



The relation of physical activity to functional connectivity between brain regions[☆]

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ABSTRACT

Objective: To investigate the relation of physical activity to functional connectivity between brain regions during an executive control task using phase-locking values (PLVs) and a graph theoretical analysis.

Methods: Twenty active and 20 sedentary young adults had their electroencephalograms recorded during a spatial priming task. The positive and negative priming conditions require greater amounts of executive control to inhibit previous trial information relative to control condition.

Results: Beta band PLVs during the priming conditions were larger relative to the control condition 300–400 ms after stimulus onset only in the active group, suggesting that physically active individuals have greater functional connectivity between brain regions during task conditions requiring greater amounts of executive control. Further, graph theoretical analysis was conducted for the PLVs in the 300–400 ms post-stimulus epoch, with analyses indicating that physical activity is associated with the strength of functional connectivity between brain regions rather than the structure of network.

Conclusions: Greater functional connectivity between brain regions and efficiency of neural network are potential mechanisms for the positive relation of physical activity to cognitive function.

Significance: The present study suggests that PLVs and graph theoretical analysis is a useful tool to investigate the relation of physical activity on human cognition.

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1. Introduction

A growing literature has emerged indicating a positive relationship between physical activity, cognition, and brain using human and non-human animal models (see Hillman et al. (2008) for review). Historically, most have focused on aging with available research indicating that physical activity is associated with sparing of age-related cognitive decline. More recently, a growing focus on executive control (i.e., processes subserving inhibitory control, working memory, and cognitive flexibility) has developed because findings have demonstrated that physical activity has a disproportionately larger relation to this aspect of cognition (Colcombe and Kramer, 2003; Kramer et al., 1999). This selectively greater effect for executive control is well-founded given that the prefrontal cortex, which exhibits disproportionately larger age-related degrada-

tion (Raz et al., 1997), is believed to mediate, to a larger extent, this aspect of cognition (Funahashi, 2001). Furthermore, investigators have begun to examine the physical activity–executive control relationship during earlier periods of the human lifespan. Several studies have emerged using event-related brain potentials (ERPs) that have observed a positive relation of physical activity to executive control in not only older adults, but also in younger adults (Hillman et al., 2006; Kamijo and Takeda, 2009; Themanson and Hillman, 2006; Themanson et al., 2006, 2008) and children (Hillman et al., 2009). Thus, it appears that physical activity may benefit executive control processes during earlier periods of the human lifespan.

Despite these interesting findings, the underlying mechanisms supporting the physical activity–cognition relationship are not well understood. Accordingly, researchers have investigated a number of potential mechanisms in both human and non-human animal models at the molecular, cellular, and systems level. It has been established that synchronization of the electroencephalographic (EEG) signal measured across electrode sites closely relates to the connectivity of perceptual and cognitive functions between brain regions when time locked to the onset of a stimulus (Rodriguez et al., 1999). Given that physical activity has been related to improvements in cognition, the underlying functional connectivity between brain regions may also be altered to support

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more effective cognitive performance. However, to our knowledge, the relationship between physical activity and EEG synchronization during cognitive performance has not been reported. It is important to clarify this issue to elucidate possible mechanisms underlying the positive relation of physical activity to cognition. In the present study, we examined the relation of physical activity on functional connectivity between brain regions using phase-locking values (PLVs) derived from stimulus-locked EEG data (Lachaux et al., 1999). PLVs refer to variations in phase synchrony between EEG signals measured from two electrodes across trials. The phases of a signal are extracted via a wavelet transformation and used to calculate the phase difference between electrodes. Higher PLVs indicate that the phase differences are constant across trials, suggesting a functional connectivity between brain regions near these electrodes. PLVs are thought to have an advantage over other coherence measures used to examine the functional connectivity during cognitive performance (Lachaux et al., 1999), and thus this phase synchrony index has been used extensively in recent studies (e.g., Phillips and Takeda, 2009; Rodriguez et al., 1999).

Beyond the examination of functional connectivity between brain regions, recent development in the methodology of graph theoretical analysis in the neurosciences allows us to further examine the efficiency of the entire neural network (i.e., whole brain) during cognitive tasks (Reijneveld et al., 2007). In graph theoretical analysis, a graph is a mathematical representation of a network consisting of a set of nodes with edges lying between them. In EEG analyses, nodes and edges correspond to electrodes and the functional connections between them, respectively. Graph theoretical analysis assumes EEG synchronization between electrode pairs above a certain threshold as existence of the functional connectivity between them (Valencia et al., 2008). This is based on the assumption that functional connectivity between brain regions is accomplished via neuronal synchrony (Engel et al., 2001). A simplified example of three networks is illustrated in Fig. 1. The graph theoretical analysis provides three important indices:

- (1) Global efficiency (E_{glob}) describes (on average) the shortest path length between nodes (i.e., electrodes). The index indicates the ease of transporting information from one node to other nodes (i.e., from one brain region to others). In Fig. 1, the shortest mean path length between node pairs in Network A is 1.82 steps, where in Network B it is 1.68 steps. For example, four steps are needed to connect from Node 6 to Node 8 in Network A (e.g., $6 \rightarrow 4 \rightarrow 3 \rightarrow 5 \rightarrow 8$), whereas the distance between any node pair is less than or equal to three steps in Network B. Thus, global efficiency is greater in Network B than in Network A. The global efficiency index ranges from 0 to 1, with a higher value indicating a more efficient network structure.

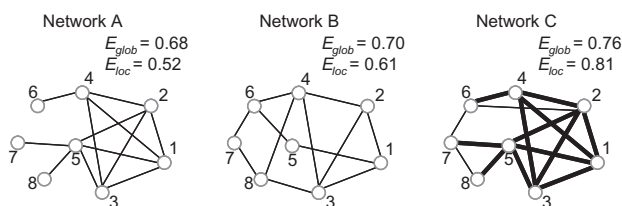


Fig. 1. Example of networks. Networks A and B have the same degree ($k = 3$), but the efficiencies are higher in Network B than Network A. Network C is constructed by adding three extra connections (thin lines) on Network A, resulted in greater degree ($k = 3.75$) and efficiency. When we chose the strongest 12 connections to examine the basic structure of the Network (i.e., fixed k analysis), Networks A and C are identical. However, when we chose the connections beyond a certain threshold of synchronization (i.e., fixed threshold analysis), Network C has available additional connections such as Nodes 2–6, 6–7, and 7–8, which result in greater global and local efficiencies.

