IMPROVED MECHANICAL EFFICIENCY IN CEREBRAL PALSY PATIENTS TREATED WITH A CRANIAL ELECTROTHERAPY STIMULATOR (CES)

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Dr. Logan received the Richmond Award from the American Academy for Cerebral Palsy and Developmental Medicine-October 1988 for this work.

Summary

Thirty subjects with spastic type cerebral palsy participated in a double-blind placebo controlled study to evaluate the antispasticity effects of very low level noninvasive cortical electrical stimulation. Each subject performed a vigorous graded exercise work task on a computerized bicycle ergometer before and after stimulation. The active group scored impressive gains in work performance, 19.1% improvement in mechanical efficiency and 43% in workload output, while performance of the placebo group declined relative to baseline scores. The results were highly statistically significant. The most likely explanation is that spasticity was reduced in the actively treated subjects.

INTRODUCTION

Cerebral Palsy (CP) is a condition characterized by pathology with several common features including static encephalopathy; motor dysfunction; and etiologic insult either before birth, in the perinatal period, or in the first few years of life. The large majority of victims suffer from the spastic type, which may be combined with the other syndromes of dyskinesia and/or ataxia. It is unusual that all three types are found in the same individual (Swaiman 1982).

Two treatment modes are of potential benefit to the CP patient: rehabilitation programs of physical and occupational therapy, and attempted reduction of spasticity through the use of surgery, drugs, or electrical stimulation.

Direct electrical stimulation of the brain to reduce spasticity can be effective (Cooper 1978 and McLellan 1982), but the technique has all the disadvantages associated with invasive procedures: it is traumatic, requiring implantation of an electrode on the brain's surface; it is expensive and requires extensive medical follow up; it carries a high risk of infection; and it is unacceptable to many patients. Even though this invasive technique has not gained widespread acceptance, interest in electrical antispasticity modalities has persisted.

Recent reports in the literature have indicated that very low level noninvasive cortical electrical stimulation promotes developmental improvement of CP patients enrolled in physical therapy programs (Malden and Charash 1985). These authors noted that approximately 1 milliampere of current applied across the temporal region for 10 minutes in the morning and evening produced an antispasticity effect that potentiated the learning of gross motor responses according to several rating scales. Notwithstanding the difficulties involved in assessing functional improvement over time in hard to match test populations, these studies did not attempt to measure an antispasticity effect directly. Therefore, a study was devised to objectify the previous findings using short-term measurements which would reflect reductions in spasticity.

A double-blind placebo controlled study was conducted to measure mechanical efficiency during a period of vigorous bicycling before and after electrical stimulation. Since reductions in spasticity of an antagonist muscle necessarily result in less energy expenditure, ergometric measurements were made in response to a graded work task. Although other factors could affect mechanical efficiency, we believe that bicycle ergometry is sufficiently sensitive to evaluate the antispasticity activity of low level noninvasive cortical electrical stimulation.

Subjects and Methods

Thirty-six subjects with established diagnoses of spastic type cerebral palsy were enrolled in the study. The evaluable population comprised 13 males and 17 females, ranging in age from 10 to 35 years, with a mean age of 23 years.

Each subject was asked to perform a graded exercise test on a Tunturi bicycle ergometer. The ergometer was mechanically braked, displaying the pedaling speed in revolutions per minute (rpm) and the resistance to pedaling in Newtons (N).

The mechanical efficiency was calculated using the formula: ME = W/E where W is the workload in watts and E is the energy consumed in lifers of 0_2. The workload was calculated from the resistance of the bicycle and the pedal velocity utilizing the formula:

$W = \frac{N \times R}{30}$, where N is the resistance in Newtons and R is the pedal velocity in rpm.

Expired respiratory gases were collected and analyzed by a Beckman Metabolic Measurement Cart (MMC). The MMC measured the volume of air expired, the amount of $C0_2$ produced, and the amount of 0_2 used. The respiratory exchange quotient (RQ) was calculated from these values. Workload and respiratory gas data were entered into a minicomputer in real time.

Informed consent was required of all subjects. Subjects were screened to assure that they were in the American College of Sports Medicine (ACSM) low risk category regarding the potential for developing cardiovascular complications during or following maximum exercise. Subjects were also given a resting 12 lead electrocardiogram.

