Protective effects of Olive oil on the stress induced behavioral changes in rats

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Abstract: The objective of the current study was to examine protective effects of olive oil having high magnitude of essential components and likely to guard the brain from damaging outcomes of stress. Stress is a key etiological feature in the development of various diseases. Olive oil is a chief constituent of Mediterranean diet, has been used from the past for nutritional and pharmacological purposes. It is a rich source of vital dietary and nutritional constituents with excellent health benefits. Therefore, this study was planned to see the potential role of olive oil on stress-related behavioral shortfalls in rats. Behavioral parameters such as open field test, light and dark activity test, forced swim test, hot plate and water maze test were used for investigations of locomotor activity, level of anxiety, depression, analgesic activity and long term memory in rats respectively. The outcomes of present study displayed increased locomotion, decreased anxiety and depressive behaviors, improvement in long term memory as well as analgesic activity in restraint rats pretreated with olive oil. The results from present study reflected that 2 h restraint stress induced anxiogenic; depressive, nociceptive and memory impairing effects in rats are decreased following repeated administration of olive oil in rats. Our finding highlights the significance of using herbal compounds in the recovery of stress related behavioral impairments as they possess minimal side effects as compared to synthetic drugs.

Key Words: Olive oil, Antidepressant, Anxiolytic, Nociceptive, Anxiogenic, Analgesic

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INTRODUCTION

Stress is not considered as a disease itself but continuous exposure to stressful episodes has been related to the onset and advancement of many physiological and neurological illnesses1-3. All living organism must keep homeostasis while facing challenging stimuli known as stressors 4. Olive oil taken from a natural herb olive, constitutes different components such as mixed triglyceride, esters of oleic acid, palmitic acid and other fatty acids 5. It is also contains high amount of antioxidants and vitamins. Phenolic mixtures, polyphenols including esters of tyrosol and hydroxytyrosol (oleocanthal and oleuropein) possess neurodefensive properties 6, 7. Other phenolic constituents include aldehydic secoiridoids, flavonoids and lignans 8. Olive oil also contains monounsaturated fatty acids and have beneficial effects on health. The long chain omega 3 fatty acid, docosahexaenoic acid (DHA) provides neuroprotection against stress induced neurological impairments, inflammation, and apoptosis 9-11. High levels of unsaturated fatty acids in serum have protective roles against stress by decreasing the release of pro-inflammatory cytokines 12. Other component hydroxytyrosol present in olive oil acting as antioxidants have also been reported to defend against markers associated with antherogenic process13-15. Stress inducing situations may cause several changes in body and develops alterations in overall behavioral patterns in humans and animals. Extensive studies to investigate behavioral, neurological and biochemical changes following repeated administration of olive oil in various animal models has been described and it was found that olive oil possess analgesic, anxiolytic as well as antidepressant properties 16, 17. Previous work in our laboratory also elucidated the antidepressant and anxiolytic properties of olive oil and suggested that these effects may be due to changes in neurotransmission levels which were attenuated by the administration of olive oil in rats 18. In view of the previously reported studies on beneficial effects of olive oil, current study was planned to monitor effects of olive oil in animal model of learned helplessness. Therefore, in present study role of olive oil on exploratory activity, anxiety, depression and memory tasks in rats will be monitored.

MATERIALS AND METHODS

Animals

Locally breed male Albino Wistar rats were obtained from the ICCBS, University of Karachi, Pakistan weighing about 150-200 g. Animals were housed separately and allowed access for diet and water one week prior to the start of experiment so that rats get adopted themselves in the environment.

Protocol

The rats were categorized into 2 groups as control and olive oil treated. Each group was given with standard rodent diet. 0.3 ml/day tap water was given orally to control rats and 0.3 ml/day olive oil was administered orally to oil group for 3 weeks, food and water were accessible for 24 hours to each group. Treatment with olive oil continued for 21 days and after this period groups were further
categorized as unrestraint and restraint groups. Restraint group was given stress for 2 h / day for 2 days.

**Restraint Procedure**

After the completion of olive oil administration protocol, rats of restraint group (control and oil) were subjected to acute restraint stress (2 h /day for 2 days) in ventilated, closed plastic tubes with length of 20 cm and diameter of 6.5 cm that permit only restricted exploration. Unrestraint rats were kept in their home cages throughout the experimentation. Behaviors were monitored after 2 h of stress procedure.

