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THE EFFECTS OF INHALING SAFFLOWER EXTRACTS ON THE AUTONOMIC NERVOUS SYSTEM IN COLLEGE STUDENTS

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ABSTRACT

Safflower is known for its effectiveness in preventing arteriosclerosis and is rich in linoleic acid. It contains various compounds including flavonoids, alkaloids, and phenolic acids, which contribute to its efficacy in cardiovascular metabolism. Hydroxysafflor yellow A (HSYA) found in safflower shows potential in treating cerebrovascular diseases by reducing neurological deficits in a cerebral infarction model. In modern society, many individuals experience stress, and humanities therapy is considered positive for relieving stress induced by emotional labor. The autonomic nervous system (ANS) regulates internal organs, and stressful situations can disrupt this balance. We investigated the effects of inhaling safflower extract and attending humanities lectures on autonomic nervous system (ANS) activity using transcranial Doppler ultrasonography. The study results showed an increase in the activity of the sympathetic and parasympathetic nervous systems after inhaling safflower extract and attending humanities lectures. Brain activity increased, indicating improved concentration and immersion, while stress on the brain remained relatively low. This study provides a foundation for understanding the influence of safflower extract on cognitive function and the autonomic nervous system, suggesting the need for further research on safflower extract and the autonomic nervous system.

Keywords: Safflower, Cerebral Blood Flow, Transcranial Doppler, Cognitive Function, Autonomic Nervous System

1. INTRODUCTION

Safflower, also known as hollyhock, is a biennial plant in the mallow family. Its seeds are pressed to extract oil, which is used for lighting and cooking. The oil obtained from the seeds is rich in linoleic acid, making it beneficial for preventing and treating atherosclerosis caused by excess cholesterol [3]. Linoleic acid is the most abundant polyunsaturated fatty acid that we can consume [11]. It plays a crucial role as a precursor to arachidonic acid (AA), essential not only for the brain and nervous system development in fetuses and infants but also for proper growth in general [11]. Linoleic acid in safflower seeds has the effect of reducing the concentration of cholesterol in the blood, making it highly effective in preventing and treating circulatory system diseases such as atherosclerosis, hyperlipidemia, and hypertension [4][5][7]. Safflower contains various chemical compounds including flavonoids, alkaloids, and phenolic acids [4]. Flavonoids are polyphenolic plant metabolites abundant in fruits and vegetables and exhibit biologically relevant protective effects in various cardiovascular disorders [12]. In particular, 3,4-DHBA, a monophenolic microbial flavonoid metabolite, has been reported as the most effective heart-protective molecule [12]. Alkaloid is an organic chemical compound with ring structure containing one or more nitrogen atoms [13]. It is widely distributed in nature and is naturally occurring secondary metabolite found in plants and animals [13]. According to previous research, alkaloids are soluble under acidic conditions in the basic state, while they become lipid-permeable when neutral after losing a proton [13]. With these properties, alkaloids have been utilized for various purposes in plant and human disease treatments including anti-cancer, antimicrobial, analgesic, anti-diabetic, and other applications [13]. Phenolic acids, which possess the characteristics of acids, have been reported to exhibit cytotoxicity in certain types of cancer cells and normal cells [14]. Moreover, it has been reported that the hydroxyl groups of phenolic acids are essential for cytotoxicity, and their methylation or loss of hydroxyl groups completely removes cytotoxicity [14]. Major active components isolated from safflower, such as Hydroxysafflor yellow A (HSYA) and Safflomin B (SYB), are widely used in cerebrovascular diseases treatments [10]. Recent studies have reported a significant reduction in neurological deficits in a cerebral infarction model with the administration of Hydroxysafflor yellow A [3]. Furthermore, Hydroxysafflor yellow A (HSYA) indicates its potential as a protective agent against atherosclerosis by lowering blood lipid levels, regulating vascular contraction and dilation functions, and alleviating vascular damage [3]. It has been reported to have antiplatelet aggregation, antithrombotic, and inhibitory effects, as well as reduction in blood pressure and heart rate [15][16]. In today's modern society, individuals are pursuing something more than just performing their tasks; they are often engaged in what is commonly referred to as emotional labor. Beyond professional life, in daily interactions with others under the pretext of social life, people may experience stressful events as they engage in emotional labor [2]. This results in feelings of depression and lethargy. Previous studies have attempted to develop humanistic therapy programs, with the assumption that therapeutic activities involving humanities and arts could inject new enthusiasm and vitality into the depleted minds of those engaged in emotional labor [2]. Humanistic therapy aims to heal various issues faced by individuals who struggle with suppressed emotional expression, fostering a fulfilling life [1]. Numerous studies have reported that humanistic literacy has a positive impact on communication skills [17][18][19][20]. Given this, humanistic literacy is considered an essential element for smooth communication in society. We sought to induce a shift in thinking by offering humanities lectures to science and engineering students who may not have been exposed to humanities literacy. Through this, we aimed to explore the correlation between such emotional changes and the autonomic nervous system.

