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# Cardiorespiratory fitness and prefrontal cortex oxygenation during Stroop task in older males

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## ABSTRACT

*Aim:* The aim of the current study was to assess whether executive function and prefrontal oxygenation are dependent on fitness level and age in older adults. *Methods:* Twenty-four healthy males aged between 55 and 69 years old were recruited for this study. They were stratified by age, leading to the creation of two groups: 55-60 years old and 61-69 years old. A median split based on CRF creates higher- and lower-fit categories of participants. Cerebral oxygenation was assessed using functional near-infrared spectroscopy (fNIRS) during a computerized Stroop task. Accuracy (% of correct responses) and reaction times (ms) were used as behavioural indicators of cognitive performances. Changes in oxygenated ( $\Delta\text{HbO}_2$ ) and deoxygenated ( $\Delta\text{HHb}$ ) hemoglobin were measured to capture neural changes. Repeated measures ANOVAs (CRF x Age x Stroop conditions) were performed to test the null hypothesis of an absence of interaction between CRF, Age and executive performance. *Results:* We also found an interaction between CRF and age on reaction times ( $p = .001$ ), in which higher fitness levels were related to faster reaction times in the 61-69 year olds but not in the 55-60 year olds. Regarding  $\Delta\text{HHb}$ , the ANOVA revealed a main effect of CRF in the right PFC ( $p = .04$ ), in which higher-fit participants had a greater  $\Delta\text{HHb}$  than the lower-fit ( $d = 1.5$ ). We also found fitness by age interaction for  $\Delta\text{HHb}$  in the right PFC ( $p = .04$ ). *Conclusion:* Our results support the positive association of CRF on cerebral oxygenation and Stroop performance in healthy older males. They indicated that high-fit individuals performed better in the 61-69 year olds group, but not in the 55-60 years old group. We also observed a greater PFC oxygenation change (as measured by  $\Delta\text{HHb}$ ) in the high-fit individuals.

## INTRODUCTION

Several reviews suggest that cardiorespiratory fitness (CRF) may protect the brain against the typical effects of aging as well as the cumulative effects of age-associated health problems [1-3]. Interventional studies with older adults support cardiorespiratory training as a method to reduce cognitive decline, which also may lead to improvements in cognition [3]. These benefits appear to be specific to executive functions [4], a subset of cognitive functions that refer to a collection of cognitive abilities such as planning, inhibitory control, working memory, and attentional control [2]. Executive functions have been related to fluid and crystallized intelligences [5]. Both of these intelligences have been shown to decline with age, particularly after the age of 60 [6, 7]. As expected, executive functions follow the same trend [8], the age of 60 representing once again a threshold for an accelerated loss [7]. The literature clearly supports a key role of CRF to explain the non-linearity of cognitive decline during aging.

Several underlying mechanisms, involving both the structure and the function of the brain, have been proposed to explain this beneficial effect of CRF on executive functions [9-12]. Oxygen availability appears to play a major role in brain functioning, since this organ is one of the greatest consumers of oxygen in the human body [13, 14]. Cerebral oxygen availability is determined in part by the interaction between cerebral vasculature and the regulation of cerebral blood flow (CBF) and also by the availability of oxygen in the environment, as evidenced by studies revealing cognitive performance impairments during hypoxia [15-17].

As executive functions, CRF is recognized to decline with age in older adults [18]. Interestingly, the longitudinal rate of decline in the peak oxygen uptake ( $\dot{V}O_{2peak}$ ) in healthy adults is not constant across the age span, and accelerates with each successive decade, especially in males, regardless of physical activity habits [18]. These specific kinetics may have substantial implications for cerebrovascular regulation and cerebral oxygenation since healthy older adults with a higher CRF generally exhibit better cerebral oxygenation than age-matched older adults with lower CRF [19-21]. The observation of an association between CRF, prefrontal cortex (PFC) oxygenation, and executive function would imply that the age-related decline in CRF is associated with a decline in PFC oxygenation during executive function tasks in older adults. To the best of our knowledge, this hypothesis has never been tested.

Therefore, the purpose of this study was to determine whether PFC oxygenation and executive function were dependent on CRF level (higher- and lower-fit). Considering the scientific literature, we hypothesized that: 1) Performance in the executive component of the Stroop task would be better in higher-fit vs lower-fit participants; 2) PFC oxygenation would be greater in higher-fit versus lower-fit participants. Considering recent results from Bherer et al, (2021) highlighting the importance of taking into account age (in older populations) in studies assessing the relationship between physical activity effect on cognitive performance and the potential effect on all our dependent variables, we also tested the effect of age in an exploratory manner.

## METHOD

### PARTICIPANTS

Considering that PFC functions can be influenced by differences in the concentration of estrogen or estradiol, and because menopause is known to affect these concentrations and to occur during the age-span targeted in this study, we decided to focus specifically on males [22-25]. Twenty-four healthy males aged between 55 and 69 years old were recruited through social medias and billboards for this study. They were stratified by age using a median split, which led to the creation of two groups: 55-60 years old and 61-69 years old. They were non-smokers, did not undergo major surgery in the past six months, did not report any neurological or psychiatric disorders, did not suffer from cognitive impairment (as assessed by the Montreal Cognitive Assessment – MoCA) or depression (as assessed by the Beck's Depression Inventory II questionnaire -BDI), did not suffer from a cardiovascular disease, and were not taking medication known to affect cognition. The protocol has been reviewed and approved by a national ethics committee for non-interventional research (CERSTAPS # 2017-23-11-17) and was conducted in accordance with recognized ethical standards and national/international laws.

