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CHRONIC EXERCISE ALTERS EEG POWER SPECTRA IN AN ANIMAL MODEL OF DEPRESSION

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Abstract : The EEG from frontal cortex, EMG and EOG were recorded from rats exposed to only exercise (Treadmill), only stress, exercise + stress and neither (control). In comparison with the control group, the percent of Delta activity in the awake was significantly increased in the depressed group and significantly decreased in the exercised groups, while for Beta-2, the reverse occurred; Theta increased and Beta-2 decreased in the NREM sleep state of the depressed group and the opposite happened for the exercised groups; Delta and Alpha-2 activity significantly increased in the depressed group, and they were significantly decreased in the exercised groups whereas the Beta-2 activity showed contrary changes in the REM sleep state. These findings indicate that exercise has the opposite effect from what stress has on qEEG and concomitant physical exercise reduces the effects of stress. Behavioral tests were done by Open Field (OF) and High Plus Maze (HPM). Slow EEG activity (Delta, Theta, Alpha) was significantly positively correlated with immobilization in the OF and defecation in both OF and HPM and negatively with the food intake, transfer latency in HPM; rearing, grooming and total ambulation in OF. Whereas, fast activity (Beta-2) was significantly negatively correlated with immobilization in OF and defecation in OF and HPM, while positively with ambulation in the central squares of OF and time spent at the central cross and number of times arms crossed in the HPM.

Key words : animal model of depression (rats)
(chronic) exercise EEG power spectra
open field high plus-maze

INTRODUCTION

Depression is one of the common underdiagnosed diseases in clinical psychiatry. EEG, in its present applied form, does not assist much diagnostically or prognostically in determining the extent of depression. Instead of analyzing only the frequency and amplitude changes, obtaining power spectra by fast Fourier transform (FFT) of EEG signals conveys more information (1). Computerization has led to more sophisticated use of EEG, even in affective disorders, where, perceptual processes are significantly distorted (2). However, no systematic study is available on the EEG power spectra changes, in the various sleep and wake

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stages, in the same subject - human or animal - in depression along with exercise.

Several valid animal models of depression, which mimic most of the somatic symptoms of clinical depression, have been developed (3-5). These symptoms are alleviated by chronic antidepressant therapy and electro-convulsive therapy. In depression, there are changes in the patterns of sleep. The two varieties of sleep - REM (Rapid eye movement) sleep and SWS (Slow wave sleep, non-rapid eye movement or NREM sleep) can be differentiated by simultaneous recording of EEG, EMG (electromyogram) and EOG (electro-oculogram) (6). In many species of animals, sleep is related with adjusting and reorganizing emotional behaviors (7). So, in depression, where emotional behaviors vary, sleep changes occur, e.g., short REM latency, increased REM frequency, and an early temporal distribution of REM sleep are noted (8). The differences between the percentage of each frequency band in the EEG power spectra during REM sleep in depressed rats have been successfully identified by an artificial neural network (9).

Regularly performed physical exercise helps in coping with environmental stress (10-13). Therefore, exercise is now being recognized as an important antidepressant measure in stress related mental disorders. In an animal model of depression, chronic swimming has demonstrated antidepressant effect (14).

This study was designed to investigate the specific frontal cortical EEG changes in depression and to find whether exercise training reverses them. Simultaneous EMG and EOG were recorded from all the rats. The REM and NREM sleep and awake states' recordings were analyzed by FFT. Behavioral tests were also compared in the test group with the control groups.

METHODS

Subjects and surgery : Thirtysix male Charles-Foster rats, 12-14 weeks of age, 200-300 gm in weight, were individually housed in polypropylene cages (30 cm x 20 cm x 15 cm) with drinking water and food *adlib* normally. The animal room was artificially illuminated with a 12:12 hours light:dark cycle changed at 08.00 hrs and 20.00 hrs. Ambient room temperature was maintained at 23 ± 1^{0}C. Electrodes were implanted, aseptically, on the rats under Pentobarbital (Loba Chemie, India) @ 35 mg/kg, ip anaesthesia. For grounding, midline Frontal stainless steel screw electrode of 1 mm diameter was used. Two other screw electrodes, 2 mm posterior to and 4 mm lateral to the Bregma were used for bilateral frontal cortical EEG. Stainless steel loop electrodes, insulated except at the tip (2 for EOG from bilateral outer canthus muscles and 2 for EMG from bilateral cervical muscles) were implanted. Their socket contacts had earlier been soldered to a 9-pin connector and the whole array was fixed to the skull bone with dental acrylic. Following up, a minimum of 1 week was allowed for handling and adapting to the recording chamber.

Experimental design and recording procedure: The rats were divided into four groups:

(i) A group of rats (n=11) was trained to exercise for 6 weeks and was subjected to chronic stress along with the scheduled exercise from the 7th week, for 2 weeks (ES group).

(ii) A group (n=5) had only exercise for 8 weeks (EO group).

(iii) A group (n=15) had only stress for 2 weeks (D group).

(iv) The handled and operated control group (n=5) had neither exercise nor stress (C group).