2. METHODS

2.1 Research Participants

This study targeted nine healthy male and female undergraduate students (2 males, 7 females) at D University in region B who volunteered for the research. The research duration was consisted of a 7-day period without any stimuli in a stable state and 15 days each in stable and aromatic states, during which participants watched the humanities lecture "Sebasi." The study was conducted after obtaining approval from the Institutional Review Board (IRB) of Dong-Eui University.

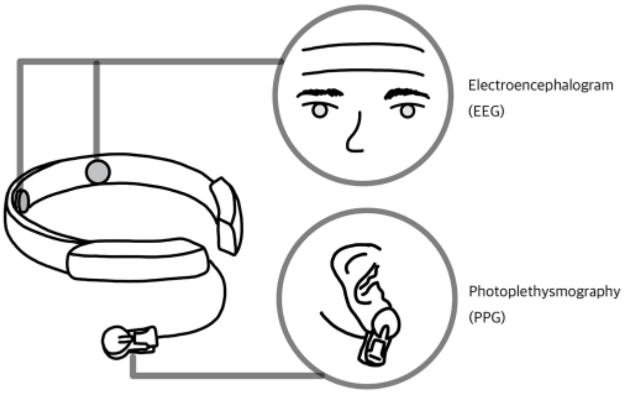
2.2 Materials

The safflower used in this experiment was purchased as a dried product after harvesting and was processed into a hot water extract. The safflower hot water extract was prepared by extracting 100g of safflower with 1L of distilled water for 3 hours and filtering it. The nebulizer used for olfactory stimulation had a spray volume of 0.32cc/minute, and the particle size of the aerosolized particles ranged from 0.5 to 5.0 μm, with more than 50% of particles falling within this range.

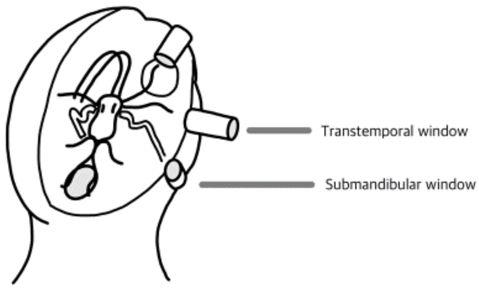
2.3 Research Method

As the autonomic nervous system was measured (Figure 3), the Mindcare device from OMNIFIT was employed to assess the activity levels of the sympathetic and parasympathetic nervous systems. The active electrode of the OMNIFIT Mindcare (Figure 1 and 2) was attached to the forehead, and the reference electrode was attached to the earlobe. The pulse wave sensor was attached to the index finger of the left hand. The LF (Low Frequency) values obtained after measurement were recorded as an indicator of sympathetic nervous system activity, while the HF

