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Brief Report

Benefits of Physical Exercise on the Aging Brain: The Role of the Prefrontal Cortex

Marika Berchicci,[1] Giuliana Lucci,[2] and Francesco Di Russo[1,2]

[1]Department of Human Movement, Social and Health Sciences, University of Rome "Foro Italico," 00135 Rome, Italy.
[2]Neuropsychological Unit, Santa Lucia Foundation IRCCS, 00144 Rome, Italy.

Address correspondence to Marika Berchicci, PhD, Department of Human Movement, Social and Health Sciences, University of Rome "Foro Italico," Piazza Lauro de Bosis 15, 00135 Rome, Italy. Email: m.berchicci@gmail.com

Motor planning in older adults likely relies on the overengagement of the prefrontal cortex (PFC) and is associated with slowness of movement and responses. Does a physically active lifestyle counteract the overrecruitment of the PFC during action preparation? This study used high-resolution electroencephalography to measure the effect of physical exercise on the executive functions of the PFC preceding a visuomotor discriminative task. A total of 130 participants aged 15–86 were divided into two groups based on physical exercise participation. The response times and accuracy and the premotor activity of the PFC were separately correlated with age for the two groups. The data were first fit with a linear function and then a higher order polynomial function. We observed that after 35–40 years of age, physically active individuals have faster response times than their less active peers and showed no signs of PFC hyperactivity during motor planning. The present findings show that physical exercise could speed up the response of older people and reveal that also in middle-aged people, moderate-to-high levels of physical exercise benefits the planning/execution of a response and the executive functions mediated by the PFC, counteracting the neural overactivity often observed in the elderly adults.

Key Words: Physical exercise—Middle aged—Prefrontal cortex—Movement-related cortical potential.

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THE literature on aging suggests that widespread morphological and physiological alterations occur in the brain, particularly in the prefrontal cortex (PFC). These alterations reflect an age-related decline in executive processes and sensorimotor functions (1). Recently, by measuring response-locked event-related potentials during visuomotor tasks, we observed an age-related overrecruitment of the PFC during the motor preparation stage (2). This increase in frontal lobe activation is a reliable finding in studies examining task-related brain activity (3). It has been proposed that PFC hyperactivity likely reflects increased reliance on cognitive control mechanisms, which, in turn, leads to both a slowing of information processing speed and a reduction of online cognitive resources available to process, store, and retrieve information (4). Two main hypotheses have been put forward to account for the neural overactivity often observed in the elderly adults: the compensation hypothesis, which suggests that the recruitment of additional brain areas or the overactivation of the involved regions compensates for various neural/behavioral deficits, and the dedifferentiation hypothesis, which posits that neural representations become less distinctive with age and that overactivation reflects the loss of neural specialization (5). The older brain acts differently from the brain of younger adults. Although their performance is comparable over a wide range of cognitive domains, a delay in motor response time (RT) represents one hallmark of the changes in sensorimotor functions. Aging-related structural and functional changes may be modified and mitigated by physical exercise programs, which are also associated with improvement of mental, social, and physical health (6). Although studies have shown that many aspects of age-related physical and cognitive decline are positively affected by physical exercise (7), few data indicate at which stage of brain processing the cognitive functions are altered by exercise (8).

An important goal is to evaluate the effects of physical activity on PFC processing, which contributes to motor planning and processing speed, but has been neglected in the electrophysiological literature. We hypothesized that physically active individuals would show reduced age-related prefrontal recruitment during motor planning and faster RTs than less active controls.

Using high-resolution EEG recording and movement-related cortical potentials (MRCPs) analysis, we examined the age-related PFC activity of 130 participants (15–86 years old) during a discriminative response task. To the best of our knowledge, this study represents the first investigation of the effects of physical exercise on executive functions mediated by the PFC across the adult life span.