During the graded exercise test, the workload was started at zero Newtons and increased by two to five Newtons every two minutes based on the subject's heart rate, blood pressure, and ability to maintain pedal velocity. The heart rate was measured every minute by an EKG utilizing lead V5. Expired gases were measured every minute and blood pressure was recorded every two minutes. As the respiratory quotient (RQ) approached 1.0 or as the subject showed signs of laboring to maintain the workload, all measurements were recorded every 30 seconds.

The test end point was reached when one or more of the following conditions was met:

1. The subject reached a respiratory quotient of 1.0;

2. The ACSM discontinuation criteria were met;

3. The subject requested that the test be stopped.

All subjects underwent a prestimulation exercise test to establish a mechanical efficiency baseline. According to a previously assigned randomization schedule, all subjects underwent a second test following a period of stimulation with either an active or placebo Cranial Electrotherapy Stimulator (CES), the Pain Suppressor^{TM} manufactured by Pain Suppression Labs, Inc., Wayne, New Jersey, USA. The second test took place 48 hours after the first. Subjects in the active group received ten minutes of noninvasive cortical electrical stimulation, with the electrodes being placed just above the ears. The applied level of current was 0.5-0.7 milliamperes. The signal consisted of a 35 microsecond square wave repeating at 15,000 Hz within a 50 ms pulse burst, which had a repetition rate of 15 Hz (Figure 1). The unit is battery operated and portable, about

the size of a small transistor radio. Placebo units applied current for the first 70 seconds and then shut off automatically. Neither subjects nor investigators knew who were assigned active units. The poststimulation exercise test was conducted 20 minutes to one hour after electrical stimulation.

Statistical Methods

A two factor analysis of covariance was used to test the outcomes of the placebo group versus the treatment group. The change in ME from the prestimulation test to the poststimulation test was the dependent variable. The covariate was the initial oxygen uptake. The subjects were grouped by the unit they drew (active or placebo), and stratified by gender to form the two factor design.

Results

Thirty of the 36 subjects who enrolled in the study were included in the analysis. Three subjects were not able to maintain pedaling motion on the ergometer and three voluntarily withdrew from the study. Eighteen subjects drew the active unit, while 12 subjects drew the placebo unit.

Table 1 lists the individual prestimulation and poststimulation mechanical efficiency (ME) values for the active and placebo groups. The mean prestimulation values were nearly identical, being 53.3 for the placebo group and 50.3 for the active group. The mean poststimulation value for the placebo group dropped by -9.1% to 48.4. However, the mean poststimulation value for the treated group increased by 19.1% to a value of 59.9.

Table 2 lists the individual prestimulation and poststimulation workload values for each group. The mean prestimulation value was 75 for the placebo group, with a drop of -5.5% to 70.9 for the poststimulation value. On the other hand, the mean poststimulation value for the active group improved by 43%, increasing from an initial mean value of 65.9 to 94.3.

Figure 2 displays the mean percentage changes in workload and mechanical efficiency for the active and placebo groups. Figure 3 shows the individual responses in mechanical efficiency for each group, and Figure 4 shows the individual responses in workload.

The absolute test value differences (rather than percentage changes) were subjected to a two factor analysis of covariance. Table 3 gives the data for each variable for all subjects in terms of ranges, means, and standard deviations.

The grouping variables were the sex of the subject and the unit that the subject drew. The dependent variable was the change in mechanical efficiency from the exercise pretest to the exercise posttest.

Table 4 gives the cell means and standard deviations for the oxygen uptake ($V\dot{O}_2$) on exercise pretest, and the change in mechanical efficiency from exercise pretest to exercise posttest. The mean change in ME between the exercise pretest and the exercise posttest for males who drew the placebo unit was -2.46, while the exercise posttest for males who drew the active unit was +8.34. The mean change in ME for females who drew the placebo unit was -7.47, whereas the females who drew the active unit registered a mean change of +8.95.

Although there was a small difference between the males and females in ME for the active unit, the direction and magnitude of the change was influenced by unit much more than gender. These observations were confirmed by the F statistic as shown in Table 5. The F statistics for the gender factor and for the gender factor by the unit factor interaction were less than 1.0. That is, test differences due to these factors are not significant ($p=0.4$-0.5). However, the F statistic for the unit factor is 17.43. This statistic is significant at the .0003 level. Therefore, the differences in test results of subjects treated with an active unit compared to subjects treated with a placebo unit are highly statistically significant.

DISCUSSION

These results indicate that noninvasive cranial electrotherapy stimulation does, in fact, improve the work performance of cerebral palsy patients. Workloads of treated patients improved by an average of 43%. This is a remarkable increase, especially when one considers that the placebo retest scores declined by -5.5%. The decline is probably reflective of incomplete muscle recovery from the first test, which is clearly overcome by the treated patients.

