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Biogenic amine changes in brain regions and attenuating action of *Ocimum sanctum* in noise exposure

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Abstract

Broadband white noise exposure (100 dB) in wistar strain male albino rats significantly increased the levels of dopamine (DA), serotonin (5-HT) and 5-HT turnover in many of the discrete brain regions (cerebral cortex, cerebellum, hypothalamus, hippocampus, pons-medulla and corpus striatum) during sub-chronic noise exposure (4 h daily for 15 days). In acute (4 h for 1 day) and chronic noise exposures (4 h daily for 30 days) the levels were significantly altered only in certain regions. The turnover study of serotonin clearly indicates that neurotransmitter level alone cannot be an indicator, as in some brain regions the rate of synthesis matched with the degradation in order to maintain the normal levels. The intraperitoneal administration of 70% ethanolic extract of *Ocimum sanctum* (OS) at the dosage of 100 mg/kg body weight to animals subjected to noise exposure has prevented the noise induced increase in neurotransmitter levels without affecting the normal levels. This indicates that OS can be a probable herbal remedy for noise induced biogenic amine alterations.

Keywords: *Ocimum sanctum*; Brain; Neurotransmitters; Noise; Dopamine; Serotonin

1. Introduction

Noise is known to produce several short and long-term physiological and biochemical responses in humans and other animals. Acute exposure to sound pressure levels above 90 dB has the potential to cause inner ear hearing loss and to stimulate the sympathetic nervous system into increasing the release of adrenaline and noradrenaline (Ising et al., 1990). Long term as well as acute exposure to noise, affects the central nervous system in many ways. Noise exposure alters the free radical scavenging enzymes in discrete regions of brain (Samson et al., 2005). Moreover DA and 5-HT are known to be involved in the expression of environmentally induced behavioral disorders in adult individuals of several species (Hierden et al., 2002). Hence estimation of noise induced alterations in DA, 5-HT and 5-HT turnover in discrete regions of brain will help in understanding the impact of three different durations of noise exposure on the central nervous system.

Since noise is a pervasive aspect in many modern communities and work environments, finding an effective antidote for noise induced changes seems to be the only solution for this distressing problem. One of the widely used medicinal herbs in indigenous systems of medicine is *Ocimum sanctum* Linn (OS), which belongs to the family Lamiaceae and commonly known as sacred basil or "Tulsi". Epidemiological studies have suggested positive associations between the consumption of phenolic-rich foods or beverages and the prevention of diseases (Scalbert and Williamson, 2000). These effects have been attributed to antioxidant components such as plant phenolics, flavonoids and phenylpropanoids among others (Rice-Evans et al., 1996). Basils (*Ocimum* spp., Lamiaceae) contain a wide range of essential oils rich in phenolic compounds (Phippen and Simon, 2000) and a wide array of other natural products including polyphenols such as flavonoids and anthocyanins. Various aspects of the stress alleviating potential of the crude extracts of OS have been established (Archana and Namasivayam, 2000).

This study focuses the alterations in brain neurotransmitters (DA, 5-HT and 5-HT turnover) in various periods of noise exposure and the role of ethanolic extract of OS in attenuating these changes.

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2. Materials and methods

2.1. Animals

Wistar strain male albino rats weighing 180 to 220 g were used. Animals were housed in groups of three (rats) per cage and maintained in a temperature controlled room with a 12-h light/dark cycle (lights on at 7:00 AM) and allowed free access to food and water. All animal procedures were approved by the institutional animal ethical committee and CPCSEA (IAEC No: 08/020/04). All efforts were made to minimize both the number of animals used and unwanted stress or discomfort to the animals during experimental procedures.

2.2. Experimental design

The animals were divided into ten groups with six animals in each group. Group I consisted of the control animals, while Group II, V and VIII consisted of animals subjected to acute (4 h for 1 day), sub-chronic (4 h daily for 15 days) and chronic (4 h daily for 30 days) noise exposures, respectively. Group III, VI and IX were the treated groups, in which the animals were subjected to acute, sub-chronic and chronic noise exposure along with OS treatment. Groups IV, VII and X were the acute, sub-chronic and chronic vehicle treated animals. To avoid circadian rhythm induced variation all the sample collection were done between 8–9 AM. Since the study involves the estimation of neurotransmitters no anesthesia was used.

