Whole-brain grey matter density predicts balance stability irrespective of age and protects older adults from falling

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A B S T R A C T

Functional and structural imaging studies have demonstrated the involvement of the brain in balance control. Nevertheless, how decisive grey matter density and white matter microstructural organisation are in predicting balance stability, and especially when linked to the effects of ageing, remains unclear. Standing balance was tested on a platform moving at different frequencies and amplitudes in 30 young and 30 older adults, with eyes open and with eyes closed. Centre of pressure variance was used as an indicator of balance instability. The mean density of grey matter and mean white matter microstructural organisation were measured using voxel-based morphometry and diffusion tensor imaging, respectively. Mixed-effects models were built to analyse the extent to which age, grey matter density, and white matter microstructural organisation predicted balance instability. Results showed that both grey matter density and age independently predicted balance instability. These predictions were reinforced when the level of difficulty of the conditions increased. Furthermore, grey matter predicted balance instability beyond age and at least as consistently as age across conditions. In other words, for balance stability, the level of whole-brain grey matter density is at least as decisive as being young or old. Finally, brain grey matter appeared to be protective against falls in older adults as age increased the probability of losing balance in older adults with low, but not moderate or high grey matter density. No such results were observed for white matter microstructural organisation, thereby reinforcing the specificity of our grey matter findings.

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1. Introduction

In healthy adults, grey matter volume or density of specific brain structures has already shown to be correlated with performance in pursuit rotor tasks [1], tracing tasks [2], manual dexterity [3], choice reaction time tasks [4], and gait [5]. However, how decisive grey matter density (GM) is in predicting motor performance remains unclear.

We investigated this question in the context of standing balance, a motor task that has also shown to be correlated with structural grey matter metrics [4,6]. Balance stability is fundamental in humans at all ages, but becomes increasingly critical with ageing to maintain functional independence and to avoid falls that may cause catastrophic injuries in this population [7,8]. Comparing the extent to which whole-brain GM and ageing predict balance instability would provide an indication about whether training-induced structural brain plasticity [6] can efficiently delay age-related deficits.

We hypothesised that age (i) and GM (ii) predict balance instability, that such predictions are dependent on task difficulty (iii), that GM predicts balance instability beyond age (iv), and that GM predicts balance loss in older adults (v). To test these hypotheses, we combined structural brain imaging and mixed-effects model analyses to analyse balance performance of young and older adults on a rotating platform. To investigate how specific

the impact of GM was, we also tested the extent to which whole-brain white matter microstructural organisation (WM) predicted balance stability and falls.

2. Materials and methods

2.1. Participants

Thirty young (age, 22 ± 3 years; height, 175 ± 9 cm; weight, 69 ± 12 kg; 16 males, 14 females) and 30 older (69 ± 5 years; 170 ± 8 cm; 78 ± 14 kg; 16 males, 14 females) healthy volunteers participated in the study. Older participants were screened for cognitive impairment with the Montreal Cognitive Assessment test using the standard cut-off score of 26. All participants gave their written informed consent and procedures were performed according to guidelines established by the ethics committee for biomedical research at KU Leuven, Belgium, and in accordance with the World Medical Association International Code of Medical Ethics.

2.2. Balance task

Standing balance was tested on an Equitest balance platform (Neurocom International, Inc., Clackamas, OR, USA). This dynamic postural system consists of a force plate (46 cm $\times$ 46 cm) moving around a mediolateral axis that is equipped with force transducers that measure X, Y, and Z forces (Fx, Fy, and Fz) as well as X, Y, and Z moments (Mx, My, and Mz). Participants stood on the surface barefoot, with the medial malleoli of the ankles vertically aligned to the platform's axis of rotation. A safety harness was used to prevent falls in case of loss of balance. To fully assess balance performance, seven platform conditions with different platform frequencies and amplitudes were tested on participants with eyes open and with eyes closed (Fig. 1). Each condition lasted 1 min and was repeated twice for a total of 28 randomised trials per participant (7 patterns $\times$ 2 visual conditions $\times$ 2 trials). Participants were instructed to minimise body sway. When a participant lost balance and fell (held by the safety harness) or took a step to regain balance, the trial was reported as a fall and was removed from the balance analysis. Participants were given another opportunity to complete the failed trials after all 28 trials had been performed.

