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RESEARCH ARTICLE

EFFECT OF DARKNESS ON SEROTONIN LEVEL AND DEPRESSION AND COMPARISON BETWEEN DIFFERENT METHODS TO INCREASE SEROTONIN LEVEL AND IMPROVE MOOD COMPARED TO ANTIDEPRESSANT DRUGS

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ABSTRACT

Serotonin is a neurotransmitter which is hypothesized to affect mood. Darkness is suggested to affect the serotonin level greatly and hence mood. This work aimed to study the effect of prolonged darkness on serotonin level in blood and detect which method is best to over come its hazardous effect on mood, and whether excess feeding of carbohydrate and chocolate or exercise training or intermittent light exposure or all of them combined together can combate this hazardous effect compared to the use of antidepressant drugs.

Seventy rats were included in this study. They were divided into seven groups. The first group was the control group fed on normal chow. The groups from two to seven were subjected to complete darkness for one month. The second group was fed on normal chow. The third group werefed on excess carbohydrate and chocolate. The fourth group its rats were fed on normal chow and subjected all through the month to undergo exercise swimming for fifteen minutes every day in a shallow beaker. The fifth group its rats were fed on normal chow and subjected to light exposure episodes for fifteen minutes twice daily. The sixth group its rats were fed on excess carbohydrate and chocolate and undergo exercise swimming for fifteen minutes in a shallow beaker every day and they were subjected to light exposure episodes for fifteen minutes twice daily. The seventh group was fed on normal chow and its rats were given antidepressant drug Nardil at a dose of 5 mg/day for one month.

At the end of the month samples of blood were collected to measure serotonin level and all rats were subjected to drowning in a deep beaker filled with water and time to resist drowning was detected for each group. Rats of each group were sacrificed and histologic slides were made to show the effect of serotonin on the brain tissue. There was significant decrease of the serotonin level and time to resist drowning in the second group compared to control group. There was a non significant increase in the serotonin level and time to resist drowning in the third group as well as in the fourth and fifth compared to the second group. There was a significant increase in the serotonin level and time to resist drowning in the sixth group compared to the second group. There was a non significant increase in serotonin level and time to resist drowning in the seventh group compared to third group as well as with the fourth and fifth groups There was a significant increase in the serotonin level and time to resist drowning in the seventh group subjected to complete darkness and fed on normal chow and given antidepressant drug Nardil at a dose of 5 mg/day for one month compared to the second group fed on normal chow and subjected to complete darkness for one month. There was a significant increase in the serotonin level and time to resist drowning in the sixth group compared to the seventh group. **Conclusion:** continuous darkness may decrease serotonin level in blood and hence may cause depression. combined effect of eating excess carbohydrates and chocolate and daily exercise for fifteen minutes and exposure to light may be beneficial to increase serotonin level and hence affect mood positively and overcome depression even more than antidepressant drugs.

INTRODUCTION

Serotonin is a chemical transmitterthat helps the relay of signals from one area of the brain to another (1). It is manufactured in the brain, where it performs its primary functions (2).

Serotonin is made via a conversion process which begins with tryptophan. Cells that make serotonin use tryptophan hydroxylase, a chemical reactor which, when combined with

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tryptophan, forms the 5-hydroxytryptamine, known as serotonin (3).

Serotonin cannot cross the blood-brain barrier. Therefore serotonin that is used inside the brain must be produced within it (4).

Serotonin is believed to influence a variety of psychological and other body functions. Most of the cells are influenced either directly or indirectly by serotonin, including the brain cells related to mood, sexual desire and function, appetite, sleep, memory and learning, temperature regulation, and some social behavior (5).

It is to be believed that any imbalance in the serotonin levels may influence the mood in a way that may lead to depression. There are many conditions which may affect serotonin and cause depression as in cases of low production of serotonin by the brain cells, lack of receptors for serotonin, inability of serotonin to reach the receptor sites, or a shortage in tryptophan, the chemical from which serotonin is made (6).

