA) and sartorius (Sart) muscles produces a premature transition to the extensor phase (i.e. reset to extension) while stimulation of Sart group II afferents enhances ongoing flexor activity (Perreault et al. J. Physiol 487:211–220, 1995). We have now examined the effects of stimulating other hindlimb flexor nerve afferents in decerebrate cats during brainstem-evoked fictive locomotion. In contrast to the extension-promoting effects of TA group II afferents, stimulation of the synergist ankle flexor, extensor digitorum longus (EDL), prolongs and/or enhances the ongoing flexor activity throughout the limb while delaying the onset of the subsequent extensor phase. The threshold for these effects is between 2 and 5T suggesting that EDL group II muscle afferents are responsible for these actions. Similar flexion enhancing actions are evoked by stimulation of the nerve to the hip flexor Psoas major. The contrasting actions of TA and EDL group II afferents obtained under identical conditions and in the same preparations indicate that separate populations of interneurons with group II input are contacted by these afferents. Unlike the case of extensor afferents, flexor muscle afferents can have excitatory actions on both the extensor and flexor portions of the central circuitry producing locomotion. We suggest that these actions evoked during fictive locomotion are a reflection of the powerful role that proprioceptive feedback from flexors has in step cycle regulation during real locomotion. Supported by: Canadian MRC.

**Program Number:** 423.15

**Day / time:** Tuesday, Nov. 7, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**COMPUTER SIMULATION OF NMDA-MEDIATED VOLTAGE-DEPENDENT EXCITATION OF CAT LUMBAR MOTONEURONS DURING FICTIVE LOCOMOTION.**

**Y. Dai** <sup>\*</sup>; R.M. Brownstone; B. Fedirchuk; L.M. Jordan

*Dept of Physiology, University of Manitoba, Winnipeg, MB, Canada*

During fictive locomotion cat lumbar motoneurons have locomotor drive potentials (LDPs, Jordan 1983) due to alternating excitatory and inhibitory synaptic inputs from the locomotor network. Brownstone et al. (1994) showed that the excitatory component of the LDPs and the locomotor-related EPSPs evoked from flexor reflex afferents and extensor Ib afferents were voltage-dependent. The mechanisms underlying the voltage-dependent excitation of the motoneurons are still unknown, but may be due to either an NMDA mediated current or activation of L-type voltage-gated calcium channels. A single cell model with five-compartments (axon, initial segment, soma, proximal dendrite, and distal dendrite) was used to investigate the possible mechanisms. The model was built with GENESIS and included nine active conductances in the somatic compartment, five in the proximal dendrite, two each in the axon and initial segment, and none in the distal dendrite. The L-type channel was blocked to probe the voltage dependency induced by NMDA channels. Simulation results showed that (1) an NMDA-mediated non-linear membrane property of the motoneuron could account for both the voltage dependence of the excitatory component of the LDPs and the generation of plateau potentials; (2) a hyperpolarization-activated inward current,  $I_{h}$ , would be required to maintain the amplitude of the LDPs within a physiological range ( $\leq 30$  mV) during locomotion; and (3) reduction of the afterhyperpolarization (AHP) could facilitate the NMDA-induced bistable firing, but had only a small effect on the generation of the plateau potentials. The simulation results support the activation of NMDA channels as a potential mechanism underlying the voltage-dependent excitation of motoneurons. Other possible mechanisms continue to be assessed using this model. Supported by: Canadian MRC and the Health Sciences Center Foundation.

