Exergaming Improves Executive Functions in Patients with Metabolic Syndrome

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Shanshan Wu[1], Eunah Jo[2], Hongqing Ji[1], Kyung-Hee Kim[3], Jung-Jun Park[1], Bo Hyun Kim[4*], and Kyoung Im Cho[2,*]

[1]Division of Sport Science, Pusan National University, Busan 46241, Korea

[2]Department of Internal Medicine, Kosin University College of Medicine, Busan 49267, Korea

[3]Department of Cardiology, Sejong General Hospital, Bucheon 22972, Korea

[4]Department of Internal Medicine, Pusan National University Hospital and Biomedical Research Institute, Busan 49241, Korea

Running Title: Exergame in Patients with Metabolic Syndrome

* Corresponding author

Kyoung-Im Cho, MD, Division of Cardiology, Department of Internal Medicine, Kosin University School of Medicine,34 Amnam-Dong, Seo-Ku, Busan 49267, Korea, Tel: (82) 51-990-6105, Fax: (82) 51-990-3005, E-mail: kyoungim74@gmail.com

* Co-corresponding author

Bo Hyun Kim, M.D., Ph.D. Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, Busan, 49241, Korea. Tel: (82)-51-240-7678, Fax: (82) 51-254-3237, E-mail: pons71@hanmail.net

Abstract

Background: Recent studies indicate that exercise-related games can improve executive function, attention processing, and visuospatial skills.

Objective: This study investigates whether exercise with exergaming can improve the executive function in patients with metabolic syndrome (MetS).

Methods: Twenty-two MetS patients were recruited and randomly assigned to the exergaming group (EXG) and treadmill exercise group (TEG). The reaction time (RT) and electrophysiological signal from the frontal (Fz), central (Cz), and parietal (Pz) cortex were collected during a Stroop task after 12 weeks' exercise.

Results: During the Stroop congruence (facilitation) judgment task, both EXG and TEG showed significantly faster RT after 12 weeks of exercise training. For N200 amplitude, EXG significantly increased on Fz and Cz. These changes were significantly larger in EXG than TEG. For P300 amplitude, EXG significantly increased on Fz, Cz, and Pz, while TEG significantly increased on Cz and Pz only. During the Stroop incongruence (interference) judgment task, both EXG and TEG showed significantly faster RT. For P300 amplitude, EXG significantly increased on Fz and Cz only, while TEG significantly increased on Fz, Cz, and Pz.

Conclusions: Exergaming improves executive function in patients with MetS as much as normal aerobic exercise. Particularly, the unique benefit of the exergaming beyond increased aerobic capacity is the improvement of selective attention among cognitive functions. Thus, exergaming could be recommended to someone who needs to improve brain responses of concentration and judgment as well as physical fitness.

Keywords: exergaming; executive functions; event-related potential; metabolic syndrome

Introduction

In recent years, the relationship between cognitive function and metabolic syndrome has been widely studied [1,2]. Metabolic syndrome (MetS) has been shown to be associated with a decline in executive function [3,4] due to multiple risk factors, including hypertension, dyslipidemia, impaired glucose homeostasis, and abdominal obesity. Executive functions include basic cognitive processes such as attentional control, cognitive inhibition, inhibitory control, working memory, and cognitive flexibility [5].

Cognitive neuroscience is using Stroop tasks to measure selective attention capacity and skills, as well as processing speed ability, indicating executive functions [6]. Electroencephalographic (EEG) activity using event-related positioning technology P300 and N200 has been widely used to measure selective attention capacity and skills, and a behavioral performance such as reaction time (RT) is commonly used to measure processing speed ability [7,8]. N200 negativity (200~350 ms post-stimulus) is an event-related potential (ERP), which indicates attentional capacity that is usually induced before motion response control and is related to the cognitive processes of stimulus recognition and differentiation [9]. P300 positivity (300~600 ms post-stimulus) is another ERP, reflecting memory-related neural processing that is involved in categorizing incoming information and updating the context of the working memory (e.g., encoding, rehearsal, recognition, and retrieval) [10].

It is well known that aerobic exercise training provides various beneficial clinical outcomes in metabolic disease patients [11,12]. Its effects on cognitive function, especially executive function, also have been reported [13]. Furthermore, recent studies reported that both aerobic and resistance exercise training facilitate overall electrophysiological effects (e.g., increased ERP P300 amplitudes) and behavior index (e.g., faster RT) in healthy elderly people [14,15].