2.3. Balance analysis

The amount of movement of the centre of foot pressure in the anteroposterior axis was computed using the root mean square of its time series and used as an indicator of balance control (CoP activity). Coordinates of the centre of pressure on the anteroposterior axis (CoPy) of the surface of the platform were computed as follows:

$$CoPy = \frac{[(CoPz)(Fy)] - Mx}{Fz}$$

where CoPz is the distance from the transducers to the surface of the platform, Fy is the anteroposterior force, and Mx is the moment about the mediolateral axis. The root mean square of the detrended time series for the centre of pressure was computed as follows:

$$CoP\,activity = \sqrt{\frac{1}{N} \times \sum_{1}^{N} (CoPy)^2}$$

where N is the number of data samples over a trial of 58 s (5.8×10^3), with the first 2 s of each 1-min trial removed from the analysis.

2.4. Structural brain image acquisition

Brain images were acquired on a 3.0 T Philips Achieva magnetic resonance imaging scanner (Philips Healthcare, Best, NL) with a 32-channel head coil. For all participants, a high resolution T1-weighted structural image was acquired using a magnetisation prepared rapid gradient echo (repetition time, 9.70 ms; echo time, 4.60 ms; flip angle, $8°$; 230 sagittal slices; voxel resolution, 0.98 mm $\times$ 0.98 mm $\times$ 1 mm; matrix, 384×384). A field map was acquired using a dual-gradient echo (TR, 750 ms; TE1, 5.75 ms; TE2, 7.76 ms; flip angle, $90°$; 35 transverse slices; gap, 0.19 mm; voxel resolution, 2 mm $\times$ 2 mm $\times$ 4 mm; matrix, 192×192). Single-shot spin-echo diffusion-weighted images (TR, 4015 ms; TE, 56 ms; flip angle, $90°$; 50 sagittal slices; gap, 0.3 mm; voxel resolution, 2.0 mm $\times$ 1.96 mm $\times$ 2.2 mm; matrix, 220×220) were acquired with diffusion sensitising gradients applied along 75 non-collinear directions (b-value of 800 s/mm^2). One b0 image with no diffusion weighting was acquired.

2.5. Imaging analysis

Images were analysed using the FMRib Software Library, FSL (Oxford University, Oxford, UK). All T1 structural images were checked manually for the presence of anatomical abnormalities and magnetic resonance artefacts. Differences in GM were determined using the FSL Voxel-Based Morphometry optimised protocol [9–11]. This method is based on three-dimensional magnetic resonance imaging with voxel intensity ranging from 0 to 1 and representing the combination of grey matter density and volume of each voxel. First, structural images were brain-extracted using the brain extraction tool [12]. To reduce the amount of 'neck tissue' included in the resulting image, the centre of the brain (i.e., massa intermedia) was specified for each participant and used as a command argument. Second, grey matter was segmented using FAST4, and normalised to the MNI152 template using the affine registration tool FLIRT [13]. The images were then averaged to create a study-specific template, to which the native grey matter images were non-linearly re-registered. The partial volume images were divided by the Jacobian of the warp field to correct for local expansion or contraction. Smoothing with an isotropic Gaussian kernel (sigma = 4 mm) was applied to the segmented images. The intensity of all the GM voxels was then averaged, extracted for each participant using the fslmeants command, and used as an indicator of whole-brain GM.

For diffusion-weighted images, the diffusion sensitising gradients ("bvecs") were rotated to correct for motion. Using the Diffusion Toolbox, the diffusion tensor model was fitted to the data, from which fractional anisotropy (FA) images were calculated. Tract-based spatial statistics (TBSS) was used for voxel-based analyses of WM [14]. This involved registering all subjects' FA images to a common space (the FA158 MNI space template) using a combination of affine and nonlinear registration, creating the mean FA image, eroding it to a skeleton, and thresholding the skeleton at FA >0.25. The resulting alignment-invariant representation of the central trajectory of white matter pathways was used as a mask. The intensity of all the FA voxels of this skeleton was then averaged, extracted for each participant using the fslmeants command, and used as an indicator of whole-brain WM.