### STUDY DESIGN

Once included, participants completed two testing sessions two days apart. During the first session, they filled the informed consent form, completed anthropometry measurements to obtain height, weight, and body composition (Tanita BC418, Tanita Corp., Tokyo, Japan) and performed the computerized Modified Stroop task. At the end of the first session, all participants were given a 24-h ambulatory measurement blood pressure (AMBP) device. The arm cuff was attached, and instructions were provided so that 24-h blood pressure monitoring could be started. During the second session, participants completed a maximal continuous graded exercise test. To avoid any residual fatigue induced by recent workouts, participants were asked to refrain from strenuous exercise the day before each session. They were also asked to abstain from alcohol and caffeine-containing beverages 24 hours before the test in order to avoid any influence of these beverages on the regulation of the cardiovascular system. Both sessions were administered between 8:00 a.m. to 4:00 p.m., with at least 48h between each. Once the experimental sessions were completed, participants were ranked according to their peak oxygen uptake ( $\dot{V}O_{2peak}$ ). We performed a median split on  $\dot{V}O_{2peak}$  (median value = 33 ml.min<sup>-1</sup>.kg<sup>-1</sup>) in each group in order to generate two subgroups with different CRF levels (higher and lower-fit).

## CARDIORESPIRATORY FITNESS ASSESSMENT

A modified Balke walking protocol performed on a motorized treadmill (Valiant 2 sport, Lode B.V., Groningen, Netherlands) was used to determine  $\dot{V}O_2peak$ . This test is well suited to assess CRF in heterogeneous populations that vary in terms of fitness level, age, adiposity or health status in general [26]. The velocity was set at 5.6 km/h throughout the test, with an initial 0% grade. The inclination was increased by 6% after the first minute, and then by 2% every minute until voluntary exhaustion. Verbal encouragement was given every minute throughout the test [27]. Oxygen uptake ( $\dot{V}O_2$ , in ml.kg<sup>-1</sup>.min<sup>-1</sup>) was determined continuously on a 30-s basis using a portable cardiopulmonary exercise testing system (MetaMax Cortex 3B, CORTEX Biophysik GmbH, Germany). Gas analyzers were calibrated before each test using ambient air and a gas mixture of known concentration (15% O<sub>2</sub> and 5% CO<sub>2</sub>). The turbine was calibrated before each test using a 3-l syringe at several flow rates. The highest  $\dot{V}O_2$  over a 30-s period during the test was considered as the peak oxygen uptake ( $\dot{V}O_2peak$ , in ml.kg<sup>-1</sup>.min<sup>-1</sup>). Perceived exertion (RPE) was assessed at the end of the test with the Borg scale (scale of 6-20) [28].

## STROOP TASK REACTION TIMES AND ACCURACY

The computerized Modified Stroop task used in this study was based on the Modified Stroop Color Test [29] and was previously used in several reports (Dupuy et al, 2014, Dupuy et al, 2015, Gornarjo et al, 2020, Mekari, et al, 2020). This task included three experimental conditions: naming, inhibition, and switching. Participants completed one block of 60 trials for each experimental condition (one naming, one inhibition, and one switching). Each block lasted between 2-4 minutes and was interspersed with 60-s resting blocks for a total time of 8-14 min. All trials began with a fixation cross (or square for switching condition) for 1.5 s, and all visual stimuli appeared in the center of the computer screen for 2.5 s. Participants provided their responses with two fingers (index and middle finger) from each of their hands on an AZERTY keyboard. In the Naming trial, participants were presented with a color-word (RED/BLUE/GREEN/YELLOW) in French as a visual stimulus. The name and color were congruent (i.e., RED presented in red ink) and participants were asked to identify the color of the ink with a button press. In the Inhibition block, each stimulus consisted of a color-word (RED/BLUE/GREEN/YELLOW) printed in the incongruent ink color (i.e., RED was presented in blue ink). Participants were asked to identify the color of the ink (i.e., blue). In the Switching block, participants also had to identify the color-word printed in incongruent ink (Inhibition type trial) and in 25% of the trials, a square appeared in the place of the fixation cross. When this occurred, participants were instructed to read the word instead of identifying the color of the ink (i.e., RED in blue ink respond red). As such, within the Switching block, there were both inhibition trials in which the participant had to inhibit their reading of the word and correctly identify the color of the ink, and there were switch trials in which the participant had to switch their response mode to read the word instead of identifying the color of the ink. To resume: the participants must respond as quickly as possible, making the least possible error by naming the colors of the ink for congruent trials (naming condition), for the incongruent trials (inhibition conditions) and alternatively during congruent or incongruent trials switching conditions). Visual feedback on performance was presented after each trial. A practice session was completed before the acquisition run to ensure the participants understood the different conditions. The practice consisted of a shorter version of the task. Dependent variables were reaction times (ms) and the number of errors committed (%).

## PFC OXYGENATION MEASUREMENT

The concentration changes of HbO<sub>2</sub> ( $\Delta\text{HbO}_2$ ) and HHb ( $\Delta\text{HHb}$ ) were measured with the PortaLite fNIRS system (Artinis Medical Systems, Elst, Netherlands). This system utilizes near-infrared light, which penetrates the skull and brain but is absorbed by hemoglobin (Hb) chromophores in the cortical layer. The light was transmitted with two different wavelengths, 760 and 850 nm. Based on different Hb absorption spectra, concentration changes of HbO<sub>2</sub> and HHb in the PFC area were calculated from the changes in detected light intensity. The calculation was done using the modified Lambert-Beer law, assuming constant light scattering [30]. A probe of PortaLite has three transmitters and one receiver, with transmitter-receiver distances of 30, 35, and 40 mm. The differential pathlength factor (DPF) was specified for DPF ( $\lambda=807\text{nm}$ , A), which is determined using the formula:  $\text{DPF}(\lambda=807\text{nm}, A) = 4.99 + (0.067 \times \text{Age}^{0.814})$  [31], and data were sampled with a frequency of 10 Hz.