It is to be documented that depression may occur when there is a suppression of new brain cells and that stress is the most important precipitator of depression. There for It is believed that common antidepressant medications, such as Celexa, Lexapro, Prozac, Paxil and Zoloft, are designed to increase the serotonin levels, and help to increase the production of new brain cells, which in turn helps to decrease the depression (7). Although it is widely believed that serotonin deficiency plays a role in depression, there is no way to measure its levels in the living brain. Blood levels of serotonin are measurable, and have been shown to be lower in people who suffer from depression (8).

The antidepressant drugs that work on serotonin levels as SSRIs (selective serotonin reuptake inhibitors) are believed to decrease the symptoms of depression, but the exact mode of work is not yet fully understood (9).

It is to be documented that the diet we have can influence our supply of serotonin, but there are no foods that can directly increase our body's serotonin ,on the other hand there are foods and nutrients that can increase levels of tryptophan, the amino acid from which serotonin is made (10).

Tryptophan appears to be present sufficiently in protein-rich foods, such as meat and chicken, and in dairy foods, nuts, and fowl. Nutritionists believe that when you eat a high-protein meal, you fill the blood with both tryptophan and its competing amino acids," all fighting for entry into the brain. That means only a small amount of tryptophan will be able to get through - and thus serotonin levels don't rise much (11).

On eating a carbohydrate-rich meal, insulin release is triggered which causesmany amino acids in the blood to be absorbed into the body but not to the brain (12). Exceptionally the tryptophan, remains in the bloodstream at high levels following a carbohydrate meal, which means that it can freely enter the brain and causes serotonin levels to increase (13).This is why it is hypothesized that excess carbohydrates can increase serotonin and hence affect mood positively (14), and also why people on regular diet excluding carbohydrates for long time may feel depressed after time (15).

Exercise can affect mood positively. Many studies have shown that regular exercise can be an effective treatment for depression (16). It is to be considered that 40-minute period of exercise can have an immediate effect on mood (17).

Exercise and its duration is believed to affect serotonin levelin blood and hence mood (17).

It is to be assured that light exposure may affect level of serotonin and hence affect mood. Depression is somehow triggered by the brain's response to decreased daylight exposure (18).

Experts think that there are two specific chemicals in the brain, which are the melatonin and serotonin. They are involved in the seasonal affective disorders and help to regulate person's sleep-wake cycles, energy, and mood. Shorter days and longer hours of darkness in fall and winter may cause increased levels of melatonin and decreased levels of serotonin, creating the biological conditions for depression (18).

Studies show that men do have slightly more serotonin than women. It is to be considered that there might be a huge difference in how men and women react to the reduction in serotonin, and this might be one reason why women suffer from depression far more than men (18).Using a technique called "tryptophan depletion," which reduces serotonin levels in the brain, researchers found that on reduction of the serotonin levels men may become impulsive but not necessarily depressed (19).

On the other hand women, may experience a marked drop in mood and become more cautious, an emotional response commonly associated with depression (20). It is to be believed that women may use serotonin in a different way than men (20).This may explain why more women than men may experience anxiety and mood disorders (21).

There is also some evidence that female hormones may also interact with serotonin to cause some symptoms to occur during the premenstrual time, the postpartum period, or around the time of menopause (22).

Serotonin is generally useful but a rare side effect of increased serotonin is called serotonin syndrome which occur when levels of this neurochemical in the brain rise too high. It happens most often when two or more drugs increasing serotonin levels are used simultaneously (23).

MATERIAL AND METHODS

Seventy white male albino rats aged one month and weighed (150-170 grams) were included in the present study which began by the end of january 2015. They were obtained from the animal house in the Baterjee medical research center at the Baterjee medical college in Jeddah and were housed in wire

mesh cages at room temperature and maintained on normal chow and had free access to water.

The rats were divided into seven groups, each group contained ten rats

Group one: Control group fed on normal chow.
Group two: Fed on normal chow and were subjected to complete darkness for one month.
Group three: subjected to complete darkness and fed on excess carbohydrate and chocolate for one month.
Group four: subjected to complete darkness and undergo exercise swimming in shallow beaker for fifteen minutes every day for one month.
Group five: subjected to complete darkness for one month and through this month the rats were subjected to light exposure episodes for fifteen minutes twice daily.
Group six: subjected to complete darkness for one month and through this month the rats were fed on excess carbohydrate and chocolate and undergo exercise swimming for fifteen minutes in a shallow beaker every day and they were subjected to light exposure episodes for fifteen minutes twice daily.
Group seven: fed on normal how and its rats were subjected to complete darkness for one month and they were given antidepressant drug Nardil at a dose of 5 mg/day for one month.

