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THE IMPACT OF INHALATION OF ACER TEGMENTOSUM MAXIM EXTRACT ON CEREBRAL BLOOD FLOW IN COLLEGE STUDENTS

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ABSTRACT

Acer tegmentosum Maxim is a deciduous hardwood tree known for its therapeutic effects in conditions such as liver cancer, hepatocirrhosis, hepatitis, and leukemia. The leaves of Acer tegmentosum Maxim are rich in potassium, contributing to its effectiveness in preventing and treating hypertension. Acer tegmentosum Maxim extract possesses anti-angiogenic, anti-inflammatory, and antioxidant properties. Studies suggest potential roles in reducing neutral fats and total cholesterol, as well as acting as a plant-based estrogen. This research explores the correlation between inhalation of Acer tegmentosum Maxim extract and cerebral blood flow. Despite improved information accessibility in modern society, stress levels and mental health issues continue to rise. Humanistic therapy, a form of mental care utilizing the humanities for self-insight and transformation, was applied to science and engineering students alongside the examination of cerebral blood flow changes using transcranial Doppler ultrasound. The results indicate an increase in mean blood flow velocity in the posterior cerebral artery (PCA) and internal carotid artery (ICA) after inhaling Acer tegmentosum Maxim extract, suggesting potential associations with cognitive function and cerebral blood flow.

Keywords: Acer tegmentosum Maxim, plant-based estrogen, transcranial Doppler, humanities, cognitive function, cerebral blood flo

1. INTRODUCTION

Acer tegmentosum Maxim is a deciduous hardwood tree found in humid valleys and ravines at altitudes above 600 meters. Known for its therapeutic effects in conditions such as liver cancer, hepatocirrhosis, hepatitis, and leukemia, Acer tegmentosum Maxim is recognized as a non-toxic herbal remedy with minimal side effects. The leaves of

Acer tegmentosum Maxim are particularly rich in potassium, making them effective in the prevention and treatment of hypertension [1]. Potassium plays a crucial role in energy metabolism, neural stimulation, cell membrane transport, blood pressure regulation, and maintaining the balance of acids and alkalis [1]. Acer tegmentosum Maxim extract has demonstrated potent anti-angiogenic activity in both in vivo and in vitro settings, influencing processes such as embryonic development, wound healing, tissue regeneration, and tumor growth [14]. Additionally, its well-documented anti-inflammatory and antioxidant properties have been the focus of various studies [15][16][17]. Obesity is a major risk factor for various metabolic disorders, including hyperlipidemia, type 2 diabetes, atherosclerosis, non-alcoholic fatty liver disease, and cardiovascular diseases [18]. Acer tegmentosum Maxim extract has been reported to decrease levels of neutral fats and total cholesterol, inducing the inhibition of lipid accumulation in the adipose tissue of models consuming a high-fat diet, a condition associated with these disorders [18]. Furthermore, recent research has isolated a novel phenolic compound, isoamericanoic acid B, with a 1,4-benzodioxane scaffold, suggesting the potential utilization of Acer tegmentosum Maxim as a plant-based estrogen [2]. Plant-based estrogens, primarily belonging to natural phenolic compounds, are known to exert their effects by binding to estrogen receptors (ER), including ER-α and ER-β [3]. In the study, isoamericanoic acid B exhibited high binding affinity to ER-β, and the activation of ER-β is known to induce cell proliferation inhibition and protection against atherosclerosis [3]. Based on these findings, we hypothesized that Acer tegmentosum Maxim could influence the vascular system, blood flow, and nervous system and aimed to investigate the correlation between the inhalation of the extract and cerebral blood flow.

