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Research report

Non-effective increase of fMRI-activation for motor performance in elder individuals

M. Loibl, W. Beutling, E. Kaza, M. Lotze*

Functional Imaging Unit, Center for Diagnostic Radiology and Neuroradiology, University of Greifswald, Greifswald, Germany

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ABSTRACT

Motor performance declines with increasing age and it has been proposed that elder people might compensate for these deficits with increased cerebral activation. However, it is not known, whether increased activation – especially in motor areas of the contralateral and the ipsilateral cerebral hemisphere – might effectively contribute to motor performance or whether it is an ineffective way to counteract age related deficits in the motor system. We tested this question by mapping brain activation during performance of differentially demanding motor tasks in 18 young (mean 25.39 years) and 17 elderly (mean 66.65 years) healthy individuals. We tested a wide range of hand motor tasks from passive wrist movements, fist clenching at different frequencies, to a somatosensory-guided finger pinch task. In the elderly group functional activation was generally increased for all tasks with comparable motor performance for ipsilateral primary and secondary motor areas. The young group showed increased contralateral primary motor cortex activation for the more difficult somatosensory guided precision grip task. We correlated motor performance of the task with high difficulty and comparable performance with fMRI-activation. Elder participants showed a negative correlation for the ipsilateral supplementary motor area (SMA) and for the ipsilateral sensorimotor cortex (SM1). Young participants showed a positive correlation for contralateral SMA and SM1. Our data suggest an increased cerebral recruitment reflects an inefficient response to an age-related higher difficulty of task and is not an effective way to counteract age-related deficits in the motor system.

1. Introduction

Motor performance decreases linearly in individuals older than 60 years for less demanding tasks and nonlinearly for complex movements [20]. The decline in motor performance with increasing age is associated with a structural decline in the neuromuscular system [4,10] and central neuronal changes [14]. For other domains, it has been demonstrated that cortical representation in elderly people, as investigated with functional magnetic resonance imaging (fMRI), differs from that in younger persons, even when the level of performance is matched [1]. Generally, task-related activation appears to be more focused and lateralized in younger individuals and more diffuse and bilateral in older individuals [1,26]. For the motor domain the reduction of functional lateralization, especially as a result of ipsilateral activation, correlates with age [16].

For the elderly functional mapping studies on simple motor tasks revealed increased activation in contralateral primary and secondary motor regions (M1, dPMC, SMA [9,14] and parietal cortex [9,14], but also in ipsilateral M1 [15,16,18,28], dPMC [15,18], and SMA [2,15].

These studies with younger and older individuals were based on experiments testing activation differences during the performance of simple motor tasks. However, highly demanding motor tasks are the first to show a decline in aged individuals [20] and should therefore be more distinguishable between groups. As an example of a more challenging motor paradigm, Heuninckx et al. [8] used an interlimb coordination task and found a positive correlation between performance and BOLD-signal of areas additionally activated by the elderly. The authors conclude that age-related changes are compensational and increased activation in the older participants is associated with better performance. This effective compensation hypothesis emphasizes that increased activation, especially in non-motor-areas, is associated with increased performance, and is therefore able to compensate for motor deficits. In older individuals, additionally activated areas – especially non-motor regions – should correlate positively with performance. However, in this study, the performance level between groups differed and is therefore only comparable in certain aspects. In contrast, a compensation of decreased motor ability should be successful in simple, repetitive motor tasks. It might be insufficient

* Corresponding author at: Functional Imaging Unit, Center for Diagnostic Radiology and Neuroradiology, University of Greifswald, Friedrich-Löffler-Straße 23a, D-17487 Greifswald, Germany. Tel.: +49 3834 866899; fax: +49 3834 866898.
E-mail address: martin.lotze@uni-greifswald.de (M. Lotze).

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in those tasks that show a high demand with respect to sensory guidance or to movement complexity or velocity.

