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Research Article

Cortical Thickness and the Correlation with Manual Motor Performance in a Community-based Sample of Older Adults in South America

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Abstract

Objectives: This study aims to investigate the relationship between cortical thickness and manual motor performance in a sample of healthy elders from a large urban cohort.

Experimental design: we examined the correlation between cortical thickness, dexterity and handgrip considering age, sex, and education in a population-based sample of 303 right-handed older adults. Cortical thickness was measured using surface-based morphometry implemented in Free surfer software.

Main points: Significant positive FDR-corrected correlations (p<0.05) were observed between right hand dexterity and left cortical thickness in the insula, postcentral, superior parietal and superior frontal gyrus. Moreover, significant positive correlations were observed between right hand dexterity and right cortical thickness in the inferior parietal gyrus, precuneus, superior frontal, precentral, superior temporal and insula. The dexterity of the left hand showed no significant association with cortical thickness, and no significant association was observed between the right or left handgrip and right or left cortical thickness. No significant effects of sex or education were observed.

Conclusion: Differences in hand dexterity contribute to differences in brain thickness even at the later stages of life, suggesting that motor skill could be a protecting factor for cortical thinning during the aging process.

Introduction

Healthy aging is associated with a progressive loss of function of multiple systems [1] associated with sensory functions [2,3], with dexterity [4], muscle strength (Dynapenia), hand function and a reduction in motor control performance [5,6]. Grip strength is a clinical marker of mobility and a strong predictor of physical function [7,8], of frailty [9] and it can be used as a universal marker of aging [10]. Lower handgrip strength values measured predict an accelerated decline in Activities of Daily Living (ADL), in cognition [11] and even mortality [12,13].

Functional abilities depend on anatomical integrity, muscle strength, and dexterity and are influenced by age, gender and mental state. Hand function can be evaluated by simulating the activities of daily living [14,15]. Thus, movement coordination is not only related to strength and dexterity but is also essential for functionality [16]. In particular, the decline in hand function has been attributed to peripheral changes, such as sarcopenia and a progressive loss of motor cortical neurons, followed by proximal axonal degeneration with reduced density of dendritic spines of pyramidal neurons in the motor cortex, prefrontal cortex, and superior temporal cortex [17], a reduction in the number of synapses in the cerebral cortex [18] and a reduction in cortical and spinal excitability by reducing the size and number of motor units [19]. All of these changes are associated with a decrease in gray matter volume [20] and changes in the structure of the white matter, resulting in significant quantitative and qualitative changes in cerebral structures related to the motor system [21].

Salat et al., [22] analyzed Magnetic Resonance Images (MRI) from 106 non-demented individuals with ages ranging from 18 to 93 years revealed that cortical thinning began at middle age in areas near the primary motor cortex (e.g., the precentral gyrus) demonstrating prominent atrophy.

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Nonetheless, many studies have shown that changes associated with aging are heterogeneous, regional and involve pre-motor regions such as superior and medial frontal areas, even more than primary motor or sensory regions [23,24]. Additionally, Bonilha et al., [25] investigated whether age-related volume loss affects the hand areas asymmetrically and showed greater decreases in specific areas of gray matter in older adults corresponding to the non-dominant hemisphere, suggesting that disuse leads to atrophy in the right hemisphere. However, those authors have not used individual measures of handgrip strength or dexterity in relation to handedness assessment. Then a study that consider just elderly being investigated should be enlightening.

Additional MRI images have suggested that positive structural and functional changes in the brain occur not only during the stage of development but also in senescence [26]. These modifications indicate that learning new abilities induces cortical plasticity in adults and elders, involving changes in the synaptic strength [27-32]. Although these studies reinforce the concept that training can increase neurogenesis, synaptic plasticity and learning and all these factors have provided evidence of improve sensorimotor performance and cognition for the elderly, there is a need to know whether these structural changes, in particular, on thickness are temporary or not and if these changes can be maintained without training. The effectiveness of plasticity changes throughout life. There are many variables, which depend on genetic factors, environmental factors and their interaction resulting in a complex scenario [33]. The increase in gray matter is detectable during the constant training of visual motor skills, and it recedes when the activity stops. According to Driemeyer and collaborators [34], it is not known whether learning a new skill or exercising this skill is more important for functional and structural change of the brain.

In 2002, Cabeza suggested that age-related neurofunctional changes are characterized by a significant reduction in the functional hemispheric lateralization in the prefrontal cortex-HAROLD model [35]. In contrast, the CRUNCH (compensation-related utilization of neural circuits hypothesis) model suggested that elderly subjects recruit additional brain regions that do not necessarily belong to the contralateral hemisphere as much as they rely on additional strategies to solve cognitive problems [21,36,37]. Evidence of both hemisphere engaged during unilateral performance have produced mixed results. Whether handgrip and dexterity influence ipsilateral or contralateral cortical thickness in older adults has not been investigated.

Evidence of brain plasticity in the hippocampus of adult mice exposed to an environment rich in stimuli Kempermann, et al., [38,39] have described a basis for the changes observed in humans. However, the direct mechanistic relationship with the previously mentioned MRI studies cannot be assumed due to confounding factors including differences in "enriched environment" through human life as well as in cortical organization. At the same way, to verify if skills acquired during life, such as manual dexterity and handgrip strength are correlated with cortical thickness, we investigated in a group of 303 healthy older adults, the correlation between manual motor performance (handgrip strength, dexterity) and cortical thickness in all brain and in particular in areas related to manual function (gyro-pre-central) and the bilateral medial temporal sulcus and left posterior parietal [29]. We predicted that cortical thickness of those areas is positively associated with motor performance.