In addition, aerobic exercise has also been reported to improve cognitive processes in cortical cognitive control (P300 amplitude) in studies of chronic stroke patients [16].

Recently, exergaming (a combination of "exercise" and "gaming") has attracted much attention as a novel exercise method to improve cognitive function because it utilizes video games that require body movements while simultaneously presenting the user with a cognitively challenging environment [17]. Along with its popular usage for leisure and entertainment, there is a growing interest in the application of exergaming to improve clinical outcomes. Recent studies using exergaming showed beneficial effects on cognitive and dual-task functions, which reduced falls in older adults [18] as well as cardiovascular disease risks such as body fat, serum adipokine levels, and lipid profiles [19]. Exergaming also promoted executive functions and cognitive processing speed in elderly and children [20,21]. This growing evidence suggests that exergaming's have the benefit of improving cognitive and physical functions.

Although many previous studies have reported improvements in cognitive function following exergaming, it is not clear whether this benefit is due to an exercise effect or video game effect. In addition, all of these studies measured RT, instead of ERP using EEG, which limits to illuminate brain activities. Considering that EEG can measure electrical activities in various cortex areas in the brain, it is necessary to investigate ERP using EEG to evaluate executive function. Therefore, we examined the benefits of exergaming compared to normal exercise and investigated executive function by measuring RT as well as N200 and P300 in three cortex areas during Stroop tasks in patients with MetS.

Methods

Participants

A total of 22 MetS male and female patients aged between 50-80 years participated in this study. MetS was defined according to the modified NCEP Adult Treatment Panel III (NCEP-ATP III) definition for South Asians. Briefly, individuals with three or more of the following criteria were defined as MetS: central obesity (waist circumference ≥90 cm for men; ≥ 85 cm for women), fasting plasma glucose ≥100 mg/dL or current treatment for diabetes mellitus, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or current treatment for hypertension, serum triglyceride ≥150 mg/dL, low HDL cholesterol (men<40 mg/dL; women<50 mg/dL) [22]. Subjects were asked to not exercise for 24 hours before the experiment. They were also instructed to eat usual meals and to finish meals 4 hours before the experiment, while avoiding alcohol 1 day before the experiment and caffeine during the 4 hours prior to the experiment. All subjects were required to complete a written informed consent approved by the Institutional Review Board of Kosin University College of Medicine.

The sample size was calculated using sample size calculation software (G*Power version 3.1.9.2 for Windows; http://www.gpower.hhu.de), with effect size 0.484, statistical power 0.8, and statistical level of significance 0.05. This effect size was calculated from the previous studies [13,14]. As a result, the sample size for each group became 8, and we decided to recruit 11 patients for each group, with a potential 30% dropout rate.

Exercise Training Interventions

Exercise training was conducted at the Kosin University Gospel Hospital U-healthcare Center. Each participant was instructed to immediately inform the supervisor if he or she experienced any unusual symptoms during exercise training and to consult a physician if needed. Subjects were excluded if they did not perform more than 80% of the exercise sessions.

All subjects were randomly divided into two groups: exergaming and treadmill exercise group. Subjects had 2 weeks of adaptation and then carried out 12 weeks of exercise training: 60 min/day, 60-80% of heart rate reserved (HRR), 3 days/week. Each exercise session consisted of 10 minutes of warm-up, 40 minutes of main exercise, and 10 minutes of warm-down.

The exergaming group (EXG) performed exercise using Exerheart® devices (D&J Humancare, Busan, South Korea) composed of a running/jumping mat [730(W) × 730(D) × 130(H)] and a tablet PC on a stand (can be adjusted to any height between 70 and 155 cm) (Supplemental Figure 1A). Exerheart® is an exergaming developed for in-situ running along with the video game called "Alchemist's Treasure" (D&J Humancare, Busan, South Korea) (Supplemental Figure 1B). To play this game, the subject has to run or jump on a spot on the mat to move a virtual avatar on the screen of the tablet PC to the front, back, left, and right along with music (Supplemental Video 1 for online). The subject can control the speed of avatar movement by running or jumping speed on the mat. The treadmill exercise group (TEG) performed exercise using commercial treadmills (MOTUS, Gyeonggi-do, South Korea). Each subject walked or ran on the treadmill at a comfortable speed.

