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Light Aerobic Exercise Modulates Executive Function and Cortical Excitability

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Abstract

Single bouts of aerobic exercise can modulate cortical excitability and executive cognitive function, but less is known about the effect of light intensity exercise, an intensity of exercise more achievable for certain clinical populations. Fourteen healthy adults (aged 22 to 30) completed the following study procedures twice (≥7 days apart) before and after 30-minutes of either light aerobic exercise (cycling) or seated rest: neurocognitive battery (multitasking performance, inhibitory control and spatial working memory), paired pulse TMS-measures of cortical excitability. Significant improvements in response times during multitasking performance and increases in intracortical facilitation (ICF) were seen following light aerobic exercise. Light

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Author contributions
TM and APL conceived the study. TM, PF, ES and APL designed the study. DCM, JGO and JMTM participated in the study design. JM performed the study set up. Data was collected by TM, JM and AS. Data was analysed by TM, PF, JGO and DCM. Data was interpreted by TM, PF, JGO, DCM, ES and APL. TM drafted the manuscript and all authors critically revised it.

Disclosure of Interest
Dr. A. Pascual-Leone serves on the scientific advisory boards for Nexstim, Neuronix, Starlab Neuroscience, Neuroelectrics, Constant Therapy, Cognito, and Neosync; and is listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation with electroencephalography and magnetic resonance imaging. Dr. Santarnecchi serves on the scientific advisory boards for EBNeuro.

Data Availability
All data pertaining to this study will be made available upon request to the corresponding author.

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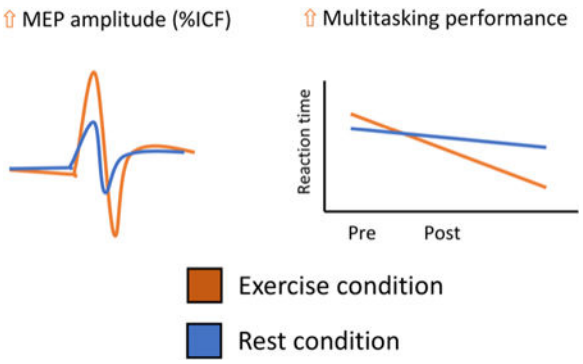
aerobic exercise can modulate cortical excitability and some executive function tasks. Populations with deficits in multitasking ability may benefit from this intervention.

Graphical Abstract

Light intensity aerobic exercise, suited to populations who may be unable to exercise at higher intensities can modulate multitasking performance and cortical excitability in a facilitative direction. Consistent with previous research however, this intensity of exercise does not appear to modulate widespread executive functions.



Keywords

Exercise; Neuroplasticity; Cortical excitability; Executive function

1. Introduction

There is a vast amount of evidence showing that participation in regular aerobic exercise has many positive effects on brain and cognitive functions, particularly on those dependent on mechanisms of neuroplasticity (Cabral et al., 2019; Cotman, Berchtold, & Christie, 2007; Gomes-Osman et al., 2018; Hillman, Erickson, & Kramer, 2008). Domain specific improvements in cognitive function have been reported and much focus has been placed on exercise-induced improvements in executive functions (Etnier & Chang, 2009). The majority of the evidence generated to date is based on moderate intensity exercise, in studies spanning various age groups (Donnelly et al., 2009; Gomes-Osman et al., 2018; Nanda, Balde, & Manjunatha, 2013; Peruyero, Zapata, Pastor, & Cervelló, 2017). It is worth noting however that certain populations, such as sedentary individuals, older adults or those with a disability or within rehabilitation may not be capable of exercising at higher exercise intensities (Franco et al., 2015; Pinto, Newman, & Hirsch, 2018), and therefore it is important to explore the effects of exercise performed at lower intensities. In one previous study, 4 weeks of light intensity exercise in previously sedentary individuals improved performance on the Stroop cognitive test (Gomes-Osman et al., 2017), suggesting that this intensity may have modulatory properties in certain populations. Single bouts of moderate intensity aerobic exercise have been shown to enhance different executive functions, such as planning, task switching, response inhibition and working memory (Chang et al., 2011; Hung, Tsai, Chen, Wang, & Chang, 2013; Kamijo et al., 2004; Kamijo, Nishihira, Higashiura, & Kuroiwa,

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2007; Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009). Of these studies Kamijo and colleagues also found that light aerobic exercise increased reaction time latencies on a Flanker task (Kamijo et al., 2007) but not after a go/no-go task (Kamijo et al., 2004).

Cortical adaptations following injury to the brain (for example after stroke or traumatic brain injury) are a key goal of rehabilitation, and aerobic exercise has been associated with short term changes in cortical excitability within the motor cortex (Mooney et al., 2016; Singh, Duncan, Neva, & Staines, 2014; Smith, Goldsworthy, Garside, Wood, & Ridding, 2014). Exercise may facilitate learning-based rehabilitation via adaptive modulation of cortical excitability (Singh et al., 2014a). Accordingly, the immediate effect of exercise on executive function tasks, specifically those measured via response times (multitasking, inhibitory control), may be driven, in part, by neuroplastic changes related to neurotransmitter signalling (glutamate and gamma-aminobutyric (GABA)) (Kujirai et al., 1993; Maddock, Casazza, Fernandez, & Maddock, 2016). Transcranial magnetic stimulation (TMS) paradigms provide a means to characterize cortical excitability balance in the motor cortex (Pascual-Leone et al., 2011). Paired-pulse TMS (ppTMS) can be applied with different inter-stimulus intervals to provide an understanding of excitatory and inhibitory GABAergic and glutamatergic systems (Kujirai et al., 1993; Valls-Solé, Pascual-Leone, Wassermann, & Hallett, 1992). Studies have shown that moderate intensity exercise can modulate TMS measures of intracortical facilitation (ICF) and inhibition, including short interval intracortical inhibition (SICI) and long interval intracortical inhibition (LICI) (Lulic, El-Sayes, Fassett, & Nelson, 2017; Mooney et al., 2016; Singh et al., 2014; Smith et al., 2014). Of these studies, Smith and colleagues were the only previous study to assess the effect of light aerobic exercise on TMS measures of cortical excitability. Therefore, less evidence exists on how intracortical circuits are modulated by a single session of light aerobic exercise. Whilst studies have evaluated the effect of exercise on motor learning (Tunovic, Press, & Robertson, 2014) and procedural memory (Ostadan et al., 2016), and one previous study associated improvements in motor learning with cortical excitability and plasticity (Mang, Snow, Campbell, Ross, & Boyd, 2014), no studies have assessed the relationship between the effect of light intensity exercise on both executive function tasks and TMS measures of cortical excitability. Kamijo and colleagues did demonstrated that the P300 amplitude of an event-related potential was increased after both light and moderate-intensity exercise indicating increased executive control (Kamijo et al., 2007), however in a previous study only moderate intensity exercise lead to an increase in P300 amplitude, which was not concomitant with increased reaction times (Kamijo et al., 2004).

