



UNIVERSITY OF
GLOUCESTERSHIRE

This is a peer-reviewed, post-print (final draft post-refereeing) version of the following published document, This is the peer reviewed version of the following article: Faulkner, James and Stoner, Lee and Grigg, Rebecca and Fryer, Simon M and Stone, Keeron J and Lambrick, Danielle (2017) Acute effects of exercise posture on executive function in transient ischemic attack patients. *Psychophysiology* ISSN 0048-5772 which has been published in final form at <http://onlinelibrary.wiley.com/doi/10.1111/psyp.12868>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving. and is licensed under All Rights Reserved license:

Faulkner, James, Stoner, Lee, Grigg, Rebecca, Fryer, Simon M ORCID: 0000-0003-0376-0104, Stone, Keeron J ORCID: 0000-0001-6572-7874 and Lambrick, Danielle (2017) Acute effects of exercise posture on executive function in transient ischemic attack patients. *Psychophysiology*, 54 (8). pp. 1239-1248. doi:10.1111/psyp.12868

Official URL: <http://onlinelibrary.wiley.com/doi/10.1111/psyp.12868/full>

DOI: <http://dx.doi.org/10.1111/psyp.12868>

EPrint URI: <https://eprints.glos.ac.uk/id/eprint/4399>

Disclaimer

The University of Gloucestershire has obtained warranties from all depositors as to their title in the material deposited and as to their right to deposit such material.

The University of Gloucestershire makes no representation or warranties of commercial utility, title, or fitness for a particular purpose or any other warranty, express or implied in respect of any material deposited.

The University of Gloucestershire makes no representation that the use of the materials will not infringe any patent, copyright, trademark or other property or proprietary rights.

The University of Gloucestershire accepts no liability for any infringement of intellectual property rights in any material deposited but will remove such material from public view pending investigation in the event of an allegation of any such infringement.

PLEASE SCROLL DOWN FOR TEXT.

ACUTE EFFECTS OF EXERCISE POSTURE ON EXECUTIVE FUNCTION IN TRANSIENT ISCHEMIC ATTACK PATIENTS

Running title: Exercise posture and executive function in TIA

James Faulkner^{1*}, Lee Stoner^{2,3}, Rebecca Grigg², Simon Fryer⁴, Keeron Stone⁴,
Danielle Lambrick⁵

¹ Department of Sport and Exercise, University of Winchester, Winchester, UK.

² School of Sport and Exercise, Massey University, Wellington, New Zealand.

³ Department of Exercise and Sport Science, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

⁴ School of Sport and Exercise, University of Gloucestershire, Gloucester, UK.

⁵ School of Health and Life Sciences, University of Southampton, Southampton, UK.

* Corresponding Author: Dr James Faulkner, Department of Sport and Exercise, University of Winchester, Winchester, UK. **E:** James.Faulkner@winchester.ac.uk **T:** +44 (0)1962 624932

Abstract

In patients with stroke or transient ischaemic attacks (TIA), a decline in executive function may limit an individual's ability to process motor tasks and re-learn motor skills. The purpose of this study was to assess the acute effect of exercise posture (seated vs. supine cycle ergometry) on executive function and prefrontal cortex perfusion, in patients with TIA. Eleven TIA patients (65±10y) and 15 age-matched, healthy-controls (HC; 62±7y) completed two graded exercise tests to maximal functional capacity (1 x seated; 1 x supine) and two 30-minute sub-maximal exercise tests (1 x seated, 1 x supine). Executive function was assessed prior-to and following (1.5-min Post, 15-min Post) the submaximal exercise tests using a Stroop Task. Prefrontal cortex perfusion (total hemoglobin) was continuously recorded using near infrared spectroscopy. There was no Posture (seated, supine) by Group (TIA, HC) interaction for the Stroop task ($P > .05$). HC completed Stroop tasks significantly faster than TIA (51.9[10.3] vs. 64.2[8.5] s, respectively); while Stroop completion time significantly improved between Baseline and 1.5-min Post (61.3[10] vs. 58.1[9.4] s, respectively) and 1.5-min Post and 15-min Post (54.8[8.9] s). Posture and Group had no significant influence on prefrontal cortex perfusion ($P > .05$). In conclusion, executive function improves to a similar extent in TIA and age-matched, healthy-controls following an acute bout of exercise, regardless of exercise posture (seated vs. supine). As acute improvements in executive function were maintained for 15 minutes, there could be an important window of opportunity for assigning executive tasks following exercise rehabilitation for patients with TIA.

Keywords: stroke, cerebral perfusion, cognition, prefrontal cortex, supine, cycling

Introduction

Following a stroke many patients suffer from impaired mobility and are at risk of losing their independence. While physical rehabilitation is effective for restoring mobility, the speed and degree of restoration to normal function may be impeded by cognitive impairments (McKinney et al., 2002). In particular, a decline in executive function may limit the ability to process motor tasks and re-learn motor skills. These cognitive impairments result from infarcted brain tissue and subsequent hypoperfusion and hypo-oxygenation of the infarcted area and adjacent regions (Baron et al., 1981; Hillis et al., 2006; Hillis et al., 2002). Indeed, the degree of hypoperfusion seems to correlate with the degree of cognitive dysfunction (Hillis, et al., 2002; Hillis et al., 2001), and restoration of perfusion has been demonstrated to improve cognitive performance in acute ischaemic stroke (Heiss et al., 1998; Hillis, Barker, Beauchamp, Gordon, & Wityk, 2000; Hillis, et al., 2006; Olivot et al., 2008). By way of logical extension, simple strategies which acutely improve cognitive function may enhance the rehabilitation process.

Exercise may be a simple, cost-effective and easily administered therapy for improving cerebral perfusion and cognitive function. A meta-analysis has identified a limited number of studies examining physical activity and cognition in stroke patients; while cognitive function was atypically the primary outcome measure, and the cognitive assessment tools were generally suboptimal, physical activity was shown to improve cognitive function (Cumming, Tyedin, Churilov, Morris, & Bernhardt, 2011). These findings are in-line with a number of randomized control trials which have demonstrated that a single bout of aerobic exercise can acutely improve various cognitive domains (Chang, Labban, Gapin, & Etnier, 2012), including spatial and executive functioning (Colcombe & Kramer, 2003).

