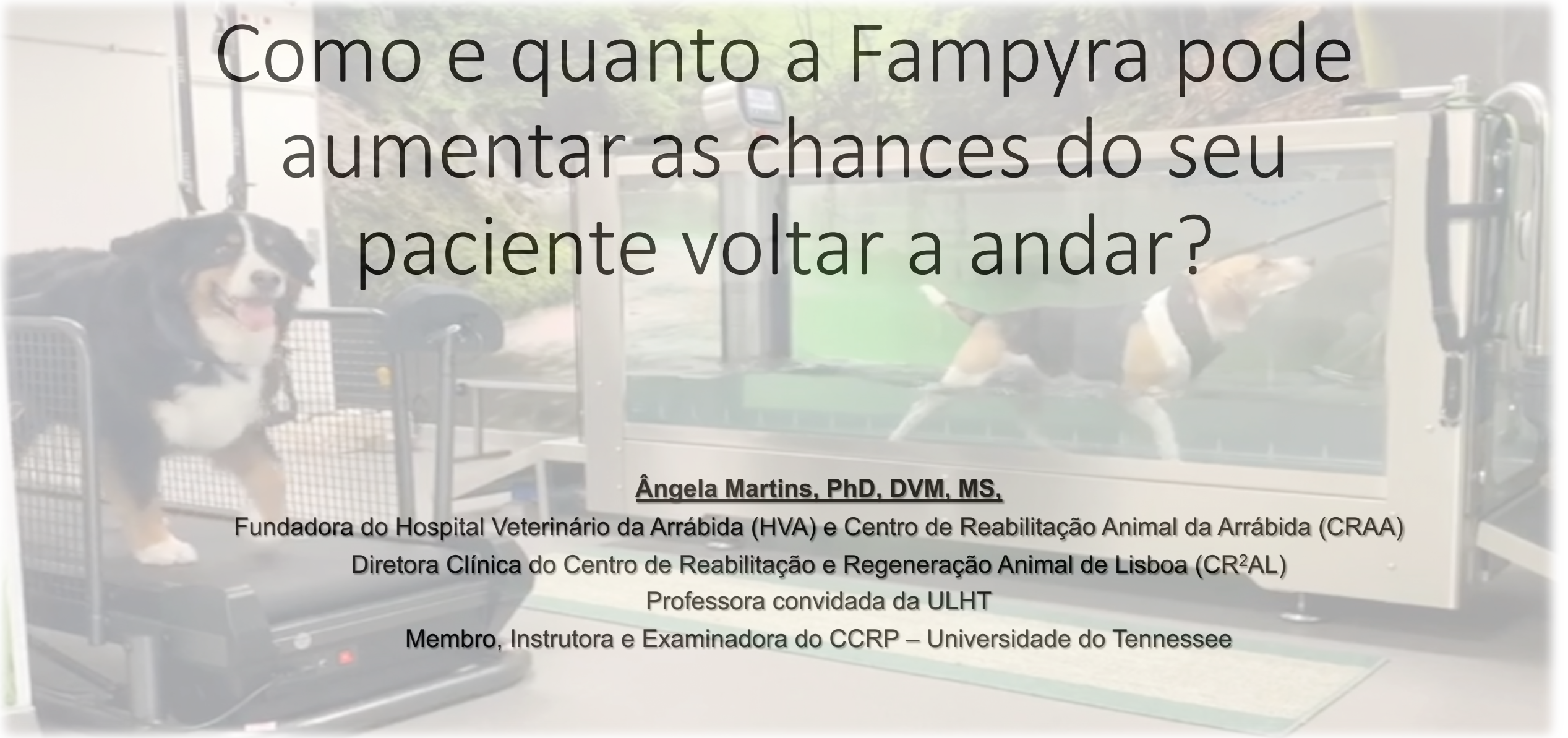
Como e quanto a Fampyra pode aumentar as chances do seu paciente voltar a andar?



Ângela Martins, PhD, DVM, MS,

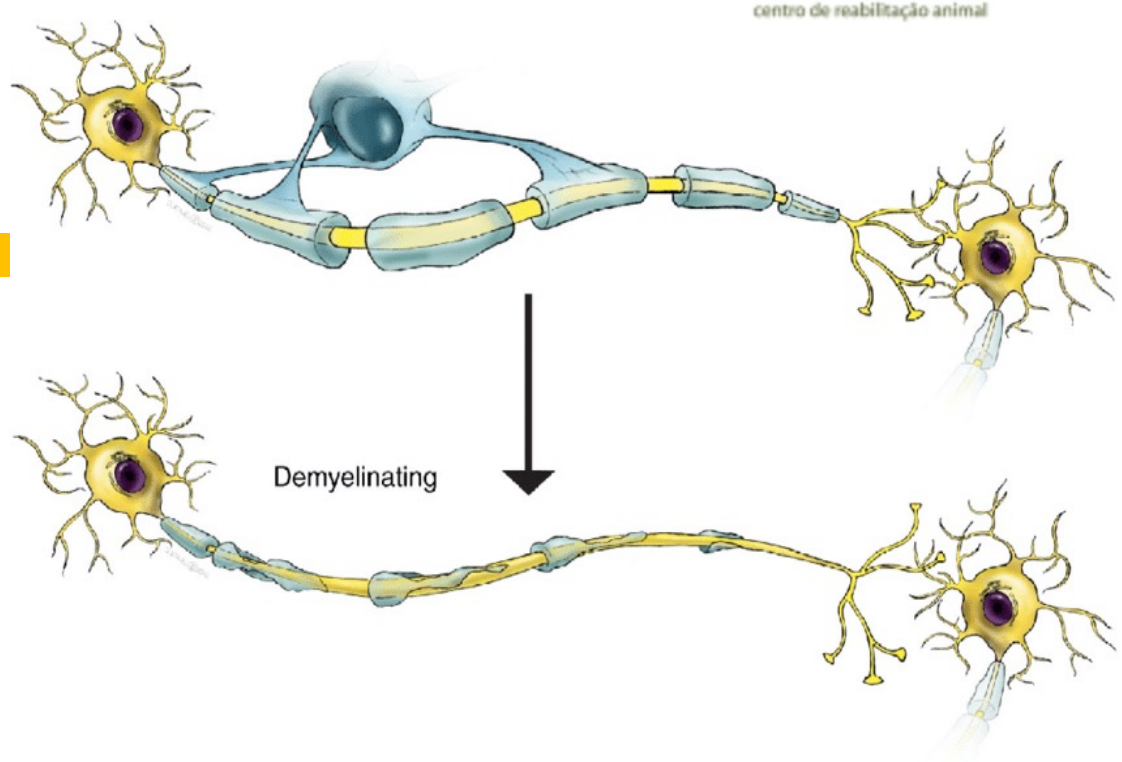
Fundadora do Hospital Veterinário da Arrábida (HVA) e Centro de Reabilitação Animal da Arrábida (CRAA)

Diretora Clínica do Centro de Reabilitação e Regeneração Animal de Lisboa (CR²AL)

Professora convidada da ULHT

Membro, Instrutora e Examinadora do CCRP – Universidade do Tennessee

Spinal Cord Injury

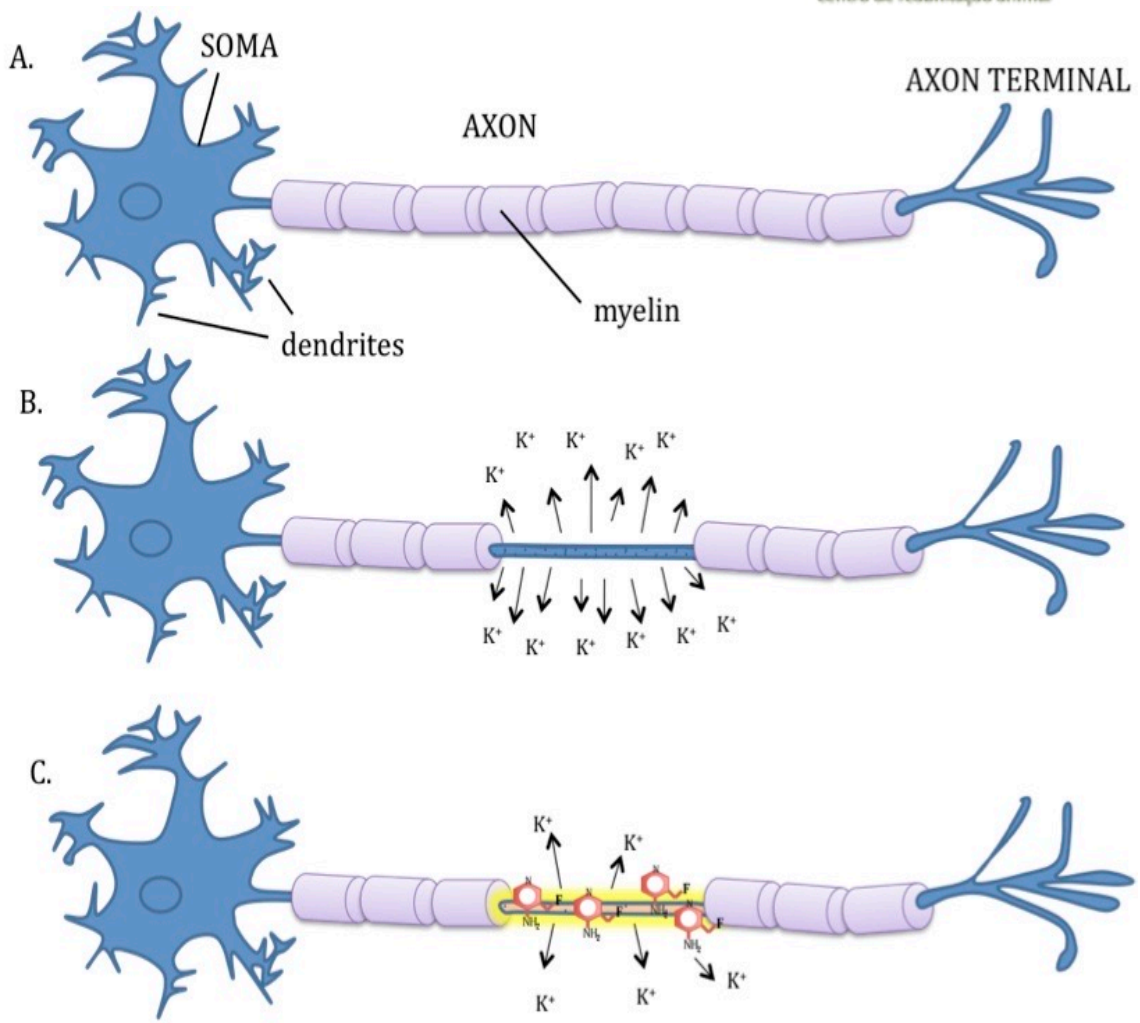


- Axonal demyelination
  - K^+ *channel exposure* (CNS internodal zone of axons)
  - Under normal circunstances, covered by the myelin sheath, not being activated by the action potential

