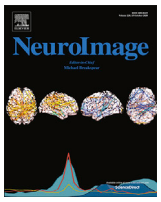
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Functional brain changes in the elderly for the perception of hand movements: A greater impairment occurs in proprioception than touch



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ABSTRACT

Unlike age-related brain changes linked to motor activity, neural alterations related to self-motion perception remain unknown. Using fMRI data, we investigated age-related changes in the central processing of somatosensory information by inducing illusions of right-hand rotations with specific proprioceptive and tactile stimulation. Functional connectivity during resting-state (rs-FC) was also compared between younger and older participants. Results showed common sensorimotor activations in younger and older adults during proprioceptive and tactile illusions, but less deactivation in various right frontal regions and the precuneus were found in the elderly. Older participants exhibited a less-lateralized pattern of activity across the primary sensorimotor cortices (SM1) in the proprioceptive condition only. This alteration of the interhemispheric balance correlated with declining individual performance in illusion velocity perception from a proprioceptive, but not a tactile, origin. By combining task-related data, rs-FC and behavioral performance, this study provided consistent results showing that hand movement perception was altered in the elderly, with a more pronounced deterioration of the proprioceptive system, likely due to the breakdown of inhibitory processes with aging. Nevertheless, older people could benefit from an increase in internetwork connectivity to overcome this kinesthetic decline.

1. Introduction

Aging is associated with changes in sensorimotor function and its neural correlates. At the brain level, neuroimaging studies have consistently demonstrated an overall increase of activation of the motor network in older people when performing hand or finger motor tasks as compared to younger adults (Hutchinson, 2002; Mattay et al., 2002; Ward and Frackowiak, 2003; Wu and Hallett, 2005; Naccarato et al., 2006; Riecker et al., 2006; Ward, 2006; Heuninckx et al., 2008, 2010; Marchand et al., 2011). This brain over-activation has been interpreted as reflecting a compensatory mechanism to maintain sensorimotor performance when they were associated with better motor performance (Mattay et al., 2002; Heuninckx et al., 2008). However, others failed to demonstrate such a relationship (Riecker et al., 2006). Alternatively, this over-activation may be due to dedifferentiated recruitment occurring in aging, in line with the breakdown of selective tuning neurons profiles in the somatosensory cortex of old rats (Godde et al., 2002), the loss of selective brain responses evidenced in the visual system in humans (Park et al., 2012), and the decrease in signal-to-noise ratio in neural firing in the elderly (Li et al., 2001). When participants were required to perform different types of movement (right index finger tapping, left index finger tapping, or both alternately), Carp et al. (2011) showed in a multivariate analysis that motor representations in older subjects were less selective than those of younger ones, supporting the dedifferentiation hypothesis.

However, alteration of body movements with aging does not only result from motor decline, but also involves the somatosensory system. Normal aging is associated with a decline in all sensory sources including muscle proprioception and touch, which are affected at multiple levels from receptors to central processing. At the level of the peripheral nervous system, neurophysiological studies showed a structural degradation and reduced density of muscle and mechanoreceptive afferents, along with an alteration of peripheral nerve conduction (see reviews Ribeiro

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and Oliveira, 2007; Shaffer and Harrison, 2007). At the central level, despite compelling evidence for structural brain changes occurring across the lifespan (Hedman et al., 2012), few studies have examined age-related brain activity changes during pure somatosensory tasks. In comparison with young subjects, a tactile stimulation of the hand, or electrical stimulation of the median nerve, results in an enlarged activation of the contralateral primary somatosensory cortex (S1) (Kalisch et al., 2009; Brodoehl et al., 2013; Gröschel et al., 2013) and a decreased deactivation of the ipsilateral S1 (Lenz et al., 2012; Gröschel et al., 2013) in the elderly. Regarding muscle proprioception, age-related brain activity changes have been evaluated using mechanical vibration that specifically stimulates muscle spindles (Roll and Vedel, 1982). When comparing brain activation during vibration applied on the ankle, Goble et al. (2011) found no difference between young and old adults, except for a lower activation in the right putamen in the older participants, which was positively correlated with postural instability.

Whereas kinesthesia seems more clearly impaired in the upper limb than in the lower limb (Landelle et al., 2018), the proprioceptive alteration of hand movement representation has, to our knowledge, never been explored. Perception of hand movements is altered in the elderly (Wright et al., 2011), as is the ability to precisely encode their velocity through a more pronounced degradation of muscle proprioception, compared to the tactile system (Chancel et al., 2018; Landelle et al., 2018). Given the fact that these two sensory systems are activated during actual body movements, this may account for the apparent discrepancies found in neuroimaging studies focusing on the motor system. Depending on the motor task used, muscle proprioception and/or tactile afference may be used to different extents.