Consideration does need to be given to the prescribed exercise intensity and modality. A meta-analysis reported that incremental exercise in healthy subjects increased prefrontal cortex oxygenation in a quadratic manner, rising between moderate and hard intensities, then falling at very hard intensities (Rooks, Thom, McCully, & Dishman, 2010). In terms of exercise modality, owing to impaired motor control in

stroke patients, the safest form of aerobic exercise is considered to be cycle ergometry. While upright cycling is most typically prescribed for these patients, we recently reported that recumbent cycle ergometry in healthy young men acutely increased prefrontal cortex oxygenation by a greater magnitude (Faulkner, Lambrick, Kaufmann, & Stoner, 2016). This may be because recumbent exercise enhances cardiac output (Quinn, Smith, Vroman, Kertzer, & Olney, 1995; Saitoh et al., 2005; Walsh-Riddle & Blumenthal, 1989), and cardiac output has been shown to have a linear relationship with cerebral blood flow (Ogoh & Ainslie, 2009). Contrary to the hypothesis, executive function was found to improve by a similar amount for both upright and recumbent exercise; however, there may be a ceiling effect in healthy young men who would not be expected to have impaired executive function.

The current study recruited patients diagnosed with a transient ischaemic attack (TIA), typically reported to be a minor form of stroke, and age-matched healthy controls. TIA patients were recruited as, i) they could engage with 30 minutes of moderate intensity cycling exercise in a seated and supine position, and ii) because recent studies investigating cognition after TIA suggest that deficits in executive function persist at least 7 days post-TIA (Ganzer, Barnes, Uphold & Jacobs, 2016). The purpose of this was to determine the effects of Group (TIA vs. control) and Posture (seated vs. supine) on, i) executive function and ii) prefrontal cortex perfusion. Four null hypotheses were tested, there is no relationship between: H1) Group and executive function; H2) Posture and executive function; H3) Group and prefrontal cortex perfusion; H4) Posture and prefrontal cortex perfusion. Accordingly, the researchers anticipated that executive function and prefrontal cortex perfusion would be greater in: i) the healthy age-matched control group than TIA group, and ii) during supine rather than seated exercise. Findings from this study may aid rehabilitation specialists in designing optimal rehabilitation strategies.

Methods

Participants

Eleven TIA patients (age: 65.1 ± 10.1 y; height: 169.7 ± 11.3 cm; body mass: 85.8 ± 16.9 kg; 9 male, 2 female) and fifteen healthy age-matched controls (age: 61.5 ± 7.1

y; height: 176.6 ± 8.0 cm; body mass: 84.9 ± 16.3 kg; 13 male, 2 female) volunteered. The TIA participants were recruited within 7 ± 3 days of the event, and were diagnosed with a high risk TIA (ABCD² score ≥ 4), after review by a specialist stroke physician. The TIA participants completed an electrocardiogram (ECG) assessment to establish appropriate cardiovascular health for this study. Patients were excluded if they had any of the following: oxygen dependence, uncontrolled angina, unstable cardiac conditions (i.e., atrial fibrillation), uncontrolled diabetes mellitus, major medical conditions, claudication, febrile illness, significant cognitive impairment, immobile. Control group participants completed a coronary artery disease risk stratification assessment to ensure that they were asymptomatic of illness, disease or mental disability and free of any injury. Due to the nature of the assessment of executive function, participants were excluded if they suffered from colour blindness or attention deficits. This research was conducted in agreement with the guidelines and policies of the institutional ethics committee and New Zealand's health and disability ethics committee.

Procedures

Participants performed two familiarisation sessions and four laboratory-based exercise protocols on a cycle ergometer (Velotron, RacerMate, Seattle, U.S.A.), within a thermo-neutral environment. Tests were performed on either an upright, seated (1 x graded exercise test [GXT], 1 x 30 minute moderate intensity exercise bout) or a supine (1 x GXT, 1 x 30 minute moderate intensity exercise bout) cycle ergometer. Tests were performed in a semi-randomized order, separated by 48 to 72 hours, as it was necessary for moderate intensity exercise bouts to proceed the respective GXTs. To reduce the risk of anticipatory effects on physiological parameters, the display screen of the physiological markers (i.e., oxygen uptake [$\dot{V}O_2$], minute ventilation [\dot{V}_E], respiratory exchange ratio [RER], heart rate [HR]), along with all cycle ergometer information (i.e., power output), was concealed from the participant during each exercise test.

The Stroop task was used to assess executive function following 10-minutes of quiet, supine rest (Baseline), and 1.5- (1.5-min Post) and 15-minutes (15-min Post)

following the completion of each moderate intensity exercise bout. Pre-frontal cortex perfusion was monitored continuously and in real-time, using near-infrared spectroscopy (Artinis Medical Systems BV, Zetten, The Netherlands), throughout the Stroop tasks and exercise protocols (Figure 1). Respiratory variables were continuously recorded throughout each moderate intensity exercise bout, and the participant's blood pressure, heart rate (HR) and ratings of perceived exertion (RPE; Borg, 1998) were recorded every 10 minutes during exercise.

Seated and supine GXT to maximal functional capacity

The GXTs were used to determine the exercise intensities that would be prescribed in both the seated and supine submaximal exercise tests. The seated and supine GXTs were continuous and incremental, commenced at 60 W and increased 12 W per minute. Criteria for termination of the maximal GXT was primarily based on volitional exhaustion, although two or more of the following secondary criteria were accepted as indicators of maximal functional capacity: HR within 10 beats/min of age-predicted maximum, $RER \geq 1.10$ or $RPE \geq 18$ on completion of the tests (ACSM, 2013). On-line respiratory gas analysis was performed using a breath-by-breath automatic gas exchange system (Sensormedics Corporation, Yorba Linda, CA, USA), following volume and gas calibration. Heart rate was monitored using a wireless chest strap telemetry system (Polar Electro T31, Kempele, Finland). The Borg 6-20 RPE scale was used to quantify the subjective perception of effort every 3 minutes during the GXTs. Participants' peak oxygen consumption ($\dot{V}O_{2peak}$) and gaseous exchange threshold (GET) were ascertained for both exercise bouts.

Seated and supine submaximal exercise tests

During these tests participants cycled at a power output equivalent to GET for 30 minutes. The GET typically equates to a moderate exercise intensity (45-60% $\dot{V}O_{2max}$) (Seiler & Tønnessen, 2009). The V-slope method was used to analyse the slopes of $\dot{V}O_2$ and carbon dioxide ($\dot{V}CO_2$) volume curves from both the seated and supine GXTs to determine each participant's power output at GET (Beaver, Wasserman, & Whipp, 1986). Three independent researchers verified the

interpretation of GET and the corresponding power outputs. Physiological markers were continuously monitored throughout the test.