Further characterization of the cognitive effects and mechanistic underpinnings of single bouts of light aerobic exercise, an intervention suited to the rehabilitation setting, therefore is especially pertinent for populations who cannot exercise at higher intensities and of interest to the growing body of literature on the effects of acute exercise on executive function.

The present study was designed to explore the effects of a single bout of light aerobic exercise on several executive function tasks and cortical excitability. We hypothesized that a single bout of light aerobic exercise would improve executive function constructs (multitask performance, inhibitory control and spatial working memory) and modulate cortical

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excitability, as measured by TMS. An exploratory aim was to assess the relationship between these two outcome measures.

2. Methods

2.1 Participants

The Institutional Review Board of the Beth Israel Deaconess Medical Center (BIDMC) approved this study and participants signed informed consent prior to participating in any research procedures. Participants were recruited via an internal repository of previous research participants from the Berenson-Allen Center for Non-Invasive Brain Stimulation at BIDMC. Interested participants were screened for eligibility using the following criteria: right-handed (confirmed by the modified version of the Edinburgh Handedness questionnaire (Milenkovic & Dragovic, 2013), between the ages of 18 and 60 years, without neurological or physical conditions that might affect performance on testing procedures or known contraindications to TMS (Rossi et al., 2009). Contraindications to exercise were screened via the Physical Activity Readiness Questionnaire (PAR-Q) (Adams, 1999). Fourteen healthy adults (9 females) with a mean (±SD) age of 26 (±3) years completed all study procedures. An initial sample size calculation based on a previous meta-analysis (Etnier, Nowell, Landers, & Sibley, 2006) calculated that we needed a sample size of 13 to detect a similar effect (effect size of .34 with a standard deviation of .30, assuming a type I error rate of 0.05 with 95% power).

2.2 Protocol and study design

Participants completed two study visits in a randomized counterbalanced order design with at least 7 days between visits. This interval was chosen to minimize carry-over effects from the first visit. Study visits consisted of the following procedures (Figure 1): cognitive testing, a TMS session, either a 30-minute aerobic exercise (cycling) or control rest intervention followed by a repeat of the cognitive tasks and finally the TMS session. Study visits were scheduled so that each procedure was undertaken at roughly the same time of day over both visits. A random number sequence generated by Microsoft Excel (Microsoft, USA) determined the order in which each participant completed the study to minimize practice effects of the cognitive tasks. A series of 20 random numbers was generated and participants were allocated an order (exercise first or rest first) based on their corresponding number being odd or even.

2.3 Intervention

The aerobic exercise intervention consisted of 30 minutes of light aerobic exercise on a Monarch 928 G3 static cycle electronic ergometer (Monarch exercise AB, Vansbro, Swenden). Prior to the intervention, a nurse recorded baseline vital signs (resting heart rate, blood pressure, oxygen saturation, respiratory rate). A Polar H7 heart rate strap (Polar, Kemple, Finland) was worn measuring second-by-second heart rate (HR), recorded via the cycle ergometer with an ANT+ / 5KHz receiver. HR data was also collected using an iPad (Apple Inc, California) and commercial software (Polar Flow, Kemple, Finland). The ergometer was then fitted to each participant who subsequently undertook a 5-minute warm-up consisting of passive cycling with no resistance. After the warm-up, participants

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undertook 30-minutes of light intensity cycling. Intensity was calculated based on the Karvonen equation and the target heart rate reserve (HRR) zone was 40 and 60% HRR:

$$\text{target HR} = ((\text{HRmax} - \text{resting HR}) * \text{intensity } [0.4 - 0.6]) + \text{resting HR}. \quad (1)$$

This exercise intensity was chosen based on prior research with TMS and cortisol, which suggests higher intensity exercise interventions abolished the neuromodulatory effects of repetitive TMS, possibly related to exercise-induced increases in cortisol (McDonnell, Buckley, Opie, Ridding, & Semmler, 2013; A. E. Smith et al., 2018). Resistance of the cycle ergometer was adjusted by study researchers to ensure participants reached the exercise intensity zone. Upon completion of the intervention, participants cooled-down for 2-minutes (no resistance cycling), after which, post-intervention vital signs were recorded by the nurse. The control intervention consisted of seated rest for 30 minutes. During this time, participants could interact with study staff, use the mobile phones or read, but were seated and made no whole-body movements during the 30 minutes. HR was also recorded during the rest intervention using the same Polar strap.

2.4 Cognitive tasks.

A battery of three tablet-based executive function tasks was completed before and after each intervention using the Food and Drug Administration (FDA)-approved CANTAB cognitive testing software (Cambridge cognition, Cambridge, UK) using an iPad Pro (Apple Inc, California) (Luca et al., 2003). The CANTAB battery has been shown to be well correlated with traditional pen and paper neuropsychological tests (Smith, Need, Cirulli, Chiba-Falek, & Attix, 2013) and demonstrates moderate to high test-retest reliability (Gonçalves, Pinho, & Simões, 2016; Lowe & Rabbitt, 1998). Participants were given verbal instructions by the CANTAB software as well as practice trials prior to each test. The tasks were identical at each time point. The following tasks were chosen to measure inhibitory control, processing of conflicting information (multitasking) and spatial working memory (Figure 2).

The *multitasking test* presented two virtual buttons on either side of the screen and a cue (side, direction) with an arrow above either button (left or right) indicating which button to select. Cues appeared (for the full duration of the trial) in consistent (single task) and in-consistent (multitask) trials and both congruent (arrow on right side pointing right) and incongruent trials (arrow on right side pointing left) were presented. The distribution of the trials was randomly ordered within the following constraints: if multiple trials are presented then 50% must be switch trials, 25% switch trials that are congruent and 25% which are switch trials that are incongruent. Outcome measures consisted of reaction times, errors and multitasking cost (mean latency of single blocks subtracted by mean latency on multitasking blocks).