- (2) Local efficiency (E_{loc}) describes the network's resilience to random error. Assume that in Fig. 1, Node 5 is temporally lost to random error in Network A, Nodes 7 and 8 would no longer be able to connect the other nodes due to the lost edges. Such dysfunction would not occur in Network B with the loss of any one node due to the overlap of edges between nodes. Thus, local efficiency is greater in Network B than in Network A. The local efficiency index ranges from 0 to 1, with higher values indicating a more efficient network structure.
- (3) Degree (k) indicates the mean number of edges that functionally connect each node (i.e., electrode). For example, $k = 3$ indicates that on average each node is functionally connected to three other nodes (such as the case in Networks A and B from Fig. 1). Further, the degree impacts both global and local efficiencies. Network C from Fig. 1 depicts a graph in which three connections are added to Network A. Although most of the connections are the same as Network A ($k = 3$), Network C ($k = 3.75$) has higher efficiencies for both the global and local indices.

As mentioned previously, the connections between nodes are defined by the magnitude of EEG synchronization in the graph theoretical analysis. Thus, the increasing number of channel pairs leading to increased EEG synchronization (i.e., $PLV \geq \text{threshold}$) increases the degree (k) and results in a more efficient neural network. That is, if the degree (k), above a certain threshold, is different between two networks (e.g., as demonstrated by the difference between A and C in Fig. 1), the network that has the larger degree (Network C in Fig. 1) could have greater efficiency compared to the smaller one (Network A in Fig. 1). The fixed threshold graph describes this difference between two networks. That is, the fixed threshold graph assumes that electrode pairs having EEG synchronization above a certain threshold are functionally connected. As shown in the comparison Networks A and B in Fig. 1, the network efficiency could be different even when the degree (k) is similar between two networks. In other words, if the structures between two networks are different, the network efficiency could also be different. Graph theoretical analysis allows us to examine such structural changes independent of the variation of degree (k) by using a fixed k graph instead of the fixed threshold graph. That is, the fixed k graph assumes that the fixed number of electrode pairs having the greatest EEG synchronization is functionally connected.

In the current study, we reanalyzed data from a previous investigation on the relationship between physical activity and executive control during a spatial priming task (Kamijo and Takeda, 2009). Tipper et al. (1990) demonstrated that the response latencies to a target were shortened when the target in the current trial (probe) appeared at the same location as the previous trial (prime). This facilitative effect is termed 'positive priming' (PP). By contrast, the response latencies became longer when the probe target appeared at the prime distractor location (Tipper et al., 1990). This inhibitory effect is termed 'negative priming' (NP). It is considered that the magnitude of the NP effect is related to executive control ability and the magnitude of the PP effect is negatively correlated with executive control ability (Kamijo and Takeda, 2009). We observed larger NP effects on reaction time (RT) and P3 latency in active individuals relative to sedentary individuals, with PP effects only observed in the sedentary group. From these findings, we concluded that regular physical activity has a positive relation with executive control processes in younger adults. Thus, reanalysis of our previous data would allow us to examine the functional connectivity between brain regions and efficiency of the whole neural network during executive control processes, which prior reports have demonstrated are influenced by physical activity (Colcombe and Kramer, 2003).

Accordingly, the purpose of this reanalysis was to investigate the relation of physical activity to functional connectivity between brain regions and the efficiency of the neural network during a cognitive task requiring variable amounts of executive control in young adults. It is important to clarify this relationship in young adults to elucidate possible mechanisms underlying the association of physical activity to cognitive function across the lifespan. To this end, we examined EEG beta and gamma band synchronization between electrodes and applied graph theoretical analysis to assess functional connectivity between brain regions and the efficiency of the neural network (Stam, 2004; Reijneveld et al., 2007). It has been well established that gamma band (≥ 30 Hz) activity is associated with a wide variety of cognitive processes (Fell et al., 2003; Herrmann et al., 2004). Further, lower spectral frequencies (including beta: 14–30 Hz, and low gamma bands) are also related to cognitive processes (von Stein et al., 1999), especially during top-down control of cognitive function (Phillips and Takeda, 2009). Accordingly, we focused on beta and gamma band activity in this study.

It was predicted that if structural differences in the neural network as a function of physical activity were associated with greater efficiency of the neural network underlying cognitive function, group differences would be observed even in the fixed k graph (e.g., the difference between Network A to B in Fig. 1). By contrast, if physical activity had a positive relation with the strength of functional connectivity between brain regions in the absence of structural differences, group differences would be shown only in the fixed threshold graph, but not in the fixed k graph (e.g., the difference between Network A to C in Fig. 1). Lastly, it was predicted that group differences would be observed selectively during both priming condition requiring greater amounts of executive control.

2. Methods

2.1. Participants

Forty students ($M = 21.1$ years, $SD = 1.8$; 19 females) were recruited from the University of Tsukuba, Japan. All participants reported being free of neurological disorders, cardiovascular disease, any medications that influenced central nervous system function, and had (corrected-to-) normal vision. Participants were separated into physically active and sedentary groups on the basis of their regular levels of physical activity, which were evaluated by the International Physical Activity Questionnaire (IPAQ) long form (<http://www.ipaq.ki.se/ipaq.htm>). The characteristics of the active and sedentary groups are summarized in Table 1. The IPAQ scores (i.e., physical activity levels) were significantly different between the active and sedentary groups, $t(38) \geq 6.2$, $p's \leq .001$. All participants provided written informed consent that was approved by

the Institutional Human Research Committee (National Institute of Advanced Industrial Science and Technology, Tsukuba, Japan).

2.2. Spatial priming task

A white fixation point and four 1.8° squares indicating the possible locations of target and distractor stimuli were provided on a black background and visible throughout each trial. The vertical visual angle between the outside upper and the lower positions of the viewing area was 6.5° , and the horizontal angle between the two outside positions was also 6.5° . The white letters “O” and “X” ($1^\circ \times 1^\circ$) were presented simultaneously at two of the four possible locations. The stimuli were presented for a 200 ms duration, with a 3000 ms response window and a 1500 ms response–stimulus interval. The viewing distance was 57.3 cm. Participants were instructed to press, as quickly and accurately as possible, one of four keys (A, X, M and L) on the computer keyboard corresponding to the position of the O (target) and to ignore the location of the X (distractor) using their index and middle fingers of each hand. Each trial served as a prime for the following trial (except the last trial in each experimental block) and as a probe for the preceding trial (except the first trial in each experimental block). The positive priming (PP) condition was defined as having the probe target appear at the same location as the prime target. The negative priming (NP) condition was defined as having the probe target appear at the same location as the prime distractor. All other trials were defined as a control condition. After 72 practice trials, 3 experimental blocks of 72 trials were administered with a brief rest period between blocks. The trials consisted of 25% PP condition (18 trials), 25% NP condition (18 trials), and 50% control condition (36 trials). The participants were engaged in the task for 7.5 min ($2.5 \text{ min} \times 3 \text{ blocks}$).