Consequently, we investigated differently demanding motor tasks (repetitive simple active and passive movements, more difficult somatosensory guided movements) in the same group of healthy volunteers and we compared representation maps of young and old individuals involved in different levels of motor performance. In order to differentiate the functional relevance of representation sites we correlated motor representation during tasks with performance. We assumed that this approach might answer the question whether increasing activation in a highly demanding motor task is capable to effectively compensate for age related decline in motor function.

2. Methods

2.1. Participants

Overall, 35 volunteers participated in this study including 18 younger individuals (7 males, 11 females, age range 23–30 years, average age 25.39 years) and 17 elderly individuals (2 males, 15 females, age range 57–72, average age 66.65 years). All participants were right-handed [average score of handedness: 90.86 ± 12.02 [17] and performed all tasks with their dominant hand. All participants were healthy, without any neural or cardio-vascular disease and were not taking any regular medication. Participants were recruited by an announcement posted at the University and a local adult education center. Full written consent was obtained from all participants in accordance to the Declaration of Helsinki. The study was approved by the ethics committee of the University of Greifswald.

2.2. Apparatus and procedure

MRI data were collected using a 1.5 Tesla MRI-scanner (Siemens Symphony) that was additionally equipped with an 8-channel head-coil. Field homogeneity was optimized prior to each session using a shimming sequence. As a structural dataset, we recorded a T1-weighted volume (MPrage; TR 2.3 s; TE 3.93 ms; 175 sagittal slices; voxel size 1 mm × 1 mm × 1 mm). During the performance tasks, 75 volumes with 33 slices each (3 mm thick, 0.75 mm gap) were acquired in the transverse direction, parallel to the AC-PC-line, using echo-planar images (EPIs; TR 3000 ms, TE 50 ms, flip angle 90°, FoV 192 mm, matrix 64 × 64, voxel size 3 mm × 3 mm × 3 mm). Each block therefore lasted for 3 min 45 s, active and resting blocks alternated all 15 s. Participants lay in a supine position on the padded scanner couch and wore hearing protection. Four different tasks were performed seven times each in a randomized order using a block design alternating rest and performance. During all conditions, a green light projected in the scanner bore indicated movement, whereas a blue light indicated rest. These signals were presented via video-projection controlled by the Presentation software (Neurobehavioral Systems. Albany, NY, USA) and triggered by the scanner. Motor tasks were continuously monitored. (1) Passive wrist extension at a frequency of 1 Hz was generated using an air pressure-operated forearm splint [11]. (2) Fist-clenching using a rubber ball attached to a force sensor was performed at a frequency of 1 Hz (acoustically paced). (3) Fist-clenching using a rubber ball attached to a force sensor was performed in the individual maximal frequency. (4) The somatosensory-guided precision grip task consisted of a nine-hole PEG test system, which was assembled on a desk, invisible to the participants and mounted above the individual's abdomen. The participants were asked to put the pegs in holes. These holes were arranged in a square to the left of a cavity containing nine pegs. Individuals used a precision grip without having any visual control over their movements performed. After each block an assistant removed the positioned pegs and counted them. The performance measure was the number of pegs correctly placed over time (15 s) and was averaged over seven trials. Conditions were trained outside the scanner room and on the scanner couch before mapping started.

