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Brain activation during executive control after acute exercise in older adults

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ABSTRACT

Previous work has shown that aerobic exercise training is associated with regional changes in functional activation and improved behavioral outcomes during the Flanker task. However, it is unknown whether acute aerobic exercise has comparable effects on brain activation during the Flanker task. The aim of this study was to examine the effects of an acute bout of moderate-intensity bicycle exercise on Flanker task functional activation and behavioral performance in older adults. Thirty-two healthy older adults (66.2 ± 7.3 years) performed two experimental visits that included 30-min of aerobic exercise and a rest condition on separate days. After each condition, participants performed the Flanker task during an fMRI scan. Significantly greater functional activation (incongruent > congruent) was found in the left inferior frontal gyrus and inferior parietal lobule after exercise compared to rest. A main effect of exercise was also observed on Flanker task performance with greater accuracy in both incongruent and congruent trials, suggesting the effects of acute exercise on Flanker performance are general across Flanker trial types. Conversely, greater executive control-related functional activations after performing a single session of exercise suggests enhanced functional processing while engaging in task conditions requiring disproportionately greater amounts of executive control.

1. Introduction

Cognitive decline often accompanies the normal aging process (Harada et al., 2013). Temporal (Jack et al., 1997), prefrontal, and parietal areas (West, 1996) are some of the most susceptible brain regions to structural and physiological deterioration which occurs with age, typically in the form of gray and white matter atrophy (Tisserand and Jolles, 2003). Executive control consists, in part, of working memory, mental flexibility, and inhibitory control, and depends heavily on the frontal lobes (Stuss, 2011). Age-related impairment in frontal cortical function often manifests as executive control dysfunction (Bialystok et al., 2006). Indeed, healthy older adults consistently perform worse on tasks requiring attention and inhibitory control than healthy younger adults (Miyake et al., 2000; Salthouse et al., 2003).

Over the past decades, an emerging body of evidence suggests exercise promotes brain health through facilitation of cognition and delaying the onset of age-related cognitive decline (Cotman and Engesser-Cesar, 2002; Erickson and Kramer, 2009). In particular, regular participation in aerobic and resistance training is linked to improved behavioral performance and neural activation during the Flanker task (Eriksen and Eriksen, 1974). Colcombe et al. (2004) used the modified Eriksen Flanker task to examine the cross-sectional association between executive control and cardiovascular fitness. They found more physically-fit older adults, compared to their less-fit counterparts, were more efficient in dealing with the incongruent flanking trials and exibited greater functional activation during response to incongruent compared to congruent trials in the superior frontal gyrus (SFG), middle frontal gyrus (MFG) and superior parietal lobule (SPL), while showing lower activation in the anterior cingulate cortex (ACC). Similarly, six months of aerobic exercise training in a seperate sample of older adults resulted in changes to executive control-related activation that paralleled the effects of physical fitness in the first study (Colcombe et al., 2004). In a 12-month randomized trial, older women who were assigned to a twice-weekly resistance training, compared to a control group, demonstrated significantly greater efficiency in response to the incongruent flanking trials with shorter additional time to respond to the incongruent relative to the congruent trials. The chronic resistance training group also demonstrated greater functional activation in brain regions associated with processing interference tasks, including the left insula, orbital frontal cortex, and middle temporal gyrus (Liu-Ambrose et al., 2012).

Despite these longitudinal evidence, less is known about the effects of acute exercise on Flanker task performance and activation. Acute effects of exercise on Flanker performance and activation in older adults were observed by Kamijo et al. (2009) who investigated the

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electrocortical underpinnings of acute exercise-induced improvements in Flanker task performance and activation. Using event-related potentials measured using electroencephalography (EEG), they observed significantly shorter P3 latency, an indication of faster stimulus classification, following both light- (36% of $\dot{V}O2_{max}$) and moderate-intensity (57% of $\dot{V}O2_{max}$) exercise compared to pre-exercise during the Flanker task. Further, moderate-intensity exercise was associated with shorter response time (RT) during the Flanker task (both congruent and incongruent trials) compared to pre-exercise, yet this effect was not observed following light-intensity exercise (Kamijo et al., 2009).

Although Kamijo et al. (2009) employed EEG, which has high temporal resolution, functional magnetic resonance imaging (fMRI) provides superior spatial resolution and allows for more spatially accurate measurement of functional brain activation (Cohen and Bookheimer, 1994). To the best of our knowledge, it has not been established whether a single session of exercise elicits similar or complementary effects on functional brain activation during the Flanker task compared to long-term exercise training interventions. This approach can therefore advance our understanding of the facilitative effects of acute exercise during the Flanker task. Understanding changes in Flanker task performance and activation in response to an acute bout of exercise is of significance, as it can provide insight regarding how the long-term accumulation of acute effects produces beneficial adaptations for executive control. Thus, this study investigated the effects of acute aerobic exercise on fMRI blood oxygen level-dependent (BOLD) activation patterns during the Flanker task in 32 healthy older adults. Based on previous studies (Colcombe et al., 2004; Kamijo et al., 2009), we hypothesized that acute aerobic exercise, compared to rest, will be associated with greater intensity and spatial extent of Flanker activation (incongruent > congruent) in the frontal and parietal regions and less functional activation in the ACC. We also predicted that Flanker task performance will improve for both congruent and incongruent trials.