There are only two hypotheses that reasonably explain the study findings. Either the electrical stimulation causes a reduction in sympathetic tone, resulting in better perfusion to muscle tissue or there is a direct reduction of tension in the spastic muscle. Reports in the literature indicate that peripheral application of either weak or relatively strong current produces a sympatholytic effect. Such effects have been measured by direct in-situ observations in animals, and indirectly by skin temperature measurements in humans (Lee 1974). However, it is highly unlikely that a vasodilation effect could produce effects of the order of magnitude seen here. In other words one would not expect a group of normal individuals to improve their work performances by 43% under these or any conditions. Nonetheless, it will be useful to test normal subjects to determine an autonomic baseline response.

Of the two alternatives, it would seem that direct reduction of spasticity provides a more mechanistically satisfying explanation of the data. Why weak noninvasive cranial electrotherapy stimulation should produce such an effect is not clear. How much current passes into the brain and precisely where it flows is likewise not well defined at this point. Preliminary data from computer simulated modeling techniques (Vresilovic et.al. 1982) indicates that cerebral tissue experiences approximately 1 microampere of current when 1 milliampere is applied transcranially (Carter and Vresilovic, in press). The thousandfold attennuation being due to the insulating capacity of the skull and cerebrospinal fluid (CSF) (Carter and Vresilovic in press). It is very interesting to note that currents of this magnitude are biologically active in the sense that the activities of membrane

receptor sites and bound ions, such as calcium are modulated within the 1 microampere amplitude window. Some of the earliest work in the field of bioelectromagnetics established that efflux or influx of membrane bound calcium in cat brains could be modulated by specific field parameters (Kaczmarek and Adey 1974). Fluxes in local ion concentrations at synapse sites could potentially modify neural transmission properties to produce an inhibitory effect. That is, the binding kinetics of neurotransmitters to membrane sites may be modulated in a manner promoting an antispasticity response.

Another possibility is that the synthesis or release of an inhibitory neurotransmitter is enhanced by the application of these currents. For instance, it has been demonstrated that extremely weak current induced in cat cerebral tissue result in both a release of calcium ions and an increase in the concentration of GABA (gamma-amino-butyric acid) (Kaczmarek and Adey 1974), the primary inhibitory neurotransmitter (Mountcastle and Sastre 1980). Determinations of GABA concentrations in cerebrospinal fluid before and after stimulation with this system have not been attempted in animals or humans. However, it is a measurement worthy of pursuit. In the immediate future, studies are being designed to define the nature of the autonomic and/or antispasticity response.

Whether weak noninvasive cranial electrotherapy stimulation ultimately finds a place in the management of cerebral palsy will be answered by future studies. Invasive electrical procedures for reduction of spasticity have been beneficial, but not without significant risk. Therefore, it seems mandatory to thoroughly investigate the noninvasive modality described here. If the results of this study can be translated into real clinical gains, then the use of noninvasive cranial electrotherapy stimulation will play a major role in the rehabilitation of the cerebral palsy individual.