Methods

Participants

This study is based on participants from the SABE study (Health, Wellbeing and Ageing, 2010), a population-based cohort study in Sao Paulo (Brazil) that is aimed at investigating the determinants of health among elderly persons. The original study pop-ulation (n=1480) consisted of individuals 60 years of age and older, of which 576 indi-viduals took part in a neuroimaging and study. In this paper, we selected 303 participants from the neuroimaging subsample using the following inclusion criteria: primarily right-handed participants according to the Edinburgh Handedness Inventory [40]; normal MRI radiological examination; and able to understand all the tests and to complete manual motor performance tests. All participants completed socio-demographic questionnaires, expanded mini-mental and were evaluated for the presence of depressive symptoms using SRQ-20 and the Beck Depression Scale [41,42]. This study was approved by the Ethics Committee from the University of São Paulo and Hospital Israelita Albert Einstein. All participants signed a written Informed Consent Form (ICF) to participate in all phases of the experiment and they have not received a financial compensation for their participation.

Manual motor tasks

Manual motor performance was measured by manual dexterity and grip force. These tests included the Purdue Pegboard test, a test of manual dexterity (Lafayette Instrument Company) and handgrip strength (Jamar hand dynamometer). The pegboard test was administered under several conditions. All trials lasted for 30 s and were completed three times. The number of pegs (unimanual condition) and the number of pairs of pegs (bimanual condition) were recorded. In the unimanual condition, participants placed one peg at a time into a row of small holes. In the bimanual condition, both hands were used simultaneously to put pegs into parallel rows of holes. The average of the trials was considered. Grip strength was measured using a hand dynamometer and the participants were asked to squeeze with maximal force and the highest value among the three trials was considered.

MRI data

All participants were scanned using a Siemens 3.0T Magnetom Tim Trio System. MPRAGE T1-weighted images were obtained using a 32Ch head coil with the following parameters: isotropic 1mm voxels, TR: 2500ms, TE: 3.45ms, IR: 1100ms, FA:7°. Images were analyzed by four trained neuroradiologists to exclude visible abnormalities or head movement artifacts.

Surface-Based Morphometry

The FreeSurfer analysis suite (vFS5.1.0 release, (http://surfer.nmr.mgh.harvard.edu/) was used to derive models of the cortical surface in each T1-weighted image. These well-validated and fully automated procedures have been extensively described elsewhere [43]. Briefly, a single filled white matter volume was generated for each hemisphere after intensity normalization, skull stripping, and image segmentation using a connected components algorithm. Then, a surface tessellation was generated for each white matter volume by fitting a deformable template. This process resulted in a triangular cortical mesh for

Table 1: Demographical information of the studied sample, n=303.

Variable	Mean (SD)
Age, years (SD)	71.5 (8.65)
Women, No. (%)	209 (70)
Mini Mental Sate Examination score	25.3 (4.46)
Formal education, No. (%)	
Never been to school	29 (9.8)
1-4	195 (65.6)
5-8 years	45 (18.5)
9 or more	30 (10.1)
Pegboard right hand(mean)	11.0 (2.70)
Pegboard left hand(mean)	10.1 (2.44)
Right handgrip force (mean/highest value)	30.3 (9.27)
Left handgrip force (mean/highest value)	28.6 (8.83)

Values indicate means and (standard deviations) unless specified otherwise.

gray and white matter surfaces consisting of approximately 150,000 vertices (i.e., points) per hemisphere. Measures of cortical thickness were computed as the closest distance from the gray and white matter boundary to the gray matter and cerebrospinal fluid boundary at each vertex on the tessellated surface. Thickness data was smoothed using a 10-mm surface-based smoothing kernel.

Data analysis

Statistical surface maps were generated by computing a General Linear Model (GLM) of the effects of each motor manual performance variable (independent variable) on cortical thickness (dependent variable) at each vertex in the cortical mantle controlling for the effects of age, sex and education, using the QDEC interface of FreeSurfer (http://surfer.nmr.mgh.harvard.edu/fswiki/Qdec). Corrections for multiple comparisons across the whole brain were performed using False Discovery Rate (FDR) with the expected proportion of false positives set at a level of p<0.05. The False Discovery Rate (FDR) is a method of conceptualizing the rate of type I errors in null hypothesis testing when conducting multiple comparisons.

Results

The characteristics of the studied sample (n=303) are shown in Table 1. The mean age was 71.5 years (range 58-102 years) and 70% were women; 29% of the sample had never been to school and most of the participants (i.e., 69%) had between 1 and 4 years of formal education. The mean number of years of formal education was 4.39±3.50 years. The mean of the higher value for the right handgrip was 30.3±9.9 kgf, and for the left handgrip, the mean was 28.6±8.9) kgf. The mean of the right hand PB was 11.0±2.7, and that for the left hand PB was 10.1±2.4.

Table 2: Regions with a significant positive correlation between left cortical thickness and right hand dexterity (FDR corrected, p <0.05).

Region	Tal x	Tal y	Tal z	t-value
Insula	-22.01	-3.87	-5.66	5.33
Superior parietal	-4.48	-63.03	44.44	4.65
Postcentral	-31.06	10.62	-3.76	4.41
Superior frontal	-30.13	49.67	44.94	4.1

*All analyses are adjusted for age, sex and years of education.