(Hayes, 2006; McBride *et al.,* 2007; Pavsic *et al.,* 2015)

Spinal Cord Injury

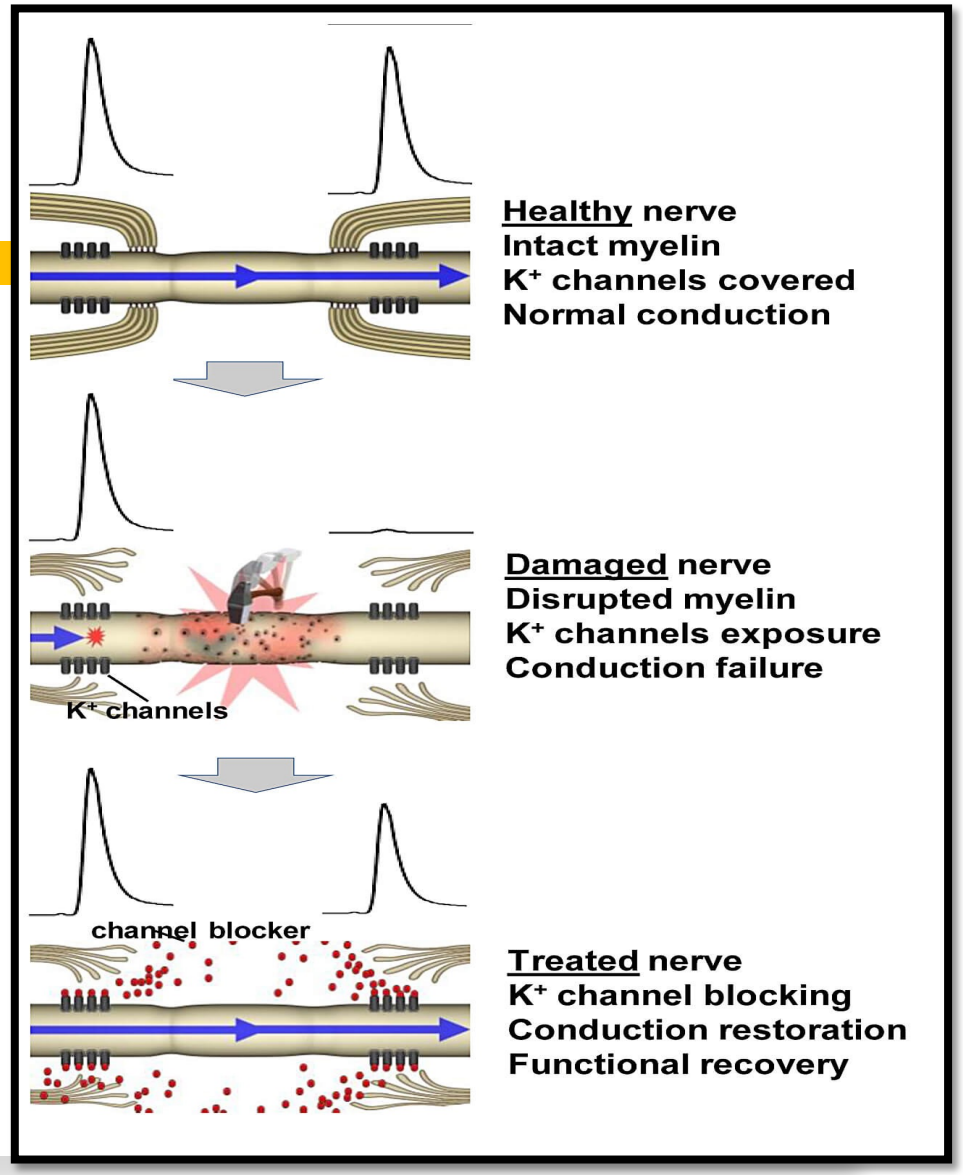
- Axonal demyelination
  - *K^+ channel exposure* → *K^+ leaves the cell, which becomes with a more negative charge*
  - *Depolarization is hard*
    - ↓
    - *neuronal conduction block*



(Hayes, 2006; McBride *et al.,* 2007; Pavsic *et al.,* 2015)

Spinal Cord Injury

Restoring nerve conduction of these axons **by blocking K^+ channels**, provides a therapeutic approach, a role played by K^+ channel antagonists

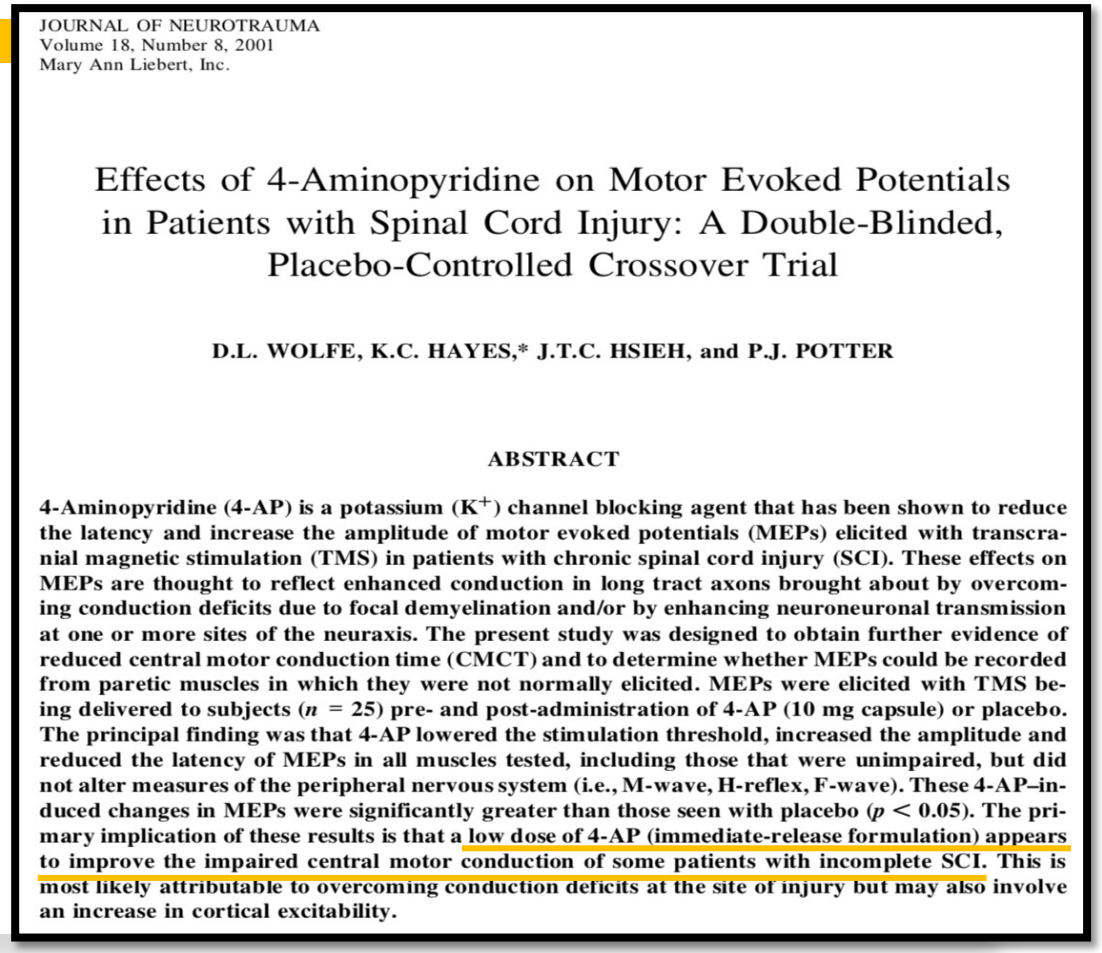


(Olby *et al.,* 2009; McBride *et al.,* 2007; Lim *et al.,* 2014)

Pharmacological Management

- 4-aminopyridine (4-AP)
  - Possible treatment for SCI
  - **Aim**

    To *restore function of anatomically intact but physiologically dysfunctional axons*



JOURNAL OF NEUROTRAUMA
Volume 18, Number 8, 2001
Mary Ann Liebert, Inc.

