



Motor repertoire and gray matter plasticity: Is there a link?

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ABSTRACT

There is a considerable amount of evidence sustaining that aerobic exercise causes positive modifications in gray matter density (GMD), especially in the hippocampus and anterior cingulate cortex. However, recent experimental researches with motor learning paradigms are consistently showing that increasing cardiorespiratory capacity is not the only mechanism able to promote positive outcomes in GMD with exercise. In the present study, we present a theoretical suggestion that expanding one's motor repertoire is another primary mechanism related to the increases in GMD. Motor repertoire can be understood as the number of movement possibilities and motor skills that can be performed by a person. Supporting our suggestion, professional athletes present higher GMD than controls, and experimental protocols repeatedly observe positive changes in GMD following motor learning. The relationship between physical inactivity, amputation, and lower GMD values also gives further support for the hypothesis. Follow-up studies monitoring GMD before and after training programs that stimulate new motor skill learning are essential to confirm this proposition. The brain regions related to sensory processing of the motor tasks and the cortical areas related to motor control (e.g., primary motor cortex, supplementary motor area) are probably the ones most affected by plastic changes. If the hypothesis turns out to be reliable, dancing, gymnastics, and other movement-rich activities are thoroughly encouraged for this purpose. Therefore, this approach might be used to attenuate GMD loss related to aging or another condition, such as Parkinson's and Alzheimer's.

Introduction

Gray matter density (GMD) is a measure related to important health outcomes. Its loss is associated with cognitive declines in aging [1], dementia [2], Alzheimer's [3], and Parkinson's [4] diseases progression. Increasing or maintaining GMD throughout adulthood and older ages seems essential to prevent these adverse outcomes. Moreover, improvements in GMD are associated with academic performance [5], mental calculation training [6], long-term memory and musical abilities [7], higher sporting performance [8], and high levels of physical activity [8].

Zlata et al. [9] suggest that age-related attenuation of GMD loss is mainly achieved through the development of high aerobic fitness levels. However, a recent study [10] emphasized that physical activity interventions requiring constant cognitive and motor learning are more efficient to induce neuroplastic modifications in GMD than repetitive physical exercises in elderly individuals. Since repetitive and cyclic activities are the most commonly used to enhance aerobic fitness levels, requiring constant motor learning and providing new movement possibilities is probably more efficient to induce plastic changes in the GMD. Within this scope, we propose a theoretical link between motor

repertoire enhancement and gains in GMD.

Plasticity is hereafter interpreted according to the theoretical approach proposed by Lövdén et al. [11], whereas a mismatch between the demand of the environment and the current capacity of the system (in this case, learning a new motor task) represents the starting point for the modifications in the brain structure. Furthermore, this mismatch must be sufficiently sustained through time to induce the plastic outcomes, and also be challenging enough according to the individual flexibility and capacity of each subject [11].

In this manuscript, we understand motor repertoire as the number of movement possibilities and motor skills that can be performed by a person. For example, a martial arts athlete has a more extensive motor repertoire than a sedentary person, due to the movements learned and performed in the sport. Thus, learning a new motor skill, as well as experiencing and being able to perform different movement combinations, always expands one's motor repertoire.

The hypothesis

The notion of plasticity induced benefits of exercise is mainly related to increased cardiorespiratory capacity. There is a considerable

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amount of evidence sustaining that aerobic exercise causes positive modifications in GMD, especially in the hippocampus and anterior cingulate cortex [12,13]. However, recent experimental research (discussed below) are consistently showing that increasing cardiorespiratory capacity is not the only mechanisms able to promote positive outcomes in GMD with exercise.

We hypothesized that expanding one's motor repertoire is another primary mechanism related to the increases in GMD observed in different interventions with exercise and motor learning programs. Learning a novel motor task demands considerable brain activation due to new processing of input and output information regarding attention, sensation, perception, decision making, and memory. Therefore, performing a new movement stimulates distinct brain areas, thus inducing positive plastic changes in the corresponding regions. The consolidation (persistent learning) of these new motor tasks expands the individuals' motor repertoire and promotes the plasticity in the GMD.