Depression model : The widely used Katz (15, 16) model was modified. The test group was subjected to chronic stress in accordance with the following schedule given in Table I, one stressor per day, for two weeks. The stressors were applied at some unpredictable time between 8.00 hrs and 12.00 hrs daily, to avoid habituation.

TABLE I : Chronic intermittent stress schedule for producing depression.

Day	*Stressor*
1.	Crowding for 24 hr
2.	Electric shock of 0.75 mA for 15 sec per min for 30 min
3.	Tail pinch by rubber damped forceps 1 cm away from the base for 1 min
4.	Water deprivation for 24 hr
5.	Heat at 40°C for 5 min
6.	Day/Night Reversal
7.	Cold swim at 4°C for 5 min
8.	Electrode Implantation
9.	Noise at 100 dB for 5 min
10.	Heat at 40°C for 5 min
11.	Electric shock of 0.75 mA for 15 sec per min for 30 min
12.	Tail pinch by rubber damped forceps 1 cm away from the base for 1 min
13.	Food deprivation for 24 hr
14.	Noise at 100 dB for 5 min
15.	Recording

Exercise regime : The rats were trained to run on a programmable Treadmill (Uni-Insta, India), gradually increasing the speed to a maximum of 1.2 km/hr i.e., 20 m/min at 0^0 inclination. The maximum duration was of 60 min per day (between 17.00 hrs and 20.00 hrs), for 6 days a week, for 8 weeks. The training was done by applying footshock at low intensity of 5 mA to avoid unnecessary trauma. Four rats could run simultaneously in lanes of 15 cm x 50 cm (17).

Other parameters : The bodyweight and food intake were measured every week. For statistical analysis, 2 dates were chosen :

(i) Zero week (EO/SO).

(ii) At end of the 8th week exercise (E8) or with two weeks of stress (S2) or both or neither (E8/S2) for respectively the EO, D, ES and the C groups.

After the recording, the animals were sacrificed by an overdose of Urethane ip and the post-mortem wet weights of the whole brain, heart and gastrocnemius muscle were noted as also the presence of any gastric ulcer. During the autopsy, the extent of brain damage, if any, by the implanted electrodes were also studied. The dissectors were blind to the experimental conditions.

The test chamber (35 cm x 25 cm x 30 cm) was constructed entirely of Plexiglas and was located in a constantly illuminated (500-600 Lux white light), sound insulated and electrically shielded chamber (300 cm x 180 cm x 240 cm).

The sleep recordings were done from 8.00 hrs to 17.00 hrs, on the 8th day post-operative. Cortical EEG, EMG, EOG were recorded through an 8-channel polygraph (Medicare, India). All recordings were done on paper @ 2 mm/sec with the parameters given in Table II. The polygraph was also connected through a 12-bit ADC (Micronics, India) and recording was done with it at a sampling frequency of 256 Hz and was stored in the hard-disk of a PC-AT (HCL, India). The digitized data was filtered by a fourth order, cascaded, Butterworth, infinite impulse response (IIR) type digital filter (18). The FFT of these were performed by a program, in Turbo (19), developed by the authors.

EEG analysis : Power in each of the 7 bands (Delta : 1-3.75 Hz, Theta : 4-7.75 Hz, Alpha-1:8-9. 75 Hz, Alpha-2:10-12.75 Hz, Beta-1 : 13-16.75 Hz, Beta-2 : 17-24.75 Hz and Beta-3 : 25-30 Hz)

TABLE II : Parameters for recording the EEG, EMG and EOG.

	Sensitivity in Microvolts/cm	*Low Freq. Cutoff-Hz*	*High Freq. Cutoff-Hz*	*Time Const. (sec)*	*50 Hz Filter*
EEG	100	1	75	0.10	In
EMG	50	3	75	0.04	Out
EOG	200	0.3	35	0.24	In

was expressed as a percent of the total power of all the bands in the epoch. Data from three successive 4 sec artifact-free epochs was averaged. Spectral power from 1-30 Hz was determined at 0.25 Hz increments. The criteria for sleep-wakefulness stages are given in Table III.

Behavioral activity monitoring : It was done between 8.00 and 9.00 hrs.

(a) *Open Field (OF) :* The field was a circular arena (20), with the outer diameter being 84 cm. Peripherally there were 16 squares. The inner concentric circle of 56 cm diameter, contained 8 squares. A 100W frosted bulb was placed 1 m above the field, in an otherwise dark room during the activity testing. The rat was initially placed at the center of the field. Each rat was tested for 3 min each time. Ambulation was counted when all the four limbs were placed in one square. Total period of immobilization, number of rearing (standing on the hindlimbs), grooming and fecal pellets were also measured. The unbiased observer watched through reflecting mirrors.

(b) *Elevated Plus-Maze (HPM) :* The maze (21) had 2 open arms (50 cm x 10 cm) and at right angles to it, 2 closed arms (50 cm x 10 cm x 40 cm), with, the roof uncovered; an open central crossing (10 cm x 10 cm) and was raising to a height of 50 cm. The Transfer Latency (TL) was the time taken to enter (all 4 limbs) in a closed arm, from the start when the rat was placed at the outer end of an open arm. The percentage of time spent in the open arms and in the central cross were measured as also the number of times the rat crossed the arms in 5 min.