Table 3: Regions with a significant positive correlation between right cortical thickness and right hand dexterity (FDR corrected, p <0.05).

Region	Tal x	Tal y	Tal z	t-value
Inferior parietal	0.2	-90.1	8.51	5.21
Precuneus	23.54	-63.11	-8.14	5.11
Superior frontal	31.28	35.59	39.5	4.72
Precentral	24.7	32.65	25.46	4.35
Superior temporal	34.23	-7.79	-15.72	4.01
Insula	22.29	-0.07	-5.86	3.77
Precentral	4.77	7.6	62.73	3.84

*All analyses are adjusted for age, sex and years of education.

The analyses of QDEC within the whole sample of right-handed older adults revealed that there was positive significant association (False discovery rate /FDR <0.05) between left cortical thickness and right-hand dexterity, particularly in areas related to manual function: superior parietal, insula, postcentral and superior frontal (Table 2).

There was also a positive association (FDR corrected, p< 0.05) between right cortical thickness and right-hand dexterity in some areas as inferior parietal, precentral, superior temporal and superior frontal gyrus, insula and precuneus (FDR corrected p<0.05) (Table 3 and Figure 1).

Cortical thickness and right-hand dexterity revealed significantly positively association in the large significant cluster of left insula (Figures 2 & 3).

No significant correlations were observed between the left-hand dexterity (non-dominant hand) evaluated by pegboard was correlated and right or left cortical thickness. We also tested whether cortical thickness was associated with right and left handgrip strength in the same way. No association was observed between cortical thickness and handgrip strength regardless of the years of education or age.

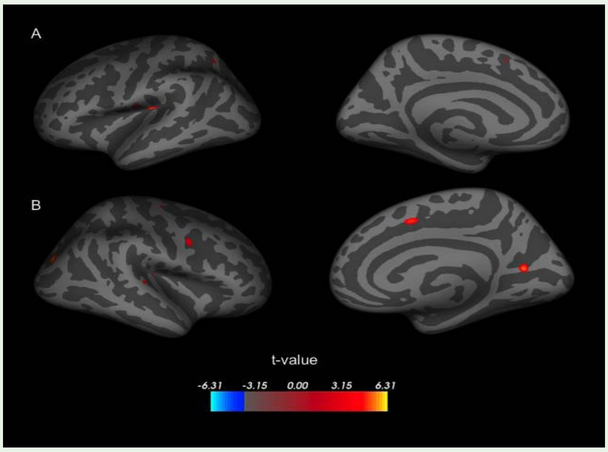

Figure 1: Increased right hand dexterity was associated with thicker cortices in portions of the A) left superior parietal gyrus, insula, postcentral and superior frontal gyrus and of the B) right inferior parietal, precentral, superior temporal and superior frontal gyrus and also in insula and precuneus (FDR corrected p<0.05).

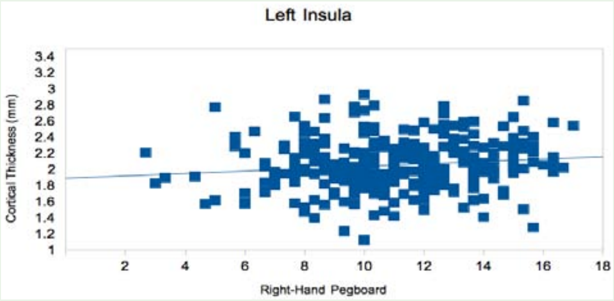

Figure 2: Scatterplot of the association between right hand peg board (dexterity) and cortical thickness in left insula.

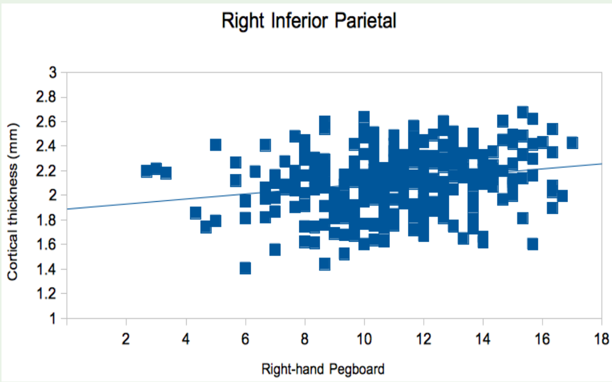

Figure 3: Scatterplot of the association between right hand pegboard (dexterity) and cortical thickness in right inferior parietal.

Discussion

We investigated the correlation between motor manual performance (handgrip strength and dexterity) and cortical thickness particularly in areas related to manual function (pre-central central, middle temporal and left posterior parietal areas) in older adults who were recruited from SABE (Health, Wellbeing and Ageing, 2010). Our findings supported our neuroanatomical hypothesis that older adults with greater dexterity would present thicker contralateral cortices in the pre-central and posterior intraparietal areas, but these results were confirmed only for the dominant hand (FDR<0.05). These data could suggest a specialization mechanism during life. We also observed a significant positive correlation between ipsilateral cortical thickness and right hand dexterity regardless of age, sex or years of formal education. No association was observed between cortical thickness and handgrip strength regardless of years of formal education, age, sex, and hand assessed, as we hypothesized.