For both EXG and TEG, all subjects' heart rates (HR) during exercise were monitored using HR monitors (polar RS400sd, Madison Height, Michigan, USA) to confirm that the value was within the target HR range. The Karvonen formula (1957) [23] was used to calculate HR reserve (HRR, estimated maximal HR– resting HR) and target HR during exercise [(HRR × given percentage of training intensity) + resting HR)].

Stroop Test

For assessment of executive function, a computer-based version of the Stroop task was administered with Telescan software (LAXTHA, Daejeon, South Korea). During the task, subjects were presented with a color word appearing in the same color on congruent trials (e.g. “blue” printed in blue) and in a different color on incongruent trials (e.g. “blue” printed in green) [24]. To provide similar visual content, blue, green, and yellow were chosen as stimuli.

Subjects performed Stroop task twice, pre- and post-exercise training. Subjects sat 1 meter from the screen, and when the color words appeared on the screen, they clicked the left keyboard for the congruent test and the right keyboard for the incongruent test. Subjects were instructed to respond as quickly and accurately as possible. The rate of measurement targeted for 50%. Each color word (vertical viewing angle: 2 °) was presented for 200 ms, and the response was allowed within 1500 ms. The inter-stimulus interval varied randomly between 1500 and 2500 ms.

Electroencephalographic (EEG) Measurements

EEG activity was recorded during the modified Stroop task using a computerized polygraph system– Type A: A total of 31-channel Poly G-A (LAXTHA, Daejeon, South Korea). Ag-AgCl electrodes (LAXTHA, Daejeon, South Korea) were placed on frontal (Fz), central (Cz), and parietal (Pz) cortex areas, according to the International 10-20 system. Midline locations referenced to link earlobe electrodes. Horizontal and vertical electrooculograms (EOGs) were monitored by electrodes placed above and below the left eye and at the outer canthus of both eyes, respectively. The impedance of all electrodes was maintained below 10 kΩ. The bandpass filter of the amplifier was 0.1–100 Hz, the sampling rate was 1000 Hz, and a notch filter was at 60 Hz.

The N200 component was defined as the largest positive peak occurring between 200-350 ms post-stimulus, and the P300 component was defined as the largest positive peak occurring between 300~600 ms post-stimulus [7]. N200 and P300 amplitudes were measured as the difference between the mean pre-stimulus baseline and maximum peak amplitude. Telescan's built-in high pass IIR filter was used for filtering. Waveforms were digitally smoothed with a low-pass filter using a half-power cut-off of 10 Hz prior to analysis.

Statistical Analysis

Due to the small sample size, we used nonparametric statistics for data analysis. We used the Wilcoxon signed-rank test to examine the changes of each dependent variable after intervention within each group. The Mann–Whitney U test was used to make comparisons of the delta values between training groups (Δ-EXG vs Δ-TEG). The effect size of partial eta-squared ($\eta 2$) was reported for significant effects, where the alpha level for all of the tests was set at 0.05. Data were expressed as mean ± standard deviation of mean. All statistical tests were processed using the software SPSS 24 version.

Results

Demographic and physical characteristics for all subjects are provided in Table 1. There were no significant group differences at baseline measurements.

Reaction Time

The changes in congruent RT after 12 weeks of exercise training were not significantly different between EXG and TEG (Table 2). EXG significantly shortened congruent RT, as did TEG (Figure 1A). The changes in incongruent RT after 12 weeks of exercise training were not significantly different between EXG and TEG. EXG significantly shortened incongruent RT, as did TEG (Figure 1B).

Event-related Potential Data

N200 amplitude

The results in Table 3 after 12 weeks of exercise training, the increases in congruent N200 amplitude on Cz, and Pz in EXG were significantly greater than in TEG, but not on Fz. EXG significantly increased congruent N200 amplitude on Cz, but not on Fz and Pz. On the other hand, TEG showed no significant changes in congruent N200 amplitude on Fz, Cz, or Pz (Figure 2A).

The changes in incongruent N200 amplitude on Fz, Cz, and Pz after 12 weeks of exercise training were not significantly different between EXG and TEG (Table 3). Interestingly, EXG did not significantly change incongruent N200 amplitude on Fz, Cz, or Pz. TEG also did not significantly change incongruent N200 amplitude on Fz, Cz, or Pz (Figure 2B). The waveforms of congruent and incongruent N200 amplitudes on Fz, Cz, and Pz for EXG and TEG before and after exercise are shown in Figure 3.