2.3. Noise stress induction

Broad band (White) noise at 100 dB intensity was used for the study. The sound was produced by a white noise generator, amplified by an amplifier connected to a loud speaker fixed 30 cm above the animal cages. A sound level meter was used to measure the intensity of noise. During the experiment, the noise level peaked at 100 dB immediately after the generator was switched on and lasted 4 h (Archana and Namasivayam, 2000). Control animals were sham exposed by placing them in the noise chamber with the noise generator turned off to counter the handling and environment induced changes.

2.4. OS extract preparation

Fresh OS plants cultivated at the IMPCOPS farm, Chennai and identified by Prof. N. Anand, Director, Centre for advanced studies in Botany, University of Madras (No. ARC/JS/2004/1090), was collected, dried under shade, powdered and 70% ethanolic extract was prepared by percolation method. The yield of the final product during the extraction procedure was 15% (w/w) of the dried starting material. The OS extract was dissolved in propylene glycol (PG) at 10 g/100 ml and given intraperitoneally at 100 mg/kg body weight (Bhargava and Singh, 1981). Since the reports reveal that pretreatment gives better response the Group III, VI and IX animals were pretreated for 15 days apart from the treatment during the noise exposure period.

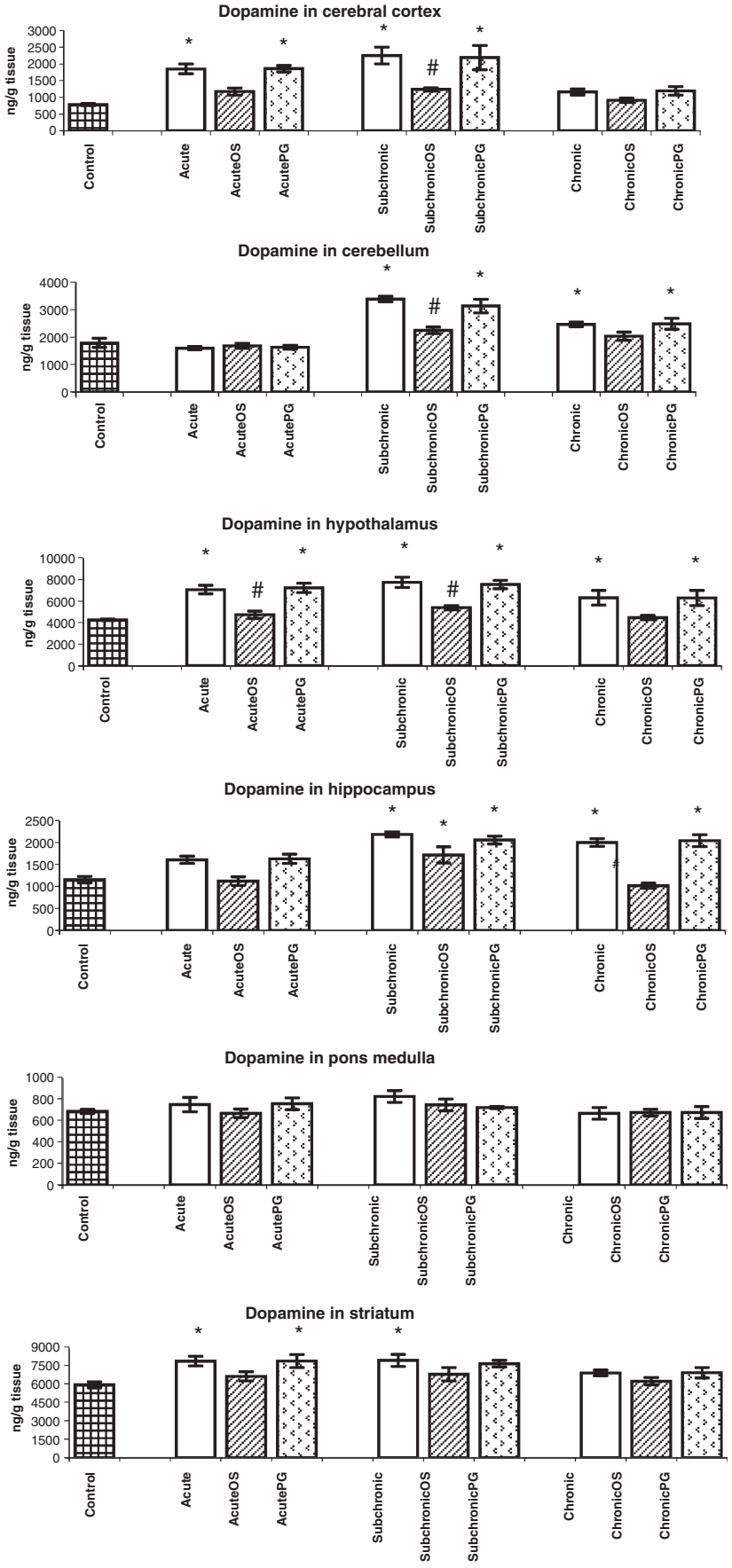
2.5. Sample preparation

The rats were decapitated and the brain was rapidly removed. Further dissection of discrete regions was made on ice-cold glass plate (Glowinski and Iverson, 1966). The brain was dissected into six discrete regions, viz.: cerebral cortex, cerebellum, hippocampus, hypothalamus, pons-medulla and corpus striatum. The inclusion of amygdala that is noted for being involved in the stress pathway along with the hippocampus is one of the weaknesses of this study. Since the effect of noise in major brain regions were analyzed, amygdala was not studied separately. The regions were weighed and homogenized with 0.1 M perchloric acid. Homogenates were centrifuged at 4000 $\times g$ in a refrigerated centrifuge at 4 °C for 2 min. Internal standard dihydroxybenzylamine (DHBA) was added with the supernatant and again centrifuged at 4000 $\times g$ at 4 °C for 20 min. Supernatant was filtered with 0.22 μm membrane filter.

2.6. Neurotransmitter estimation by HPLC

