The impact of water immersion during exercise on cerebral perfusion

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Abstract

Introduction. Regular exercise induces recurrent increases in cerebrovascular perfusion. In peripheral arteries, such episodic increases in perfusion are responsible for improvement in arterial function and health. We examined the hypothesis that exercise during water immersion augments cerebrovascular perfusion compared to intensity-matched land-based exercise. **Methods.** Fifteen normotensive participants were recruited (26±4yrs, 24.3±1.9kg/m^2). We continuously assessed mean arterial blood pressure (MAP), heart rate (HR), stroke volume, oxygen consumption and blood flow velocities through the middle and posterior cerebral arteries before, during and after 20-min bouts of water- and land-based stepping exercise of matched intensity. The order in which the exercise conditions were performed was randomized between subjects. Water-based exercise was performed in 30°C water to the level of the right atrium. **Results.** Water- and land-based exercise were closely matched for oxygen consumption [13.3ml.kg^{-1}.min^{-1} (95% CI=12.2, 14.6) vs. 13.5ml.kg^{-1}.min^{-1} (95% CI=12.1, 14.8); P=0.89] and HR [95bpm (95% CI=90, 101) vs. 96bpm (95% CI=91, 102); P=0.65]. Compared with land-based exercise, water-based exercise induced an increase in MAP [106mmHg (95% CI=100, 111) vs. 101mmHg (95% CI=95, 106) P<0.001], middle cerebral artery velocity [74cm/s (95% CI=66, 81) vs. 67cm/s (95% CI=60, 74) P<0.001], posterior cerebral artery velocity [47cm/s (95% CI=40, 53) vs. 43cm/s (95% CI=37, 49) P<0.001] and expired CO_2 [44.5mmHg (95% CI=42.8, 45.9) vs. 42.8mmHg (95% CI=40.6,) P<0.001]. **Conclusion.** Our findings suggest that water-based exercise augments cerebrovascular perfusion, relative to land-based exercise of a similar intensity, in healthy humans.

Key words: Cerebral blood flow, water immersion, exercise, transcranial Doppler.

Introduction

Paragraph 1. Exercise induces recurrent increases in blood flow and shear stress in micro- and macrovessels of the peripheral circulation. Episodic increases in endothelial shear stress represent a dominant stimulus for enhanced nitric oxide (NO) bioavailability, which is associated with improved cardiovascular health (18, 19). Exercise has also been reported to have a beneficial impact on cerebral function (20, 23), with some animal studies relating such benefits to enhanced cerebrovascular endothelial function (3, 11, 13, 17, 24).

Paragraph 2. During mild to moderate intensity exercise (≤60% maximal oxygen uptake), cerebral blood flow increases globally by ~10-20% in response to increases in neuronal activation and cerebral metabolism (28, 30, 32). Although some studies indicate that regional differences might exist within the cerebral circulation during exercise (32, 39, 40), the prominent mechanisms driving the increase in global cerebral blood flow during exercise seem to be related to alterations in cerebral neuronal metabolism, partial pressure of arterial carbon dioxide and/or arterial pressure (28, 30, 34).

Paragraph 3. Water-based exercise is a non-weight-bearing exercise modality for individuals with impaired functional capacity, which over the past two decades has emerged as a popular alternative for the management of clinically vulnerable groups (22). Previous studies have compared physiological responses to water- and land-based exercises in healthy (4-6, 12, 14, 26) and diseased populations (7, 10, 16, 33, 37), but *no* previous study has reported the impact of water-based exercise on cerebral perfusion using transcranial Doppler. This is of particular importance, since we

recently demonstrated that water immersion under resting conditions induces an increase in middle and posterior cerebral artery perfusion, which is associated with elevated mean arterial pressure (MAP) and end-tidal carbon dioxide (8). The purpose of this study was therefore to examine the impact of an acute bout of land-based exercise *versus* exercise during water immersion on cerebral perfusion in healthy volunteers. We hypothesised that exercise performed during water immersion would be associated with augmented cerebral perfusion compared with land-based exercise.