2. Methods

2.1. Participants

Thirty-two physically active, right-handed older adults (ages 55–80 years) were recruited from local senior fitness classes, recreation centers, and swimming clubs. In the initial pre-screening session, participants completed a structured interview questionnaire, which included items specific to MRI safety (e.g. regarding the presence of metal implants, pacemakers, aneurysm clips, and other potential safety hazards). Individuals who reported a history of heart attack, stroke, diabetes, high blood pressure, neurological disease, major psychiatric disturbance, hypertension, or who were taking psychoactive prescriptive medications were considered ineligible. Prior to the first MRI scan, eligible participants attended the in-person screening session in which they provided informed consent approved by the Institutional Review Board at The University of Maryland. They also completed the 7-Day Physical Activity Recall (Blair et al., 1985) to estimate physical activity energy expenditure and the Mini-Mental State Exam (MMSE) (Folstein et al., 1975), a 30-point questionnaire used to screen for global cognitive impairment and dementia. All eligible participants obtained physician approval before engaging in moderate-intensity exercise. This study was conducted according to the Helsinki Declaration of 1975. Demographic, physical, and cognitive data for all participants are illustrated in Table 1. Details about the participant recruitment process are illustrated in Won et al. (2019).

2.2. Experimental conditions

We used a within-subject, counter-balanced design where participants underwent two experimental visits (exercise and rest) on separate days, with 12.00 ± 17.01 days interval between sessions. Prior to experimental conditions, participants were fitted with a heart rate (HR) monitor (Polar Electro, Kempele, Finland) and were provided standardized instruction for the Borg 6–20 ratings of perceived exertion (RPE) scale (Borg, 1970) and self-assessment manikin (Bradley and Lang, 1994) to assess subjective affect. The exercise condition consisted of 30 min of continuous cycling on a mechanically-braked cycle ergometer (Monark 828E, Varbro, Sweden). The exercise protocol included a 5-min warm-up session with self-selected intensity, followed by 20 min of moderate-intensity exercise, a 5-min cool-down, and a 5-min recovery period. During moderate-intensity exercise, participants were instructed to maintain a pedal cadence of 60 to 80 rpm and to select a flywheel resistance that maintained their intensity at an RPE of 15 (associated with the verbal anchor 'Hard'). Moderate-intensity exercise was chosen based on previous studies suggesting that moderate-intensity exercise enhances cognition to a greater degree than light- or high-intensity exercise (Chang et al., 2012). HR, RPE, and subjective affect were recorded every 5 min. The seated rest condition was also administered for a total of 35 min, including a 5-min recovery period. During the rest condition, participants remained seated in a chair while HR and RPE were collected during each 5-min interval. Reading, writing, technology use, and excessive talking were prevented throughout the rest session.

Table 1
Participant characteristics.

		Total sample (n = 32)
		Mean ± SD
Demographics	Age (years)	66.2 ± 7.3
	Sex (n,%)	
	Male	8 (25%)
	Female	24 (75%)
	Race (n,%)	
	White	25 (78%)
	Black	2 (6%)
	Hispanic	2 (6%)
	Asian	3 (9%)
	Education (n,%)	
	≤College	11 (34%)
	≥Graduate	21 (66%)
Physical characteristics	Height (cm)	166.6 ± 9.0
	Weight (kg)	71.3 ± 14.2
	BMI (kg/m^2)	25.5 ± 4.1
7-Day Physical Activity Recall Score	kJ/kg/day	135.6 ± 17.2
Cognitive function	MMSE	29.1 ± 1.1

Note: SD, standard deviation; BMI, body mass index; 7-Day Physical Activity Recall Score, scores based on approximate number of hours spent in light, moderate, hard, and very hard activities as well as estimated kcal/kg/day during past weekdays and weekends; MMSE, Mini-Mental Status Exam.

2.3. MRI data acquisition

Whole-brain, event-related fMRI was conducted on a Siemens 3.0 Tesla MR scanner (Magnetom Trio Tim Syngo, Munich, Germany). A 32-channel head coil was used for radio frequency transmission and reception. Foam padding was positioned around the sides and top of the head to minimize head movement within the coil. A high-resolution T1-weighted anatomical image was acquired for coregistration with the following sequence parameters: Magnetization Prepared Rapid Acquisition of Gradient Echo (MPRAGE), matrix = 256, field of view (FOV) = 230 mm, voxel size = 0.9 × 0.9 × 0.9 mm, slices = 192 (sagittal plane, acquired right to left), slice thickness = 0.9 mm, repetition time (TR) = 1900 ms, echo time (TE) = 2.32 ms, inversion time (TI) = 900 ms, flip angle = 9°, and sequence duration = 4:26 min. The Flanker event-related data were acquired using the following sequence parameters: single-shot gradient echo planar images (EPI), matrix = 64, FOV = 192 mm, voxel size = 3.0 × 3.0 × 3.0 mm, slices = 36, slice thickness = 3.0 mm, GRAPPA acceleration factor = 2, TR/TE = 2000/

24 ms, volumes = 175, flip angle = 70°, bandwidth = 2232 Hz/Px, multi-slice mode = Interleaved, and sequence duration = 9:42 min. The MPRAGE and the Flanker sequences began approximately 10 and 30–40 min after the completion of the exercise or rest session, respectively.