This hypothesis can explain a series of experimental evidence regarding GMD plasticity in training programs, expert athletes and motor learning paradigms. Furthermore, the hypothesis is readily testable and, if reliable, could have a significant impact on how exercise and training interventions should be programmed. Older adults might be the ones most benefited from this mechanism, as aging declines in GMD negatively impacts different aspects of everyday life. Training interventions based on motor learning could counteract this effect.

Evaluation of the hypothesis

Movement representation in cortical areas can be modified after motor learning protocols. This functional plasticity has been documented in rodents [14], monkeys [15], and humans [16]. An expansion of the corresponding processing area characterizes this phenomenon, as well as an increased number of cortical representations related to the trained movement [17]. As a possible mechanism responsible for this functional plasticity, it is suggested that improvements in performance with practice are due to reorganization of cortical synapses in the motor cortex [18]. Agreeing with our hypothesis, the synaptic reorganization is known to mediate the relationship between learning and structural changes in the brain within specific processing areas required to perform and learn the novel task [19]. Changes in glial number and morphology, axon sprouting, and synaptogenesis are also well-documented mechanisms responsible for gray matter plasticity after learning protocols [20]. Hence, it is reasonable to believe that motor learning would lead to increases in GMD.

An essential piece of evidence supporting the hypothesis that a more extensive motor repertoire might increase GMD is higher values of this measure verified in endurance and martial arts athletes when compared to non-athletes [21]. Although their aerobic fitness levels are also higher when compared to controls, Schlaffke et al. [21] proposed that GMD is greater in areas related to motor learning and planning. The plurality of movements performed in martial arts could also be the underlying factor behind these results. Furthermore, expert athletes much likely have an increased motor repertoire when compared to controls, even those of cyclic modalities (e.g., running, cycling), since their training program always involves another type of exercise and coordinative movements. Thus, we can safely assume both these athletic populations have a wider motor repertoire than controls.

Another experiment comparing athletes and non-athletes found increased GMD in various brain regions of world-class gymnasts when compared to non-athletes [22]. The left inferior frontal gyrus, bilateral inferior and superior parietal lobe, among other areas, showed higher values of GMD in the gymnasts. The authors attribute this result to the gymnasts' increased capacity of movement execution and prediction, and spatial consciousness of their own body. In line with our hypothesis, this population clearly have an increased motor repertoire due to their extensive and complex sports practice, which demands distinct coordinative patterns and movement combinations.

Directly analyzing a motor learning paradigm, Driemeyer et al. [23] research showed that learning a three-ball cascade juggling skill altered gray matter in the occipital-temporal cortex as early as after seven days of training. After five weeks of training, significant increases in GMD were verified in the cingulate cortex, medial temporal gyrus, superior frontal gyrus, and inferior parietal lobe. This finding suggests that qualitative changes (i.e., learning of a new task) are critical for the brain to change its structure, inducing plastic modifications very early after training onset. Additionally, we should highlight that, in this case, the juggling training did not involve high cardiorespiratory demands. Therefore, this result clearly shows a link between motor repertoire enhancing and gains in GMD, as none of the participants knew how to juggle before experimental protocol, and no cardiovascular demand occurred during training.

In the same direction, Draganski et al., [24] showed that three months of juggling could increase GMD in the mid-temporal area and the left posterior intraparietal sulcus. Interestingly, after three months without practicing, those changes in GMD were not sustained, as well as the performance on the juggling skill. This data evidences a transient change in brain structure due to the novel motor stimulus. Hence, we can speculate that consolidation of motor learning and constant practice of the newly learned tasks are necessary to promote persistent changes in GMD. The plasticity notion by Lövdén et al. [11] fits well this experimental result [24]. According to their approach, a mismatch between the system functional capacity and the environmental demand must occur to induce plastic changes in the brain structure [11]. Thus, the demand of learning a new motor skill causes the initial mismatch that promotes the GM gains in the given area, whereas the lack of practice promotes another mismatch with a downwards adaptation, reverting the gains previously acquired with practice. This overall approach fits the other motor learning paradigms revisited by this hypothesis as well.