Methods

Participants

Paragraph 4. Fifteen healthy participants were recruited to the study (8 males, 7 females: age: 26±4yrs, BMI: 24.3±1.9kg/m^2). All participants were normotensive, recreationally active (≤2 hours of physical activity per week), non-smokers with no history of cardiovascular, musculoskeletal or metabolic disease or any contra-indications to exercise. None of the participants reported taking any (prescribed) medication. Female participants were tested during the early follicular phase of the menstrual cycle, defined as day 1-7 of the menstrual cycle. The study conformed to the *Declaration of Helsinki* and was approved by the Human Research Ethics Committee of the University of Western Australia. Participants were informed of the methods and study design verbally and in writing before providing written informed consent.

Experimental Procedures

Paragraph 5. Participants arrived at the laboratory having fasted for a minimum of 8 hours and abstained from alcohol, caffeine and vigorous exercise for at least 24 hours.

Upon arrival, participants were seated and instrumented (~30 mins). Following this, participants were positioned in a water tank (1.4m diameter, 1.55m height, 2386L) in an upright standing position with their arms resting comfortably on a platform at heart level. The experimental protocol involved two separate 20 min bouts of low intensity stepping exercise which consisted of water-based and land-based stepping exercise. These distinct exercise conditions were separated by a 15 min period of land-based seated rest and the order in which they were performed was randomized between participants. Based on the real-time heart rate (HR) and oxygen consumption (VO_2) data, the cadence of stepping exercise was adjusted to match exercise intensity to that observed during the initial exercise bout. We adopted a low intensity exercise protocol because previous research has demonstrated that mild to moderate intensity exercise increases cerebral blood flow by ~10-20%, whereas during higher intensities, cerebral blood flow decreases to basal levels (28, 30, 32). Therefore, we wanted to ensure that the exercise intensity was sufficient to stimulate an increase in CBFv in all participants without reaching this threshold. Data were measured and recorded continuously throughout the entire protocol. For every outcome parameter, data were averaged from the last 1-2 min of each 5 min time-period.

Paragraph 6. *Water-based exercise:* Two submersible water pumps (KPA 600A; Grundfos, South Australia) were placed in an adjacent heated swimming pool. These pumps filled the tank at a constant rate with 30°C water to the level of the right atrium (RA). This process was completed in 9 min. Preliminary experiments indicated that 30°C was consistent with skin temperatures in our young healthy subjects. We also selected this temperature because it is typical of temperatures used in rehabilitation centers which focus on hydrotherapy. This experimental approach avoided the

potential for confounding effects of physical movement into, or out of, the tank on hemodynamics, cutaneous and cerebral blood flow velocities. Once immersed in water, participants remained in the resting upright position for 5 min, which was followed by a 20 min bout of low intensity exercise consisting of a repetitive stepping protocol (~100 bpm). Upon completion of the exercise bout, participants remained in the resting upright position for a further 5 minutes, after which the pumps were reversed in order to empty the tank.

Paragraph 7. *Land-based exercise:* Participants remained in the upright standing position and avoided movement for 5 min. This was followed by a 20 min bout of low intensity exercise consisting of a repetitive stepping protocol (~100 bpm). Upon completion of the exercise bout, participants remained in the resting upright position for a further 5 min.

Experimental Measures

Paragraph 8. *Systemic hemodynamics.* A Finometer PRO (Finapres Medical Systems, Netherlands) was used to monitor relative changes in MAP, cardiac output (CO) and stroke volume (SV) via photoplethysmography. These data were exported to a data acquisition system PowerLab (LabChart 7, ADInstruments, Sydney, Australia) in real time. A finger cuff was placed around the middle finger of the left arm, which was supported at right atrium level on a platform. Participants were instructed not to move their arm or finger during recording and vigilant supervision ensured this was the case. Total peripheral resistance (TPR) was calculated in real time in LabChart, whilst the cyclical measurement feature used systolic peaks to calculate HR.

Paragraph 9. *Middle and posterior cerebral artery velocities.* Middle and posterior cerebral artery velocities (MCAv and PCAv, respectively) were measured using a 2 MHz pulsed ST3 transcranial ultrasound system (Spencer Technologies, Seattle, USA). Search techniques adopted to identify the MCA and PCA are described in detail elsewhere (1). Two 2-MHz probes were secured bilaterally at the temporal window with a Marc 600 headframe (Spencer Technologies, Seattle, USA) to allow for adjustments to the insonation angle until an optimal M-mode image was found. Raw analogue MCAv and PCAv cerebral velocity traces were exported from PowerLab to LabChart for *post-hoc* analysis.

