

Instrumental Balinese Flute Music Therapy Improves Cognitive Function and Serum Dopamine Level in the Elderly Population of West Denpasar Primary Health Care Center

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Abstract

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BACKGROUND: Musical artwork using Balinese flutes made from bamboo (timing buluh) by Agus Teja Sentosa, S.Sn is a combination of music played with flute as the main instrument which contains certain components resembling music therapy such as in western classical music by Antonio Lucio Vivaldi.

AIM: This study aims to determine the improvement of cognitive function and increase in serum dopamine in the elderly after listening to music with Balinese flute as the main instrument.

METHOD: The current study allocated 18 subjects in the control group listened to western classical music by Antonio Lucio Vivaldi, while 18 subjects in the intervention group listened to western classical music and music from Balinese flute as the main instrument by Agus Teja Sentosa, S.Sn. MoCA-Ina assessment and examination of serum dopamine levels were carried out initially and 21 days after listening to music intervention.

RESULTS: The mean increase in cognitive function score was higher in the intervention group (5.22; $p < 0.001$) than in the control group (4.67; $p < 0.001$), this increase was not statistically significant with a value of $p = 0.562$ ($p > 0.005$). The mean increase in dopamine levels in the control group (3.60) was greater than in the treatment group (3.56), but the mean increase was not statistically significant ($p = 0.085$).

CONCLUSION: There was a significant relationship between listening to the main instrumental Balinese flute music and the improvement of cognitive function, especially in the memory domain in all study subjects, but the mean increase in cognitive function and serum dopamine level did not reach statistical significance.

Introduction

The balance between brain, body, and soul is an integral part of human life. In Hindu religion, the philosophy of life is called *Tri Hita Karana*, which refers to a harmonious relationship that manifests happiness. The three major pearls of wisdom consist of *Parahyangan* or the harmony of life between human with God, *Pawongan* or the harmony of life between human with each other, and *Palemahan* or the harmony of life between humans and their natural surroundings.

Music can vibrate and resonate rhythm in our nature, in which as a metaphor, every cell in our body plays a role as a rhythmical sound resonator. Listening to music including in elderly associates with an improvement of brain plasticity, which is beneficial

to stimulate cognitive function [1]. The process of brain neuroplasticity in its relationship with music is a part of enhancing cognitive ability or intelligence in the form of auditory intelligence. Listening to music induces powerful modulation activity on the mesolimbic pathway, impacts the nucleus accumbens and ventral tegmental area, as well as the hypothalamus and insula [2].

Musical listening experience necessitates complex auditory pattern-processing mechanisms, attention, memory storage and retrieval, and sensory-motor integration [3]. Music activates stored memory and stimulates cognitive function, also, recent brain imaging studies have shown that neural activity associated with listening to music extends well beyond the auditory cortex involving a wide-spread bilateral network of the frontal, temporal, parietal and subarachnoid pathway [4]. Right cerebral hemisphere receives musical impulse and activates both

hemispheres via the corpus callosum. Cognitive process is related to memory. Memory can be divided into 3 categories; it consists of sensory information storage, short-term memory, and long-term memory. Music impacts the encoding process of sensory memory. Positive emotion which people get from listening to music will encourage cognitive repair process [5]. Listening to pleasant music may increase cerebral blood flow or brain vascularisation in the mesocorticolimbic system, ventral striata (nucleus accumbens and mesencephalon), thalamic structure, cerebellum, insula, anterior cingulate cortex, and orbitofrontal cortex. The nucleus accumbens will be activated when a person is listening to pleasant music although it is never heard before [6].

Instrumental music is a type of music in which there are no vocals. The flute is a family of musical instruments in the woodwind group made from bamboo [7]. There are two principles in music reception which are equal loudness level (phone) and perceived level (sone). Phon is used to solve problems which cannot be fixed using only the decibel and hertz. In the human being, there is a natural human principle about surrounding things called senses [8]. The frequency range of human hearing which will travel to auditory cortex is 20-20.000 Hz [9].

Instrumental, low-pitched music with harmonious slow rhythm (60-80 beats per minute) are pleasing to the listeners, it may affect body physiology, slowing down both heart and respiratory rate, and might influence emotions through the limbic system [10], [11], [12]. This study utilised music from Balinese bamboo flute (*timing buluh*) as the main instrument, arranged together with modern music and played by Gus Teja (Agus Teja Sentosa, S.Sn). The song "Morning Happiness" has a tempo of 70-90 beats per minute and a frequency of 440 Hz.