Two probes were placed on the forehead of the participants, at a height corresponding to 10 % of the nasion-inion distance from nasion, and the middle of the device was placed at 5 % of the head circumference to the left and right from midline, corresponding to the Fp1 and Fp2 according to the international EEG 10–20 system. These locations roughly target left and right Brodmann's areas 9 and 10, which represent the dorsolateral and anterior PFC. Probes were shielded from ambient light with a black cloth fixed by an elastic strap. Oxysoft software version 3.0 (Artinis Medical Systems, Elst, Netherlands) was used for data collection. These procedures conform with a recent publication on this topic [32].

Initially resting PFC oxygenation was acquired in a seated position for 2 minutes. During the practice phase, no oxygenation data was acquired. During the experimentation, a tight-fitting band was used to optimize the hemodynamic signals' quality. For the same objective, our participants were asked to always face forward during the test, avoid making a sudden head movement, clenching their jaw, frowning, and other facial expressions.

NIRS data analysis was performed on unfiltered data. The artifacts in the signal were identified by visual inspection and replaced by interpolation of adjacent data. Conversion of optical density to change in HbO<sub>2</sub> and HHb occurred in the Oxysoft software with the modified Beer-Lambert law. The change in prefrontal oxygenation was calculated as the average of the three NIRS channels on the same side of PFC. As in all fNIRS calculations, the experimental condition activity was subtracted from the baseline activity in order to have a change in cerebral oxygenation for each condition. This preprocessing and calculation of mean changes in cerebral oxygenation have been successfully used and documented in previous research projects [32, 33].

## STATISTICAL ANALYSIS

Standard statistical methods were used for the calculation of means and standard deviations. Normal Gaussian distribution of the data was verified by the Shapiro–Wilks test and homoscedasticity by a modified Levene Test. The compound symmetry, or sphericity, was checked by the Mauchly's test. T-tests for independent samples were used to compare the baseline characteristics of subgroups. A two-way ANOVA (CRF x age) with Bonferroni post-hoc test was conducted to test the null hypothesis of an absence of interaction between CRF level (higher-fit or lower-fit) and age (YO = young-old and OO = old-old) on PFC oxygenation and Stroop conditions (naming, inhibition, switching). The magnitude of the difference was assessed by the Cohen's  $d$  ( $d$ ). The magnitude of the difference was considered small ( $0.2 < d < 0.5$ ), moderate ( $0.5 < d < 0.8$ ), or large ( $d > 0.8$ ) [34]. The significance level was set at  $p < .05$  for all analyses. All calculations were made with Statistica 7.0 (StatSoft, Tulsa, USA).

## RESULTS

The characteristics of our participants are presented in Table 1. As expected, the median split based on CRF led to a large baseline difference in  $\dot{V}O_{2peak}$  between groups, which created higher- and lower-fit categories of participants.

### STROOP TASK REACTION TIMES AND ACCURACY

Results obtained during the computerized modified Stroop task are presented in Table 2. The ANOVA assessing differences in accuracy revealed a main effect of Stroop condition [ $F(2, 69) = 36.89, p < .001$ ]. Participants completed naming and inhibition conditions with higher accuracy than switching condition ( $97.4\% \pm 2.7, 96.7\% \pm 4.6, \text{ and } 73.1\% \pm 22.9$ , respectively,  $0.2 < d < 1.5$ ). There was no effect of CRF on accuracy and no interaction between conditions.

Regarding reaction times, the ANOVA revealed an important effect of age [ $F(2, 70) = 9.89, p < 0.01; 1.1 < d < 1.9$ ]. Individuals 55-60 years old had faster overall reaction times than individuals 61-69 years old ( $1012.6 \pm 284.9$  vs  $1289.3 \pm 460.6$  ms, respectively,  $d = 0.8$ ). There was also a main effect of Stroop condition on reaction time ( $p < .001$ ). Participants completed the naming condition faster than inhibition, and inhibition conditions faster than switching ( $0.9 < d < 2.1$ ). Moreover, there was an interaction between age and Stroop condition ( $p = .03$ ). Bonferroni post-hoc analysis revealed that 55-60 year olds were significantly faster than the 61-69 year olds in all conditions ( $1.1 < d < 1.9$ ). We also found an interaction between CRF and age on reaction times ( $p = .001$ ), in which higher fitness levels were related to faster reaction times in the 61-69 year olds but not in the 55-60 year olds.

## CEREBRAL OXYGENATION CHANGES

PFC oxygenation changes during the computerized modified Stroop task are presented in Table 3. There was a main effect of Stroop condition on  $\Delta\text{HbO}_2$  in both the right and left PFC [ $F(2, 69) = 3.72, p < .05$  and  $F(2, 69) = 3.82, p < .05$ , respectively], in which  $\Delta\text{HbO}_2$  was greater in the switching condition when compared to the naming and inhibition conditions. We also found a main effect of Stroop condition on  $\Delta\text{HHb}$  in the right PFC [ $F(2, 69) = 3.81, p < .05$ ] and the left PFC [ $F(2, 69) = 4.92, p < .05$ ], in which the  $\Delta\text{HHb}$  in switching condition was greater than in naming and inhibition conditions ( $0.2 < d < 0.5$ ).

Regarding  $\Delta\text{HHb}$ , the ANOVA revealed a main effect of CRF in the right PFC [ $F(1, 70) = 6.40, p < .05$ ], in which higher-fit participants had a greater  $\Delta\text{HHb}$  than the lower-fit ( $d = 1.5$ ). We also found fitness by age interaction for  $\Delta\text{HHb}$  in the right PFC ( $p = .04$ ).