Paragraph 10. *Oxygen consumption and expired carbon dioxide.* VO_2 and carbon dioxide production were continuously recorded throughout the protocol and calculated from expired gas fractions (Ametek Gas Analysers, Applied Electrochemistry, SOV S-3A/1 and COV CD-3A, Pittsburgh, PA, USA) and ventilation (Morgan, 225 A, Kent, England) using a metabolic cart. Due to the use of a mixing chamber, all variables were averaged across a 15 s time window; including partial pressure of expired carbon dioxide (PCO_2).

Paragraph 11. *Skin temperature and flux.* Integrated laser Doppler probes (Model 413; Periflux 5001 System, Perimed AB, Sweden) were used to continuously monitor skin flux of the forearm and chest (i.e. both measured above the level of water immersion). Skin thermistors were also placed at these sites to assess forearm and chest skin temperature (°C). These data were exported to a data acquisition system (LabChart 7, ADInstruments, Sydney, Australia) in real time. Flux data were

converted to cutaneous vascular conductance (CVC), calculated as Flux/MAP (PU $mmHg^{-1}$).

Statistics

Paragraph 12. Analyses were performed using the Statistics Package for Social Sciences for windows, version 21.0 (SPSS Inc. Chicago, IL, USA). Statistical significance was delimited at $P<0.05$ and exact P values are cited (P values of "0.000" provided by the statistics package are reported as "<0.001"). A two-factor (condition vs. time) repeated measures ANOVA was employed to compare the impact of water-based exercise with land-based exercise (i.e. 'condition') on hemodynamics and cerebral perfusion. Correlation coefficients (two-tailed) were used to describe the strength of relationships between the change in CBFv and hemodynamic variables during exercise relative to resting values. Statistically significant interactions were assessed using the least significant difference approach to multiple comparisons (29). Data are presented mean (95% confidence interval), unless stated otherwise.

Results

Paragraph 13. The water- and land-based exercise bouts were successfully matched for VO_2 [13.3ml.kg^{-1}.min^{-1} (95% CI=12.2, 14.6) vs. 13.5ml.kg^{-1}.min^{-1} (95% CI=12.1, 14.8); P=0.89; Figure 1A]. HR increased throughout both exercise protocols (P<0.001), however, we found a significant main effect of water immersion on HR (Figure 1B). Subsequent pair-wise comparisons revealed that HR was significantly lower during water immersion at rest and during recovery, but not during exercise (Figure 1B). VO_2 and HR returned to baseline following 5 min recovery (P=0.83 and P=0.11, respectively).

Impact of water immersion on cerebral perfusion and expired carbon dioxide at rest and during exercise

Paragraph 14. MCA and PCA blood velocities increased throughout both exercise protocols (P<0.001) and returned to baseline following the 5 min recovery period (P=0.10, P=0.12 respectively). MCA and PCA blood velocities were elevated during water immersion at rest, throughout exercise and during recovery (Figure 2A-B). PCO_2 increased during both exercise protocols (P<0.001) and normalised following 5 min recovery (P=0.96). A significant main effect and time x condition interaction-effect of water immersion was found for PCO_2 (Figure 2C). Post-hoc analysis revealed that PCO_2 was significantly elevated during water immersion across all time points of the protocol (Figure 2C).

Impact of water immersion on systemic hemodynamics at rest and during exercise

Paragraph 15. SV increased throughout both exercise protocols and a significant time x condition interaction effect was observed (Figure 3A). Subsequent post-hoc comparisons revealed that water-immersion was associated with a significantly larger SV at rest and recovery, but not during exercise (Figure 3A). CO increased during both exercise protocols, but there was no effect of water immersion on the magnitude of increase in CO (Figure 3B). MAP was elevated during water immersion at rest, throughout exercise and during recovery (Figure 3C). TPR decreased throughout both exercise protocols and a main effect of water immersion was observed across all time points (Figure 3D). Finally, we found that SV, CO, MAP and TPR all returned to baseline following the 5 min recovery period (P=0.15, P=0.10, P=0.19, and P=0.33, respectively).

Impact of water immersion on skin temperature and CVC at rest and during exercise

Paragraph 16. We found no impact of exercise or water immersion on forearm or chest skin temperature (Figure 4A-B). Forearm and chest CVC increased throughout both exercise protocols (Figure 4C-D) and returned to baseline following the 5 min recovery period (P=0.38, P=0.43 respectively). Forearm and chest CVC was attenuated during water immersion at rest and throughout exercise (P=0.03; and P=0.06 respectively; Figure 4C-D).