Although we observed an increase in cortical thickness in selected areas related to specific skills, dexterity can change the structural gray matter regardless of aging and the type of motor activity performed during life. It is possible that these transformations can be maintained by macroscopic alterations based on changes at the synaptic level; the skills learned during life form new networks of neurons that could even be reduced if not encouraged, but still present; or they can still include increased numbers of glial cells or even neuronal cells [44]. Recent research confirmed that plasticity is accompanied by the activity of glial cells, especially astrocytes. It can influence the activity and survival of neurons due to its ability to monitor the constituents of the extracellular space and absorb excess neurotransmitter synthesizing neuroactive molecules [45].

An important technical aspect of our study deserves a comment: most studies investigate cortical volume changes instead of cortical thickness. We used cortical thickness and surface-based methods since this approach has been shown to have better performance and similarities compared to cortical volume measures and even genetic heritability [46,47].

Although published studies have indicated an asymmetric and regionally accentuated decline in gray matter thickness [48,49] and the atrophy of motor cortical regions [22,50,51] as a result of aging, our data suggested that motor skill ability in right-handed persons could be a protective factor for the effects of aging in cortical thickness. These findings could be partially interpreted as a response to environmental demands [29,52] and they also provide indirect evidence for the HAROLD model in that a dynamic asymmetry between the dominant and non-dominant hand and the continuous demand during life requirements could represent a protective factor against loss of function [25].

The correlation found between left cortical thickness and the Pegboard test for dominant hand is in agreement with functional imaging studies revealing that the activation of the motor area to the moving hand is asymmetric mainly when simple tasks are executed [53-55], which reflected the stronger involvement of the left versus right hemisphere in performing demanding motor tasks. According to van den Berg, these asymmetries were most consistently reported for areas upstream from the cerebral cortex (M1) and parietal and premotor regions, which is likely because functional imaging offers only limited sensitivity for studying M1. Similarly, Rose et al., [56] have shown leftward gray matter density asymmetry for right-handed subjects within the pre-central gyrus hand representation area. This region has several major white matter interhemispheric connections to the brain stem, thalamus, cerebellum, postcentral, caudal middle and superior frontal and inferior parietal corticomotor regions and corticospinal tracts that were significantly higher in the left hemisphere compared with the right one. The involvement of these brain regions and hand ability skills can be explained by the fact that all dexterity depends on a sustained and rapid transfer of sensorimotor information between M1 (corticospinal neuron originating from the supplementary motor area, anterior cingulate, postarcuate, parietal and insular cortex) and the cervical spinal cord. In fact, M1 is not the only region controlling motor output. Motor representations can be found in other areas, such as the premotor cortex, the supplementary motor area, and the cingulate motor cortex and their neurons send projections to the spinal cord [57].

Our cohort of older adults showed increased cortical thickness not only in the left superior parietal lobe, similarly to what was observed in Draganski and Boyle`s study, but also in the ipsilateral side when right hand pegboard performance (dominant hand) was analyzed. This association has been observed across many different brain regions that are involved in manipulative manual dexterity. The Superior Parietal Lobe (SPL) is among these areas, and it has a crucial role in the visual guidance of action [58]. The anterior region of the inferior parietal lobe which area we found large clusters seems to integrate visual and somatosensory information which is in agreement with the significant association that was observed with the Pegboard test [59,60]. The positive correlation observed between the right Pegboard test and ipsilateral cortical thickness reinforces the hypothesis of the loss of laterality with aging in the ipsilateral side [61,62]. However, this could not be confirmed in our cohort because our sample did not include younger volunteers. In fact, some authors suggested that additional brain areas are positively associated with task performance, which is a compensatory mechanism for age-related brain structural and biochemical declines [21,62-64] and another authors suggested that brain structure–function become less precise with age, recruiting additional regions of the brain compared to young adults [65,66].

Although recent research suggests that age-related neural dedifferentiation is reduced in older adults in several motor control areas, including the primary motor cortex, the supplementary motor area and insula, we observed significant positive relationships between thicker areas such as insula (large clusters), postcentral gyrus, superior frontal area and right hand dexterity [67]. Our results were supported by studies which showed that the neuronal tracts controlling manual dexterity originate from cortical regions in the frontal lobe and include the supplementary motor area, anterior cingulate, and post-arcuate gyrus, as well as the parietal and insular cortices suggested that hyper-activations were present in several brain regions, areas involved in sensory processing and integration, such as insula cortices, frontal operculum, superior temporal gyrus, supramarginal gyrus and the secondary somatosensory area [68,69].

Additionally, several studies have shown age differences in gray matter volume in the pre- and postcentral gyrus for older adults, in prefrontal and parietal cortices. Although we have measured thickness, not volume, this aspect can be relevant to motor performance deficits in old age since motor control is more dependent on higher hierarchical motor regions [48]. This fact could suggest that improved dexterity is related to a positive adaptation. Similarly, our data revealed a positive association between right hand dexterity with left postcentral and right precentral gyrus cortical thickness. The anatomical changes found in superior frontal areas can be related to previous findings showing that the lateral and posterior portion of the left Superior Frontal Gyrus (SFG) is a key component of the neural network. This region is involved in tasks requiring the highest level of executive processing, and it is also involved in spatially oriented processing [70]. Additionally, SFG has an important role in the bilateral control of complex movements and in bimanual coordination that is the supplementary motor area [71].

Our cohort of adults ages 60 years and older showed thickening in the same area known for processing and the storage of complex visual motion [29,52,72,73]. However, a positive and significant association was observed between dominant hand and right superior temporal thickness.