The *inhibitory control task (stop signal task)* required participants to respond to an arrow stimulus pointing in a given direction. The first set consisted of 16 trials where the participant practiced the response. In the second set, the participant was told to inhibit their response if they heard an auditory signal (a beep). An adaptive *staircase* was employed for the stop signal delay allowing the task to adapt to the performance of the participant to

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narrow in on a 50% success rate. An inter-stimulus interval of 1000ms was applied. The outcome measure was stop signal reaction time, the estimate of when an individual can successfully inhibit their response 50% of the time. This is inferred as the time before all actions become ballistic and the person is no longer able to stop the action.

A *spatial working memory task* required participants to find tokens hidden behind covered boxes and transfer them to empty boxes on the right-hand side of the screen without re-opening a box that has previously been selected. This task displayed four, six or eight boxes and outcome measures consisted of errors (trials when a participant revisits a box in which a token has been previously found) and strategy. It has been suggested that an efficient strategy to complete this task is to follow a predetermined sequence beginning with a given box and once a token has been found return to the same box to begin the next search (Owen, Sahakian, Semple, Polkey, & Robbins, 1995). Participants were not informed of this strategy. To estimate how well this strategy was utilized, the number of times a subject begins a new search with the same box was calculated. A high score represents poor use of this strategy and a low score, effective use.

2.6 Transcranial magnetic stimulation (TMS) and Electromyography (EMG)

To measure the amplitude of TMS-induced motor evoked potentials (MEPs), surface electrodes were placed in a belly-tendon montage on the right first dorsal interosseus (FDI; target muscle) and the abductor pollicis brevis (APB; reference muscle) with a ground on the ulnar styloid process. Electrodes were connected to a PowerLab 4/25T data acquisition device (ADInstruments, Colorado Springs, CO, USA). EMG data epochs (100 ms pre-trigger to 500 ms post-trigger) were digitized at 1 kHz and amplified with a range of ±10 mV (band-pass filter 0.3–1000 Hz) and peak-to-peak MEP amplitude of the non-rectified signal was calculated on individual waveforms using LabChart 8 software (ADInstruments).

All TMS parameters used in this study conform to the guidelines of the International Federation of Clinical Neurophysiology (Rossi, Hallett, Rossini, Pascual-Leone, & Safety of TMS Consensus Group, 2009). In accordance with these guidelines the following TMS procedures were applied before and after each intervention: The optimal spot for the maximal responses of the right FDI muscle was localized and deemed the “motor hotspot.” Resting motor threshold (rMT) was obtained and used to set the intensity of subsequent TMS. rMT was defined as the lowest stimulation intensity required to evoke MEPs ≥ 50 μV in the relaxed right FDI muscle, in five out of ten trials. TMS was applied to the left primary motor cortex using a passive-cooled handheld MagPro MC-B70 Butterfly Coil (outer diameter: 97 mm) connected to a MagPro X100 stimulator (MagVenture A/S, Farum, Denmark). The coil was placed tangential to each participant’s head with the handle oriented approximately 45° relative to the mid-sagittal axis. A monophasic current flowing anterior-posterior (AP) through the coil center was used to induce a posterior-anterior (PA) current approximately orthogonal to the central sulcus. Consistent targeting of the motor hotspot throughout the experiment was achieved by means of a Polaris infrared optical tracking system (Northern Digital Inc., Waterloo, ON, Canada) and a Brainsight TMS neuronavigation system (Rogue Research Inc., Montreal, QC, Canada) using the Montreal Neurological Institute structural MRI template brain. The head-tracker (headband) was

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removed between each TMS session and at the beginning of each subsequent session, the motor hotspot and rMT were re-checked. Anatomical landmarks (fiducial points) were used to register the subjects head into the frameless stereotaxic system that allowed accurate targeting of the motor hotspot during each of the TMS sessions. If the RMT changed (see results), the TMS protocols were subsequently applied as percentages of the new RMT value.

After determining the motor hotspot and rMT, interleaved single pulse TMS (spTMS) and ppTMS were applied over the course of three separate blocks. Each block consisted of spTMS (5 trials each at 80% rMT and 120%rMT), 10 trials of SICI (80%-rMT conditioning stimulus, 120%-rMT test stimulus, 3ms interval), 10 trials of ICF (80%-rMT conditioning stimulus, 120% test stimulus, 12ms interval), and 10 trials of LICI (120%-rMT conditioning stimulus, 120%-rMT test stimulus, 100ms interval). The trial order and the inter-trial interval were pseudorandomized to avoid any block effects or train effects, respectively. Unconditioned cortico-motor reactivity was determined by combining trials of spTMS at 120% with the conditioning stimulus of LICI. Conditioned MEPs were averaged across each ppTMS protocols. Like protocols were averaged across the three blocks. Outcome measures consisted of all ppTMS protocols, baseline MEP amplitudes and RMT values.

2.8 Statistical analysis

All statistical analyses were performed using JMP Pro (v 13.0, The SAS Institute Inc., Cary, North Carolina, USA). Following a within-subjects design, data corresponding to cognitive function scores and TMS measures were each entered into separate 2*2 random-effects linear models, with *intervention* (exercise, rest) and *block* (pre-intervention, post-intervention) as main factors and an interaction term of *intervention*block.* TMS measures consisted of rMT (% of maximum stimulator output; %MSO), unconditioned cortical reactivity (spTMS at 120% and the LICI conditioning pulse), and ppTMS measures of SICI, LICI and ICF (% change of conditioned MEP from unconditioned cortical reactivity [TS-CS/CS*100]). As practice effects have been evidenced for the cognitive tasks (Cacciamani et al., 2018), our main hypothesis was that exercise would improve cognitive test scores more so than rest. Accordingly, planned pairwise comparisons using Bonferroni correction to correct for multiple comparisons were used on the executive function outcomes. For the TMS data, post-hoc pairwise comparisons using Bonferroni corrections were used when an intervention by block interaction was found. All p values from the pairwise comparisons are the corrected values. The effect size for each main effect was presented as partial eta squared (η_p^2) for significant effects. As an exploratory step, simple bivariate correlations (Pearson's R coefficient) were performed on variables highlighted by the linear models to show significant changes across and within interventions. We also performed a power analysis (using STATA version 15.1, StataCorp, USA) on our sample size to ensure sufficient power was gained to detect a difference. Given our sample size (n=14) and an assumed type 1 error rate of 0.05 we calculated an estimated power of 99.8% to detect a true difference of $\Delta = -1.402$ with a standard deviation of 49.7 from a two sample paired means test on one of our main outcome measures (multitasking performance).