Effects of 4-Aminopyridine on Motor Evoked Potentials in Patients with Spinal Cord Injury: A Double-Blinded, Placebo-Controlled Crossover Trial

D.L. WOLFE, K.C. HAYES,* J.T.C. HSIEH, and P.J. POTTER

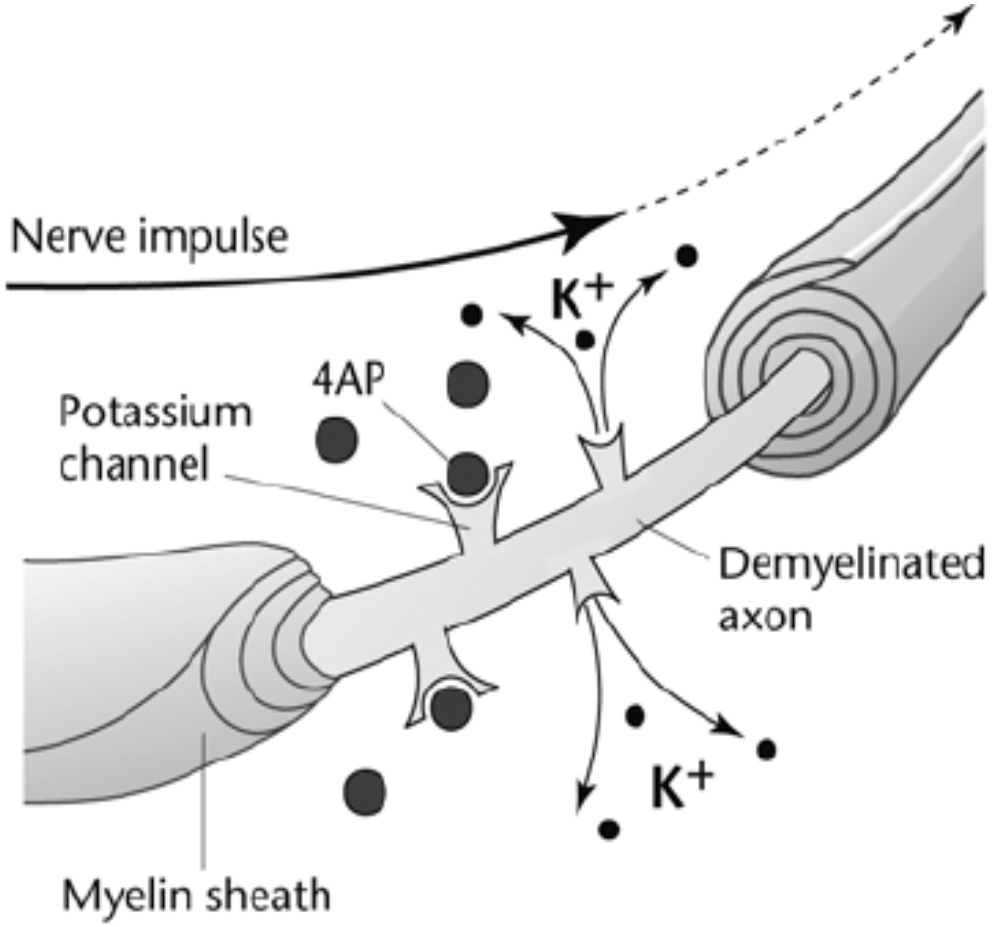
ABSTRACT

4-Aminopyridine (4-AP) is a potassium (K^+) channel blocking agent that has been shown to reduce the latency and increase the amplitude of motor evoked potentials (MEPs) elicited with transcranial magnetic stimulation (TMS) in patients with chronic spinal cord injury (SCI). These effects on MEPs are thought to reflect enhanced conduction in long tract axons brought about by overcoming conduction deficits due to focal demyelination and/or by enhancing neuroneuronal transmission at one or more sites of the neuraxis. The present study was designed to obtain further evidence of reduced central motor conduction time (CMCT) and to determine whether MEPs could be recorded from paretic muscles in which they were not normally elicited. MEPs were elicited with TMS being delivered to subjects (n = 25) pre- and post-administration of 4-AP (10 mg capsule) or placebo. The principal finding was that 4-AP lowered the stimulation threshold, increased the amplitude and reduced the latency of MEPs in all muscles tested, including those that were unimpaired, but did not alter measures of the peripheral nervous system (i.e., M-wave, H-reflex, F-wave). These 4-AP–induced changes in MEPs were significantly greater than those seen with placebo ($p < 0.05$). The primary implication of these results is that a low dose of 4-AP (immediate-release formulation) appears to improve the impaired central motor conduction of some patients with incomplete SCI. This is most likely attributable to overcoming conduction deficits at the site of injury but may also involve an increase in cortical excitability.

(Park *et al.,* 2012; Lim *et al.,* 2014; Lewis *et al.,* 2018)

Pharmacological Management

- 4-aminopyridine (4-AP)
  - Promotes action potential
  - Restores nerve conduction in peripheral nerves demyelinated axons
  - Improves synaptic transmission
  - Improves nerve conduction speed
  - Improves muscle contraction strength
  - ↑ the excitability of intrinsic motor neuron circuits
  - Promotes re-myelination



(Tseng *et al.,* 2016; Lewis *et al.,* 2018).

Pharmacological Management

- 4-aminopyridine (4-AP)
  - Side effects

- ✓ Anxiety
- ✓ Hyperesthesia
- ✓ Tremors
- ✓ Seizures
- ✓ Nausea
- ✓ Diahrreia

Treatment::
- ***Maropitant*** *SC: 1ml/10kg*
- ***Omeprazol*** *IV: 1-1.4 mg/kg*
- ***Metronidazol*** *IV: 12.5 mg/kg (2.2 ml/kg)*
- ***Diazepam - rectal****: 1mg/kg or*
  per os *- 0.3-0.5 mg/kg*

Pharmacological Management

- 4-aminopyridine (4-AP)
  - *Synthetic substances similar to 4-AP have been developed with the aim of*

↑ *axonal conductivity, with fewer side effects*

RESEARCH ARTICLE

Potassium Channel Antagonists 4-Aminopyridine and the T-Butyl Carbamate Derivative of 4-Aminopyridine Improve Hind Limb Function in Chronically Non-Ambulatory Dogs; A Blinded, Placebo-Controlled Trial

Ji-Hey Lim[1,3], Audrey C. Muguet-Chanoit[1], Daniel T. Smith[2], Eric Laber[4], Natasha J. Olby[1,3]*

2014

Pharmacological Management

- 4-aminopyridine (4-AP)

Side Effects

STOP pharmacological management

- ✓ **Protocol:**
  - 0.3 mg/kg BID *per os* 3 days;
  - 0.5 mg/kg BID *per os* 3 days;
  - 0.7 mg/kg BID *per os* 3 days;
  - 1.1mg/kg BID *per os* 21 days.

Maximum dose : 1.2 mg/kg → therapeutic dose 1.1 mg/kg

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

- ***Nine years of study, a prospective clinical study …***

AIM

*To verify if an **intensive neurorehabilitation protocol (INRP)** could improve the ambulatory status **faster** than spontaneous recovery or conventional physiotherapy*

animals

MDPI

Article

A Controlled Clinical Study of Intensive Neurorehabilitation in Post-Surgical Dogs with Severe Acute Intervertebral Disc Extrusion

Ângela Martins [1,2,3,4,*], Débora Gouveia [2,4], Ana Cardoso [2], Carla Carvalho [2], Tiago Coelho [2], Cátia Silva [2], Inês Viegas [2], Óscar Gamboa [5] and António Ferreira [3,5]

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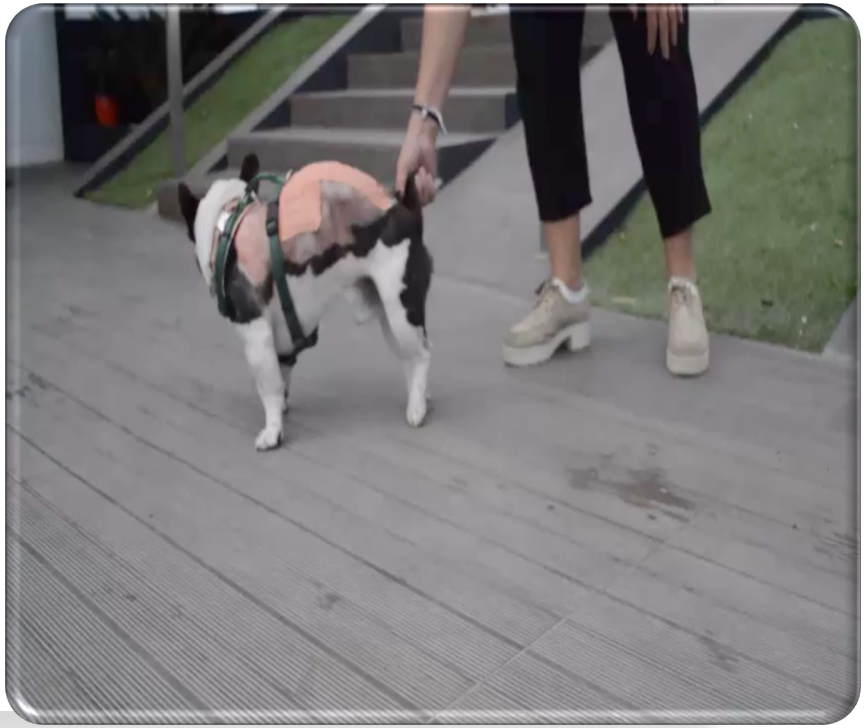
(2021)