Muller et al. [10] reported another relevant finding in this context. These authors verified that elderly individuals who enrolled in a dancing program presented higher GMD gains in the left precentral and right parahippocampal gyrus when compared to a control exercise group. It is worth noting the control group performed endurance and resistance exercise mainly consisting of cyclic and repetitive movements (e.g., treadmill, curls, sit-ups), presenting a low coordinative demand during training. Thus, learning new motor skills was a primary outcome only in the dancing group. Therefore, it is clear that performing distinct coordinative combinations and novel movement patterns while dancing stimulates motor learning and enhances the motor repertoire. Additionally, brain-derived neurotrophic factor (BDNF) was increased only in the dancing group. This result is specifically relevant for the suggestion of underlying mechanisms responsible for the plastic changes in the brain. El-Sayes et al. [25] verified in their review that increases in BDNF lead to both neurogenesis and synaptogenesis, which are mechanisms known for increasing GMD [20]. Thus, increases in BDNF levels might be one of the responsible signaling pathways of this process [10,20].

Balance exercises can also lead to increases in GMD. Taubert et al. [26] verified significant gains in GMD of young adults after six weeks of balance training on an unstable platform that oscillated in the medio-lateral direction, compared to a control group without training. Learning this new motor task increased GMD in the left supplementary motor area, left superior frontal gyrus and left medial orbitofrontal cortex. The experimental task applied in this protocol was definitely novel compared to previous motor experiences. Hence, it is safe to assume this intervention also added to the participants motor repertoire. The correlation between the behavioral (performance) and brain structural measures is in line with our hypothesis.

Besides exercise, playing instruments also involve skilled manual action and motor learning. In this direction, James et al. [27] compared musicians with three different levels of expertise, but age-, sex- and intelligence-matched, and found the experts had increased GMD in

distinct brain regions (left intraparietal sulcus and the left inferior frontal gyrus). These areas are related to visuomotor coordination and working memory, corroborating with our proposition that the brain areas stimulated during the performance of the motor tasks are the ones most affected by the plasticity mechanisms. We can also explain their results based on the increased motor repertoire that expert musicians have, compared to the amateur ones. The number of coordinative combinations and temporal synchronization of complex movement patterns seen in the more experienced musician can all be considered to enhance one's motor repertoire. Even though this experiment did not promote an intervention, it is clear that the expertise level is associated with more extended periods of practice and motor learning.

The analysis of transcranial magnetic stimulation (TMS) related to map cortical representations also gives support to our hypothesis. A greater cortical map was verified in the dominant cortical hemisphere (left), which has a larger motor repertoire than the non-dominant one (right), for the control of upper extremity muscles [28]. In the same direction, volleyball players also had greater cortical representations of the proximal medial deltoid muscle when compared to runners, mainly due to the specific adaptation provided by the sport [29]. Furthermore, increasing the use of hand muscles causes an enlargement of motor and sensory cortical representations of the reading finger in Braille readers [30]. Altogether, these results reinforce the plasticity of the cortex due to learning. Since gains in GMD generally occur in the cortical areas associated with the information processing and control of the motor task, it is reasonable to suggest that increased cortical maps due to motor learning will consequently induce plastic alterations in the corresponding cortical structure.

Adding to the hypothesis foundation, physical inactivity, which consequently leads to declines in motor repertoire due to lack of movement, is also related to GMD loss [31]. An essential finding of this study is that a pronounced effect of pro-inflammatory cytokines was associated with inactivity in older people, further compromising GMD and cognition. Thus, avoiding inactivity is a proper approach to fight both developments of an inflammatory profile and declines of motor repertoire, contributing to GMD preservation. Indeed, Arenaza-Urquijo et al. [32] suggested both physical activity and cognitive training as suitable interventions to promote brain health, even in late adulthood.