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3. Results

Fourteen adults (9 female), aged 26 ± 3 years (range of 22 to 30 years) participated. Mean exercise HRR for the exercise condition was 48 ± 5% HRR and was significantly different compared to the rest condition (5 ± 4% HRR).

3.1.1 Executive functions

Table 1 presents mean ± SD scores for the executive function tasks at each time point. Random-effects linear models showed significant main effects of *block* for mean latency reaction times on the multitasking test for all congruent trials ($F_{1,17}$ = 25.27, p = <.001, η_p^2 = .60), incongruent trials ($F_{1,13}$ = 23.04, p = <.001, η_p^2 = .64), multitasking trials where both rules (side and direction) were used ($F_{1,13}$ = 23.73, p = <.001, η_p^2 = .68) as well as the multitasking cost ($F_{1,13}$ = 9.39, p = .009, η_p^2 = .42). A *block* intervention* interaction was observed in the incongruent trials, though it did not reach significance ($F_{1,13}$ = 2.35, p = .095, η_p^2 = .20). Planned comparisons showed significant improvements in the exercise condition (p = .003) but not in the rest condition (p = .338). Further planned pairwise comparisons of the significant effects of *block* in these outcomes revealed significant pre/post differences in the exercise condition for the congruent (p = .007) and incongruent (p = .019) trials but not in the rest condition (congruent: p = .101; incongruent: p = .338). No change in either condition was seen for the multitasking cost (Figure 3).

No significant effects of *block* or *block* intervention* interaction were seen in stop signal reaction time (*block*: $F_{1,13}$ = 4.01, p = .066, η_p^2 = .02; *block* intervention*: $F_{1,13}$ = 0.12, p = .734, η_p^2 = .00), spatial working memory between errors (*block*: $F_{1,13}$ = 0.24, p = .632, η_p^2 = .01; *block* intervention*: $F_{1,13}$ = 0.02, p = .965, η_p^2 = .00) or strategy (block: $F_{1,13}$ = 0.08, p = .787, η_p^2 = .01; *block* intervention*: $F_{1,13}$ = 0.01, p = .953, η_p^2 = .00).

3.1.2 TMS measures

The random-effects linear model revealed a significant main effect of *block* ($F_{1,13}$ = 7.29, p = .018 η_p^2 = .36) for rMT. Specifically, there was a change pre-to-post intervention of −1.12 ± .40 %MSO (95% CI's .22, 1.99) (Table 2). A significant main effect of *block* ($F_{1,12}$ = 5.38, p = .040 η_p^2 = .31) and an *intervention* block* interaction for ICF was found ($F_{1,11}$ = 7.51, p = .018 η_p^2 = .41). Post hoc comparisons showed a significant increase in ICF pre-to-post exercise (p = .021). No main effects of *block* were seen for SICI ($F_{1,13}$ = 2.44, p = .626, η_p^2 = .02), LICI ($F_{1,11}$ = 1.56, p = .189, η_p^2 = .13) or MEP amplitude ($F_{1,13}$ = 1.18, p = .885, η_p^2 = .07) (Figure 4).

3.1.3 Correlational analyses between significant outcomes and cognitive improvements

Simple linear regression yielded no relationships between %Δ in ICF and %Δ in multitask performance for any multitask outcome (congruent trials: $r_{(12)}$ = −.06, R^2 = .004; incongruent trials: $r_{(12)}$ = −.04, R^2 = .001 ; multitask trials: $r_{(12)}$ = .09, R^2 = .008; multitask cost: $r_{(12)}$ = .21, R^2 = .047).

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1. Discussion

A vast majority of studies on the effects of acute bouts of exercise have assessed the effects of moderate intensity exercise (Hung, Tsai, Chen, Wang, & Chang, 2013; Lulic et al., 2017; Pontifex, Hillman, Fernhall, Thompson, & Valentini, 2009b; Singh, Duncan, Neva, & Staines, 2014b). The present study found that 30-minutes of light aerobic exercise improved response times on multiple outcomes of a multitasking task in healthy adults. Exercise-mediated increases in cortical excitability (ICF) were also observed.

Meta-analyses on the effect of single bouts of exercise on executive functions show a small but consistent improvement (Chang, Labban, Gapin, & Etnier, 2012). Nevertheless, some studies have failed to show an effect (Wang et al., 2015), suggesting exercise may not have broad widespread effects on all executive function domains. Indeed, our results show exercise enhanced several measures of the multitasking test, yet failed to modulate inhibitory control and spatial working memory. In previous research, moderate intensity aerobic exercise has shown more consistent effects on improving executive functions (Chang et al., 2011; Hung et al., 2013; Pontifex et al., 2009). Our results therefore potentially add to the debate regarding the interactions of intensity of exercise and cognitive improvements. That is, in two previous studies comparing the effects of different exercise intensities (light, moderate and intense) on inhibitory control (Go/No-Go) and response inhibition (Flanker task), light aerobic exercise improved reactions times on Flanker task (Kamijo et al., 2007) but not the Go/No-Go task (Kamijo et al., 2004), comparable to our results. It is conceivable that light aerobic exercise may not be sufficiently intense to induce an adaptive plastic response necessary to improve widespread executive functions.