Executive Function

Executive function was assessed using the Stroop task (Xavier Educational Software Ltd., Bangor, Wales), a classic measure of prefrontal cortex function which has been widely used to assess the effects of acute exercise on cognition (Hogervorst et al., 2008; Lucas et al., 2012; MacLeod, 1991; Vasques, Moraes, Silveira, Deslandes, & Laks, 2011). Participants were habituated with the Stroop task during two familiarisation sessions, as well as following each GXT. In this study, the Stroop interference task was administered as it is more sensitive to executive function than the traditional Stroop word task (Durgin, 2000). Participants completed the Stroop interference task wherein four words ('blue', 'yellow', 'green', 'red') were randomly presented, consecutively, on a computer screen. The colour each word was presented in was either congruent or incongruent with the relevant semantic information (e.g., 'red' presented in the colour red or the colour green, respectively). Participants were tasked with identifying the colour of each word being presented as quickly as possible, responding by clicking on the respective answer button (blue, yellow, green, red). Each presentation of a word constituted a sequence; each test comprised 36 sequences. The total time to complete the test (completion time), average time per response (reaction time), and number of correct answers (response accuracy) were recorded as measures of performance (Baseline, 1.5-min Post, 15-min Post). Although a time-control (no exercise) condition was not included in the study design, unpublished findings from our laboratory has demonstrated good reliability when assessing Stroop performance before and after 30 minutes quiet seated rest in a young, healthy population. Similar findings have generally been shown for Near-infrared Spectroscopy (NIRS) measures (Supplementary Table A).

Near-infrared spectroscopy

Near infrared spectroscopy assessments have been demonstrated to provide a metric of cognitive activation similar to functional magnetic resonance imaging during cognitive performance tasks (Cui, Bray, Bryant, Glover, & Reiss, 2011). A

continuous wave NIRS device (PortaLite, Artinis Medical Systems BV, the Netherlands), which emits infrared light at wavelengths of 760 and 850 nm, was used to detect relative changes in concentrations of oxygenated hemoglobin [O₂Hb] and deoxygenated hemoglobin [HHb], respectively, as well as the main parameter of interest: total blood volume (tHb = [O₂Hb + HHb]), before, during and after the 30-minutes of upright and supine exercise (Figure 1). Both wavelengths were emitted from three transmitters at 3.0, 3.5, and 4.0 cm from the photo diode detector, allowing for theoretical penetration distances between 1.5-2 cm (Chance, Dait, Zhang, Hamaoka, & Hagerman, 1992). Data was collected at 10 Hz, and a differential path-length factor of 4.0 was used to correct for photon scattering within the tissue (Ferrari, Wei, Carraresi, De Blasi, & Zaccanti, 1992). Depending on individual head geometry, the probe was positioned over the participant's prefrontal cortex at Fp1 for right sided dominant participants and at Fp2 for left sided dominant participants according to the International 10-20 system of Electrode Placement (Klem, Luders, Jasper, & Elders, 1999). For the TIA participants, the NIRS probe was placed on the side in which their TIA event occurred. The effect of ambient light on NIRS was reduced by conducting all exercise tests and Stroop tasks in a dimly lit laboratory. The NIRS device was fixed to the skin with bi-adhesive tape and covered with a dark opaque cloth to prevent signal contamination by ambient light, as per manufacturer recommendations.

Data Analysis

Statistical analyses were performed using Statistical Package for Social Sciences version 21 (SPSS, Inc., Chicago, Illinois, USA). All data are reported as means (standard deviation, SD) or mean differences (95% confidence intervals [CI]), unless otherwise specified. For all statistical tests, alpha was set at 0.05 with an adjustment made via the Bonferroni technique to protect against type 1 error. Effect size are represented using partial eta squared (η_p^2), with 0.0099, 0.0588, and 0.1379 representing a small, medium, and large effect (Cohen, 1988).

H1 and H2: Independent *t*-tests were used to compare Stroop task performance at Baseline between TIA and healthy-control (HC) participants for both seated and

supine exercise. A repeated-measures ANOVA: Group (TIA vs. HC) by Posture (Seated vs. Supine) by Time (Baseline, 1.5-min Post, 15-min Post), was used to assess the rate of change in Stroop task performance (time taken and number of correct answers). Where assumptions of sphericity were violated, the critical value of F was adjusted by the Greenhouse–Geisser epsilon value from the Mauchly Test of Sphericity. Where significant differences were identified, post-hoc analysis using dependent t -tests were performed.

H3 and H4: Changes in primary (tHb) and secondary (O₂Hb, HHb) NIRS markers were analysed using a repeated-measures ANOVA, as above. Regression analysis was used to assess whether the change in tHb, O₂Hb and HHb (independent variables [IV]) (Baseline to 1.5-min Post) accounted for a significant amount of variance in the change in Stroop performance scores (dependent variable [DV]).

Results

There were no differences in demographic characteristics between TIA and HC participants (all $P > .05$; Table 1). The diagnostic location of the 11 TIA patients were as follows; Anterior circulation ($n = 7$), posterior circulation ($n = 3$), uncertain territory ($n = 1$).

Graded Exercise Test and Submaximal Exercise Test

There were no Posture by Group interaction effects for any GXT or GET variables (all $P > .05$; Table 2). Significant Posture main effects were observed for $\dot{V}O_{2\text{peak}}$ (mean difference [95 %CI]; 2.0 [0.4 to 3.7] mL·Kg⁻¹·min⁻¹), HR (mean difference [95 %CI]; 11 [8 to 14] b·min⁻¹) and power output (mean difference [95 %CI]; 21 [15 to 28] W) on completion of the GXTs (all $P < .05$), with higher values reported during the seated GXT compared to the supine GXT. A Group main effect was also observed for $\dot{V}O_{2\text{peak}}$ ($P < 0.05$), with higher values reported for HC compared to TIA (mean difference [95 % CI]; 8.6 [1.1 to 16.0] mL·Kg⁻¹·min⁻¹). At GET, despite differences in absolute $\dot{V}O_2$ and power output between Posture and Group ($P < .05$), when expressed as a proportion of peak values, there were no differences in $\dot{V}O_2$ or power

output for Posture or Group ($P > .05$; Table 2). Similar findings were observed for other physiological (minute ventilation, respiratory exchange ratio, heart rate) and perceptual responses at the end of the seated and supine submaximal exercise tests ($P > .05$; Supplementary Table B).