Statistical analysis : All the analyses were done by computer programs written by the authors. They were tested with textbook examples and standard packages for checking the efficacy. ANOVA was performed to compare the various parameters followed by posthoc comparison with 2-tailed Student's t-test. Pearson r correlations were calculated for finding out the relation between the various EEG frequencies and the behavioral activities.

RESULTS

The results are presented under separate sub-headings for better understanding.

Post-mortem weight of organs : Macroscopic gastric ulcers (pinpoint to hemorrhagic) were present in all the rats of the depressed group but not in the other groups. No brain damage was found due to electrode implantation in any rat. Exercise significantly increased the relative weights of the brain ($F_{3,32}$=18.91, P<<0.001), the heart ($F_{3,32}$=27.86, P<<0.001) and the gastrocnemius muscle ($F_{3,32}$=228.59, P<<0.001).

Body weight and food intake : To compare properly, for the C and D groups, the SO body weight was measured twice with a gap of 6 weeks in between and only handling was done in that period. At EO/SO, ($F_{3,32}$=1.37) no

TABLE III : Criteria for the staging of sleep/wakefulness.

Stage	*EEG*	*EMG*	*EOG*
SWS (Slow Wave Sleep)	About 50% synchronized, Amplitude 50 - 300 μV Frequency 6- 24 Hz.	Muscle tone less than in awake	No movements
REM (Rapid Eye Movement Sleep)	Desynchronized waves Amplitude >40 μV	No muscle tone	Frequent monophasic eye movements
Awake	Synchronization < 25% Amplitude about 30 μV Frequency 30 - 40 Hz.	Movement artifacts	Frequent irregular eye movements

significant difference was there as they were well matched controls. At SO after 6 weeks i.e., E6, ($F_{3,32}$=19.017), P << 0.001) there were very significant differences ($F_{3,32}$=15.0626, P << 0.001). Two weeks after continuing the respective schedules (E8/S2), there was again a significant difference ($F_{3,32}$=14.172, P<<0.001). The maximum increase in body weight was in the sedentary control animals. The EO group had the least weight gain.

Similar tests were performed for the food intake also. One way ANOVA showed no significant difference at EO/SO, ($F_{3,32}$=2.14). At S2/E8 week, ($F_{3,32}$=46.2769, P<<0.001) the exercised groups had a significantly increased appetite. The D group had a reduced appetite, which was not, however, significantly different from the controls.

Behavioral tests : Behavioral changes are summarized in Table IV.

(a) Open field : For immobilization in the OF, one way ANOVA at EO/SO, ($F_{3,32}$=4.8754, P<0.01) was significantly different due to individual variations. The same was significantly different at S2/F8 week ($F_{3,32}$=32.0111, P<<0.001). In the D group it was significantly increased from the control, whereas in the exercise groups, it was significantly decreased from the D group but similar to the control.

For the rearing activity one way ANOVA at EO/SO week, ($F_{3,32}$=1.8528) was not significant, but it showed significant difference at S2/E8 week ($F_{3,32}$=22.88, P<<0.001). In the D group it was significantly decreased and in the ES group was significantly increased compared to the control groups.

For the grooming activity, at EO/SO week, ($F_{3,32}$=2.6836) there was negligible difference between the 4 groups. At S2/E8 week ($F_{3,32}$=3.17, P<0.05) there were significant differences, as it was greatly reduced in the EO group.

For the fecal pellet count in OF, one way ANOVA at EO/SO week ($F_{3,32}$=0.34) showed no significant difference between the groups. At

TABLES IV : (a) - (d) Behavioral activity in the 4 groups: control (at zero week, 8th week after that without any stress or exercise), depressed (at zero week, and after 2 weeks of stress), exercise (at zero week, and after 8 weeks of exercise) and exercise+stress (at zero week, and after 8 weeks of exercise + 2 weeks of stress).

TABLE IV (a) : Control (n=5).

	S_O		S_{O+2}	
Open Field :				
Immobilization	12	(1.22)	16.6	(1.36)
Rearing	13	(2.81)	10.6	(2.62)
Grooming	7.8	(2.03)	6.8	(0.8)
Squares - Periph.	58.8	(6.11)	51	(7.86)
Central	10.2	(2.4)	5.2	(0.86)
Total	69	(8.19)	56.2	(7.41)
Fecal pellets	2	(1.22)	0	(0)
High Plus-Maze :				
Transfer Latency	42.8	(7.37)	49.4	(5.3)
% Time (Open Arm)	30.4	(17.78)	32.4	(17.18)
% Time (Center)	4	(1.7)	4.6	(2.03)
No. Arms Crossed	2.4	(1.16)	2	(0.55)
Fecal pellets	1.2	(0.73)	0	(0)

TABLE IV (b) : Depressed (n=15)

	S_O		S_{O+2}	
Open Field :				
Immobilization	17.33	(0.67)	25.4	(0.7)
Rearing	12.6	(0.48)	5.87	(0.69)
Grooming	4.6	(0.64)	5.27	(0.74)
Squares - Periph.	70.6	(2.34)	48.13	(2.67)
Central	8.93	(0.55)	5.13	(0.74)
Total	79.2	(2.51)	53.27	(2.68)
Fecal pellets	1.47	(0.52)	3.47	(0.52)
High Plus-Maze :				
Transfer Latency	57.73	(9.18)	22.26	(3.23)
% Time (Open Arm)	29.6	(3.13)	11.33	(1.11)
% Time (Center)	5.6	(0.55)	2.67	(0.5)
No. Arms Crossed	6.13	(0.6)	3.2	(0.42)
Fecal pellets	0.93	(0.37)	3.53	(0.52)

TABLE IV (c) : Exercise only (n=15).