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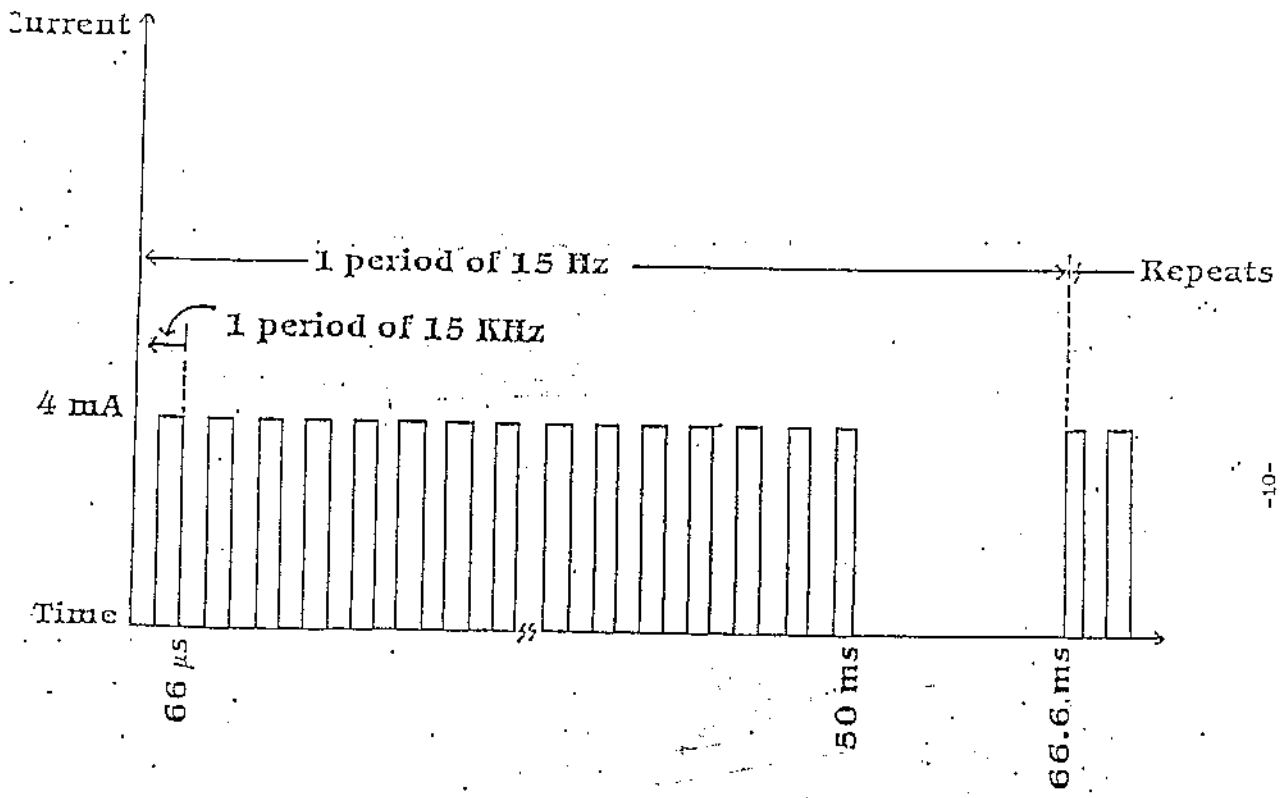

Figure 1. Electric current waveform of the Cranial Electrotherapy Stimulator manufactured by Pain Suppression Labs, Inc. Wayne, New Jersey 07470