2.4. fMRI task

The computerized modified Eriksen Flanker task (Colcombe et al., 2004), presented electronically using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA), was used to assess executive control. Participants completed the task in the scanner using an MRI-compatible button box in their right hand. On each trial, participants were presented with a row of five horizontally-arranged arrows and instructed to respond to the direction of a centrally-positioned target arrow as quickly and accurately as possible. Each trial began with a 1500–9500 ms fixation blank screen followed by a pre-cue (500 ms) consisting of dashed lines to indicate the stimulus was about to appear. Flanker stimuli were presented for 500 ms each followed by a 1500 ms response window. The schedule of trial presentation was generated using optseq2 (https://surfer.nmr.mgh.harvard.edu/optseq) to optimize estimation of the incongruent minus congruent contrast. The two generated orders of stimulus presentation were counterbalanced across participants. The task stimuli consisted of a total of 80 trials including 40 congruent (five flanking arrows horizontally facing the same direction) and 40 incongruent (five flanking arrows facing the opposite direction of the target arrow) trials. There were equal numbers of trials with the arrows pointing left and right. The duration of the test was 9:42 min during which time both accuracy and RT (ms) were recorded. The interference score was calculated based on the following equation: $[(\text{incongruent RT} - \text{congruent RT})/\text{congruent RT}] * 100$ (Colcombe et al., 2004; Liu-Ambrose et al., 2012). Before the MRI scan, a practice session including five congruent and five incongruent trials was administered for 1:30 min outside of the MRI environment.

2.5. Neuroimaging data analysis

2.5.1. Preprocessing

Functional and anatomical images were converted into 3D space using the Analysis of Functional NeuroImages (AFNI)'s Dimon program (Cox, 1996). The anatomical volumes were then processed using Freesurfer's automated processing stream (recon-all) to generate cortical and subcortical reconstructions based on tissue-specific intensities and atlas probabilities (Fischl et al., 2002). All estimated reconstructions were visually inspected for segmentation errors.

The first 3 volumes (TRs) of each functional time series were automatically discarded by the scanner and additional 3 TRs were removed manually using AFNI's 3dTcat to avoid magnetization disequilibrium. The truncated time-series were realigned using a slice-oriented motion correction algorithm (SLOMOCO) (Beall and Lowe, 2014). Next, AFNI's align_epi_anat was executed to coregister the functional time series with the Freesurfer-normalized native space anatomical images. The coregistered anatomical and functional data were visually inspected and used for AFNI's proc.py processing stream. Slices within each volume of the time series were time-shifted to the beginning of the TR. Image volumes were despiked, the time-series were spatially registered to censor TRs when the head movement exceeded 0.3 mm relative to the previous TR and minimize the artifacts from head movement, and were then aligned to the participant's high-resolution anatomical image. Non-linear registration of the anatomical images to standard space was performed using AFNI's tlrc_NL_warp. The functional time-series was also warped to standard space (AFNI's MNI2009c template) from normalized T1-weighted anatomical images using nonlinear transformation matrices.

2.5.2. Flanker task processing

Incongruent minus congruent contrasts were computed by convolving a square wave (duration = 1s; amplitude = 1) with the default canonical hemodynamic response function in AFNI (3dDeconvolve). The resulting parametric maps for each participant were submitted to the group analysis. Incorrect trials were not modeled in this analysis, therefore this convolution created continous predictors representing only correct congruent and incongruent trials. Incorrect trials were excluded from the analysis in order to isolate activation associated with only correct executive control performance, consistent with the approach used by others (Colcombe et al., 2004; Liu-Ambrose et al., 2012). While exercise could effect error-related processing during conflict monitoring, the Flanker task is relatively easy to perform and produces relatively few error trials, and is not designed to effectively address error-related processing using fMRI.

2.5.3. Whole brain voxel-wise analysis

The magnitude and spatial extent of Flanker executive control-related activation (incongruent minus congruent) was created for the exercise (see Supplementary Fig. 1) and rest (see Supplementary Fig. 2) conditions, respectively. AFNI's cluster-size threshold computation program (3dClustSim) was used to control the whole brain family-wise error rate (FWER) at $p < .05$ based on a voxel-wise probability threshold of $p < .001$ and minimum cluster size $k \geq 20$ (first nearest-neighbor clustering, separate clustering of positive and negative values above the threshold). Executive control-related activation maps were defined where significant difference between the incongruent and congruent contrast was present at FWER corrected $p < .05$.

Using AFNI's voxel-by-voxel arithmetic computation function (3dcalc), activation maps for each condition were created and combined into a disjunction ("OR") mask by conjoining activated regions identified in the voxel-wise analysis for the exercise and rest conditions. Based on the incongruent minus congruent contrast, any significantly activated clusters in each condition contributed to the disjunction map (Fig. 1). Voxels identified in the disjunction map were applied as a mask to each participant's individual data and AFNI's time-series extraction function (3dmaskave) was used to extract the mean activation intensities (β coefficients) for each participant within each distinct region for both the exercise and rest conditions. Using this method, we computed the interaction between Flanker trial types (incongruent versus congruent) and experimental condition (exercise versus rest).

2.6. Statistical analysis

The executive control-related activation maps, HR, RPE, behavioral measures of the Flanker task between the exercise and rest conditions in each region were compared using paired *t*-test within SPSS (version 21), with statistical significance at $p < .05$. The False Discovery Rate (FDR) correction was conducted for further adjustment in functional activation intensity with ten ROIs. Upon inspection of the Flanker performance data, we determined that the Flanker accuracy data were not normally distributed, with a negative skewness and high kurtosis; thus, a non-parametric statistical test (Wilcoxon sign-rank) was used to compare the exercise and rest conditions.