2.3. Analyses of functional imaging

The first two EPI images in each session were discarded prior to analysis to allow for T1-saturation effects. Spatial pre-processing and data analysis were performed with SPM5 (Wellcome Department of Imaging Neuroscience, London, England) running on Matlab version 7.4. (MathWorks Inc.; Natick, MA, USA). Each time-series was realigned, resliced and spatially normalized to the MNI-template using the coregistered and segmented T1-image as a reference. For group comparisons, data were smoothed with a Gaussian filter of 9 mm (full width at half maximum; FWHM), high pass filtered (128 s) and statistically evaluated individually. A fixed effect, single participant analysis was calculated for each condition using the movement parameters as an additional regressor. The corresponding contrast images of each participant were entered into a second level random effects analysis, which takes variance among individuals into account. Main effects were calculated with significance thresholds for multiple comparison correction over the whole brain [adjusted $p < 0.05$; false discovery rate (FDR) [7]; see Fig. 1]. Comparison between groups was restricted to regions of interest (ROIs) known to be active during performance of simple and complex motor tasks and areas that may participate in successful motor compensation [8,26]. These ROIs comprise areas in both hemispheres such as bilateral SM1, the secondary somatosensory cortex (S2), the dorsal (dPMC) and ventral premotor cortex (vPMC reaching into the inferior frontal gyrus pars opercularis, BA44), pars triangularis of the inferior frontal gyrus (BA 45), superior parietal lobe (SPA, BA 5 and 7), SMA, MCC and the bilateral anterior cerebellar hemispheres (aCH, Larsell lobules H III–VI). We restricted our analysis to these ROIs using a statistical threshold of $p \leq 0.001$, uncorrected (see Fig. 2). Whenever possible, we used cytoarchitectural probability masks (ANATOMY [5]). In addition, to avoid overlapping contributions, we used the 50% cytoarchitectural probability ROIs if not further indicated. For dPMC and SMA, which do not vary cytoarchitecturally, we differentiated BA 6 spatially. The SMA was defined as the BA 6 medial to the superior frontal sulcus of the mini-template ($-30 < x < 30$). The dPMC reached to $z = 50$ at its inferior border. If cytoarchitectural masks were not available (cerebellar hemisphere, middle cingulate gyrus), we used the "Automated Anatomical Labeling" software (AAL; [22]). Differences between groups were compared with two-sample random effect t-tests.

Table 1
Motor performance during scanning.

Task		Young subjects	Older subjects
Fist clenching at max.	Mean	2.37	2.29
frequency (Hz)	SD	0.77	0.89
Precision grip task average	Mean	3.50	3.29
of achieved pegs	SD	0.71	0.42

2.4. Correlation analysis

Activation magnitude of those tasks with no predefined performance level was correlated with motor performance. We performed this correlation analysis using multiple regression in SPM5 ($p \leq 0.001$, uncorrected) for the whole brain (to encompass possible correlation in frontal regions, which have been described by others [8].

3. Results

3.1. Motor performance

Older participants matched the performance level of the younger ones for all motor conditions (see Table 1).

3.2. fMRI findings; main effects

A detailed listing of activation sites during each task is provided in the Supplementary Table 1. In the group of young participants passive wrist movements evoked cortical activation in MCC, contralateral SMA, dPMC and bilateral SM1, S2, BA 5, BA 7 and BA 44, as well as cerebellar activation was higher ipsilateral to movement execution.

During the fist-clenching task at 1 Hz, young participants showed activation in bilateral SM1, S2, SMA, dPMC and ipsilateral aCH.

When this task was performed with the individually maximal frequency activated areas comprised bilateral MCC, SM1, SMA, dPMC, S2, BA 7 and BA 44, as well as the cerebellar hemispheres and only contralateral activation in BA5. The precision grip task for young participants involved activation in the same ROIs described for the fist clench task. No activation in BA 45 was observed in the young group.

In the group of elderly passive wrist movements evoked cortical activation in MCC, bilateral SM1, S2, SMA, dPMC, BA 5, BA 44 and BA 45 and contralateral BA 7. Cerebellar activation was higher in the ipsilateral hemisphere. During the fist-clenching task at 1 Hz, elderly participants showed activation in MCC, bilateral in SM1, S2, SMA, dPMC, BA 7, BA 44, BA 45, aCH, and contralateral BA 5. Cerebellar activation was observed bilaterally, with a higher activation ipsilaterally. At individual maximal frequency the fist clenching task evoked also activation in ipsilateral BA 5. For the precision