Correlations of cerebral blood flow velocity

Paragraph 17. Changes in MCAv were correlated with changes in MAP (r=0.32, P=0.002; Figure 5) and changes in PCO_2 (r=0.27, P=0.003; Figure 5) during exercise. Changes in PCAv were correlated with changes in MAP (r=0.21, P=0.04) and changes in PCO_2 (r=0.36, P=0.001) during exercise.

Discussion

Paragraph 18. The aim of the present study was to examine whether an acute bout of exercise during water immersion would stimulate a greater increase in cerebral perfusion than land-based exercise of matched intensity. Our principal finding was that water-based exercise is associated with higher MCA and PCA blood flow velocity, relative to land-based exercise, in healthy humans.

Paragraph 19. This study examined acute hemodynamic and cerebrovascular responses to water- and land-based exercise. Importantly, the water- and land-based exercise bouts were successfully matched for VO_2 and HR, indicating that the exercise protocols were of similar relative intensity within subjects and that any observed

differences in cerebrovascular and/or hemodynamic responses between exercise bouts were a function of water immersion *per se*. Participants were immersed in 30°C water in order to avoid any reflex responses elicited by cold or heat. To this end, we observed no changes in skin temperature during the water immersion period. We suggest that the use of this water temperature allowed for direct and specific examination of the hydrostatic effects of water immersion, but it must be acknowledged that future studies will be required to address the compound impact of exercise performed in warmer or cooler water, which elicit reflex cardiovascular effects.

Paragraph 20. Previous studies have reported an increase in CBFv during mild to moderate intensity exercise (28, 32, 34, 40) and we have previously demonstrated that water immersion induces an increase in middle and posterior cerebral artery perfusion at rest (8). In the current study, the increases in CBFv during water immersion at rest persisted throughout exercise and correlated with increases in both MAP and PCO_2. This suggests that a synergistic relationship may exist in the contribution of these variables to enhanced cerebral perfusion during water-based exercise. Given the complexity of cerebral blood flow regulation during exercise and its multi-factorial nature, attempting to isolate a sole mediator responsible for the increase in cerebral perfusion is complex, but causal relationships between MAP, arterial carbon dioxide and CBFv have been consistently reported in the literature (28, 30, 34). Regardless of the precise mechanism(s) responsible, this is the first experiment to characterize the impact of water immersion during exercise on cerebral perfusion in humans.

Paragraph 21. Our previous report demonstrated that water immersion at similar temperatures to those adopted in the present study elicits an increase in MAP and SV and a decrease in HR at rest (8). These findings are consistent with the resting values observed in the subjects recruited for this study. However, the increase in SV and reduction in HR during resting water immersion was not maintained during exercise, suggesting that increased hydrostatic pressure and cephaloid redistribution of blood volume, which most likely increases end-diastolic volume and SV (5, 38) via a *Frank-Starling* effect, are not as relevant during exercise. We propose that the impact of hydrostatic pressure on blood centralization and cardiac hemodynamics is less prominent during exercise, when venous return is substantially augmented by the muscle pump (31).

Paragraph 22. As HR and SV did not differ between conditions in the present study, we did not observe any differences in CO during exercise. Whilst this finding contradicts some previous reports of increased CO during water immersion at rest (2, 5, 15) and during exercise (9, 35), our observation corroborates other previous work (21, 25). The differences between these previous studies with respect to the influence of water immersion on CO may relate to differences in methodology, in particular water temperature, exercise intensity and the duration of immersion, all of which may elicit reflex changes. In any event, we observed elevated MAP during water immersion at rest and throughout exercise, despite the similarity in CO. This indicates that the increase in MAP was related to elevated TPR during water immersion. We are reassured that this finding is robust as we simultaneously used laser Doppler flowmetry to measure forearm and chest cutaneous blood flows, which decreased during immersion, in agreement with the TPR findings. We do not believe that the

increased TPR we observed was due to a cold water effect, since we went to great lengths to ensure that the water temperature was close to the resting skin temperatures we observed at rest in our cohort and because skin temperatures did not vary throughout the immersion period.