## DISCUSSION

The study investigated the interactions between CRF, Stroop task performance, and PFC oxygenation in healthy older males stratified by age (55-60 years old and 61-69 years old). Based on the literature, we hypothesized that individuals with higher-CRF would have better executive cognitive performance (ie shorter reaction time) and greater PFC oxygenation than individuals with lower-CRF. We also hypothesized that the benefits of higher-CRF on executive function and PFC oxygenation would be greater in 61-69 years olds compared to 55-60 year olds. Our main findings were that 1) PFC oxygenation change during the Stroop task, specifically the  $\Delta\text{HHb}$  in the right PFC, was greater in higher-fit participants compared to lower-fit. 2) Once stratified by age, CRF was related to improved Stroop task reaction time in switching conditions and greater change in the right PFC  $\Delta\text{HHb}$  in the 61-69 years old compared to the 55-60 years old.

In Stroop task performance findings, overall, participants responded with faster reaction times and higher accuracy when performing the naming condition in comparison to performance during inhibition and switching conditions. This effect supports the complexity manipulation in the Stroop task, in that participants are slower to respond and less accurate in the more executive inhibition and switching conditions. Regarding Stroop task reaction time, 55-60 year olds were faster overall than 61-69 year olds. This results in agreement with several studies, which have reported progressive age-related declines in executive functions in males after the age of 50 [35] or 60 [7].

No effect of CRF on reaction time was found in overall healthy older males. This ambiguous finding might be attributed to the differences in  $\dot{V}O_2\text{peak}$  level across the older age spectrum, as mentioned previously [18]. Indeed, the rate of decline in CRF accelerated from 10% every ten years in the 40s to greater than 20% every decade in the 70s and beyond [18]. This difference in CRF level between age groups might influence the association between CRF and switching condition performance in older males. Interestingly, after stratifying by age, higher-fit participants were faster in switching conditions than the lower-fit in the 61-69 year olds but not in the 55-60 year olds. Considering that both age groups have similar mean  $\dot{V}O_2\text{peak}$  values for their higher-fit and lower-fit categories, these results suggest that better CRF enhances Stroop task reaction time performance only in the 61-69 year olds and not the 55-60 year olds. These results are in accordance with recent observations from Bherer et al (2021) which highlights the importance of considering age (in older populations) when assessing the relationship between physical activity and cognitive performance. Indeed, their results suggest

that physical exercise training improves performance differently in a dual-task paradigm when comparing younger-old adults (<70 years old) and older-old adults (>70 years old).

Using the same Stroop task paradigm, our laboratory and others have previously demonstrated that greater CRF or higher physical activity level was positively associated with enhanced cognitive flexibility performance (Dupuy et al, 2015, Pedrovan et al, Goenarjo et al, 2020, Mekari et al, 2020)). This association is regularly observed by faster reaction times without impact on the number of errors. In contrast, the executive function of inhibition and the naming processes, also measured with this Stroop task, seems less sensitive to CRF. In a cross-sectional study, Dupuy et al. [9] reported that higher fit women had a better flexibility performance during the switching condition of the Stroop task when compared with lower fit women. A similar observation has been made with physical activity, since the cross sectional studies by Goenarjo et al., (2020) and Odrien (2021) reported a better flexibility performance in the participants who had the higher physical activity level, whatever their age (i.e. young or old). Longitudinal studies testing the effect of aerobic training on cognitive performance reported similar results (Pedrovan et al., Mekari et al, 2020).

In order to interpret the fNIRS results, it is important to remember that cerebral oxygenation response typically expected over an activated cortical area consists of a decrease in  $\Delta\text{HHb}$ , accompanied by an increase in  $\Delta\text{HbO}_2$ , thus resulting in an increase in total hemoglobin ([HbT]). When cortical “activation” is defined based on NIRS measurements, a decrease in  $\Delta\text{HHb}$  (Obrig et Villringer, 2003) is the most valid parameter since the decrease in  $\Delta\text{HHb}$  corresponds to an increase in BOLD contrast, as has been shown by several studies (Kleinschmidt et al., 1996; Me- hagnoul-Schipper et al., 2002).

In this study, regarding the changes in PFC oxygenation during Stroop task, both higher-fit and lower-fit participants responded with greater  $\Delta\text{HbO}_2$  and  $\Delta\text{HHb}$  to the switching condition than the inhibition and naming condition on both sides of PFC. These results align with a previous article that demonstrates increased task or condition complexity results in greater change in cerebral oxygenation in the PFC in older adults (Dupuy et al, 2015, Agbangla et 2019). We also found that higher-fit individuals had a greater decrease in  $\Delta\text{HHb}$  in the right PFC, without a significant change in  $\Delta\text{HbO}_2$ , when compared to lower-fit individuals. After age stratification, we found an interaction between CRF and age group on  $\Delta\text{HHb}$ , suggesting that the decrease of  $\Delta\text{HHb}$  had a greater effect in the 61-69 years old group than in the 55-60 years old group. In left PFC, no effects of CRF nor age group were observed on both  $\Delta\text{HHb}$  and  $\Delta\text{HbO}_2$ . This specific effect of CRF on  $\Delta\text{HHb}$  was already observed during dual task in young adults (Goenarjo et al, 2020). This relation supports the CRF hypothesis that PFC hemodynamic is influenced by the regulation of the cardiovascular system [37]. According to this hypothesis, high-fit individuals have a greater regional cerebral blood flow than lower-fit individuals, which facilitates a greater PFC activation, then contributing to improved executive performances [16].