METHODS

Participants

A total of 130 participants volunteered; they were divided into physical exercise participants (PEP; n = 73; aged between 16 and 80; 36 women) and not-physical exercise participants (N-PEP; n = 57; aged between 17 and 86; 25 women) based on a self-report questionnaire about physical exercise participation administered at the beginning of each experimental session in accordance with International classification (9). The N-PEP group included participants not involved in any structured or planned physical exercise programs. The PEP group included those who reported involvement in regular physical exercise and sports at least 3 days/week, 1 hour/session (ie, swimming, martial arts, fencing, and low- and high-impact exercise). All of the participants were healthy and without histories of neurological, psychiatric, or chronic somatic diseases. They were not taking psychoactive or vasoactive medication and had normal or corrected-to-normal vision. All participants were right handed (Edinburgh handedness inventory) (10). General cognitive functions in older participants were assessed using the Mini-Mental State Examination (11) (averaged score was 29/30, range: 28–30). The older participants were recruited through the *Vitattiva Association* in Rome, the middle-aged participants were recruited among friends of the authors, and the younger participants were recruited from the local student population. The two groups were matched for education levels (years of study: 15.2, SE = 1.3, for the N-PEP group; 15.0, SE = 1.4, for the PEP group). The participants' written consent was obtained (from parents for minors) according to the Declaration of Helsinki after approval by the ethical committee of the IRCCS Santa Lucia Foundation.

Materials and Tasks

Each participant was tested individually in a sound-attenuated dimly lit room after a 64-channel EEG cap was mounted on his/her scalp. Visual stimuli (ie, four-squared figures made by vertical and horizontal bars) were randomly displayed for 260 ms with equal probability (p = .25); the stimulus-onset asynchrony varied from 1 to 2 s to prevent time prediction effects on RT (for more details on the paradigm (2). The participants performed a discriminative response task, also known as Go/No-go task, which is widely used to assess sustained attention, response control, and executive/inhibitory functions (12). The participants had to press a button as fast as possible with the right hand when the target (Go stimuli; p = .5) appeared on the screen and withhold a response when the non target (No-go stimuli; p = .5) appeared (see Supplementary Figure 1 for more details).

Statistical Analysis

RTs, omissions, and false alarms, as well as the onset latency, peak amplitude, and latency of premotor activity at the AFz electrode site (placed over the medial PFC), were separately correlated with age for the N-PEP and PEP groups. The data were first fit with linear functions and then with higher order polynomial functions. The function with the highest correlation value (Pearson's adjusted R^2 coefficient) was accepted. The statistical significance of each fitting was tested by ANOVA. A sample-by-sample t test (two tailed) was performed between fit functions for each sample (100 per function) using bootstrap statistics. Age was treated as a continuous variable. The overall alpha level was fixed at .05 after the Geisser-Greenhouse correction.

RESULTS

Behaviorally, the RTs increased with age following a second-order polynomial function (linear and higher order functions yielded lower correlations). The function was RT = 399 − 0.068 × Age + 0.025 × Age^2 (adjusted R^2 = .910, $F_{2,54}$ = 365.1, $p < .0001$) for the N-PEP group and RT = 391 − 0.267 × Age + 0.022 × Age^2 (adjusted R^2 = .911, $F_{2,70}$ = 286.5, $p < .0001$) for the PEP group. The sample-by-sample t-test performed between the fit functions of the two groups showed significant differences from 36.7 years ($p < 0.029$) up to the end of the comparable fit functions (Figure 1A). No correlations between age and response accuracy (adjusted R^2 < .128) were found (Figure 1B). In line with previous investigations, we confirmed on a large sample that although response speed decreases with age, response accuracy does not change across life span.