Blood samples were taken at the end of experimental period for determination of serotonin level in blood.

Exercise was done for the fourth group by minimizing the light in the lab to minimal and then the rats were subjected to swim in a shallow beaker put under cover of a cartoon cap to ensure darkness for 15 minutes every day for one month (24).

At the end of the experimental period rats of all groups were put in deep baker filled with water put under the cartoon cap and time to resist drowning was calculated for each group (25).

Rats of group five were subjected to day light for fifteen minutes every day and to white light for fifteen minutes every day during night.

Antidepressant drug Nardilpresent in the market was given to the rats of group seven orally at a dose of5 mg/day. At the end of the experiment rats of all groups were sacrificed and brains were harvested for histopathologic examination as the brain tissue were fixed in 10% buffered neutral formal saline solution then after fixation tissues were embedded in paraffin.

Solid sections were cut at four micro meter and stained with haematoxylin and eosin. The sections were examined under light microscope and photomicrographs were taken.

Statistical analysis

The data were encoded and entered using the statistical package SPSS version 15. The data were summarized using mean, comparison between studied groups was done using unpaired t-test. P value < 0.05 were considered statistically significant.

RESULTS

The obtained results showed significant decrease in the serotonin level in blood and time to resist drowning in group two subjected to complete darkness compared to control group.

The obtained results showed non significant increase in serotonin levels and time to resist drowning in group three fed on excess carbohydrates and chocolate and group four fed on normal chow and subjected to exercise swimming for fifteen minutes per day and group five fed on normal chow and subjected to light exposure for fifteen minutes twice times per day all compared to group two subjected to complete darkness and fed on normal chow.

The study showed significant increase in the serotonin level in blood and time to resist drowning in groupsix subjected to completedarkness and fed on excess carbohydrates and chocolate and subjected to exercise swimming for fifteen minutes every day and subjected to light exposure for fifteen minutes twice daily compared to group two subjected to complete darkness and fed on normal chow.

The study showed significant increase in serotonin level and time to resist drowning in group seven subjected to complete darkness and fed on normal chow and was given the antidepressant drug Nardilcompared to group two fed on normal chow and subjected to complete darkness.

The study showed non significant increase in serotonin level and time to resist drowning in group seven compared to group three subjected to darkness and fed on excess carbohydrates and chocolate and group four subjected to darkness and fed on normal chow and subjected to exercise swimming and group five subjected to darkness and subjected to light exposure per day.

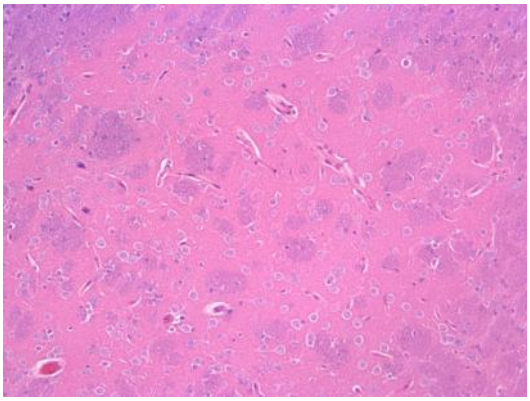
The results of the study showed a significant increase in serotonin level and time to resist drowning in group six subjected to complete darkness and fed on excess carbohydrates and subjected to exercise swimming and light exposure compared to group seven subjected to darkness and fed on normal chow and was given the antidepressant drug.

Table 1 The serotonin levels in blood and time to resist drowning for the seven groups.