2.6. Statistical analysis

Our dataset is structured with repeated and nested measurements from each participant that are crossed with each condition. Therefore, data were analysed using mixed-models with cross-random factors. Mixed-models process both participant and condition factors as randomly distributed. Conversely, traditional
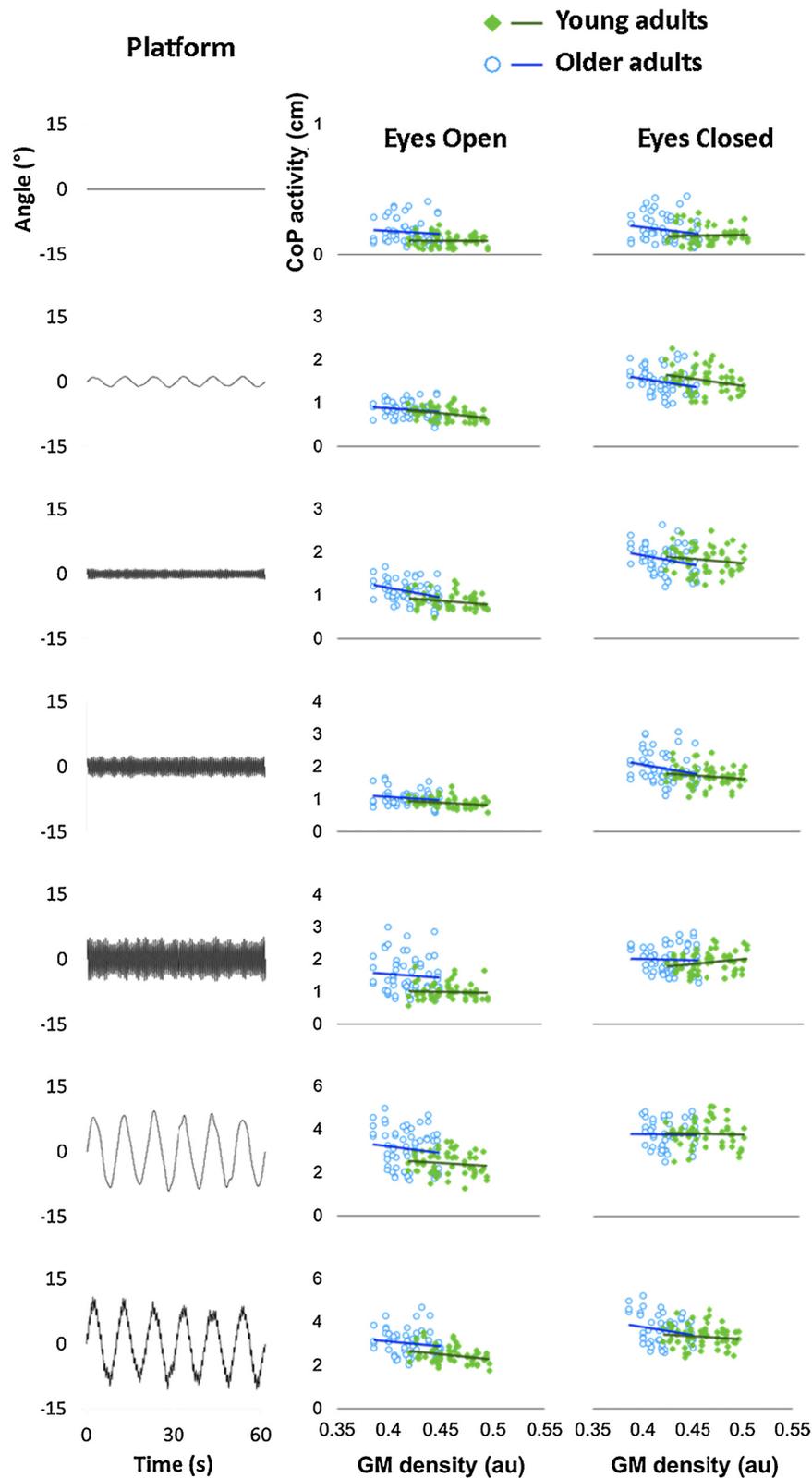
Fig. 1. Platform conditions and balance performance. Platform angle across time in the 7 conditions and corresponding root mean square of the centre of pressure time series in the antero-posterior axis (CoP activity) in young (green diamonds) and older participants (blue circles) as a function of grey matter density (GM) with eyes open and eyes closed. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

analyses of variance disregard the sampling variability of conditions despite numerous warnings about the shortcomings of such practice [15–17]. A likely consequence of treating only participants as a random effect is a large inflation of Type I errors.