Although previous studies reported that advancing age was associated with greater task-related activation in the right (ipsilateral) primary Motor Cortex (M1), our results do not show a correlation between handgrip and gyro-precentral (primary Motor Cortex (M1) of the dominant or non-dominant hand in right-handed older adults [21,61]. The last author has been attributed the result to a putative reduction in Interhemispheric Inhibition (IHI) between the motor cortices in older subjects and the linear increase in Blood Oxygen Level Dependent (BOLD) signal normally observed with parametric increases in peak grip force in the contralateral motor cortex that diminishes with age. The possible reason for our results is that in older brains, inputs to M1 could be insufficient to increase output to spinal cord motor neurons when higher grip forces are required [74]. In normal primates rostral PMv (area F5) has dense connections to M1 and it is able to enhance M1 output to upper limb spinal cord motor neurons [75,76]. Fathi et al., [77] reported that in older adults, electrical stimulation of the median nerve does not result in increased amplitude of the motor-evoked potential differs between young and middle age individuals. These findings have shown that aging results in reduced motor cortical excitability, a loss of functional asymmetry and reduced cortical plasticity.

Talelli et al., [78] investigated whether aspects of brain activity during a motor task (handgrip) were influenced not only by age but also by neurophysiological parameters of the motor cortex contralateral to the moving hand. They observed that advancing age was associated with greater task-related activation in the right (ipsilateral) primary Motor Cortex (M1) during gripping with the right hand, and left ventral premotor cortex was greater in older subjects and in those in whom contralateral M1 was less responsive to TMS stimulation.

Conversely, cortical regions showing activity when stimulated may not necessarily be recruited when performing a unimanual task according to Bernard. A greater number of ipsilateral Motor Evoked Potentials (iMEPS) were elicited in less lateralized individuals when the number of iMEPS was correlated with the duration of interhemispheric transfer [79].

Consistent with our results, it was recently shown that the development of skilled forelimb movements, but not increased forelimb strength, was associated with a reorganization of forelimb movement representations within rat motor cortex [80]. According to Otten [81], the strength was related to neural pathway connectivity particularly between the primary motor cortex and supplementary motor area and the difference was driven mostly by decreases in interhemispheric connectivity between the left and right primary motor cortex, but our method was not sensitive enough to detect this difference.

Another interesting possibility is that corticospinal projections directly from the medially located supplementary motor area (M2) to the spinal cord lamina-containing neurons could also play a role in maintaining handgrip forces, an alteration that might be too subtle to be detected in our approach [82]. Additionally, a recent study confirmed the significant positive association between hand motor performance (grip force and manual dexterity) with cerebellar gray matter in healthy older adults using several other methods including functional magnetic resonance imaging (fMRI) and BOLD activity [83]. On the other hand, Ward and colleagues [84] investigated the effects of aging on the fMRI blood oxygen level, and observed that the motor cortex of older adults is less able to increase activity when increased handgrip force is required. All of these findings could explain the loss of relationship between HG and cortical thickness in our study.

Considering the whole motor system involved in handgrip task, one could argue if the handgrip strength changes could also be related peripheral adaptations due to the recruitment of limb motor units, therefore the force changes might not be reflected in cortical thickness. The results of these peripheral changes on handgrip were not assessed in our analysis [85]. Thus, a possible shift in muscle fiber properties with a greater proportion of slower fibers in most muscles could not be detected, a factor that suggest that our method may lack sufficient sensitivity if one considers whole motor system [86].

For the purpose of comparison with other studies, one limitation of our results is the transversal design (single cohort observation). Because it was not a longitudinal study, we cannot assess whether subjects acquired skills or were trained in hand tasks for this specific study. In that sense, findings associating the acquisition of new motor skills - such as the ones reported by Draganski and Boyle and changes in the structure of the brain are not directly comparable. Another point to consider is that juggling seems to be a more complex task compared to the Purdue Pegboard Test. Our findings related to the correlation observed between cortical thickness and the pegboard test might also have been modulated by exercise demands during participants' life time and that we can improve and keep these new neurons [87]. Physical activity and learning a new skill seem to be the output [30,39]. Our results indicated that structural changes are detectable by MRI [1].

Acknowledgments

The current analysis incorporates data from the SABE (Health, Wellbeing and Ageing- wave, 2010) Longitudinal Study, a population-based cohort study in Sao Paulo (Brazil) that is aimed at investigating the determinants of health among elderly persons. The original study population (n=1480) consisted of the general population 60 years and older. The following members of the core SABE team were involving in the design, set-up, maintenance and the support of the database: Yeda Maria Duarte, Maria Lucia Lebrão (in memory).