Classical music is defined by Indonesian Language Dictionary (2008) as music composed and born from European culture and categorised according to certain periods. Listening to classical music will produce a positive effect, called a Mozart effect or Vivaldi effect. Western classical music used in such study is titled Spring by Antonio Lucio Vivaldi. Instrumental music with 60-80 beats per minute may affect brainstem neurons, activating neurotransmitters norepinephrine in conjunction with cholinergic and dopaminergic in the brainstem, mediating sensory and motor functions, with some influencing the cognitive function. Music directly activates the neuro-vegetative system (hypothalamus, hypophysis, suprarenal gland) to release neurotransmitters [2]. Cognitive function amelioration by listening to music is due to the relationship between orbitofrontal cortex (OFC) and a dopaminergic mesocorticolimbic circuit (nucleus accumbens/NAc and ventral tegmental area/VTA). Dopaminergic neurotransmitter in the neuronal pathway has a critical role in the brain's ability to process heard music [6].

The brain will have difficulty in recalling (memory function) along with the ageing process, reduces its ability to make decisions and slower in carrying out activities which are known as cognitive function changes. MoCA (Montreal Cognitive Assessment) is a questionnaire to assess global cognitive function including executive function and memory [13], [14].

Methods

This research was an experimental study using a pretest-posttest control group design. This study was conducted between November 2017 and December 2018 over 21 days in a primary geriatric facility located in West Denpasar primary health centre. Pocock formula was used to calculate the sample size of this study. There were 32 healthy geriatrics aged 60-74 years old given their consent to be subjects in this study. These subjects were healthy and did not have any history of systemic illnesses including stroke, diabetes mellitus, dyslipidemia, hypertension, epilepsy, history of brain injury, brain tumour, brain infection, and hearing impairment. These subjects were divided into two groups, control, and intervention group. Subjects on control group listened to western classical music by Antonio Lucio Vivaldi, titled "Spring", while intervention group listened to western classical music "Spring" with additional music piece of main Balinese flute "Morning Happiness" by Agus Teja Sentosa S.Sn. Each song was played for 20 minutes one time a day in the morning before subjects did their daily activity. All of the subjects used earphone to listen to the songs which were played from the recording tool provided by the researcher.

Cognitive function assessment in this study used the MoCA-Ina instrument, in which subjects were examined 2 times, before intervention and 21 days after the intervention of listening to music. Examination of serum dopamine levels also was carried out two times, before and 21 days after the intervention.

Descriptive analysis was carried out to see the characteristics of the research subjects. The Shapiro Wilk test was used to determine the numerical scale data normality, which was mean an increase in cognitive function scores and means an increase in serum dopamine levels. Comparative analysis of two mean increases in cognitive function scores and the mean increase in serum dopamine levels used unpaired T-test, significance level with p, and a 95% confidence interval.

Results

There were 36 subjects on this study, each group of a control group and intervention group consisted of 18 subjects. Male and female gender was distributed normally in each subject group consisting of 16 male and 16 female. Both groups had the same age interval, ranging from 60 to 74 years old. The subject baseline characteristics in this study including age, gender, education level, occupation, and mean score of the initial cognitive function are shown in Table 1.

Table 1: Baseline characteristics of research subjects

Variable	Group		p-value
	Control (n = 18)	Intervention (n = 18)	
Mean Age (years)	65.83 ± 4.27	69.44 ± 4.48	0.856
Gender			1.000
Male	9 (50%)	9 (50%)	
Female	9 (50%)	9 (50%)	
Education Level			
Junior High School	10 (55.6%)	8 (44.4%)	
Senior High School	2 (11.1%)	4 (22.2%)	
Academy/Diploma/Bachelor	6 (33.3%)	6 (33.3%)	
Occupation			
Retired Civil Servants	7 (38.9%)	8 (44.4%)	
Private Employees	5 (27.8%)	5 (27.8%)	
Entrepreneur	4 (22.2%)	1 (5.6%)	
Others	2 (11.1%)	4 (22.2%)	
Mean Initial MoCA-Ina Score	20.94 ± 3.45	21.33 ± 3.07	0.971
Mean Initial Dopamine Serum Level	36.50 ± 16.40	23.08 ± 8.63	0.002*

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Table 2 shows the mean increase of cognitive function score on each subject group. The mean increase of cognitive function score on the intervention group (5.22 ± 2.02) was higher than in the control group (3.89 ± 1.55).