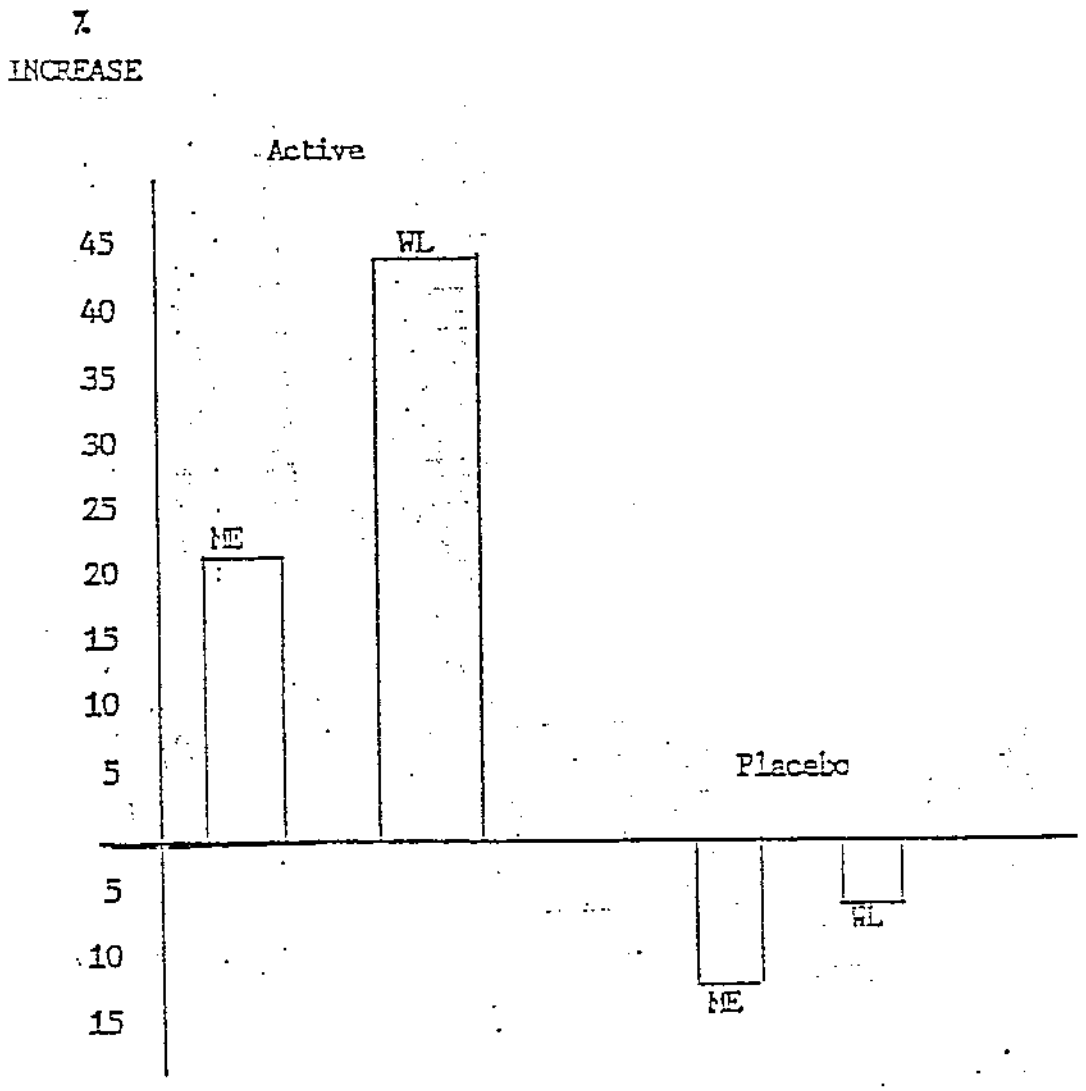

Figure 2. Mean percentage changes in mechanical efficiency and workload for active and placebo groups.