In today's modern society, advancements in communication devices, including smartphones, have made information exchange more convenient for members of the community. While individuals now have greater access to information than before, there is a growing trend of people becoming isolated in their own worlds, with a reduction in conversations among family and friends [4]. As a consequence of these technological developments, there is an increasing number of individuals experiencing what is commonly referred to as stress, a mental ailment [4]. Humanities have been employed as a means to treat such mental distress [4]. Humanistic therapy involves utilizing humanistic methods to induce self-insight and epistemological changes, securing mental well-being for individuals or groups at risk of psychological pain or experiencing emotional distress [4]. The study aims to induce a shift in thinking among science and engineering students who had relatively limited exposure to humanities by encouraging them to enroll in humanities courses. Through this process, we sought to investigate the changes in cerebral blood flow that manifest during the course of exposure to humanities.

2. METHODS

2.1 Research Participants

This study targeted healthy male and female volunteers with an interest in research among undergraduate students at D University in Region B. A total of 9 participants were included, consisting of 2 males and 7 females. The research duration encompassed 7 days of baseline measurements without any external stimuli, followed by 15 days of watching the humanities lecture titled "Sebasi" in both baseline and exposure conditions. The research was conducted after obtaining approval from the Institutional Review Board (IRB) of Dong-Eui University.

2.2 Materials

The Acer tegmentosum Maxim used in this experiment was purchased as dried products after collection and processed into a hot water extract. The hot water extract was prepared by boiling 100g of Acer tegmentosum Maxim with 1L of distilled water for 3 hours, followed by filtration. The nebulizer used for olfactory stimulation had a spray volume of 0.32 cc/min, and particle size ranged from 0.5 to 5.0 μm, with more than 50% of particles within this range.

2.3 Research Method

Transcranial Doppler (TCD) examination is a non-invasive method utilizing ultrasound to examine the hemodynamic abnormalities of the extracranial and intracranial blood vessels [13]. The brain is supplied with nutrients through two arterial systems [13]. The basilar artery (BA) is formed by the convergence of the internal carotid artery (ICA), branching from the common carotid artery (CCA) originating from the brachiocephalic artery and aortic arch, and the vertebral artery (VA), which begins at the subclavian artery and travels beneath the subclavian artery [13]. The internal carotid artery (ICA) passes through the carotid canal of the temporal bone, entering the intracranial space and giving rise to the anterior cerebral artery (ACA) and middle cerebral artery (MCA) near the lateral fissure around the external part of the brain [13]. The basilar artery (BA) ascends along the brainstem, branching at the superior cerebellar artery to form MCA, ACA, and posterior cerebral artery (PCA), forming the cerebral arterial circle [13]. In Transcranial Doppler (TCD) examination, the major criteria for distinguishing blood vessels include the acoustic window, orientation of the probe, sample volume depth, direction of flow, and contour of the waveform [19]. These criteria were considered during the measurements in this study.

Cerebral blood flow velocity was measured using the Delica EMS-9BP device, with a 2MHz probe for the MCA, ACA, and PCA, and a 4MHz probe for the CCA and ICA. Measurements were taken through the temporal bone window and submandibular window, adjusting the probe's angle accordingly. During olfactory stimulation, the nebulizer was positioned approximately 30cm away from the subject's face, and delivery was stopped upon the subject's recognition of the scent. The stimulation was conducted at 10-minute intervals. Humanities lectures were provided through a monitor and speaker in the laboratory, and participants continued attending until the measurements were completed.

2.4 Data Analysis

In this study, the brain vascular data, measured five times for each experimental group, were analyzed using a multivariate approach under the assumption that the data were associated with the location of blood vessels (LMCA, LACA, LPCA, RMCA, RACA, RPCA, LCCA, RCCA, LICA, RICA). Hence, the selected statistical model was the Repeated Measures Multivariate Analysis of Variance (RM-MANOVA), and the entire data analysis was divided into five modules (vessel depth, maximum frequency, average frequency, pulsatility index, and resistance index) based on the experimental design. SPSS 23.0 was used for data analysis.