	Control group	Second group	Third group	Fourth group	Fifth group	Sixth group	Seventh group
Serotonin level (mg/day)	166	89*	115	105	102	145*	125*
Time to resist drowning (minutes)	4.25	2.36*	3.10	2.58	2.50	3.57*	4.10*

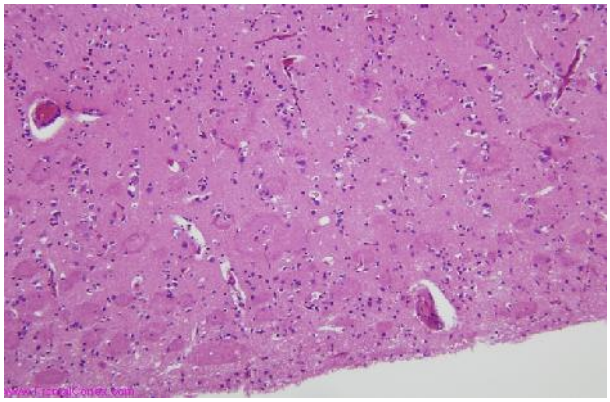
* Significant (*P* value < 0.05)

Slide 1



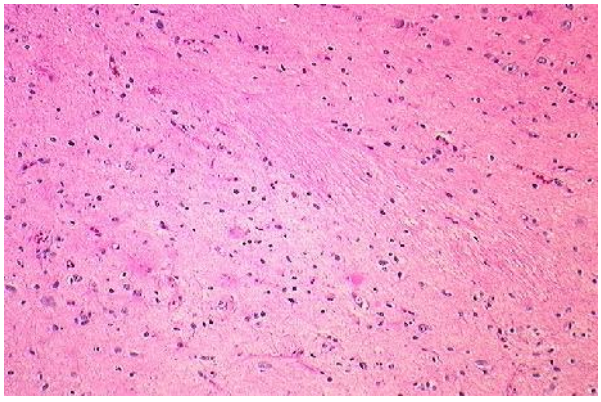
Histologic observation in the brain tissue of the control group of rats showing normal structure.

Slide 2



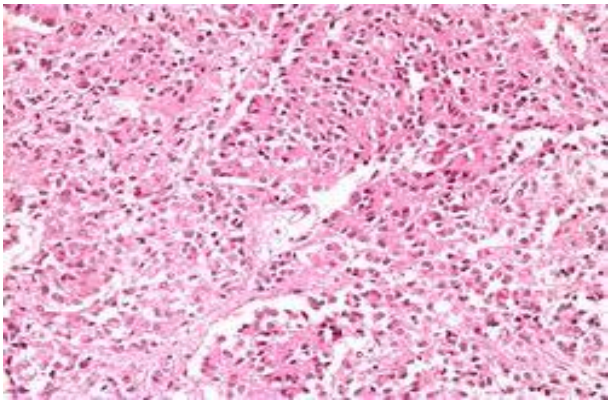
Histopathologic slide of rat brain of group two subjected to complete darkness showing degeneration of axon terminal and cell body and striation and decrease cellularity consistent with depression and stupor.

Slide 3



Histopathologic slide of rat brain of group six subjected to complete darkness and fed on excess carbohydrates and undergo exercise swimming every day and subjected to light exposure for fifteen minutes daily showing returning increased cellularity, numerous glial cells and tissue resembles normal.

Slide 4



Histopathologic slide of rat brain of group seven subjected to complete darkness and given antidepressants or subjected to complete darkness and fed on excess carbohydrates and undergo exercise swimming every day and subjected to light exposure for fifteen minutes daily showing returning increased cellularity, numerous glial cells and tissue resembles normal.

DISCUSSION

The objective of the present study was to find the effect of darkness on serotonin level and hence on mood and find out whether excess feeding of carbohydrate and chocolate or exercise training or intermittent light exposure or all of them combined together can combate its hazardous effect compared to the use of antidepressant drugs.

The results of the study showed that prolonged darkness may exert a hazardous effect on mood through decreasing serotonin level the condition which may lead to depression and may earge persons even to commit suicide. These results are consistent with the results of Burger and his colleagues where they stated that people in countries subjected to prolonged months of darkness may suffer seasonal affective disorders (S.A.D.) due to this darkness and that they are among the largest consumers for the antidepressant drugs in the whole world and that these countries have the highest percentage of those persons who commit suicide world wide.