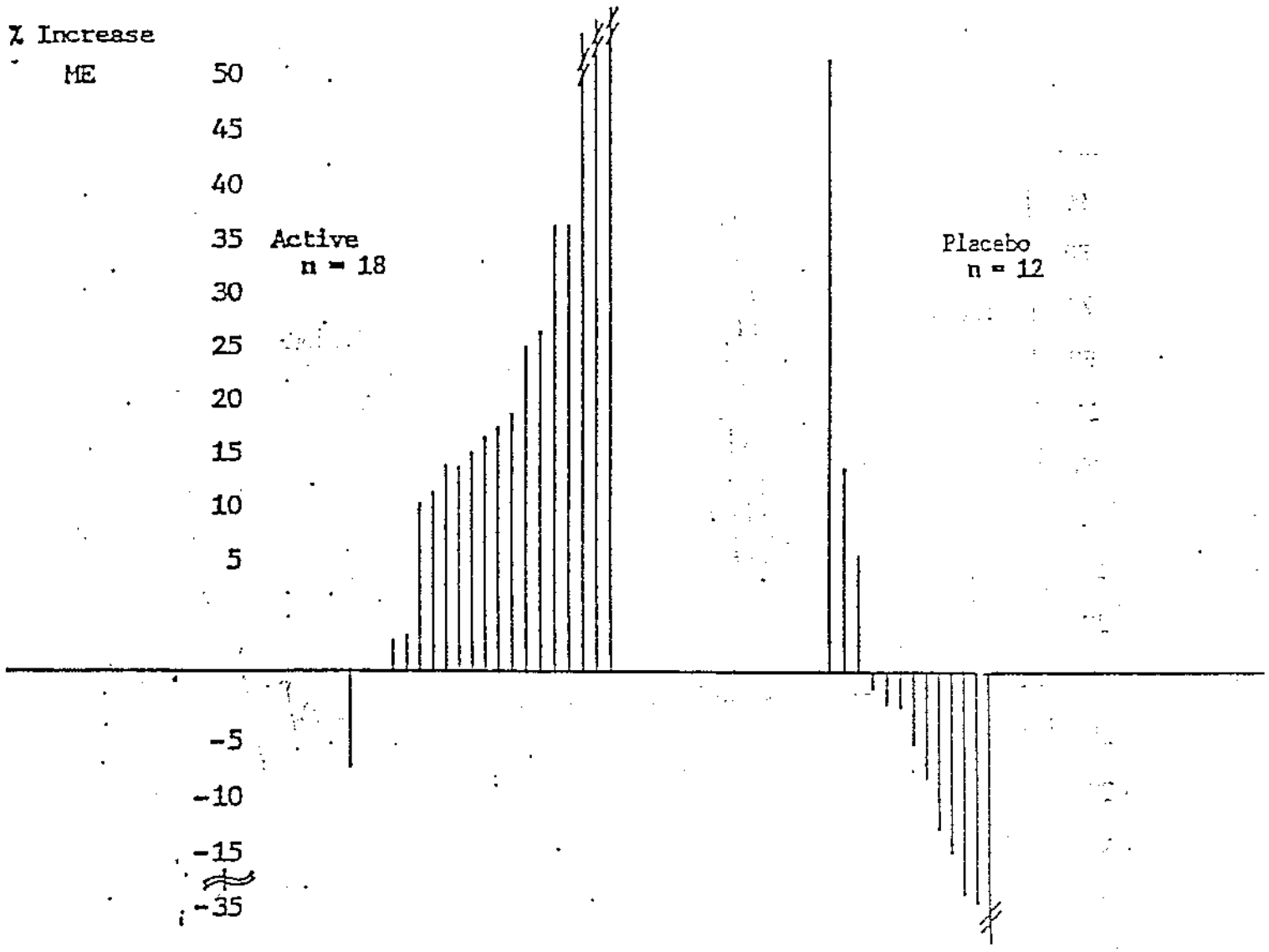

Figure 3. Individual percentage changes in mechanical efficiency for active and placebo groups.

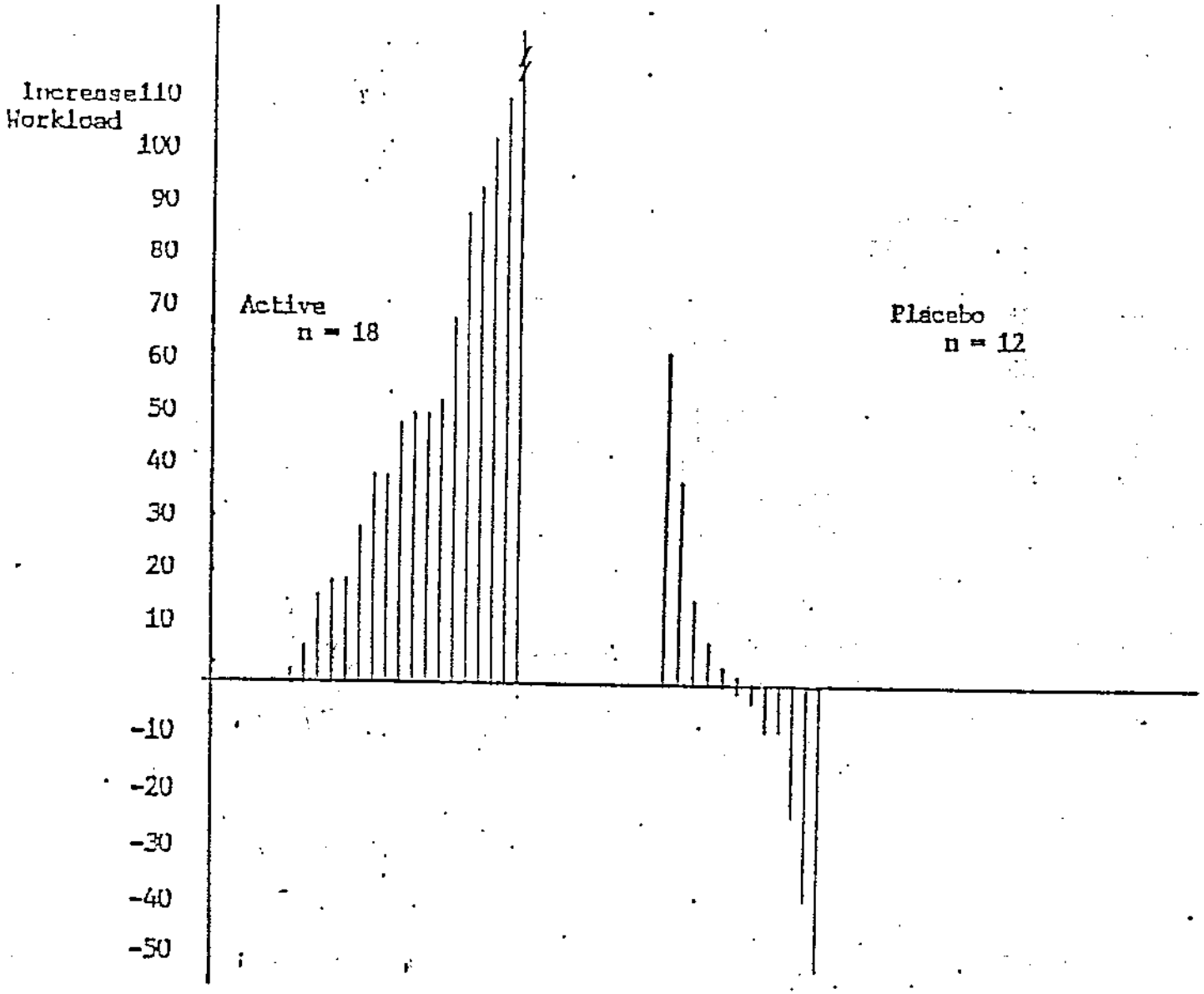

Figure 4. Individual percentage changes in workload for active and placebo groups.