	E_0S_0	E_8S_2
Open Field :		
Immobilization	19 (2.45)	17 (2.55)
Rearing	15.8 (1.93)	13.4 (2.25)
Grooming	4.8 (2.13)	2.6 (0.24)
Squares - Periph.	56.8 (9.1)	53.6 (11.31)
Central	9.6 (2.25)	14.6 (4.15)
Total	66.4 (9.97)	68.2 (15.38)
Fecal pellets	2 (0.84)	0 (0)
High Plus-Maze :		
Transfer Latency	26.8 (4.14)	29.6 (7.08)
% Time (Open Arm)	34.2 (16.49)	27.2 (2.99)
% Time (Center)	5.2 (1.66)	5.4 (2.1)
No. Arms crossed	5.8 (1.68)	4.2 (1.06)
Fecal pellets	1 (1)	0 (0)

TABLE IV (d) : Exercise+Stress (n=11).

	E_0S_0	E_8S_2
Open Field :		
Immobilization	15.45 (0.91)	12.73 (0.93)
Rearing	15.45 (1.47)	21.45 (1.88)
Grooming	2.03 (0.62)	6.18 (0.74)
Squares - Periph.	60.18 (5.83)	50.18 (5.75)
Central	6.91 (0.67)	16.1 (1.4)
Total	67.09 (5.65)	67.18 (5.87)
Fecal pellets	1.1 (0.58)	0 (0)
High Plus-Maze :		
Transfer Latency	83.36 (21.2)	52.45 (8.15)
% Time (Open Arm)	33.55 (4.13)	42 (8.39)
% Time (Center)	5.18 (0.57)	4.64 (1.23)
No. Arms Crossed	6.82 (0.63)	6.55 (0.56)
Fecal Pellets	0.09 (0.09)	0 (0)

S2/E8 week ($F_{3,32}$=20.1255, P<<0.001) it showed highly significant difference because the C and the exercised groups did not defecate due to habituation, whereas the D rats defecated during those anxiety periods.

For ambulation in the central squares of OF, by one way ANOVA, at EO/SO week ($F_{3,32}$=1.65) no significant difference was found. However, at S2/E8 week ($F_{3,32}$=15.18, P<<0.001) there was a highly significant difference as there was more ambulation in the central squares by the exercised groups compared to the C and the D groups, which had no significant difference between them. For the peripheral and total number of squares, the groups showed no significant difference.

(b) *High Plus-maze :* The Transfer Latency (TL), by one way ANOVA at EO/SO week, showed no significant difference ($F_{3,32}$=2.027). At the S2/E8 week ($F_{3,32}$=6.6518, P<0.01) ANOVA showed significant difference due to the less time taken by the D rats to enter the closed arm, compared to the control. The time taken by the ES group was not very different from the control but the EO group did show low TL. However, once entering a closed arm, they immediately left it and started exploring the open arms again.

For the % time spent in the open arm, one way ANOVA for S2/E8 ($F_{3,32}$=4.73, P<0.01) showed significant difference between the groups as it was significantly higher in the E groups compared to the D group. However, for the % time in the central cross, ANOVA showed no significant difference.

For the number of arm crossings, one way ANOVA for SO ($F_{3,32}$=3.72, P<0.05) and for S2/E8 week ($F_{3,32}$=10.64, P<<0.001) were significant with the highest number of arm crossings being in the E groups.

The fecal pellet count in the HPM showed significant difference only at S2/E8 week ($F_{3,32}$=20.91, P<<0.001) the differences were due to defecation, induced by stress, only in the D group.

EEG analysis : Sleep-Wakefulness changes - Table V shows the relative percentages of REM sleep, NREM sleep and awake states. The REM state was significantly ($F_{3,32}$=99.62, P<<0.001) increased in the D group and decreased in the exercised groups. The SWS was also significantly ($F_{3,32}$=5.15, P<<0.01) increased by exercise and reduced in the depression model. However, the percentage of wakefulness did not vary significantly.

TABLE V : Percentage distribution of REM, NREM and awake states in all the groups. (Mean±S.E.) P<0.01=**, P<0.001=***

	REM*** ($F_{3,32}$=99.62)	NREM** $F_{3,32}$=5.1537)	Awake
Control (n=5)	12.52(0.19)	63.54(2.2)	23.94(2.27)
Depressed (n=15)	15.93(0.21)	61.17(0.48)	22.89(0.48)
Exercise Only (n=5)	11.97(0.07)	64.76(0.69)	23.27(0.64)
Exercise+stress (n=11)	12.12(0.14)	64.07(0.28)	23.81(0.28)

REM latency - One way ANOVA showed that the onset of the first REM epoch from the beginning of the sleep recording was significantly different ($F_{3,32}$=26.82, P<<0.001). In the C group, it was 204±52.31 sec, in the D group 31.73±5.49 sec, in the EO group 3042±674.81 sec. and in the ES group, it was 2325.46±346.74 sec. In the D group it was significantly increased from the control, in the exercised groups, it was significantly decreased from C.