2.7. Post-hoc analysis

To more appropriately test whether our results were in agreement with those of previous exercise training studies (Colcombe et al., 2004; Liu-Ambrose et al., 2012) employing a less conservative voxel-wise thresholds relative to the one used in the present study, we conducted a post-hoc analysis using FWER corrected $p < .05$ based on a voxel-wise probability of $p < .005$ and minimum clusters size $k \geq 63$ (first nearest-neighbor clustering, separate clustering of positive and negative values above the threshold). Briefly, a disjunction mask was created by combining exercise and rest maps based on the threshold before

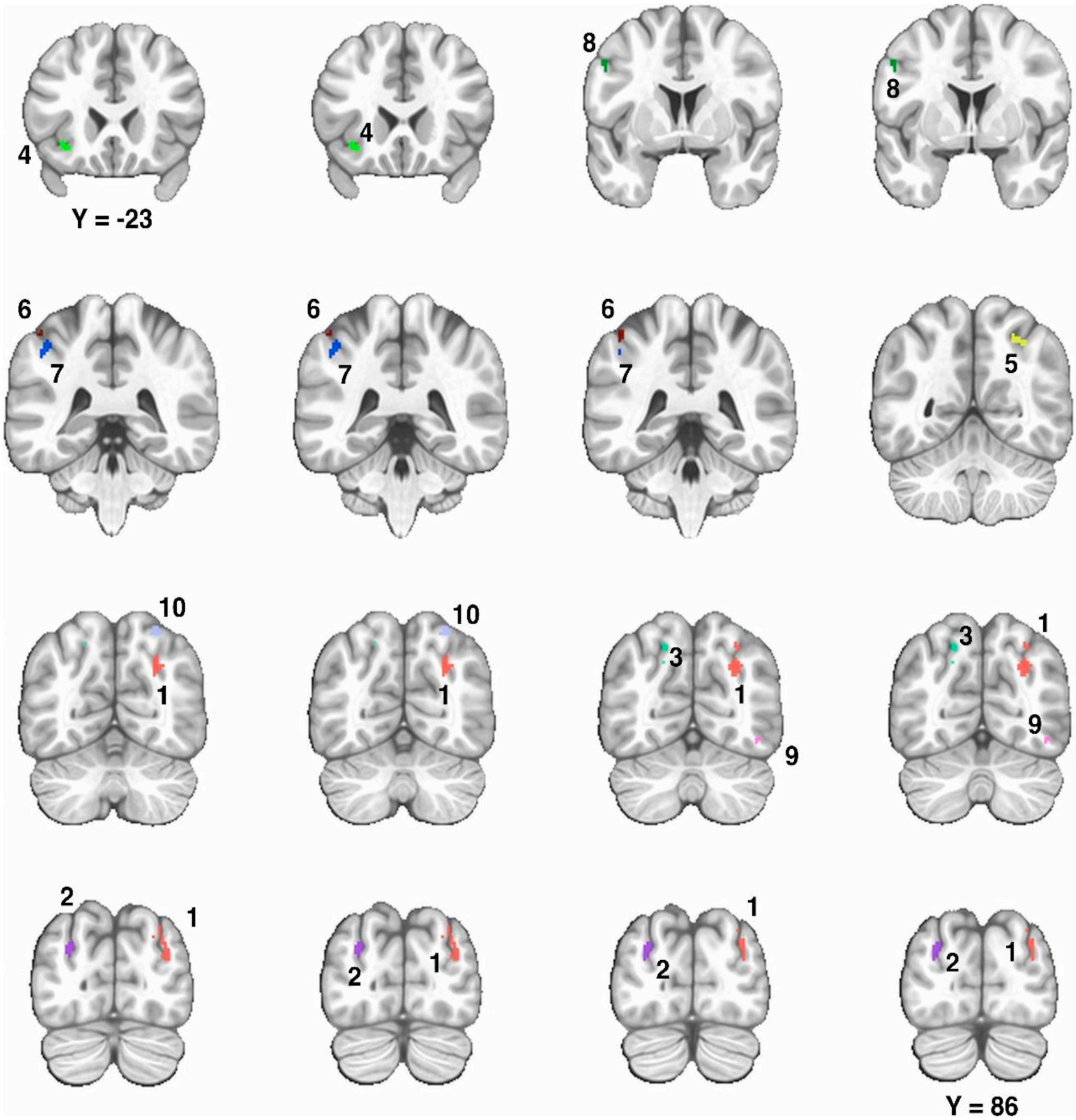

Fig. 1. A montage of coronal slices showing the ten regions derived from a disjunction (OR) mask activated in both the exercise and rest conditions. The numerical labels correspond to the region numbers shown in Table 3. The colors only denote the spatial location of the distinct regions and may appear in multiple slices of the montage.

extracting the mean activation intensities from each experimental condition and compared using paired *t*-tests.

3. Results

3.1. Exercise and behavioral flanker performance

HR and RPE data during the exercise and rest conditions are reported in Table 2. HR (± SD) was significantly higher during exercise (135.9 ± 20.3 bpm) compared to rest (66.7 ± 9.0 bpm) [Exercise main effect, $t(31) = 19.209$, $p < .0001$, $d = 4.81$]. Similarly, RPE during the exercise was significantly greater (14.3 ± 1.4) relative to rest (6.1 ± 0.3) [Exercise main effect, $t(31) = 37.612$, $p < .0001$, $d = 9.18$]. The mean RPE during exercise was located between the verbal anchors "somewhat hard" and "hard", indicating participants subjectively perceived the exercise at a moderate intensity, as intended. Moreover, our participants subjectively perceived both the exercise (6.4 ± 1.9) and rest (6.9 ± 1.5) conditions as neutral to mildly pleasant based on self-assessment manikin valence ratings (Bradley and Lang, 1994), suggesting the both conditions were not associated with unpleasant affective states (e.g., boredom).