H1 and H2: Executive Function

There were no Posture by Group by Time interactions for Stroop completion time or the number of correct answers ($P > .05$; Table 3). Across groups, Stroop completion time significantly improved between Baseline and 1.5-min Post (61.3 [10] vs. 58.1 [9.4] s, respectively) and 1.5-min Post and 15-min Post (54.8 [8.9] s). There was a significant Group (H2) main effect, with HC completing the Stroop task significantly faster than TIA (51.9 [10.3] vs. 64.2 [8.5] s, respectively; mean difference [95 % CI]; 12.3 [4.9 to 19.8] s). There was no Posture (H1) main effect ($P > .05$).

H3 and H4: Prefrontal Cortex Perfusion

There was no Posture by Group by Time interaction, or Group (H3) or Posture (H4) main effects for each NIRS measure (all $P > .05$). Time main effects were observed for tHb, O₂Hb, and HHb ($P < 0.001$; η_p^2 all 0.81 – 0.90; Figure 2). Post-hoc analysis demonstrated significant increases in these measures between Baseline and 1.5-min Post (mean difference [95 % CI], tHb 15.9 [12.4 to 19.3] %; O₂Hb 14.4 [11.3 to 17.5] %; HHb 1.5 [0.9 to 2.1] %).

Prefrontal Cortex Perfusion and Executive Function

As there were no between Group differences for prefrontal cortex perfusion, regression analysis was implemented with the entire sample (TIA + HC). Neither tHb ($P > .05$; $R^2 = 0$; beta [standardized coefficient] = -.07; Standard error = 0.126; beta [unstandardized coefficient] = -0.06), O₂Hb ($P > .05$; $R^2 = 0$; beta [standardized coefficient] = -0.06; Standard error = 0.09; beta [unstandardized coefficient] = -0.04) or HHb ($P > .05$; $R^2 = .03$; beta [standardized coefficient] = -0.18; Standard error = 0.20; beta [unstandardized coefficient] = -0.24) explained a significant amount of the variance in the change in Stroop task performance (Baseline to 1.5-min Post; all $P > 0.05$).

Discussion

Findings from this study show that TIA patients have a lower baseline executive function than age-matched healthy controls, but executive function improves similarly for both Groups following exercise, and these benefits are maintained for at least 15-minutes. However, exercise Posture (seated, supine) does not influence the improvement in executive function. Further, cerebral perfusion was shown to improve irrespective of Group (TIA, control) or Posture. These novel findings support the use of exercise to improve executive function, which may in-turn improve rehabilitation practice.

Executive Function

For the present study, the hypothesis that Group would effect executive function was rejected (H1), while the hypothesis that Posture will effect executive function (H2) was not rejected. The Group main effect can be attributed to baseline differences (Table 3), as the relative improvement in executive function 15-minutes post-exercise was similar for both TIA and controls (10.5 vs. 10.6 %, respectively). While changes in executive function following moderate intensity exercise have been shown previously in various populations (Chang, et al., 2012; Lambourne & Tomporowski, 2010; McMorris, Sproule, Turner, & Hale, 2011; Tomporowski, 2003), to our knowledge, this is the first study to demonstrate that acute exercise improves executive function in TIA patients, and that these patients respond similarly to healthy, age-matched individuals.

The current study explored the association between Posture and executive function (H2) following a recent study from our group, which demonstrated that, compared to seated cycle ergometry, recumbent cycle ergometry in healthy young men acutely increased prefrontal cortex oxygenation by a greater magnitude (Faulkner, et al., 2016). The failure to reject H2 may be attributable to the lack of effect of Posture on cerebral perfusion (tHb) in the current study, or the lack of direct association between cerebral perfusion and executive function, both of which are discussed below.

Prefrontal Cerebral Perfusion

In this study we used tHb as a measure of prefrontal cortex perfusion, and found that moderate exercise intensity (~52 % of $\dot{V}O_{2peak}$) increased perfusion by 15 u/mol. However, the increase in perfusion was not influenced by either Group (H3) or Posture (H4). As previously mentioned, the failure to reject H4 is contrary to a recent study by our group (Faulkner, et al., 2016). This may, at least in part, be explained by the wide variation in prefrontal cortex perfusion (tHb) and oxygenation (O₂Hb) responses to exercise for participants in the current study (Figure 2), whereas for our previous study the responses were fairly consistent between participants. This variation may be explained by differences in the respective cohorts; the previous study recruited a young (24.6 ± 4.3 y), healthy and physically-active homogenous population.

Regression analysis demonstrated that, regardless of Posture or Group, the NIRS markers (tHb, O₂Hb, HHb) did not explain a significant portion of the variance for change in executive function. This is contrary to a previous study by Endo et al. (2013) who found that, following arm ergometry at 40% maximal functional capacity (but not at 20 or 60 % of maximal capacity), improvements in oxygenation to the prefrontal cortex correlated with improved executive function (Stroop). The contrary findings may be explained by the heterogeneous responses for the participants in the current study, or may suggest that other mechanism/s contributed to the observed exercise-induced improvements in executive function. It has been suggested that the exercise-induced up-regulation of neurotransmitters such as dopamine, serotonin, norepinephrine and endorphine (Barenberg, 2012; Best, 2010; Meeusen, Watson, Hasegawa, Roelands, & Piacentini, 2006), as well as brain-derived neurotropic factor (Saucedo Marquez, Vanaudenaerde, Troosters, & Wenderoth, 2015) play a crucial role in improving executive function (Barenberg, 2012; Robbins & Arnsten, 2009).

Clinical implications

These findings may have important implications for rehabilitation of TIA and stroke patients. Previously, recumbent/supine cycling exercise has been suggested to be a safer alternative to upright/seated cycling, and may provide practical advantages for muscle and aerobic training in patients with impaired physical function (Gregor et al.,

2002; Kerr, Rafferty, Moffat, & Morlan, 2007). In the present study, a similar level of improvement was observed in executive function between the two body positions. This may be due to the fact that participants were exercising at a similar proportion of their maximal functional capacity at the end of both (seated and supine) exercise tests (see Table 2 and Supplementary Table B). Participants were also exercising at a similar perception of exertion during the seated and supine exercise, at approximately a 'somewhat hard' to 'hard' perception of exertion according to the Borg 6-20 RPE Scale. Although both exercise modes and the prescribed exercise intensity could be useful in the rehabilitation setting, supine exercise may be deemed more appropriate as it may be a safer exercise modality for those populations who lack mobility.

