Antidepressant effect of bright white LED combined with classical music

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Abstract: The treatment of bright white LED combined with classical music was proposed by laboratory mice. Mice suffered from chronic mild stress were divided randomly into three groups and exposed to 12: 12 h bright light:dark (350 lx) conditions. The control group (C) received no treatment. The classical music group (M) was treated with classical music of 2 h per day. The classical music + bright light group (M+B) was treated daily with classical music of 2 h and 5 000 lx white LED light. Thirty days later, depression-like behaviors were assessed using saccharin solution preferences and forced swim tests. Mice in M and M+B demonstrated signi cantly shorter immobility times and longer climbing times and swimming times compared to those in C (p<0.001). It was observed that M+B experienced shorter immobility times (52.3±25.18 s) than M (78.9±14.82 s), and there was significant difference between two groups(t(9)=3.414, p=0.008<0.05). The combination therapy of bright white LED and classical music raised the vitality of mice and possessed antidepressant effect.

Key words: bright white LED; classical music; depression; photoperiod

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亮白光 LED 结合古典音乐疗法的抗抑郁效果

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摘 要: 通过小鼠实验提出了一种亮白光 LED 联合古典音乐疗法。遭受过慢性不可预知性应激的小鼠被随机分成 3 组,均饲养在 350 lx、光周期为 12 小时明亮 12 小时黑暗的环境中。对照组(C):不做任何处理。五行音乐组(M):每天播放 2 个小时古典音乐。五行音乐+光照组(M+B):每天播放 2 小时古典音乐并采用 5 000 lx 的白光 LED 照射。30 天后用糖水偏爱度测试和强迫游泳实验来评估抑郁程度。与 C 组相比,M 和 M+B 组的小鼠表现出更短的游泳不动时间和更长的游泳和攀爬时间 (p<0.001)。M+B 组小鼠的游泳不动时间(52.3±25.18 s)要短于 M 组(78.9±14.82 s),且差异存在统计学意义(t(9)=3.414, p=0.008<0.05)。亮白光 LED 联合古典音乐疗法能够提高应激小鼠的活力,具有一定的抗抑郁作用。

关键词: 亮白光 LED; 古典乐; 抑郁症; 光周期

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0 Introduction

Depression is a common disorder, with significant and long-lasting low mood as the main clinical feature. Seasonal affective disorder (SAD) is exacerbated in winter and alleviated in summer. However, non-seasonal depression is much more common, with chronic and recurrent symptoms, along with serious consequences such as suicide. The pervasive competition has increased the number of people with depression. Depression has become the world′s fourth most common disease and, by 2020, might become the second most common human disease after cardiovascular disease. Therefore, depression must be treated as much as possible.

Previous studies have shown that distur-bances in brain serotonin systems, melatonin secretion, and circadian rhythms may influence the symptoms of depression[1]. Investigations revealed that most of depression patients had sleep disorders which is the expression of circadian rhythm disorders. Rhythmical melatonin secretion can adjust circadian rhythm. Instability of melatonin can lead to endogenous depression. Even so, it seems that there are still other neural pathways that contribute to depression, and the exact pathogenesis is complex. Accordingly, the treatment of depression is challenging.

Antidepressants are the most commonly used for depression nowadays. However, anti-depressants have side effects, which affect physical health. Light therapy, a non-pharmaceutical treatment, is initially used to treat SAD, as some studies report that bright light apparently helps influence the brain′s production of melatonin then can alleviate depression caused by SAD[2]. However, the use of light therapy in treating non-SAD remains controversial. Besides, the existing res-earch used cool white fluorescent for treatment. Fluorescent lamp contains ultraviolet light, which is not only without effect upon the mood but also harmful to human. While LED contains no ultra-violet, is safe and environmental [3], which makes up the defect of fluorescent lamp. Therefore, LED as a photosource for alleviating symptoms of depression is very promising.

Currently, music therapy and phototherapy are used separately to treat depression, but there are no studies on their combined effect. The present study was therefore designed to explore the effects of bright white LED combined with classical music treatment on mammals maintained in chronic mild stress and to develop a safer and more effective therapy for depression.

1 Materials and methods

1.1 Animals

Fortytwo KM male mice (3 weeks old) weighing 25.17 ±0.34 g were purchased from Shanghai Laboratory Animal Center (SLAC) Laboratory Animal Co., Ltd. The animals were housed in the plastic cages. One was excluded due to the disease in the process of breeding.