2.3. EEG recording

EEG were measured from the following 19 electrode sites of the International 10–20 system: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2, with AFz as the ground electrode. To monitor possible artifacts due to eye movements, vertical electrooculogram (EOG) was recorded using electrodes placed above and below the right orbit, and a horizontal EOG was recorded from the outer left and right canthi. Prior to testing all electrodes had an impedance $< 5 \text{ k}\Omega$. The time constant was set at 5 s with a high-cut filter of 300 Hz. Continuous data were digitized at a sampling rate of 1000 Hz. The EEG data were re-referenced to mathematically averaged earlobes (A1–A2) off-line. Trials with eye movements (rejection levels: $\pm 80 \mu\text{V}$) and response errors were excluded from the analyses. Based on visual inspection, trials were rejected due to artifacts during off-line analysis, in addition to the automatic

Table 1
Group means for participant characteristics.

	Active		Sedentary	
	Female	Male	Female	Male
Sample size (n)	10	10	9	11
Age (years)	19.9 \pm 0.9	20.9 \pm 1.4	22.4 \pm 1.9	22.2 \pm 1.8
Height (cm)	164.5 \pm 5.3	172.7 \pm 6.8	158.8 \pm 5.9	171.5 \pm 6.4
Weight (kg)	56.0 \pm 8.2	64.2 \pm 5.0	52.4 \pm 6.7	62.8 \pm 9.9
Body mass index (kg/m^2)	20.7 \pm 2.6	21.5 \pm 1.4	20.7 \pm 1.7	21.3 \pm 2.4
Beck Depression Inventory	6.1 \pm 4.1	3.6 \pm 2.5	7.2 \pm 5.2	6.3 \pm 5.9
IPAQ total PA score (kcal/week)	8473.3 \pm 3479.0	9985.4 \pm 5739.7	2056.7 \pm 1363.3	1404.9 \pm 778.8
IPAQ leisure-time domain sub-score (kcal/week)	5328.2 \pm 2349.8	7856.0 \pm 5228.8	680.8 \pm 877.3	501.8 \pm 508.6
IPAQ vigorous-intensity sub-score (kcal/week)	4440.0 \pm 2260.6	7152.0 \pm 4774.3	400.0 \pm 678.8	283.6 \pm 489.7

Values are mean \pm SD. The maximum obtainable score on the Beck Depression Inventory is 63.

rejection. On average, about 35% of trials were discarded due to artifacts and response errors.

2.4. Data analysis

2.4.1. Phase synchronization

PLVs were computed from stimulus-locked EEG data. As the first step, the phase $\varphi_{(t,f,n,e)}$ at time (t), frequency (f), trial (n), and electrode (e) was calculated by convolving the data with a complex Morlet wavelet. The wavelet was defined as:

$$M_{(t,f)} = (\sigma_t \sqrt{\pi})^{-0.5} \cdot e^{-\frac{t^2}{2\sigma_t^2}} \cdot e^{2i\pi ft}$$

where $\sigma_t = FTR/2\pi f$. Following Lachaux et al. (1999), we set $FTR = 7$. In the present study, we varied f from 12 to 60 Hz at intervals of 2 Hz. PLV for electrode pair (e_i, e_j) was defined as:

$$PLV_{(t,f,e_i,e_j)} = \frac{1}{N} \left| \sum_{n=1}^N e^{i(\varphi_{(t,f,n,e_i)}) - \varphi_{(t,f,n,e_j)}} \right|$$

where N is the number of trials in each condition. PLVs were evaluated relative to a 100 ms pre-stimulus baseline.

To examine the regions significantly synchronized, we compared PLVs with surrogate data. The surrogate values were estimated in each participant and condition by the same EEG data as calculated for PLVs, but after permuting the order of trials for channel e_j . That is, the values were computed by the following equation:

$$PLV_{\text{surrogate}(t,f,e_i,e_j)} = \frac{1}{M} \sum_{m=1}^M \left| \frac{1}{N} \sum_{n=1}^N e^{i(\varphi_{(t,f,n,e_i)}) - \varphi_{(t,f,\text{perm}(\text{trial},e_j)})} \right|$$

where M indicates the number of surrogate data. In the present study, we set $M = 200$.

It is well known that scalp EEG signals reflect the postsynaptic activity not only in brain region immediately under the electrode but also peripheral regions (i.e., volume conduction). Therefore, it is impossible to specify the sources of EEG signal recorded from each electrode. Some researchers have proposed a technique for measuring PLVs by using data from source modeling analysis instead of scalp EEG signals to specify brain regions underlying functional connectivity (Gruber et al., 2006). Adopting the source modeling analysis may be better to examine the functional connectivity between brain regions. However, the source modeling analysis is based on a solution to the inverse problem, which has no unique solution. That is, the results from the source modeling analysis are variable depending on arbitrary initial settings, and are sometimes far from actual neural activity. In the present study, we make no assumption for the adequate initial settings for source modeling analysis. In addition, a high-density EEG recording is required for the accurate modeling. The present study (19-channel EEG) was not suitable for the source modeling analysis. Thus, we used scalp EEG signals for PLV analysis.

For the statistical analysis, we calculated the PLV averaged over all electrode pairs for 6 time epochs (0–100 ms, 100–200 ms, 200–300 ms, 300–400 ms, 400–500 ms, and 500–600 ms) \times 2 frequency bands (14–30 and 32–60 Hz for beta and gamma bands). A mixed-model analysis of variance (ANOVA) was performed with the following factors: 2 (Group: active, sedentary) \times 3 (Priming: PP, NP, control) \times 6 (Time) for beta and gamma bands separately.