**Program Number:** 406.2

**Day / time:** Tuesday, Nov. 7, 8:15 AM – 8:30 AM

**Presentation Type:** Slide

**Presentation Location:** Room 388

**EXPRESSION OF DLX HOMEODOMAIN GENES IN THE EMBRYONIC AND POSTNATAL VERTEBRATE RETINA.**

**J. de Melo** <sup>1</sup>; X. Qiu <sup>1</sup>; J.L. Rubenstein <sup>2</sup>; D.D. Eisenstat <sup>1</sup> \*

*1. Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg, MB, Canada*

*2. University of California, San Francisco, CA*

Several homeobox genes are expressed in the developing eye, including Crx, located in photoreceptors, and Pax6, expressed in retinal ganglion cells. The onset of expression of two Distal-less (Dlx) homeobox genes, Dlx-1 and Dlx-2, is detected in progenitor cells throughout the neural retina by E12.5. By P0, DLX-2 is expressed in two retinal cell layers, the nascent inner nuclear layer (INL) and the retinal ganglion cell layer (RGL). There is coincident expression of DLX-2 and the inhibitory neurotransmitter GABA in some cells of both the INL and RGL. By P7, there is better definition of the INL, containing amacrine, horizontal and bipolar interneurons, and the RGL. Combined DLX-2/GABA immunoreactive cells are evident in both the INL and RGL. In INL subpopulations, DLX-2 is also co-expressed with GAD-67 and/or calbindin. Similar patterns of expression are found in the adult retina. There is an absence of expression of DLX-2 in the inner and outer plexiform layers as well as the outer nuclear layer of the retina. DLX-1 expression resembles DLX-2 from E12.5 to E16.5, but appears to be decreased during late embryogenesis, with expression limited to the retinal neuroepithelial-iris boundary region at P0. Dlx-1-2 are also localized to inhibitory interneurons of the developing olfactory bulb and neocortex. There is concomitant loss of these interneurons in the Dlx-1 double knockout mouse. Hence, co-expression of DLX-2 and GABA GAD in cells of the INL supports our hypothesis that Dlx genes are expressed in GABAergic inhibitory interneurons of the developing retina. Supported by: Children's Hospital Foundation, Winnipeg, Canada

**Program Number:** 625.19

**Day / time:** Wednesday, Nov. 8, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**HYDROGEN PEROXIDE–MEDIATED OXIDATIVE STRESS INHIBITS GLUTAMATE AND ADENOSINE TRANSPORT IN RAT ASTROCYTES AND C6 CELLS.**

**T. Othman;** C.J.D. Sinclair; L. Mazur; N. Haughey; J.D. Geiger; F.E. Parkinson\*

*Dept. of Pharmacology and Therapeutics, Univ. of Manitoba, Winnipeg, MB, Canada*

Failure of glutamate uptake can lead to neurotoxic accumulations in brain extracellular space, resulting in increased activation of excitatory glutamate receptors causing neuronal damage. Glutamate transporters in neurones and glia play a crucial role in controlling the extracellular glutamate concentration in the brain. Equilibrative nucleoside transporters regulate extracellular concentrations of adenosine, a neuromodulator that inhibits glutamate release. Oxidative stress occurs in a range of acute and chronic neurodegenerative diseases. The aim of this work was to determine whether the activities of glutamate or nucleoside transporters are affected by oxidative stress induced by H<sub>2</sub>O<sub>2</sub>. C6 cells or astrocytes were incubated in assay buffer containing either [<sup>3</sup>H]glutamate or [<sup>3</sup>H]adenosine, 24 hours after exposure to 50, 100 or 200 μM H<sub>2</sub>O<sub>2</sub> for 30 min. The amount of radioactive compound taken up by the cells was assayed at specific time intervals. Exposure to H<sub>2</sub>O<sub>2</sub> produced 0%, 35% (P<0.01), 58% (P<0.001) reductions in [<sup>3</sup>H]adenosine uptake in C6 cells and a 1.7 (P<0.001), 1.8 (P<0.001), and 2.3 (P<0.001) fold reductions in astrocytes, following 50, 100 or 200 μM H<sub>2</sub>O<sub>2</sub> exposures respectively. Similarly, exposure to 50, 100 and 200 μM H<sub>2</sub>O<sub>2</sub> produced a 1.74 (P<0.01), 2.1 (P<0.001) and 2.6 (P<0.001) fold decrease in [<sup>3</sup>H]glutamate uptake by C6 cells. 100 and 200 μM H<sub>2</sub>O<sub>2</sub> produced 5.2 and 6.9 fold reductions in [<sup>3</sup>H]glutamate uptake in astrocytes. Reductions in adenosine uptake did not appear to be the result of changes in the expression of either nucleoside transporter subtypes ENT1 or ENT2. These data show that exposure of brain to free radicals can cause failure of both glutamate and adenosine homeostasis, rendering the brain vulnerable to excitotoxic damage.

**Program Number:** 655.11

**Day / time:** Wednesday, Nov. 8, 10:00 AM – 11:00 AM

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**BRAIN GLYCOGEN LEVELS ARE DECREASED WITH INCREASED WAKEFULNESS AND MAY REPRESENT A HOMEOSTATIC DRIVE FOR SLEEP.**