Changes in cortical excitability are a necessary precursor to sustained changes in synaptic strength underpinned by long-term potentiation and long-term depression (Daoudal & Debanne, 2003). And such increases in cortical excitability may render neuronal pools more susceptible to plasticity induction through targeted rehabilitation strategies, when preceded by a bout of exercise (Cotman et al., 2007; Griesbach, 2011). Recently TMS measures have been studied as a means to assess such exercise-mediated changes in cortical excitability (McDonnell et al., 2013; Mooney et al., 2016; Singh et al., 2014a; A. E. Smith et al., 2014) One key difference in our results from previous research is a lack of significant change in cortical inhibition measures (SICI, LICI) (Mooney et al., 2016; Singh et al., 2014a; A. E. Smith et al., 2014). Previous research has suggested that cortical excitability increases are a product of a reduction in cortical inhibition, creating a more favourable environment for potentiation-like excitability changes (Singh et al., 2014a) and whilst in our study, increases in ICF were seen, comparable to previous studies (Lulic et al., 2017; Singh et al., 2014), these were not associated with a concomitant reduction in cortical inhibition (SICI). The mechanisms of exercise-mediated changes in cortical function are not fully understood however modulation of neurotransmitter function, specifically GABA and glutamate (which mediate SICI and ICF, respectively) are thought to play a key role. An interaction between intensity of exercise and excitability changes is possible and may explain why we did not see changes in SICI however a comparison of different exercise intensities is required to fully answer such a question. In a previous study using continuous theta-burst stimulation to measure LTD-like plasticity, McDonnell and colleagues found that a preceding bout of light

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aerobic exercise enhanced the LTD-like inhibitory effect of cTBS (McDonnell et al., 2013). However, similar to ICF, research has suggested that the inhibitory after-effects of cTBS are modulated by NMDA receptors (Huang, Chen, Rothwell, & Wen, 2007). Consequently, our results add to the evidence that single sessions of light aerobic exercise can modulate cortical excitability in a facilitative direction. A key question that remains to be answered is whether such changes in cortical excitability are widespread or confined to the motor cortex. Previous research has suggested that exercise may exert a more widespread effect on the brain. For example increases in activation of diverse brain regions has been shown following exercise (Weng et al., 2017). Indeed, exercise can also modulate behavioural measures such as mood, pain and stress (Glass et al., 2004).

In a prior study by Ostadan and colleagues (2016), a correlation between exercise-increased cortico-spinal excitability (as measured by MEP amplitude) and procedural memory consolidation was shown, highlighting how TMS measures may be related to the effect of exercise on cognitive functions. Whilst our results add to previous research showing exercise-mediated increases in ICF (McDonnell et al., 2013; Singh et al., 2014a), the change in ICF was not correlated with the improvements in multitask performance. This finding suggests the effects of exercise on response times during processing of conflicting information and motor cortex excitability were independent. Although the motor cortex is involved in motor planning and execution (Cheney, 1985) and motor cortex excitability (as measured by ICF and SICI) is associated with voluntary movement (Christova et al., 2006; Nikolova, Pondev, Christova, Wolf, & Kossev, 2006), the ability to process conflicting information (incongruent trials and multitask cost) is dependent on higher-order cognitive regions outside of the primary motor area (Banich et al., 2000). Whereby the total response times of such tasks are a function of the sum of the encoding, decision and response output processes of task execution (Ratcliff & McKoon, 2008). Neuroimaging studies show associations between multitask performance and fronto-parietal networks, including regions such as the anterior cingulate cortex, lateral prefrontal cortices, parietal lobule and the anterior insula (Roberts & Hall, 2008). As such, the direct effect of exercise on ICF within the motor cortex may not completely reflect the more global effect exercise may exert on the brain (Weng et al., 2017). Advances in technology that allow real-time integration of TMS with electroencephalography (Farzan et al., 2016; Pascual-Leone et al., 2011; Tremblay et al., 2019) may provide a means to better assess exercise-improved cognitive performance in regions outside of the motor area. Future research characterizing the cognitive and neurophysiological effects of exercise beyond the motor cortex may benefit from this technique.

Our results should be interpreted in light of the relatively small sample of participants with a narrow age range, and so our results may not be generalizable to older populations. Regardless of the sample size however, our power calculations suggest we have sufficient power (95%) to detect an effect. Additionally, the use of the ipad during the cognitive tasks, which engages the intrinsic hand muscles, may have potentially affected the TMS results. A previous study by Classen and colleagues (Classen, Liepert, Wise, Hallett, & Cohen, 1998) showed that practice movements (repetition of a movement of an individual finger in a given direction) led to a temporary shift in the angular direction of TMS-evoked finger movements. Nevertheless, the Classen study did not report changes in excitability (i.e MEP

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amplitude) and their study was specific to repetitive movements of a single finger at a set frequency, which is distinct to the more-random and temporally inconsistent multi-muscle activity when using an ipad. Consequently, given no change in MEP amplitude or ppTMS measures were seen in the control condition, we believe the likelihood of this is minimal.

2. Conclusions

A greater understanding of the mechanistic underpinnings of exercise's effect on cognitive performance will lead to the development of optimal exercise interventions for various clinical populations. Multitasking performance is modulated following light aerobic exercise as is motor cortical excitability. Consequently, patients with deficits in this domain, who cannot reach higher exercise intensities due to illness severity, may benefit from bouts of light aerobic exercise.