TABLE 1
MECHANICAL EFFICIENCY

Placebo Group				Active Group			
Subject	Before	After	Percent Change	Subject	Before	After	Percent Change
1	28.2	27.2	-3.5	1	60.2	61.3	1.8
2	34.9	23.0	-34.0	2	68.6	79.7	16.2
3	5.2	7.7	+48.1	3	56.7	52.9	-6.7
4	34.8	39.4	+13.2	4	23.5	31.8	35.3
5	75.3	74.6	-0.9	5	31.4	50.3	60.2
6	76.2	80.6	+5.7	6	32.3	52.1	61.3
7	58.5	56.6	-3.2	7	73.7	86.0	16.7
8	64.1	46.0	-28.2	8	45.6	51.0	11.8
9	72.5	54.8	-24.4	9	58.8	59.8	1.7
10	49.2	44.4	-9.7	10	53.2	62.3	17.0
11	69.7	59.3	-14.9	11	44.4	47.3	6.5
12	71.6	67.6	-5.5	12	56.1	60.2	7.3
				13	42.9	52.3	21.9
				14	13.6	32.6	139.7
Means	53.3	48.4	-9.1%	15	68.4	75.9	11.0
				16	52.7	60.5	14.8
				17	46.1	57.4	24.5
				18	77.5	104.7	35.1
				Means	50.3	59.9	+19.1%

TABLE 2
WORKLOAD

Placebo Group				Active Group			
Subject	Before	After	Percent Change	Subject	Before	After	Percent Change
1	51.3	37.7	-26.5	1	52.4	77.9	48.7
2	62.8	37.7	-40.0	2	66.0	73.3	11.1
3	6.0	6.3	+5.0	3	68.0	100.5	47.8
4	18.8	25.6	+36.1	4	16.7	25.1	50.3
5	156.6	150.8	-3.7	5	42.4	58.9	38.9
6	144.0	146.6	+1.8	6	43.9	83.8	90.9
7	94.2	94.2	0.0	7	146.6	197.9	35.0
8	88.5	41.9	-52.7	8	68.0	100.5	47.8
9	66.0	104.7	+58.6	9	104.7	131.0	25.0
10	33.0	37.7	+14.2	10	65.4	75.4	15.3
11	94.2	89.0	-5.5	11	68.0	78.5	15.4
12	83.8	78.5	-6.3	12	125.7	132.5	5.4
				13	33.5	67.0	100.0
				14	25.1	83.8	233.8
				15	58.9	110.0	86.7
Means	75.0	70.9	-5.5%	16	69.1	113.1	63.7
				17	51.8	106.8	106.2
				18	80.6	80.6	0.0
				Means	65.9	94.3	+43%

TABLE 3

MEANS AND STANDARD DEVIATIONS OF THE VARIABLES

Variable	Range	Mean	Standard Deviation
Age	10-35	23.00	07.40
WL	6.00-156.6	39.90	68.30
VO21	0.54-002.2	01.34	00.45
Me 1	5.20-077.5	51.50	19.40
WL 2	6.30-197.9	84.80	42.00
VO22	0.65-002.5	01.51	00.52
Me 2	7.60-099.5	55.10	19.50
Ch Me	-18.10-027.0	03.40	10.60
Rec 1	02.00-008.0	05.10	01.40
Rec 2	02.00-009.0	05.10	01.80

WL = prestimulation workload in watts
VO21 = prestimulation oxygen uptake in liters/minute
Me 1 = prestimulation mechanical efficiency
WL 2 = poststimulation workload in watts
VO22 = poststimulation uptake in liters
Me 2 = poststimulation mechanical efficiency
Ch Me = change in mechanical efficiency
Rec 1 = prestimulation recovery time in minutes
Rec 2 = poststimulation recovery time in minutes