**C.P. Holden** 1; P.N. Shepel 1; M. Mackiewicz 2; A.I. Pack 2\*; J.D. Geiger 1

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Sleep is thought to be restorative in function. Increased wakefulness (sleep deprivation) results in an increased drive to sleep. We tested the hypothesis that glycogen levels, a major energy source in brain, would decrease with sleep deprivation and thereby represent a homeostatic drive for sleep. Male Sprague–Dawley rats deprived of sleep for 12 or 24 hours were killed by high–energy focussed microwave irradiation, and 11 brain regions were dissected and assayed using an enzyme–linked assay system adapted for a fluorescence plate reader. Levels of glycogen in rats killed using 6.0 and 10 kW were significantly higher (approximately 10–fold) than levels in rats killed using 3.5 kW or decapitation; microwave times were adjusted for brains to reach 85°C. In rats sleep–deprived for 12 hours, levels of glycogen were decreased significantly by as much as 52% (posterior hypothalamus) when compared to corresponding brain regions in control rats. In rats sleep–deprived for 24 hours, levels of glycogen were decreased significantly by as much as 59% (basal forebrain) when compared to corresponding brain regions in control rats; levels were 52% lower in posterior hypothalamus. By immunoblot, levels of glycogen that decrease with increased wakefulness and are replenished with sleep may function as an important link between cerebral metabolism and sleep drive. Supported by: SCOR grant HL60287 from NHLBI

**Program Number:** 629.5

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

**Presentation Type:** Poster

**Presentation Location:** Hall G–J

**CHOLINERGIC NEURONS AND TERMINALS WITHIN THE L6 AND S1 VENTRAL HORN OF THE ADULT AND NEONATAL RAT SPINAL CORD.**

**K.L. Paroschy**\*; S.J. Shefchyk

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Cholinergic neurons and fibres in the dorsal, ventral intermediate regions have been described in adult and neonatal rat spinal cord (Barber et al. '84 JCN 229; Phelps et al. '84 JCN 229). However, L6 sphincter motoneurons (MNs) S1 parasympathetic preganglionic neurons were not the focus of these examinations. There is evidence suggesting possible cholinergic actions on striated sphincter MNs (Sasaki, '94, JCN 349) and parasympathetic preganglionic neurons (Morgan et al. '91, PNAS 88; O'Donnell '90, J Urol 143). Using an antibody directed against the vesicular acetylcholine transporter (VAcHT), we examined cholinergic terminals in the dorsolateral (DL; urethral ischioavernosus) and dorsomedial (DM; anal bulbospongiosus) motor nuclei in L6, as well as in and around the sacral preganglionic neurons in adult and neonatal rats (male female). In both male female adult rats there was VAcHT terminal labelling within the DL and DM nuclei in L6. Prior to postnatal (PN) day 8, cholinergic terminals were not observed on the DM DL motoneurons although some labelling on limb motoneurons was evident. At about PN day 13 there appeared to be more VAcHT terminals associated with the DL motoneurons as compared to the DM motoneurons in both sexes. At all ages examined, VAcHT labelling on limb motoneurons was greater than that within the DM or DL nuclei. Starting at about PN day 20, VAcHT labelling was also evident just dorsal to, and within, the region of the S1 preganglionic neurons. It would appear that MNs innervating sphincter and pelvic muscles as well as neurons within the intermediate region, including the parasympathetic preganglionic neurons associated with the bladder colon, receive cholinergic inputs. The source(s) of these cholinergic inputs as well as their actions on these various neurons and sacral reflexes remain to be defined. Funded by the MRC of Canada.

**Program Number:** 747.6

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**ACTIVITY OF HIP FLEXORS PRECEDES THAT OF ANKLE FLEXORS DURING FICTIVE LOCOMOTION AND SCRATCHING.**

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In this study we explored the extent to which the spinal circuits controlling locomotion and scratching (CPGs) are similarly organized. Decerebrate cat preparations were used in which fictive locomotion was elicited by electrical stimulation of the brainstem and fictive scratching by topical application of curare to the cervical spinal cord and manual stimulation of the pinna. Intracellular records from hindlimb motoneurons and electroencephalograms were compared during fictive scratching and locomotion in the same experiment. The onsets of efferent activity in nerves to proximal and distal muscles were determined from normalized records. During locomotion the onset of activity in hip flexors (sartorius and psoas major) preceded activity in the ankle flexor tibialis anterior (TA) by 17–35 ms. Activity in another ankle flexor, extensor digitorum longus, was often delayed from that of TA and could persist well into extension. During scratching this sequence of flexor motoneuron activation was preserved. In both locomotion and scratching the onset of activity in proximal and distal extensor motoneurons was synchronous. Although the cycle period during scratch is considerably shorter than that during locomotion, the sequence of motoneuron activation appears similar in the two behaviours. This is consistent with a similar organization of the CPGs for scratch and locomotion. One clear difference is that during scratch flexor motoneurons are subject to a large depolarization during flexion and a smaller depolarization during extension. During fictive locomotion, flexor motoneurons are rhythmically hyperpolarized and depolarized around the resting membrane potential. The timing for activity in flexors is consistent with a CPG organization where the onset of hip flexor activity leads that of other flexors. Supported by: Canadian MRC and the Neurotrauma Initiative.