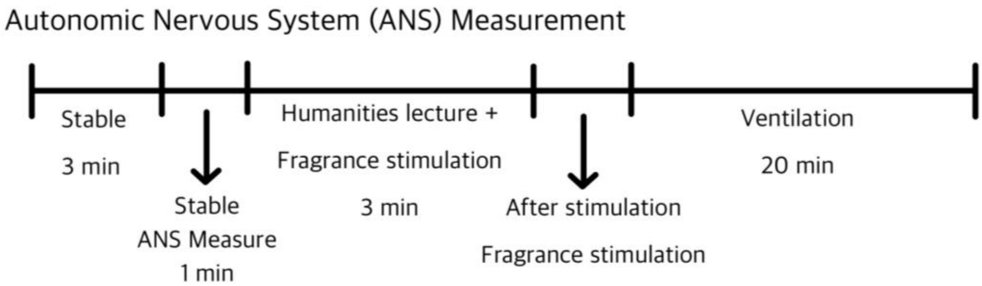
(High Frequency) values were recorded as an indicator of parasympathetic nervous system activity. After sitting in a comfortable chair and maintaining a stable state for 3 minutes, the ANS (Autonomic Nervous System) was measured for 1 minute during the stable state. Subsequently, ANS was measured for another 1 minute after olfactory stimulation and attending a humanities lecture. During olfactory stimulation, the nebulizer was positioned approximately 30cm away from the participant's face and sprayed. The stimulation was stopped once the participant perceived the scent. The experiment was conducted at 10-minute intervals. After completing all measurements, the laboratory window was opened and ventilated for a minimum of 20 minutes. Humanities lectures were provided through the monitor and speaker in the laboratory and continued until the end of the measurements.