The literature on the relationship between Stroop performance and PFC activity is consistently showing a left-sided bias (e.g., mainly implicated left lateral prefrontal (particularly inferior frontal regions of BA44/45/47) and left parietal cortices in Stroop task performance (e.g., Song and Hakoda, 2015; Cipolotti et al., 2016; Parris et al., 2019). However, the CRF seems to affect more specifically right side of the PFC, since the greatest  $\Delta\text{HHb}$  difference between higher-fit and lower-fit participants in the 61-69 years old group is observed in this region. This result is in accordance with previous reports using fNIRS techniques in young (Goenarjo et al, 2020) and old adults (Dupuy et al, 2015) and highlights

the importance of lateralization to explain the better cognitive performance observed in higher fit individuals. In line with this observation, Colcombe et al. (2004) found that the right middle frontal gyrus showed greater signal increases in physically active older people during a Flanker task [10]. Altogether, these results confirm that physical activity level and CRF have the potential to modulate cortical activity (see review Volcker Rehager et al, 2013). This observation can be attributed to a greater volume of gray matter, since it has been shown to mediate the relationship between CRF and Stroop interference (Weintein et al, 2012). In addition to previous reports, our findings support this mediation and the possible contribution of right PFC structures in executive tasks in higher-fit older individuals.

Using the fNIRS technique, this study supports that higher-fit older males displayed a greater hemodynamic change in PFC during executive function task [38]. Furthermore, in contrast to recent study findings that reported a greater  $\Delta\text{HbO}_2$  during Stroop task [19], n-back (Abganbla et al, 2019) or Trail making test (Mekari et al, 2020) in higher-fit older compared to their lower-fit counterparts, our study reports difference in  $\Delta\text{HHb}$  but no difference in  $\Delta\text{HbO}_2$  between CRF groups in all conditions. These hemodynamic attributes may be related to the characteristics of the older males. The change in  $\Delta\text{HHb}$  is more related to cellular metabolism due to greater cerebral activity, event while change in  $\Delta\text{HbO}_2$  is more related to the vascular event. As older males have less capacity of vascular modulation compared to young males (Ungvari et al, 2020), we could hypothesize that the cellular metabolism factor may have a greater effect on the hemodynamics change in this population.

## CONCLUSION

The purpose of this study was to determine whether PFC oxygenation and executive function were dependent on CRF level (higher- and lower-fit) and age (young-old and old-old healthy males). We hypothesized that individuals with higher-CRF would have better Stroop task performance and greater PFC oxygenation than individuals with lower-CRF. We also hypothesized that the benefits of higher-CRF on Stroop task performance and PFC oxygenation would be greater in 61-69 years olds compared to 55-60 year olds. Our results partially support the positive effects of CRF on PFC oxygenation and Stroop performance in healthy older males. They indicated that high-fit individuals performed better in the 61-69 year olds group, but not in 55-60 years old group. We also observed a greater PFC oxygenation change (as measured by  $\Delta\text{HHb}$ ) in the high-fit individuals. Consequently, high CRF might enable healthy older males, more specifically between 61-69 years old, to have a greater PFC oxygenation and a better performance in the switching condition in Stroop task. Our study also underscores the importance of age-grouping when studying the relation between CRF and executive performance.

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## REFERENCES

- [1] McAuley, E., Kramer, A. F., Colcombe, S. J. Cardiovascular fitness and neurocognitive function in older adults: a brief review. *Brain Behav Immun.* 2004,18:214-20.
- [2] Kramer, A. F., Colcombe, S. J., McAuley, E., Scalf, P. E., Erickson, K. I. Fitness, aging and neurocognitive function. *Neurobiol Aging.* 2005,26 Suppl 1:124-7.
- [3] Bherer, L., Erickson, K. I., Liu-Ambrose, T. A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. *J Aging Res.* 2013,2013:657508.
- [4] Colcombe, S., Kramer, A. F. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci.* 2003,14:125-30.
- [5] van Aken, L., Kessels, R. P., Wingbermuhle, E., van der Veld, W. M., Egger, J. I. Fluid intelligence and executive functioning more alike than different? *Acta Neuropsychiatr.* 2016,28:31-7.
- [6] Murman, D. L. The Impact of Age on Cognition. *Semin Hear.* 2015,36:111-21.
- [7] Treitz, F. H., Heyder, K., Daum, I. Differential course of executive control changes during normal aging. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn.* 2007,14:370-93.
- [8] Drag, L. L., Bieliauskas, L. A. Contemporary review 2009: cognitive aging. *J Geriatr Psychiatry Neurol.* 2010,23:75-93.
- [9] Hillman, C. H., Erickson, K. I., Kramer, A. F. Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci.* 2008,9:58-65.
- [10] Colcombe, S. J., Kramer, A. F., Erickson, K. I., Scalf, P., McAuley, E., Cohen, N. J., et al. Cardiovascular fitness, cortical plasticity, and aging. *Proc Natl Acad Sci U S A.* 2004,101:3316-21.
- [11] Hayes, S. M., Hayes, J. P., Cadden, M., Verfaellie, M. A review of cardiorespiratory fitness-related neuroplasticity in the aging brain. *Front Aging Neurosci.* 2013,5:31.
- [12] Kramer, A. F., Colcombe, S. Fitness Effects on the Cognitive Function of Older Adults: A Meta-Analytic Study-Revisited. *Perspect Psychol Sci.* 2018,13:213-7.
- [13] Obrig, H., Villringer, A. Beyond the visible--imaging the human brain with light. *J Cereb Blood Flow Metab.* 2003,23:1-18.
- [14] Dienel, G. A. Brain Glucose Metabolism: Integration of Energetics with Function. *Physiol Rev.* 2019,99:949-1045.
- [15] Ando, S., Yamada, Y., Kokubu, M. Reaction time to peripheral visual stimuli during exercise under hypoxia. *J Appl Physiol (1985).* 2010,108:1210-6.
- [16] Ainslie, P. N., Cotter, J. D., George, K. P., Lucas, S., Murrell, C., Shave, R., et al. Elevation in cerebral blood flow velocity with aerobic fitness throughout healthy human ageing. *J Physiol.* 2008,586:4005-10.
- [17] Novak, V., Hajjar, I. The relationship between blood pressure and cognitive function. *Nat Rev Cardiol.* 2010,7:686-98.
- [18] Fleg, J. L., Morrell, C. H., Bos, A. G., Brant, L. J., Talbot, L. A., Wright, J. G., et al. Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation.* 2005,112:674-82.
- [19] Dupuy, O., Gauthier, C. J., Fraser, S. A., Desjardins-Crepeau, L., Desjardins, M., Mekary, S., et al. Higher levels of cardiovascular fitness are associated with better executive function and prefrontal oxygenation in younger and older women. *Front Hum Neurosci.* 2015,9:66.
- [20] Albinet, C. T., Mandrick, K., Bernard, P. L., Perrey, S., Blain, H. Improved cerebral oxygenation response and executive performance as a function of cardiorespiratory fitness in older women: a fNIRS study. *Front Aging Neurosci.* 2014,6:272.
- [21] Guiney, H., Lucas, S. J., Cotter, J. D., Machado, L. Evidence cerebral blood-flow regulation mediates exercise-cognition links in healthy young adults. *Neuropsychology.* 2015,29:1-9.
- [22] Keenan, P. A., Ezzat, W. H., Ginsburg, K., Moore, G. J. Prefrontal cortex as the site of estrogen's effect on cognition. *Psychoneuroendocrinology.* 2001,26:577-90.
- [23] Hausmann, M. Why sex hormones matter for neuroscience: A very short review on sex, sex hormones, and functional brain asymmetries. *J Neurosci Res.* 2017,95:40-9.
- [24] Villa, E., Vukotic, R., Camma, C., Petta, S., Di Leo, A., Gitto, S., et al. Reproductive status is associated with the severity of fibrosis in women with hepatitis C. *PLoS One.* 2012,7:e44624.