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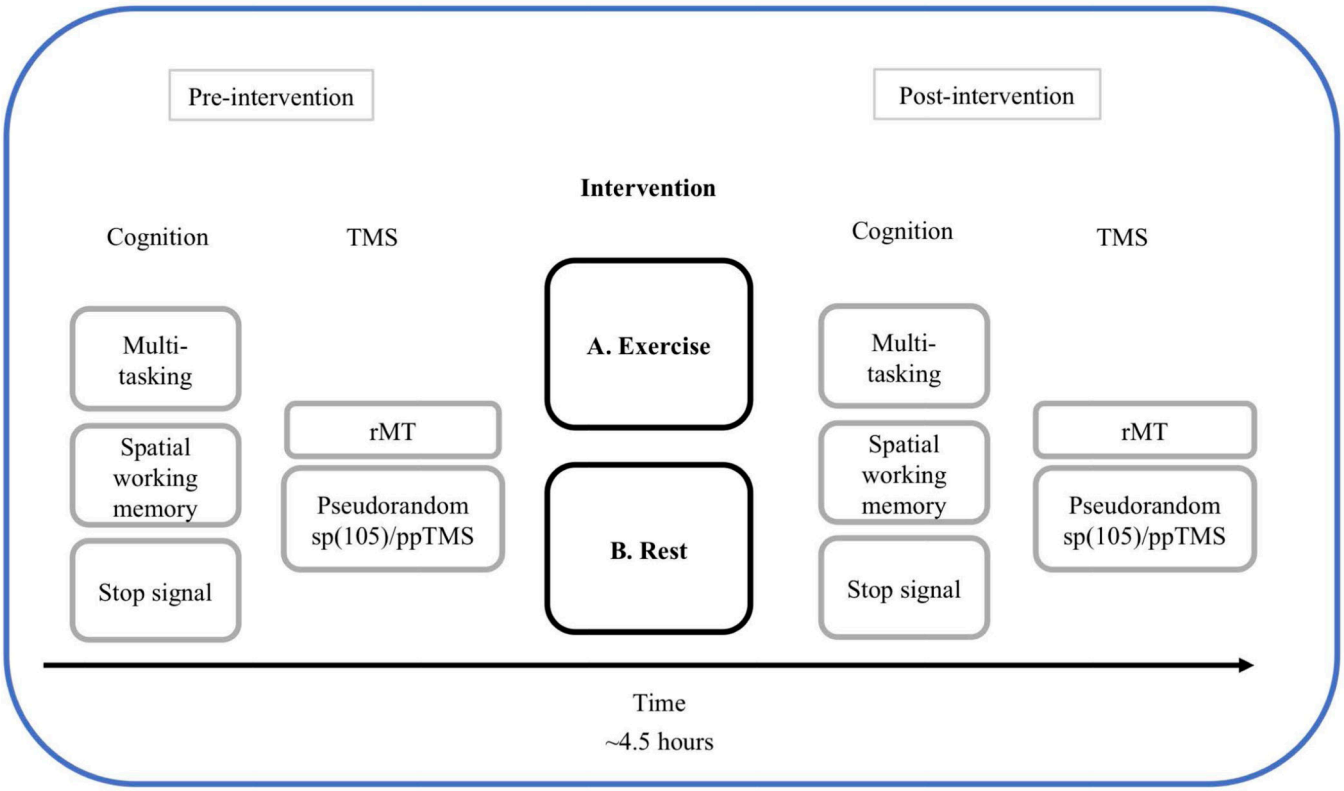

Figure 1.

Timeline of study procedures. The study employed a 2*2 (intervention by block) within-subjects A-B randomized protocol whereby participants were randomized to either perform the exercise intervention or rest control first, followed by the remaining intervention ≥7days later. The post-intervention cognitive tasks and TMS sessions were identical to the pre-intervention sessions. The time between the end of the pre-intervention TMS session the start of the post-intervention TMS session was 3 hours.

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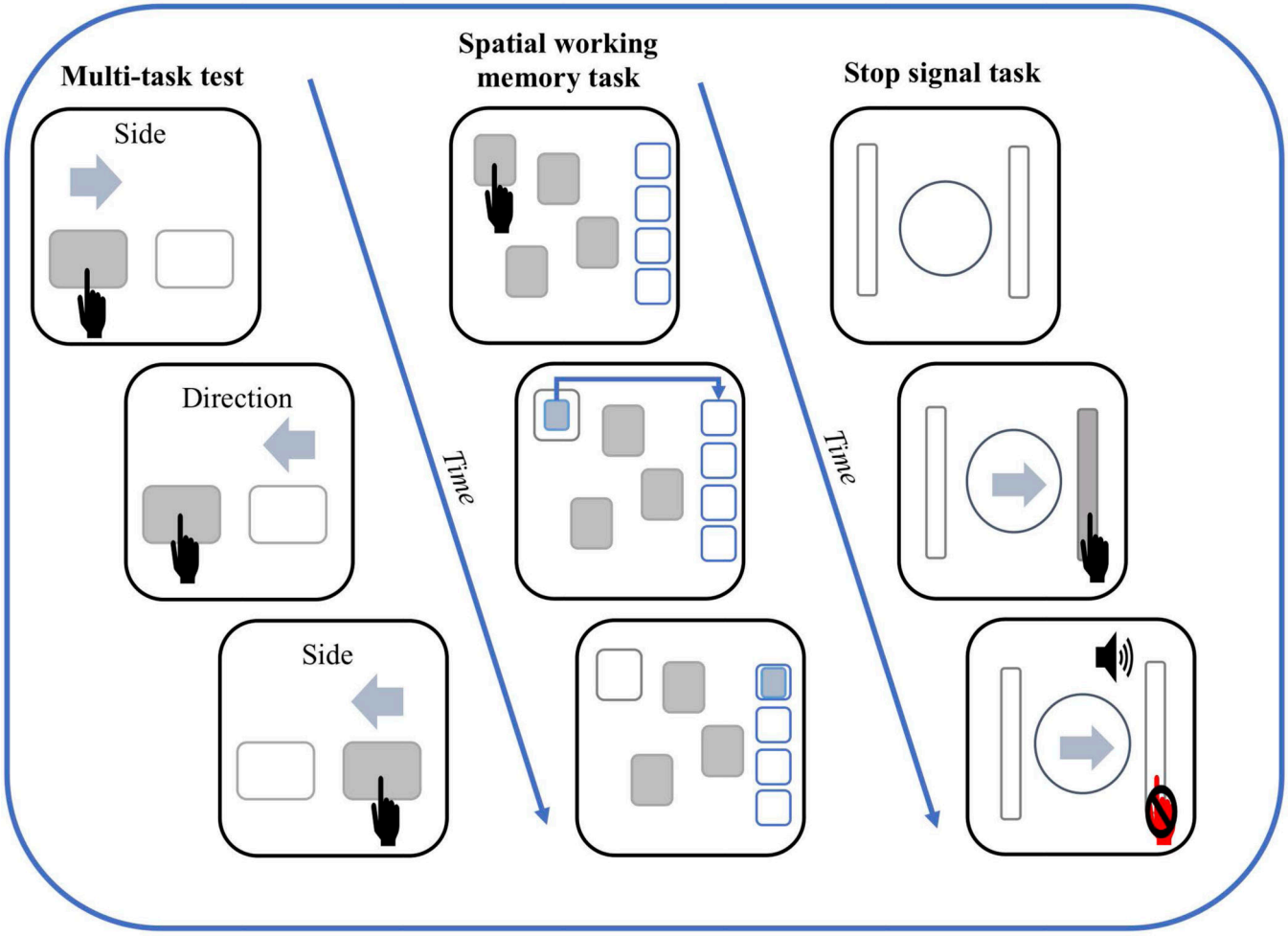

Figure 2.