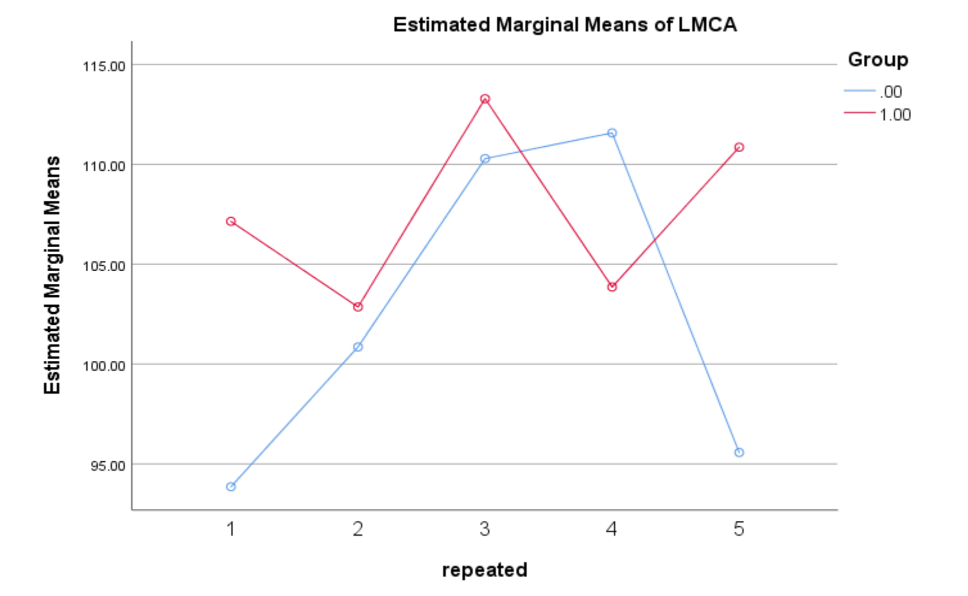
3. FINDINGS

In the current paper, the analysis results of the maximum frequency module among the five modules are presented. In the multivariate test, the difference between the two groups' mean vectors for the ten variables was not significant, but differences due to repeated measures were found to be significant (based on Roy's largest root criterion, $F(10, 42) = 3.616$, $p = 0.002$). When considering individual measurement locations, particularly for LMCA ($F(4, 48) = 2.601$, $p = 0.048$) and LACA ($F(4, 48) = 4.468$, $p = 0.003$), differences due to repetition were notably significant. No significant interaction between groups and repeated measures was observed, and the results of contrasts among repetitions will be presented in this analysis. The preliminary analysis results are summarized with a profile plot (Figure 1) and corresponding numerical values (Table 1).

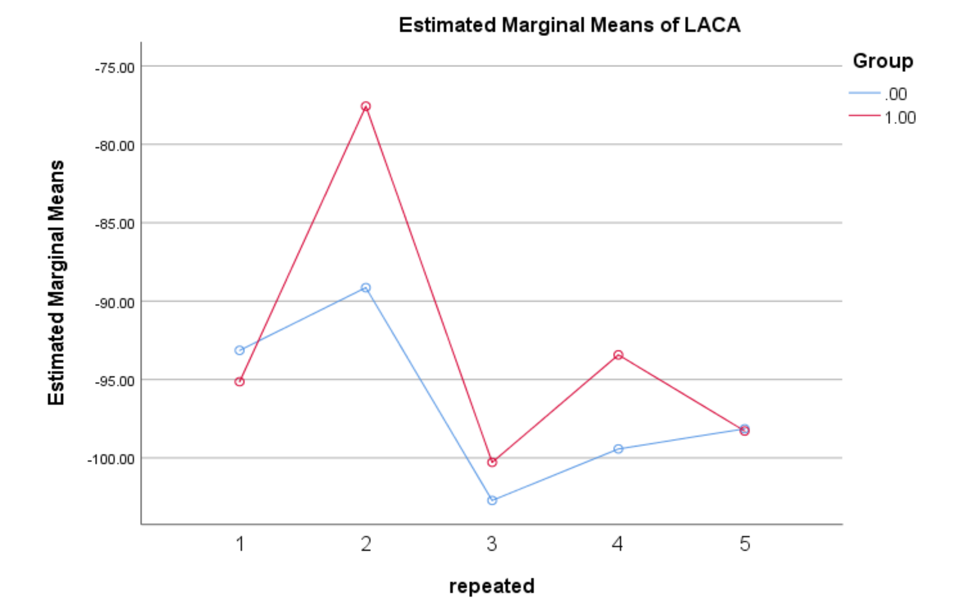
[Table 1] Estimated group means across repetitions by cerebral blood vessels