[Figure 1] EEG electrodes and pulse wave sensor



[Figure 2] Transtemporal and Submandibular window



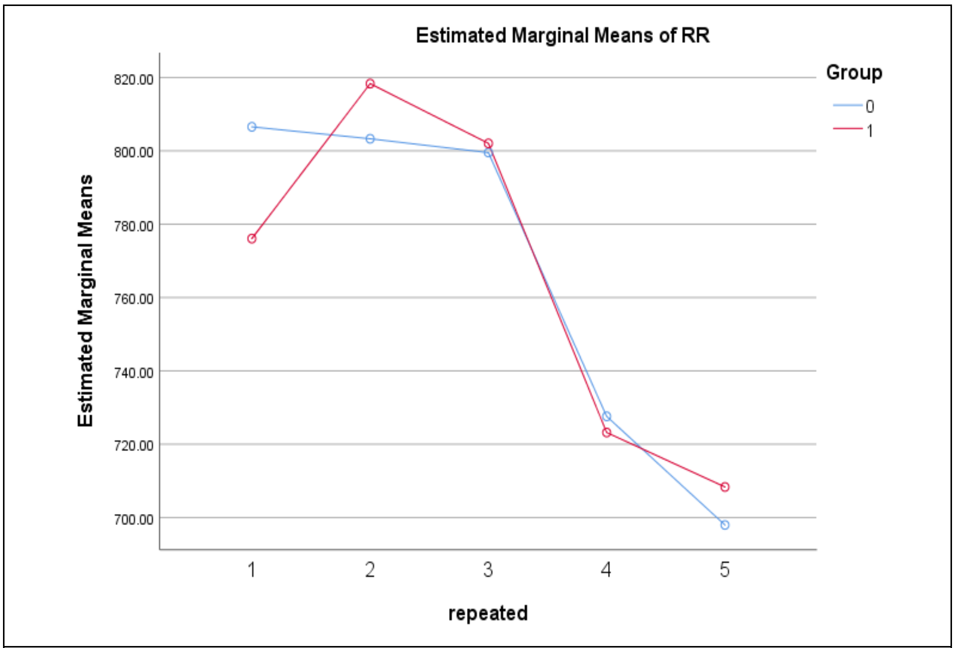
[Figure 3] ANS measurement

2.4 Data Analysis

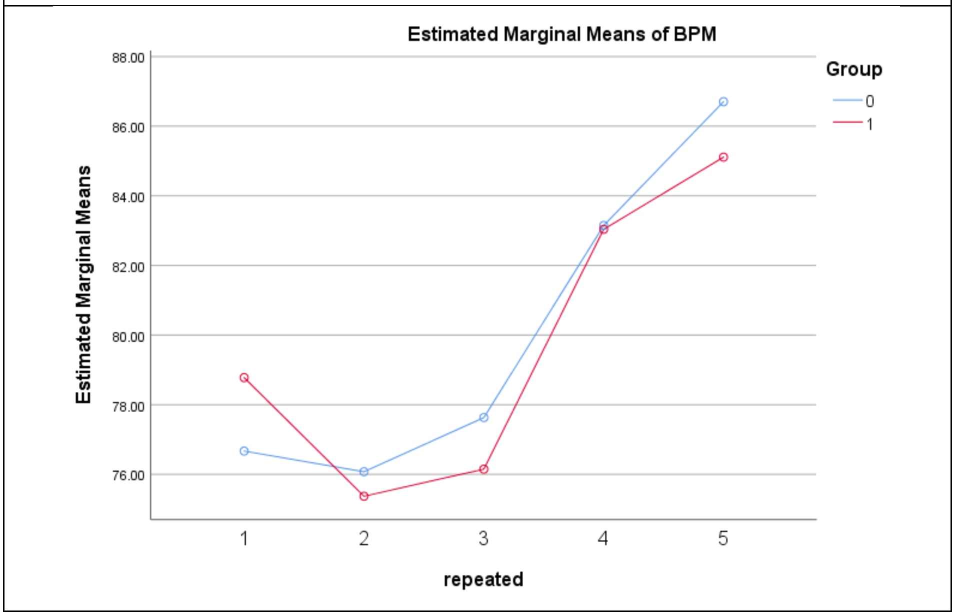
In this study, the autonomic nervous system data measured in five repeated sessions for each experimental group were analyzed using a multivariate approach under the assumption that the data related to seven indicators (RR, BPM, LF, HF, stress, BA, BS). A repeated measures multivariate analysis of variance (RM-MANOVA) model was selected as the statistical model for the analysis.

3. FINDINGS

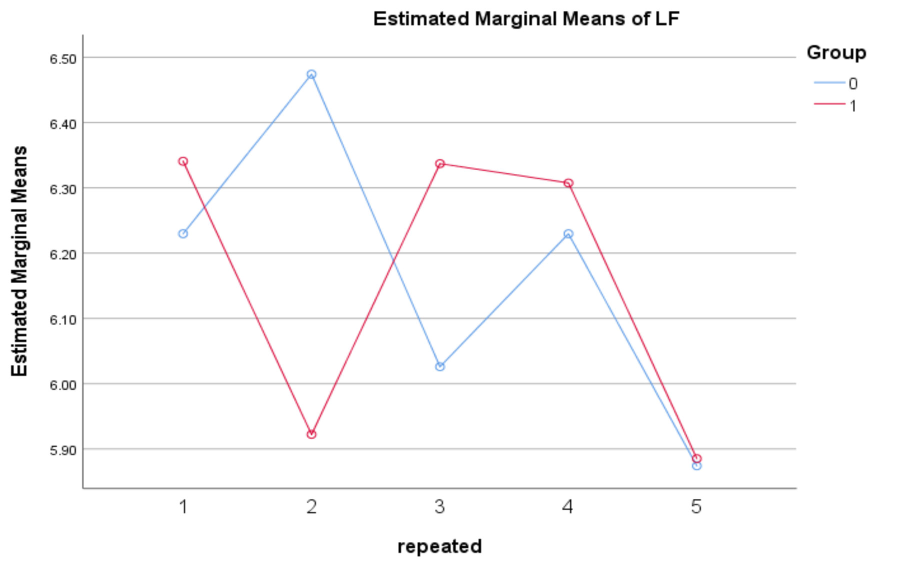
In the multivariate test, the difference between the two groups was not significant for the seven mean vectors; however, a significant difference was observed due to repeated measurements ($F(28, 25) = 3.880$, $p = 0.001$). When considering individual measurement locations as the basis, the repeated measurement effects were significant for five variables (RR, BPM, HF, stress, BS; for example, in the case of RR, $F(4, 208) = 15.441$, $p < 0.001$). There was no observed interaction between groups and repeated measurements. The analysis results are summarized in the profile plot (Figure 4) and corresponding numerical values (Table 1).