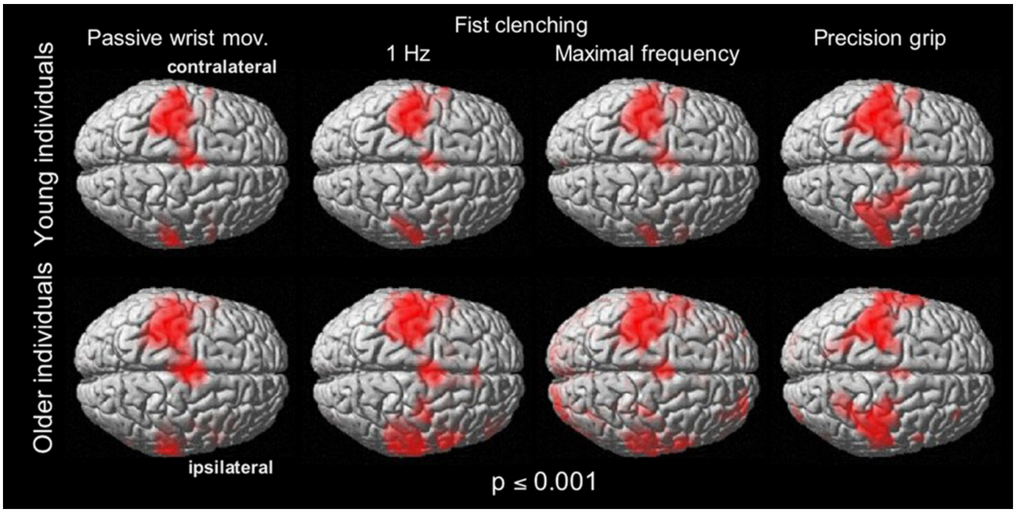

Fig. 1. Main effects for each group and task; in order to provide an overview on activation maps with the same threshold we here use $p \leq 0.001$; uncorrected projected on the render brain view. In the upper row: young participants; in the lower one: older participants.

grip task activation pattern were observed in all described ROIs in the group of the elderly.

3.3. fMRI findings; group comparison

A comparison between older and younger participants revealed increased fMRI-activation among the elderly (see Fig. 2; Table 2). For the passive wrist movement, we found increased ipsilateral activation in the SM1, dPMC, MCC and SMA, as well as in the contralateral aCH. For the 1 Hz fist-clenching, additional activation was seen bilaterally in the SM1, SMA, dPMC, MCC, BA 45, BA 5, BA 7 and aCH, as well as in the ipsilateral BA 44 and S2. For the fist-clenching task with maximal frequency, additional activation in the elderly was observed in the bilateral SM1, BA 45, BA 7 and aCH, ipsilateral SMA, BA 5, contralateral MCC and BA 44. During the precision grip task, increased activation in the contralateral BA 45 and ipsilateral SM1 was observed for the elderly.

Only during the more difficult somatosensory-guided precision grip task a comparison between younger and older participants showed an activation increase among the younger in the contralateral SM1 (Fig. 2, Table 2).

3.4. Correlation analysis

Only in the elderly activation magnitude during clenching the fist with maximal frequency showed a negative correlation with frequency in ipsilateral SMA ($r = -0.74$; MNI coordinates (x, y, z): 15, −27, 72) and ipsilateral SM1 ($r = -0.78$; 45, −15, 39). Young participants did not show any significant correlation during this task.

Only for the elderly group the activation magnitude during the precision grip task was negatively correlated with the performance (number of pegs correctly placed) in the ipsilateral SMA ($r = -0.78$; 27, −24, 75), and in the ipsilateral SM1 ($r = -0.72$; 48, −36, 57; Fig. 3). In contrast, for the young group, fMRI-signal intensity correlated positively with performance of the precision grip task in the contralateral SMA ($r = 0.76$; −9, 9, 57) and in the contralateral SM1 ($r = 0.72$; −15, −33, 57; Fig. 3). We did not observe any positive correlations between performance and cerebral activations in the elder group for the whole brain volume.