- [25] Shanmugan, S., Epperson, C. N. Estrogen and the prefrontal cortex: towards a new understanding of estrogen's effects on executive functions in the menopause transition. *Hum Brain Mapp.* 2014,35:847-65.
- [26] Fletcher, G. F., Ades, P. A., Kligfield, P., Arena, R., Balady, G. J., Bittner, V. A., et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation.* 2013,128:873-934.
- [27] Andreacci, J. L., LeMura, L. M., Cohen, S. L., Urbansky, E. A., Chelland, S. A., Von Duvillard, S. P. The effects of frequency of encouragement on performance during maximal exercise testing. *J Sports Sci.* 2002,20:345-52.
- [28] Borg, G. A. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc.* 1982,14:377-81.
- [29] Bohnen, N., Jolles, J., Twijnstra, A. Modification of the stroop color word test improves differentiation between patients with mild head injury and matched controls. *Clin Neuropsychol.* 1992,6:178-84.
- [30] Sakatani, K., Yamashita, D., Yamanaka, T., Oda, M., Yamashita, Y., Hoshino, T., et al. Changes of cerebral blood oxygenation and optical pathlength during activation and deactivation in the prefrontal cortex measured by time-resolved near infrared spectroscopy. *Life Sci.* 2006,78:2734-41.
- [31] Duncan, A., Meek, J. H., Clemence, M., Elwell, C. E., Fallon, P., Tyszczuk, L., et al. Measurement of cranial optical path length as a function of age using phase resolved near infrared spectroscopy. *Pediatr Res.* 1996,39:889-94.
- [32] Goenarjo, R., Bosquet, L., Berryman, N., Metier, V., Perrochon, A., Fraser, S. A., et al. Cerebral Oxygenation Reserve: The Relationship Between Physical Activity Level and the Cognitive Load During a Stroop Task in Healthy Young Males. *Int J Environ Res Public Health.* 2020,17.
- [33] Goenarjo, R., Dupuy, O., Fraser, S., Perrochon, A., Berryman, N., Bosquet, L. Cardiorespiratory fitness, blood pressure, and cerebral oxygenation during a dual-task in healthy young males. *Behav Brain Res.* 2020,380:112422.
- [34] Cohen, J. *Statistical power analysis for the behavioral sciences.* 2nd ed. Hillsdale: L. Erlbaum Associates; 1988.
- [35] Zaninotto, P., Batty, G. D., Allerhand, M., Deary, I. J. Cognitive function trajectories and their determinants in older people: 8 years of follow-up in the English Longitudinal Study of Ageing. *J Epidemiol Community Health.* 2018,72:685-94.
- [36] Lindauer, U., Dirnagl, U., Fuchtemeier, M., Bottiger, C., Offenhauser, N., Leithner, C., et al. Pathophysiological interference with neurovascular coupling - when imaging based on hemoglobin might go blind. *Front Neuroenergetics.* 2010,2.
- [37] Dustman, R. E., Ruhling, R. O., Russell, E. M., Shearer, D. E., Bonekat, H. W., Shigeoka, J. W., et al. Aerobic exercise training and improved neuropsychological function of older individuals. *Neurobiol Aging.* 1984,5:35-42.
- [38] Voelcker-Rehage, C., Niemann, C. Structural and functional brain changes related to different types of physical activity across the life span. *Neurosci Biobehav Rev.* 2013,37:2268-95.
- Bherer, L., Langeard, A., Kaushal, N., Vrinceanu, T., Desjardins-Crépeau, L., Langlois, F., & Kramer, A. F. (2021). Physical Exercise Training Effect and Mediation Through Cardiorespiratory Fitness on Dual-Task Performances Differ in Younger-Old and Older-Old Adults. *The journals of gerontology. Series B, Psychological sciences and social sciences*, 76(2), 219–228. <https://doi.org/10.1093/geronb/gbz066>
- Ungvari Z, Tarantini S, Sorond F, Merkely B, Csiszar A. Mechanisms of Vascular Aging, A Geroscience Perspective: JACC Focus Seminar. *J Am Coll Cardiol.* 2020 Mar 3;75(8):931-941. doi: 10.1016/j.jacc.2019.11.061. PMID: 32130929.
- Weinstein AM, Voss MW, Prakash RS, Chaddock L, Szabo A, White SM, Wojcicki TR, Mailey E, McAuley E, Kramer AF, Erickson KI. The association between aerobic fitness and executive function is mediated by prefrontal cortex volume. *Brain Behav Immun.* 2012 Jul;26(5):811-9. doi: 10.1016/j.bbi.2011.11.008. Epub 2011 Dec 7. PMID: 22172477; PMCID: PMC3321393.
- Predovan D, Fraser SA, Renaud M, Bherer L. The effect of three months of aerobic training on stroop performance in older adults. *J Aging Res.* 2012;2012:269815. doi: 10.1155/2012/269815. Epub 2012 Dec 11. PMID: 23304504; PMCID: PMC3530182.

