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Mozart's or murotal, which is more effective for spatial memory? an experimental study on mice (*Mus musculus*)

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ABSTRACT

Introduction: Many studies have found the effect of Mozart's music on the spatial memory of humans, but there are still very few studies that examine the effect of the Murotal Alquran approach on spatial memory improvement. This study aimed to evaluate the effect of Mozart's classical music and the Murotal approach on improving spatial memory in mice. This is an experimental study with 24 adult BALB/c male mice.

Method: The mice were divided into four groups: K (untreated control), P1 (Murotal approach with surah *Al-Fatihah* and *Al-Baqarah by Qori' Al-Mathrud*), P2 (Mozart's classical music approach "Sonata in D for two pianos KV448-Allegro con spirito"), and P3 (combined approach). Each group was placed in a cage and treated for 2 hours/day for 20 days. The memory level was measured with an eight-arm radial maze instrument for ten days. The data were analyzed with non-parametric Kruskal Wallis and Mann-Whitney tests.

Result: This study found there were no significant differences between groups toward increasing spatial memory. The highest and fastest memory score was in the P3 group compared to the others.

Conclusion: There is no difference in the effect between classical music Mozart's and Murotal approach on increasing the spatial memory of mice (Mus musculus), but mice given a combination of approaches have a better level of spatial memory with a higher level of aggressiveness.

Keywords: mice, Mozart's classical music, Murotal Alquran, spatial memory, therapy.
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INTRODUCTION

Memory is a complex biological function that combines several neural networks.[1] The role of memory is very important for human life as a bridge to record and recall all forms of information for decision-making in solving a problem. Memory itself is formed from the process of repeated learning of the information obtained.[2] The type of memory was divided into two, namely declarative memory (explicit) and non-declarative memory (implicit). One form of declarative memory that is related to the ability to remember space fields, recognize shapes, distances, and areas, and know the direction or position of a person is spatial memory. Uniquely in rodents, spatial memory is considered the equivalent of human declarative memory. Two structures in the brain that have the most important role in the formation of spatial memory are the entorhinal cortex (EC) and the hippocampus (especially in the CA1 and CA3 hippocampus regions) as sites of memory formation, memory consolidation, and memory optimization during sleep.[1]

A previous study stated that the provision of classical music stimulated Mozart's Sonata K-488 in mice succeeded in significantly improving short-term memory. Research by Suteja Putra et al. (2018) stated that giving Murotal audio to human respondents significantly increased short-term memory.[3] However, the research of Suteja Putra et al. (2018) has the possibility of bias, especially towards the level of knowledge, the majority of respondents are Muslim, and age (performance bias).[4,5] Previous studies have shown that Murotal can improve depressive behavior in mice[6] as well as increase immunity in mice with breast cancer models.[7] These studies may have answered the bias, but further research on Murotal Alquran is still needed.

Muslims have known the Alquran for a long time as an effective treatment method, as is the case with the classical music approach in curing various diseases, especially psychological diseases.[8] Our previous study showed that stress and depression are associated with a decrease in brain-derived neurotrophic factor (BDNF), resulting in decreased memory skills which may be related to brain neuroplasticity.[9] This condition causes individuals to be less able to make reward predictions to feel motivated. Music acts as an external stimulus that may help individuals escape the downward spiral due to the loss of motivation. Mozart's classical music and Murotal have been proven to have an influence on the human body's work system in reducing stress

levels and creating inner peace. The calm created by music and the Murotal approach is good for memory formation, absorbing information, doing therapy, accelerating the healing process, increasing immunity, and also reducing stress.[10,11]

This study examines the effect of exposure to the classical music of Mozart and Murotal on the level of spatial memory in mice (mus musculus). This study uses classical music, "Sonata in D for two pianos KV448-Allegro con spirito" and Murotal Alquran *surah Al-Fatihah* and *Al-Baqarah* by *Qori' Al-Mathrud* which has a calming and relaxing effect. This relaxed state will further facilitate the learning process of absorbing information and even being able to create a conducive learning atmosphere.

RESEARCH METHODS

Research Design

This is a true experimental study with a post-test-only control group design approach. Male mice (Mus musculus) strain BALB/c aged 10-12 weeks were used in this study. According to Federer's formula, it takes 24 mice which are divided into 4 groups (Figure 1).