The extent to which age group (young vs. older adults), GM, and WM predicted balance instability was analysed using mixed-effects models. These models offer a comprehensive approach to multiple crossed-random effects, explicitly modelling variability

around fixed effects [18]. The fit of these models was compared using Akaike's information criteria (AIC). Specifically, a series of 7 mixed-effect models specifying both participants ($n = 60$) and conditions ($n = 14$) as random factors were built using the R language lmerTest package, version 1.1-7 (http://www.r-project.org/). This package, like SAS proc mixed, uses Satterthwaite's method to compute the degrees of freedom of the t tests. All models controlled for weight, height, trial number (1 vs. 2), vision (eyes closed vs. eyes open), and trial order (1–28).

Model 1 was designed to evaluate the random effects of participants and conditions on CoP activity. Accordingly, a random error component for the intercept was specified for these two factors. These specifications allowed the modelling of different levels of intercept across participants and across conditions. The random intercept across conditions corresponds to the diversity of the average levels of CoP activity between conditions and can therefore be viewed as the variability of the level of difficulty associated with each condition.

Model 2 was designed to estimate (a) the fixed effect of age on CoP activity, (b) the random effect of age across conditions, and (c) whether the age effect was dependent on the intercept level of conditions. Accordingly, a random error component for age and a covariance between the intercept and the effect of age for conditions were added to Model 1.

Model 3 was designed to estimate (a) the fixed effect of GM on CoP activity, (b) the random effect of GM across conditions, and (c) whether the GM effect was dependent on the intercept level of conditions. Accordingly, a random error component for GM and a covariance between the intercept and the effect of GM for conditions were added to Model 1.

Model 4 was designed to compare the effects of age and GM, and to estimate the fixed effect of GM on the average level of CoP activity, beyond the fixed effect of age. Accordingly, a random error for GM and a covariance between the intercept and the GM effect for conditions were added to Model 2. The decreases in random effects variance between models 1 to 2, 1 to 3, and 2 to 4 were used to evaluate the ability of age and GM to improve the fit of the model and therefore the predictions made at the levels of participants and conditions.

Models 5 and 6 followed the same logic as models 3 and 4, with WM replacing GM.

Model 7 was designed to get a full picture of the effects investigated here. The equation for this model is the following:

$$Y_{ij} = (\beta_0 + \gamma_{0i} + \theta_{0j}) + \beta_1 \text{Order}_{ij} + \beta_2 \text{Weight}_i + \beta_3 \text{Height}_j$$
$$+ \beta_4 \text{Trial}_{ij} + \beta_5 \text{EyesOpen}_{ij} + (\beta_5 + \gamma_{5i}) \text{AgeGrp}_j$$
$$+ (\beta_6 + \gamma_{6i}) \text{Grey Matter Density}_j$$
$$+ (\beta_7 + \gamma_{7i}) \text{White Matter Integrity}_j + \in_{ij}$$

where Y_{ij} is the score of participant at condition i, β_0 to β_7 are the fixed effect coefficients, θ_j is the random effect for the participant j (random intercept), γ_{0i}, γ_{5i}, γ_{6i}, and γ_{7i} are the random effects for the condition i (one random intercept and 3 random slopes) and ϵ_{ij} is the error term. The γ's correlate with each other.

To test the protective role of GM in falls in older adults (0 = no falls; 1 = falls), a logistic mixed-effect model was built specifying both participants ($n = 30$) and conditions ($n = 7$) as random factors. A fixed effect was introduced for age as a continuous variable, GM, and their interaction. Age and GM were centred. A random component was specified for the intercept for participants and for the intercept for conditions. These random components were specified to model the diversity of the average level of falls between participants and between conditions. This model controlled for vision (eyes closed vs. open) and participants'

height. The model for falls is the same as the ones used for balance stability except that what is predicted is the logarithm of the odds of a fall, or $\log(\pi_{ij}/1 - \pi_{ij})$ where π_{ij} is the probability of fall of participant at condition i, and the quantity $\pi_{ij}/1 - \pi_{ij}$ is the odd of a fall.

