10th Annual Conference of the International FES Society
July 2005 – Montreal, Canada

SURGICALLY BRAIN DAMAGED PIG AS A MODEL TO INVESTIGATE FES's APPLICATIONS ON SPASTICITY OF CEREBRAL PALSY AND RELATED DESEASES

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ABSTRACT

Our aim is to create a more adapted animal model to experiment FES's methods in spastic cerebral palsy .Classically, decerebrated animal by mesencephalic lesion is considered as the paradigm for experimental study of spasticity accompanying cerebral palsy, but, this situation is not corresponding with anatomo-pathological reality, so we needed to create a new model simulating more precisely the common findings in this disease, a mixture of ulegiria (motor cortical lesion), and subcortical lesion, both produced by perinatal anoxic brain damage. To simulate these pathological conditions pigs were used, in which a double surgical lesion was produced: a resection of rolandic and peri-rolandic area (cortical lesion) and by aspiration and coagulation of sub-cortex (subcortical lesion), to give as a result a pathogenic configuration similar to human spastic cerebral palsy. Confirmatory pre and post-operative cervical motor evoked potentials and abnormally propagated electromyographic recordings were made, and they showed significant differences.

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KEY WORDS

Animal model- Brain Damage- Fes's Applications-Functional Electrical Stimulation-Neurostimulation-Reproducibility of Results-Spastic Cerebral Palsy-Spasticity

INTRODUCTION

Sherrington and Moruzzi described decrease in muscle tonus after paravermal cerebellar stimulation in decerebrate cat preparation (11,12,16).
This model has been employed to study some aspects of spastic phenomena (14,15).
Nevertheless, a model that clearly mimics spastic cerebral palsy is still not available (19).
We design this different model as close as possible to commonly present lesions in cerebral palsy: ulegiria and subcortical lesion (10), with the objective to ilnvestigate the effect of lateral cord electrical stimulation on spasticity of Cerebral Palsy and related diseases.
Cortical and subcortical lesions were made by means of a right craniectomy.
In a previous attempt to test basic conditions, motor evoked potentials with stimulation in cervical region with simultaneous electromyographic recording technique (7) were made bilaterally, and a 4th lumbar root stimulation, supplying cuadriceps muscle, to test any current electromyographic spreading on semitendinous muscle, supplied by 7th root, was applied.
After brain lesion a similar sequence of electrical records was also performed.
The rational of this last procedure is to declenche abnormally propagated current spreading (3-4 segments below the stimulated root L4), of polysynaptic basis by upper motor lesion(3,8) which is not normally present (1).Electrical parameters were adapted taking clinical (1, 17) and experimental (15) as reference. Frequency of 45HZ, 100 microsecond p.p. were used in reason of our equipment limitations. Discharges of increasing electrical intensity of 0,5 mA each 0,5 sec, starting of 0,5 mA, every three seconds were delivered. In pre-operative preparation the step current was stopped at 4,5 mA. In post-operative one the current was delivered till a fully electromyographic response was obtained in semitendinous muscle, innervated by 7th lumbar root.

MATERIALS AND METHODS

Young pigs weighting 30-40 kg were used. All animals were anesthetized with ketamine clorhidrate 50 mg per kilo by intravenous perfusion, and prometazide 20 mg kilo IV as premedication, after a short induction with isofluorane which was discontinued in cases of neuro-physiological measures to avoid neuro-muscular interaction as much as possible(5).
A previous motor evoked potentials (MEPs) were made with cervical stimulation technique and simultaneous bilateral electromyographic (EMG) recording (7), measuring bilateral responses on rectus femoris muscle making a mean value of ten measures each one. Several minutes later, a laminectomy L3 toL6 was made to expose left 4th lumbar root which was electrophysiological identified by successive steps of current (0,5 mA) and by EMG recording on rectus femoris.
Standart intramuscular electrodes were placed on it to record EMG responses on semitendinous muscle,

innervated by L7. Serial steps of stimulation were made, starting from 0,5 mA and stopping at 4,5 mA, with already described adapted parameters.
Cranial operation was performed some days later, by means of a right arciform unilateral incision, extended from supraorbitary to retroauricular region , and cutaneous flap was retracted exposing the cranial bone . Posteriorly, a trephine was made over skull surface an a craniotomy was completed using a gouge, exposing the duramater which was opened with scissors, and a cortical and sub-cortical lesion are done, as follows:
Cortical surface belonging to sylvian girus and sulcus and its vicinity are coagulated with bipolar forceps extending the lesion to midline in the posterior margin of coronal sulcus, grossly corresponding to pyramidal areas in man (18).
Later, aspiration of coagulated tissue continues by sub-cortical dissection.
Then, the operation is finished with several unipolar coagulations directed to deep gray matter lesioning internal capsulae between caudate and putamen nuclei.
Twenty days after or later (mean 26.6 days), an identical set of measures of MEP and EMG record were made by re-opening the lumbar surgical wound.