Group	RM*	LMCA	LACA	LPCA	LCCA	LICA	RMCA	RACA	RPCA	RCCA	RICA
0	1	93.86	-93.14	59.29	47.43	-41.71	102.14	-96.71	64.86	45.14	-48.86
	2	100.86	-89.14	61.57	49.86	-43.71	100.29	-83.71	57.43	55.71	-50.57
	3	110.29	-102.71	67.86	57.71	-46.43	96.29	-84.43	61.00	47.00	-56.00
	4	111.57	-99.43	62.00	50.14	-49.29	104.71	-81.29	63.71	50.57	-54.14
	5	95.57	-98.14	61.57	50.57	-50.29	105.57	-83.43	66.14	48.29	-50.43
1	1	107.14	-95.14	71.29	53.71	-39.43	108.43	-86.43	65.14	54.43	-44.71
	2	102.86	-77.57	68.29	52.00	-34.43	105.43	-91.29	66.14	51.71	-41.43
	3	113.29	-100.29	70.14	53.29	-41.71	110.00	-92.29	73.71	52.00	-42.71
	4	103.86	-93.43	69.86	55.14	-38.29	114.57	-90.43	73.86	51.43	-40.57
	5	110.86	-98.29	65.71	55.86	-38.00	110.71	-95.29	72.57	47.29	-39.43