In our study, continued improvements in Stroop performance were observed 15 minutes after exercise cessation (Table 3). This is in support of the findings of Chang and colleagues' (2012), whose meta-analysis found that the greatest positive effect on cognition occurs 11-20 minutes after exercise cessation. More recent research has shown that improvements in cognition can be maintained for a period of at least 30 minutes post-exercise (Lambrick, Stoner, Grigg, & Faulkner, 2016; Peiffer, Darby, Fullenkamp, & Morgan, 2015; Tsukamoto et al., 2016). These previous findings, together with the current findings, may have practical implications for the rehabilitation environment. Following moderate-intensity exercise there may be a window of opportunity for presenting patients with neurological deficit with tasks that challenge executive function.

Future considerations

To determine the mechanistic link between acute exercise and executive function, studies with larger sample size are required, and which simultaneously record cerebral perfusion, neurotransmitters and psychological factors (arousal, mood state). Understanding the mechanism(s) of action will enable the identification of the optimal exercise paradigm for enhancing executive function. For example, while moderate intensity exercise is most effective for increasing cerebral blood flow (Ogoh & Ainslie, 2009), high-intensity intermittent exercise may elicit greater elevations in serum BDNF (Saucedo Marquez, et al., 2015). Furthermore, compared to continuous

and moderate intensity exercise, short periods of intense exercise have been shown to result in greater elevations of BDNF and peripheral catecholamines, and can improve vocabulary learning by 20% in just one week (Winter et al., 2007). Although this may be evident, the severity and location of the stroke may have a significant impact on the use of exercise in improving executive function, as some stroke survivors may be unable to exercise at low, moderate or high intensities, or for prolonged durations (i.e., 30 minutes of submaximal exercise). It would also be useful if future research investigated the effect of exercise on executive function in a homogenous sample of stroke patients. From a clinical/rehabilitation perspective, besides determining the optimal exercise prescription, further research is needed to determine the optimal timing post-exercise for assigning tasks that challenge executive function. Additionally, when undertaking such research investigations into the utility of exercise for improving cognition or cerebral perfusion, it would also be beneficial to include a time-control condition.

In conclusion, the present study has demonstrated that an acute bout of moderate intensity exercise improves executive function in TIA patients, and that TIA patients appear to respond similarly to healthy, age-matched controls. The improvements were not moderated by exercise Posture (seated vs. supine), and were not associated with prefrontal cortex perfusion. Importantly, the improvements in executive function were maintained for 15 minutes, suggesting that there could be an important window for assigning tasks that challenge executive function.

References

ACSM's guidelines for exercise testing and prescription (2013). Philadelphia: Lippincott, Williams and Wilkins.

Barenberg, J. (2012). Executive functions in learning processes: do they benefit from physical activity. *Educational Research Review*, 6, 208-222. doi:10.1016/j.edurev.2011.04.002

Baron, J. C., Bousser, M. G., Rey, A., Guillard, A., Comar, D., & Castaigne, P. (1981). Reversal of focal "misery-perfusion syndrome" by extra-intracranial arterial bypass in hemodynamic cerebral ischemia: A case study with 15O positron emission tomography. *Stroke*, 12, 454-459. doi: 10.1161/01.STR.12.4.454

Beaver, W., Wasserman, K., & Whipp, B. (1986). A new method for detecting anaerobic threshold by gas exchange. *Journal of Applied Physiology*, 60, 2020-2027.

Best, J. R. (2010). Effects of physical activity on children's executive function: contributions of experimental research on aerobic exercise. *Developmental Review*, 30, 331-351. doi:10.1016/j.dr.2010.08.001

Borg, G. (1998). *Borg's perceived exertion and pain scales*. Leeds, UK: Human Kinetics.

Chance, B., Dait, M. T., Zhang, C., Hamaoka, T., & Hagerman, F. (1992). Recovery from exercise-induced desaturation in the quadriceps muscles of elite competitive rowers. *American Journal of Physiology-Cell Physiology*, 262, C766-C775.

Chang, Y. K., Labban, J. D., Gapin, J. I., & Etnier, J. L. (2012). The effects of acute exercise on cognitive performance: A meta-analysis. *Brain Research*, 1453, 87-101. doi:10.1016/j.brainres.2012.02.068

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed). Hillsdale, NJ: Erlbaum.

Colcombe, S., & Kramer, A. F. (2003). Fitness effects on the cognitive function of older adults: A Meta-Analytic Study. *Psychological Science*, 14, 125-130. doi: 10.1111/1467-9280.t01-1-01430

Cui, X., Bray, S., Bryant, D. M., Glover, G. H., & Reiss, A. L. (2011). A quantitative comparison of NIRS and fMRI across multiple cognitive tasks. *NeuroImage*, 54, 2808-2821. doi:10.1016/j.neuroimage.2010.10.069

Cumming, T. B., Tyedin, K., Churilov, L., Morris, M. E., & Bernhardt, J. (2012). The effect of physical activity on cognitive function after stroke: a systematic review. *International Psychogeriatrics*, 24, 557-567. doi:10.1017/S1041610211001980

Durgin, F. H. (2000). The reverse Stroop effect. *Psychonomic Bulletin & Review*, 7, 121-125. doi:10.3758/BF03210730

Endo, K., Matsukawa, K., Liang, N., Nakatsuka, C., Tsuchimochi, H., Okamura, H., & Hamaoka, T. (2013). Dynamic exercise improves cognitive function in association with increased prefrontal oxygenation. *The Journal of Physiological Sciences*, 63, 287-298.

Faulkner, J., Lambrick, D., Kaufmann, S., & Stoner, L. (2016). Effects of upright and recumbent cycling on executive function and prefrontal cortex oxygenation in young, healthy, men. *Journal of Physical Activity & Health*. [Epub ahead of print].

Ferrari, M., Wei, Q., Carraresi, L., De Blasi, R. A., & Zaccanti, G. (1992). Time-resolved spectroscopy of the human forearm. *Journal of Photochemistry and Photobiology B: Biology*, 16, 141-153.

Ganzer, C. A., Barnes, A., Uphold, C., & Jacobs, A. R. (2016). Transient ischemic attack and cognitive impairment: a review. *Journal of Neuroscience Nursing*, 48, 322-327.