The mean (± SD) performance accuracy for the congruent condition after exercise (97.0 ± 10.1%) was statistically greater than rest (87.7 ± 24.1%), [Exercise main effect, Z = 2.109, $p = .035$]. Also, participants demonstrated higher incongruent trial accuracy after exercise (93.2 ± 13.3%) relative to rest (84.8 ± 24.2%) [Exercise main effect, Z = 2.264, $p = .024$]. The mean RT for congruent trials [Exercise main effect, $t(31) = 0.683$, $p = .500$, $d = 0.077$], incongruent trials [Exercise main effect, $t(31) = 0.644$, $p = .524$, $d = 0.051$] and the interference score [Exercise main effect, $t(31) = -0.342$, $p = .734$, $d = 0.053$] did not show a significant difference between the two conditions (Table 2). In order to confirm that there were no effects elicited by the order of experimental session, we compared the differences in behavioral performance between Day 1 and Day 2 where no statistical differences were found in any Flanker performance indices.

Table 2
Exercise and fMRI task outcome data for study participants.

		Total sample (n = 32)		Exercise main effect
		Exercise	Rest	
		Mean ± SD	Mean ± SD	p-Value (d)
Exercise outcome	HR (BPM)	135.9 ± 20.3	66.7 ± 9.0	**< 0.0001 (4.81)**
	RPE (Borg 6–20 scale)	14.3 ± 1.4	6.1 ± 0.3	**< 0.0001 (9.18)**
fMRI task outcome	Congruent accuracy (%)	97.0 ± 10.1	87.7 ± 24.1	**0.035 (0.54)**
	Incongruent accuracy (%)	93.2 ± 13.3	84.8 ± 24.2	**0.024 (0.45)**
	Congruent RT (ms)	588.8 ± 104.0	580.6 ± 95.6	0.500 (0.07)
	Incongruent RT (ms)	673.7 ± 154.8	666.1 ± 139.3	0.524 (0.05)
	Interference score (ms)	13.9 ± 9.8	14.5 ± 12.6	0.734 (0.05)

Note: SD, standard deviation; HR, heart rate; BPM, beats per minute; RPE, rating of perceived exertion; RT, response time; ms, millisecond; Interference Score = [(Incongruent RT–Congruent RT)/Congruent RT]*100; d, Cohen's d; p-values and effect sizes reflect within participant differences; Non-parametric t-test was used for Flanker accuracy comparison; comparisons in **bold** font are significant at $p < .05$.

3.2. fMRI data processing

Maximum censored motion during fMRI data preprocessing for exercise (0.94 ± 0.48 mm) and rest (1.03 ± 0.66 mm) was not statistically different (p = .415). Also, there was no statistical difference between the percentage of censored TRs for exercise (0.20 ± 0.65%) and rest (0.53 ± 1.81%) (p = .129), suggesting the amount of head movement during the scan between conditions were not a confounding factor when interpreting the present fMRI datasets.

3.3. Executive control fMRI activation

Supplementary Table 1 illustrates results from the voxel-wise analysis and volumes of regions that were activated when comparing incongruent minus congruent trials after the exercise and rest conditions. Exercise was associated with a greater spatial extent of executive control-related activation (volume 3632 mm^3; see Supplementary Fig. 1) compared to rest (volume 400mm^3; see Supplementary Fig. 2), although the spatial extent of activation did not include a statistical comparison.

Table 3 depicts the results of the paired t-test comparing activation of the exercise and rest conditions in ten regions with significant executive control-related activation (incongruent > congruent). Three out of the ten regions showed greater activation after exercise compared to rest (Fig. 2; Panel A, B, C). FDR correction for multiple comparisons with ten ROIs was then conducted and we found the p-value of ROI 4 was greater than FDR correction threshold. In a post-hoc analysis, using a less conservative voxel-wise probability threshold of $p < .005$ and a cluster threshold to maintain whole brain FWER at $p < .05$, significantly less activation after exercise compared to rest was found (p = .041, d = 0.400) in the right cingulate gyrus (BA = 32, Talairach coordinates x = 3, y = 13, z = 45, volume 228 mm^3) (Fig. 2; Panel D).

4. Discussion

The present study assessed the functional activation and behavioral indices of executive control via the Flanker task in response to a single session of exercise among healthy older adults. Our prediction of greater functional activation in the frontal and parietal cortices was supported by a voxel-wise main effect of exercise (incongruent > congruent) in the left inferior frontal gyrus (IFG) and left inferior parietal lobule (IPL). Although the p-value of IFG was greater than FDR correction threshold, because a conservative approach during voxel-wise analysis was employed, we cannot dismiss the possibility that type II error might have occurred due to overcorrection.

The IFG plays a role in inhibitory processes engaged in the context of identifying misleading information (Novick et al., 2005) and the IPL

Table 3
Comparison of executive control-related activation (incongruent minus congruent) between the exercise and rest conditions in ten brain regions. The region numbers correspond to the regions in the brain activation maps identified in Fig. 1.