RESULTS

We have operated twelve pigs and we have two deaths after cranial operation in the beginning of the experiment (1st and 3rd operation), one by meningeal infection and other by post-operative hydrocephalus.
After we had mastered the technique, nine animals did well post – operatively, and a total of ten has been completely studied.
In two cases they had vomits that improved with intramuscular dexametasone and metoclopramide.
Those 10 animals were able to walk and eat shortly after the operation, but when they tried to run they limped at the left hindlimb in all but one case (7th animal).
Several days after, they became increasingly spastic, but always able to stand and walk in all cases, and feed by themselves.
The pre-operative MEPs show no significant differences comparing sides, and EMG record of semitendinous muscle showed any EMG activity after L4 stimulation (see table in figure 1).

FIGURE 1

	Mean	Standart Direction	P. Value
pre operative right potential	**2,88**	**0,2**	**0,27**
post operative right potential	**2,98**	**0,45**	

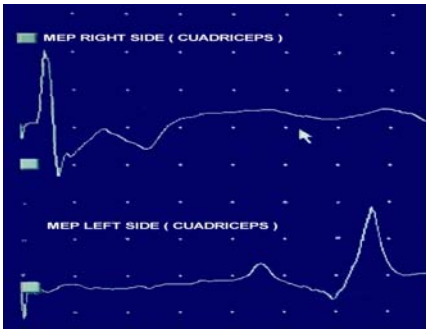
	Mean	Standart Direction	P. Value
pre operative right latence	**20**	**2,06**	**0,23**
post operative right latence	**19,5**	**1,84**	

	Mean	Standart Direction	P. Value
pre operative left potential	**2,94**	**0,19**	**0,001**
post operative left potential	**1,97**	**0,39**	

	Mean	Standart Direction	P. Value
pre operative left latence	**20,8**	**1,9**	**0,001**
post operative left latence	**29,8**	**3,5**	

By the contrary, in brain damaged pigs both latences and amplitude were significantly different (an example is shown in figure 2).

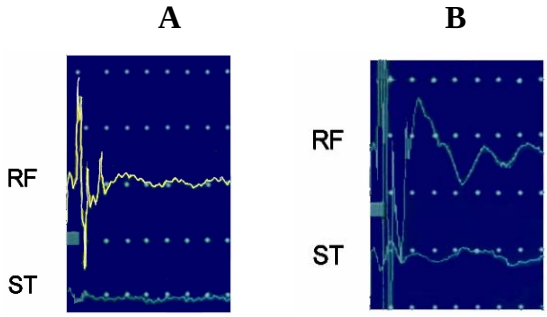
FIGURE 2



DIFFERENCES OF EMGRAPHIC LATENCE AND VOLTAGE OBTAINED FROM HEALTHY (RIGHT) AND DAMAGED (LEFT) SIDES, ARE SHOWN

Fully spreading EMGraphic activity on semitendinous muscle was seen in all animals with a mean of 1,83 mA (an example is shown in figure 3)

FIGURE 3



RF = RECTUS FEMORIS (CUADRICEPS)
ST = SEMITENDINOUS
5Th Animal
A)No disseminated EMGraphic response is seen on semitendinous muscle at 4.5mA
B)After brain lesion fully EMGraphic response Spreading on semitendinous muscle is obtained at 2.5mA

DISCUSSION/CONCLUSIONS

The alterations on both, latencies and amplitude on the stroke side compared to previous and also simultaneous contralateral normal ones demonstrates chronic long motor tract lesion (7).

Data obtained from Sherrington's decerebrate cat preparation (16) has been longer used for clinical (1, 17), and experimental research in spasticity (14, 15) but it's not related with the real anatomic and physiological conditions present in cerebral palsy.

Some alternative models has been proposed: hypoxic rats (19) or rabbits (4), by endogenous toxicity in rats (13).These models are expensive because the need of huge technical resources, trained technical staff and they are time- consuming,

A model with hypoxia-ischemia in piglets has been studied with any published practical research on FES's applications, till the moment (9). The unilaterallity of the brain lesion looks promising as producing abnormal neural connections (2) and it's surgically easier, so we have adopted it.

Our preparation is handling, easy to perform and cheaper than currently employed models because it doesn't require complicated means for intra or postoperative care.

Besides, our neurophisiological records show significant signs of chronic motor damage and reflex release to propose this model as usefull to investigate FES's applications for human spasticity.

Equipment used was MEDELEC model Synergy, range 2,5 volt, Sew Ecp 5º mseg, Low frquency filter 1Kj, monitor reliability 200 micro volts, 2 channels, setup adquisition.

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Acknowledgments:

No finantial source, neither private nor governmental, supported this work. The authors thank to Esteban Miele VD for his orientation and animal care, and Mr Luis Sanjurjo for his technical assistance.