2.4.2. Graph theoretical analysis

To evaluate the efficiency of the neural network during the task, PLV was used for a graph theoretical analysis as an index of functional connectivity between electrodes (Valencia et al., 2008). The graph theoretical analysis provides three indices (Latora and Marchiori, 2003): degree (k), global efficiency (E_{glob}), and local

efficiency (E_{loc}). The maximum k was 18 (i.e., 19 electrodes). The average efficiency of the unweighted graph G was defined as:

$$E(G) = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{d_{(ij)}}$$

where N indicates the number of nodes involved in the graph G and $d_{(ij)}$ indicates the shortest path length between Nodes i and j . The global efficiency was defined as:

$$E_{\text{glob}} = \frac{E(G)}{E(G^{\text{ideal}})}$$

where G^{ideal} indicates the ideal case of graph G , in which all nodes directly connect to each other. The global efficiency index ranges from 0 to 1, and higher value indicates efficient network structure. The local efficiency was defined as:

$$E_{\text{loc}} = \frac{1}{N} \sum_{i \in G} \frac{E(G_i)}{E(G_i^{\text{ideal}})}$$

where G_i indicates the subgraph of the neighbors of Node i . Similar to the global efficiency, the local efficiency index ranges from 0 to 1, and higher value indicate more efficient network structure. For the statistical analysis, a mixed-model ANOVA was performed for each graph theoretical index with the following factors: 2 (Group: active, sedentary) \times 3 (Priming: PP, NP, control).

Lastly, the network having better global and local efficiencies relative to the random network with the same k is known as ‘small-world’ network (Watts and Strogatz, 1998). To examine whether the neural network observed in the present study had a small-world network structure, the observed graph was compared with a randomly generated graph with the same degree (k) distribution (i.e., $E_{\text{glob}}/E_{\text{glob}}^{\text{Rand}}$, $E_{\text{loc}}/E_{\text{loc}}^{\text{Rand}}$). That is, if the values are greater than 1, the neural network is considered to be more efficient than a random network (i.e., ‘small-network’ structure). For the statistical analysis, paired t -tests were performed to determine whether global and local efficiency were greater than 1 in each group and priming condition.

Analyses with three or more within-subject levels employed the Greenhouse–Geisser statistic, if the assumption of sphericity was violated. Post-hoc comparisons were conducted using univariate ANOVA and Tukey’s HSD multiple-comparison test. The family-wise alpha value was set at $p = .05$.

3. Results

3.1. Task performance

Although the task performance data have already been reported in our previous study (Kamiyo and Takeda, 2009), the results are briefly reviewed here and in Table 2.

For the PP effect on RTs, the analysis revealed a significant Group \times Priming interaction, $F(1, 38) = 5.3$, $p = .03$, $\eta_p^2 = .12$. Post-hoc analyses indicated that RTs in the PP condition were shorter than in the control condition for the sedentary group (i.e., general PP), $t(19) = 2.6$, $p = .02$, whereas no such difference was observed for the active group, $t(19) = .06$, $p = .96$. For the NP effect on the RTs, there was a marginal Group \times Priming effect, $F(1, 38) = 3.5$, $p = .07$, $\eta_p^2 = .09$. This interaction may indicate larger NP for the

Table 2
Mean RTs (ms) across groups and task conditions.

	PP	Control	NP
Active	409.6 \pm 45.0	409.9 \pm 46.5	431.6 \pm 46.4
Sedentary	428.7 \pm 64.1	450.0 \pm 94.7	460.5 \pm 89.4

Values are mean \pm SD.

active group ($M = 21.7$ ms) relative to the sedentary group ($M = 10.5$ ms). No effects were observed for response accuracy.

3.2. Phase synchronization

Fig. 2 (upper) shows PLVs observed in each condition and group. We calculated the PLVs averaged over all electrode pairs for 6 time epochs and 2 frequency bands (Fig. 2, lower). The beta band analysis revealed a Time main effect, $F(3.5, 131.5) = 11.6$, $p < .001$, $\eta_p^2 = .23$, and a Group \times Time interaction, $F(3.5, 131.5) = 2.6$, $p = .04$, $\eta_p^2 = .07$, qualified by a Group \times Priming \times Time interaction, $F(5.9, 224.8) = 2.2$, $p = .02$, $\eta_p^2 = .05$. Breaking down the three-way interaction by examining Group \times Priming for each Time revealed a significant interaction at the 300–400 ms time epoch, $F(2, 76) = 5.0$, $p = .009$, $\eta_p^2 = .12$. Post-hoc univariate ANOVA revealed a Priming main effect for the active group, $F(2, 38) = 4.3$, $p = .02$, $\eta_p^2 = .19$, but not for the sedentary group, $F(2, 38) = 1.6$, $p = .22$, $\eta_p^2 = .08$. Tukey's HSD post-hoc analysis indicated greater synchronization for both priming conditions relative to the control condition in the active group, p 's $< .042$. Additional post-hoc t -tests to examine the group difference for each task condition indicated

greater synchronization in the active group during the PP condition relative to the sedentary group, $t(38) = 2.7$, $p = .01$, although the group difference did not reach significance during the NP and control conditions. Such an interaction was not observed at the other time epochs. These results indicate functional connectivity between brain regions was stronger during both priming conditions relative to the control condition at 300–400 ms after stimulus onset only for the active group.

The gamma band analysis revealed a Time main effect, $F(3.2, 122.1) = 6.5$, $p < .001$, $\eta_p^2 = .15$. Tukey's HSD post-hoc analysis indicated that mean PLV at the 300–400 ms time epoch was significantly greater than 0–100, 100–200, 200–300, and 500–600 ms time epochs, p 's $\leq .02$. These results indicate functional connectivity between brain regions was stronger at 300–400 ms after stimulus onset relative to the above-mentioned other time epochs across groups.