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

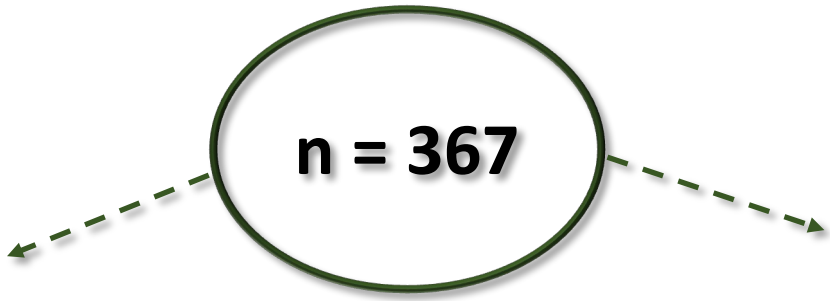
❑ Material and Methods

- ❑ May 2011 → May 2020
- ❑ Retrospective controlled clinical study using a large cohort of dogs (**n=367**)



Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Material and Methods → *Participants*



Study group (SG)

- n = **262**
- **Prospective clinical cases**
- Data collected and registered during the rehabilitation period

Control group (CG)

- n = **105**
- Data from HVA system and the **medical records retrospectively** investigated

Breed, age, weight, etiology, surgical treatment, neurological examination at admission and at discharge

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Material and Methods → *Participants*

Compressive myelopathy (**Hansen type I IVDE**)

Hemilaminectomy 3-5 day after injury

T10-L3 diagnosed by **CT** (with/without myelogram) or **MRI**

Classified with MFS **grade 0 (DPP^-) or grade 1 (DPP^+)**

n = 367

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Material and Methods → *Participants*

Inclusion criteria

- ❑ Acute IVD
- ❑ ≤ 7 years old;
- ❑ Weight ≤ 25 kg;
- ❑ Most chrondodystrophic breed;
- ❑ Lacked other concomitant diseases

Exclusion criteria

- ❑ SCI other than T10-L3;
- ❑ Surgery before 3 days > 5 days after injury;
- ❑ OFS scores >1
- ❑ Higher grades of FNRS-DPP- (>1)
- ❑ SG dogs: admitted with >7 days

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

SG
n = 262

Admitted to the rehabilitation center **≤ 7 days after surgery**

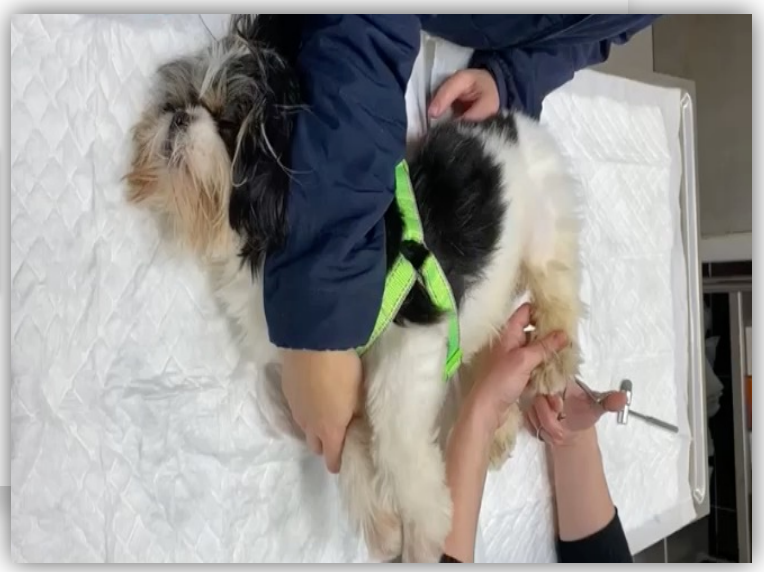
n= 94 DPP $^{-}$

New scale → **Grade 0 or 1** (if patellar reflex present)

Functional NR scale for dogs with thoracolumbar SCI without DPP (FNRS-DPP^{-})

n=168 DPP $^{+}$ (OFS 1)

Absent flexor reflex



Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Study Design

SG
n = 262

- ❑ Gait evaluation for DPP $^{+}$ → **OFS**
- ❑ Gait evaluation for DPP $^{-}$ → **FNRS-DPP $^{-}$**

FUNCTIONAL NEUROREHABILITATION SCALE (FNS) FOR DOGS WITH TORACOLOMBAR INJURY, WITHOUT DEEP PAIN SENSATION			
Nociception Evaluation	Deep pain sensation present in the digits		(+1)
	Deep pain sensation present in the tail		(+1)
	Deep pain sensation present in the perineum (dermatomes S3)		(+1)
	Deep pain sensation present in the vulva (dermatomes S2)		(+1)
Spinal Reflexes Evaluation	Patellar reflex	Absent	0
	Cranial tibial reflex	Decreased	1
	Withdrawal reflex	Normal	2
		Increased	3
	Crossed extensor reflex	Absent	0
		Present	1
Muscle Tone Evaluation	Hypotonic extensors muscles and hypotonic flexors muscles		0
	Hypertonic extensors muscles and hypotonic flexors muscles		1
	Spasticity of the extensors muscles and hypotonic flexors muscles, with passive range of motion difficult or absent ROM		2
	Hypertonic extensors muscles and hypotonic flexors muscles, with decreased ROM		3
	Normal muscle tone or slightly hypotonic flexors muscles		4
Gait Evaluation	Paraplegy		0
	Presence of movement without deep pain sensation, non-functional		1
	Presence of movement with deep pain sensation, non-functional		3
	Presence of movement without deep pain sensation, functional		2
	Presence of movement with deep pain sensation, functional		4
Proprioception and Locomotor #Coordination Evaluation	Coordination between PL and TL < 10% of the time*; +/- knuckling		0
	Coordination between PL and TL between 10-25% of the time*; +/- knuckling		1
	Coordination between PL and TL between 25-50% of the time*; without knuckling		2
	Coordination between PL and TL between 50-75% of the time*; without knuckling		3
	Coordination between PL and TL > 75% of the time*; without knuckling		4

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Pharmacological Management

❑ **3rd - 4th weeks (T4-T5)**

↓

If the flexion/extension locomotor pattern was present with DPP-

❑ **4 aminopyridine (4-AP)**

↳ K+ channel blocking compound

→ Implemented for a **maximum of 2 months!**

(Hayes 2006,2007; Lewis et al 2019; Lim et al 2014; Zorner et al 2016)

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

Definitions!

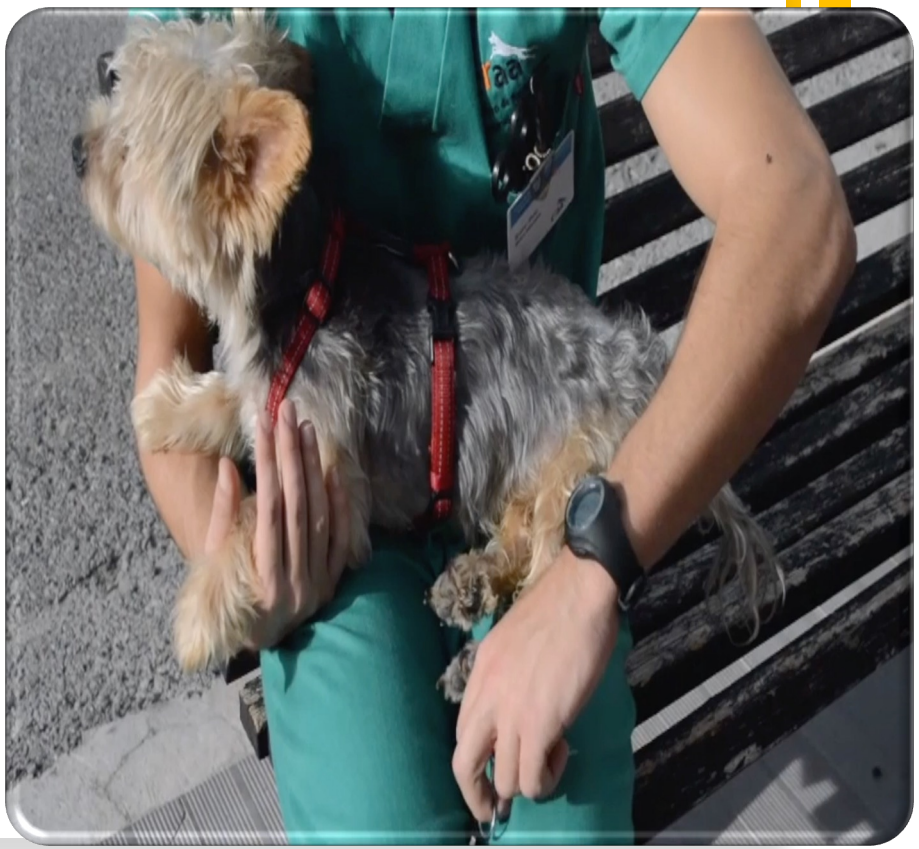
- **Autonomous ability** in movement control → Some **conscious control**!!!

Spinal Reflex Locomotion : Promote the autonomous ability to stand up and walk in DPP - dogs, maintaining some coordination forelimbs-hindlimbs and the ability to not fall when changing direction on a non-slippery floor

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

SG

- **DPP $^{-}$** Dogs→ Ambulatory if **SRL** (**FNRS-DPP^{-} score ≥ 14**)
- **DPP^{+}** Dogs → Ambulation when **OFS ≥ 11**



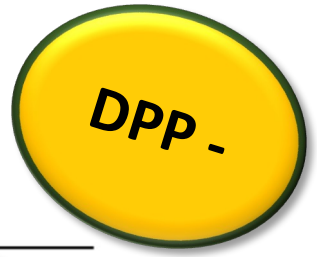
Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

SG

- **DPP$^-$** dogs with signs compatible with progressive myelomalacia → euthanized
- **CG dogs** were evaluated at admission and at discharge (FMS and neurological exam)

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Results



DPP⁻ population characterization at admission (n = 137).