Procedure

Mice were divided into 4 groups: K (control without treatment), P1 (Murotal Alquran), P2 (Mozart's), and P3 (combined approach of Murotal Alquran and Mozart's). The mice were placed in a plastic cage with a music box above the cage at an effective distance of about 40 cm. Mice were treated for two hours/day for 20 days. The mice were adapted to a radial maze on days 18, 19, and 20, respectively (Figure 2).

Data Collection

Observation data were collected through mice daily observation before and after the intervention. Mice memory and test duration were measured using a radial eight-arm maze instrument for 10 days (Figure 3). To find out the memory score of each mouse, the memory score formula was used as follows[12]:

$$\text{Memory Score} = \frac{\text{correct number of arms} - (\text{wrong number of arms})}{\text{correct number of arms} + (\text{wrong number of arms})}$$

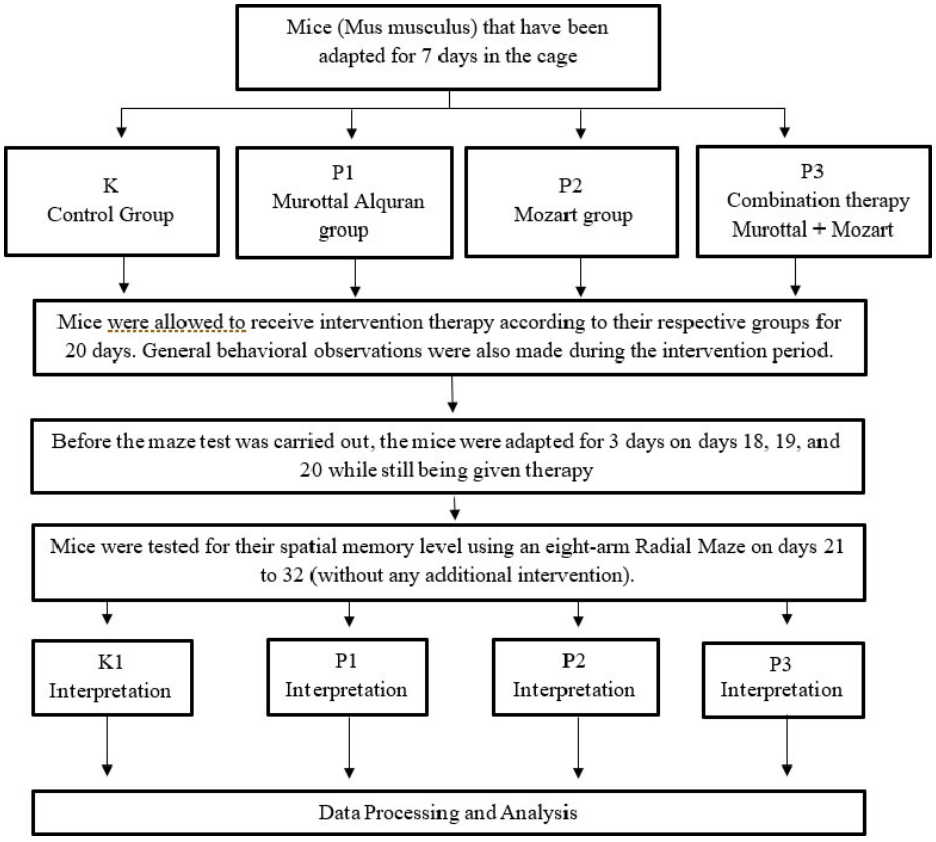

Figure 1. Research Framework.

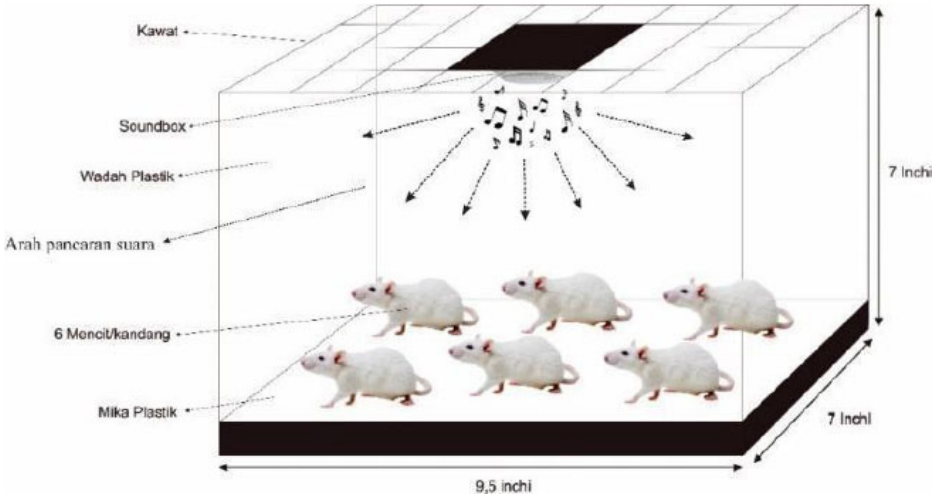

Figure 2. Mice Research Cage.