The electrophysiological recordings were time locked to response onset. PFC activity was analyzed in the premotor preparation phase (Supplementary Materials) on the medial prefrontal electrode (AFz), and the peak latency was used as a dependent variable (hereafter called PFC_PL). The PCF_PL was earlier with increasing age following a second-order polynomial function. The function was PFC_PL = 373 − 0.431 × Age + 0.099 × Age^2 (adjusted R^2 = .930, $F_{2,54}$ = 373.1, $p < .0001$) for the N-PEP and PFC_PL = 394 − 1.839 × Age + 0.082 × Age^2 (adjusted R^2 = .860, $F_{2,70}$ = 222.9, $p < .0001$) for the PEP. The sample-by-sample t test performed between the fit functions of the two groups showed significant differences from the age of 38.0 years (p = .024) up to the end of the comparable fit functions (Figure 2A). Although the onset latency and peak amplitude of PFC activity were significantly correlated with age and physical exercise, the determination coefficients were lower. Thus, we do not provide additional information. Furthermore, the correlations between PFC_PLs and RTs were also significant ($p < .0001$) in both the N-PEP

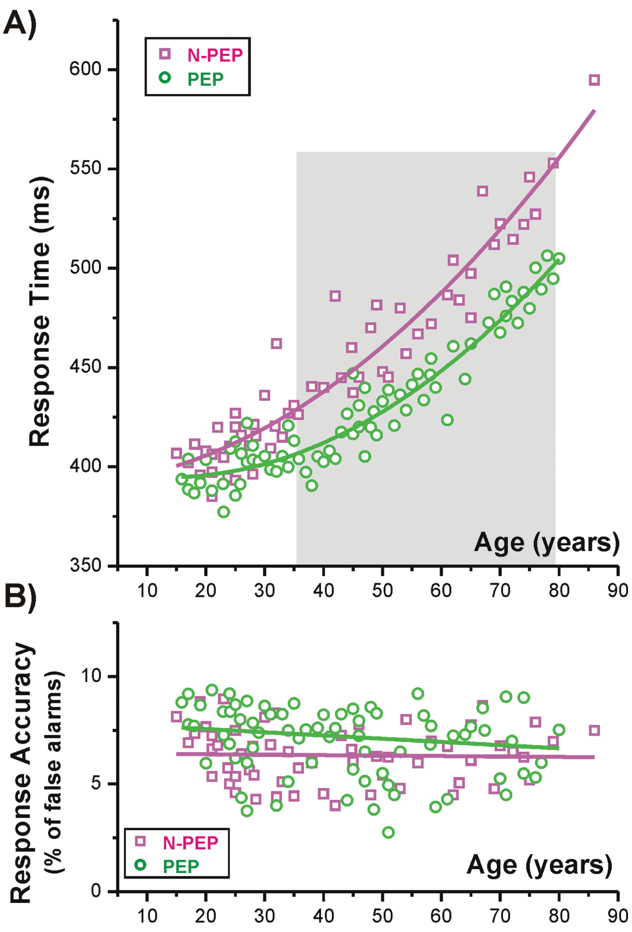

Figure 1. (**A**) Motor response time increases as a function of age. Significant differences between groups are shown by the gray area behind the plots. (**B**) Lack of correlation between response accuracy (expressed as percentage of the false alarms) and age.