The HPLC estimation of neurotransmitters is based on the principle that the current of oxidation is proportional to the concentration of the amine concerned. The sample (20 μl) was injected into a rheodyne injector (USA) of HPLC system, which was connected to an isocratic pump (Waters Model 501, Waters Association, Millipore, MA, USA) and reverse phase column (LiChroCART RP-18), for separation of biogenic amines. The mobile phase contained citric acid, di-sodium hydrogen orthophosphate, EDTA, octane-1-sulphonic acid sodium salt, 14% methanol and was adjusted to the pH of 4.0 using di-sodium hydrogen orthophosphate. The reaction products were detected with electrochemical detector (Waters 460 MA, USA). The flow rate was maintained at 0.8 ml/min. The electrochemical detector coupled to the HPLC system was set at a potential of +0.60 V for the detection of neurotransmitters. The neurotransmitters were quantified using Shimadzu C-R8A data processor and expressed as nanograms of neurotransmitter per gram of wet weight of brain tissue. A constant amount of the internal standard (DHBA) was used for the tissue samples to calculate the recovery (Wagner et al., 1982). DA, 5-HT, 5-hydroxy indole acetic acid (5-HIAA) and DHBA were purchased from Sigma and the rest of the reagents were of HPLC grade. The 5-HIAA/5-HT ratio was calculated to indicate the 5-HT turnover.

Fig. 1. Noise induced alterations in dopamine levels and effect of OS treatment (ng/g wet tissue). *Indicates significance compared with control, # indicates significance in treated groups compared with respective noise exposed groups. In acute noise exposure the DA levels in cerebellum, hippocampus and pons-medulla were not altered whereas in the other regions the DA levels were increased. During sub-chronic exposures pons-medulla alone was unaffected. In chronic exposure, the DA levels in cerebral cortex, pons-medulla and striatum were not increased. OS treatment prevented the DA changes in all the regions except hippocampus in sub-chronic exposure.


Dopamine in cerebral cortex
ng/g tissue
3000
2500
2000
1500
1000
500
0
Control
Acute
AcuteOS
AcutePG
Subchronic
SubchronicOS
SubchronicPG
Chronic
ChronicOS
ChronicPG
Dopamine in cerebellum
ng/g tissue
4000
3000
2000
1000
0
Dopamine in hypothalamus
ng/g tissue
10000
8000
6000
4000
2000
0
Dopamine in hippocampus
ng/g tissue
2500
2000
1500
1000
500
0
Dopamine in pons medulla
ng/g tissue
1000
800
600
400
200
0
Dopamine in striatum
ng/g tissue
9000
7500
6000
4500
3000
1500
0

2.7. Statistical analysis

Statistical analysis of the data was performed by one way analysis of variance followed by Tukey's multiple comparison tests, to evaluate the significance between the various groups studied. $P<0.05$ was considered as statistically significant. The results are expressed as mean±SE.

3. Results

3.1. Dopamine levels

The DA levels in various groups are given in Fig. 1.

3.1.1. Cerebral cortex

In cerebral cortex the acute and sub-chronic noise exposure significantly increased DA levels, ($F(9,50)=10.4$) whereas it remained unaltered during chronic noise exposures. OS treatment prevented this increase in both acute and sub-chronic treated group.