3. Results

The statistical assumptions were examined. Plots of the residuals against the predicted scores of CoP activity and against all independent variables showed no major signs of heteroscedasticity. Residuals were normally distributed and centred on zero. Descriptive statistics of the relationship between balance performance and GM density in young and older adults are illustrated in Fig. 1.

3.1. Predicting CoP activity: Age

Model 1 tested the random effects of conditions on CoP activity and confirmed that the level of difficulty was different across conditions ($\sigma^2 = 1.088$). Adding the fixed and random effects of age (young vs. older adults) allowed model 2 to predict the data more accurately than model 1 (ΔAIC = 117.379). As expected, model 2 showed a significant fixed effect of age on CoP activity ($b = 0.291$, df = 55.6, $t = 3.263$, $p = 0.001$, one-tailed; Table 1), indicating that, on average, older adults showed greater balance instability than young adults. In addition, the random effect of age on CoP activity across conditions ($\sigma^2 = 0.039$) increased the prediction power of the model,[2] indicating that the fixed effect of age on CoP activity varied across conditions. Specifically, the positive correlation between the intercepts of the conditions and age at the random level ($r = 0.709$) indicated that balance stability was more dependent on age in more difficult than in easier conditions. Furthermore, the unexplained variability between participants, i.e., the random intercept at the level of participants, decreased from 0.054 in model 1 to 0.042 in Model 2, indicating that age explained 22.3% of the inter-individual variability in the intercept.

3.2. Predicting CoP activity: Grey matter density

Adding the fixed and random effects of GM allowed model 3 to predict the data more accurately than model 1 (ΔAIC = 84.706). Importantly, model 3 showed a significant fixed effect of GM on CoP activity ($b = -4.384$, df = 57.7, $t = -3.199$, $p = 0.001$, one-tailed; Table 1), indicating that, on average, participants with lower GM showed greater balance instability than participants with higher GM. In addition, the random effect of GM on CoP activity across conditions ($\sigma^2 = 8.278$) increased the prediction power of the model,[3] indicating that the fixed effect of GM on CoP activity varied across conditions. Specifically, the negative correlation between the intercepts of the conditions and GM at the random level ($r = -0.880$; Table 1) indicated that balance stability was more dependent on GM in more difficult than in easier conditions. Furthermore, the unexplained variability between participants decreased from 0.054 in model 1 to 0.043 in Model 3, indicating that GM explained 20.4% of the inter-individual variability in the intercept.

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[2] The model (not shown) with the fixed effect for age but without this random effect displayed an AIC of 1492, i.e., 104 points higher than this model, showing the importance of this random effect.

[3] The model (not shown) with the fixed effect for GM but without this random effect displayed an AIC of 1494, i.e., 73 points higher than this model, showing the importance of this random effect.

Table 1

Summary of mixed-effects model analyses for predicting the centre of pressure activity. Model 1 evaluates the random effects of participants and conditions on the centre of pressure activity. Model 2 adds a fixed and random effect for age. Model 3 adds a fixed and random effect for grey matter. Model 4 adds a fixed and random effect for both age and grey matter. Model 5 adds a fixed and random effect for white matter. Model 6 adds a fixed and random effect for both age and white matter. Model 7 adds a fixed and random effect for age, grey matter, and white matter. GM, grey matter density; WM, white matter microstructural organisation; $*p < 0.05$; $**p < 0.01$; $***p < 0.001$; $†$one-tailed tests corresponding to the hypotheses; b = estimate; SE = standard error; σ^2 = variance; r = correlation.