3.3. Graph theoretical analysis

Based on the results of the phase synchronization analyses, we defined a temporal region of interest at the 300–400 ms

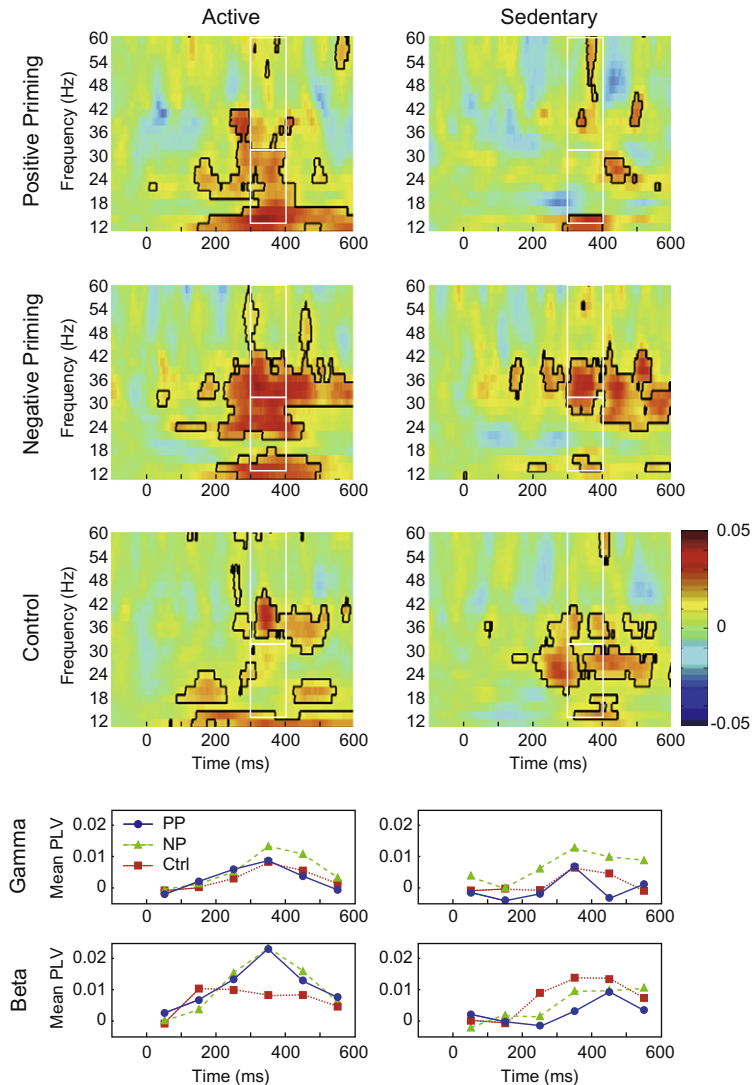


Fig. 2. Time-frequency plots (upper panel) of PLVs in each priming condition and group. The regions surrounded by black lines indicate a significant increase in synchronization compared to the surrogate value ($p < .05$, uncorrected). White boxes indicate region of interest (300–400 ms after stimulus onset for beta and gamma bands) for the following graph theoretical analysis. Line graphs (lower panel) of PLVs for gamma (top row) and beta (bottom row) bands. The PLVs were averaged over all electrode pairs.

post-stimulus epoch. Figs. 3(left) and 4(left) depict the degree, global efficiency, and local efficiency as the function of the threshold in PLV for beta and gamma bands, respectively. For the statistical analysis of fixed threshold graphs, several studies have reported that k -cost (k /possible edges) between 0.2 and 0.25 is sensitive enough to examine small-world properties (Achard and Bullmore, 2007; Liu et al., 2008). It is important to note that this criterion (around 0.2) of k -cost yields the middle level (about 0.5) of the global and local efficiencies in a randomly generated graph. Thus, we adopted a threshold of 0.05 for beta band and 0.03 for gamma band, which were defined by the k -cost greater than 0.2 in all conditions. It is important to note that the consistent difference between conditions of the network efficiency was observed for a broad PLV cut-off range in the present study. For example, in the beta band analysis of the active group, the differences in global and local efficiencies between conditions could be observed in the PLV cut-off range between 0.02 and 0.12 (Fig. 3, 1st column). The threshold used in the present study is positioned within this range. Similar to the fixed threshold analysis, it is necessary to decide the mean number of edges for the fixed k analysis. In the present study, EEG was measured from 19 electrodes allowing for a maximum of 18 possible edges from one node (electrode). Accordingly, we used the criterion of $k = 4$ for the fixed k analysis (i.e., k -cost = $4/18 = 0.22$).

3.3.1. Beta band

Fig. 3 (3rd column) depicts the degree, global efficiency, and local efficiency of the fixed threshold graphs. The degree analysis revealed a Priming main effect, $F(2, 76) = 6.2$, $p = .003$, $\eta_p^2 = .14$, qualified by a Group \times Priming interaction, $F(2, 76) = 3.9$, $p = .02$,

$\eta_p^2 = .09$. Post-hoc univariate ANOVA revealed a Priming main effect for the active group, $F(2, 38) = 11.3$, $p < .001$, $\eta_p^2 = .37$, but not for the sedentary group, $F(2, 38) = 0.2$, $p = .82$, $\eta_p^2 = .01$. Tukey's HSD post-hoc analyses indicated that degree in the two priming conditions were larger than the control condition in the active group, p 's $\leq .001$. These results indicate that the amount of synchronization between electrodes was greater during both priming conditions relative to the control condition only for the active group.

The global efficiency analysis revealed a Priming main effect, $F(2, 76) = 6.0$, $p = .004$, $\eta_p^2 = .14$, qualified by a Group \times Priming interaction, $F(2, 76) = 4.3$, $p = .017$, $\eta_p^2 = .10$. The post-hoc univariate ANOVA revealed a Priming main effect for the active group, $F(2, 38) = 9.7$, $p < .001$, $\eta_p^2 = .34$, but not for the sedentary group, $F(2, 38) = 0.8$, $p = .48$, $\eta_p^2 = .04$. Tukey's HSD post-hoc analyses indicated that global efficiency in the two priming conditions were larger than the control condition for the active group, p 's $\leq .002$. These results indicate that transporting information from one brain region to others was enhanced during both priming conditions relative to the control condition only for the active group.

