SOMATIC AND BEHAVIORAL CHANGES ASSOCIATED WITH DIFUSE TRANSCRANIAL ELECTRICAL STIMULATION IN ANAESTHETIZED AND UNANAESTHETIZED NORMAL WISTAR RATS.

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ABSTRACT

AIMS: The effects of diffuse transcranial electrical stimulation on somatic and behavioral changes in anaesthetized and unanaesthetized normal male and female Wister rats was studied.

METHOD: Diffuse transcranial electrical stimulation (0-25v, frequency 90Hz,pulse width 1ms) was administered via two electrodes clipped to the ear lobes of the rat.

RESULTS: DTES causes apparent-irritability, apprehension, micturation, and piloerection and increase activity in unanaesthetised wistar rats at voltage below 10v. Tonic-clonic seizures were observed at voltages above 10v.

In anaesthetized normal wistar rats, DTES has no effects on the rats at voltages below 20v. At voltages 20v and above, tonic- clonic seizures were observed.

CONCLUSION: These results suggest that higher voltages are needed to induce seizures in anaesthetized rats than unanaesthetized wistar rats. Some of the response to diffuse transcranial electrical stimulation can be abolished or attenuated by administering anaesthetic.

KEY WORDS: DTES, Hypermotility, Anaesthesia, Urethane, Wistar rats.

INTRODUCTION:

Diffuse transcranial electrical stimulation has been employed as a method of stimulating the whole brain of an animal. It is also been used as form of therapy in the management of affective disturbances (anxiety, depression) in alcoholic patients [1]. It was also suggested that diffuse transcranial electrical stimulation increases sympathetic outflow and arterial blood pressure in anaesthetized wistar rats [2]. Electrical stimulation of the posterior nucleus of the hypothalamus has been reported to cause arousal, emotional stress-like behavior and elevation of blood pressure and heart rate.[3-5]

Changes in the behavioral output of normal animal or man are generally believed to be due to changes resulting from alternations in central neuronal system activity. Alternation in central nervous system activity may lead to changes in the overall activity of the various organs and vessels in the animal.

Ruch and Patton [6] noted that such alternation in central nervous system activity could be influenced by humoral mechanisms, by intrinsic activity or by electrical stimulation of the brain. Electrical stimulation of the brain modifies levels of humoral activity in the brain to bring about some somatic manifestations.

Passage of low DC electric current through various parts of the brain increases the catecholamine levels in the portion of the brain concerned [7]. This in turn may lead to the stimulation of the postsynaptic cell membrane and increase in the activity of the sympathetic out flow to the periphery [3].

The objective of this study is to establish the effect of diffuse transcranial electrical stimulation on normal Wistar rats and on anaesthetized Wistar rats (Using urethane as the anaesthetic).

Materials and Methods: Adult male and female Wister rats (200-250g) inbred in the animal Production Unit of the National Veterinary Research Institute Vom were used. The animals had access to tap water and feed (24% protein: Pfizer Products, Lagos, Nigeria) ad libitum. The rats were housed at 25°-2° C and acclimatized on approximately 12 hours light and 12 hours dark cycle in the animal house. They were randomly selected from colony of Male and Female rats.

Diffused transcranial electrical stimulation was effected via steel electrodes clipped on the left and right ear lobe of the rat. Electrical stimulation (0-25v, frequency 90Hz, pulse width 1 ms) was delivered for duration of 10 seconds or 20 seconds depending on the experimental design using a CFP stimulator model 8048 (C. F. Palmer, London, UK.). The animal's body temperature was maintained at 37°C on a small operating table for studies under anaesthesia.

For studies under anaesthesia, the rats were anaesthetized using urethane (BDN Chemicals, Dagenham, UK), 125/100g, and injected interperitonially. The depth of anaesthesia was assessed by the loss of righting or corneal reflex. For awake studies rats were isolated and placed in the stimulating chamber (individually). Diffuse transcranial electrical stimulation or activity measurement were carried out. Conscious Wistar rats were also visually observed to determine somatic and behavioral changes. The somatic and behavioral changes observed were noted and recorded.