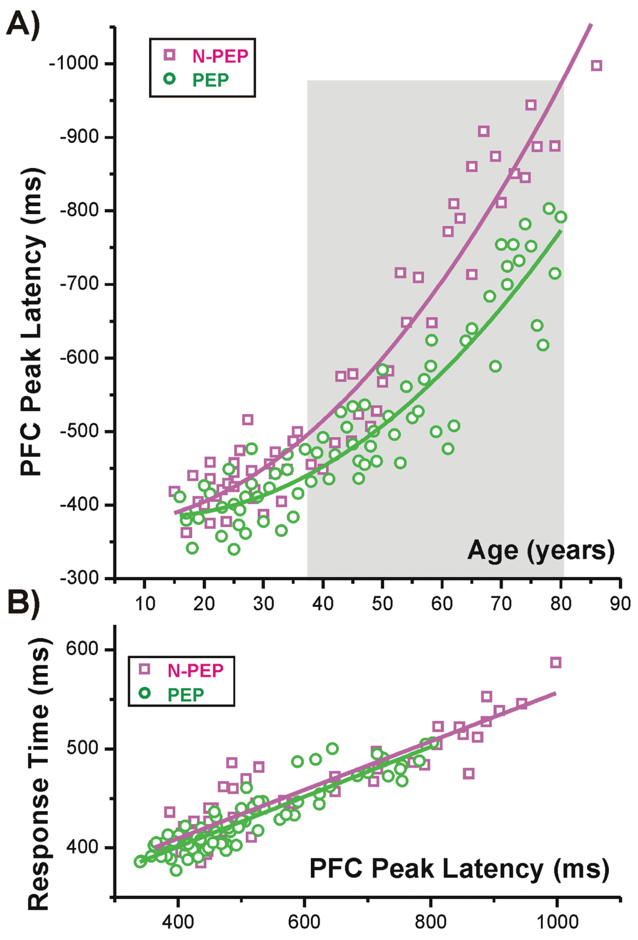

Figure 2. (**A**) Correlation between age and premotor activity in the prefrontal cortex (PFC). Significant differences between groups are shown by the gray area. (**B**) Linear correlation between motor response time and premotor activity in the PFC.

(adjusted R^2 = .835; slope = 0.245) and PEP (adjusted R^2 = .846; slope = 0.253) groups, indicating that anticipation in the PFC_PL corresponded with slow RTs (Figure 2B).

Figure 3A shows MRCP waveforms over the medial prefrontal areas in the N-PEP and PEP groups divided into two age cohorts (*n* = 25): younger (mean age: 25 years) and older (mean age: 65 years). Activity started earlier and was larger in the N-PEP than in the PEP group. The minimum norm estimation (Supplementary Materials) of the cerebral sources that generate prefrontal activity at its peak latency were consistently bilaterally localized within the PFC in the frontal pole (Figure 3B) and showed an increasing gradient of intensity from the younger PEP (the lowest) to the older N-PEP (the highest) participants. This localization agrees well with previous studies that used the same paradigm but a different source localization method (2).

Discussion

The issue of population aging will be a challenge in the coming decades in both advanced and developing countries. Although the clinical literature has recognized for years that exercise affects overall health and brain function (13), less is known about the benefits of physical exercise on executive functions mediated by the PFC across the adult life span. We extended previous investigations by studying a population with a greater age range (15–86 years). Using high-resolution 64-channel EEG, we showed novel results concerning the timing of PFC activity during motor planning, its modulation by physical activity and its relationship with behavioral parameters. Physical activity did not affect PFC activity during young adulthood, but its effect was evident in participants older than 38 years of age: active individuals engaged the PFC less and were faster than less active individuals. We did not observe significant differences in the executive processes of the young participants between the two groups. This suggests that compared with middle-aged and older participants, the young participants were easily able to accomplish the task, showing decreased effortful task preparation, especially in the PFC. The beneficial effects of physical exercise on cognitive functions in