3.1.2. Cerebellum

In cerebellum the sub-chronic and chronic noise exposures significantly increased the DA levels ($F(9,50)=19.9$) while in acute noise exposure the level remained unaltered. OS treatment was able to prevent the increase in the sub-chronic and chronic noise exposed groups.

3.1.3. Hypothalamus

In hypothalamus all the three different durations of noise exposures have significantly increased ($F(9,50)=9.1$) the DA levels. OS treatment prevented the increase in all the noise exposed groups.

3.1.4. Hippocampus

In hippocampus sub-chronic and chronic noise exposure significantly increased the DA levels ($F(9,50)=17.1$), while the level was not altered in acute noise exposure. OS treatment prevented this increase in DA level in the chronic treated group. However in the sub-chronic treated group the level was similar to that of noise exposed animals and remained elevated when compared to control levels.

3.1.5. Pons-medulla

In pons-medulla no variations was observed ($F(9,50)=1.2$) in the test group when compared to the controls indicating only in certain brain regions DA levels were altered during noise exposure.

3.1.6. Corpus striatum

In striatum acute and sub-chronic exposures significantly ($F(9,50)=3.3$) increased the DA levels, while the levels remained unaltered in chronic noise exposure. OS treatment was able to prevent this increase in acute and sub-chronic treated groups.

3.2. 5-HIAA levels

The 5-HIAA levels in various groups are given in Table 1. The 5-HIAA levels were estimated to calculate the 5-HT turnover.

3.2.1. Cerebral cortex

Acute and sub-chronic noise exposure significantly increased ($F(9,50)=69.5$) the 5-HIAA levels while OS treatment prevented the increase in acute exposure.

3.2.2. Cerebellum

Acute and sub-chronic noise exposure significantly increased ($F(9,50)=49.1$) the 5-HIAA levels while OS treatment prevented the increase in acute exposure.

3.2.3. Hypothalamus

All three durations of noise exposure significantly increased the 5-HIAA levels ($F(9,50)=29.3$), while OS treatment prevented the increase.

3.2.4. Hippocampus

All the three durations of noise exposure significantly increased the 5-HIAA levels ($F(9,50)=33$), while OS

Table 1
Noise induced alterations in 5-HIAA levels and effect of OS treatment (ng/g wet tissue)

	Cerebral cortex	Cerebellum	Hypothalamus	Hippocampus	Pons-medulla	Striatum
Control	57±6	143±14	961±92	312±46	389±31	780±68
Acute	257±11[a]	622±56[a]	3352±320[a]	1735±119[a]	1586±62[a]	3325±114[a]
Acute OS	108±7[b]	311±26[b]	1385±138[b]	897±68[a,b]	436±26[b]	1484±97[b]
Acute PG	260±20[a]	622±48[a]	3495±356[a]	1897±82[a]	1563±94[a]	3479±233[a]
Subchronic	320±19[a]	783±39[a]	4646±360[a]	1528±104[a]	1718±114[a]	4733±333[a]
Subchronic OS	157±17[a,b]	389±25[a,b]	1815±165[b]	837±91[a,b]	957±92[a,b]	2020±167[a,b]
Subchronic PG	250±18[aa]	692±66[a]	4496±284[a]	1443±133[a]	1643±111[a]	4570±312[a]
Chronic	52±3	166±7	2367±213[a]	1117±71[a]	542±40	1902±94[a]
Chronic OS	54±1	156±1	1383±126	464±22[b]	418±19	1189±97
Chronic PG	52±3	169±9	2430±179[a]	1147±115[a]	554±46	2035±152[a]
F value	69.504	49.104	29.315	33.026	64.341	53.747
df	9,50	9,50	9,50	9,50	9,50	9,50

[a] Indicates significance compared with control.
[b] Indicates significance in treated groups compared with respective noise exposed groups.

treatment prevented the increase in chronic noise exposed group.

3.2.5. Pons-medulla

Acute and sub-chronic noise exposure significantly increased ($F(9,50)=64.3$) the 5-HIAA levels while OS treatment prevented the increase in acute exposure.

3.2.6. Corpus striatum

All the three durations of noise exposure significantly increased the 5-HIAA levels ($F(9,50)=53.7$), while OS treatment prevented the increase in acute and chronic noise exposed group.