RESULTS: Preliminary experiments were carried out to determine the suitable voltage for brain stimulation. We found that between 5v to 25v produced reproducible actions and activity on the rats. 5v, 10v, 15v and 20v were then chosen for these experiments.

Effects of DTES (0v, 5v, 10v, 15v, and 20v) on unanaesthetized wistar rats.

The rats in the control group were calm, and have normal activity. Table 1 shows some of the somatic and behavioral changes associated with diffuse transcranial electrical stimulation in conscious rats. DTES induces apparent irritability in conscious rats at sub-convulsive voltages (fig. 1) and tonic-clonic convulsion at voltages (fig 2, table 1).

Figure 1; Sub-convulsive (5-10v) diffuse transcranial electrical stimulation causes apparent irritability, hyper-motility and apprehension in conscious wistar rats

Voltage	Number of rats	Convulsion (%)	Other changes
Control	10	0	Calm, Normal activity.
5v.	10	0	Apparent irritability, apprehension, micturation, increased breathing, piloerection.
10v.	10	0	Apparent irritability, apprehension, micturation, increased breathing, piloerection.
15v	10	100	Transient loss of consciousness, Micturation, Increased breathing, Piloerection, tonic-clonic seizures.
20v	10	100	Transient loss of consciousness, Micturation, Increased breathing, Piloerection, tonic-clonic seizures.

Table 1; Some somatic and behavioral changes produced by graded voltages of diffuse transcranial electrical stimulation in conscious rats.

Figure 2 Convulsive (15-25v) diffuse transcranial electrical stimulation causes transient loss of consciousness and tonic- clonic seizure in Wister rats.

1. Effects of diffused transcranial electrical stimulation on the activity of unanaesthetized wistar rats.

The activity of the animal was observed to have generally increased.

Table 2 below show that higher voltage is needed to induce tonic- clonic seizures in anaesthetized rat than in unanaesthetized rats.

Table 2; Effects of diffused transcranial electrical stimulation on anaesthetized rats.

Voltage	No of rats	% Convulsion	Other Changes
0	6	0	
5	6	0	
10	6	0	
15	6	0	
20	6	100	
25	6	100	

DISCUSSION:

From the results above, diffuse transcranoal stimulation causes apparent irritability, apprehension, piloerection, micturation and increase locomotor activity in unanaethtized Wister rats. The increase in activity observed may have been due to an increase in the turn over of catecholamines in the brain.[7]. There by leading to an increase in the sympathetic outflow to the periphery. The increased brain catecholamine turnover may explain the somatic manifestations observed during sub-convulsive diffuse transcranial electrical stimulation. During sub-convulsive diffuse transcranial electrical stimulation, the low voltage currents delivered to the brain via the ear clips may radiate (spread) to various centers of the brain (e.g. *posterior hypothalamic regions, Locus coeruleus*). This spread of low voltage currents across the brain may lead an increase in the turnover of catecholamine in some regions of the brain. The somatic manifestations observed mimic what is seen in animals and man under stress.

At higher voltages, conscious wistar rats go into tonic-clonic convulsion. This convulsion may have resulted from the over-activation of some brain centers especially the motor area of the cortex. Stimulation at convulsive voltages causes massive release of catecholamines from adrenergic neurons in various centers of the brain [11]. In this study, it was observed that DTES induces generalized increased activity) in the experimental animal. The increased in activity observed may be as a result of the increase in the sympathetic outflow to the periphery.

The mechanism by which diffuse transcranial electrical stimulation induces hypermotility in the animal may be the same the mechanism involved in the increase in arterial blood pressure which is thought to result from increase sympathetic vasomotor activity and adrenomedulary catecholamines[12, 13,14]. Von Eiff and Piekarski[15] have postulated that stimuli creating defense and attach behavior, rises the blood pressure and muscle tone in animal acts on the ``dynamogenic zone" of the hypothalamus. It may therefore be conceived that diffuse transcranial electrical stimulation might result in the spread of electric current to the hypothalamus and the posterior nucleus to cause the somatic, behavioral effects and the hypermotility observed during DTES. The precise area of the brain activated during DTES to produce hypermotility cannot be ascertained from our studies.