Illustrations of the tablet-based (Cantab software) executive function tasks. The left column depicts the multi-tasking test with the top and middle boxes showing a congruent trail whereas the bottom box illustrates an incongruent trail. Participants must tap the corresponding virtual button as fast as the can. The middle column illustrates a 4 box spatial working memory task. Participants must tap covered boxes to unveil hidden tokens and place them in the stack on the right once they are found. This task has trials where 4, 6 and 8 boxes are displayed. The far-right column displays the stop signal task where by the participant must press the virtual button corresponding to the direction of the arrow as fast as they can. However, upon hearing a auditory beep, the participant must inhibit their response (as shown in the bottom box).

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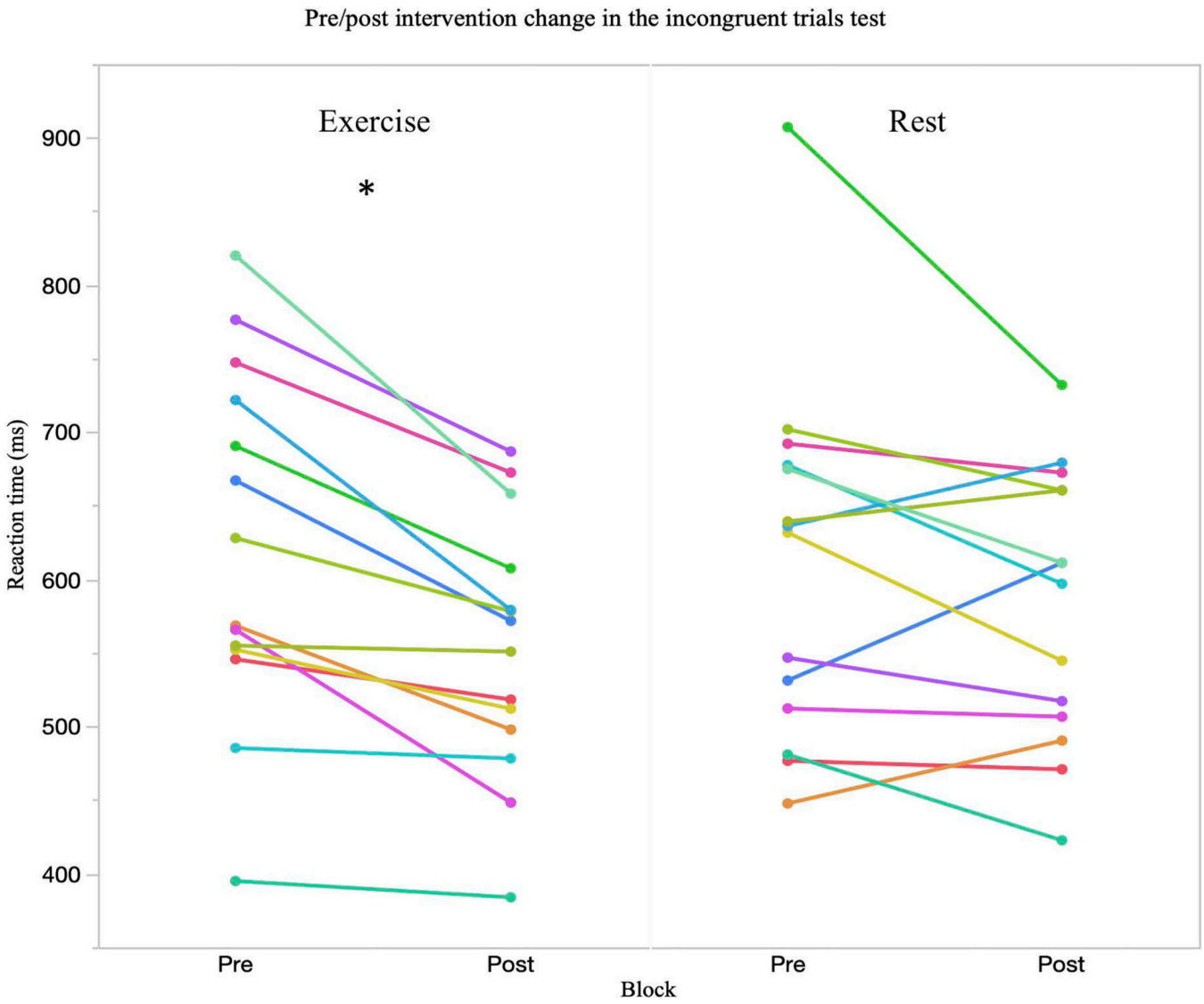

Figure 3.

Evidence of an improvement in the multitasking test when incongruent trials were presented. At the group level a non-significant block *intervention interaction was observed (p = .095) and planned comparisons showed a significant pre/post change in the exercise condition (p = .003) but not in the rest condition (p = .338). An improvement in incongruent reaction time was seen in every subject after the exercise condition. * indicates significant post hoc change in the exercise condition at the group level.