3.3. Serotonin levels

The 5-HT level in various brain regions are given in Table 2. The 5-HT turnover (5-HIAA / 5-HT ratio) in various regions are given in Fig. 2. Since many of the stressors are known to alter the serotonin levels, the turnover for serotonin was also calculated in this study.

3.3.1. Cerebral cortex

In the cerebral cortex no variations ($F(9,50)=2.3$) in 5-HT level was observed in all the noise exposed groups studied. The OS treatment also did not alter the levels when compared to control group. However the 5-HT turnover was significantly increased ($F(9,50)=27.4$) in acute and sub-chronic noise exposure indicating that, an increased synthesis of 5-HT was matched with the increased degradation of 5-HT. The OS treatment was able to prevent this increase in 5HT turnover in the acute stress exposed group. This observation denotes that OS could modulate the key enzymes levels. The 5-HT turnover was not altered in chronic noise exposure.

3.3.2. Cerebellum

In cerebellum, the sub-chronic and chronic noise exposure significantly ($F(9,50)=23.5$) increased the 5-HT levels, while the level was similar to controls in acute noise exposed group. When the turnover was calculated the 5-HT turnover in acute and sub-chronic noise exposed group showed a marked increase ($F(9,50)=26.1$), while in chronic noise exposure it remained unaltered. Collectively these results show that the unaltered neurotransmitter level in acute noise exposure is due to its increased turnover in both synthesis and degradation levels. Similarly the increase in neurotransmitter level in chronic noise exposure may be due the increased synthesis and decreased degradation levels. OS treatment prevented the increase in serotonin level in the chronic treated group. OS was also able to prevent the drastic increase in turnover seen in the sub-chronic group, though it was not able to restore it to normal levels.

3.3.3. Hypothalamus

In hypothalamus acute and sub-chronic exposure significantly ($F(9,50)=5.4$) increased the 5-HT levels, while the levels were unaltered in chronic noise exposure. OS treatment prevented this increase in 5-HT level in acute and sub-chronic treated groups. The 5-HT turnover was significantly increased ($F(9,50)=7.8$) in acute and sub-chronic noise stress in hypothalamus and OS treatment prevented the increase in both acute and sub-chronic treated group by decreasing the synthesis of 5-HT without affecting the degradation. Further in the chronic exposure group, the 5-HT turnover remained unaltered even after OS treatment.

3.3.4. Hippocampus

In the hippocampus no variations ($F(9,50)=1.3$) were observed in 5-HT level in the noise exposed groups as well as in the OS treated groups, when compared to control. However the 5-HT turnover was significantly increased ($F(9,50)=14.7$) in the three durations of noise exposure while OS treatment prevented the increase in sub-chronic and chronic treated group.