The results of the study showed that excess feeding of carbohydrates as well as exercise swimming and light exposure per day may have a beneficial effect on serotonin level and hence on mood improvement yet any of them is not sufficient alone. On the other hand the study showed that the combined effect of excess carbohydrates and exercise swimming and light exposure may bebeneficial against the hazardous effect of darkness. This is consistent with the results of Kang and his colleagues where they stated that people living in areas having long times of darkness along the year should consume larger amounts of carbohydrates and undergo exercise and subject themselves to light intermittently along the day to increase the serotonin level and protect themselves from depression which they may suffer due to the prolonged darkness.

It is to be documented that Serotonin-releasing brain neurons are unique in that the amount of neurotransmitter they release is normally controlled by food intake where Carbohydrate

consumption--acting via insulin secretion and increasing plasma tryptophan ratio to increase serotonin release. Carbohydrates, when digested by the body, are effectively broken down into sugar molecules. When these molecules are absorbed and released in the bloodstream, blood concentration of glucose increases. Almost immediately, there will be a significant increase in plasma insulin levels as a result of the pancreas releasing its stored insulin. Insulin then steps in to do what it is genetically program to do--it breaks it down some more to produce energy and transport the extra glucose from the blood to the body cells. Insulin then makes it easy for tryptophan to enter the brain by eliminating its other amino acid competitors (28).

Tryptophan, which is an important ingredient in serotonin synthesis, is one of the substances allowed by the brain to enter from the blood. Tryptophan is the less occurring amino acid in the body and competes with the other amino acids in entering the blood-brain barrier. It was observed that the concentration of the majority of the amino acids, including alanine and glutamine, are significantly reduced each time insulin is secreted. Tryptophan is then able to enter the brain at a higher rate. An increased level of tryptophan in the brain means more available tryptophan for conversion. Tryptophan then undergoes hydroxylation to serotonin (28).

The existence of a retinoraphe tract may help to explain why, in experimental animals, neuronal firing rates, and the serotonin content in the raphe nuclei are responsive to retinal light exposure (29).

Lamps designed for the treatment of seasonal affective disorder, which provide more light than is ever achieved by normal indoor lighting, are readily available, although incorporating their use into a daily routine may be a challenge for some. However, other strategies, both personal and institutional, exist. “Light cafes” pioneered in Scandinavia have come to the United Kingdom and an Austrian village that receives no sunshine in the winter because of its surrounding mountains is building a series of giant mirrors to reflect sunlight into the valley (29).

The study showed that the use of antidepressant drugs although it may exert a beneficial effect to improve serotonin and hence improve mood as shown in the results where group seven given antidepressant drug Nardil showed significant increase in serotonin level and time to resist drowning compared to group two fed on normal chow and subjected to complete darkness. yet this increase was non significant when compared to the results recorded for group three fed on excess carbohydrates, and groups four and five subjected to exercise swimming and light exposure respectively indicating that the increase in serotonin and time to resist drowning exerted by the carbohydrates and light exposure and exercise swimming each of them alone was much high to the extent that make the increase exerted by the antidepressant drugs when compared to them non significant.

It is to be documented that physical activity increases serotonin but it is not clear whether this may be due to increased serotonin turnover or due to mixing of CSF from higher regions, which contain higher levels of serotonnin, with lumbar CSF or to the combination of both mechanisms. Young and colleagues showed that exercise increased tryptophan and serotonin in rat ventricles. More recent studies have shown that exercise increases extracellular serotonin in various brain areas, including the hippocampus and cortex. Two different mechanisms may be involved in this effect. It is to be documented that motor activity increases the firing rates of serotonin neurons, and this results in increased release and synthesis of serotonin. In addition, there is an increase in the the serotonin precursor tryptophan that persists after exercise(30).

The study showed that the combined effect of excess carbohydrates and exercise swimming and light exposure may be even much more beneficial to increase serotonin level and improve mood and combat depression even more than the antidepressant drugs as the study showed that group six subjected to complete darkness and fed on excess carbohydrates and subjected to exercise swimming and subjected to light for fifteen minutes every day recorded a significant increase in the serotonin level and time to resist drowning compared to group seven fed on normal chow and subjected to darkness and given the antidepressant drug Nardil. The study reveals the need for exercise training to be done on regular basis and light exposure and consumption of considerable amounts of carbohydrates daily to combat depression and improve mood.

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