Song Y, Hakoda Y. An fMRI study of the functional mechanisms of Stroop/reverse-Stroop effects. *Behav Brain Res.* 2015 Sep 1;290:187-96. doi: 10.1016/j.bbr.2015.04.047. Epub 2015 May 5. PMID: 25952963.

Cipolotti L, Spanò B, Healy C, Tudor-Sfetea C, Chan E, White M, Biondo F, Duncan J, Shallice T, Bozzali M. Inhibition processes are dissociable and lateralized in human prefrontal cortex. *Neuropsychologia.* 2016 Dec;93(Pt A):1-12. doi: 10.1016/j.neuropsychologia.2016.09.018. Epub 2016 Sep 23. PMID: 27671485.

Parris BA, Wadsley MG, Hasshim N, Benattayallah A, Augustinova M, Ferrand L. An fMRI Study of Response and Semantic Conflict in the Stroop Task. *Front Psychol.* 2019 Oct 31;10:2426. doi: 10.3389/fpsyg.2019.02426. PMID: 31736827; PMCID: PMC6834775.

Mekari S, Neyedli HF, Fraser S, O'Brien MW, Martins R, Evans K, Earle M, Aucoin R, Chiekwe J, Hollohan Q, Kimmerly DS, Dupuy O. High-Intensity Interval Training Improves Cognitive Flexibility in Older Adults. *Brain Sci.* 2020 Oct 29;10(11):796. doi: 10.3390/brainsci10110796. PMID: 33137993; PMCID: PMC7693870.

Mekari S, Dupuy O, Martins R, Evans K, Kimmerly DS, Fraser S, Neyedli HF. The effects of cardiorespiratory fitness on executive function and prefrontal oxygenation in older adults. *Geroscience.* 2019 Oct;41(5):681-690. doi: 10.1007/s11357-019-00128-5. Epub 2019 Nov 15. PMID: 31728899; PMCID: PMC6885073.

O'Brien MW, Kimmerly DS, Mekari S. Greater habitual moderate-to-vigorous physical activity is associated with better executive function and higher prefrontal oxygenation in older adults. *Geroscience.* 2021 Jun 3. doi: 10.1007/s11357-021-00391-5. Epub ahead of print. PMID: 34081258.

Obrig H, Villringer A. Beyond the visible--imaging the human brain with light. *J Cereb Blood Flow Metab.* 2003 Jan;23(1):1-18. doi: 10.1097/01.WCB.0000043472.45775.29. PMID: 12500086.

Table 1: Characteristics of Study Participants. Data are presented as mean (SD)

	Overall (n = 24)		Higher-fit (n = 13)		Lower-fit (n = 11)		Cohen's d	55-60 Years Old				61-69 Years Old					
								(n = 14)		Cohen's d	(n = 10)		Cohen's d				
								Higher-fit (n = 8)	Lower-fit (n = 6)		Higher-fit (n = 5)	Lower-fit (n = 5)					
Age (yrs)	60.4	(4.3)	61.9	(4.6)	59.5	(4.3)	0.5	57.9	(1.6)	57.3	(2.0)	0.3	64.8	(3.6)	65.7	(2.9)	0.3
Height (cm)	174.7	(6.6)	175.7	(7.3)	173.9	(6.2)	0.3	178.0	(6.7)	173.7	(2.9)	0.8	174.6	(8.2)	170.6	(7.1)	0.5
Weight (kg)	80.9	(12.4)	79.9	(12.7)	81.9	(12.6)	0.1	80.4	(15.2)	88.3	(10.9)	0.6	79.3	(9.1)	74.1	(10.4)	0.5
$\dot{V}O_{2peak}$ (ml.kg <sup>-1</sup> .min <sup>-1</sup> )	32.8	(5.1)	36.2	(3.2)	28.7	(3.6) *	2.2	35.8	(3.8)	28.2	(3.8) *	2.0	36.8	(2.4)	29.4	(3.8) *	2.3

\*different from Higher-fit ( $p < 0.05$ )

Table 2. Accuracy and reaction time during Stroop tasks. Data are presented as mean (SD)