P300 amplitude

Table 3 shows the results of Mann–Whitney U test for changes in congruent P300 amplitude on Fz, Cz, and Pz after 12 weeks of exercise training was not significantly different between EXG and TEG. EXG significantly increased congruent P300 amplitude on Fz, Cz, and Pz. However, TEG significantly increased congruent P300 amplitude on only Fz and Cz, but not on Pz (Figure 2C).

There were no significant differences in the changes in incongruent P300 amplitude on Fz, Cz, and Pz between EXG and TEG after 12 weeks of exercise training (Table 3). EXG significantly increased incongruent P300 amplitude on Cz and Pz, but not on Fz. On the other hand, TEG significantly increased incongruent P300 amplitude on Fz, Cz, and Pz (Figure 2D). The waveforms of congruent and incongruent P300 amplitudes on Fz, Cz, and Pz for EXG and TEG before and after exercise are shown in Figure 3.

Discussion

This study was the first to investigate the benefits of exergaming compared to normal exercise on the behavioral performance and executive function of patients with MetS. We found that 12 weeks of both exergaming and treadmill exercise training similarly and effectively improved behavioral performance and congruent and incongruent memory-related neural processing. However, only exergaming training improved congruent selective attention, while neither exergaming nor treadmill exercise training affected incongruent selective attention. These results suggest similar overall effects of exergaming and normal exercise on behavioral performance and executive function of patients with MetS, but exergaming could be more effective than normal exercise for congruent selective attention.

The present study showed that both 12 weeks of exergaming and treadmill exercise training effectively improved reaction time in MetS patients, and these changes were not different between exergaming and treadmill exercise training. These results indicate that both exergaming and normal exercise improve behavioral performance, but exergaming does not have more beneficial effects compared to normal exercise. In our previous study, we examined the performance of control tasks using a simple acute aerobic exercise and complex exercise [25]. The results indicated that participants did not have different performance when participating in simple exercise compared to very skilled complex exercises. In another study, contrary to our results, an acute single-bout study comparing the effects of standard normal exercise to exergaming on attention performance in young adults found no significant improvement with exergaming [7]. The result of that study suggests that, after 20 minutes of unskilled Wii Fit ™, the brain needs more information processing, which may be the source of control requirements and pressure increases, offsetting the potential benefits of the exercise component. However, compared to the Wii Fit™, exergaming with exerheart® is running-based aerobic exercise on an air cushion board with game-based contents such as adventures, racing, and quizzes, which continue to arouse interest in exercise. So, with exerheart®, an individual is running constantly with changing visual stimuli; these repeated effects will simultaneously increase physical activity and cognitive function via interactive virtual reality engagement [20]. Therefore, through exergaming and treadmill exercise, the reaction time of Stroop task conditions of MetS patients could be shortened, which would promote basic information processing and executive function of suppression control.

In this study, the congruent and incongruent P300 amplitudes were increased after both 12 weeks of exergaming and treadmill exercise training, with no difference between EXG and TEG. These results indicate that both exergaming and normal exercise improve memory-related neural processing, but exergaming has no more beneficial effects than normal exercise. In other words, participation in exercise, regardless of exercise modality, induces an increase in working memory in executive function. However, our previous study showed that P300 amplitude increased during a control task following futsal relative to seated rest or treadmill exercise, indicating that complex control of the brain stimulates the executive control network of the cortex [25]. It was found that, as age increases, the P300 amplitude in the central (Cz) region decreases, and the scalp distribution of the P300 amplitude is transferred to the frontal region [26]. Pontifex *et al*. [27] examined P300 components and found that older adults with high cardiorespiratory fitness only exhibited greater P300 amplitudes, and Tsai and colleagues [28] found that different exercise types have greater amplitudes for older P300. However, as they pointed out, regardless of the type of older people to participate in sports, physical exercise is a lifestyle factor that is crucial to preventing age-related biological degeneration in the frontal-to-parietal areas, thus delaying the cognitive declines associated with later life. Considering that exergaming is a kind of aerobic exercise, it stands to reason that exergaming could improve not only cardiovascular health, but also cognitive plasticity, thereby improving categorization of incoming information and updating the context of working memory in MetS patients.