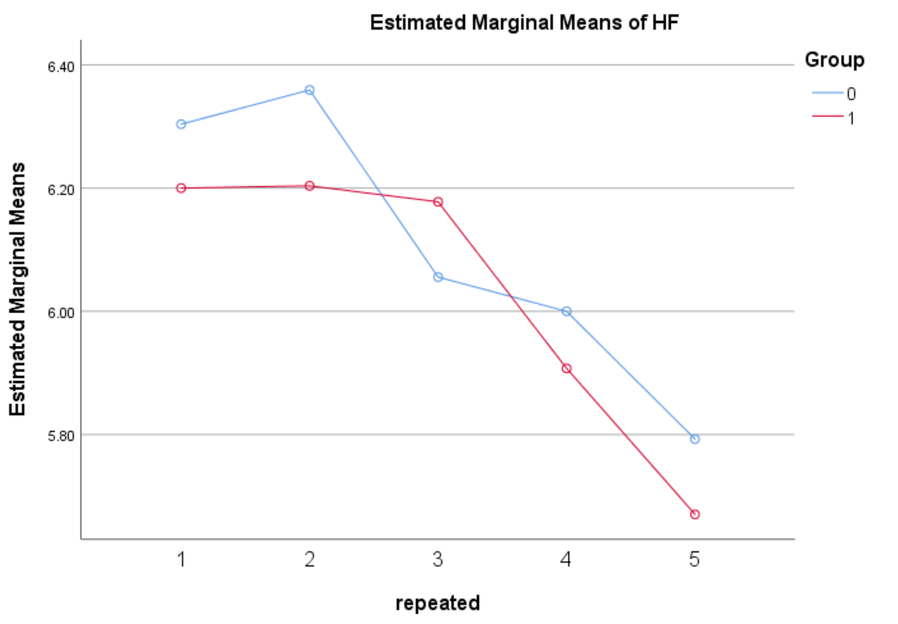
RR



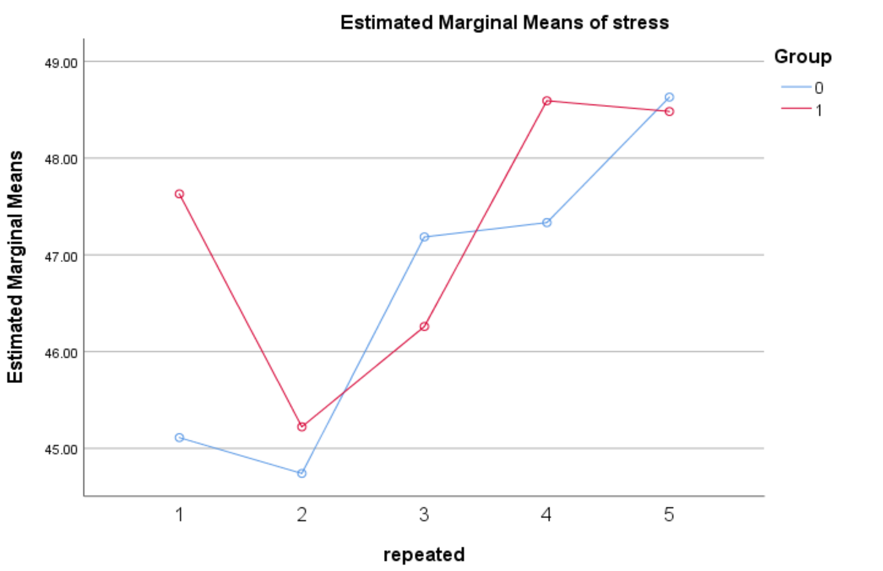
BPM


Estimated Marginal Means of LF
Estimated Marginal Means
6.50
6.40
6.30
6.20
6.10
6.00
5.90
1
2
3
4
5
repeated
Group
0
1