	Overall (n = 24)	55-60 Years Old (n = 14)				61-69 Years Old (n = 10)				
		Higher-fit (n = 13)	Lower-fit (n = 11)	Cohen 's d	Higher-fit (n = 8)	Lower-fit (n = 6)	Cohen 's d	Higher-fit (n = 5)	Lower-fit (n = 5)	Cohen 's d
<b>Accuracy (% of correct responses)</b>										
Naming	97.4 (2.7)	97.4 (3.2)	97.3 (2.1)	0.1	96.3 (3.7)	97.5 (1.8)	0.4	99.3 (0.9)	97.0 (2.7)	1.1
Inhibition	96.7 (4.6)	98.2 (2.4)	94.9 (5.8)	0.8	98.3 (1.5)	94.7 (7.2)	0.8	98.0 (3.6)	95.0 (4.6)	0.7
Switching	73.1 (22.9)	81.2 (15.7)	63.5 (26.9)	0.8	80.0 (15.4)	71.4 (21.9)	0.5	83.0 (17.7)	54.0 (31.8)	1.1
<b>Reaction time (ms)</b>										
Naming	861.3 (132.3)	846.3 (68.9)	879.1 (184.1)	0.2	841.7 (89.2)	744.3 (99.6)	1.0	853.7 (13.6)	1040.8 (111.4) *	2.3
Inhibition	1009.9 (206.5)	990.4 (136.8)	1032.8 (273.1)	0.2	930.7 (106.6)	840.0 (160.9)	0.7	1085.9 (132.9)	1264.1 (177.4)	1.1
Switching	1512.6 (408.9)	1433.3 (229.1)	1606.2 (551.2)	0.4	1437.7 (171.9)	1223.9 (197.4)	1.2	1426.4 (324.9)	2064.9 (478.3) *	1.6

\*different from Higher-fit ( $p < .05$ ). 1) Naming (Color naming of congruent trials); 2) Inhibition (Color naming of incongruent trials); 3) Switching (Switching between color naming of word reading and of incongruent trials).

Table 3. Cerebral oxygenation changes from baseline during computerized Stroop tasks. Data are presented as mean (SD).

Overall (n = 24)	Higher-fit (n = 13)	Lower-fit (n = 11)	Cohen 's d	55-60 Years Old (n = 14)	Cohen 's d	61-69 Years Old (n = 10)	Cohen 's d
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		Higher-fit (n = 8)				Lower-fit (n = 6)				Higher-fit (n = 5)				Lower-fit (n = 5)			
<b>Naming</b>																	
<i>Right PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	2.00	(1.39)	2.17	(1.22)	1.80	(1.60)	0.3	2.57	(1.37)	1.84	(1.46)	0.5	1.54	(0.60)	1.74	(1.93)	0.1
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.23	(0.67)	-0.36	(0.64)	-0.07	(0.70)	0.4	-0.18	(0.65)	-0.39	(0.54)	0.3	-0.65	(0.56)	0.30	(0.73)	1.5
<i>Left PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	2.42	(1.74)	2.49	(1.22)	2.32	(2.27)	0.1	2.93	(1.26)	1.71	(0.85)	1.1	1.80	(0.83)	3.07	(3.27)	0.5
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.12	(1.18)	-0.11	(0.54)	-0.14	(1.15)	0.03	-0.16	(0.53)	-0.52	(0.59)	0.6	-0.03	(0.47)	0.31	(2.54)	0.2
<b>Inhibition</b>																	
<i>Right PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	2.38	(1.39)	2.57	(1.23)	2.16	(1.59)	0.3	2.71	(1.36)	2.43	(1.45)	0.2	2.35	(1.12)	1.83	(1.85)	0.3
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.48	(0.57)	-0.65	(0.56)	-0.29	(0.53)	0.6	-0.63	(0.70)	-0.52	(0.56)	0.2	-0.68	(0.30)	-0.02	(0.38) *	1.9
<i>Left PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	2.93	(1.93)	2.88	(1.40)	2.99	(2.50)	0.06	3.18	(1.57)	2.63	(1.89)	0.3	2.39	(1.05)	3.42	(3.27)	0.4
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.34	(1.15)	-0.37	(0.59)	-0.30	(1.62)	0.06	-0.43	(0.61)	-0.72	(0.46)	0.5	-0.28	(0.61)	0.21	(2.39)	0.2
<b>Switching</b>																	
<i>Right PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	3.17	(1.74)	3.40	(1.58)	2.90	(1.95)	0.3	3.85	(1.81)	3.42	(1.87)	0.2	2.67	(0.86)	2.27	(2.07)	0.3
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.69	(0.75)	-0.93	(0.70)	-0.40	(0.81)	0.8	-0.82	(0.75)	-0.65	(0.76)	0.2	-1.12	(0.64)	-0.09	(0.61) *	1.6
<i>Left PFC</i>																	
$\Delta$ O <sub>2</sub> Hb (umol.L <sup>-1</sup> )	3.58	(1.92)	3.66	(1.67)	3.47	(2.26)	0.1	4.23	(1.69)	3.37	(1.81)	0.5	2.76	(1.30)	3.59	(2.93)	0.6
$\Delta$ HHb (umol.L <sup>-1</sup> )	-0.54	(1.18)	-0.65	(0.96)	-0.40	(1.44)	0.2	-0.63	(1.02)	-0.54	(1.12)	0.1	-0.68	(0.99)	-0.24	(1.88)	0.3

PFC, Pre-frontal cortex;  $\Delta$ O<sub>2</sub>Hb, changes in oxyhemoglobin concentrations;  $\Delta$ HHb, changes in deoxyhemoglobin concentrations

\*different from higher-fit group ( $p < .05$ )