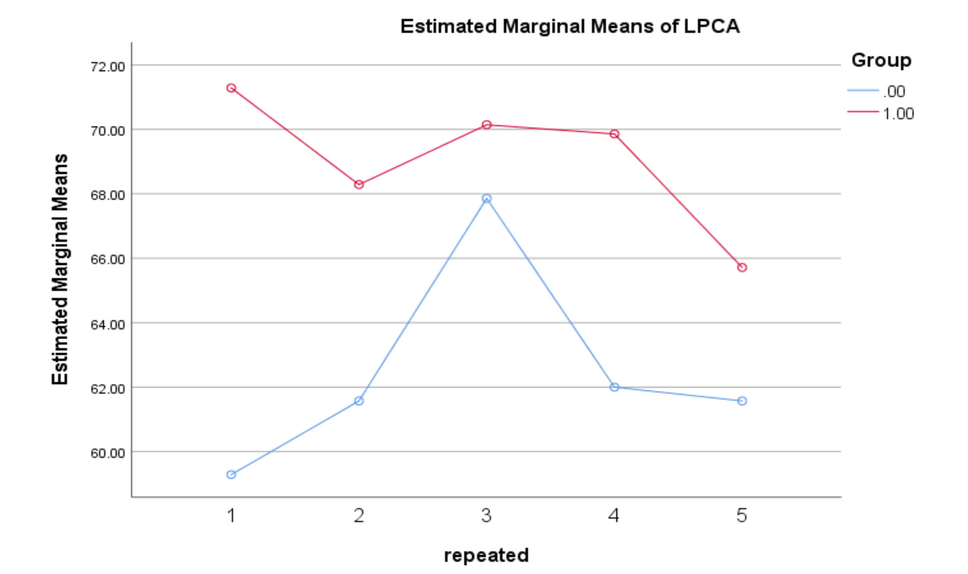
* RM: repeated measures



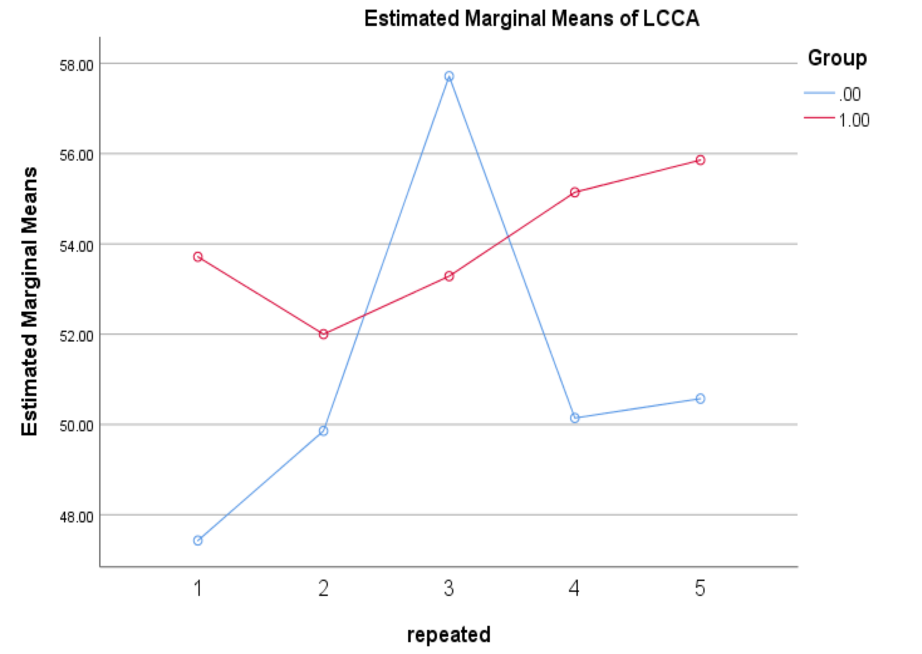
LMCA



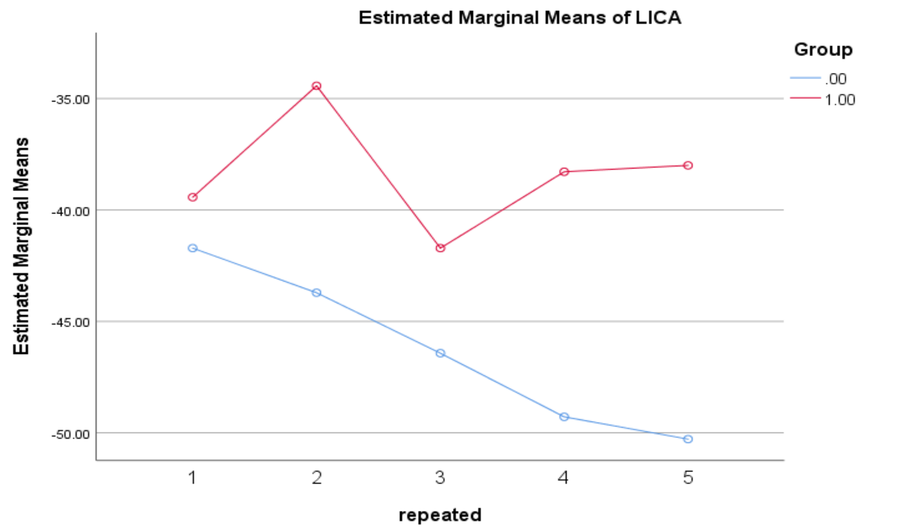
LACA



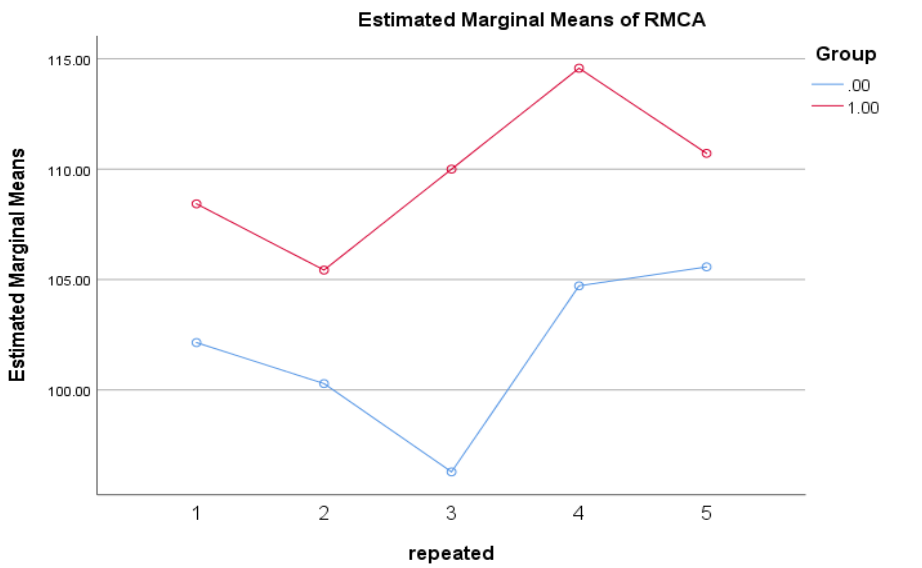
LPCA



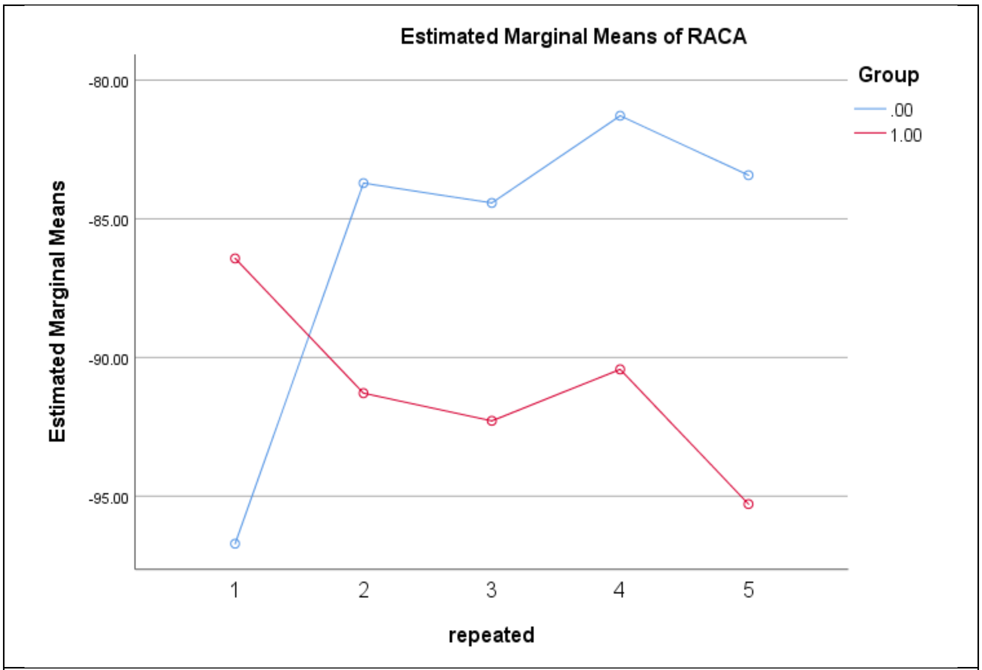
LCCA



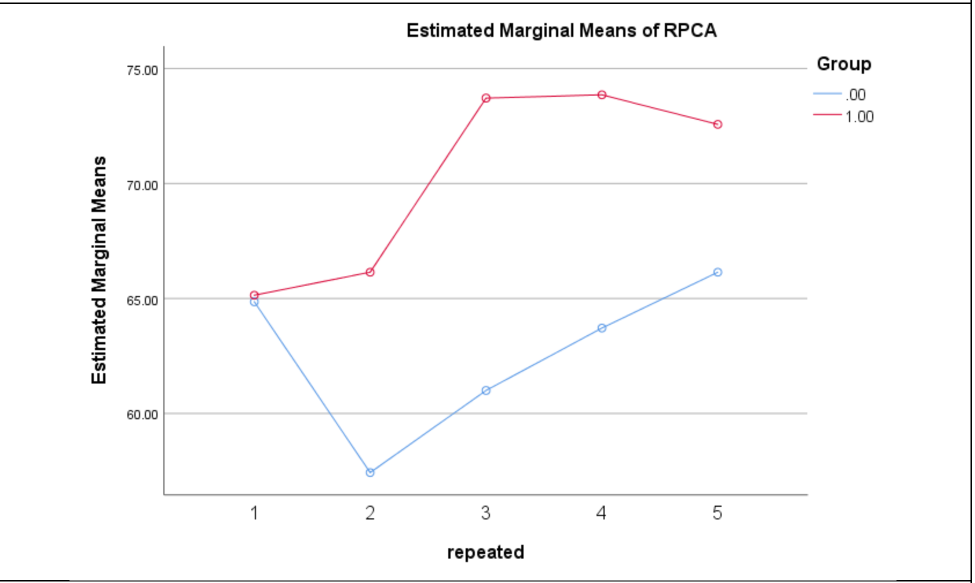
LICA



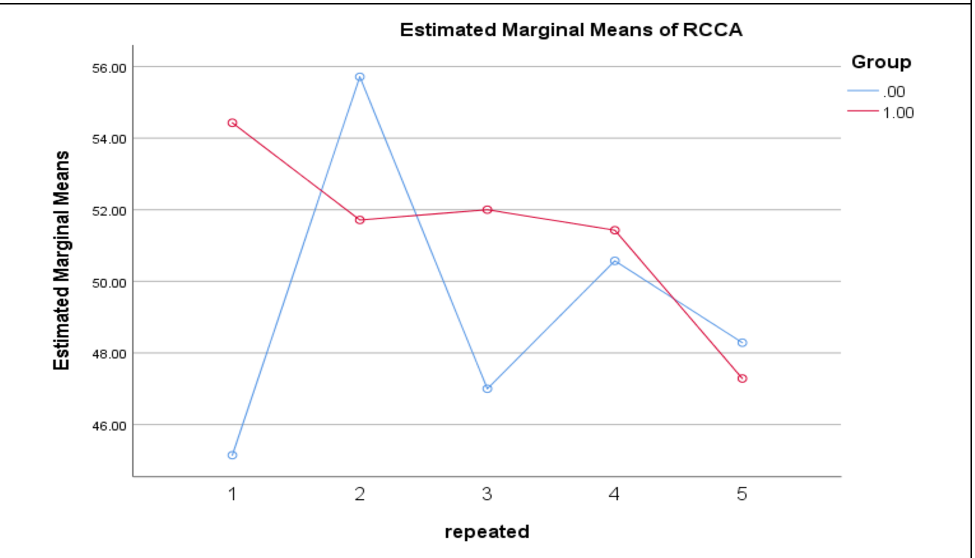
RMCA



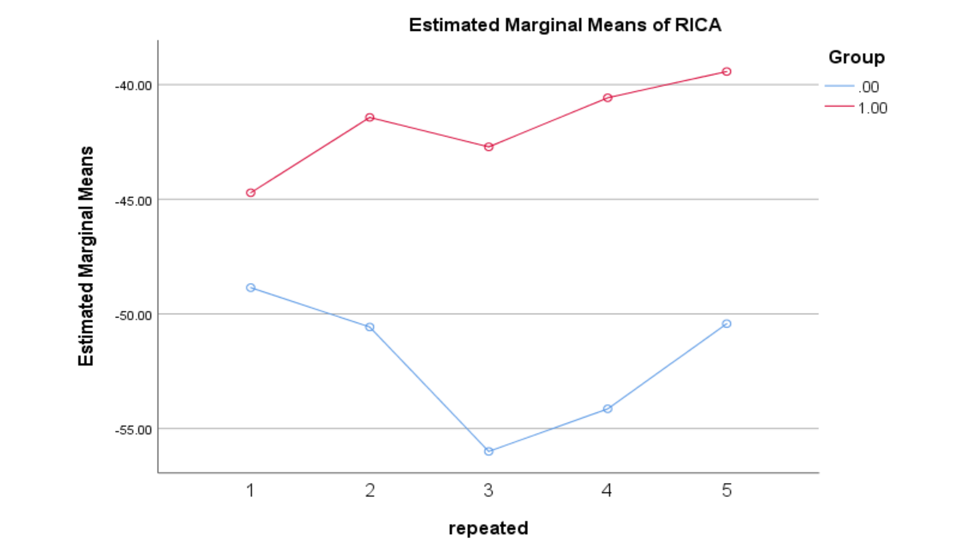
RACA



RPCA



RCCA



RICA

[Figure 1] Profile plots for peak frequency (0: control group; 1 safflower group)

4. DISCUSSION

Doppler ultrasound examination of the cerebral arteries is a non-invasive, safe, and efficient method for real-time evaluation of cerebral vascular circulation [20]. This is particularly useful in assessing peripheral circulation, which is influenced by the hemodynamics of critical arteries such as the carotid arteries and potential stenosis in the intracranial vessels [20]. In a recent study, the correlation between the lifetime exposure to estrogen and the area of cerebral white matter degeneration was analyzed. The research results indicated that women with longer exposure to estrogen throughout