1.2 Chronic mild stress procedure

All mice were exposed to chronic mild stress (CMS) stimulations. The six stimulations were: 95 dB noise of 8 h, horizontal oscillation of 3 min, continuous light of 36 h, food and water deprivation of 24 h, tilted cage (45°) of 24 h , and a reversed light cycle with lights on at 19:00. Each day consisted of two CMS stimulation and every stimulation was utilized discontinueously. Mice were maintained in the unpredictable stimulations for 12 days.

1.3 Animal feeding and grouping

All mice were housed in a 12:12 h bright light:dark (light on at 07:00) environment. Light was supplied by cool white LEDs and the light intensity at cage level was approximately 350 lx.

The environment temperature was 20±2° C with 60±10% relative humidity. Food and water were provided ad libitum except when the CMS procedure required deprivation. After 12 days of CMS, mice were randomly divided into three groups. In the control group (C), mice were maintained in the above-mentioned conditions, untreated. In the classical music group (M), mice were treated daily with Chinese classical music of 2 h (′Ambush From All Sides′ and ′Plum Blossom Melody′, volume approximately 50 dB). Each song was played on alternating days. In the classical music + bright light group (M+B), mice were treated daily with classical music and bright white LED light of 2 h (5 000 lx, started at 09:30 am). Following 4 weeks of treatment, all mice underwent two behavioral tests to quantify depression levels.

1.4 Behavioral testing

1.4.1 Saccharin solution preference test

Saccharin solution preference test (SSP) is generally used to evaluate anhedonia of depression model mice. Animals were adapted to the sugary drink 24 hours before the experiment and each cage was supplied with two bottles of 1% saccharin solution dissolved in tap water, on top of the regular supply of food. After 24 h each cage was provided with a bottle containing 1% saccharin solution and a bottle of tap water. Two bottles were weighed at the beginning of the experiment and again after 24 h. The test started around 30 min after the treatment. The ratio of saccharin solution consumption and total liquid consumption was used to calculate saccharin solution preference. SSP was performed on the twenty-ninth day of treatment.

1.4.2 Forced swim test

The forced swim test (FST) is among the most frequently used model for antidepressant effects of manipulations and treatments in mice. Here, each mouse was placed into the transparent cylindrical tank, 20 cm in diameter and 20 cm high. The tank was filled with water (25±1°C) to a depth of 10 cm. Mice individually swam for 8 min and the immobility time, climbing time and swimming time of 3-8 min was calculated. Mice were tested in alternating order from the three groups. FST started approximately 30 min after the treatment on the thirtieth day.

1.4.3 Statistical analysis

Data from the experiment were analyzed using a student′s t-test and analysis of variance (ANOVA) in Statistica 19.0 software. Data were expressed as mean ±SD or % and statistical significance was set at $p<0.05$.

2 Results

2.1 Saccharin solution preference

The light or music treatment had no effect on SSP (as shown in Tab.1). Mice in M+B and M slightly increased their saccharin consumption than those in C, while there was no significant difference among three groups ($p>0.05$).

2.2 Weights

After CMS, the measured weight of mice was 30.12±2.21 g. The weight of mice in M+B and M was slightly higher than those in C at the end of experiment (as shown in Tab.1). However, differences between three groups was not statistically significant ($F(2,38)=1.698$, $p=0.197$).

Tab.1 Behavioral tests of mice in each group

Test	M+B	M	C	Statistic
Weight/g	48.71±3.58	48.38±4.23	46.31±2.97	$F(2,38)=1.698$, $p=0.197$
Saccharin consumption	45.60±13.30	46.07±6.07	41.40±9.56	$F(2,6)=0.194$, $p=0.828$
Water consumption	48.71±3.58	48.71±3.58	48.71±3.58	$F(2,6)=0.848$, $p=0.474$
Saccharin preference	95.7%	96.8%	91.9%	$F(2,6)=0.805$, $p=0.49$

2.3 Forced swim test

Mice in C showed significantly higher immobility time compared to those in M+B ($t(9)$= 11.552, p<0.001) and M($t(9)$=6.797, p<0.001) (as shown in Tab.2, Fig.1). The frequency of climbing and swimming behavior increased obviously in M+B ($t(9)$=7.416, p<0.001; $t(9)$=4.75, p=0.001) and M($t(9)$=2.352, p=0.043<0.05; $t(9)$=4.717, p= 0.001) relative to C, and the climbing time of mice in M+B was almost twice as much as those in C. Moreover, the immobility time for mice in M+B was lower than those in M, and significant difference was observed between two groups ($t(9)$= 3.414, p= 0.008<0.05).