The involvement of gamma amino butyric acid (GABA) in the mechanism of action of electrical stimulation has been reported, [16] during electrical stimulation of the brain, there is inhibition of the release of GABA near the adrenergic neurons thereby leading to an increase in the brain turnover of catecholmine[17]. Reduction in GABA- brain levels leads to over activity of the neurons (adrenrgic neuroses) it synapses with thereby increasing the sympathetic outflow to the periphery. This may account for the increased activity and somatic behavioral changes observed in rats treated with diffuse transcranial electrical stimulation.

The involvement of dopamine in the induction of Hypermotility by Morphine has also been reported[18]. It is not possible to categorically say dopamine is involved in DTES induced hypermotility, but its involvement cannot be ruled out.

In most studies, animals are anaesthetized before DTES is delivered [2]. The result obtained shows that the anesthetics administered may affect the results of such experiments, as it will not give the true picture of the happenings in the animal. The results above show that anesthetic influence the result obtained when an animal is anaesthetized before DTES is administered.

REFERENCES;

1. Kruptsky, E.M., Burakov, A.M. Karandashova, G.F., Katsnelson,J.S, Lebedev, V.P.,Grinenko,A.J.,and Borodkin,J.S. (1991). Drug and alcohol Dependence, 27, 1-6, Elsevier Scientific Publishers, Ireland Ltd.
2. Osunkwo U. A. Ihezue C.H. Onuminya J. E.and Ogunranti J.O.(1994). Med.Sci.Res, 22, 107- 109.
3. Scherrer, H.F and Friedman, S.M 1958. Acta Endocrinol, 27, 89-98.
4. Bunag, R.D., Eferakeya, A.E. and Langdon, D.S. 1975. Am. J. Physiol., 228, 217-222.
5. Bunag, R.D. and Eferakeya, A.E. 1976, Cardiovasc. Res., 10, 363-371
6. Ruch T.C. and Patton H.D. (1966). Science, 191,310.
7. Hollister, L.E.(1971),Antidepresant drugs: in Drill`s Pharmacology in Medicine. Edn. J.R.Dipama. 4th edn. McGraw-Hill Book Company New York pp 499-513.
8. Longoni, R., Spina, L.and Di Chiara, G. (1987). PsychoPharmacology,93: 401-402.

9. Maurel-Reny, Audinot, V., Lejeune, F. Bervoets, R. and Milllan M.J. 1995): Br. J. Pharmacology. Suppl.
10. Snedecor, G.W, and Cochran, W.G. 1967, Statistical Methods, 6th edn. Ames Iowa State University Press, pp. 432.
11. Welch, B.L. and Welch A.S. (1970): In : Amphetamines and related compounds (eds. Costa ,E and Garattini, S), pp. 415-445, Reven Press, New York.
12. Morpugo, C. 1968 Br. J, Pharmaco., 34, 534-542
13. Morpugo C, and Morillo,A. 1962. Life Sci., 1, 263-269.
14. Hacualer, G. 1975. Circ. Res, 36 and 37 (Suppl. 1 0, 223-232
15. Von Eiff A. W. and Piekarski, C 1977. In: de Jong,W., Shapiro.A.P. and Provost, A P. (eds.) Hypertension and brain Mechanism,pp 289-300. Elsevier Scientific Publishing Co. Inc., new York.
16. Green, A,R., Minchin, M.C.W. and Vincent, N. D.(1987); Br. J. Pharmacol. 92(1): 13-18.
17. Rand H.P. and Dale M.M> (1994). In: Pharmacology by Churchill Livingstone Medical Division of Longman Group UK Ltd. 2nd edn. pp 684-696.
18. Carroll B.J, Sharp P (1972). Br. J. Pharmacol. 46, 124-139.