their lives tend to exhibit less cerebral white matter degeneration. When the small blood vessels in the brain are damaged over an extended period, myelin sheaths, which connect nerve cells, are stripped away, leading to the interruption of signal transmission between nerve cells and the risk of dementia or stroke increases [6]. This highlights the importance of estrogen in cognitive function and cerebral vasculature [6]. Furthermore, numerous studies have suggested that estrogen-based therapies play a neuroprotective role in preventing cognitive aging and brain damage. In addition, in other studies, Acer tegmentosum Maxim has been found to contain isoamericanoic acid B, a plant-based estrogen. This component has confirmed estrogenic activity [21][22][23]. Particularly, it shows a high affinity for ER-β, and is present in the hippocampus, a critical area for learning and memory [2]. The Posterior Cerebral Artery (PCA) supplies blood to structures related to vision and memory, potentially influencing memory and learning processes [11]. Specifically, some portions supplied by the PCA belong to the hippocampus, an area associated with memory [11]. The hippocampus is involved in the storage and retrieval of new information, spatial memory, and is related to the memory capacity [11]. In cases where blood flow to the PCA is insufficient or problems arise, there may be a decline in memory and learning abilities [11]. Additionally, the decrease in sex hormones reduces ligand binding to steroid receptors present in various brain areas, including those related to cognition such as the hippocampus and prefrontal cortex [11]. The activation of brain steroid receptors plays a crucial role in normal cognitive function [9]. The Internal Carotid Artery (ICA) is a vascular structure responsible for collateral circulation, and its stenosis is characterized by a reduction in cerebral blood flow, leading to chronic cerebral hypoperfusion [8]. Prolonged cerebral hypoperfusion can damage neuronal energy metabolism and induce cognitive impairment [8][10]. Although the impact of carotid artery stenosis on cognitive function may be mild, some studies suggest a broad and potentially harmful influence [12]. In this study, we measured cerebral blood flow while inhaling the scent of Acer tegmentosum Maxim and simultaneously attending humanities lectures. In all sessions, the average blood flow velocity of both the left and right Posterior Cerebral Artery (PCA) and Internal Carotid Artery (ICA) showed a higher tendency after inhaling Acer tegmentosum Maxim compared to before. Considering previous research indicating a decrease in average blood flow velocity in the ICA stenosis model, the study suggests the significance of increased blood flow velocity due to vascular dilation [8]. On the other hand, the results of measuring the left and right Middle Cerebral Artery (MCA), Anterior Cerebral Artery (ACA), and Common Carotid Artery (CCA) did not show a distinct difference before and after inhaling the scent of Acer tegmentosum Maxim. However, considering the tendency of increased average cerebral blood flow velocity in other blood vessels, this provides a basis for suggesting the positive impact of inhaling the scent of Acer tegmentosum Maxim on improving cognitive function by enhancing cerebral blood flow.

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