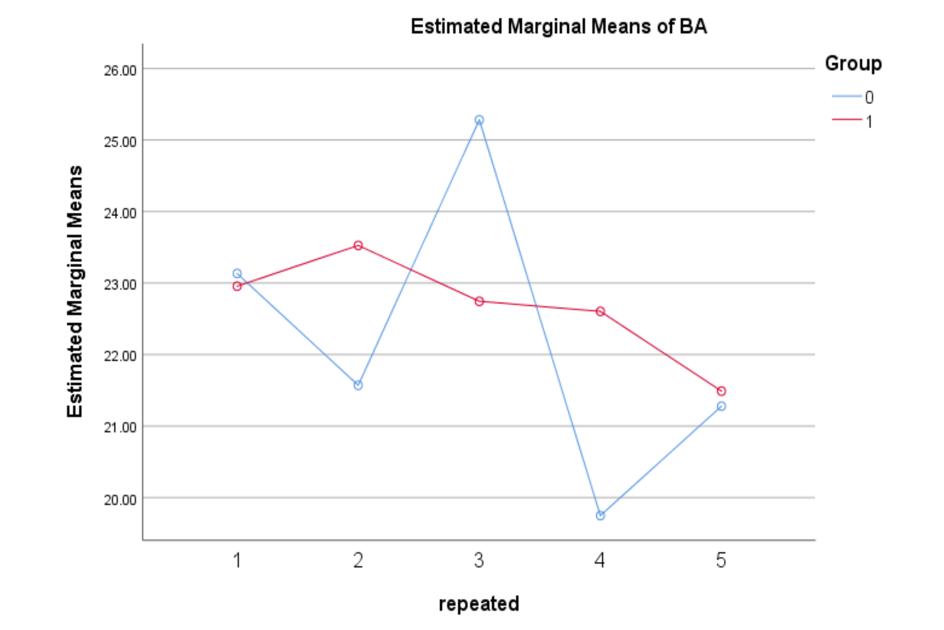
LF


Estimated Marginal Means of HF
Estimated Marginal Means
6.40
6.20
6.00
5.80
1
2
3
4
5
repeated
Group
0
1

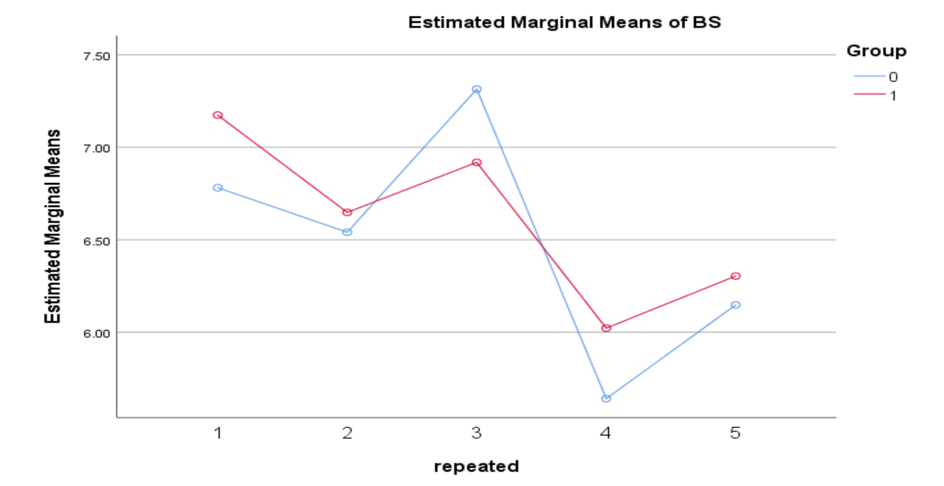
HF


Estimated Marginal Means of stress
Estimated Marginal Means
49.00
48.00
47.00
46.00
45.00
1
2
3
4
5
repeated
Group
0
1

stress



BA



BS

[Figure 4] Profile plots (0: control group; 1 safflower group)

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

Group	RM*	RR	BPM	LF	HF	stress	BA	BS
0	1	806.56	76.67	6.23	6.30	45.11	23.13	6.78
	2	803.30	76.07	6.47	6.36	44.74	21.57	6.54
	3	799.52	77.63	6.03	6.06	47.19	25.28	7.31
	4	727.59	83.15	6.23	6.00	47.33	19.75	5.64
	5	697.96	86.70	5.87	5.79	48.63	21.28	6.15
1	1	776.07	78.78	6.34	6.20	47.63	22.96	7.17
	2	818.33	75.37	5.92	6.20	45.22	23.53	6.65
	3	802.04	76.15	6.34	6.18	46.26	22.74	6.92
	4	723.19	83.04	6.31	5.91	48.59	22.60	6.02
	5	708.33	85.11	5.89	5.67	48.48	21.49	6.30