Centre of pressure activity	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6			Model 7		
Fixed effects	b	SE	p-Value	b	SE	p-Value	b	SE	p-Value	b	SE	p-Value	b	SE	p-Value	b	SE	p-Value	b	SE	p-Value
Intercept	1.393	0.743	0.003**	0.860	0.740	0.026*	1.013	0.346	0.009**	1.027	0.331	0.006**	1.111	0.386	0.012*	1.030	0.320	0.005**	1.105	0.316	0.002**
Order	−0.002	<0.001	0.032*	−0.002	0.001	0.004**	−0.002	0.001	0.019*	−0.002	0.001	0.005**	−0.002	<0.001	0.024*	−0.003	<0.001	0.006**	−0.002	0.001	0.009**
Weight	0.004	0.003	0.101	−0.002	0.003	0.411	−0.001	0.003	0.809	−0.003	0.003	0.281	0.003	0.003	0.234	−0.002	0.003	0.595	−0.002	0.003	0.431
Height	<0.001	0.003	0.962	0.010	0.004	0.022*	0.006	0.004	0.122	0.010	0.004	0.017*	0.005	0.004	0.277	0.009	0.004	0.035*	0.010	0.004	0.027*
Trial	0.009	0.017	0.616	0.008	0.017	0.620	0.009	0.017	0.614	0.008	0.017	0.610	0.007	0.017	0.666	0.007	0.017	0.669	0.007	0.017	0.658
Eyes open (vs. eyes closed)	0.734	0.558	0.210	1.531	0.417	0.003**	1.502	0.343	<0.001***	1.294	0.339	0.002**	1.266	0.518	0.028*	1.155	0.364	0.006**	1.088	0.319	0.003**
Age (young vs. older adults)				0.291	0.089	0.001**†				0.193	0.098	0.037*†				0.300	0.124	0.009**†	0.020	0.126	0.042*†
GM							−4.384	1.371	0.001**†	−2.571	1.411	0.026*†							−2.407	1.434	0.049*†
WM													−2.243	1.280	0.043*†	1.010	1.690	0.264†	1.259	1.657	0.225†

Random effects	σ^2	r	σ^2	r	σ^2	r	σ^2	r	σ^2	r	σ^2	r	σ^2	r
Participants														
Intercept	0.054		0.042		0.043		0.039		0.046		0.040		0.038	
Condition														
Intercept	1.088		1.092		1.237		1.084		1.127		0.929		0.972	
Age			0.039				0.028				0.055		0.038	
GM					8.278		2.008						1.817	
WM									3.345		3.025		3.105	
Correlation (Intercept, Age)				0.709				0.448				0.753		0.618
Correlation (Intercept, GM)						−0.880		−0.997						−0.998
Correlation (Age, GM)								−0.393						−0.661
Correlation (Intercept, WM)										−0.48		0.978		0.974
Correlation (Age, WM)												0.873		0.779
Correlation (WM, GM)														−0.985
Residual	0.125		0.114		0.117		0.113		0.117		0.111		0.110	
Akaike Information Criterion	1505.5		1388.1		1420.8		1381.5		1357.0		1287.6		1284.7	
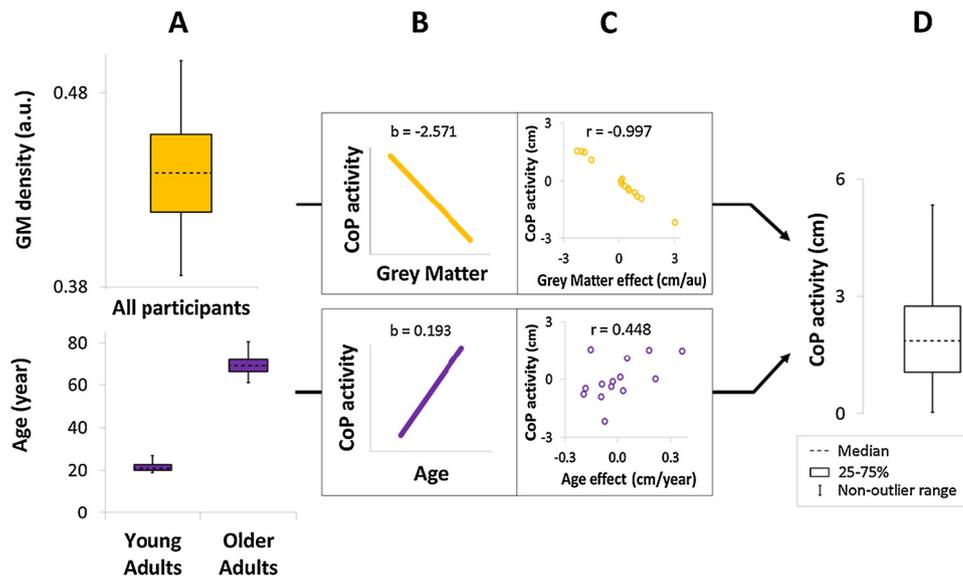
Fig. 2. Fixed and random effects. (A) Distributions of the whole-brain grey matter mean density (yellow box plot) and age (purple box plot) within the study sample. (B) Prediction of the fixed effect of grey matter (yellow line) and age (purple line). (C) Prediction of the random effect of grey matter (yellow circles), and age (young vs. older adults; purple circles) plotted against the random intercept of conditions, i.e. the predicted value of the centre of pressure (CoP) activity. Each circle represents a condition (7 platform × 2 vision conditions). Both the negative effect of grey matter density and the positive effect of age on CoP activity were reinforced when the intercepts of the conditions increased, i.e., when the difficulty of the task increased. (D) Distribution of the centre of pressure activity within the sample. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.3. Predicting CoP activity: Age vs. grey matter density