FFT changes - The F_C EEG changes in each sleep-wakefulness stage during the recording period are shown in Table VI.

(a) Awake changes : The percent of Delta ($F_{3,32}$=6.1136, P<0.01) activity was significantly increased in the D group and significantly decreased in the exercised groups while for Beta-2 ($F_{3,32}$=8.6184, P<0.001), the reverse occurred, all in comparison with the C group.

(b) NREM sleep changes : Theta increased ($F_{3,32}$=3.33, P<0.05) and Beta-2 decreased ($F_{3,32}$=4.3534, P<0.01) in the NREM sleep state of the D group and the opposite happened for

TABLE VI : Percentage of power in each frequency band in all the groups (Mean ± S.E.) REM Delta ($F_{3,32}$=5.2249, P<0.01); REM Alpha-2 ($F_{3,32}$=7.7716, P<0.001); REM Beta-2 ($F_{3,32}$=5.7685, P<0.01); SWS Theta ($F_{3,32}$=3.3269, P<0.05); SWS Beta-2 ($F_{3,32}$=4.3534, P<0.01); Awake Beta-2 ($F_{3,32}$=8.6184, P<0.001); Awake Delta ($F_{3,32}$=6.11360 P<0.01).

	Delta	*Theta*	*Alpha-1*	*Alpha-2*	*Beta-1*	*Beta-2*	*Beta-3*
Control (n=5)							
REM :	10.03 (0.1)	14.05 (0.1)	6.81 (0.11)	10.32 (0.05)	13.64 (0.04)	26.89 (0.19)	18.17 (0.14)
SWS :	9.79 (0.11)	13.36 (0.36)	6.86 (0.07)	10.23 (0.08)	13.63 (0.09)	26.47 (0.27)	19.64 (0.47)
Awake :	10.02 (0.09)	13.36 (0.02)	6.8 (0.2)	9.92 (0.11)	13.66 (0.01)	27.05 (0.26)	19.19 (0.47)
Depressed (n=15)							
REM :	10.26 (0.09)	13.65 (0.05)	6.93 (0.04)	10.56 (0.1)	13.61 (0.07)	26.47 (0.13)	18.56 (0.16)
SWS :	10.03 (0.13)	13.82 (0.09)	6.79 (0.05)	10.08 (0.13)	13.55 (0.13)	26.89 (0.13)	19.71 (0.3)
Awake :	10.51 (0.08)	13.77 (0.16)	6.88 (0.07)	10.04 (0.16)	13.7 (0.1)	25.86 (0.16)	19.23 (0.24)
Exercise Only (n=15)							
REM :	9.6 (0.25)	13.51 (0.27)	6.83 (0.13)	9.741 (0.11)	13.671 (0.14)	27.15 (0.2)	19.35 (0.43)
SWS :	10.05 (0.17)	13.56 (0.11)	6.68 (0.28)	10.3 (0.2)	13.44 (0.15)	27.15 (0.26)	19.1 (0.39)
Awake :	9.65 (0.16)	13.22 (0.08)	6.9 (0.08)	10.31 (0.16)	13.74(0.09)	26.77(0.04)	19.31(0.27)
Exercise+Stress (n=11)							
REM :	9.98 (0.06)	13.79 (0.09)	6.73 (0.07)	10.36 (0.08)	13.59 (0.07)	26.35 (0.09)	19.03 (0.23)
SWS :	9.89 (0.18)	13.25 (0.15)	6.75 (0.08)	10.15 (0.15)	13.45 (0.11)	26.89 (0.29)	19.59 (0.31)
Awake :	10.07 (0.18)	13.95 (0.15)	6.86 (0.12)	10.24 (0.02)	13.63 (0.1)	26.27 (0.14)	19.07 (0.34)