Other findings indicate that limb amputation is also related to GMD loss [33]. The authors verified significant losses in the posterolateral thalamus contralateral to the side of the amputation. Losing a limb inevitably diminishes one's movement possibilities and motor repertoire. Furthermore, aging promotes GMD loss [1] and is usually associated with diminished physical activity levels. Both these pieces of evidence suggest that a lack of movement and motor skills practice can lead to GMD decreases.

The plurality of areas reported to increase GMD is probably due to the distinct experimental protocol applied in each research. Characteristics of the motor tasks vary between the revised experiments (e.g., juggling, dancing, balance training), as well as the analyzed population and training duration/structure. Nonetheless, what all of these studies have in common is the increase in the motor repertoire found after training and its impact on brain structure remodeling. Thus, there is compelling evidence to provide an overall explanation of these results, suggesting a link between increases in the motor repertoire and gains in GMD.

This hypothesis can be tested with interventions programs promoting a variety of exercises, motor tasks, movement combinations, and coordinative demands. Pre- and post-testing with voxel-based morphometry can answer if our hypothesis is reliable, especially if a quantitative MRI approach is used [34]. We speculate the brain regions related to sensory processing of the new motor skill and the cortical areas related to motor control (e.g., primary motor cortex, supplementary motor area) would be most affected by the plastic changes.

Consequences of the hypothesis and discussion

This novel insight into the benefits of increased motor repertoire and its association with higher GMD can be applied in everyday-life at a population level without any high investment. This strategy requires training programs with novel motor tasks that can even be performed at home, like the ones with juggling [23,24]. Clinical populations and older adults can also benefit from this mechanism, as it might be used to attenuate GMD loss related to aging or another condition, such as Parkinson's and Alzheimer's.

The suggestion of motor-repertoire induced modifications in gray matter agrees with both plasticity and flexibility notions proposed Lövdén et al. [11]. Initially, the shift in behavior (motor practice) will trigger the physiological processes responsible for altering the processing efficiency. In this phase, flexibility is necessary to meet the new demand for task processing within the preexisting knowledge and efficiency of the system. Afterward, the behavioral modifications meet the altered demand by inducing the plastic modifications in the brain structure, acquiring new processing efficiency (likely via synaptogenesis, increases in myelin, and remodeling of neural processes). As proposed by Lövdén et al. [11], these modifications can shift the range of functioning and performance, in line with our hypothesis (i.e., motor learning).

We should highlight the need for a critical reappraisal of previous findings that did not use quantitative MRI measures, as suggested by Lorio et al. [34]. These authors verified that iron, myelin, and water concentration could impact the MRI measures, leading to spurious conclusions of modifications in gray matter volume, for example. Indeed, the implication of the microstructural analysis and the underlying neurophysiological process responsible for the plasticity verified in those experiments are hindered to some extent, and specific interpretations are limited within this context. We believe, however, this evidence does not nullify the previous findings, either the theoretical evidence supporting the hypothesis framework. In fact, it is well documented in studies with rats that synaptogenesis and functional reorganization in the brain areas occurs after motor learning, mediating the anatomical changes verified in GMD [35]. We suggest that remodeling of the neuronal process via synaptogenesis [19,20], and increase in myelin along the major motor pathways [34] might be responsible for the volume/density modifications in the cortex area corresponding to that motor behavior.

Finally, as neuroplasticity might induce changes as fast as seven days after practicing a complex novel motor skill [23], not much time should be needed for positive benefits in GMD to appear with a varied and multimodal training program. If the hypothesis turns out to be reliable, dancing, gymnastics, and other movement-rich activities are thoroughly encouraged for this purpose. Despite the amount of evidence, this initial hypothesis does require further empirical testing. Follow-up studies monitoring GMD before and after training programs that stimulate new motor skill learning, are essential to confirm this novel proposition. Further research focusing on motor learning and promoting distinct motor experiences should be conducted.

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Declaration of Competing Interest

None of the authors have any conflict of interest or financial and/or personal relationships with other people or organizations that could bias the development and results of the paper.