Combining the fixed and random effects of age and GM allowed model 4 to predict the data more accurately than model 2 (ΔAIC = 6.5609) and 3 (ΔAIC = 39.234). The fixed effect of age ($b = 0.193$, df = 63.1, $t = 1.980$, $p = 0.037$, one-tailed; Table 1 and Fig. 2B) and GM ($b = -2.571$, df = 62.8, $t = -1.822$, $p = 0.026$, one-tailed) on CoP activity were still significant, indicating that older age and lower GM were associated with higher instability. The random effects of age ($\sigma^2 = 0.028$) and GM ($\sigma^2 = 2.008$) on CoP activity added prediction power to the model, indicating that balance control was more dependent on age and GM in more difficult than in easier conditions.

When compared to model 2, the fixed and the random effect of age weakened in model 4. This result suggested that the variability assigned to age in model 2 was in fact at least partially due to the variability of GM. Specifically, at the fixed level, the effect of age on CoP activity weakened from model 2–4 ($b = 0.291$ to $b = 0.193$). This result indicated that part of this fixed effect was incorrectly attributed to age in model 2 and was actually due to GM. At the random level, adding GM in model 4 reduced the random effect of age by 28.1%, indicating that part of the random effect of age at the level of conditions was again incorrectly attributed to age in model 2 and was actually due to GM. Furthermore, adding GM to the model reduced the correlation between the intercepts of conditions and age (from $r = 0.709$ to $r = 0.448$). This result indicated that, once GM was added to the model, the effect of age was less dependent on the intercepts of the conditions (i.e., of their level of difficulty). The negative correlation between the intercepts of the conditions and GM at the random level ($r = -0.997$[4]) was particularly high as compared to the positive correlation with age ($r = 0.448$; Table 1 and Fig. 2C), suggesting that GM was more consistent than age in predicting balance instability across conditions.

3.4. Predicting CoP activity: Age, grey matter density, and white matter microstructural organisation

Model 5 showed a significant fixed effect of WM on CoP activity ($b = -2.243$, df = 62.2, $t = -1.749$, $p = 0.043$, one-tailed; Table 1) indicating that, on average, participants with lower WM showed greater balance instability than participants with higher WM. However, unlike the fixed effect of GM (model 4), the fixed effect of WM on CoP activity disappeared when the effect of age was added (model 6). This result suggested that WM was not related to balance stability. Model 7 confirmed that both age and GM, but not WM, had a specific contribution to balance stability. This result implies that in conjunction with age, GM accounted for unique variance in balance stability, whereas the unique variance of WM in conjunction with age was negligible.

### 3.5. Falls and grey matter in older adults

Results of the model testing the protective role of GM in falls in older adults revealed a significant age × GM interaction ($b = -10.846$, $Z = -2.076$, $p = 0.037$; Table 2).[5] This interaction indicated that the fixed effect of age on the probability of falls was dependent on GM. Specifically, age increased the probability of falls in older adults with low (GM mean − 1 SD; $b = 0.332$, $Z = 2.495$, $p = 0.012$), but not moderate (GM mean; $b = 0.132$, $Z = 1.459$, $p = 0.144$) or high GM (GM mean + 1 SD; $b = -0.066$, $Z = -0.506$, $p = 0.612$). To evaluate the effect size, we computed the odds ratio for participants with a low level of GM between older old (mean age + 1 SD; i.e., 74.5 years) and younger old adults (mean age − 1 SD; i.e., 64.5 years). It was equal to 27.7, meaning that the odds of losing balance was 27.7 times higher in older than younger old adults when the level of GM was low. The odds ratio for participants with moderate or high GM were 3.8 and 0.5, respectively, but not significant (Fig. 3).