Table 2: Mean Increase of MoCA-Ina score before and after listening to music on the control and intervention group

Group	Mean Initial MoCA-Ina	Mean Final MoCA-Ina	Mean Increase MoCA-Ina	p-value
Control	20.94 ± 3.45	24.83 ± 3.54	3.89 ± 1.55	< 0.001*
Intervention	21.33 ± 3.07	26.56 ± 2.77	5.22 ± 2.02	< 0.001*

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Statistical analysis using unpaired T-test to measure the effectiveness of MoCA-Ina score improvement between 2 subject groups showed that the increase was not statistically significant with a value of $p = 0.562$ ($p > 0.05$). The results of the analysis are presented in Table 3 below.

Table 3: Mean Increase of MoCA-Ina score between control and intervention group

Group	Mean Increase of MoCA-Ina score	p-value
Control	3.89 ± 1.55	0.562
Intervention	5.22 ± 2.02	

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Independent t-test was performed to know the significance or effectiveness of each cognitive function domain between control and intervention group. The highest mean increase was found in memory domain

on the intervention group (1.56 ± 0.78) compared to the control group (1.56 ± 0.78) with a value of $p = 0.023$ ($p < 0.05$). The mean increase of memory domain in the intervention group was statistically significant compared to in the control group. The analysis result for other cognitive function domains is presented in Table 4.

Table 4: Mean Increase of each cognitive function domain score (MoCA-Ina) on intervention and control group

Variable	Group		p-value
	Control	Intervention	
Visuospatial/Executive	0.89 ± 0.58	1.22 ± 1.06	0.093
Naming	0.17 ± 0.71	0.00 ± 0.34	0.377
Memory	1.56 ± 0.78	2.39 ± 1.24	0.023
Attention	1.06 ± 1.11	0.94 ± 1.35	0.453
Language	0.44 ± 0.62	0.33 ± 0.59	0.534
Abstract thinking	0.33 ± 0.49	0.28 ± 0.46	0.487
Orientation	0.06 ± 0.24	0.00 ± 0.00	0.331

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

The Shapiro Wilk test was used to determine the data normality since the sample size was less than 50 subjects. Mean increase of serum dopamine level data on both groups were being tested and showed that the data were not distributed normally with $p = 0.000$ ($p < 0.05$). Nonparametric study for the related sample, Wilcoxon test, was further conducted to test the mean difference of two groups that were not distributed normally. The analysis result is presented in Table 5.

Table 5: Mean concentration of serum dopamine before and after listening to music on the control and intervention group

Group	Mean initial dopamine concentration	Mean final dopamine concentration	Mean increase of dopamine	p-value
Control	36.50 ± 16.40	40.06 ± 72.50	3.60 (37.63-30.51)	0.085
Intervention	23.08 ± 8.63	26.65 ± 24.87	3.56 (16.84-9.71)	0.094

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

The mean increase in the control group was higher than in the intervention group, but this result was not statistically significant with a value of $p = 0.085$ ($p > 0.05$). The analysis result is showed in Table 6 below.

Table 6: Mean increase of serum dopamine concentration between control and intervention group

Group	Median (Minimum-Maximum)	p-value
Control	3.60 (37.63-30.51)	0.085
Intervention	3.56 (16.84-9.71)	

MoCA-Ina = Montreal Cognitive Assessment-Indonesia.

Discussion

All of the subjects in this study had the same range of age which was 60 to 74 years old. World Health Organization (WHO) in 1999 divided age range for geriatrics into 4 categories, consisting of middle age, elderly, old, and oldest-old. The range of age 64 to 74 years old in this study is classified as elderly [15]. A cross-sectional study found that the incidence

of hearing loss in the elderly occurred in 45% of people at the age of > 70 years [16]. Mean of age from the previous study was 74.1 years old [17]. The age range 60-74 years in this study is by the category of elderly by WHO and it was chosen to minimise the possibility of research subjects having hearing loss.