We found that neither exergaming nor treadmill exercise training affected incongruent N200 amplitude. However, the consistent N200 amplitude only increased by exergaming training. These results indicate that, while neither exergaming nor normal exercise affects incongruent selective attention, only exergaming improves congruent selective attention, which suggests that exergaming have a more beneficial effect on congruent selective attention compared to normal exercise. The results of many studies on the relationship between exercise and N200 amplitude indicate show that exercise has no significant effect on N200 amplitude [28,29]. Pontifex and his colleagues showed that general decreases in N200 amplitudes across scalp sites were observed during exercise relative to rest [29]. The N200 component plays a key role in the anterior cingulate cortex (ACC), which is part of the potential prefrontal cortex and regulates dopaminergic neurons in cognitive functions, such as working memory, attention, and decision making [30-32]. Therefore, the reduction of N200 amplitude caused by normal aerobic exercise severely limits ACC activity [29]. In light of our N200 amplitude findings, these results suggest that exergaming better regulates the activity of ACC in the prefrontal cortex than aerobic exercise, thereby effectively increasing consistent selective attention.

Recent studies suggest that combining motor and cognitive demands during exercising can improve cognitive function more than training these domains separately [17,33]. In addition, cognitive video game training can have beneficial effects on memory, attention, and reaction time in older adults [34,35]. In previous studies, when participants consistently performed exercises in a virtual environment, an increase in N200 amplitude positively promoted decision-making (frontal and central) and visual perception (occipital) [36]. Therefore, the exergaming positively promotes visual perceptual stimulation in the virtual environment to enhance the selective attention activity associated with the cerebral cortex, thereby strongly promoting executive function. Exercise and video games can each improve brain structure and function [37-40]; thus, their combination can have a complementary effect on brain stimulation and protection.

Our study provides evidence that exergaming improves reaction time and incongruent memory-related neural processing in MetS patients as much as normal aerobic exercise. In addition, exergaming improves congruent selective attention, which was not changed by normal aerobic exercise. Therefore, exergaming could provide an innovative way to enjoy aerobic exercise compared to repetitive, conventional exercises.

Although this study found significant results, there are some limitations in this study as follows: 1) the sample size in this study is relatively small, even though all patients were very hard motion for 12 weeks; 2) the range of age was relatively large, 50~80 years old. Considering that with age, response time and brain activity are usually slower, we cannot rule out the possibility that age will affect the performance of executive function. However, the mean age was similar in both groups, so this possibility might be low in this study; 3) the intensity of the

Exerheart® using "Alchemist's Treasure" game was not able to be controlled.

Conclusions

The results of this study suggest that exergaming enhances brain response to concentration and judgment, resulting in increased behavioral response of the MetS patients, comparable to that of normal aerobic exercise. Furthermore, the unique advantage of exergaming is that it improves selective attention among cognitive functions, unlike normal aerobic exercise. Therefore, exergaming could be recommended to some patients who need to improve executive function as well as physical fitness.

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Conflicts of Interest

None declared.

Multimedia Appendix 1. MP4.

Participants played the video game with Exerheart®.

[Author- Kyoung Im Cho, videographer - Shanshan Wu, 15 seconds length and 1.48 MB size]

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Figure Legends

Figure 1. Mean reaction time (RT) during stroop task (A. congruent/ B. incongruent) performance after exergaming group (EXG) and treadmill exercise group (TEG) before and after the exercise intervention.

Figure 2. N200 and P300 amplitudes (mean ± SE) on three electrodes (Fz, Cz, and Pz) during the Stroop task (A. congruent/ B. incongruent N200 amplitudes; C. congruent/ D. incongruent P300 amplitudes) in the exergaming group (EXG) and treadmill exercise group (TEG) before and after 12 weeks of exercise training.

Figure 3. Average event-related potential waveforms of electrodes (Fz, Cz, Pz) for mean N200 and P300 amplitudes during the Stroop test (A. congruent/ B. incongruent) in the exergaming group (EXG) and treadmill exercise group (TEG) before and after 12 weeks of the exercise training.

Supplement Figure 1. A. The exergaming group performed exercise using Exerheart® devices by permission of D&J Humancare which had the copyright holder of Exerheart®. B. Features of the video game "Alchemist's Treasure".

Table 1. Baseline characteristics of demographic information.