The maximum memory score that can be obtained is 1. The closer to 1 means the better spatial memory of the experimental animals being tested.

Data Analysis

Data analysis was carried out using the one-way ANOVA parametric test if the data were normally distributed and the Mann-Whitney test if the data were not normally distributed. Data were analyzed with significance ($P<0.05$).

RESULT

Subject Characteristics

Observation data showed that mice induced by the murotal approach tended to be calmer and less aggressive than other groups. Meanwhile, the combination group had the most aggressive and hyperactive tendencies, as evidenced by the injuries found in almost every combination treatment group (Table 1).

Furthermore, the mice were tested using a radial eight-arm maze instrument to determine the level of spatial memory for each treatment group. During the radial maze test, mice intentionally fasted for 12 hours to trigger reward and punishment mechanisms in the limbic system that were shown to correlate with memory ability. During data collection, two mice in the combined and control groups were excluded for cannibalistic behavior. In contrast, the Murotal and Mozart's groups did not get a dropout sample at the time of data collection.

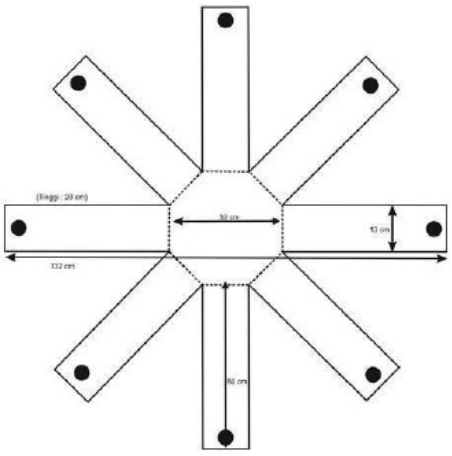

Figure 3. Radial Eight-Arms Maze.

Table 1. Results of general behavioral observations during the treatment intervention period

Groups	n	General Behavior	
		Aggressiveness	Agility
K	6	++	++
P1	6	-	+
P2	6	+	++
P3	6	+++	+++

Note: Description: + (low), ++ (medium), +++ (high).

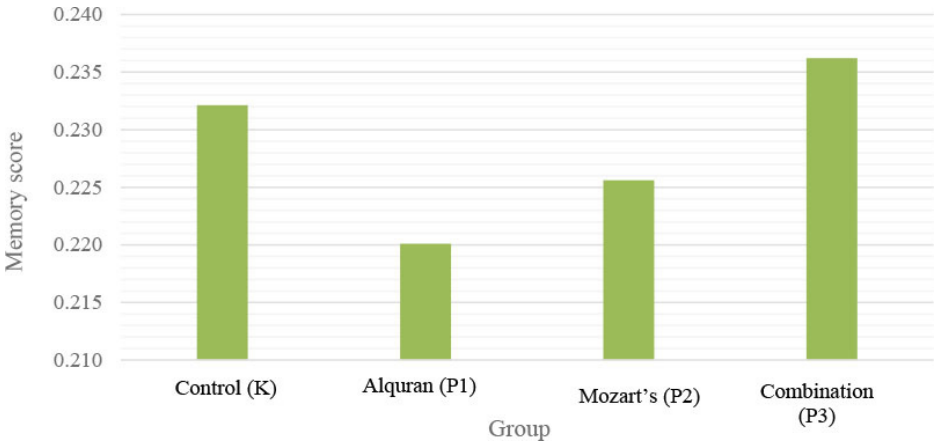

Figure 4. The average level of spatial memory in all study groups, K = Negative control (n=0.323), P(1) = Mice given the Murotal (n=0.220), P(2) = Mice given Mozart's classical music (n=0.226), P(3) = Mice given combination approach of the Alquran and Mozart's (n=0.236).