Baseline characteristic for mean serum dopamine level on both groups had a statistically significant difference ($p = 0.002$). There have been no similar studies before assessing serum dopamine levels in the elderly. The mean level of dopamine on both groups was below normal range, and the difference of initial serum dopamine level on control and intervention group was likely due to several factors, including the diversity of daily stressors experienced by the two groups, different feelings of comfort when listening to music and different daily habits such as smoking. The previous study in experimental animals found that psychological stress affects the level of dopamine release in mesolimbic, the assessment of dopamine level on this study was carried out by Positron Emission Tomography (PET) [18]. Nicotine consumption as in cigarette smoking is known for their effect in stimulating dopamine production [19]. The result from previous research using experimental animal found that as the increase of age, the basal ganglia structure changes and affects dopamine level [20]. The difference of mean initial cognitive function score between the two groups was not statistically significant with a value of $p = 0.856$ ($p > 0.05$). The result of the cognitive function examination on the elderly in this study is similar to the result from the previous study; it showed that the average cognitive function of the elderly aged 60-70 years was 21.48 [21]. The previous research about listening to Balinese flute music as a therapy showed the mean cognitive function score on the elderly was 20.75 [22].

The paired test found that both groups experienced a statistically significant increase in their mean cognitive function after listening to music ($p < 0.001$). The mean increase of cognitive function score in the intervention group was greater than in control group, the difference of the value based on the unpaired comparative test was not statistically significant ($p = 0.562$; $p > 0.05$). The intervention group listened to two types of music so that the possibility of improving their mean cognitive function was bigger than in the control group who only listened to one type of music, which was classical music. This condition may be caused by the weakness of this study which could not control the overall daily activities that can affect cognitive function. The subjects in this study listened to the music for 21 days (3 weeks) similar with the previously conducted study which concluded that experiencing music therapy for 2-3 times a week for 1-6 weeks period enhanced cognitive function [23]. Listening to western classical music for at least 10 minutes was able to improve cognitive function [24], [25].

The mean increase of cognitive function score after listening to classical music from the previous study was 3.17 which was less than the result from this current study that could happen because the subjects from the previous study listened to classical western music with a smaller frequency of 2 times a week for 7 weeks [26]. Both the control and intervention group were having improvement in their cognitive function score since the main Balinese flute instruments had similar characteristics with classical western music. Those two types of music have the appropriate component of music therapy. The mean increase of cognitive function score in the intervention group was higher than in the control group, that could be caused by the fact that all of the subjects on this study were Balinese people in which they were accustomed to listening to the Balinese flute. Balinese flute was earlier only played in the spiritual ceremony, but nowadays Balinese flute had developed and combined with modern music and played as recreational music. The intervention group had a higher increase in their cognitive function score compared to the control group since they were listening to two kinds of music that contained suitable components of therapeutic music. A prior research entitled *The Effect of Exposure to Classical and Javanese Music on Cognitive Function in Patients with Acute Ischemic Stroke* conducted at Dr. Sardjito Hospital Yogyakarta stated that the results of a cognitive function of subjects who received exposure to Javanese music and classical music were better than those who did not receive musical exposure [27]. The way people receive music is different from each other; it is influenced by history, place, culture, and taste of the listeners [6].

The previous research found that the mean scores of cognitive function in Balinese flute players were higher than in player of other types of musical instruments in the *Gong Kebyar* group in Bali. Metronome program was used to find out the components of music contained in the *Gong Kebyar* group. Music produced from the main flute instrument used in this study had some similar components to classical music, in terms of they did not have any lyrics, the frequency was 440 Hertz, and the tempo was 70-90 beat/minute, then the subjects listened with the volume of 40-70 decibel [28]. No similar research was found regarding the role of listening to the main Balinese flute instruments in improving cognitive function, especially in the elderly.