4. Discussion

By using a combined approach of mapping movements with different motor demand in younger and older individuals together

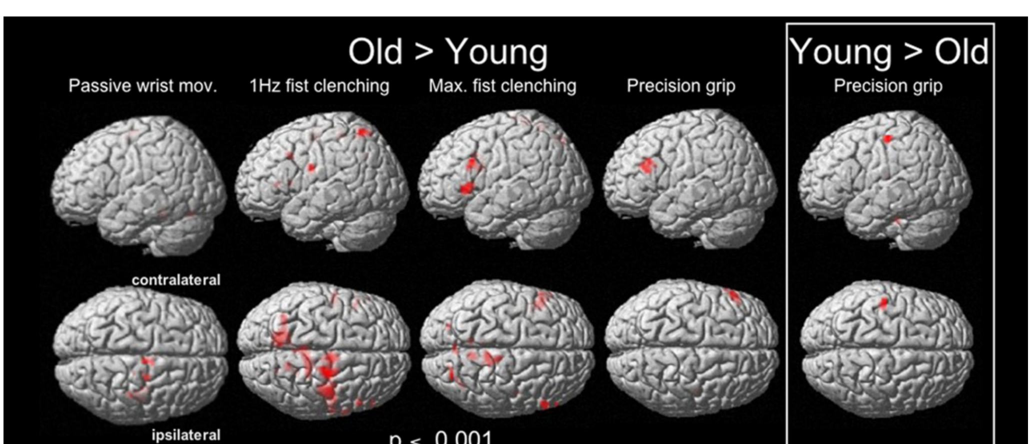

Fig. 2. Comparisons between groups; $p \leq 0.001$; in order to provide an overview on activation maps with the same threshold we here use $p \leq 0.001$; uncorrected projected on the render brain view. During the task of fist clenching the highest age related differences were observable. For the less demanding task young individuals did not show any additional activations in comparison.

Table 2
Group comparison: $p \leq 0.001$; uncorrected.

Region	Side	*T*-value	MNI coordinates		
			x	*y*	*z*
Elder > Young					
Passive wrist movement					
Primary sensorimotor cortex (SM1)	Right	3.70	39	−21	45
Supplementary motor area (SMA)	Right	4.15	6	−15	66
Dorsal premotor cortex (dPMC)	Right	3.55	24	−9	66
Middle cingulate cortex (MCC)	Right	3.72	6	−9	42
Anterior cerebellar hemisphere (H 1–3)	Left	4.21	−9	−42	−21
Anterior cerebellar hemisphere (H 4–7)	Left	4.94	−15	−42	−18
Fist clenching at 1 Hz					
Primary sensorimotor	Left	3.54	−3	−36	57
cortex (SM1)	Right	4.56	36	−18	42
Supplementary motor area	Left	3.95	−9	18	54
(SMA)	Right	5.15	12	−6	51
Dorsal premotor cortex	Left	4.92	−30	6	57
(dPMC)	Right	5.32	21	−9	63
Middle cingulate cortex	Left	3.5	−6	15	36
(MCC)	Right	4.87	6	−12	48
Inferior frontal gyrus pars opercularis (BA44)	Right	3.49	60	9	21
Inferior frontal gyrus pars	Left	3.48	−54	27	9
triangularis (BA45)	Right	4.11	54	18	33
Secondary somatosensory cortex (S2)	Right	5.08	42	−21	27
Superior parietal cortex	Left	3.46	−6	−51	57
(BA5)	Right	3.85	15	−54	66
Superior parietal cortex	Left	4.34	−15	−63	63
(BA7)	Right	3.80	18	−54	66
Anterior cerebellar	Right	4.40	15	−78	−33
hemisphere (H 1–3)	Left	3.53	−21	−72	−36
Anterior cerebellar hemisphere (H 4–7)	Left	3.47	−9	−57	−21
Fist clenching at maximal frequency					
Primary sensorimotor	Left	3.48	−6	−42	69
cortex (SM1)	Right	4.92	9	−39	72
Supplementary motor area (SMA)	Right	4.08	9	−27	75
Middle cingulate cortex (MCC)	Left	4.64	−3	−39	36
Inferior frontal gyrus pars opercularis (BA44)	Left	3.41	−48	12	36
Inferior frontal gyrus pars	Left	3.98	−48	18	27
triangularis (BA45)	Right	3.96	57	21	27
Superior parietal cortex (BA5)	Right	4.27	9	−54	66
Superior parietal cortex	Left	3.81	−24	−78	48
(BA7)	Right	4.06	30	−75	48
Anterior cerebellar hemisphere (H 4–7)	Right	3.59	21	−69	−33
Lateral cerebellar hemisphere (H 8–9)	Left	4.37	−9	−45	−39
Precision grip task					
Primary sensorimotor cortex (SM1)	Right	3.54	45	−12	36
Inferior frontal gyrus pars triangularis (BA45)	Left	3.61	−57	27	21
Young > Old					
Precision grip task					
Primary sensorimotor cortex (SM1)	Left	3.73	−48	−21	57