References

- [1] Haller S, Montandon M-L, Rodriguez C, Ackermann M, Herrmann FR, Giannakopoulos P. APOE*E4 is associated with gray matter loss in the posterior cingulate cortex in healthy elderly controls subsequently developing subtle cognitive decline. *Am J Neuroradiol* 2017;38(7):1335–42.
- [2] Vijverberg EGB, Tijms BM, Dopp J, Hong YJ, Teunissen CE, Barkhof F, et al. Gray matter network differences between behavioral variant frontotemporal dementia and Alzheimer's disease. *Neurobiol Aging* 2017;50:77–86.
- [3] Doan NT, Engvig A, Zasko K, Persson K, Lund MJ, Kaufmann T, et al. Distinguishing early and late brain aging from the Alzheimer's disease spectrum: consistent morphological patterns across independent samples. *Neuroimage* 2017;158:282–95.
- [4] Rektor I, Svátková A, Vojtíšek L, Zikmundová I, Vaniček J, Király A, et al. White matter alterations in Parkinson's disease with normal cognition precede grey matter atrophy. *PLoS One* 2018;13(1):e0187939.
- [5] Wang S, Zhou M, Chen T, Yang X, Chen G, Wang M, et al. Examining gray matter structure associated with academic performance in a large sample of Chinese high school students. *Sci Rep* 2017;7(1):893.
- [6] Takeuchi H, Taki Y, Sassa Y, Hashizume H, Sekiguchi A, Fukushima A, et al. Working memory training using mental calculation impacts regional gray matter of the frontal and parietal regions. *PLoS One* 2011;6(8):e23175.
- [7] Groussard M, La Joie R, Rauchs G, Landeau B, Chételat G, Viader F, et al. When music and long-term memory interact: effects of musical expertise on functional and structural plasticity in the hippocampus. *PLoS One* 2010;5(10):e13225.
- [8] Jacini WFS, Cannonieri GC, Fernandes PT, Bonilha L, Cendes F, Li LM. Can exercise shape your brain? Cortical differences associated with judo practice. *J Sci Med Sport* 2009;12(6):688–90.
- [9] Zlatar ZZ, McGregor KM, Towler S, Nocera JR, Dzierzewski JM, Crosson B. Self-reported physical activity and objective aerobic fitness: differential associations with gray matter density in healthy aging. *Front Aging Neurosci* 2015;7:5.
- [10] Müller P, Rehfeld K, Schmicker M, Hökelmann A, Dordevic M, Lessmann V, et al. evolution of neuroplasticity in response to physical activity in old age: the case for dancing. *Front Aging Neurosci* 2017;9:56.
- [11] Lövdén M, Bäckman L, Lindenberger U, Schaefer S, Schmiedek F. A theoretical framework for the study of adult cognitive plasticity. *Psychol Bull* 2010;136(4):659–76.
- [12] Erickson KI, Leckie RL, Weinstein AM. Physical activity, fitness, and gray matter volume. *Neurobiol Aging* 2014;35:S20–8.
- [13] Hayes SM, Hayes JP, Cadden M, Verfaellie M. A review of cardiorespiratory fitness-related neuroplasticity in the aging brain. *Front Aging Neurosci* 2013;5:1–16.
- [14] Kleim JA, Hogg TM, VandenBerg PM, Cooper NR, Bruneau R, Remple M. Cortical synaptogenesis and motor map reorganization occur during late, but not early, phase of motor skill learning. *J Neurosci* 2004;24(3):628–33.
- [15] Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *J Neurosci* 1996;16(2):785–807.
- [16] Pearce AJ, Thickbroom GW, Byrnes ML, Mastaglia FL. Functional reorganization of the corticomotor projection to the hand in skilled racquet players. *Exp Brain Res* 2000;130(2):238–43.
- [17] Conner JM, Culbertson A, Packowski C, Chiba AA, Tuszynski MH. Lesions of the Basal forebrain cholinergic system impair task acquisition and abolish cortical plasticity associated with motor skill learning. *Neuron* 2003;38(5):819–29.
