Shorter term aerobic exercise improves brain perfusion, cognition, and cardiovascular fitness in aging

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Introduction: Physical exercise, particularly aerobic exercise, shows promise as a low-cost regimen to improve cognitive health such as memory and executive functions in middle-age to older adults. Several neural mechanisms have also emerged to support the salutary effect of physical exercise on brain health. Structural imaging showed a reversal from the typical hippocampal volume loss associated with aging following one year of aerobic training (Erickson et al., 2011). Functional MRI studies revealed increased task-related brain activity in the anterior cingulated cortex following 6 months of aerobic exercise (Colcombe et al., 2004). Resting cerebral blood flow (CBF) is a functional marker that may provide earlier indications of brain changes compared to structural markers. It also allows the examination of a broader area of brain regions compared to fMRI which only probes specific areas activated by the task. In the present study, we evaluated whether short term exercise (≤ 3 months) engenders gains in three domains: brain blood flow, cognition, and cardiovascular fitness. We hypothesized that 12 weeks of physical training would increase CBF in key areas of the brain, improve cognition in the domains of memory/executive functions and enhance VO2max (a physiological measure of cardiorespiratory fitness).

Methods: A total of 37 cognitively normal older adults (mean age=64.0±3.6) were randomized to two different groups: physical training (PT) and control (CN). The PT group underwent three 60 minute sessions of aerobic exercise training per week for a period of 12 weeks. The participants' aerobic exercise alternated each session between exercise bike and treadmill. The PT group's participants sustained their heart rate at 50-75% of their maximum achieved heart rate on VO2max testing during exercise. Physiological markers (e.g. weight, heart rate, rating of perceived exertion [RPE], and VO2 Max) were assessed at three time points: baseline/pre-training (T1), mid-training, week 6 (T2), and upon completion of the training, week 12 (T3). Additionally, the participants underwent pseudo-continuous ASL (pCASL) MRI scans on a 3T Philips scanner at each three time points. The pCASL data were routinely preprocessed and absolute CBF (aCBF)/relative CBF (rCBF) maps were estimated. Then, the global CBF value and regional CBF (via VBA) were compared between the groups. Last, a battery of neurocognitive measures was administered at each time point, i.e. T1, T2, and T3, to assess executive function (Trails A & B), memory (CVLT-II, immediate/delayed logical memory), and complex attention (stroop condition 3/4 and backward digit span). Statistical Analysis involved a "Group x Time" Interaction with two orthogonal polynomial contrasts: Linear (increase from T1 to T3) and Quadratic (maximal increase at T2) for imaging and neurocognitive measures.

Results: Physical training measures: The VO2 max improved maximally at T2 in the physical training group relative to controls (p=.02), and the rating of perceived exertion (RPE) improved from T1 to T3 in the physical training group compared to control group (p=.01) (Figure 1C & D). Neural cognitive measures: No significant differences were noted in the baseline scores (i.e. T1) between the physical training and control groups (p>.05). Tests of cognitive performance found that the physical training group significantly improved over training sessions relative to the control group. Specifically, two measures of memory function, i.e. immediate and delayed logical memory, showed improvement from T1 to T3 (p=.003 and p=.03, respectively) (Figure 1A & B). MRI measurements: The global aCBF at T1 for both CN and PT groups were similar; 47.2 and 46.8 ml/100g/min, respectively (p=.91) and did not change significantly across time points. To evaluate local resting CBF changes, we conducted voxel-wise analyses on CBF maps. In the VBA, the PT group showed an increase in resting-state blood flow from T1 to T3 in bilateral anterior cingulate (ACC) compared to the control group (FWE corrected p<.05), shown in figure 2. Since hippocampus has previously been suggested to manifest structural changes following physical exercise, we specifically examined CBF in the hippocampal ROI. CBF of the hippocampal ROI did not change significantly between CN and PT groups (p=.42), but its variation across individuals was correlated with cognition (see below). Neural Correlates of Brain, Cognition and Cardiovascular Changes. Figure 3 shows the scatter plots of relationships between logical memory changes and hippocampal CBF changes. A positive relationship was evident in physical trainers in both the left and right hippocampus (p = 0.025 and p < 0.001, respectively). Last, we found a positive trend for the physical trainers between anterior cingulate cortex from T1 to T3 and VO2 Max at maximal T2 (p=0.13) as well as a negative trend for the physical trainers between anterior cingulate cortex from T1 to T3 and RPE from T1 to T3 (p=0.11).

Discussions: The present research suggested that aerobic exercise in sedentary adults (55 – 75 years) can improve brain health. Physical activity augmented three domains; brain function (resting regional CBF), cognition (i.e. immediate and delayed memory), and cardiovascular fitness (VO2max and RPE). The benefits were measured after shorter term exercise (<3 months), extending prior evidence of gains from longer-term exercise (>3 months). The significant gains in the anterior cingulate region are intriguing since this region has recently been linked to superior cognitive agers in late life (Colcombe et al., 2004). It is also interesting to note that regions that manifest perfusion increase due to physical exercise appear to be complementary to those due to cognitive training (ISMRM Abstract #2359), although both improve cognition. In summary, the findings of the present study suggest that healthy life style changes in exercise habits can help to mitigate unnecessary losses. The sooner one starts the better since the slope of declines in brain and cognitive health become steeper from age 50 and forward.

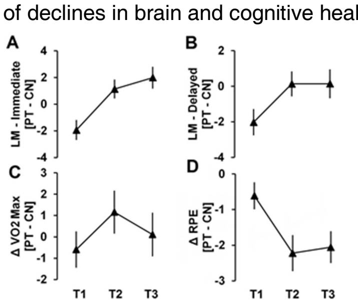

Fig 1. The mean difference between PT and CN groups over training sessions are shown for A) immediate LM, B) delayed LM, C) VO2 Max, and D) RPE.

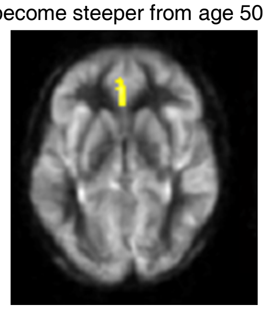

Fig 2. ACC's CBF increased from T1 to T3 in the PT group (shown in yellow) compared to the CN group, p<0.05 (FWE corrected) and k≥664 mm^3.

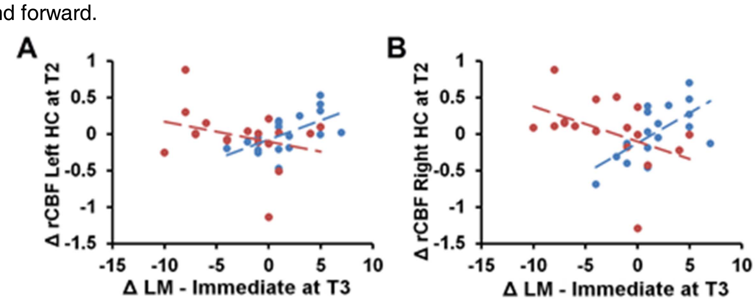

Fig 3. Scatterplots of immediate logical memory (LM) change from T1 to T3 against maximal T2 change of rCBF in the hippocampus (HC). The PT group shows positive relationships between LM immediate scores and bilateral hippocampus that differ significantly from CN (Panel (A): p=0.015; Panel (B): p<0.001).