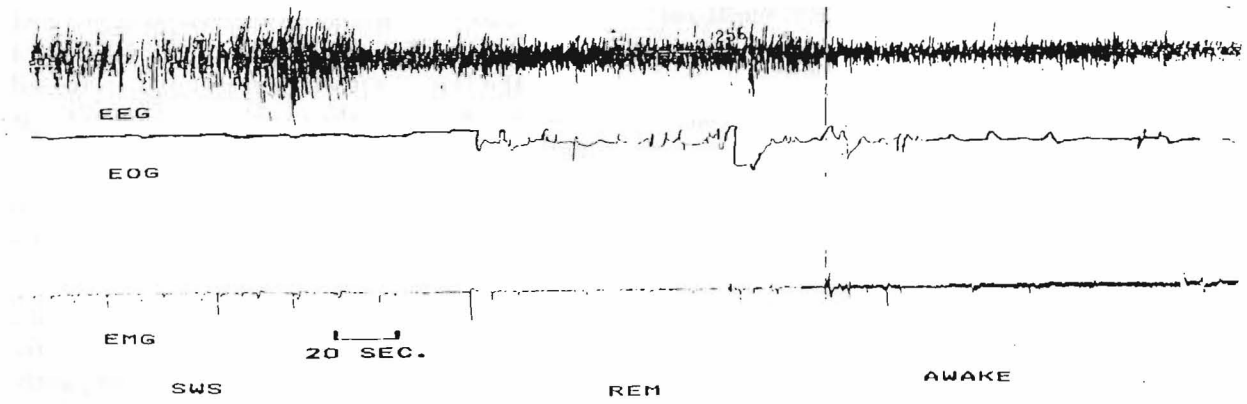

Fig. 1 : Simultaneous EEG, EMG, EOG tracing showing successive changes from SWS to REM to Awake stages in a control rat.

the exercised groups, all in comparison with the C group.

(c) REM sleep changes : Delta ($F_{3,32}$=5.2249, P<0.01) and Alpha-2 ($F_{3,32}$=7.7716, P<0.001) activity significantly increased in the D group, and they were significantly decreased in the exercised groups whereas the Beta-2 activity ($F_{3,32}$=5.7685, P<0.01) showed contrary changes, in comparison with the controls.

Correlation between the EEG changes and behavioral activity : In the REM state, Beta-2 activity was significantly positively (r=0.3576, P<0.05) correlated with the ambulation in the central squares of the OF (Fig. 2) and was

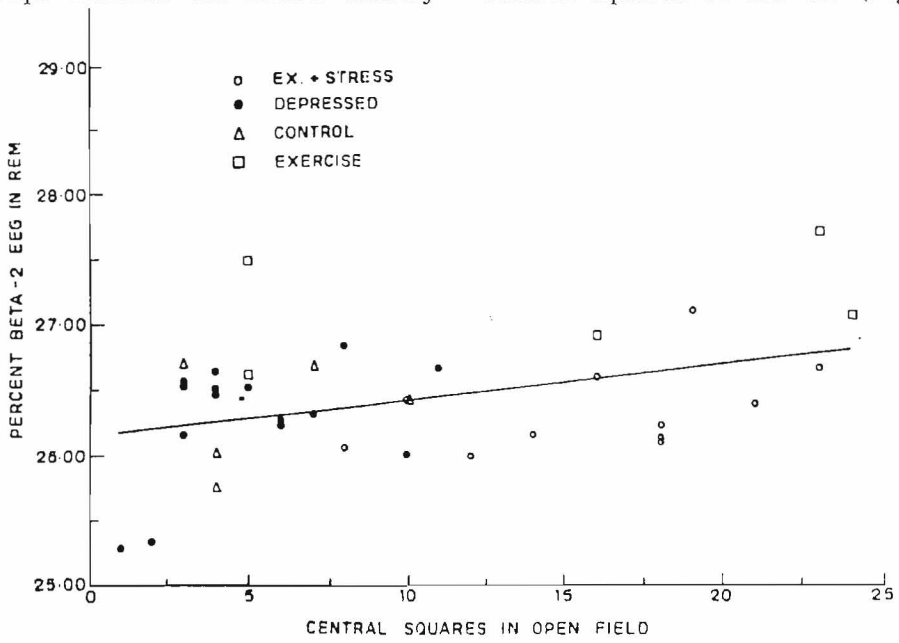

Fig. 2 : Scatterplot showing significant postitive correlation (r=0.3576, P<0.05) between ambulation in the central squares of the open field at the end of the 2nd week of stress and/or 8th week of exercise training or the 8th week after the start of the experiment and the percent power in the Beta-2 band of EEG during the REM sleep period.

significantly negatively (r=–0.3939, P<0.05) correlated with the fecal pellet counts there. The alpha activity was significantly positively (r = 0.3995, P<0.05) correlated with the fecal pellet count in the HPM and also with the same in OF (r=0.433, P<0.01). In the NREM state, Theta activity was significantly negatively correlated with the ambulation in the total (r=–0.371, P<0.05) number of squares; rearing (r=–4384, P<0.01) in the OF; TL in HPM (r=–0.4974, P<0.01) and significantly positively correlated with the OF immobilization (r=0.5293, P<0.01) and fecal pellet count in OF (r=0.3593, P<0.05) and HPM (r=0.3649, P<0.05). Beta-2 activity was significantly positively correlated with % time spent in central crossing in HPM (r=0.592, P<0.001); number of arm crossings (r=0.36, P<0.05) and negatively with the defecation in HPM (r=–0.4328, P<0.01). In the awake state, Delta activity was significantly positively (r=–0.5083, P<0.01) correlated with the fecal pellet counts in OF and HPM (r=0.4973, P<0.01); with immobilization in OF (r=0.3655, P<0.05) and significantly negatively (r=–0.38, P<0.05) correlated with the food intake; TL in HPM (r=–0.3328, P<0.05). The Alpha-2 activity was significantly positively (r=0.378, P<0.05) correlated with the food intake and negatively with grooming (r=–0.3842, P<0.05) in OF. The Beta-2 activity was significantly negatively (r=–0.4007, P<0.05) correlated with the fecal pellet counts in OF (r=–0.4766, P<0.01) and HPM (r=–0.3847, P<0.05) and with OF immobilization (r=–0.3564, P<0.05).