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References

1. Mahncke HW, Bronstone A, Merzenich MM. Brain plasticity and functional losses in the aged: scientific bases for a novel intervention. Progress in brain research. 2006; 157: 81-109.
2. Salthouse TA, Atkinson TM, Berish DE. Executive functioning as a potential mediator of age-related cognitive decline in normal adults. Journal of experimental psychology General. 2003; 132:566-594.
3. Sheppard AL, Davies LN. The effect of ageing on in vivo human ciliary muscle morphology and contractility. Investigative ophthalmology & visual science. 2011; 52: 1809-1816.
4. Ranganathan VK, Siemionow V, Sahgal V, Yue GH. Effects of aging on hand function. Journal of the American Geriatrics Society. 2001; 49: 1478-1484.
5. Clark BC, Manini TM. Sarcopenia dynapenia. The journals of gerontology A, Biological sciences and medical sciences. 2008; 63: 829-834.
6. Delmonico MJ, Harris TB, Visser M, Park SW, Conroy MB, Velasquez-Mieyer P, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. The American journal of clinical nutrition. 2009; 90: 1579-1585.
7. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol (1985). 2003; 95: 1851-1860.
8. Iannuzzi-Sucich M, Prestwood KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. The journals of gerontology Series A, Biological sciences and medical sciences. 2002; 57: 772-777.
9. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001; 56: 146-156.
10. Koopman JJ, van Bodegom D, van Heemst D, Westendorp RG. Handgrip strength, ageing and mortality in rural Africa Age and ageing. 2015; 44: 465-470.
11. Taekema DG, Gussekloo J, Maier AB, Westendorp RG, de Craen AJ. Handgrip strength as a predictor of functional, psychological and social health. A prospective population-based study among the oldest old. Age and ageing. 2010; 39: 331-337.
12. Cooper R, Kuh D, Hardy R. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. BMJ. 2010; 341: 4467.
13. Ling CH, Taekema D, de Craen AJ, Gussekloo J, Westendorp RG, Maier AB. Handgrip strength and mortality in the oldest old population: the Leiden 85-plus study. CMAJ. 2010; 182: 429-435.
14. Jebsen RH, Taylor N, Trieschmann RB, Trotter MJ, Howard LA. An objective and standardized test of hand function. Archives of physical medicine and rehabilitation. 1969; 50: 311-319.
15. Shim JK, Lay BS, Zatsiorsky VM, Latash ML. Age-related changes in finger coordination in static prehension tasks. J Appl Physiol (1985). 2004; 97: 213-224.
16. Diermayr G, McIsaac TL, Gordon AM. Finger force coordination underlying object manipulation in the elderly - a mini-review. Gerontology. 2011; 57: 217-227.
17. Dickstein DL, Kabaso D, Rocher AB, Luebke JI, Wearne SL, Hof PR. Changes in the structural complexity of the aged brain. Aging cell. 2007; 6: 275-284.
18. Johansen-Berg H, Scholz J, Stagg CJ. Relevance of structural brain connectivity to learning and recovery from stroke. Frontiers in systems neuroscience. 2010; 4: 146.
19. McNeil CJ, Doherty TJ, Stashuk DW, Rice CL. Motor unit number estimates in the tibialis anterior muscle of young, old, and very old men. Muscle & nerve. 2005; 31: 461-467.
20. Resnick SM, Pham DL, Kraut MA, Zonderman AB, Davatzikos C. Longitudinal magnetic resonance imaging studies of older adults: a shrinking brain. The Journal of neuroscience. 2003; 23: 3295-3301.
21. Ward NS. Compensatory mechanisms in the aging motor system. Ageing research reviews. 2006; 5: 239-254.
22. Salat DH, Buckner RL, Snyder AZ, Greve DN, Desikan RS, Busa E, et al. Thinning of the cerebral cortex in aging. Cereb Cortex. 2004; 14: 721-730.
23. Chetelat G, Desgranges B, Landeau B, Mezenge F, Poline JB, de la Sayette V, et al. Direct voxel-based comparison between grey matter hypometabolism and atrophy in Alzheimer's disease. Brain. 2008; 131: 60-71.
24. Kalpouzos G, Chetelat G, Baron JC, Landeau B, Mevel K, Godeau C, et al. Voxel-based mapping of brain gray matter volume and glucose metabolism profiles in normal aging. Neurobiology of aging. 2009; 30: 112-124.
25. Bonilha L, Eckert MA, Fridriksson J, Hirth VA, Moser D, Morgan PS, et al. Age-related relative volume preservation of the dominant hand cortical region. Brain research. 2009; 1305: 14-19.
26. Wang DD, Li Z, Chang Y, Wang RR, Chen XF, Zhao ZY, et al. Neural circuits and temporal plasticity in hindlimb representation of rat primary somatosensory cortex: revisited by multi-electrode array on brain slices. Neuroscience bulletin. 2010; 26: 175-187.

27. Draganski B, Gaser C, Kempermann G, Kuhn HG, Winkler J, Buchel C, et al. Temporal and spatial dynamics of brain structure changes during extensive learning. The Journal of neuroscience. 2006; 26: 6314-6317.

28. Gaser C, Schlaug G. Brain structures differ between musicians and non-musicians. The Journal of neuroscience. 2003; 23: 9240-9245.

29. Draganski B, Gaser C, Busch V, Schuierer G, Bogdahn U, May A. Neuroplasticity: changes in grey matter induced by training. Nature. 2004; 427: 311-312.

30. Pereira AC, Huddleston DE, Brickman AM, Sosunov AA, Hen R, McKhann GM, et al. An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proceedings of the National Academy of Sciences of the United States of America. 2007; 104: 5638-5643.

31. Wan CY, Schlaug G. Music making as a tool for promoting brain plasticity across the life span. The Neuroscientist. 2010; 16: 566-577.

32. Fields RD. Neuroscience. Change in the brain's white matter. Science. 2010; 330: 768-769.

33. Adamson MM, Samarina V, Xiangyan X, Huynh V, Kennedy Q, Weiner M, et al. The impact of brain size on pilot performance varies with aviation training and years of education. Journal of the International Neuropsychological Society. 2010; 16: 412-423.