Paragraph 23. Whilst this study benefited from a randomized within-subjects experimental design and contemporary methodology, there are some limitations that warrant consideration. The recruitment of the present study was limited to young healthy volunteers, therefore, we cannot extrapolate these findings to older populations or clinical groups. A second limitation is that we only investigated the impact of low intensity water-based exercise on cerebral blood flow. Given the potential implication that water-based exercise may benefit individuals with cerebrovascular disease, many of whom are elderly and have impaired functional capacity, we wanted to adopt an exercise intensity that potentially could be tolerated by a diverse range of clinical populations. Nevertheless, previous research has demonstrated that mild to moderate intensity exercise increases cerebral blood flow by ~10-20% (28, 30, 32) and future studies would benefit from a dose-response assessment of the impacts of exercise intensity on CBFv.

Paragraph 24. Our findings of increased CBFv during water-based exercise raise the possibility of acute and chronic impacts of water-based exercise on cerebrovascular function and health. The recurrent episodic increases in blood flow and shear that occur as a result of exercise training are potent stimuli for improvement in endothelial function and arterial remodelling in peripheral arteries in humans (18, 27, 36). Recent animal studies have also suggested that exercise improves cerebrovascular endothelial

function by up-regulating endothelial nitric oxide synthase expression through repeated exposure to elevations in blood flow and shear rate (13, 17). We speculate, based on our current findings, that water-based exercise training may induce a greater cerebrovascular health benefit than traditional land-based exercise training. However, further research examining the chronic impact of water- *versus* land-based exercise training on cerebrovascular function and cerebral autoregulation is required to substantiate this claim.

Paragraph 25. In summary, this study indicates that water-based exercise induces a greater increase in CBFv than land-based exercise of matched intensity. This observation provides a rationale to investigate the therapeutic impact of water-based exercise training on cerebrovascular function and health in humans.

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Conflict of interests:

Paragraph 27. None of the authors have declared any conflict of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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List of Figures

Figure 1. Oxygen consumption (A; VO_2/kg/min) and heart rate (B; bpm) before ('rest'), during (5, 10, 15 and 20 min) and after ('recovery') a 20 min repetitive stepping land-based (○) and water-immersion (●) exercise bout in 15 healthy participants. Error bars represent SE. *P*-values for the 2-way ANOVA data are presented ('time', 'condition', and 'time*condition'). *$P<0.05$ following post-hoc analysis when a significant 'time*condition' interaction was observed.

Figure 2. Middle cerebral artery (A; cm/s) and posterior cerebral artery blood velocity (B; cm/s), and PCO_2 (C; mmHg) before ('rest'), during (5, 10, 15 and 20 min) and after ('recovery') a 20 min repetitive stepping land-based (○) and water-immersion (●) exercise bout in 15 healthy participants. Error bars represent SE. *P*-values for the 2-way ANOVA data are presented ('time', 'condition', and 'time*condition'). *$P<0.05$ following post-hoc analysis when a significant 'time*condition' interaction was observed.

Figure 3. Stroke volume (A; mL) and cardiac output (B; L/min), mean arterial pressure (C; mmHg) and total peripheral resistance (D; mmHg/mL/min) before ('rest'), during (5, 10, 15 and 20 min) and after ('recovery') a 20 min repetitive stepping land-based (○) and water-immersion (●) exercise bout in 15 healthy participants. Error bars represent SE. *P*-values for the 2-way ANOVA data are presented ('time', 'condition', and 'time*condition'). *$P<0.05$ following post-hoc analysis when a significant 'time*condition' interaction was observed.

Figure 4. Forearm and chest skin temperature (A; Forearm, B; Chest; °C) and cutaneous vascular conductance (C; Forearm, D; Chest; CVC) before ('rest'), during (5, 10, 15 and 20 min) and after ('recovery') a 20 min repetitive stepping land-based (○) and water-immersion (●) exercise bout in 15 healthy participants. Error bars represent SE. *P*-values for the 2-way ANOVA data are presented ('time', 'condition', and 'time*condition').

Figure 5. The relationship between ΔMCAv and ΔPCO_2 (A) and ΔMAP (B) following water-based (●, dashed trend line) and land-based exercise (○, dotted trend line). The pooled water-and land-based exercise data set is represented by a solid trend line (ΔPCO_2: r=0.27, P=0.003. ΔMAP: r=0.32, P=0.002).