	DPP⁻ (n = 137)			SG (n = 94)			CG (n = 43)		
	Mean (SD)	95% CI	Median	Mean (SD)	95% CI	Median	Mean (SD)	95% CI	Median
Age (years)	4.03 (1.576)	3.76–4.30	4.00	3.90 (1.566)	3.58–4.23	4.00	4.30 (1.582)	3.82–4.79	4.00
Body weight (kg)	8.14 (3.218)	7.59–8.68	8.00	8.51 (3.466)	7.80–9.22	8.00	7.33 (2.437)	6.58–8.08	7.00

Abbreviations: DPP, deep pain perception; SG, study group; CG, control group; CI, confidence interval; and SD, standard deviation.

- ❑ **72.3% chondrodystrophic** breeds;
- ❑ 39.4 % ♀ ; 60.6% ♂
- ❑ Neurolocation: **T12-T13 (30.4%) ; T13-L1 (26.1%);**
- ❑ Mean age: **4.03 years**; Mean weight: **8.14 kg**

- ❑ **Breed:**
  - →**French Bulldog** (27%; n=37);
  - →**Mixed breed** (25.5%; n=35);
  - →**Dachshund** (15.3%;n=20)

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Results

❑ T-test for independent samples (**age and weight**)

→ **No diference** between two groups → **Comparable!!**

DPP recovery : **SG** was **33.2 % (n=35)** VS **CG** was **21 % (n=9)**

SG: 59 dogs **did not recover DPP** → 22 dogs achieved SRL → Maximum of 3months!

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

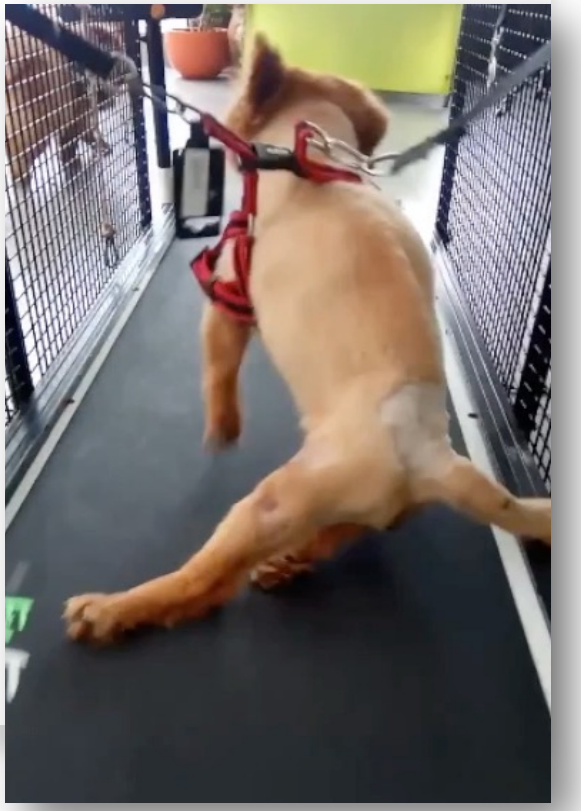
❑ Results

DPP -

❑ **Ambulation:** **58.5%** (n=55) in **SG** vs **32.6%** (n=14) in the **CG**;

- Strong difference with statistical significance **regarding ambulation recovery!!**

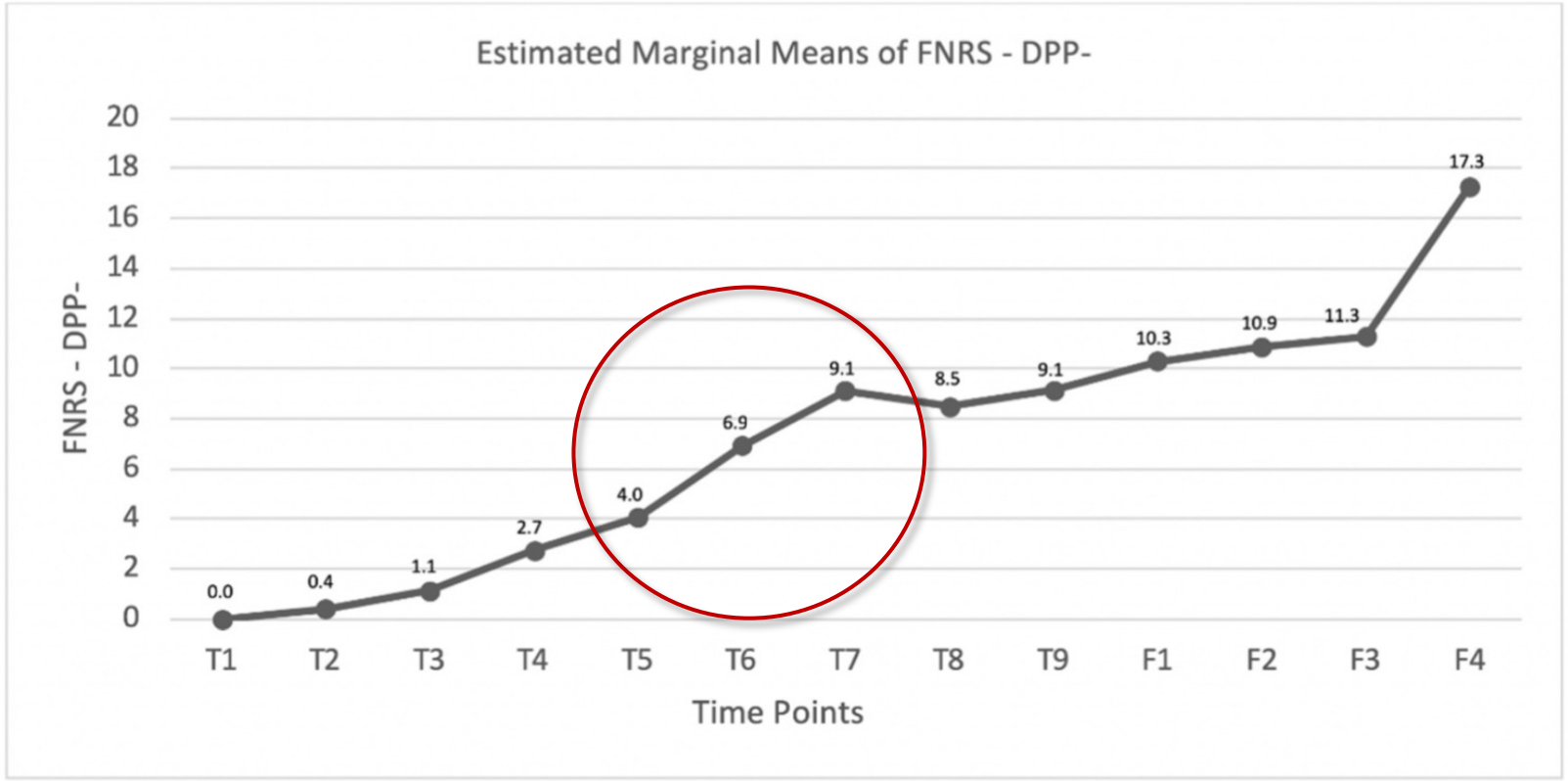
  → (*X2* (1, *n* = 137) = 7.311; ***p* = 0.007**).



Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Results

n - 59

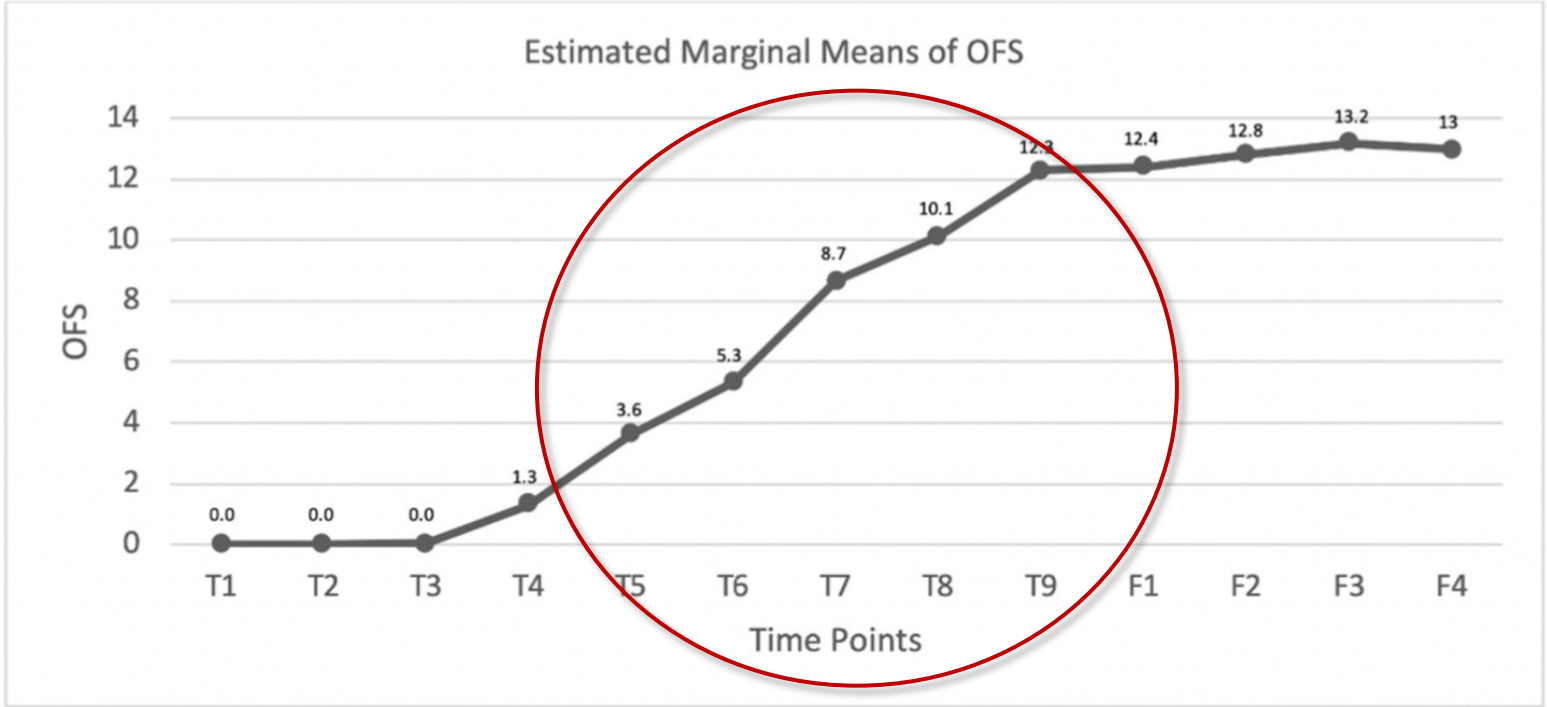


Graphic describing the FNRS-DPP⁻ mean evolution within the DPP⁻ dogs in the study group (SG). T1: admission, T2: day 3, T3: day 7, T4: day 15, T5: day 30, T6: day 45, T7: day 60, T8: day 75, T9: day 90, F1: 8–10 days follow-up, F2: 1-month follow-up, F3; 6-month follow-up, and F4; one-year follow-up.

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Results

n =35



Graphic describing the OFS mean evolution within the DPP⁻ dogs that recovered DPP in the study group (SG). T1: admission, T2: day 3, T3: day 7, T4: day 15, T5: day 30, T6: day 45, T7: day 60, T8: day 75, T9: day 90, F1: 8–10 days follow-up, F2: 1-month follow-up, F3: 6-month follow-up, and F4: one-year follow-up.

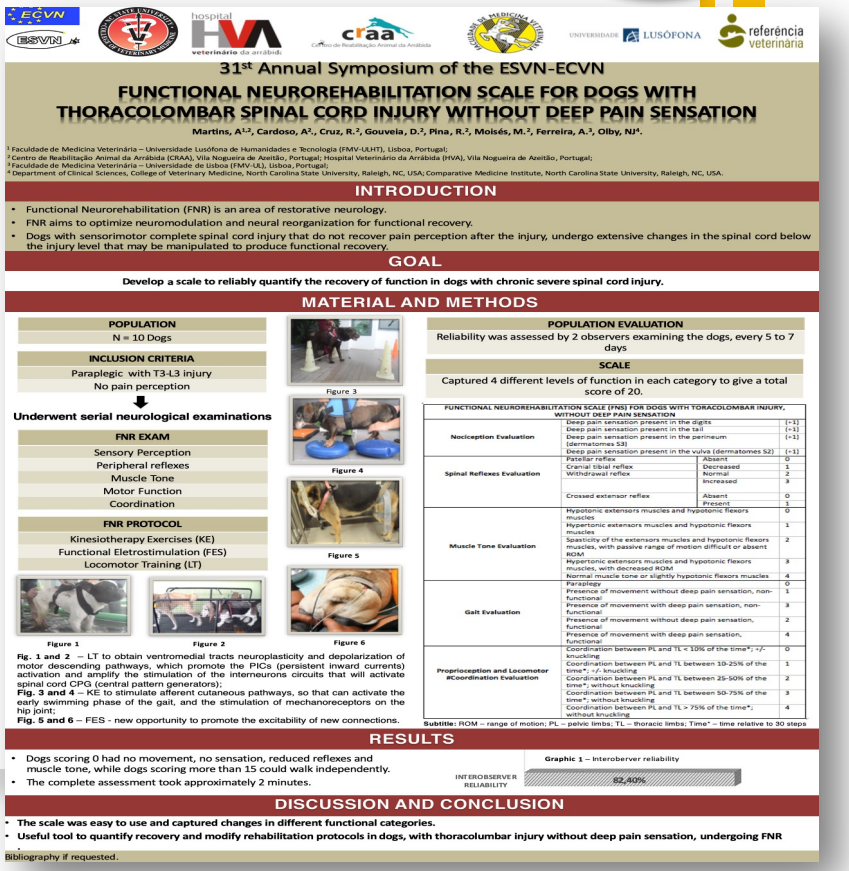
Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

DPP -

❑ Discussion

- ❑ n=137
- ❑ OFS limited value

- ❑ To evaluate **peripheral reflexes (flexion/extension locomotor pattern)**
  - ❑ **Scale** → 31st ESVN-ECVN Symposium in Copenhagen 2018



31st Annual Symposium of the ESVN-ECVN

FUNCTIONAL NEUROREHABILITATION SCALE FOR DOGS WITH THORACOLOMBAR SPINAL CORD INJURY WITHOUT DEEP PAIN SENSATION

Martins, A.[1,2], Cardoso, A.[2], Cruz, R.[2], Gouveia, D.[2], Pina, R.[2], Moisés, M.[2], Ferreira, A.[3], Olby, NJ[4].

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[2] Centro de Reabilitação Animal da Arrábida (CRAA), Vila Nogueira de Azeitão, Portugal; Hospital Veterinário da Arrábida (HVA), Vila Nogueira de Azeitão, Portugal;
[3] Faculdade de Medicina Veterinária – Universidade de Lisboa (FMV-UL), Lisboa, Portugal;
[4] Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC, USA; Comparative Medicine Institute, North Carolina State University, Raleigh, NC, USA.

INTRODUCTION

- Functional Neurorehabilitation (FNR) is an area of restorative neurology.
- FNR aims to optimize neuromodulation and neural reorganization for functional recovery.
- Dogs with sensorimotor complete spinal cord injury that do not recover pain perception after the injury, undergo extensive changes in the spinal cord below the injury level that may be manipulated to produce functional recovery.

GOAL

Develop a scale to reliably quantify the recovery of function in dogs with chronic severe spinal cord injury.

MATERIAL AND METHODS

POPULATION
N = 10 Dogs

INCLUSION CRITERIA
Paraplegic with T3-L3 injury
No pain perception

Underwent serial neurological examinations

FNR EXAM
Sensory Perception
Peripheral reflexes
Muscle Tone
Motor Function
Coordination

FNR PROTOCOL
Kinesiotherapy Exercises (KE)
Functional Eletrostimulation (FES)
Locomotor Training (LT)

Figure 1 Figure 2 Figure 3 Figure 4 Figure 5 Figure 6

Fig. 1 and 2 – LT to obtain ventromedial tracts neuroplasticity and depolarization of motor descending pathways, which promote the PICs (persistent inward currents) activation and amplify the stimulation of the interneurons circuits that will activate spinal cord CPG (central pattern generators);
Fig. 3 and 4 – KE to stimulate afferent cutaneous pathways, so that can activate the early swimming phase of the gait, and the stimulation of mechanoreceptors on the hip joint;
Fig. 5 and 6 – FES - new opportunity to promote the excitability of new connections.

POPULATION EVALUATION
Reliability was assessed by 2 observers examining the dogs, every 5 to 7 days

SCALE
Captured 4 different levels of function in each category to give a total score of 20.

FUNCTIONAL NEUROREHABILITATION SCALE (FNS) FOR DOGS WITH TORACOLOMBAR INJURY, WITHOUT DEEP PAIN SENSATION

Nociception Evaluation	Deep pain sensation present in the digits		(+1)
	Deep pain sensation present in the tail		(+1)
	Deep pain sensation present in the perineum (dermatomes S3)		(+1)
	Deep pain sensation present in the vulva (dermatomes S2)		(+1)
Spinal Reflexes Evaluation	Patellar reflex	Absent	0
	Cranial tibial reflex	Decreased	1
	Withdrawal reflex	Normal	2
		Increased	3
	Crossed extensor reflex	Absent	0
		Present	1
Muscle Tone Evaluation	Hypotonic extensors muscles and hypotonic flexors muscles		0
	Hypertonic extensors muscles and hypotonic flexors muscles		1
	Spasticity of the extensors muscles and hypotonic flexors muscles, with passive range of motion difficult or absent ROM		2
	Hypertonic extensors muscles and hypotonic flexors muscles, with decreased ROM		3
	Normal muscle tone or slightly hypotonic flexors muscles		4
Gait Evaluation	Paraplegy		0
	Presence of movement without deep pain sensation, non-functional		1
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Proprioception and Locomotor #Coordination Evaluation	Coordination between PL and TL < 10% of the time*; +/- knuckling		0
	Coordination between PL and TL between 10-25% of the time*; +/- knuckling		1
	Coordination between PL and TL between 25-50% of the time*; without knuckling		2
	Coordination between PL and TL between 50-75% of the time*; without knuckling		3
	Coordination between PL and TL > 75% of the time*; without knuckling		4

Subtitle: ROM – range of motion; PL – pelvic limbs; TL – thoracic limbs; Time* – time relative to 30 steps

RESULTS

- Dogs scoring 0 had no movement, no sensation, reduced reflexes and muscle tone, while dogs scoring more than 15 could walk independently.
- The complete assessment took approximately 2 minutes.