with correlation analysis of performance with fMRI-activation, we demonstrated that an activation increase in the elderly was not associated with effective performance compensation. Accordingly, we observed increased activation in ipsilateral motor areas in the elderly during all types of movement and we found a negative correlation of fMRI-activation in the ipsilateral SMA and SM1 with motor performance. More intriguing, this negative correlation between ipsilateral activation and performance was associated with increased motor demand.

Our study confirmed previous findings observed for simple motor paradigms showing that older individuals recruit more widespread and bilateral areas [2,15,18,27]. Especially for the ipsilateral hemisphere, the extent of observed additional activation declined with increasing demand of task (Fig. 3, Table 2). Ward et al. [28] used a fist force modulation task to demonstrate that the motor cortices of older persons are less able to increase activity when increasing force output is required.

With increasing demand of the motor task the younger individuals also took those areas into account that the elderly already recruited during more simple tasks. This provides insight to the physiological genesis of additional activations in the elderly and is in line with the notion that additional recruitment of cerebral areas is a general mechanism to respond to more demanding motor tasks [25]. A similar mechanism can be stated also on a cerebellar level: Schlerf et al. [19] reported a bilateral activation in neocerebellar lobes (containing lobules VI and VIIa), which was especially high during high demanding movements. In the group of elderly we observed bilateral cerebellar activity already for the simple and repetitive 1 Hz fist clenching