34. Driemeyer J, Boyke J, Gaser C, Buchel C, May A. Changes in gray matter induced by learning--revisited. PloS one. 2008; 3: 2669.

35. Cabeza R. Hemispheric asymmetry reduction in older adults: the HAROLD model. Psychology and aging. 2002; 17: 85-100.

36. Berlingeri M, Danelli L, Bottini G, Sberna M, Paulesu E. Reassessing the HAROLD model: is the hemispheric asymmetry reduction in older adults a special case of compensatory-related utilisation of neural circuits? Experimental brain research. 2013; 224: 393-410.

37. Schaefer SY. Preserved motor asymmetry in late adulthood: is measuring chronological age enough? Neuroscience. 2015; 294: 51-59.

38. Kempermann G, Kuhn HG, Gage FH. More hippocampal neurons in adult mice living in an enriched environment. Nature. 1997; 386: 493-495.

39. Kempermann G, Gast D, Gage FH. Neuroplasticity in old age: sustained fivefold induction of hippocampal neurogenesis by long-term environmental enrichment. Annals of neurology. 2002; 52: 135-143.

40. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 1971; 9: 97-113.

41. Gomes-Oliveira MH, Gorenstein C, Lotufo Neto F, Andrade LH, Wang YP. Validation of the Brazilian Portuguese version of the Beck Depression Inventory-II in a community sample. Rev Bras Psiquiatr. 2012; 34: 389-394.

42. Mari JJ, Williams P. A validity study of a psychiatric screening questionnaire (SRQ-20) in primary care in the city of Sao Paulo. The British Journal of Psychiatry. 1986; 148: 23-26.

43. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proceedings of the National Academy of Sciences of the United States of America. 2000; 97: 11050-11055.

44. Trachtenberg JT, Chen BE, Knott GW, Feng G, Sanes JR, Welker E, et al. Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. Nature. 2002; 420: 788-794.

45. Pekny M, Wilhelmsson U, Bogestal YR, Pekna M. The role of astrocytes and complement system in neural plasticity. International review of neurobiology. 2007; 82: 95-111.

46. Winkler AM, Kochunov P, Blangero J, Almasy L, Zilles K, Fox PT, et al. Cortical thickness or grey matter volume? The importance of selecting the phenotype for imaging genetics studies. NeuroImage. 2010; 53: 1135-1146.

47. Glahn D. Imaging Genetics: Heritability, Linkage & Association. 2011; 1-58.

48. Good CD, Johnsrude IS, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. A voxel-based morphometric study of ageing in 465 normal adult human brains. NeuroImage. 2001; 14: 21-36.

49. Hedden T, Gabrieli JD. Insights into the ageing mind: a view from cognitive neuroscience. Nature reviews. Neuroscience. 2004; 5: 87-96.

50. Lemaitre H, Goldman AL, Sambataro F, Verchinski BA, Meyer-Lindenberg A, Weinberger DR, et al. Normal age-related brain morphometric changes: nonuniformity across cortical thickness, surface area and gray matter volume? Neurobiology of aging. 2012; 33: e1-9.

51. Rathi Y, Pasternak O, Savadjiev P, Michailovich O, Bouix S, Kubicki M, et al. Gray matter alterations in early aging: a diffusion magnetic resonance imaging study. Human brain mapping. 2014; 35: 3841-3856.

52. Boyke J, Driemeyer J, Gaser C, Buchel C, May A. Training-induced brain structure changes in the elderly. The Journal of neuroscience: the official journal of the Society for Neuroscience. 2008; 28: 7031-7035.

53. Swinnen SP, Vangheluwe S, Wagemans J, Coxon JP, Goble DJ, Van Impe A, et al. Shared neural resources between left and right interlimb coordination skills: the neural substrate of abstract motor representations. NeuroImage. 2010; 49: 2570-2580.

54. Callaert DV, Vercauteren K, Peeters R, Tam F, Graham S, Swinnen SP, et al. Hemispheric asymmetries of motor versus nonmotor processes during (visuo)motor control. Human brain mapping. 2011; 32: 1311-1329.

55. Van den Berg FE, Swinnen SP, Wenderoth N. Excitability of the motor cortex ipsilateral to the moving body side depends on spatio-temporal task complexity and hemispheric specialization. PloS one. 2011; 6: e17742.

56. Rose S, Rowland T, Pannek K, Baumann F, Coulthard A, McCombe P, et al. Structural hemispheric asymmetries in the human precentral gyrus hand representation. Neuroscience. 2012; 210: 211-221.

57. Stepniewska I, Preuss TM, Kaas JH. Architectonics, somatotopic organization, and ipsilateral cortical connections of the primary motor area (M1) of owl monkeys. The Journal of comparative neurology. 1993; 330: 238-271.

58. Singh-Curry V, Husain M. The functional role of the inferior parietal lobe in the dorsal and ventral stream dichotomy. Neuropsychologia. 2009; 47: 1434-1448.

59. Nickel J, Seitz RJ. Functional clusters in the human parietal cortex as revealed by an observer-independent meta-analysis of functional activation studies. Anatomy and embryology. 2005; 210: 463-472.

60. Rizzolatti G, Matelli M. Two different streams form the dorsal visual system: anatomy and functions. Experimental brain research. 2003; 153: 146-157.

61. Naccarato M, Calautti C, Jones PS, Day DJ, Carpenter TA, Baron JC. Does healthy aging affect the hemispheric activation balance during paced index-to-thumb opposition task? An fMRI study. NeuroImage. 2006; 32: 1250-1256.