- [18] Kleim JA, Swain RA, Czerlanis CM, Kelly JL, Pipitone MA, Greenough WT. Learning-dependent dendritic hypertrophy of cerebellar stellate cells: plasticity of local circuit neurons. *Neurobiol Learn Mem* 1997;67(1):29–33.
- [19] Ilg R, Wohlschläger AM, Gaser C, Liebau Y, Dauner R, Wöller A, et al. Gray matter increase induced by practice correlates with task-specific activation: a combined functional and morphometric magnetic resonance imaging study. *J Neurosci* 2008;28(16):4210–5.
- [20] Zatorre RJ, Fields RD, Johansen-Berg H. Plasticity in gray and white: neuroimaging changes in brain structure during learning. *Nat Neurosci* 2012;15(4):528–36.
- [21] Schlaffke L, Lissek S, Lenz M, Brüne M, Juckel G, Hinrichs T, et al. Sports and brain morphology – a voxel-based morphometry study with endurance athletes and martial artists. *Neuroscience* 2014;259:35–42.
- [22] Huang R, Lu M, Song Z, Wang J. Long-term intensive training induced brain structural changes in world class gymnasts. *Brain Struct Funct* 2015;220(2):625–44.
- [23] Driemeyer J, Boyke J, Gaser C, Büchel C, May A. Changes in gray matter induced by learning–revisited. *PLoS One* 2008;3(7):e2669.
- [24] Draganski B, Gaser C, Busch V, Schuierer G, Bogdahn U, May A. Changes in grey matter induced by training. *Nature* 2004;427(6972):311–2.
- [25] El-Sayes J, Harasym D, Turco CV, Locke MB, Nelson AJ. Exercise-induced neuroplasticity: a mechanistic model and prospects for promoting plasticity. *Neuroscientist* 2019;25(1):65–85.
- [26] Taubert M, Draganski B, Anwander A, Müller K, Horstmann A, Villringer A, et al. Dynamic properties of human brain structure: learning-related changes in cortical areas and associated fiber connections. *J Neurosci* 2010;30(35):11670–7.
- [27] James CE, Oechslin MS, Van De Ville D, Hauert C-A, Descloux C, Lazeyras F. Musical training intensity yields opposite effects on grey matter density in cognitive versus sensorimotor networks. *Brain Struct Funct* 2014;219(1):353–66.
- [28] Wassermann EM, McShane LM, Hallett M, Cohen LG. Noninvasive mapping of muscle representations in human motor cortex. *Electroencephalogr Clin Neurophysiol* 1992;85(1):1–8.
- [29] Tyc F, Boyadjian A, Devanne H. Motor cortex plasticity induced by extensive training revealed by transcranial magnetic stimulation in human. *Eur J Neurosci* 2005;21(1):259–66.
- [30] Pascual-Leone A, Wassermann EM, Sadato N, Hallett M. The role of reading activity on the modulation of motor cortical outputs to the reading hand in Braille readers. *Ann Neurol* 1995;38(6):910–5.
- [31] Papenberg G, Ferencz B, Mangialasche F, Mecocci P, Cecchetti R, Kalpouzos G, et al. Physical activity and inflammation: effects on gray-matter volume and cognitive decline in aging. *Hum Brain Mapp* 2016;37(10):3462–73.
- [32] Arenaza-Urquijo EM, de Flores R, Gonneaud J, Wirth M, Ourry V, Callewaert W, et al. Distinct effects of late adulthood cognitive and physical activities on gray matter volume. *Brain Imaging Behav* 2017;11(2):346–56.
- [33] Draganski B, Moser T, Lummel N, Gänssbauer S, Bogdahn U, Haas F, et al. Decrease of thalamic gray matter following limb amputation. *Neuroimage* 2006;31(3):951–7.
- [34] Lorio S, Kherif F, Ruef A, Melie-Garcia L, Frackowiak R, Ashburner J, et al. Neurobiological origin of spurious brain morphological changes: a quantitative MRI study. *Hum Brain Mapp* 2016;37(5):1801–15.
- [35] Kleim JA, Barbay S, Cooper NR, Hogg TM, Reidel CN, Remple MS, et al. Motor learning-dependent synaptogenesis is localized to functionally reorganized motor cortex. *Neurobiol Learn Mem* 2002;77(1):63–77.