Table 2. Results of Differences in Memory Scores Using One-Way ANOVA Test

Groups	Total (n)	Asym. Sig. (2-sided)	Spatial Memory Score (Mean±SD)
K	6	P = 0.997	0.220 ± 0.138
P1	6		0.225 ± 0.038
P2	6		0.232 ± 0.207
P3	6		0.236 ± 0.056

Memory Test

Memory test results showed the average spatial memory varied greatly in each group. The highest level was found in the combined group, (memory score = 0.236), while the lowest level of spatial memory was found in the Murotal group (memory score = 0.220) (Figure 4).

Furthermore, the average score of the mice's spatial memory was tested by the normality and homogeneity tests. The Shapiro-Wilk normality test showed that all groups were normally distributed with a p-value >0.05. The Levene homogeneity test showed that all groups were homogeneously distributed with a P-value >0.05. Furthermore, we used the One-way ANOVA parametric test to determine differences in spatial memory levels within groups. The results showed no significant difference in the sample group's average value of the spatial memory levels (Table 2).

Memory Test Time Duration

Memory Test Time Duration was also measured in this study. The duration of time it took the mice to enter the entire arm was measured using a stopwatch for every mouse tested. The average time duration measured in this study was the percentage of minutes for each mouse to enter eight different arms successfully.

Based on the results obtained from Figure 5, it can be seen that the average duration of the radial labyrinth test in the control group shows the longest average time (173 seconds or 2 minutes 53 seconds). In comparison, the Alquran group showed the average radial maze test time of 171 seconds or 2 minutes 51 seconds. Mozart's group got almost the same result as the Alquran group, namely 172 seconds or 2 minutes 52 seconds. Then the group with a combined approach showed the lowest average percentage of maze test time, which was 162 seconds or 2 minutes and 42 seconds.

Memory Test Time Average was tested with normality and homogenity test. The Shapiro-Wilk normality test showed that all groups were normally distributed with a p-value >0.05. The Levane homogeneity test showed that all groups were homogeneously distributed with a P-value >0.05. One Way ANOVA test was used

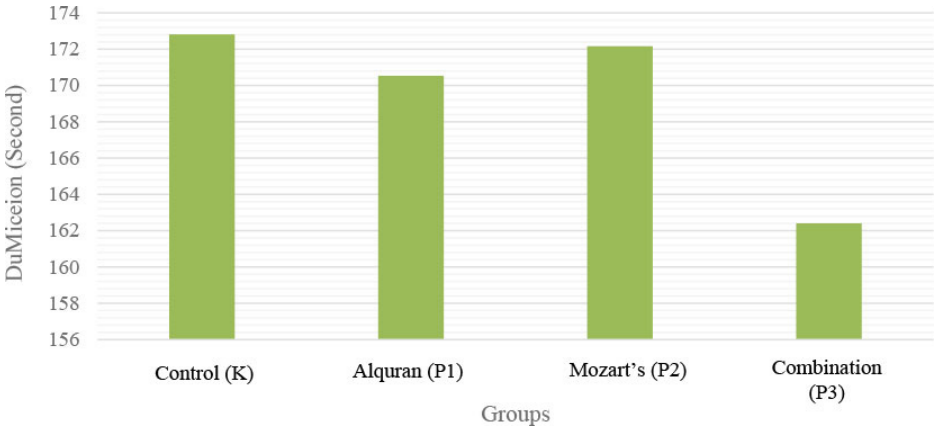

Figure 5. Average radial maze test time in all study groups, K = negative control (n=173), P(1) = mice given the Murotal (n=171), P(2) = Mice given Mozart's classical music (n=172), P(3) = Mice given combination approach from the Alquran and Mozart's (n=162).

Table 3. Results of Differences in Memory Test Time Average Using One-Way ANOVA Test

Groups	Total (n)	Asym. Sig. (2-sided)	Average Test Time Memory
K	6	P = 0.956	162.33 ± 41.08
P1	6		165.33 ± 49.28
P2	6		170.50 ± 26.39
P3	6		172.83 ± 20.53

to determine group differences (Table 3). Statistically, the results were found to be insignificant with P>0,05. However, the trend showed that the combination group has a better memory test time compared to the other group.