Graphic 1 – Interobserver reliability

INTEROBSERVER RELIABILITY 82,40%

DISCUSSION AND CONCLUSION

- The scale was easy to use and captured changes in different functional categories.
- Useful tool to quantify recovery and modify rehabilitation protocols in dogs, with thoracolumbar injury without deep pain sensation, undergoing FNR .

Bibliography if requested.

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Discussion

❑ **58.5%** Ambulation in the **SG**

❑ DPP recovery: **33.2%** (35/94) > CG recovery → (**p=0.058**)

- lower when compared to ~60% CANSORT –SCI (105)

❑ DPP recovery in the **CG limited assessment** !!

- ❑ euthanasia
- ❑ not able to evaluate spontaneous motor recovery over time

31st Annual Symposium of the ESVN-ECVN

FUNCTIONAL NEUROREHABILITATION SCALE FOR DOGS WITH THORACOLOMBAR SPINAL CORD INJURY WITHOUT DEEP PAIN SENSATION

Martins, A.[1,2], Cardoso, A.[1], Cruz, R.[2], Gouveia, D.[2], Pina, R.[2], Moisés, M.[2], Ferreira, A.[3], Olby, N.[4].

INTRODUCTION

- Functional Neurorehabilitation (FNR) is an area of restorative neurology.
- FNR aims to optimize neuromodulation and neural reorganization for functional recovery.
- Dogs with sensorimotor complete spinal cord injury that do not recover pain perception after the injury, undergo extensive changes in the spinal cord below the injury level that may be manipulated to produce functional recovery.

GOAL

Develop a scale to reliably quantify the recovery of function in dogs with chronic severe spinal cord injury.

MATERIAL AND METHODS

POPULATION: N = 10 Dogs

INCLUSION CRITERIA: Paraplegic with T3-L3 injury; No pain perception

Underwent serial neurological examinations

FNR EXAM: Sensory Perception; Peripheral reflexes; Muscle Tone; Motor Function; Coordination

FNR PROTOCOL: Kinesiotherapy Exercises (KE); Functional Eletrostimulation (FES); Locomotor Training (LT)

POPULATION EVALUATION: Reliability was assessed by 2 observers examining the dogs, every 5 to 7 days

SCALE: Captured 4 different levels of function in each category to give a total score of 20.

FUNCTIONAL NEUROREHABILITATION SCALE (FNS) FOR DOGS WITH TORACOLOMBAR INJURY, WITHOUT DEEP PAIN SENSATION

Nociception Evaluation	Deep pain sensation present in the digits		(+1)
	Deep pain sensation present in the tail		(+1)
	Deep pain sensation present in the perineum (dermatomes S3)		(+1)
	Deep pain sensation present in the vulva (dermatomes S2)		(+1)
Spinal Reflexes Evaluation	Patellar reflex	Absent	0
	Cranial tibial reflex	Decreased	1
	Withdrawal reflex	Normal	2
		Increased	3
	Crossed extensor reflex	Absent	0
		Present	1
Muscle Tone Evaluation	Hypotonic extensors muscles and hypotonic flexors muscles		0
	Hypertonic extensors muscles and hypotonic flexors muscles		1
	Spasticity of the extensors muscles and hypotonic flexors muscles, with passive range of motion difficult or absent ROM		2
	Hypertonic extensors muscles and hypotonic flexors muscles, with decreased ROM		3
	Normal muscle tone or slightly hypotonic flexors muscles		4
Gait Evaluation	Paraplegy		0
	Presence of movement without deep pain sensation, non-functional		1
	Presence of movement with deep pain sensation, non-functional		3
	Presence of movement without deep pain sensation, functional		3
	Presence of movement with deep pain sensation, functional		4
Proprioception and Locomotor #Coordination Evaluation	Coordination between PL and TL < 10% of the time*; +/- knuckling		0
	Coordination between PL and TL between 10-25% of the time*, +/- knuckling		1
	Coordination between PL and TL between 25-50% of the time*, without knuckling		2
	Coordination between PL and TL between 50-75% of the time*, without knuckling		3
	Coordination between PL and TL > 75% of the time*, without knuckling		4

Subtitle: ROM – range of motion; PL – pelvic limbs; TL – thoracic limbs; Time* – time relative to 30 steps

Figure 1 Figure 2 Figure 3 Figure 4 Figure 5 Figure 6

Fig. 1 and 2 – LT to obtain ventromedial tracts neuroplasticity and depolarization of motor descending pathways, which promote the PICs (persistent inward currents) activation and amplify the stimulation of the interneurons circuits that will activate spinal cord CPG (central pattern generators);
Fig. 3 and 4 – KE to stimulate afferent cutaneous pathways, so that can activate the early swimming phase of the gait, and the stimulation of mechanoreceptors on the hip joint;
Fig. 5 and 6 – FES - new opportunity to promote the excitability of new connections.

RESULTS

- Dogs scoring 0 had no movement, no sensation, reduced reflexes and muscle tone, while dogs scoring more than 15 could walk independently.
- The complete assessment took approximately 2 minutes.

Graphic 1 – Interobserver reliability

INTEROBSERVER RELIABILITY: 62,40%

DISCUSSION AND CONCLUSION

- The scale was easy to use and captured changes in different functional categories.
- Useful tool to quantify recovery and modify rehabilitation protocols in dogs, with thoracolumbar injury without deep pain sensation, undergoing FNR

Bibliography if requested.

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

DPP -

❑ Discussion

✓ **22 dogs** in the **SG** regained ambulation by SRL (**37.3%)**

Maximum period of 3 months !

→ Higher than reported by Olby et al (2003) : **32 %** within **9 months** (range 4-18 months);

→ A cohort of 94 chronic dogs, **9 became ambulatory** median of **12 months** (3-89 months)

Other studies T3-L3 lesions → Shorter average of time associated to an early post-injury intensive rehabilitation !!!

(Lewis et al 2017, 2020;Gallucci et al 2017; Hu et al 2018)

Controlled Clinical Study of INR in Post-surgical Dogs with Acute IVDE

❑ Discussion

❑ **58.5% ambulation within 3 months**

→ **INR ↓ time of revovery**

❑ ↑ prevalence of **SRL (37.3%** within 3 months)

→ **↓ Euthanasia**

❑ Dogs with **DPP recovery** → Max. OFS mean was **12.3 at T9** , increasing in the 6 month and 1 year follow-ups

→ **Spinal Cord memorization**

✓ *Olby et al (2020) and CANSORT-SCI (2021) → ~ **61%** IVDE dogs **recovered DPP and ambulation 6 months** after SCI; **31% did not recovered DPP but regained ambulation** within a mean time of **9 months (2-28 months)***

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

- **Chronic Dogs**

animals

MDPI

Article

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Intervertebral Disc Surgery: A Case Series

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(2021)

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

Keynotes!!

❑ Chronic Dogs

- ❑ Not modulated considering peripheral spinal reflexes;
- ❑ Non-coordinated and non-synchronized flexion/extension locomotor pattern with clonic reflexes;

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

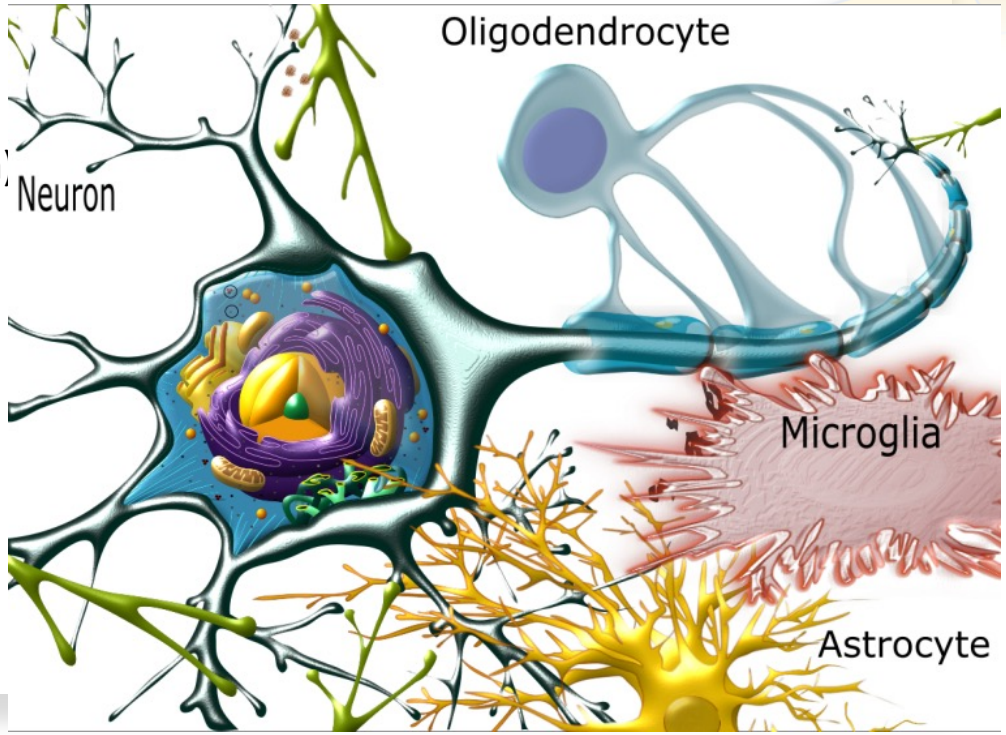
Keynotes!!

❑ Chronic Dogs

❑ Central Nervous System

- **Complex neural connections**;\
- Population of glial cells (**astrocytes, oligodendrocytes, and microglia**) Important role in neural plasticity;
- Astrocytes → **Fibroglial scar** at the injury site after SCI.

Stabilized the injured parenchyma by re-establishing its physical and chemical integrity through different mechanisms → ***Pro-regenerative role***



Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

Keynotes!!