DISCUSSION

In the present study, quantitative analysis of the EEG (qEEG) changes induced by stress, exercise and exercise+stress, in each of the three sleep-wakefulness stages in the freely moving rats revealed that exercise and stress have opposite effects. The qEEG changes could also be significantly correlated with the behavioral changes, which are established indicators of depression. The present study is probably the first report analyzing the effects of chronic exercise on the qEEG in the awake as well as both the sleep states in an animal model of depression. Researchers (22) have studied the qEEG (8 hours' recordings) in normal cats following some anxiolytic drugs.

Exercise increased the relative wet weights of brain and heart, in the exercised groups, similar to the reported findings (23). This shows that there was a significant training effect in the present study.

In comparison with the control, there was a significant increase in the percent of Delta activity and a significant decrease in the Beta-2 activity, in the awake state, in the D group while for the exercised groups, the reverse occurred. In the NREM sleep state, compared to the C group, Theta increased and Beta-2 decreased in the D group and the opposite happened for the exercised groups. In the REM sleep state, Delta and Alpha-2 activity significantly increased in the D group, and they were significantly decreased in the exercised groups whereas the Beta-2 activity showed contrary changes compared to the control animals.

These findings indicate that exercise has the opposite effect from what stress has on qEEG. Also, concomitant physical exercise reduces the effects of stress, so the qEEG findings in the rats subjected to stress were quite different from those in the depressed rats not used to exercise. However, it is difficult to explain the significance of each of these changes at the present level of investigation.

The anxiolytic drug Buspirone (24) increases wakefulness and decreases both REM and NREM sleep in freely moving rats. In this study, exercise did increase the period of wakefulness (albeit not significantly) compared to that in the D group, but not compared to the C group, whereas, REM was decreased compared to both the C and D groups. However, NREM was increased compared to both the D and the C groups. Like the anxiolytic drugs diazepam, buspirone and DN-2327 (22), exercise also had reduced the Delta and Theta activities and enhanced the Beta-2 activity in the awake state, in both the EO and the ES groups.

Recent research has also stressed on human Slow Wave Sleep more than on REM sleep (25, 26). The results from the present study show that the SWS percentage had increased in the animals of the exercised groups (both with and without stress) compared to that of the C group, whereas in the depressed group it had been significantly reduced. Similar to the clinical findings, in the present study, an increase in the SWS by exercise had corrected some of the behavioral deficits. This implies that regular physical exercise may be helpful in counteracting some of the behavioral abnormalities observed in this model of depression.

An increase in activity above 16 Hz (Beta-2) bands in awake cortical EEG of monkeys, following minor tranquilizers had been reported (27). That this parameter may have anxiolytic activity, can also be surmised by the fact that in the present study, exercise had increased Beta-2 activity highly significantly ($P<<0.01$) in awake and REM stages and significantly ($P<<0.05$) in the NREM stage. Also as there was a positive correlation with the ambulation in the central squares (away from the wall) in the OF, further corroboration of this hypothesis is obtained. This is because, in anxiety states, the animals tend to stay beside the wall and are afraid to go to the unprotected center of the field.

In future this may be tried in human beings too. Already some work is being done on quantifying the awake-EEG findings in depression, where, slow waves (Theta-2 i.e., 6-8 Hz and Alpha-1 i.e., 8-9 Hz) have been found to be positively correlated with psychomotor retardation (28). In the present study, in the awake state, slow Delta activity was found to be negatively correlated with the food intake and grooming and significantly positively correlated with the immobilization in the OF implying that there is some psychomotor retardation, even in animals. Also here the slow Delta activity, in the awake state, was found to be significantly positively correlated ($r=0.3637$, $P<0.05$) with the immobilization in the Open Field.

Modern computational tools can be very helpful in measuring the mental states, including those in animals (29). Taking continuous digital recordings and storing them in magnetic tapes for further analysis will also be helpful in determining the temporal variations of the various sleep stages. Instead of performing the WDFT (Windowed Discrete Fourier Transform), the Wavelet analysis will be more informative, in case of transient signals (29). Other animal models, and finally, different types of depression in human beings have to be meticulously investigated for a reliable qEEG diagnosis. Other methods like measuring the phase-space plots (29), also can be tried for a definitive EEG diagnosis for the depressive states. Computerized diagnosis and clinical acumen, are however, not mutually exclusive and will only reinforce each other (30).

In the present study, the behavioral changes have been compared with the help of the behavioral tests. The EEG changes have been compared separately by FFT. As the EEG power spectra changes were rather distinctive in stress and in exercise, it should be verified clinically. The EEG-behavioral correlations were also quite promising.

In conclusion, prophylactic exercise may prove beneficial in preventing depression and qEEG may be used as a diagnostic and prognostic tool for depression.