**Behavioral Parameters**

24h after restraint stress behavioral activities of unrestrained and restrained animals were monitored. All experiments were carried out by the formal approval from the department ethical committee for animal care in agreement with NIH Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985).

**Open Field Test (OFT)**

OFT was used to monitor locomotion in rats. The method followed in current study was same as described previously. The parameter noted to observe exploratory activity were in terms of number of square crossed by rats as described in earlier studies.

**Forced Swim Test (FST)**

FST is the most accepted model for the assessment of depression in animals. In the present study the parameter noted was struggling by rats to observe depressive behavior, method was followed same as described and performed earlier in our laboratory.

**Light / Dark Activity Box**

Anxiety level in animal is observed by using light and dark activity box. Time expended in light box was noted, method was same as performed previously in our laboratory. Increased time of stay in light compartment will served as an index of decrease anxiety state in rats.

**Hot Plate Test**

The method of hot plate test used is same as described earlier. The apparatus consist of metal plate surrounded by a transparent cylinder. The metal plate is maintained at a constant temperature which can be varied between 50-55 °C. It seems to produce reliable and fairly stable pain threshold to measure analgesic activity. Animal to be tested is placed in a cylinder on metal plate. Most often the animal initial response is to sit on its hind legs and lick its fore paws. Decrease number of licks served as reduce pain threshold in rats.

**Water maze test**

Water maze test was performed in a similar manner as reported earlier. Time to reach hidden platform served memory retention in rats.

**Statistical Analysis**

Data is displayed as mean ± S.D. The software used for data analysis is SPSS Version 20. Two way analysis of variance (ANOVA) was done to understand the results of treatment between groups and Tukey’s post hoc analysis was done. The significance level was considered as p≤0.05.

**RESULTS**

The beneficial effects of olive oil on behavioral parameters in restraint rats were observed. Locomotor activity was observed by using OFT. In Fig. 1 significant effects of stress (F= 211.98; df=1, 20; p<0.01), olive oil (F= 168.471; df =1, 20; p<0.01), and non-significant relationship among stress and olive oil (F=2.866; df=1, 20; p>0.05) were observed. Tukey’s test shows decreases number of square crossed in 2 h restraint stress rats.

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**Figure 1:** Values are represented with mean + SD (n=6). Tukey’s test was performed and significant levels **p <0.01 from their relevant controls (water treated) while, ++p<0.01 from their relevant unrestraint controls.
Olive oil pretreatment significantly \((p < 0.01)\) increased number of square crossed in restraint as well as unrestraint rats when compared with control. Anxiolytic effects of olive oil in rats were observed by light/dark transition box. In Fig. 2 significant effects of stress \((F= 78.327; \text{df}=1, 20; p<0.01)\), olive oil \((F= 57.232; \text{df}=1, 20; p<0.01)\), and non-significant relationship among stress and olive oil \((F=0.722; \text{df}=1, 20; p>0.05)\) were observed. Tukey’s test shows decrease time spent in light box.

Olive oil pretreatment significantly \((p<0.01)\) increased time spent in light box in restraint and unrestraint rats when compared with respective control. This result shows the anxiolytic effect of olive oil. Forced swim test is suitable to monitor depressive behaviors in rats. In Fig. 3 non-significant effect of stress \((F= 3.419; \text{df}=1, 20; p>0.05)\), significant effects of olive oil \((F= 313.315; \text{df}=1, 20; p<0.01)\), and significant relationship among stress and olive oil \((F=145.019.; \text{df}=1, 20; p<0.01)\) were observed. Tukey’s test shows that 2 h restraint stress significantly \((p<0.01)\) increased number of licks in restraint rats.