The comparison of the mean increase scores for each domain between the control and intervention group did not differ statistically ($p > 0.005$). Memory domain in both groups experienced the highest mean increase. The intervention group experienced a greater increase in their memory domain than in the control group, and the difference was statistically significant ($p = 0.023$). Primary auditory cortex (area 41) is located in the superior temporal gyri whereas the brain region responsible for memory function is

located in the temporal region. The result from the previous experimental study showed the dominant activity of the temporal region on functional Magnetic Resonance (fMR) imaging when subjects were asked to repeat words [29]. The outcome of the latter study parallel with the result from a previous experimental study which held in Italy, it was found that listening to western classical music increased mean memory function (recall memory) and visuospatial [24], [25]. Previous experimental studies yielded the same corresponding result where the increase of the memory domain was greater than of the other domains [30]. Improvement of cognitive function did not occur in all domains but there was an increase in memory function in elderly who listened to music therapy, the highest mean increase was found in the elderly listened to classical music titled Spring by Vivaldi then followed by the increase of memory domain in the elderly who listened to Mozart's White Noise music and the lowest score in the elderly who did not listen to music [31].

Attention and visuospatial/executive domains have increased higher than other domains after the memory domain. Previous research on the elderly showed that listening to music can improve the various domains of cognitive function, especially the domain of memory and attention [32], [33]. The domain of orientation and naming in the intervention group did not experience any increase in their average scores, because the initial and final scores were equally good. The fMRI scanning was done while subjects listened to music and the result showed activation of NAc and ventral tegmental area (VTA). The connection between NAc and VTA regulates the autonomic system, emotion, and cognitive function. Insula is activated since it is connected with NAc and play a role in addictive behaviour [6]. Functional Transcranial Doppler sonography (fTCD) was performed while subjects listened to music, the description of the results was music contains elements of harmony, and the music tempo increases cerebral blood flow velocity (CBFV) in the right hemisphere compared to the left hemisphere [34]. The music contains pitch elements which are processed in the auditory cortex of the right hemisphere and located in the temporal lobe, so the process of listening to music activates right hemisphere more than the left [35].

There was an increase in mean dopamine level of the control and intervention groups in this study, but this increase was not significant statistically. Similar research has never been done before. There was an improvement in cognitive function with music listening activities from the fMRI examination which done when subjects listened to music, it is due to the association between OFC and mesocorticolimbic dopaminergic circuits (NAc and VTA), but this study could not directly assess the serum dopamine levels [6].

The previous study in an experimental animal

model with fMRI scanning produced an equal result as in this study, as auditory stimulation (music) increased the serum dopamine and serotonin levels, but no changes were found in the basolateral amygdala and NAcc dopamine level when listening to music. The difference between brain dopamine and the one in systemic circulation levels must be taken into account since dopamine metabolism may cause variation in measured levels [36]. The increase in mean serum dopamine level was not statistically significant. This might be caused by the ageing process itself. A study in a healthy animal model showed a decreased metabolism in the striatum and decreasing numbers of dopamine receptors D1 and D2 in older age. Other reasons not limited to other conditions and daily routine may also contribute to the insignificant result. The increase in dopamine levels may result from cocaine use and consuming preferred meals, elaborated in another study [20].

The weakness of this study was its inability to control daily activities of the research subjects which possibly capable of improving cognitive function; research subjects were not under monitored for 24 hours per day. Other obstacles were scattered sample location over several districts within the working area of West Denpasar primary health care and limited sample collector, making blood sample acquisition from each subject's residences could not be done at the same time. All the limitations above may affect the mean serum dopamine level due to various timespan between the moment the study subjects finished listening to music and the blood sample collection from each subject. Not all the factors influencing serum dopamine levels such as medical condition, emotional stress, smoking and/or history of smoking, daily meal intake can be controlled. Study subjects listened to music individually at home with recording devices prepared by researchers, so supervisions were conducted indirectly through the music listening record.

The strength of this study lies in the homogenous control and intervention arms, strict eligibility criteria, and also have been randomized so possible bias or confounding variables have been reduced. There was no loss to follow up in this study.

In conclusion, this study proved that music listening intervention increased the cognitive function significantly in both the control (listening to classical music) and intervention group (listening to both classical music and main instrumental Balinese flute music). There was a substantial increase in the memory domain after listening to music. The differences from the cognitive function score increase and serum dopamine levels between both arms were not significant.

It is recommended to listen to classical and instrumental Balinese flute music regularly on a daily basis to maintain and/or increase the cognitive function in the elderly. Music can be utilised as one of

the non-pharmacological treatment modalities and raising the quality of geriatric home care. Further research might be necessary with different method and supervision.

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