Gregor, S. M., Perell, K. L., Rushatakankovit, S., Miyamoto, E., Muffoletto, R., & Gregor, R. J. (2002). Lower extremity general muscle moment patterns in healthy individuals during recumbent cycling. *Clinical Biomechanics*, 17, 123-129. doi:10.1016/S0268-0033(01)00112-7

Heiss, W. D., Grond, M., Thiel, A., von Stockhausen, H. M., Rudolf, J., Ghaemi, M., Lottgen, J., Stenzel, C., & Pawlik, G. (1998). Tissue at risk of infarction rescued by early reperfusion: a positron emission tomography study in systemic recombinant tissue plasminogen activator thrombolysis of acute stroke. *Journal of Cerebral Blood Flow & Metabolism*, 18, 1298-1307. doi: doi: 10.1097/00004647-199812000-00004

Hillis, A. E., Barker, P. B., Beauchamp, N. J., Gordon, B., & Wityk, R. J. (2000). MR perfusion imaging reveals regions of hypoperfusion associated with aphasia and neglect. *Neurology*, 55, 782-788. doi: <http://dx.doi.org/10.1212/WNL.55.6.782>

Hillis, A. E., Kleinman, J. T., Newhart, M., Heidler-Gary, J., Gottesman, R., Barker, P. B., Aldrich, E., Llinas, R., Wityk, R., Chaudhry, P. (2006). Restoring cerebral blood flow reveals neural regions critical for naming. *The Journal of Neuroscience*, 26, 8069-8073. doi: 10.1523/JNEUROSCI.2088-06.2006

Hillis, A. E., Wityk, R. J., Barker, P. B., Beauchamp, N. J., Gailloud, P., Murphy, K., Cooper, O., & Metter, E. J. (2002). Subcortical aphasia and neglect in acute stroke: the role of cortical hypoperfusion. *Brain*, 125, 1094-1104. DOI: <http://dx.doi.org/10.1093/brain/awf113>

Hillis, A. E., Wityk, R. J., Tuffiash, E., Beauchamp, N. J., Jacobs, M. A., Barker, P. B., & Selnes, O. A. (2001). Hypoperfusion of Wernicke's area predicts severity of semantic deficit in acute stroke. *Annals Neurology*, 50, 561-566. doi: DOI: 10.1002/ana.1265

Hogervorst, E., Bandelow, S., Schmitt, J., Jentjens, R., Oliveira, M., Allgrove, J., Carter, T., Gleeson, M. (2008). Caffeine improves physical and cognitive performance during exhaustive exercise. *Medicine & Science in Sports & Exercise*, 40, 1841-1851. doi: 10.1249/MSS.0b013e31817bb8b7

Kerr, A., Rafferty, D., Moffat, F., & Morlan, G. (2007). Specificity of recumbent cycling as a training modality for the functional movements; sit-to-stand and step-up. *Clinical Biomechanics*, 22, 1104-1111. doi:10.1016/j.clinbiomech.2007.06.006

Klem. G.H., Luders. H.O., Jasper. H.H., & Elders, C. (1999). The ten-twenty electrode system of the international federation. the international federation of clinical neurophysiology. *Electroencephalography and Clinical Neurophysiology*, Suppl. 52 3-6.

Lambourne, K., & Tomporowski, P. (2010). The effect of exercise-induced arousal on cognitive task performance: A meta-regression analysis. *Brain Research*, 1341, 12-24. doi:10.1016/j.brainres.2010.03.091

Lambrick, D., Stoner, L., Grigg. R, & Faulkner, J. (2016). Effects of continuous and intermittent exercise on executive function in children aged 8-10 years. *Psychophysiology*, doi: 10.1111/psyp.12688. [Epub ahead of print].

Lucas, S. J., Ainslie, P. N., Murrell, C. J., Thomas, K. N., Franz, E. A., & Cotter, J. D. (2012). Effect of age on exercise-induced alterations in cognitive executive function: Relationship to cerebral perfusion. *Experimental Gerontology*, 47, 541-551. doi:10.1016/j.exger.2011.12.002

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: an integrative review. *Psychological Bulletin*, 109, 163-203. <http://dx.doi.org/10.1037/0033-2909.109.2.163>

McKinney, M., Blake, H., Treece, K. A., Lincoln, N. B., Playford, E. D., & Gladman, J. R. (2002). Evaluation of cognitive assessment in stroke rehabilitation. *Clinical Rehabilitation*, 16, 129-136.

McMorris, T., Sproule, J., Turner, A., & Hale, B. J. (2011). Acute, intermediate intensity exercise, and speed and accuracy in working memory tasks: A meta-

analytical comparison of effects. *Physiology & Behavior*, 102, 421-428.
doi:10.1016/j.physbeh.2010.12.007

Meeusen, R., Watson, P., Hasegawa, H., Roelands, B., & Piacentini, M. F. (2006). Central fatigue: the serotonin hypothesis and beyond. *Sports Medicine*, 36, 881-909.

Ogoh, S., & Ainslie, P. N. (2009). Cerebral blood flow during exercise: mechanisms of regulation. *Journal of Applied Physiology*, 107, 1370-1380. doi: 10.1152/jappphysiol.00573.2009

Olivot, J. M., Mlynash, M., Thijs, V. N., Kemp, S., Lansberg, M. G., Wechsler, L., Schlaug, G., Bammer, R., Marks, M. P., & Albers, G. W. (2008). Relationships between infarct growth, clinical outcome, and early recanalization in diffusion and perfusion imaging for understanding stroke evolution (DEFUSE). *Stroke*, 39, 2257-2263. doi: 10.1161/STROKEAHA.107.511535

Peiffer, R., Darby, L. A., Fullenkamp, A., & Morgan, A. L. (2015). *Journal of Sports Science and Medicine*, 14, 574-583.

Quinn, T. J., Smith, S. W., Vroman, N. B., Kertzer, R., & Olney, W. B. (1995). Physiologic responses of cardiac patients to supine, recumbent, and upright cycle ergometry. *Archives of Physical Medicine & Rehabilitation*, 76, 257-261.

Robbins, T., & Arnsten, A. (2009). The neuropsychopharmacology of fronto-executive function: Monoaminergic modulation. *The Annual Review of Neuroscience*, 32, 267-287.

Rooks, C. R., Thom, N. J., McCully, K. K., & Dishman, R. K. (2010). Effects of incremental exercise on cerebral oxygenation measured by near-infrared spectroscopy: a systematic review. *Progress in Neurobiology*, 92, 134-150. doi:10.1016/j.pneurobio.2010.06.002

Saitoh, M., Matsunaga, A., Kamiya, K., Ogura, M. N., Sakamoto, J., Yonezawa, R., Kasahara, Y., Watanabe, H., & Masuda, T. (2005). Comparison of cardiovascular responses between upright and recumbent cycle ergometers in healthy young volunteers performing low-intensity exercise: assessment of reliability of the oxygen uptake calculated by using the ACSM metabolic equation. *Archives of Physical Medicine and Rehabilitation*, 86, 1024-1029. doi:10.1016/j.apmr.2004.09.030

Saucedo Marquez, C. M., Vanaudenaerde, B., Troosters, T., & Wenderoth, N. (2015). High-intensity interval training evokes larger serum BDNF levels compared with intense continuous exercise. *Journal of Applied Physiology*, 119, 1363-1373. doi: 10.1152/jappphysiol.00126.2015

Seiler, S., & Tønnessen, E. (2009). Intervals, thresholds, and long slow distance: the role of intensity and duration in endurance training. *Sports Science*, 13, 32-53.