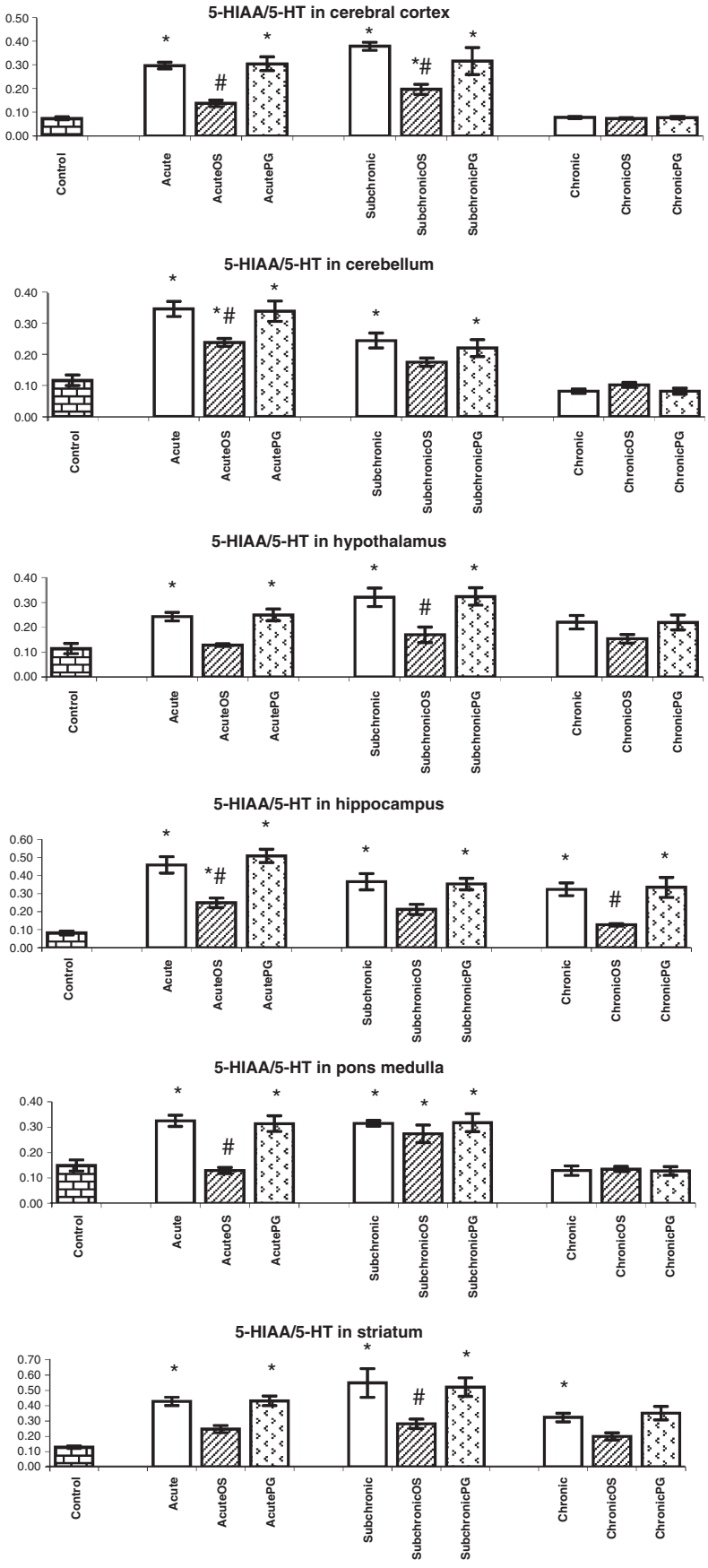
3.3.5. Pons-medulla

In pons-medulla all the three different durations of noise exposure significantly increased ($F(9,50)=9.8$) the 5-HT levels. OS treatment prevented the increase in all the treated groups. The 5-HT turnover was significantly increased

Table 2
Noise induced alterations in 5-HT levels and effect of OS treatment (ng/g wet tissue)

	Cerebral cortex	Cerebellum	Hypothalamus	Hippocampus	Pons-medulla	Striatum
Control	772±57	1271±65	8942±630	3777±121	2783±254	5975±250
Acute	873±45	1800±97	13,752±798[a]	3838±169	4941±223[a]	7886±403
Acute OS	811±50	1309±92	10,768±898	3701±225	3483±260[b]	6114±294
Acute PG	875±74	1889±153	14,015±874[a]	3829±306	5076±272[a]	8149±489
Subchronic	847±31	3336±309[a]	14,812±808[a]	4350±343	5449±308[a]	9339±1040[a]
Subchronic OS	805±38	2245±98[a,b]	11,471±1194	3990±123	3702±423[b]	7300±315
Subchronic PG	853±73	3201±109[a]	14,219±862[a]	4108±222	5312±296[a]	9221±874[a]
Chronic	672±29	2080±98[a]	11,127±937	3526±175	4502±408[a]	5998±267
Chronic OS	746±32	1579±118	9294±696	3688±170	3157±150	6085±272
Chronic PG	684±29	2161±160[a]	11,680±1159	3596±257	4545±336[a]	6021±418
F value	2.299	23.511	5.371	1.256	9.779	6.629
df	9,50	9,50	9,50	9,50	9,50	9,50

[a] Indicates significance compared with control.
[b] Indicates significance in treated groups compared with respective noise exposed groups.


5-HIAA/5-HT in cerebral cortex
5-HIAA/5-HT in cerebellum
5-HIAA/5-HT in hypothalamus
5-HIAA/5-HT in hippocampus
5-HIAA/5-HT in pons medulla
5-HIAA/5-HT in striatum
Control
Acute
AcuteOS
AcutePG
Subchronic
SubchronicOS
SubchronicPG
Chronic
ChronicOS
ChronicPG

($F(9,50)=16.1$) in acute and sub-chronic noise exposure. The 5-HT turnover was not altered in chronic exposure though the level of 5-HT was increased. This may be due to a synchronized increase in synthesis and degradation.