								Total sample (n = 32)		Exercise main effect
								Exercise	Rest	
Region #	Side	Region label	BA	x	y	z	vol	Mean ± SD	Mean ± SD	p-Value (d)
Frontal lobes										
2	L	Cuneus	19	−29	−85	19	408	0.08 ± 0.06	0.05 ± 0.09	0.135 (0.39)
3	L	Precuneus	7	−23	−69	37	192	0.07 ± 0.07	0.05 ± 0.12	0.188 (0.20)
4	L	Inferior frontal gyrus		−33	23	−11	152	0.11 ± 0.09	0.05 ± 0.11	**0.020 (0.59)**
8	L	Inferior frontal gyrus		−49	1	35	128	0.09 ± 0.08	0.05 ± 0.04	0.108 (0.63)
Parietal lobes										
5	R	Inferior parietal lobule		33	−57	47	152	0.08 ± 0.08	0.06 ± 0.12	0.300 (0.19)
6	L	Inferior parietal lobule	40	−45	−47	53	152	0.07 ± 0.06	0.002 ± 0.10	**0.0007 (0.82)**
7	L	Inferior parietal lobule		−47	−39	43	136	0.07 ± 0.06	−0.007 ± 0.08	**0.0004 (1.08)**
10	R	Superior parietal lobule		25	−65	57	120	0.11 ± 0.12	0.08 ± 0.15	0.242 (0.22)
Occipital lobes										
1	R	Superior occipital gyrus	19	37	−87	21	1280	0.10 ± 0.07	0.08 ± 0.11	0.223 (0.21)
10	R	Inferior occipital gyrus		43	−71	−11	120	0.04 ± 0.08	0.09 ± 0.09	0.050 (0.58)

Note: ROI, regions of interest; Positive, right (x), anterior (y), and superior (z), representing peak activation in Talairach coordinates; BA, Broadmann area; vol, volumes in mm^3; SD, standard deviation; d, Cohen's d; p-values and effect sizes reflect within participant differences; comparisons in **bold** font are significant at $p < .05$.

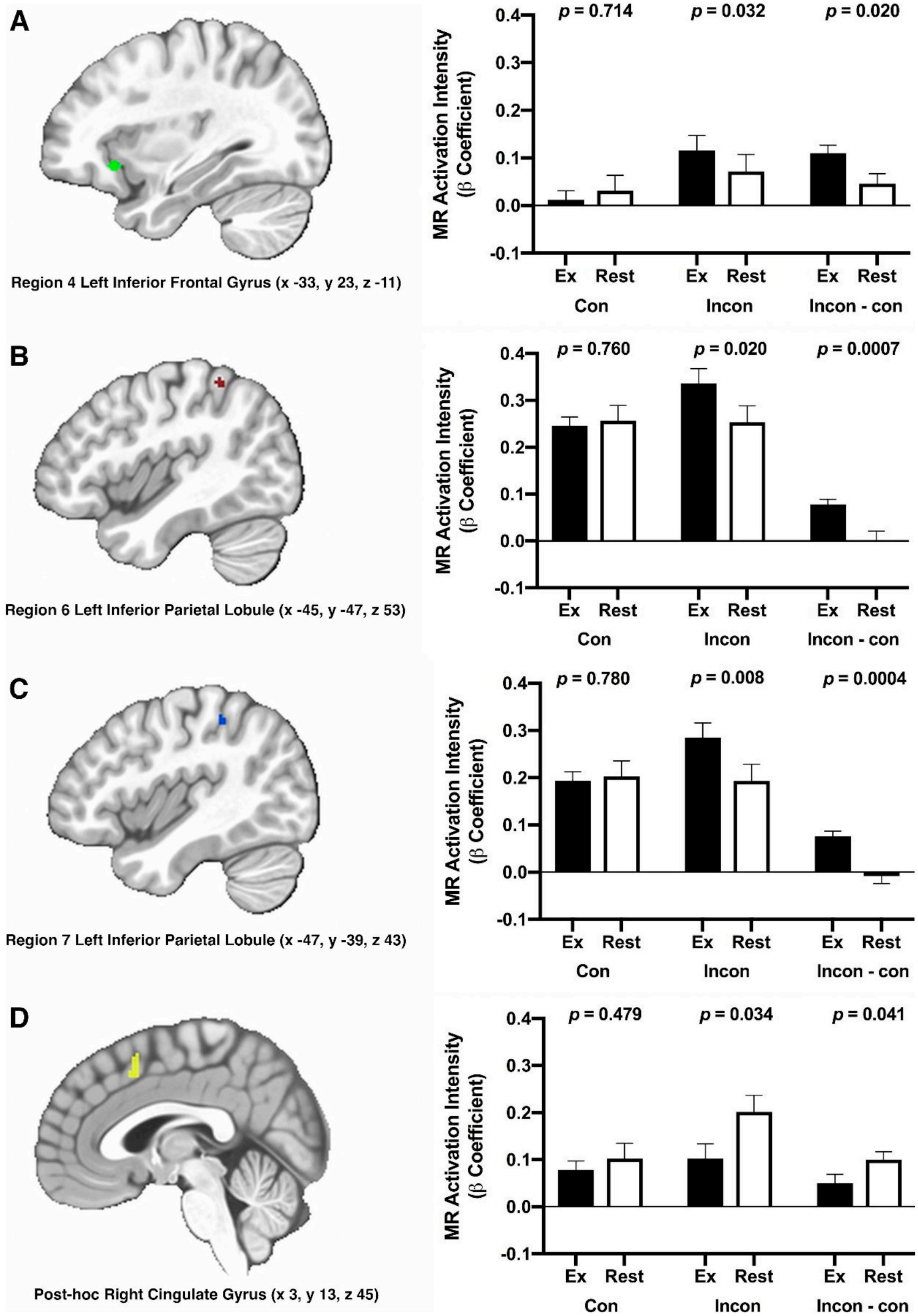

Fig. 2. Sagittal montages demonstrate results of regions in the disjunction (OR) mask presenting significant differences between the experimental conditions and include brain area and peak activation in Talairach coordinates. Adjacent bar graphs illustrate the mean executive control activation (± SEM) of each Flanker trial type for the exercise and rest condition. *p*-Values above bar graphs indicate statistical difference between the experimental conditions. (A) represents region 4, (B) represents region 6, and (C) represents region 7 in Table 3 and Fig. 1. (D) represents a post-hoc analysis (voxel-wise probability threshold $p < .005$) result showing *less* activation after exercise compared to rest. Note: Ex, exercise; Con, congruent; incon, incongruent; incon-con, incongruent-congruent.