Tomprowski, P. D. (2003). Effects of acute bouts of exercise on cognition. *Acta Psychologica*, 112(3), 297-324. doi:10.1016/S0001-6918(02)00134-8

Tsukamoto, H., Suga, T., Takenaka, S., Tanaka, D., Takeuchi, T., Hamaoka, T., Isaka, T., & Hashimoto, T. (2016). Greater impact of acute high-intensity interval exercise on post-exercise executive function compared to moderate-intensity continuous exercise. *Physiology & Behavior*, 155, 224-230. doi:10.1016/j.physbeh.2015.12.021

Vasques, P. E., Moraes, H., Silveira, H., Deslandes, A. C., & Laks, J. (2011). Acute exercise improves cognition in the depressed elderly: the effect of dual-tasks. *Clinics*, 66, 1553-1557. doi.org/10.1590/S1807-59322011000900008

Walsh-Riddle, M., & Blumenthal, J. (1989). Cardiovascular responses during upright and semirecumbent cycle ergometry testing. *Medicine & Science in Sports & Exercise*, 21, 581-585.

Winter, B., Breitenstein, C., Mooren, F. C., Voelker, K., Fobker, M., Lechtermann, A., Krueger, K., Frommer, A., Korsukewitz, C., Floel, A., & Knecht, S. (2007). High impact running improves learning. *Neurobiology of Learning & Memory*, 87, 597-609. doi:10.1016/j.nlm.2006.11.003

Author Notes:

ACKNOWLEDGEMENTS: We would like to thank Jeremy Lanford and Laikin Wong from Wellington, Regional Hospital for assisting with the identification of eligible TIA patients. We would also like to thank Yu-Chieh Tzeng, Terrence O'Donnell and Philip Allan for assisting TIA patient screening at the University of Otago.

SOURCE(S) OF FUNDING: Paykel Trust

CONFLICT(S) OF INTEREST/DISCLOSURE(S): None

Figure Legends

Figure 1: Example of total hemoglobin (tHb), oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) before, during and following the upright exercise protocol. A – Baseline rest; B – Baseline Stroop task; C – 30-minutes of upright exercise; D – 1.5-minutes Post-exercise Stroop task; E – 15-minutes Post-exercise Stroop task.

Figure 2: Absolute change (mean, SD) in tHb, O₂Hb and HHb at each baseline (rest) and each Stroop task assessment time point (Baseline, 1.5-min Post, 15-min Post). Significant Time effect: $P < 0.05$ vs. Baseline Stroop.

Table 1: Mean (SD) participant demographics

	TIA	HC	Mean Diff	95 % CI	P value
Age (y)	65 (10)	61 (7)	3.64	-3.6 to 10.9	0.310
Weight (kg)	86 (17)	85 (16)	0.95	-13.5 to 15.4	0.893
Height (m)	1.70 (0.10)	1.71 (0.08)	-0.01	-0.1 to 0.1	0.096
BMI (kg·m ²)	29.8 (7.1)	27.2 (3.9)	2.56	2.2 to -2.0	0.260
BF (%)	33 (12)	26 (8)	7.49	4.0 to -1.0	0.080
SBP (mmHg)	133 (16)	133 (24)	0.44	9.0 to -18.3	0.961
DBP (mmHg)	79 (5)	76 (5)	2.93	2.2 to -1.6	0.195
RHR (b·min ⁻¹)	59 (9)	59 (7)	0.58	3.2 to -6.0	0.857

Abbreviations: CI = Confidence interval; BMI = Body mass index; BF = Body Fat; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; RHR = Resting heart rate.

Table 2: Mean (SD) data reported on completion of the GXT and at GET for both Groups (TIA, HC) and Posture (seated, supine). Effect sizes are also reported (η_p^2)

	Posture by Group Interaction									Group main effect					Posture main effect					
	TIA				HC				η_p^2	TIA		HC		η_p^2	Seated		Supine		η_p^2	
	Seated	Supine	Seated	Supine	Total	Total	Total	Total												
X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	X	SD	η_p^2
GXT	$\dot{V}O_{2max}(mL \cdot kg^{-1} \cdot min^{-1})$	28.2	(7.7)	28.5	(8.6)	39.1	(8.9)	34.8	(8.9)	0.27	28.4	(9)	36.9*	(8.6)	0.22	33.6	(8.7)	31.7*	(9.3)	0.20
	$\dot{V}O_{2max}(L \cdot min^{-1})$	2.4	(0.6)	2.4	(0.8)	3.2	(0.6)	2.9	(0.6)	0.26	2.4	(0.6)	3.1	(0.6)	0.23	2.8	(0.7)	2.6	(0.7)	0.23
	RER	1.1	(0.1)	1.1	(0.1)	1.1	(0.1)	1.1	(0.1)	0.04	1.1	(0.1)	1.1	(0.1)	0.03	1.1	(0.1)	1.1	(0.1)	0.00
	HR (b·min⁻¹)	149	(20)	141	(23)	160	(11)	147	(10)	0.16	145	(15)	153	(15)	0.07	154	(16)	144*	(16)	0.70
	RPE	17	(2)	17	(2)	18	(1.4)	18	(1)	0.02	17	(1.5)	18	(2)	0.09	18	(2)	18	(2)	0.04
	PO (W)	161	(34)	149	(44)	205	(49)	173	(41)	0.33	155	(43)	189	(43)	0.14	182	(48)	161*	(45)	0.69
GET	$\dot{V}O_2(L \cdot min^{-1})$	1.2	(0.5)	1.3	(0.4)	1.8	(0.4)	1.5	(0.4)	0.29	1.3	(0.4)	1.7*	(0.4)	0.21	1.5	(0.5)	1.4*	(0.4)	0.21
	$\dot{V}O_2(\%)$	52	(12)	54	(7)	56	(7)	53	(9)	0.06	53	(7)	55	(7)	0.02	54	(9)	53	(8)	0.00
	PO (W)	87	(19)	81	(26)	109	(30)	91	(20)	0.09	84	(23)	100*	(23)	0.11	98	(29)	86*	(24)	0.31
	PO (%)	55	(8)	54	(6)	53	(5)	54	(8)	0.01	55	(6)	53	(6)	0.02	54	(7)	54	(8)	0.00