- Evidence that suggests that the **glial scar can support CNS repair**
- Plasticity in **pre-existent pathways** and the **formation of new circuits**

SYNAPTIC AND ANATOMICAL NEUROPLASTICITY

Promote the sprouting of lesioned fibers, contributing to **regeneration**!

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

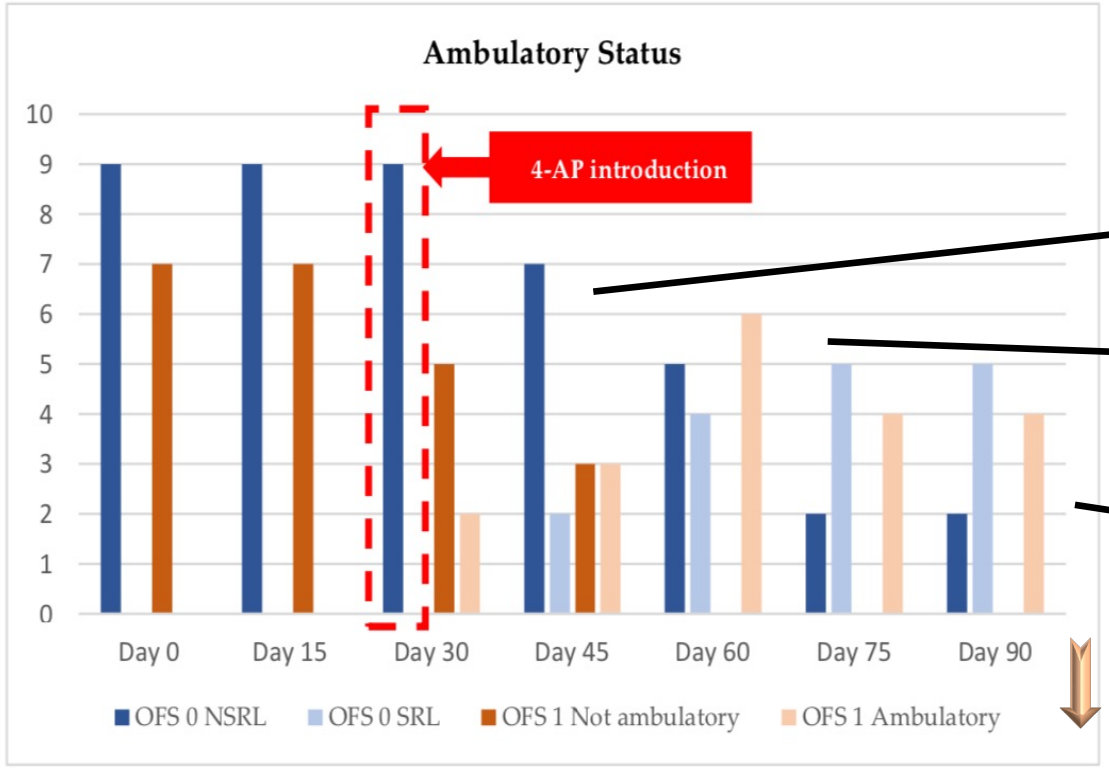
- The induction of activity → Spinal cord plasticity → **ROLE OF NEUROREHABILITATION!**

- **4-AP** → Enhance motor neuron pool excitability in dogs !! → **MORE STUDIES!**

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

❑ Results

DPP -



Evolution of ambulatory status and medical discharge from admission (day 0) until day 90. OFS—open field score [64]; SRL—Spinal Reflex Locomotion; NSRL—Non-Spinal Reflex Locomotion; OFS 0: blue color; OFS 1: brown color.

Day 45: **2 dogs SRL** with medical discharged at day 60;

Day 60: **2 dogs SRL** with medical discharged at day 90;

Day 90: **Only 2 dogs** remained with **NSRL**

Always after starting 4-AP (Day 30) !!

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

❑ Discussion

❑**Neurorehabilitation Multimodal Protocol (NRMP)**

→ Locomotor training:

BWSTT land treadmill + UWTM + kinesiotherapy exercises

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

Discussion

→**DPP⁻ dogs**: Improved after **4-AP implementation**

One dog achieved SRL after 15 days

78% achieved SRL by day 45

→Mean time to achieve SRL was **62 days**;

→**Follow-up** → maintained neurological status.

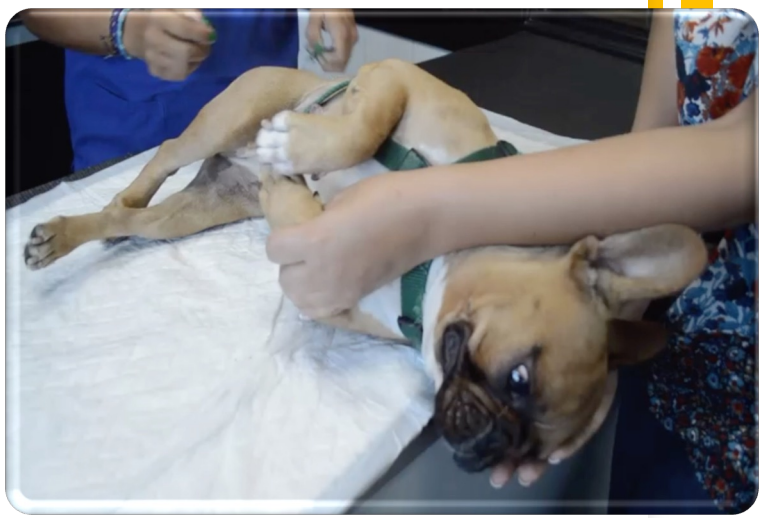
Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

❑ 4 - AP

- ❑ *Lewis and colleagues (2019)*
  Mean dosage - **0.78 mg/kg** (min 3 doses separated by at least 8 hours) → **reported seizure activity**

- ❑ **Our study**:
  Gradually administered from **0.3-1.1mg/kg** *per os* BID

- ❑ → Avoid increased drug related side effects!!!
- ❑ → No adverse effects ----► **SAFE AND NON-HARMFUL PROTOCOL**

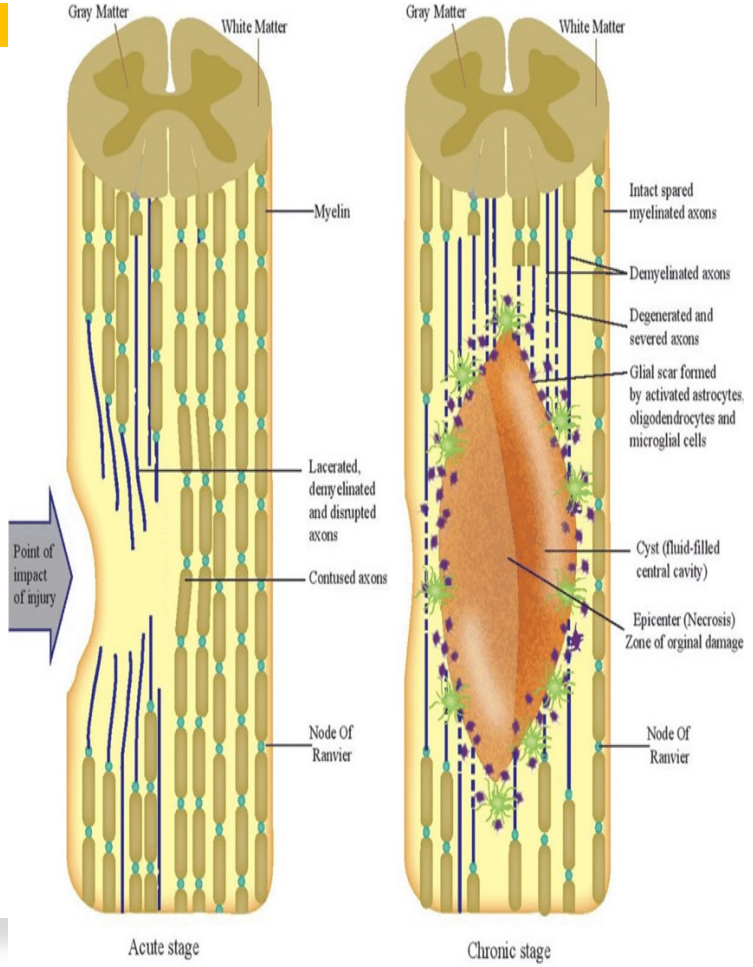


Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

Axons fail to regrow → Could be inhibited by scar tissue formation

The glial scar and cavity formation → Main pathophysiological feature **in chronic SCI !**

Reactive astrocytes in the chronic phase after the injury



Hu et al 2010

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

Recent analysis → Transcranial magnetic motor evoked potential suggested that spinal locomotion could be associated with **remaining intact conduction through the descending motor tracts !**

Hypotheses: **Spinal walking** ⟷ **Long tract conduction**

Dogs complete SCI → persistent passage of electrophysiological stimuli across the lesion with recorded evoked potentials above the injury

Granger et al (2012) Hu et al (2018)

Functional Neurorehabilitation in Dogs with an Incomplete Recovery 3 Months following Disc Surgery: A case series

DPP -

- There was **no DPP recovery** in contrast to the acute dogs (usually regain 41-62% of ambulation);
- According to the CANSORT-SCI (2021), DPP$^-$ dogs recover DPP to ambulation ~ 60% within 6 months after injury;

↓

- **DPP $^-$ chronic dogs achieved 78% of ambulation** within **2 and a half months**, however all achieved flexion/extension locomotor pattern within the first 2 weeks → **4-AP**

QUESTIONS ?!


Obrigada!!