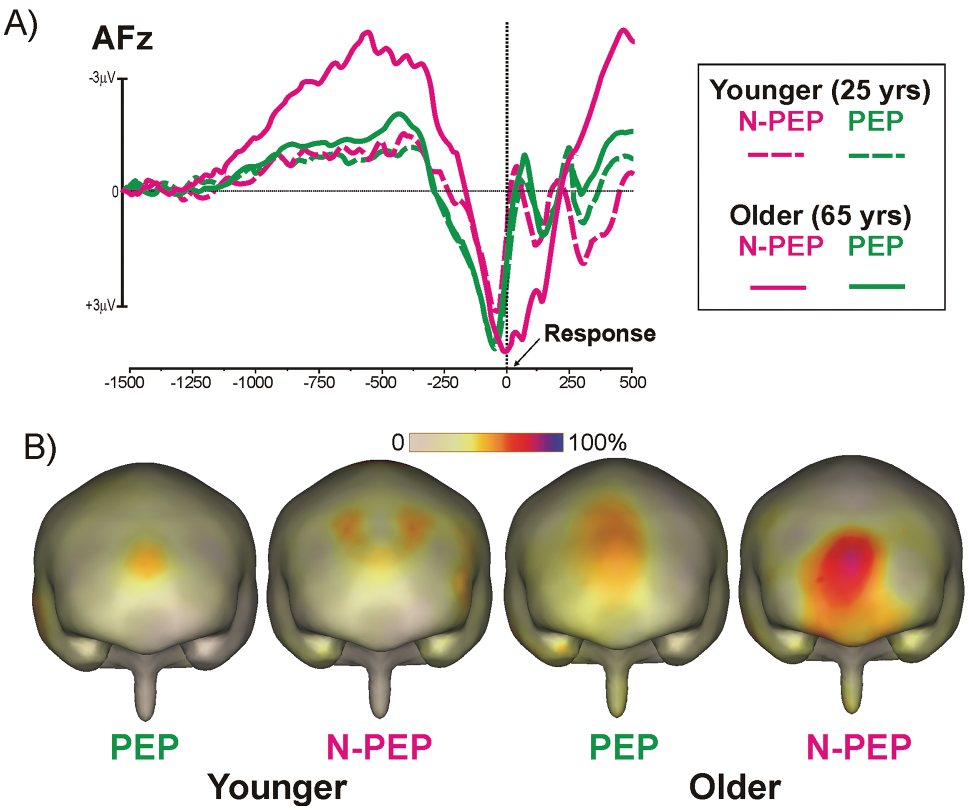

Figure 3. (**A**) MRCP waveforms over the medial prefrontal cortex (PFC; recorded on AFz) across the four cohorts. Premotor activity shows a gently rising negativity peaking around the stimulus onset. Time zero represents the response onset. (**B**) Source localization of the aforementioned activity using MNE rendered on a realistic template of the brain (frontal point of view) at PFC_PL. The activation foci were within the mid-dorsal PFC in the middle-frontal gyrus (BAs 9–10).

young people were not detected during the performance of the present task, but they cannot be excluded.

We observed that physical exercise is particularly important from middle age onwards, when the brain faces a series of challenges that can include neurodegenerative diseases. We extended previous fMRI findings, which revealed lower activation of the PFC in older adults during executive control tasks following an exercise intervention (14). The present findings reveal that in middle-aged and older individuals, moderate-to-high levels of physical exercise has beneficial effects on the planning and execution of a response, as well as on the executive functions mediated by the PFC; thus, public policy should focus on ways of increasing volitional activity in adults, starting from middle age.

There are accumulating animal and human studies explaining the metabolic and molecular changes induced by physical exercise that promote cognitive health in older people. Physical exercise has been shown to promote angiogenesis (15,16), neurogenesis (17) (see also *the neurogenic reserve hypothesis*) (18), and synaptogenesis (19) and to modulate central and peripheral levels of key neurochemicals, such as insulin like growth factor 1 and brain-derived neurotrophic factor (20). Physical exercise also induces structural and functional changes across different brain regions, as revealed by neuroimaging findings in response to specific physical exercise interventions (21–23). This study reports the first evidence of changes in the electrophysiology of the PFC induced by physical exercise.

Further studies combining different techniques and behavioral measures would contribute to improving our understanding of the mechanisms underpinning cortical overrecruitment in older adults and how it might be mitigated. Furthermore, further studies should identify methods to choose the most appropriate tools to investigate the aging brain and to propose individually tailored interventions using a combination of physical and cognitive programs for successful aging.

A critical issue of this study is its correlational nature and the lack of a programmed intervention. Future work should seek to replicate the present findings with controlled longitudinal intervention programs.

In summary, these findings are of great importance to researchers in different related fields for fully understanding the aging process and developing effective multidisciplinary therapeutic and prevention strategies to counteract brain diseases.

SUPPLEMENTARY MATERIAL

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/.

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