Olive oil pretreatment significantly increases \((p<0.01)\) struggling time in restraint and unrestraint rats when compared with respective control. These results show the antidepressant properties of olive oil. Present study also investigates the analgesic activity of olive oil in rats by using Hot plate test. In Fig. 4 significant effect of stress \((F= 306.816; \text{df}=1, 20; p<0.05)\), olive oil \((F= 554.007; \text{df}=1, 20; p<0.01)\), and significant relationship among stress and olive oil \((F=145.019.; \text{df}=1, 20; p<0.01)\) were observed. Tukey’s test shows that 2 h restraint stress significantly \((p<0.01)\) increased number of licks in restraint rats.
Olive oil significantly (p<0.01) decreased number of licks in restraint rats. The effect of repeated administration of olive oil on memory and learning behaviors was monitored by water maze test. In Fig. 5 non-significant effect of stress (F=2.440; df=1, 20; p>0.05), significant effect of olive oil (F=275.043; df=1, 20; p<0.01), and significant relationship among stress and olive oil (F=13.198; df=1, 20; p<0.01) were observed. Tukey’s test shows that 2 h restraint stress significantly (p<0.01) increases the time to reach the hidden platform control rats. Olive oil pretreatment significantly reduced time to be placed on hidden platform in restraint and unrestraint rats when compared with respective control.

![Figure 5: Values are represented with mean ± SD (n=6). Tukey’s test was performed and significant levels **p <0.01 from their relevant controls (water treated) while, ++p<0.01 from their relevant unrestraint controls.](image)

**DISCUSSION**

Olive oil is widely used all over the world because of its advantageous health effects. The present study investigated that olive oil pretreatment might be useful in stress induced alterations in behaviors in rats. In present study 2 h restraint stress induced decrease in locomotor activity, increased anxiety and depression with concomitant impairment in memory state as well as increase in nociception were observed. Stress decreases exploratory activity of animals have also been stated earlier. However, increased locomotor activity after repetitive administration of olive oil has also been described. The restraint stress induced decrease in locomotor activity as evident by reduced number of squares crossed in OFT and increased anxiogenic behaviors with decrease time spent in light dark activity box were not observed in restraint rats pretreated with olive oil in present study. Changes in neurotransmitter levels contribute in the development of anxiety states. Stress increases serotonin levels in the brain, thereby causing fear and anxiety in animals. In present study it is suggested that anxiolytic effects of olive oil may be due to the modifications in 5-HT levels mainly by decreasing 5-HT levels in the brain. Olive oil decreases 5-HT levels were also observed in previous studies. Anxiety and depression are the most prevalent neuropsychiatric illnesses. Antioxidants have ability for removal of stress related generation of reactive oxygen species. Olive oil also serve as antioxidants as they are rich in polyphenol containing compounds oleic acid, tocopherols, oleuropein and unsaturated fatty acids and are suspected to reduce anxiety states in present study. Increased immobility time in FST observed in restraint stress was not observed in olive oil pretreated restraint stress suggesting their antidepressant actions. The ameliorative effects of Mediterranean dietary component containing polyunsaturated fatty acids in depression have been studied previously. In present study the antidepressant potential of olive oil as observed by increased struggling time in restraint rats might be due to the presence of omega 3 fatty acids. Studies in animal models reported that decrease in 5-HT levels contribute to the development of depression. Omega 3 fatty acids increase 5-HT levels and therefore suggested in present study that antidepressant actions of olive oil is due to the omega 3 fatty acids. Similarily linoleic acid, omega 6 poly unsaturated fatty acids present in olive oil also reduced symptoms of depression. Restraint stress induced depression and concomitant decline in cognition were observed in present study as restraint rats took more time to be placed on submerged unseen platform in water maze test. Stress related generation of oxidative species may disrupt neurons leading to memory impairments. It is therefore suggested that polyphenols may play contributing role in the
maintenance of neuronal integrity and improve cognitive and thinking processes. Outcomes of present study consistently support that olive oil improve memory functions and attenuate stress related memory dysfunction in rats. Strong analgesic activity of olive oil has been reported previously. Licking of paws, number of jumps and latency to lick indicates rat’s perception to pain. Stress inducing situation releases pain and inflammatory mediators and enhanced nociception. Potential analgesic properties of olive oil has been stated in different animal models. Results from the present study suggested that polyphenols produced analgesia via the inhibition of pain and inflammatory pathways. Analgesic properties of olive oil observed in present study are consistent with several other reported studies.

CONCLUSION

Results of present study show that olive oil attenuate stress induced behavioral deficits. Majority of the components present in olive oil are beneficial and provide positive outcomes in altered behaviors due to restraint stress. Results from present study suggested that olive oil exerts peripheral to central actions and it can be used as herbal therapy for various ailments. However, more studies are recommended to explain the particular action by which olive oil produces its effects on behavior.

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