

Title: FUNCTIONAL RECOVERY AFTER CLOSED IMPACT INJURY TO THE SPINAL CORD USING DIMETHYL SULFOXIDE AND CENTROPHENOXINE

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Introduction: We have recently developed a new model for producing experimental impact injury to the spinal cord that is more akin to the trauma suffered in man since it is a closed system that does not necessitate laminectomy and hence, obviates infections and other cellular changes found in the open model; does not necessitate the removal of anatomical energy attenuating structures; and allows for a rapid determination of the biomechanical forces involved during and after impact. In this study we evaluate the effect of centrophenoxine (CPO), an antioxidant enzyme stimulator and dimethyl sulfoxide (DMSO), a free radical scavenger and platelet-aggregation inhibitor on acute, closed, impact injury to the spinal cord.

Methods: Closed impact injury was accomplished using a gas powered missile impacting on an impounder resting on the T₉-T₁₀ interpace. The impounder is seated on an electronic collar that records the force exerted on impact. Sixteen acclimated, barrier raised cats were anesthetized with 20mg/kg pentobarbital, intubated and ventilated to normoxia and normocarbica. During the procedure and until extubation, heart rate, respiratory rate, the EKG and temperature were continuously monitored. They were then assigned to either the control (no therapy-Group 1)-5 animals; DMSO, 2.5g/kg (Group 2)-5 animals; or CPO, 50 mgm/kg (Group 3) -6 animals. All animals were traumatized with closed impact forces greater than 0.7 x 10⁷ dynes/kg. Functional evaluation was carried out daily during the subsequent 4 weeks using a neurobehavioral recovery index in which the ability to run, move and climb, were tested. A score of 16 indicated normal function and a score of 3 signified paraplegia. The neurobehavioral changes found in each group were compared against each other and analyzed for statistical significance using paired t test with alpha splitting.

Results: Table 1 indicates the impact forces and Recovery Index Scores seen in group 1 (Control). Group II (DMSO) and Group III (CPO).

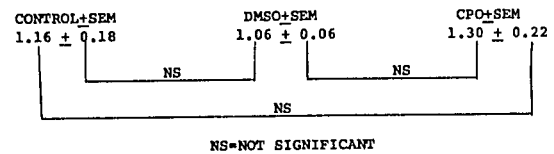
TABLE 1

Group I (Control)			Group II (DMSO)			Group III (CPO)		
Subject No.	Force 10 ⁷ dynes/kg	Recov. Index	Subject No.	Force 10 ⁷ dynes/kg	Recov. Index	Subject No.	Force 10 ⁷ dynes/kg	Recov. Index
1	1.67	3	6	1.32	11	11	1.07	15
2	0.80	7	7	1.06	10	12	1.38	16
3	0.67	7	8	1.0	10	13	1.46	3
4	1.61	3	9	0.97	15	14	1.68	3
5	1.05	3	10	0.96	16	15	0.92	16
Mean	1.16	4.6		1.06	12.4		1.30	10.6
S.E.M	0.18	0.9		0.06	1.2		0.22	2.8

It is to be noted that all controls are at 7.0 or below in the Recovery Index. All animals in the DMSO group showed good levels of functional recovery, while 2 subjects in the CPO Group were paraplegic, the remaining 4 showing excellent return of function. Statistical analysis of both Impact Forces and Recovery Index against all 3

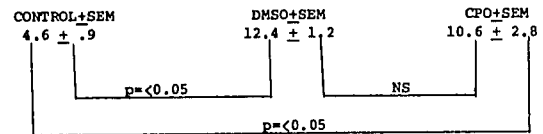
groups were carried out using The Mann-Whitney Rank Sum Test. In Fig 1 we note no statistical differences between the Impact Forces used in all 3 groups.

Fig 1. IMPACT FORCES



In Fig 2, the Recovery Index scores between DMSO and CPO are not significant, while significance exists (p<0.05) between DMSO against control and CPO against control (p<0.05).

Fig 2. RECOVERY INDEX



Discussion:² The early pathogenesis of acute spinal cord injury probably involves the generation of oxygenated arachidonic acid derivatives including prostaglandins, thromboxanes and leukotrienes. It is thought that CPO may effectively quench the arachidonic acid cascade by stimulating release of antioxidants such as superoxide dismutase and catalase. DMSO, aside from its free radical scavenging properties, has been noted to inhibit thromboxane and cyclooxygenase products such as prostaglandins and enhance prostacyclin release. This spinal cord injury model may prove to be superior to the presently used open (after laminectomy) impact injury technique by being a more suitable model for drug studies. We are presently awaiting the results of an ancillary study that will allow us to compare the neurobehavioral recovery index in each of the three groups against histological findings related to lesion volumes and white matter sparing. Our data indicates that significant functional recovery occurred from acute closed impact injury of the spinal cord using DMSO and CPO. Supported by a grant from the Moody Foundation, Galveston, Texas.

References:

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