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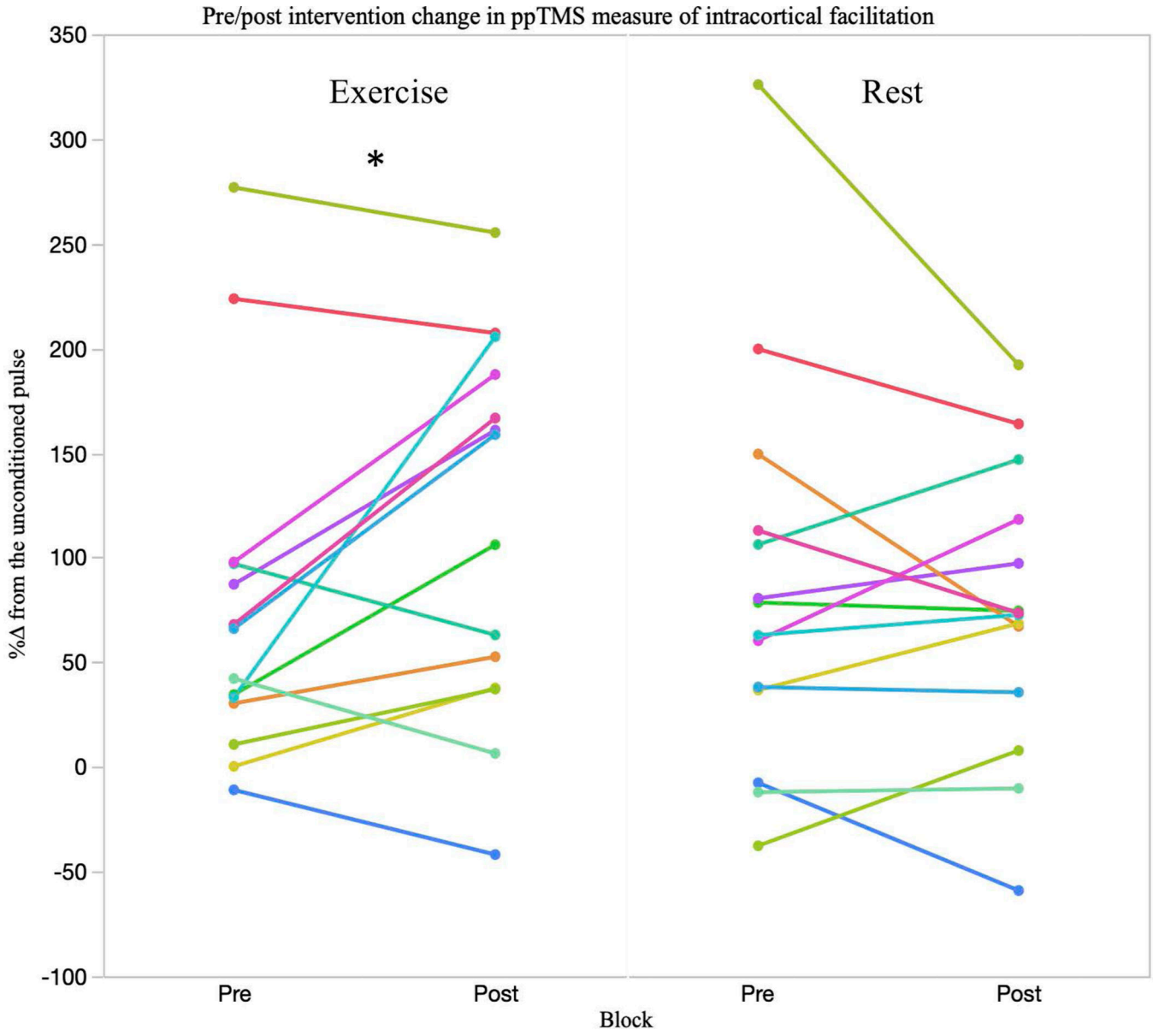

Figure 4.

A significant group level block by intervention interaction ($p = .018$) in ICF was seen. A significant increase in ICF following exercise ($p = .021$) was observed. As shown in the exercise condition, 9 out of 14 subjects (~65%) demonstrated an increase %ΔICF whereas in the rest condition only 4 subjects saw larger %ΔICF after rest, with the remaining subjects either not changing or seeing a reduction in %ΔICF. * indicates significant post hoc change in the exercise condition at the group level.

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Table 1.

Mean and SD scores for executive function tasks in healthy adults

Task	Pre-exercise	Post-exercise	Δ	*P*	Pre-rest	Post-rest	Δ	*P*
Multitasking test								
Congruent	555.6 ± 112.7	499.3 ± 78	−47.9 ± 52.9	.001	554.5 ± 102.8	518.6 ± 78.8	−35.9 ± 53.2	.083
Incongruent	622.8 ± 119.9	553.1 ±125.2	−69.4 ± 49.7	<.001	611.2 ± 122.4	584.6 ± 92.7	−27.2 ± 65.3	.324
Multitasking	690.3 ± 184.4	597.2 ±125.2	−93.1 ± 88.3	.007	682.5 ± 178.2	630.2 ± 116.4	−52.3 ± 98.3	.204
Cost	201.7 ± 150.4	141.9 ±100.1	−59.8 ± 97	.178	198.7 ± 139.9	157.9 ± 74.5	−40.8 ± 97.8	.437
SST								
RT	206.7 ± 29.7	221.6 ± 40	14.4 ± 43.4	.174	211.2 ± 42.5	219.7 ± 34.8	8.5 ± 32.9	.418
SWM								
BE	4.4 ± 5.2	5.7 ± 6.3	0.4 ± 1.6	.748	5.1 ± 5.3	6.2 ± 8.1	0.5 ± 9.2	.802
Strategy	5.3 ± 2.7	5.4 ± 3.1	0.1 ± 1.6	.921	5.5 ± 2.8	5.6 ± 3.2	0.1 ± 3.4	.843

P statistic derived from planed comparisons following 2*2 linear models. Values <.05 remained significant after Bonferroni corrections. SST= stop signal task; RT = reaction time; SWM= spatial working memory; BE= between errors.

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Table 2.

Mean and SD scores for TMS measures

Task	Pre-exercise	Post-exercise	Δ	*P*	Pre-rest	Post-rest	Δ	*P*
TMS measures								
rMT	56 ± 11.5	55 ± 11.1	−1 ± 2.3		56.6 ± 11.2	55.4 ± 11.2	1.2 ± 1.9	
MEP amplitude (uV)	856.7 ± 570.3	1097.1 ± 630.7	191.4 ± 598.4		1216.4 ± 710.7	1191.5 ± 629.6	−24.9 ± 438.9	
ICF	75.5 ± 82.1	114.5 ± 89.2	40 ± 63.2	.021	85.3 ± 94.2	74.87 ± 68.2	−10 ± 53.5	
SICI	−34.7 ± 36.6	−43.9 ± 48.4	−9.2 ± 60.9		−38 ± 46.5	−40.1 ± 31.5	−2 ± 52.4	
LICI	−65.1 ± 33.9	−84.5 ± 28.1	−19.4 ± 36.5		−74.8 ± 47.3	−77.9 ± 19.6	−2.1 ± 51.5	

P statistic derived from planed comparisons following 2*2 linear models. Values <.05 remained significant after Bonferroni corrections.