The local efficiency analysis also revealed a Priming main effect, $F(2, 76) = 4.8$, $p = .01$, $\eta_p^2 = .11$, qualified by a Group \times Priming interaction, $F(2, 76) = 3.1$, $p = .05$, $\eta_p^2 = .08$. A post-hoc univariate ANOVA revealed a Priming main effect for the active group, $F(1.5, 28.8) = 7.8$, $p = .004$, $\eta_p^2 = .29$, but not for the sedentary group, $F(2, 38) = 0.4$, $p = .65$, $\eta_p^2 = .02$. Tukey's HSD post-hoc analyses indicated that local efficiency in the two priming conditions were larger than the control condition for the active group, p 's $\leq .013$. These results indicate that resilience to random error was greater during both priming conditions relative to the control

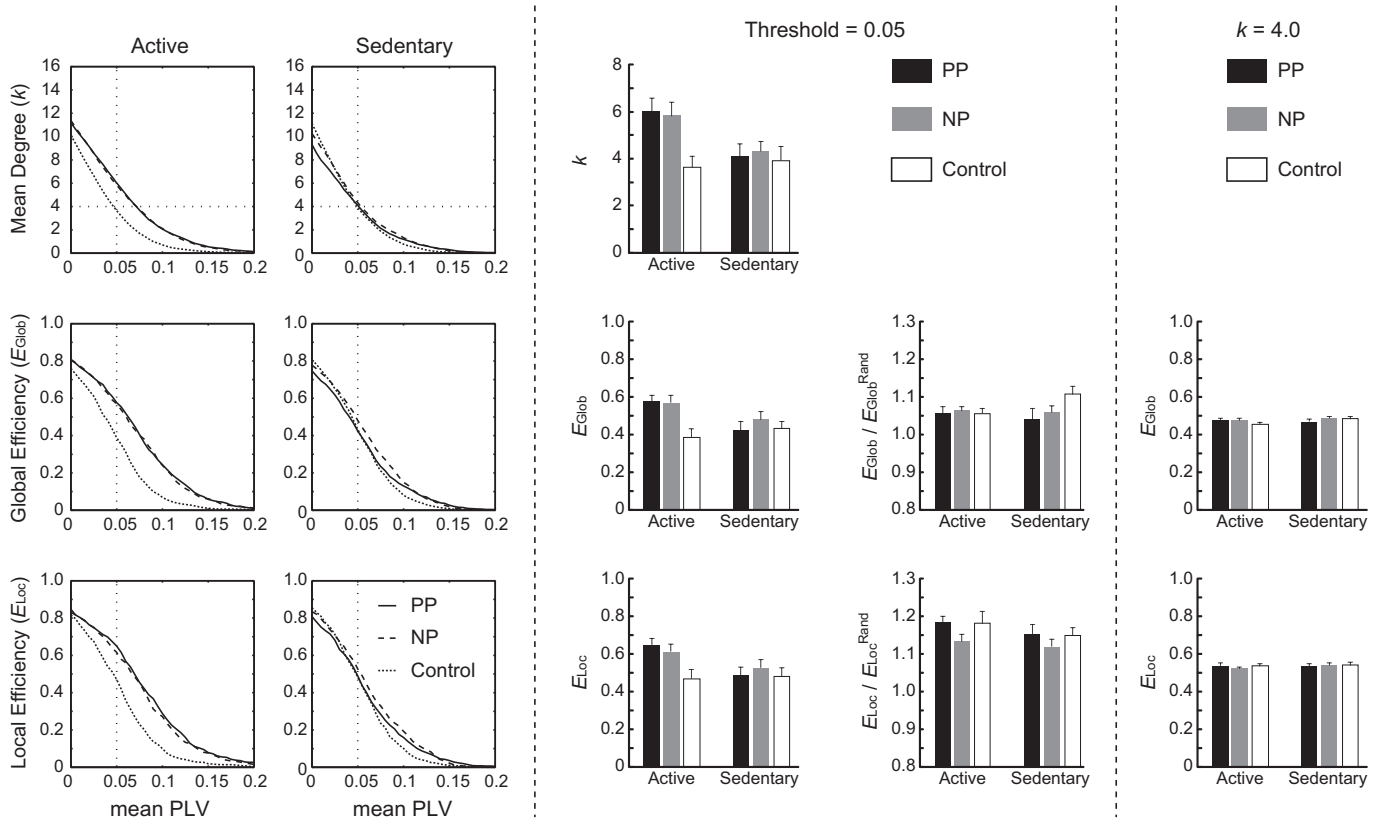


Fig. 3. Results of the graph theoretical analyses for beta band. The degree, global efficiency, and local efficiency as a function of PLV threshold in each group are presented in the 1st and 2nd columns. The degree, global efficiency, and local efficiency of the fixed threshold graphs are presented in the 3rd column. Comparisons between the fixed threshold graphs and random graphs in the global efficiency and local efficiency are depicted in the 4th column. The global efficiency and local efficiency of the fixed k graphs are depicted in the 5th column.

condition only for the active group. Thus, the networks for the two priming conditions were more efficient than the network for the control conditions in the active, but not in the sedentary group.

In addition, to examine whether the neural network observed in the present study had a small-world network structure, the observed graph was compared with a randomly generated graph with the same degree (k) distribution. Fig. 3 (4th column) depicts two efficiency indices compared with the random graph. Both global and local efficiencies were greater than 1 in both the active and sedentary groups, t 's(19) ≥ 3.19 , p 's $\leq .005$ with the exception of global efficiency for the PP condition in the sedentary group, $t(19) = 1.44$, $p = .17$. This indicates the observed neural network was more efficient than a random network (i.e., 'small-network' structure). The Group \times Priming ANOVA indicated no significant main effects or interactions for the global or local efficiencies, p 's $\geq .14$.

Finally, to examine the structure of the network, we fixed $k = 4$ instead of using the fixed threshold (Fig. 3, 5th column). The Group \times Priming ANOVA indicated no significant main effects or interactions for either global or local efficiency, p 's $\geq .24$. This indicates that there were no structural differences between groups. Thus, the greater efficiency of the priming conditions in the active group observed in the fixed threshold analysis may depend on a greater degree (k) rather than a structural difference.

3.3.2. Gamma band

Fig. 4 (3rd column) depicts the degree, global efficiency, and local efficiency of the fixed threshold graphs. The degree analysis revealed a Priming main effect, $F(2, 76) = 7.3$, $p = .001$, $\eta_p^2 = .16$. Tukey's HSD post-hoc analyses indicated that degree in the NP condition was larger than the control condition across groups, $p = .001$.

These results indicate that the amount of synchronization between electrodes was greater during the NP conditions relative to the control condition across groups.

The global efficiency analysis revealed a Priming main effect, $F(2, 76) = 9.76$, $p < .001$, $\eta_p^2 = .20$. Tukey's HSD post-hoc analyses indicated that global efficiency in the two priming conditions were larger than the control condition across groups, p 's $\leq .03$. These results indicate that transporting information from one brain region to others was enhanced during both priming conditions relative to the control condition across groups.

The local efficiency analysis revealed a Priming main effect, $F(2, 76) = 11.30$, $p < .001$, $\eta_p^2 = .23$. Tukey's HSD post-hoc analyses indicated that local efficiency in the two priming conditions were larger than the control condition across groups, p 's $\leq .02$. These results indicate that resilience to random error was greater during both priming conditions relative to the control condition across groups. Thus, it is considered that the networks for the two priming conditions were more efficient than the control condition irrespective of physical activity.