3.3.6. Corpus striatum

In striatum, sub-chronic exposure significantly increased ($F(9,50)=6.6$) the 5-HT levels, while the 5-HT levels were unaffected in acute and chronic noise exposure. OS treatment was able to prevent this increase in 5-HT level in sub-chronic treated group. However the 5-HT turnover was significantly increased ($F(9,50)=9.8$) in acute and sub-chronic noise exposure. The unaltered neurotransmitter level and altered turn over during acute exposure indicates that the rate of synthesis is matched for the rate of degradation. OS treatment prevented the increase in both acute and sub-chronic treated group. The 5-HT turnover was not altered in chronic exposure.

4. Discussion

The WHO has declared that noise is an international health problem. The noise level of 100 dB intensity, which is used in this study, is comparable with the noise frequently detected in discos and some industrial workplaces. The overall results of this study show that noise induces alterations in the brain neurotransmitters, and the alterations in neurotransmitters are more pronounced during the sub-chronic exposures. However the level of DA, 5-HT and 5-HT turnover were not altered in few regions after chronic noise exposure. This indicates that a slow adaptation occurs in noise exposure. But this adaptation phenomenon could not be observed in some other regions even after thirty days of noise exposure. OS treatment was able to prevent these noise induced changes by increasing the synthesis rather than inhibiting the degradation of the 5-HT.

The observed results indicate that the noise induced alterations in neurotransmitters are not confined to specific regions in the brain. Lopez et al. (1999) reported that the brain regions activated by the acute stressors includes neocortex, allocortex, hippocampus, nucleus accumbens, lateral septum, several hypothalamic nuclei, medial and cortical amygdaloid nuclei, dorsal raphe, locus coeruleus, and several brain stem nuclei. According to them these brain regions are activated largely irrespective of the type of acute stressor administered, perhaps indicating that these structures are involved in a more "general," integrative stress response. More over noise stimulates the brain's reticular activating system to induce wakefulness. Neural impulses spread from the reticular system to the higher cortex and throughout the central nervous system (Stansfeld et al., 2000). It is also known that stressful situations stimulate various areas of the hypothalamus and activates hypothalamus–pituitary–adrenal (HPA) axis. These reports justify the observations in this study showing noise induced alterations of neurotransmitters in many regions apart from auditory cortex.

In the present study, a consistent increase of the DA in cerebral cortex, hypothalamus and striatum was observed in animals subjected to acute noise exposure. Most of the stressors are known to initiate sympathetic "mass discharge" of catecholamines, during the acute phase of stress, as in the fight-or-flight response. However the stress responses are not similar. Various workers have given different opinions about the level of brain DA in stress, a decrease in isolation stress (Blanc et al., 1980) and an increase in foot shock stress (Reinhard et al., 1982). The DA levels were significantly increased in sub-chronic noise exposure in all the regions except pons-medulla, which did not show any change in all the three durations of noise exposure. This indicates that noise exposure do not affect all the brain regions in a uniform way. Recent research suggests that the nature of the physiological response to stressors may be much more stressor-specific than was earlier believed. Increased dopaminergic activity in the striatum and increased serotonergic activity in the frontal cortex and amygdala was reported following forced swim test-exposure (Conner et al., 1997). In another study forced swim test exposure increased serotonergic activity in the amygdala, frontal cortex, hippocampus and increased dopamine turnover in the striatum (Connor et al., 1999). These available reports correlate with the findings of this study. The OS treatment has prevented the increase in DA levels, caused by the exposure to three different durations of noise. This shows that OS acts as an anti-stressor. Such anti-noise stressor activity of OS has been reported for the central cholinergic system (Sembulingam et al., 2005) and immunological system (Archana and Namasivayam, 2000).

The differences in the serotonergic response observed in specific regions may be due to the variations in their level of distribution, their rate of synthesis and degradation as indicated by the turn over results. Because the 5-HT turnover in cerebral cortex, hippocampus indicates that the increased degradation is stabilized by the increase in their synthesis. Many studies, using tests such as an elevated plus maze (Sajdyk et al., 1997), footshock (Bernardis and Bellinger, 1998) and restraint stress (DeSouza and CanLoon, 1986) show a correlation in the stress response with an increase in 5-HT levels. In the present study also there was a significant increase in 5-HT turnover in all the three different durations of noise exposure, however with a regional specificity within the brain. The noise induced increase in neurotransmitter level is also associated with the increase in the degradation of 5-HT into 5-HIAA. Singh et al. (1990) found that acute or repetitive exposures to noise activates tryptophan hydroxylase, which is the enzyme involved in 5-HT biosynthesis. Hence increased activity of