62. Rowe JB, Siebner H, Filipovic SR, Cordivari C, Gerschlager W, Rothwell J, et al. Aging is associated with contrasting changes in local and distant cortical connectivity in the human motor system. NeuroImage. 2006; 32: 747-760.

63. Reuter-Lorenz PA, Lustig C. Brain aging: reorganizing discoveries about the aging mind. Current opinion in neurobiology. 2005; 15: 245-251.

64. Heuninckx S, Wenderoth N. Swinnen SP. Systems neuroplasticity in the aging brain: recruiting additional neural resources for successful motor performance in elderly persons. The Journal of neuroscience: the official journal of the Society for Neuroscience. 2008; 28: 91-99.

65. Logan JM, Sanders AL, Snyder AZ, Morris JC, Buckner RL. Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging. Neuron. 2002; 33: 827-840.

66. Carp J, Park J, Hebrank A, Park DC, Polk TA. Age-related neural dedifferentiation in the motor system. PloS one. 2011; 6: e29411.

67. Darian-Smith I, Galea MP, Darian-Smith C. Manual dexterity: how does the cerebral cortex contribute? Clinical and experimental pharmacology & physiology. 1996; 23: 948-956.

68. Heuninckx S, Wenderoth N, Debaere F, Peeters R, Swinnen SP. Neural basis of aging: the penetration of cognition into action control. The Journal of neuroscience. 2005; 25: 6787-6796.

69. du Boisgueheneuc F, Levy R, Volle E, Seassau M, Duffau H, Kinkingnehun S, et al. Functions of the left superior frontal gyrus in humans: a lesion study. Brain: a journal of neurology. 2006; 129: 3315-3328.

70. Martino J, Gabarros A, Deus J, Juncadella M, Acebes JJ, Torres A, et al. Intrasurgical mapping of complex motor function in the superior frontal gyrus. Neuroscience. 2011; 179: 131-142.

71. Bisley JW, Pasternak T. The multiple roles of visual cortical areas MT/MST in remembering the direction of visual motion. Cereb Cortex. 2000; 10: 1053-1065.

72. Sereno MI, Pitzalis S, Martinez A. Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. Science. 2001; 294: 1350-1354.

73. Oliviero A, Profice P, Tonali PA, Pilato F, Saturno E, Dileone M, et al. Effects of aging on motor cortex excitability. Neuroscience research. 2006; 55: 74-77.

74. Dancause N, Barbay S, Frost SB, Plautz EJ, Stowe AM, Friel KM, et al. Ipsilateral connections of the ventral premotor cortex in a new world primate. The Journal of comparative neurology. 2006; 495: 374-390.

75. Shimazu H, Maier MA, Cerri G, Kirkwood PA, Lemon RN. Macaque ventral premotor cortex exerts powerful facilitation of motor cortex outputs to upper limb motoneurons. The Journal of neuroscience: the official journal of the Society for Neuroscience. 2004; 24: 1200-1211.

76. Fathi D, Ueki Y, Mima T, Koganemaru S, Nagamine T, Tawfik A, et al. Effects of aging on the human motor cortical plasticity studied by paired associative stimulation. Clinical neurophysiology: official journal of the International Federation of Clinical Neurophysiology. 2010; 121: 90-93.

77. Talelli P, Ewas A, Waddingham W, Rothwell JC, Ward NS. Neural correlates of age-related changes in cortical neurophysiology. NeuroImage. 2008; 40: 1772-1781.

78. Bernard JA, Taylor SF, Seidler RD. Handedness, dexterity, and motor cortical representations. Journal of neurophysiology. 2011; 105: 88-99.

79. Remple MS, Bruneau RM, VandenBerg PM, Goertzen C, Kleim JA. Sensitivity of cortical movement representations to motor experience: evidence that skill learning but not strength training induces cortical reorganization. Behavioural brain research. 2001; 123: 133-141.

80. Otten ML, Mikell CB, Youngerman BE, Liston C, Sisti MB, Bruce JN, et al. Motor deficits correlate with resting state motor network connectivity in patients with brain tumours. Brain: a journal of neurology. 2012; 135: 1017-1026.

81. Darling WG, Pizzimenti MA, Morecraft RJ. Functional recovery following motor cortex lesions in non-human primates: experimental implications for human stroke patients. Journal of integrative neuroscience. 2011; 10: 353-384.

82. Koppelmans V, Hirsiger S, Merillat S, Jancke L, Seidler RD. Cerebellar gray and white matter volume and their relation with age and manual motor performance in healthy older adults. Human brain mapping. 2015; 36: 2352-2363.

83. Ward NS, Swayne OB, Newton JM. Age-dependent changes in the neural correlates of force modulation: an fMRI study. Neurobiology of aging. 2008; 29: 1434-1446.

84. Clark BC, Taylor JL. Age-related changes in motor cortical properties and voluntary activation of skeletal muscle. Current aging science. 2011; 4: 192-199.

85. Brunner F, Schmid A, Sheikhzadeh A, Nordin M, Yoon J, Frankel V. Effects of aging on Type II muscle fibers: a systematic review of the literature. Journal of aging and physical activity. 2007; 15: 336-348.

86. Colcombe SJ, Erickson KI, Scalf PE, Kim JS, Prakash R, McAuley E. Aerobic exercise training increases brain volume in aging humans. The journals of gerontology. 2006; 61: 1166-1170.