DISCUSSION

To the best of our knowledge, this study is the first study to compare the therapeutic effects of Mozart's classical music and Murotal Alquran on the level of spatial memory. In addition, this study is the first to assess the combined effect of the two on spatial memory. The results showed an increase in memory in the combination group (P3) compared to the control group. This situation is caused by the effects of two combined sound therapies that are thought to increase BDNF and affect memory quality.[13] An increase did not follow this increase in the P1 and P2 groups. Both appear to have lower memory scores than the control group, but they are not significantly different when viewed from the one-way ANOVA test. This condition is unique and interesting, whereas other studies show the opposite result on average.[13,14]

The Murotal approach and Mozart's classical music approach have the same characteristics. Both are sound-based therapies that have anxiolytic and relaxing effects, lower pain thresholds, reduce stress levels, and even improve short-term memory and spatial memory in several studies.[3,10,11,13,15] The mechanism underlying the improvement of short-term and spatial memory in both types of approach is the ability of brain neuroplasticity which is influenced by external stimuli, as indicated by a significant increase in the neurotrophic factor BDNF.[16,17] The synergistic effect of the two seems to show better results in this study, while the short duration of classical music and the Murotal approach may impact the lower spatial memory ability in groups P1 and P2 compared to controls.

The interesting thing is obtained from the observations of the behavior of mice in the 4 research groups. This study shows that Murotal and Mozart's classical music group had better habits than the combination and control group during the study period and spatial memory test. Mice that were given the Alquran approach showed the lowest level of aggressiveness and were the calmest compared to other treatment groups. This can be attributed to the optimal effect of dopamine and endorphins in the Alquran group compared to other groups. Both can potentially create a state of calmer mice and less likely to be obsessive.[18] On the other hand, the combined group had the highest level of aggressiveness and agility compared to the other groups. This study also shows that the average time for the fastest memory test was the combined group compared to the other groups. Researchers argue that this is a hormonal influence or an unexpected stress response due to the simultaneous administration of Murotal and Mozart's approach in the combination group.[19]

Jonan and Nicola's research states that the secretion of the hormone dopamine will cause the brain to feel pleasure and enjoyment and as a result will always be motivated to keep looking for sources of pleasure or what is called "seeking behavior".[20] This is what underlies the hypothesis that the suboptimal effect of dopamine will make a person curious and trigger the search for the information he wants more aggressively.

The involvement of dopamine in regulating aggressive behavior arises from the competitive motivation that arises from the dopamine reward system. The mice became sensitive and involved in the conflict as a form of interpretation of the confrontation with the attitude of "against" in the struggle for what they wanted. In addition, dopamine also causes a decrease in the "restraint" mechanism, which causes courage to take riskier decisions to get the desired reward.[21]

Research by Burhan and Morazadeh, the two "want" (dopamine) and "like" (opioids) systems complement each other. The dopamine system is stronger than the opioid system. This system will make a person constantly look for satisfaction and continue to feel less so that he always wants more than before or it is called a dopamine loop. This condition can lead to addictive behavior where dopamine becomes very active, and at a point when dopamine activity drops, unwanted aggressive behavior emerges.[22]

Dopamine and oxytocin are both secreted in a happy and happy state.[23] This hypothesizes the relationship between

dopamine and oxytocin levels in the body and a person's social cognition. Dopamine has a system that supports a person to tend to seek (stalking) while oxytocin has a system and mechanism that makes a person easily provoked and tends to sacrifice himself for something he loves (self-sacrificing). Both of these systems will then create a social drive that is easy to hate, rejects everything, and tends to conflict with others. This will later lead to destructive involvement in the social dynamics of a community.[24]

This phenomenon follows the results of observations in this study, where the mice that experienced a reduction in number were the control and the combination groups. Combination groups that have high aggressiveness tend to be hostile to their friends and bite each other. This was exacerbated by the incidence of cannibalism in which one of the mice was victimized when fasted for 12 hours according to the research instructions before the 8-arm labyrinth test was carried out. However, the group with high dopamine likelihood will tend to be more active with better cognitive task performance abilities such as working memory.[18]

Further research needs to find a comparison of the doses of classical music Mozart's and Murotal, further effects given at optimal doses, and see the effect of the approach on increasing spatial memory from the histology, biochemistry, and hormonal point of view.

CONCLUSIONS

There is no difference in the effect between classical music Mozart's and Murotal approach on increasing the spatial memory of mice (Mus musculus), but mice given a combination of approaches have a better level of spatial memory with a higher level of aggressiveness.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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ETHICAL CLEARANCE

This research received ethical approval from the Universitas Nahdlatul Ulama Surabaya, with certificate number 2.KE.101.11.2021.

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AUTHOR CONTRIBUTIONS

A.R.M., D.Y., and I.F. organized the idea. H.A. and F.K.F. developed the theory and verified the analytical methods. A.R.M. and I.F. analyzed the data and interpreted it. F.K.F. and H.A. supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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