Similar to beta band analyses, the observed graph was compared with a randomly generated graph with the same degree (k) distribution. Fig. 4 (4th column) illustrates two efficiency indices compared with the random graph. Both global and local efficiencies were greater than 1 in the active and sedentary groups, $t(19) \geq 2.87$, $p \leq .01$. This indicates the observed neural network was more efficient than a random network (i.e., 'small-network' structure). The Group \times Priming ANOVA indicated no significant main effects or interactions for either the global or local efficiencies, p 's $\geq .06$.

Similar to beta band analyses, we used fixed $k = 4$ rather than the fixed threshold (Fig. 4, 5th column). The Group \times Priming

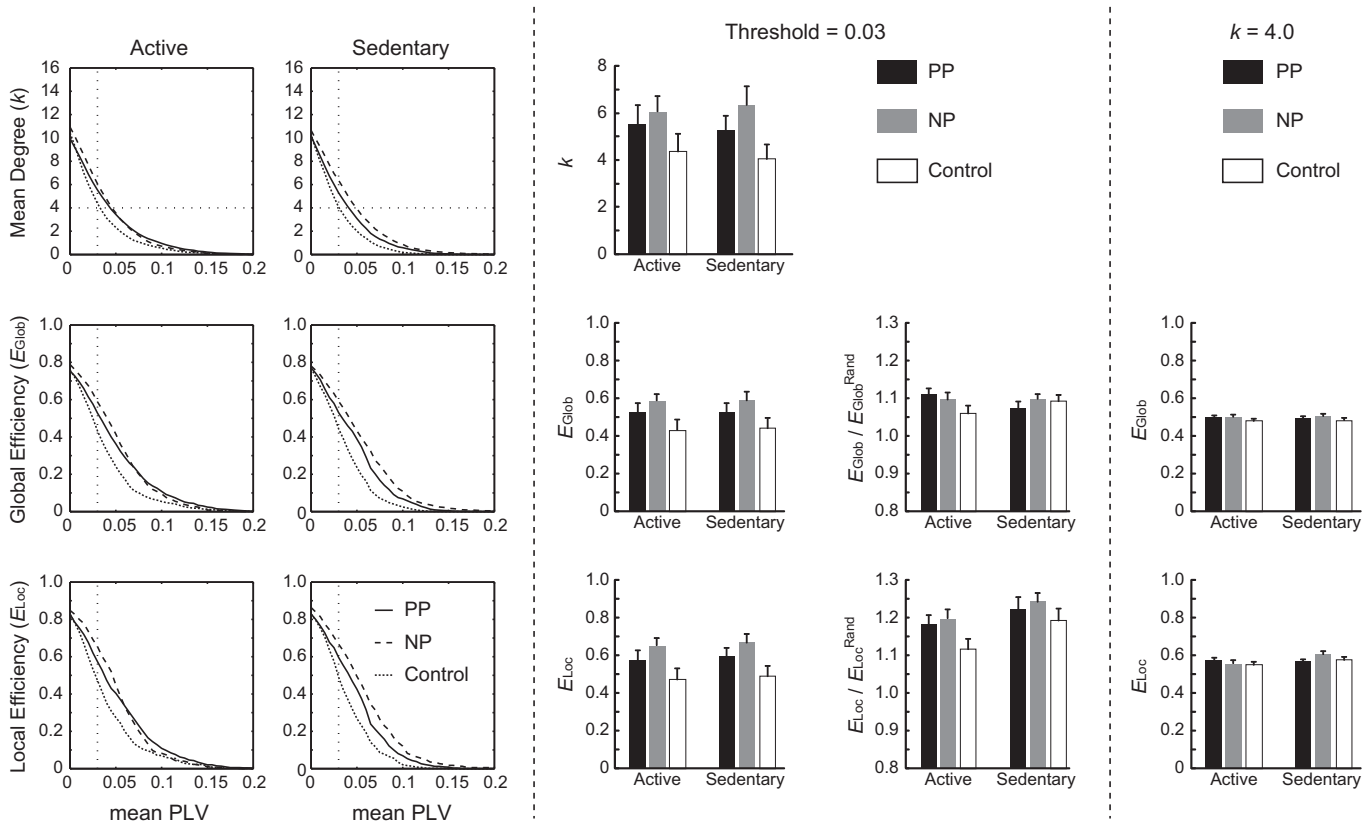


Fig. 4. Results of the graph theoretical analyses for gamma band. The degree, global efficiency, and local efficiency as a function of PLV threshold in each group are presented in the 1st and 2nd columns. The degree, global efficiency, and local efficiency of the fixed threshold graphs are presented in the 3rd column. Comparisons between the fixed threshold graphs and random graphs in the global efficiency and local efficiency are depicted in the 4th column. The global efficiency and local efficiency of the fixed k graphs are depicted in the 5th column.

ANOVA indicated no significant main effects or interactions for either the global or local efficiencies, p 's $\geq .14$. Thus, the greater efficiency of the priming conditions across groups observed in the fixed threshold analysis may depend on a greater degree (k) rather than a structural difference.

4. Discussion

In this study, we investigated the relation of physical activity to functional connectivity between brain regions and efficiency of the neural network during an executive control task using PLVs and a graph theoretical analysis, respectively. The main findings indicated that beta band PLVs during both priming conditions were larger relative to the control condition only for the active group at the 300–400 ms post-stimulus epoch. For the graph theoretical analyses, the degree, global efficiency, and local efficiency during both priming conditions were larger relative to the control condition only for the active group in the fixed threshold graphs of beta band synchrony. By contrast, no relation of physical activity and priming condition were observed in the fixed k graph. These results suggest that physically active individuals have greater functional connectivity between brain regions, but that both groups have similar network structures.