is imperative in sustaining attention and switching between task-sets (Singh-Curry and Husain, 2009). Greater activation in the IFG (Rubia et al., 2003) and IPL (Blasi et al., 2006; Bunge et al., 2002; Chen, 2014) was consistently observed during successful completion of interference tasks, reflecting the engagement of both the IFG and IPL during execution of selective spatial attention and inhibitory control to reduce interference and facilitate the correct response. Our findings were in agreement with the prior study showing increased activations in regions devoted to selective attention processing (the SFG, MFG, and SPL) after 6 months of aerobic exercise training (Colcombe et al., 2004). In this sense, greater recruitment of both the IFG and IPL, regions involved in executive control as reflected by greater activation in response to incongruent versus congruent trials following an acute bout of exercise, suggests an enhanced function of this neural network to suppress interference derived by incongruent flanking cues and to implement attentional selection to isolate target cues.

Nevertheless, our hypothesis of decreased neural activity in the ACC after exercise was not supported using our conservative analytic approach. We chose to use a more stringent voxel-wise probability threshold to increase the validity of our data which was based on Woo et al. (2014) suggesting less conservative voxel-wise probability threshold (e.g. $p < .01$) raises the vulnerability of the data to noise and possibility of cluster-level false positive rate; thus, setting the primary threshold at $p < .001$ ($Z > 3.219$) is recommended. Earlier exercise training studies have reported reduced BOLD activation in the ACC (Colcombe et al., 2004) and the insula and middle temporal gyrus (Liu-Ambrose et al., 2012) during the Flanker task. We speculate that this discrepancy might be due to differences in voxel-wise thresholding. Indeed, relatively less conservative voxel-wise thresholds were used in Colcombe et al. (2004) with $Z > 2.33$ and Liu-Ambrose et al. (2012) with $Z > 1.65$, compared to our more conservative threshold of $Z > 3.219$. Notably, the regions displaying reduced activation in the previous studies had relatively smaller cluster sizes compared to those showing increased activation, with cluster sizes of 60 in Colcombe et al. (2004) and 1215 with a maximum Z statistic of 3.07 in Liu-Ambrose et al. (2012). While not meeting current fMRI recommendations for voxel-wise thresholding (e.g., $p < .001$) (Woo et al., 2014), we conducted a post-hoc analysis using a slightly greater voxel-wise threshold of $p < .005$ in order to permit comparison with these earlier studies. In this analysis, we observed significantly reduced activation as a function of exercise in the cingulate gyrus ($p = .041$, $Z > 2.807$; Fig. 2, panel D). Although we did not detect decreased executive control-related activation in the ACC using a more stringent threshold, similar pattern of reductions in activation was observed with voxel-wise thresholds that may not be as reliable, and thus should be interpreted with caution until these effects can be replicated in larger samples.

Another important point to address is that the present study is at odds with the prior finding demonstrating shorter Flanker response time after an acute bout of exercise (Kamijo et al., 2009). While RT was not improved in the present study, we observed significantly greater Flanker accuracy (both incongruent and congruent trials) after exercise relative to rest. This discrepancy presumably arises from the difference in duration between cessation of exercise and performance of the Flanker task in the scanner. The present study had a 30–40 min interval between exercise cessation and the Flanker task due to MRI session preparation and the preceding anatomical MRI scan. In contrast, the Flanker task was conducted immediately following exercise in Kamijo et al. (2009). The lasting effects of acute exercise on upregulation of neurochemical biomarkers related to cognitive improvement including dopamine, norepinephrine, and brain-derived neurotrophic factors are known to persist for up to 2 h (Meeusen et al., 2001; Rasmussen et al., 2009). In a randomized controlled study, the positive effects of moderate-to-high intensity acute exercise on executive function performance persist for up to 2 h following the conclusion of exercise (Basso et al., 2015), although this study was unable to answer if there were time-dependent performance differences between RT and accuracy in the composite measurement used. Based on this evidence, we postulate that acute benefits on speed of trial conflict evaluation elicited by acute exercise may dissipate more quickly, while improved classification accuracy may persist longer.

There are possible neurophysiological mechanisms that drive the acute exercise-induced effects we observed. Performing an acute bout of exercise induces cognitive arousal characterized by increased norepinephrine (Chmura et al., 1994) in brain regions associated with prefrontal cortex functioning (McMorris and Hale, 2012) with subsequent enhancement in allocation of neural resources during executive function task (Mc Morris et al., 2000). Another mechanism suggests that acute exercise promotes a transient increase in neural growth factors including brain-derived neurotrophic factor (Van Praag et al., 2005; Ferris et al., 2007) which is related to prefrontal-dependent cognitive functioning (Hwang et al., 2016). The other possible underlying mechanism lies in dopaminergic neurocircuitry which involves in reward process where the brain triggers its release after accomplishment of task (Wise and Rompre, 1989). According to rodent studies, the nucleus accumbens, a major component of the ventral striatum connected to prefrontal cortex, mediates the dopamine receptor pathways and rewarding aspect of exercise (Greenwood et al., 2011; Roberts et al., 2012). Performing exercise is associated with increased dopaminergic activity in the basal ganglia and, through ascending dopaminergic projections, greater availability of dopaminergic neurotransmission (Hattori et al., 1994; Petzinger et al., 2010) facilitates cognition during tasks involving prefrontal cortex.