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[4] Using a log transform on the dependent variable, this correlation was brought back to −0.95, whereas all other parameters stayed essentially unchanged. This shows that the random effect of GM is statistically separate from the intercept.

[5] The same model was used for WM but revealed no main effect of Age ($p = 0.26$) and WM ($p = 0.99$) and no interaction effect ($p = 0.56$).

Table 2
Summary of the mixed-effects model analysis for predicting falls. GM, grey matter density; *p < 0.05; ***p < 0.001.

Falls			
Fixed effects	b	SE	p-Value
Intercept	−15.807	3.760	<0.001***
Height	−0.009	0.054	0.859
Eyes open (vs. eyes closed)	3.684	0.579	<0.001***
Age (continuous)	0.132	0.091	0.144
GM	0.613	25.477	0.980
Age × GM	−10.846	5.225	0.037*
Random effects	σ^2		
Participants			
Intercept	3.857		
Condition			
Intercept	87.837		
Akaike information criterion		246.4	
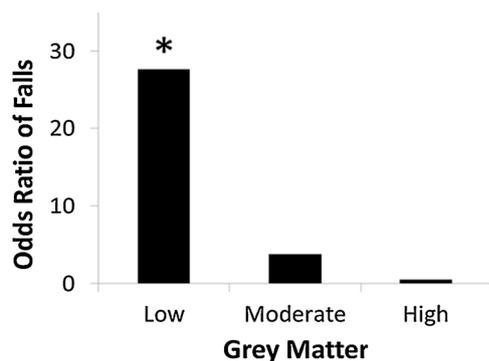
Fig. 3. Odds ratio of falls between younger old adults and older old adults (mean age − 1 SD; mean age + 1 SD, respectively) as a function of brain grey matter density: low, moderate, and high (GM mean − 1 SD; GM mean; GM + 1 SD, respectively). *p < 0.05; GM, grey matter density; SD, standard deviation.

In summary, (i) older adults showed higher instability than young adults, irrespective of GM density, (ii) participants with lower GM density showed higher instability than participants with higher GM density, irrespective of age, (iii) these effects were reinforced when the level of task difficulty increased, (iv) GM predicted balance instability beyond age, and GM predicted balance loss in older adults (v). Conversely, WM was not predictive of balance instability or balance loss.

4. Discussion

In this study, we combined brain structural imaging and mixed-effects model analyses to investigate the extent to which age (young vs. older adults), GM and WM predict balance instability. Results showed that the negative effect of age on balance stability was reinforced as the level of difficulty of the balance task increased. This result supports previous studies showing that task difficulty is a key factor when investigating age-related differences in balance control [19]. Our results also revealed that GM density, but not WM, predicted balance instability irrespective of participants' age. This finding supports and extends previous results, which showed that structural grey matter metrics were correlated with balance performance in older adults [4,6], to the group of young adults. Furthermore, our results showed that the positive effect of GM density on balance stability was stronger in more difficult conditions than in easier conditions. Therefore, future studies investigating the specific neural correlates of balance instability could make use of difficult tasks that are more sensitive to differences in GM density. Results also revealed that GM density was at least as critical as age

for predicting balance instability and may be more consistent across different levels of difficulty. In sum, for balance stability, the level of whole-brain GM is at least as decisive as being young or old. Finally, this study revealed that age has a dramatic effect on loss of balance in older adults with a low GM, while older adults with a moderate or high GM appear better protected against this effect of ageing. Training-induced grey-matter expansion [6] makes our results extremely encouraging for the prevention of falls and the promotion of functional independence.

Disclosure statement

The authors declare no competing interests.

Author contributions

Experimental conception and design: MPB. Experimental conduct: MPB. Analysis of postural data: MPB with assistance from OL. Analysis of imaging data: MPB. Statistical analysis: BC, OR, JC with assistance from MPB. First draft preparation: MPB, BC. Manuscript preparation: MPB, BC, PVR, OR, SPS.

Acknowledgments

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