Fig. 2. Noise induced alterations in 5-HT turn over and effect of OS treatment (5 HIAA/5HT). *Indicates significance compared with control, # indicates significance in treated groups compared with respective noise exposed groups. In acute and sub-chronic noise exposure all the brain regions showed a significant alteration in the turnover ratio. In chronic noise exposure the turnover was affected only in hippocampus and striatum. The OS treatment could prevent the increase in the turnover in cerebral cortex, hypothalamus, pons-medulla and striatum in the acute noise exposed group. In sub-chronic exposure OS could prevent the increase in the turnover in cerebellum, hypothalamus, hippocampus and striatum. In chronic noise exposed group, it could prevent the changes in the hippocampus and striatum.

this enzyme could result in increase in the 5-HT levels. However Mennini et al. (1993) mentioned that noise could reduce serotonergic uptake of synaptosomes in many areas of the brain, including hippocampus, hypothalamus and cerebral cortex. From these observations it can be understood that the level of neurotransmitters depend not only on their turnover, but also on the alterations in reuptake. These reports suggest the possible cause for the significant increase in 5-HT level and its turnover. OS treatment was able to prevent the alteration in neurotransmitter levels. Hence it can be assumed that OS acts by influencing either the activity of tryptophan hydroxylase or the reuptake of neurotransmitter.

The phenomenon associated with stress adaptation at neuronal level is also observed in this study. The chronic noise exposure could not induce any neurotransmitter changes either in its content or in its turnover in most of the brain areas, indicating that neural adaptation could occur during chronic noise exposures. Such adaptation appears to represent an active process. In this study chronic exposure appear to promote a compensatory or moderation mechanism resulting in the reversal of the elevated neurotransmitter concentrations towards the normal levels. This may be due to habituation (a stimulus, when repeated over and over leads to the gradually disappearing response) which is associated with the decreased release of neurotransmitter form the pre synaptic terminal because of decreased intracellular calcium by inactivating calcium channels (Ganong, 2001). Side effects such as hair loss, weight loss which can be attributed either to the effects of noise stress or OS treatment, were not observed in this study.

The changes in the brain neurotransmitter levels after the noise exposure was well protected and were brought towards normal levels in the OS treated groups. This indicates that some of the active principles present in OS can cross the blood brain barrier. Active principles present in Ocimum species such as rosmarinic acid, lithospermic acid, phenolics and flavonoids have been attributed to be responsible for their diverse medicinal activities (Kelm et al., 2000; Hase et al., 1997; Juliani and Simson, 2002). Therefore it can be assumed, that the activity of OS in reducing the elevated neurotransmitter levels may depend on one or many of its active principles such as eugenol, methyleugenol, urosolic acid, α- and β-caryophyllene, methylchavicol, linalool, 1,8-cineole and flavonoids such as orientin, vicenin etc which may act on the synthesis or reuptake of neurotransmitters. This hypothesis is well supported by the reports that OS can act through D_2 receptor. Studies on OS activity on dopaminergic neurons have shown that OS along with bromocriptine act as a D_2 receptor agonist while OS is blocked by haloperidol and sulphride (Pare and Glavin, 1986). Moreover it also further reported that OS normalized the stress induced membrane changes in the hippocampus and sensorimotor cortex (Sen et al., 1992). These reports also indicate that OS is a non-specific anti-stressor.

In this study OS prevented the stress induced changes in neurotransmitters in the regions where it was altered and it did not affect the regions that were not altered. Therefore this activity of OS and the probable interaction of OS with the D_2 receptors can be assumed to play a major role in the normalization of the elevated neurotransmitter levels. Similar activity of OS demonstrating adaptogenic and anti-stressor properties has been reported by other authors (Singh et al., 1991). Thus it is evident that OS increases the capacity to cope and adapt to changing and challenging environments, and reduces the negative biochemical effects of noise exposure emphasizing its stress resilience activity. This reinforces the popular belief that daily consumption of OS in small quantities may be beneficial and due to its high LD_{50} value it may be a safe solution for those who are exposed to one or other type of stress in this modern era of urbanized life style.

Moreover, if the specific active principle responsible for this action are identified and isolated, the quantity of the compound required to produce similar effects will be much smaller and then it will become applicable in practical life. The various compounds present in the phenolic and flavonoid content of OS are being held responsible for its medicinal properties (Hase et al., 1997; Juliani and Simson, 2002). Estimation of these compounds in the OS used in this study has revealed the presence of substantial amount of phenolic and flavonoid content. Therefore this study suggests OS as a probable remedy for noise induced changes, based on its effectiveness in attenuating the noise induced alterations in the neurotransmitter levels.

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