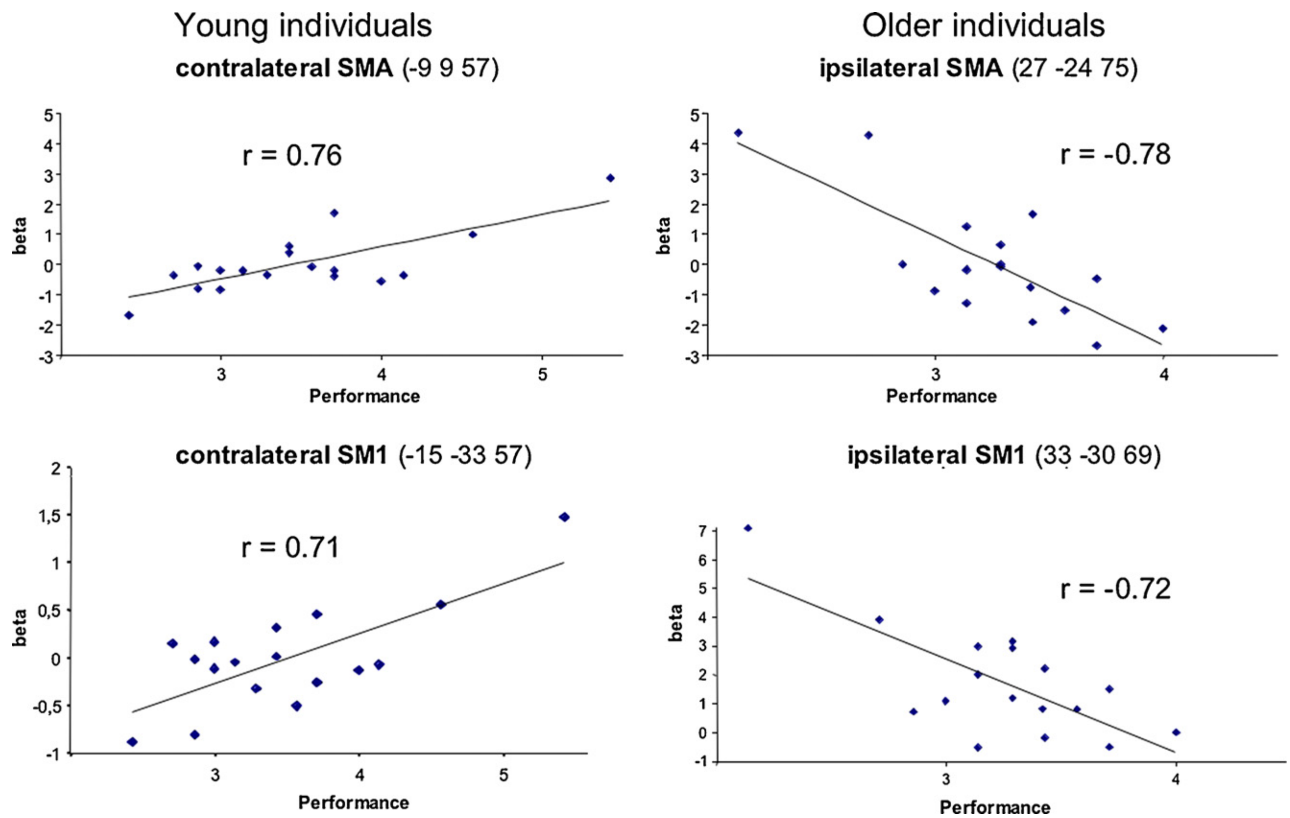

Fig. 3. Left side: correlation analyses of the contralateral SMA and contralateral M1 within the group of young participants. Right side: correlation analyses of ipsilateral SMA and ipsilateral SM1 within the group of elderly. *x*-axis: performance as the average of achieved pegs during the precision grip task; *y*-axis: blood oxygenation dependent fMRI signal (SPM-betas) of the highest activated voxel in ipsilateral SMA.

task. When the task becomes more demanding, as for maximal frequency fist clenching [18], the young also engage the cerebellum bilaterally, suggesting that the elderly respond to a higher difficulty of task in the same manner but sooner as the young.

Interestingly, the younger group showed an increased recruitment of the contralateral M1 during performance of the high demanding precision grip task. An increased recruitment of M1 has also been demonstrated for highly experienced groups of subjects. Professional musicians performing a complex tapping task of left hand string movements demonstrated increased activation in cM1 compared to less experienced amateurs [12]. The finding in musicians pointed to a focus of neural processing during more experienced motor performance in cM1. Our present data additionally demonstrated that a better performance capability of demanding motor tasks in younger healthy persons, in comparison to elder individuals. This might be generally associated with increased cM1-activation.

Because the motor performance was comparable between groups, additional activations in the elder group can be considered compensational. For the precision grip task – the most demanding one in our study – the group contrast revealed an additional activation in ipsilateral SM1 and BA 45. Others described BA 45 as a compensational area [8].

Representatives of an effective compensation hypothesis [8,15] described higher activation in individuals who showed best performance. These overactivations were seen in areas that are not primarily associated with the task (contralateral middle frontal gyrus, inferior frontal gyrus (BA44/45), superior frontal sulcus, anterior insula, superior parietal gyrus (BA7)) and that are hence compensational. In contrast to their findings, our group of elderly did not show any positive correlation of activation and motor performance, neither in areas additionally activated, nor in a global analysis for the whole brain. This might be due to substantial methodological differences between our experimental conditions and those of Heuninckx et al. [8]. They used synchronous and asynchronous movement of the wrist and ankle, a task that increases coordination effort in a predominantly cognitive manner, but that is less challenging with respect to an "every day use" movement performance. In addition, the performance level of the elderly group (1 Hz frequency) differed from that of the younger individuals (1.5 Hz frequency), therefore the elderly performed worse. A similar performance level is important for valid comparisons. Van Impe et al. [24] applied the same paradigm as Heuninckx et al. using a self-preferred frequency, which varied within the young individuals between 0.8 and 0.81 Hz and within the elderly between 0.62 and 0.64 Hz. Van Impe et al. do not show any correlation between performance and fMRI-activation. Other groups, whose data support the successful compensation theory, used a visually paced reaction time task [15] or complex go/no go tasks [23]. Valessi et al. [23] produced high conflict within the no go stimuli. They found neural overrecruitment in the older group, which was positively correlated with a lower error rate. Like the temporal synchronization task used by Heuninckx et al., these tasks are demanding in a cognitive manner. For those paradigms, a compensatory view seems plausible, but does not purely reflect motor function.