* RM: repeated measures

4. DISCUSSION

The autonomic nervous system is a part of the central and peripheral nervous systems that regulates and controls visceral functions[22]. The effects of the autonomic nervous system manifest through smooth muscles, cardiac muscles, and endocrine glands, maintaining the homeostasis of the body by integrating and regulating sensory inputs from the viscera in the central nervous system, including the hypothalamus, periaqueductal gray matter, parabrachial nucleus, nucleus ambiguus, and various regions of the medulla [22]. he balance of the autonomic nervous system is achieved through the interaction between the sympathetic and parasympathetic nervous systems [21]. When chronic stress persists, the body's homeostatic regulation system becomes impaired [21]. As a result, the activation of the sympathetic nervous system leads to prolonged contraction of the blood vessels within muscles, causing a decrease in blood circulation. This, in turn, leads to the accumulation of waste products within the muscles over an extended period, leading to feelings of fatigue, discomfort, or pain [21]. The RR interval represents the variation in the time between consecutive R peaks, the highest peaks in the continuous waveform of an electrocardiogram. In this study, changes in the RR interval were not prominently observed [23]. BPM represents the number of heartbeats per minute, and in this study, changes in BPM were not prominently observed [24]. This indicates that the participants were in a physically stable state, rather than undergoing physical exertion during the study. LF is a relative low-frequency domain that serves as an indicator of sympathetic nervous system activity [22]. In this study, LF values were generally higher than the standard range of 5.2, and the results tended to be higher after safflower extract inhalation compared to before, suggesting an activation of the sympathetic nervous system. In contrast, HF represents the relative high-frequency domain indicative of parasympathetic nervous system activity [22]. This measurement also showed values higher than the standard range of 5.42 overall during the study. Considering that the balance between the two results did not change significantly and the overall values were higher, it is suggested that both the sympathetic and parasympathetic nervous systems were activated by safflower extract inhalation and humanities lectures. BA (Brain Activity) is an indicator of the mental workload of the brain, signifying whether cognitive activities are at an efficient level. It reflects SEF (Spectral Edge Frequency) 90, determined as the frequency corresponding to 90% of the total brain wave sum, and the electrode's location is Fp1 [25]. The optimal range is 11.719.5Hz; however, the study generally showed results ranging from 19.7523.13Hz, indicating a level higher than the normal range. Although the difference before and after safflower extract inhalation was not striking, it should be considered that the study focused on university students whose brains are frequently activated due to academic activities. Although the difference before and after inhaling safflower extract was not clear, it should be considered that the study focused on university students whose brains are frequently activated due to academic activities. Nevertheless, the overall tendency to show levels higher than the normal range suggests that the brain activity measured while attending humanities lectures induced cognitive workload, indicating a state of concentration and immersion in the brain [25]. In addition, BS, an indicator of Brain Stress, was analyzed based on the magnitude of the increase in High Beta power in stress situations [23]. High stress is indicated if the value is above 7, but in this study, most values were around 5~6, suggesting that significant brain stress was not induced. The basic mechanism of HSYA, a chemical component of safflower, includes reducing lipid peroxidation, inhibiting the activity of SOD and GSH-Px (glutathione peroxidase), upregulating eNOS (endothelial nitric oxide synthase) protein expression, and reducing cell death [8]. Recent studies suggest the potential impact of HSYA on improving autonomic nervous system function in rat ischemia models with lymphostatic encephalopathy-related nerve damage [8]. Several studies have indicated that Hydroxysafflor yellow exhibits activity in the blood supply to the brain and heart, including conditions like atherosclerosis [6][9]. Most of these studies focus on preventive and therapeutic aspects to facilitate smooth blood supply. This study associated the findings with brain activity levels and the autonomic nervous system, providing a positive foundation for the data. Further research is needed to explore the relationship between safflower components and the autonomic nervous system.

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