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REFERENCES

1. Niedermeyer E, Lopes da Silva FH. Electroencephalography - Basic Principles, Clinical Applications and Ralated Fields, 2nd ed., Urban and Schwarzenberg, Baltimore-Munich, 1987.
2. Morstyn R, Duffy FH, McCarley RW. Altered topography of EEG spectral content in schizophrenia. *Electroenceph Clin Neurophysiol* 1983; 56 : 263-271.
3. Thiebot MH, Martin P, Puech AJ. Animal behavioural studies in the evaluation of antidepressant drugs. *Brit J Psychiatry* 1992; 160 (Suppl. 15) : 44-50.
4. Willner P. The validity of animal models of depression. *Psychopharmacology* 1984; 83 : 1-16.
5. Willner P. Animal models of depression : An overview. *Pharmacol Therap* 1990; 45 : 425-445.
6. Dement WC, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility and dreaming. *Electroenceph Clin Neurophysiol* 1957; 9 : 673-690.
7. Cai Z. The functions of Sleep : Further analysis. *Physiol Behav* 1991; 50 : 53-60.
8. Vogel GW, Roth T, Gillin JC, Mendelson WB, Buffenstein A. REM Sleep and Depression. In, Oniani, T. Ed, Neurobiology of Sleep-Wakefulness Cycle. *Metsniereba Tbilisi* 1988; 187-213.
9. Sarbadhikari SN, Ray AK. Identifying EEG Power Spectra of Depressed Rats Using a Neural Network, In, Reddy DC, Ed, Recent Advances in Biomedical Engineering, Tata Mcgraw-Hill, New Delhi, 1994; 76-79.
10. Harris SS, Caspersen CJ, DeFriese GH, Estes EH Jr. Physical activity counseling for healthy adults as a primary preventive intervention in the clinical setting. Report for the US Preventive Services Task Force. *JAMA* 1989; 261 : 3590-3598.
11. Liebowitz CS. To release stress - Exercise! *NY State Dent J* 1989; 55 : 36-37.
12. Overton JM, Kregel KC, Davis-Gorman G, Seals DR, Tipton CM, Fisher LA. Effects of exercise training on responses to central injection of CRF and noise stress. *Physiol Behav* 1991; 49 : 93-98.
13. Stephens T. Physical activity and mental health in the United States and Canada : evidence from four population surveys. *Prev Med* 1988; 17 : 35-47.
14. Dey S. Physical exercise as a novel antidepressant agent : possible role of serotonin receptor subtypes. *Physiol Behav* 1994; 55 : 323-329.
15. Katz RJ. Animal model of Depression : Pharmacological sensitivity of a hedonic deficit. *Pharmacol Biochem Behav* 1982; 16 : 965-968.
16. Soblosky JS, Thurmond JB. Biochemical and Behavioural Correlates of Chronic Stress : Effects of Tricyclic Antidepressants. *Pharmacol Biochem and Behav* 1986; 24 : 1361-1368.
17. Chaouloff F, Elghozi JL, Guezennec Y, Laude D. Effects of conditioned running on plasma, liver and brain tryptophan and on brain 5-hydroxytryptamine metabolism of the rat. *Eur J Pharmac* 1985; 86:33-41.
18. Stearns SD, David RA. Signal Processing Algorithms. Prentice-Hall Inc., Englewood Cliffs, New Jersey, 1988.
19. Hutchings H. Interfacing with C, part 9. *Electronics World + Wireless World* January 1991; 48-52.
20. Kierniesky N, Sick N, Kruppenbacher F. Open Field activity of albino rats as a function of age, sex and repeated testing. *Psychol Rep* 1977; 40 :1250-1260.
21. Pellow S, chopin P, File SE, Briley M. Validation of open : closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *J Neurosci Methods* 1985; 144 : 149-167.
22. Hashimoto T, Hamada C, Wada T, Fukuda N. Comparative study on the behavioral and EEG changes induced by diazepam, buspirone and a novel anxioselective anxiolytic, DN-2327, in the cat. *Neuropsychobiology* 1992; 26 : 89-99.
23. Brown BS, Van Huss W. Exercise and rat brain catecholamines. *J Appl Physiol* 1973 ; 34 : 664-669.
24. Lerman JA, Kaitin KI, Dement WC, Pertouka SJ. The effects of buspirone on sleep in the rat. *Neurosci Lett* 1986; 72 : 64-68.
25. Horne JA. Human Sleep, Sleep Loss and Behaviour; Implications for the Prefrontal Cortex and Psychiatric Disorders. *Brit J Psychiatry* 1993; 162 : 413-419.
26. Spiegel R, Koberle S, Allen SR. Significance of slow wave sleep; Consideration from a clinical viewpoint. *Sleep* 1986; 9 : 66-79.
27. Gehrmann JE, Killam KF Jr. Studies of central functional equivalence. I. Time-varying distribution of power in discrete frequency bands of the EEG as a function of drug exposure. *Neuropharmacology* 1978; 17 : 747-759.
28. Nieber D, Schlegel S. Relationships between psychomotor retardation and EEG power spectrum in major depression. *Neuropsychobiology* 1992; 25 : 20-23.
29. Klemm WR. Are there EEG correlates of mental states in animals? *Neuropsychobiology* 1992; 26 : 151-165.
30. Sarbadhikari SN. Biomedical Engineering - Relevant or Not? *J Indian Med Assoc* 1993; 91 : 145.