Group / Factor	EXG (N=11)	TEG(N=11)	*P* value
Age(years)	64±10	60 ±7	.298
Height(cm)	154.24±5.73	161.66±7.1	.014
Weight(kg)	69.38±10.54	71.47±11.62	.663
BMI(kg/m^2)	29.07±3.3	27.31±3.52	.24
WC(cm)	97.36±10.95	93.6±8.78	.399
Glucose(mg/dl)	123.55±25.68	112.36±29.37	.353
HDL-chol (mmol/L)	46.32±8.91	50.59±10.52	.316
LDL-chol (mmol/L)	66.19±22.8	78.38±19.52	.193
TC (mmol/L)	134.81±25.52	146.67±12.04	.179
TG (mmol/L)	136.82±78.88	145.73±142.74	.858
SBP (mmHg)	127.09±16.86	128.09±17.39	.892
DBP (mmHg)	75.55±9.43	77.73±11.99	.64

Values are mean ± SD. EXG, exergame group; TEG, treadmill exercise group; BMI, body mass index; WC, waist circumference; TG, triglycerides; HDL-chol, high-density lipoprotein cholesterol; LDL-chol, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2. Comparison of Stroop task congruent and incongruent reaction time of EXG and TEG groups

Effects	Group	pre	post	*P* value[a]	*η2*	*P* value[b]
Congruent	EXG	1265.91±383.15	1012.09±221.64	0.003	0.053	0.279
	TEG	1124.18±161.21	957.82±138.05	0.003		
Incongruent	EXG	1299.09±367.48	984.73±204.81	0.003	0.008	0.670
	TEG	1171.36±163.26	974.55±120.97	0.003		

[a] Wilcoxon Signed Rank Test: comparison pre vs. post within group.
[b] Mann Whitney *U* Test: comparison the delta values between groups (Δ-EXG vs Δ-TEG).

Table 3. Comparison of Stroop task congruent and incongruent N200 / P300 amplitudes of EXG and TEG groups

Components	Effects		Group	pre	post	*P* value[a]	$\eta 2$	*P* value[b]
N200 Amplitude	Congruent	Fz	EXG	-1.33±1.95	-4.1±3.02	0.091	0.138	0.088
			TEG	-0.98±3.14	-0.41±3.82	0.328		
		Cz	EXG	-1.59±2.54	-5.13±2.94	0.016	0.291	0.010
			TEG	-1.61±3.89	-0.97±4.59	0.424		
		Pz	EXG	-1.58±1.89	-4.06±2.89	0.062	0.207	0.034
			TEG	-1.32±3.62	-0.89±3.99	0.534		
	Incongruent	Fz	EXG	-2.85±2.3	-2.78±3.02	0.477	0.041	0.365
			TEG	-1.37±3.3	-0.73±3.18	0.424		
		Cz	EXG	-3.23±2.69	-3.93±2.92	0.286	0.099	0.151
			TEG	-1.9±3.82	-1.1±3.65	0.213		
		Pz	EXG	-2.86±2.45	-3.07±2.62	0.722	0.008	0.699
			TEG	-1.4±3.66	-1.01±3.52	0.477		
P300 amplitude	Congruent	Fz	EXG	2.3±1.94	7.12±5.73	0.003	0.008	0.699
			TEG	3.21±1.95	4.82±3.78	0.011		
		Cz	EXG	1.92±1.63	6.49±5.28	0.004	0.006	0.748
			TEG	2.36±0.93	5.08±3.03	0.013		
		Pz	EXG	1.44±1.69	5.2±5.88	0.004	0.099	0.151
			TEG	1.74±1.26	4.87±3.64	0.328		
	Incongruent	Fz	EXG	2.26±3.14	4.48±3.27	0.091	0.018	0.562
			TEG	1.93±2.26	3.85±3.04	0.004		
		Cz	EXG	2.03±2.8	4.38±2.81	0.016	0.002	0.847
			TEG	1.59±1.63	3.74±2.99	0.021		
		Pz	EXG	1.58±2.44	3.2±2.73	0.021	0.000	0.949
			TEG	1.05±0.92	3.33±2.59	0.033		

[a] Wilcoxon Signed Rank Test: comparison pre vs. post within group.
[b] Mann Whitney *U* Test: comparison the delta values between groups (Δ-EXG vs Δ-TEG).