Tab.2 Time required for each state of mice for the forced swim test in three groups

Test	M+B	M	C
Immobility	52.3±25.18**	78.9±14.82**	157.2±36.41
Climbin	116.4±29.87**	88.6±22.02*	59.9±24.42
Swimming	131.3±29.10**	132.5±33.10**	82.9±19.19

Compared to a control group, * indicated significant difference (p<0.05) and ** indicated significant difference (p<0.001).

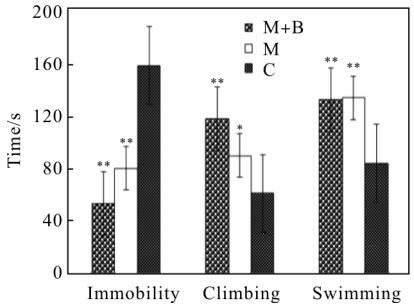

Fig.1 Time required for each state of mice for the forced swim test in three groups

3 Discussion

KM mice were treated with bright light combined with classical music. The SSP test and the FST were used to evaluate mice for anhedonia and antidepressant-like effects, respectively. The test results indicated that the bright white LED treatment in conjunction with classical music slightly increased saccharin consumption but not statistically significant (p > 0.05). Whereas, the FST immobility time of mice exposed to the same conditions was significantly reduced, and the immobility time of mice in the combined treatment group was significantly lower than those in the classical music group. In addition, the climbing time of mice treated by combined therapy was nearly twice as much as those in the group with no treatment, which means that bright white LED combined with classical music had an antidepressant-like effect in the FST, but they did not affect the SSP. SSP was not successful every time, as constant saccharin consumption was observed in some experiments [4]. While some studies have shown that mice′s response to saccharin solution intake can be quick to adapt, this remains to be confirmed. Meanwhile, there were individual differences in the sensitivity of mice to treatment. Mice were not isolated in the SSP due to experimental conditions, and the resulting deviation in measured data was so large that measurements could not reflect the therapeutic effect precisely.

Test results indicated that both bright white LED and classical music could alleviate symptoms of depression. Although it is only reflected in the FST, we cannot deny potential antidepressant effect of combination treatment. For this study, we chose two songs belong to Gong tone and Yu tone of five-element music separately. Compared with other music therapy, five-element music therapy is a kind of special music prescription based on the theory of TCM. The five musical tones correspond to the five internal organs and can relieve uneasiness of mind and body. Several studies have shown that the vibration of sound

waves was received by body through the conduction of bone, soft tissue and meridian, so as to affect the human heart rate, respiration and blood pressure, etc. This is the theoretical basis of five-element music therapy regulate mood. Previous research has shown that the concentration of 5-HT and noradrenaline (NE) are directly related to depression [5], and that five-element music increases the concentration of 5-HT and NE in the brain [6]. Therefore, we speculated that classical music regulates central nervous activeities by promoting the secretion of 5-HT to stimulate the locus coeruleus to secrete NE, which in turn alleviates depression. The rate of production of 5-HT by the brain was directly related to the prevailing duration of bright light, and rose rapidly with increased luminosity. Furthermore, there is evidence to show that human circadian rhythm disorders could cause depression. Melatonin controls circadian rhythm and bright white LED significantly affect the secretion of melatonin [3]. Photic information is passed on to the suprachiasmatic nucleus by a direct retinal projection, then is relayed to the retinohypothalamic tract and the pineal gland through specific neu ral pathways. The pineal gland produces rhythmic melatonin by a circadian rhythm of the activity of pineal N-acetyl-transferase, which synthesizes the N-acetyl-serotonin . Accordingly, bright light may work via melatonin, which can generate phase shifting or synchronize the internal clock. Although the specific therapeutic mechanism is extremely complex and remains to be studied further, combined treatment with bright white LED and classical music is more effective than either therapy alone, based on our test results.

4 Conclusions

The combination therapy of bright white LED and classical music has an antidepressant effect and alleviates symptoms of depression. This combined therapy might reduce the level of depression by changing the concentration of 5-HT, NE and melatonin in the brain to regulate the central nervous activities and circadian rhythms. Following 30 days of treatment, the immobility time of mice in M+B shortened compared to those in M which means that the emotion has meliorated in mice. Kronfeldschor expressed that mice need a period of time for physiological acclimation to a new condition [7], the effect of combination therapy might improve if the duration of treatment is extended. Although combination therapy effect is weaker than antidepressants, its curative effect is still obvious. It is safe without side effects of antidepressants. Therefore, we hold the opinion that combined therapy of bright white LED and classical music will be an excellent candidate for treatment of seasonal and non-seasonal depression in the near future.

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