TABLE 4

CELL MEANS AND STANDARD DEVIATIONS

Variable	Placebo Males	Placebo Females	CES Males	CES Females
VO2 X	1.58	1.21	1.58	1.12
VO2 sd	.71	.37	.43	.29
Me X	-2.46	-7.47	8.34	8.95
Me sd	8.29	8.10	7.47	8.85
Adjusted Cell Means Me	-1.96	-7.75	8.86	8.48

VO2 X = the mean oxygen uptake on the exercise pretest

CO2 sd = the standard deviation for the oxygen uptake on the exercise pretest

Me X = the mean change in mechanical eficiency between the exercise pretest and the exercise posttest

Me sd = the standard deviation of the change in mechanical efficiency between the exercise pretest and the exercise posttest

Me = change in mechanical efficiency between the exercise pretest and the exercise posttest

TABLE 5

ANALYSIS OF COVARIANCE

Source	Sum of Squares	df	Mean Square	F	P
Unit	1207.44	1	1207.44	17.43	.0003
Sex	0049.95	1	0049.95	00.72	.40
U x S	0048.11	1	0048.11	00.69	.41
VO_2	0020.05	1	0020.05	00.29	.59
error	0017.31	25	0069.26		

Unit = treatment unit (CES or Placebo)
Sex = male or female
U x S = the unit by sex interaction
VO_2 = the exercise pretest oxygen uptake

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Tarrant/Texas

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An Arlington physiologist is using electricity to treat cerebral palsy. Page 16.

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Cerebral palsy work praised

BY CAROLYN POIROT
Fort Worth Star-Telegram

An Arlington counselor and physiologist is using instantaneous bursts of very low-energy electricity to reduce spasticity and increase flexibility in people with cerebral palsy.

His research is praised by experts because it could make cerebral palsy patients more self-sufficient.

Dr. Michael Logan will be honored tomorrow at the international meeting of the American Academy for Cerebral Palsy and Developmental Medicine in Toronto for his research in neurotransmitter modulators and their application to spasticity reduction.

Logan will be honored for developing an objective technique to measure the affect of stimulating the muscles of cerebral palsy patients.

Cerebral palsy is a type of paralysis caused by a lesion in the brain, which is usually the result of a lack of oxygen at birth. It is characterized by stiffness and spasticity.

The only established treatments for cerebral palsy are surgery to reduce stiffness and drugs to reduce spasticity, both considered much more invasive than electrical stimulation.

Using bicycle pedaling as his test, Logan found that electrical stimulation improved the workloads of such patients.

"There is no question people treated with the working unit (in his double blind study of 30 patients) did 50-percent better than those treated with the placebo unit, and they could continue to do better 24 to 48 hours after electrical stimulation," Logan said.

Sandra Short, executive director of United Cerebral Palsy of Tarrant County, said the research could prove valuable because the treatment is non-invasive and could give people with cerebral palsy greater control over their ability to function.

"If taken a step further, the research could make it possible for patients who currently lie in bed, stiff as boards, to sit up and perhaps even feed themselves," she said.

Fort Worth Star-Telegram/MICKEY TORRES

Dr. Michael Logan and his secretary, Shellee Stack, display equipment used by Logan

Short said there are an estimated 5,000 to 7,000 Tarrant County residents with varying degrees of cerebral palsy, ranging from mild cases to those requiring lifelong institutional care.

Short said the American Academy for Cerebral Palsy and Developmental Medicine is a prestigious organization concerned with research in cerebral palsy and similar neurological disorders.

Logan, who specializes in the treatment and rehabilitation of people with neuromuscular and pain problems, primarily through biofeedback, said he became interested in the project when a manufacturer of TENS (transcutaneous electrical nerve stimulator) units wanted to promote the device for use among cerebral palsy patients.

"I wasn't interested because they lacked proof of its effectiveness," Logan said.

The manufacturer asked him to see if he could come up with a way to objectively measure the treatment's affects, he said.

He did that with a double blind study — neither the researcher nor the subject knowing which treatment was being studied. In the study, treated and untreated subjects pedaled stationary bicycles, and the amount of work they were able to do and their oxygen uptake were measured.

Subjects did 10- to 100-percent better with the electrical treatment than they did without it, according to a device attached to the bicycles to measure the amount of work being done, Logan said.

The treatment uses an electrical current of one-half to one milli volt — one one-thousandth of a volt — pulsating at the rate of 15,000 bursts per second, Logan said. It cannot be felt. The treatment relaxes the muscles, which are fighting each other in patients, and somehow causes neurotransmitters, the chemical messengers between the brain nerves, to function better.