4.1. Phase synchronization

300–400 ms after stimulus presentation, beta band PLVs were greater for both priming conditions relative to the control condition only in the active group, indicating greater functional connectivity between brain regions during conditions requiring greater amounts of executive control. By contrast, no such physical activity effects were observed during the priming conditions for the gamma band PLV, indicating that physical activity has a selective relation to the frequencies comprising beta activation. Buschman and Miller (2007), in a study of non-human primates, suggested that top-down and bottom-up control processes are mediated by neural synchrony at lower frequency bands (22–34 Hz; i.e., beta) and higher frequency bands (36–56 Hz; i.e., gamma), respectively. Similar results were reported in a human EEG study (Phillips and Takeda, 2009), indicating that greater PLVs during inefficient visual search, requiring greater amounts of top-down control, relative to efficient visual search were observed for the beta band, but not for the gamma band. Accordingly, the current dataset are consonant with these prior findings and suggest that differences in physical activity may only be related to conditions requiring greater amounts of executive control as reflected by beta band activation. This finding is also consonant with previous ERP studies indicating positive relation of physical activity to executive control processes in young adults (Hillman et al., 2006; Kamiyo and Takeda, 2009; Themanson and Hillman, 2006; Themanson et al., 2006, 2008). It is interesting to note that in our previous report (Kamiyo and Takeda, 2009) NP effects on RT and P3 latency in active individuals were larger than in the sedentary individuals, whereas the opposite relationship was observed for the PP condition with a smaller PP effect in active individuals relative to sedentary individuals. These findings indicate that active individuals could inhibit previous trial information to perform current trial efficiently irrespective of target or distractor locations, suggesting that regular physical activity may have a positive relation with inhibitory control. The present findings indicating stronger functional connectivity reflected by larger beta band PLVs during both priming conditions for the active group may reflect stronger inhibition for previous trial information, resulting in the larger NP effect and the smaller PP effect. Thus, the present study suggests that stronger functional connectivity between brain regions may be one of

the possible underlying mechanisms for the positive relation of physical activity to executive control.

4.2. Graph theoretical analysis

The fixed threshold analyses indicated that the degree, global efficiency, and local efficiency in the two priming conditions were greater than the control condition only for the active group, with no differences observed for the sedentary group. These results suggest that physical activity might be related to the efficiency of the neural network underlying executive control processes involved in spatial priming. By contrast, the physical activity effects disappeared in the fixed k analysis, indicating no structural differences between groups. Taken together, the present results support our hypothesis that physical activity may have a positive relation with the strength of functional connectivity between brain regions in the absence of structural differences (e.g., Network A to C in Fig. 1) during task conditions requiring greater amounts of executive control. That is, these data are in opposition to another hypothesis suggesting that structural differences in a neural network, as a function of physical activity, are associated with the efficiency of that network (e.g., Network A to B in Fig. 1). Similar to PLVs, greater efficiency of the priming conditions reflected by the graph theoretical analyses in the active group were only observed for the beta band, suggesting that top-down control may be selectively associated with physical activity. The present graph theoretical analyses further indicates positive differences in the efficiency of the neural network as a function of physical activity.

4.3. General discussion

The present results indicate that functional connectivity between brain regions and efficiency of the neural network during an executive control task may be related to physical activity participation. However, such a finding does not directly shed light on the underlying mechanisms responsible for physical activity–cognition relation. Accordingly, speculation for this positive relationship may be garnered from several lines of research using non-human animal models. Such studies have indicated that physical activity engendered via wheel running increases nerve growth factors such as brain-derived neurotrophin factor (BDNF; Neepser et al., 1995) and insulin-like growth factor I (Carro et al., 2001). Increases in nerve growth factors may relate to increases in the number of synaptic connections and the development of new neurons that support learning and memory (Lu and Chow, 1999; van Praag et al., 1999). Recently, human studies have also indicated that aerobic fitness training increases plasma concentration of peripheral BDNF (Zoladz et al., 2008), which may reflect cortical BDNF levels (Karege et al., 2002). Accordingly, if these changes were to occur in the human brain, it may provide one mechanism for differences in functional connectivity between brain regions and efficiency of the neural network as a function of physical activity.

It is noteworthy that physical activity effects were dependent on task conditions (i.e., executive control requirements) in the present study. A recent functional magnetic resonance imaging study demonstrated that physical activity improves functional connectivity between brain regions during a task requiring variable amounts of executive control. Specifically, Colcombe et al. (2004) examined the relationship between aerobic fitness and the attentional network supporting performance on a modified flanker task, requiring inhibitory control, via both cross-sectional assessment and a randomized clinical trial. They found increased activation of task-related prefrontal and parietal brain regions and decreased activity in the anterior cingulate cortex (ACC), with better cognitive performance in higher-fit compared to lower-fit older adults, and in aerobically trained compared to nonaerobic control older adults

(Colcombe et al., 2004). These results suggest that increased attentional control (increases in prefrontal and parietal activation) may result in decreases in activation of conflict monitoring processes (reduction in ACC activation) in higher-fit and aerobically trained older adults. Although the previous study did not directly examine functional connectivity (Colcombe et al., 2004), it appears that better cognitive performance in higher-fit and aerobically trained individuals are associated with the more effective activation of the neural networks from lower-fit and aerobically untrained individuals (i.e., greater efficiency of neural network). Thus, physical activity may improve functional connectivity requiring inhibitory control, supporting the present task condition-dependent association.

4.4. Limitations

The present study was cross-sectional in design, and thus other factors besides physical activity level may have contributed to the observed activity group differences. However, this possibility was minimized through the collection of variables that have been found to relate to physical activity participation and cognitive function, with similar findings observed across groups for self-reported depressive symptoms (Beck Depression Inventory), education (recruitment of students from same university), and the calculation of body mass index. Despite these efforts, future research using longitudinal studies of randomized control interventions are needed to better establish a direct effect of physical activity to functional connectivity between brain regions and efficiency of the neural network.

Given that the present study only focused on young adults, it remains unclear whether the mechanisms underlying the relation of physical activity on cognition are age-dependent. If underlying mechanisms for the physical activity–cognition relationship differ based on age, graph theoretical analyses may be able to detect age-dependent difference. That is, for example, if physical activity changes the structure of the network for older adults, the fixed k graph should differ between physically active and sedentary older adults. Further studies are needed to clarify this issue using the graph theoretical analysis.

4.5. Conclusion

In this study, we observed that the relation of physical activity to functional connectivity between brain regions and efficiency of the neural network may serve as potential mechanisms for the positive relation of physical activity to executive function in young adults. Additionally, this relation was observed to be unrelated to differences in network structures in the young adults sampled. The present study also suggests the PLVs and graph theoretical analysis may be a useful tool to investigate the relation of physical activity on human cognition during young adulthood. Future studies using this analysis may contribute to our understanding of the positive relation of physical activity on brain and cognition across the lifespan.

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