Since identification of the fMRI blood oxygen level dependent (BOLD) signal is based on hemodynamic response of the brain (changes in the balance between oxygenated and deoxygenated hemoglobin) (Buxton et al., 1998), one might wonder if the effects observed in the present study could simply be explained by increased cerebral blood flow (CBF) after exercise. However, it is unlikely that increased CBF after acute exercise adequately accounts for these results, for the following reasons: First, while some have found that global brain blood flow is controlled and maintained at a nearly constant level throughout exercise (Ide and Secher, 2000), there are conflicting reports regarding changes in CBF after acute exercise. For example, exercise has been shown to increase global CBF (Smith et al., 2010), to decrease CBF (MacIntosh et al., 2014), and to not change CBF (Pontifex et al., 2018). Thus, it still remains unclear if there is an increase in CBF during and after a single session of exercise that could impact the fMRI BOLD signal. Second, our analytic approach subtracted the BOLD response for the congruent trials from BOLD response for the incongruent trials, only for the correct trials. This subtraction cancels possible changes derived by global exercise-induced shifts in CBF (if they occurred), which presumably would affect the BOLD signal of both the incongruent and congruent stimuli equally, and removes the activation related to errant responding. This approach also subtracts the BOLD response common to the sensory and motor aspects of both types of trials (e.g., visual processing, the button press), revealing the BOLD response that is unique to the executive control processes invoked by the incongruent condition. Finally, we did not include error trials in the model of the activation response to congruent and incongruent trials, which places the variance from errors in the residual term of the model and possibly dampening the effects of interest. While it is possible that our effects may have been larger if the variance from error trials had been regressed as a nuisance variable, we did not observe a significant interaction between Exercise and Trial Type on the number of errors ($p = .62$, data not shown), further suggesting that our effects were not systematically confounded by activation due to response errors.

One important limitation of the present study is the homogeneity of the study sample. All individuals who completed the study regularly participated in physical activity (≥3 days/week), were highly educated (93% had college or graduate degree), did not have a diagnosis of cardiovascular disease (e.g. hypertension or diabetes), and were predominantly Caucasian (78%). As such, the present sample is not representative of the general older population. Whether acute exercise has similar effects in clinical population or a varied sample with different demographic characteristics and cognitive abilities should be investigated in future studies. Second, due to the MRI scan preparation and protocol, the Flanker task was performed 30–40 min post-exercise, meaning short-term effects of acute exercise on executive control may have been missed, particularly changes in RT. Next, while the present study lacked of maximal exercise test to determine maximal HR, our study was not designed to compare different exercise intensities. Alternatively, participants were instructed to self-adjust the resistance during cycling exercise to meet the Borg RPE 6–20 scale of rating of 15 (associated with verbal anchor "Hard"). We used a seated rest control condition during which participants were restricted from interacting with external stimuli (e.g., books, phone, etc.). While one could hypothesize that the rest condition was considered boring and could produce a negative affective response, our participants rated both the exercise and rest conditions as affectively pleasant. In addition, due to time and cost constraints, we were not able to conduct MRI scans both before and after the rest and exercise conditions. Performing a pre-test scan to control any effects of day and expectancy effects of exercise, and possible attentional decrements induced by the rest condition, is warranted in future studies. Finally, we did not assess the effects of light-intensity exercise. Light-intensity (< 30% of $\dot{V}O_{2max}$) is a feasible form of exercise for most elders, whereas performing moderate to strenuous (> 60% of $\dot{V}O_{2max}$) exercise requires a greater degree of cardiovascular fitness, which may be limited in older adults. Future research is warranted to assess the effects of light-intensity exercise on functional executive control activation.

5. Conclusion

Earlier studies suggest while long-term exercise enhanced performance during the Flanker trials demanding greater interference, only general behavioral improvements were observed after acute exercise. The present study supports this evidence by showing the salutary effects of a single bout of exercise on behavioral measurement were general, with greater Flanker task performance accuracy across Flanker trial types. Conversely, we did not detect exercise-induced improvements in RT, inconsistent with Kamijo et al. (2009), indicating benefits derived by acute exercise on processing speed during the Flanker task may last < 30–40 min. Although the behavioral performance effects related to acute exercise were general (i.e., during both congruent and incongruent trials), our fMRI results showed that acute exercise facilitated a specific inhibitory response-related functional activation (incongruent > congruent) in the IFG and IPL. These findings are in line with previous evidence (Colcombe et al., 2004) that demonstrated greater functional hemodynamic activity in the frontal and parietal regions following exercise training. These findings further suggest that the underlying neural changes associated with long-term exercise are likely to immediately occur following a single bout of exercise. In contrast, the behavioral improvements in interference control, defined by improvements in response time interference score, may be driven by accumulated effects of repeated exercise sessions. This raises questions for future studies that should examine if other executive control tasks (e.g. task-switching, Stroop) engender similar behavioral and functional patterns for acute and long-term exercise. The acute and chronic exercise relationship on other cognitive domains (e.g., episodic memory) should be also assessed in the future.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2019.10.002.

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