For force modulation especially the ipsilateral primary motor cortex showed a considerable increase of activation in the elderly [28]. In our study, additional ipsilateral activations among the elderly were even observed for the passive wrist movements and persist up to the most demanding precision grip task. An association of ipsilateral activation and bad performance is known from stroke recovery studies, in which patients with increased functional impairment show increased contralesional activation [3,27]. It seems that ipsilateral activation during simple motor performance in stroke patients is a general marker for poor motor abilities. However, ipsilateral activation in the elderly appears to be of inferior relevance for function, as the TMS disruption of ipsilateral motor areas did not result in increased response latencies in healthy controls [6,13]. Overall, the increased recruitment of ipsilateral motor areas in the elderly might be associated with a decrease of interhemispheric inhibition. Talelli et al. [21] found that modulation in the activity of the pathway mediating interhemispheric inhibition is at least one of the mechanisms regulating the amount and potentially the functional role of ipsilateral SM1 activation during the execution of a simple grip task and that the same mechanism could be responsible for the changes seen in the system with advancing age. They further conclude that the neurophysiological measures of cortical excitability and/or corticocortical connectivity appear to reflect the functional configuration of distributed brain networks more fully than chronological age. In this line it seems plausible that the functional integrity ultimately reflects itself in motor performance.

Correlation analysis of performance and BOLD magnitude of ipsilateral SM1 and SMA showed a negative association in the group of elderly, whereas young subjects showed a positive correlation in the contralateral SMA and SM1 (Fig. 3). This substantiates the relationship of motor ability and cortical representation, especially for the ipsilateral hemisphere. Because performance in both groups was comparable, ipsilateral activations in the elderly can be considered compensatory, although they were associated with bad performance. Since no association of performance and fMRI signal was found in non-motor regions, we refuse the term of an effective compensation, in the sense that one structure compensates for another. It seems more plausible that overactivations reflect a response to an age related higher task difficulty.

In our study we observed, that compensational resources were restricted to motor areas and were associated with poor motor performance. When these compensational resources are exploited, motor performance declines. This opinion is in line with previous findings of Riecker et al. [18], who describe an absence of increased age-related overactivations with increasing functional demand during movements of the index finger at different frequencies.

An increase of activation of the ipsilateral motor cortex during passive movements in the elder group might be associated with increased stabilization of the left hand on the scanner couch during passive wrist movements of the right hand. Future studies should *consider* for this possibility by using continuous EMG-recording.

Our study demonstrates that increased fMRI-activation in ipsilateral motor areas in the elderly does not represent an effective way to compensate for motor performance. Overall, when comparing fMRI-maps of different groups their performance level should be equal. For differentiating between compensation and activation necessary for movement execution, an ideal task should be leveled at a high demand but with comparable performance. In this study, we observed more diffuse and bilateral activation even during those tasks with low to almost no (passive movement) demand on performance, which makes an effective compensation unlikely. Additional activations, supposing a physiological genesis, may be considered compensational as the same mechanisms that young individuals use to respond to a more demanding task occur in the elderly. Overall the observed overactivations in the group of elderly can be considered as a non-effective cerebral adaptation to an age related higher task difficulty.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bbr.2011.04.040.

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