*Significant Group or Posture main effect ($P < .05$)

Abbreviations: HR, heart rate; PO, power output; RER, Respiratory exchange ratio; RPE, ratings of perceived exertion

Table 3: Mean (SD) Stroop completion time at baseline, Post and 15-min Post for Posture (Seated, Supine) and Group (TIA, HC)

			Seated			Supine			Seated + Supine		
			Baseline	Post	15-min Post	Baseline	Post	15-min Post	Baseline	Post	15-min Post
Time	TIA	X	67.2	65.0	59.4	67.4	65.2	61.1	67.3	65.1	60.3
		SD	11.2	10.6	11.8	14.8	13.6	8.9	9.7	9.1	8.7
	HC	X	53.5	51.1	50.1	56.9	51.1	48.5	55.2	51.1	49.3
		SD	6.5	7.7	8.2	9.6	8.4	8.4	9.3	8.8	8.4
#Correct	TIA	X	36.0	36.0	35.9	36.0	35.3	36	36.0	35.7	35.9
		SD	0	0	0.3	0	1.4	0	0	0.5	0.3
	HC	X	36.0	35.8	35.9	35.8	36.0	35.9	35.9	35.9	35.8
		SD	0	0.6	0.5	0.6	0	0.5	0.2	0.4	0.3

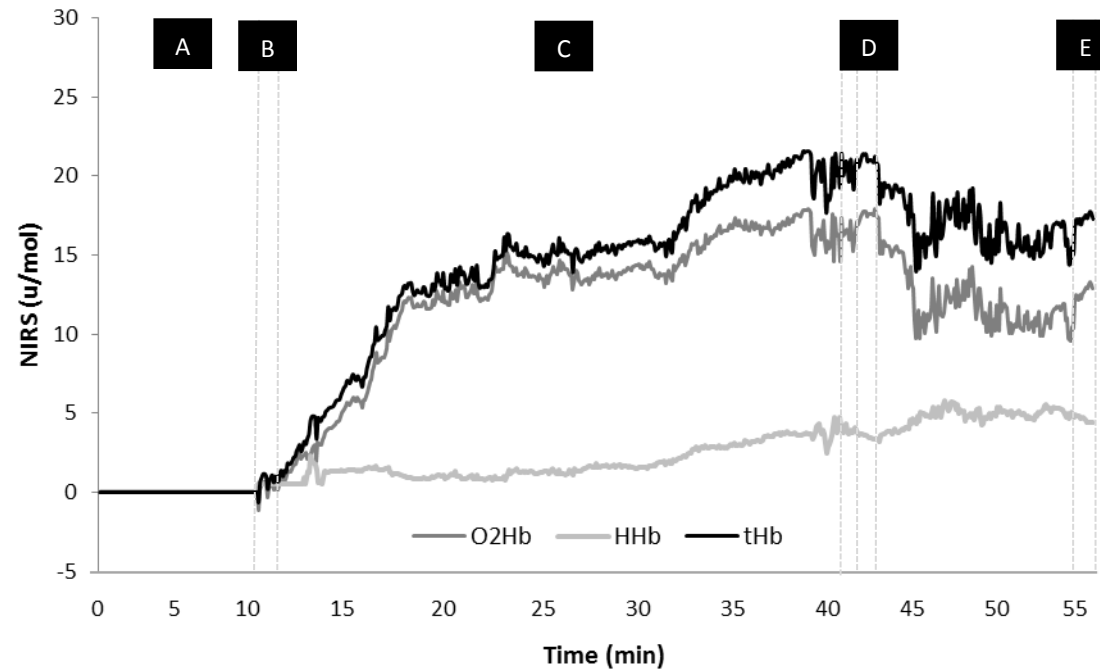


Figure 1: Example of total hemoglobin (tHb), oxyhemoglobin (O₂Hb) and deoxyhemoglobin (HHb) before, during and following the upright exercise protocol. A – Baseline rest; B – Baseline Stroop task; C – 30-minutes of upright exercise; D – 1.5-minutes Post-exercise Stroop task; E – 15-minutes Post-exercise Stroop task.

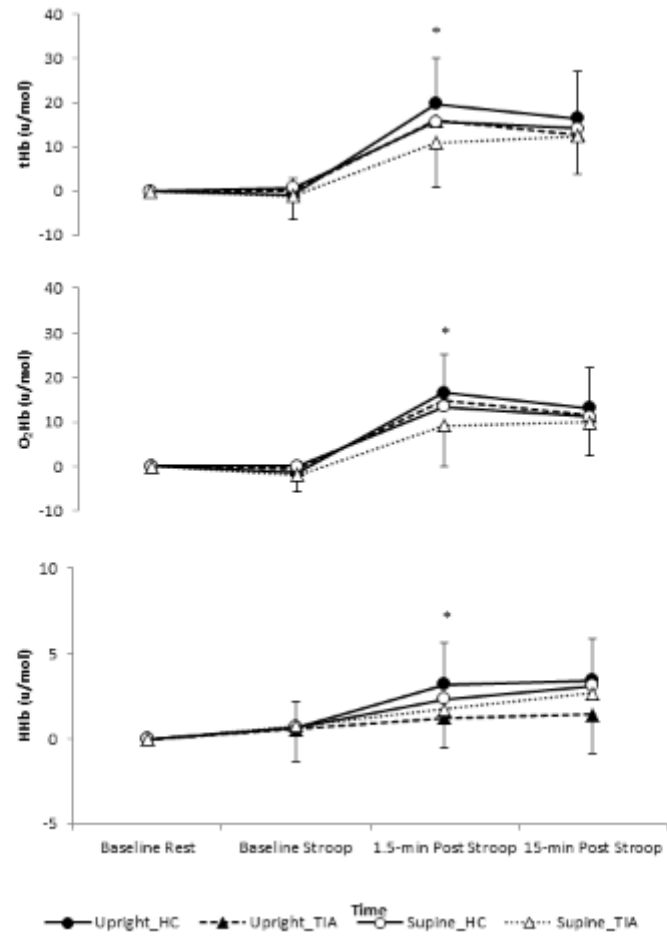


Figure 2: Absolute change (mean, SD) in tHb, O₂Hb and HHb at each baseline (rest) and each Stroop task assessment time point (Baseline, 1.5-min Post, 15-min Post). Significant Time effect: $P < 0.05$ vs. Baseline Stroop.