In addition to task-related brain changes, many recent studies reported age-related changes in resting state functional connectivity (rs-FC; see review Damoiseaux, 2017). They showed both reduced connectivity in the default mode network and increased internetworks functional connectivity (including the sensorimotor network), which is functionally separated in young adults (Ferreira et al., 2016; Grady et al., 2016; King et al., 2017), and less coherent and segregated with aging (Chan et al., 2014; Song et al., 2014; Geerligs et al., 2015). These findings were generally interpreted within the dedifferentiation hypothesis framework (Ferreira et al., 2016), although these studies brought little evidence for a link between increased rs-FC with other networks and a deterioration in motor performance. In addition, with regard to the rs-FC in the sensorimotor network, neuroimaging experiments have brought conflicting results. Yet, while some studies have reported an age-related decrease of connectivity strength (Wu et al., 2007; Bo et al., 2014), others have evidenced an age-related increase (Langan et al., 2010; Fling et al., 2011; Tomasi and Volkow, 2012; Solesio-Jofre et al., 2014; Seidler et al., 2015), or no difference (Geerligs et al., 2015).

Therefore, the present study aimed at examining age-related functional brain changes during the perception of hand movements based on muscle proprioception or touch individually, as these two sensory systems are not equally affected by aging (Chancel et al., 2018; Landelle et al., 2018). These sensory sources were specifically tested using a mechanical vibration applied on the right wrist muscle tendon and a tactile-textured disk rotating under the participant's right hand, as these two stimulation are known to elicit illusory movement sensations in participants whose hands are perfectly still (Blanchard et al., 2011; Kavounoudias et al., 2008). We hypothesized greater age-related brain changes associated to proprioceptive-induced illusions compared to tactile-induced illusions in correlation with participant discrimination performance. The potential spreading of rs-FC from the sensorimotor cortex toward other networks, as well as changes between the regions within the sensorimotor network were also expected in relation to the level of kinesthetic impairment in the elderly.

2. Materials and methods

2.1. Participants

Twenty elderly volunteers aged from 65 to 75 years old (6 men; mean: 69.2 ± 3.3 years) and 20 gender-matched young volunteers aged from 20 to 28 years old (7 men; mean: 23.7 ± 2.8 years) participated in the present study. The sample size of the present study was predicted by a power method (the neuropower toolbox, http://neuropowertools.org) based on a previous independent study we published in 2008 (Kavounoudias et al., 2008). In this previous study, 10 young adults were tested using a comparable set-up (vibrator at 50 Hz and rotating disk at 30°/s) and comparable design (event protocol). The prediction of the sample size required for a new fMRI study to reach 80% statistical power was 16 participants. However, these predictions applied to young adults. Since the variability is generally higher among older adults, we increased the sample size to 20 participants in the two groups. All participants were right handed according to the Edinburgh handedness scale (Oldfield, 1971). A systematic inclusion medical examination prior to the experiment confirmed that none of the young or old participants had a neurological history, cardiovascular risk factors or sensory-muscular disease. None of them was under medical treatment. A Mini Mental State (MMS) score of 26 and preserved daily life autonomy were required

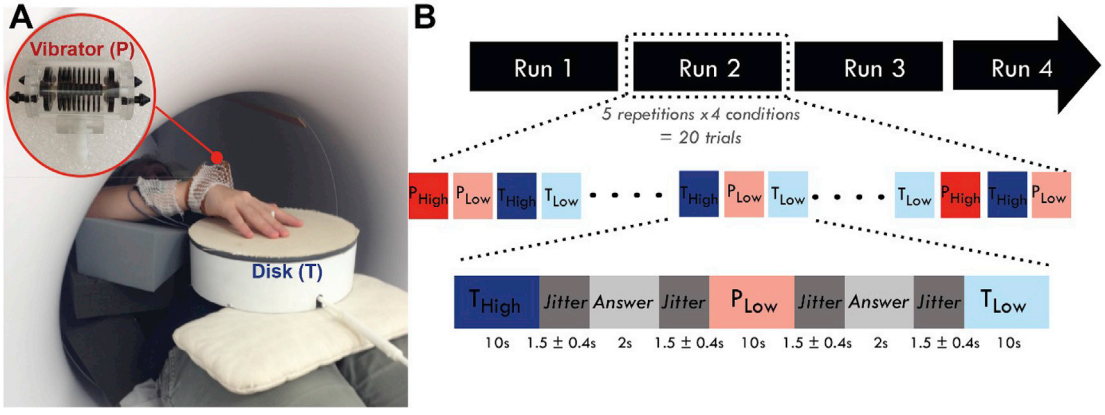


Fig. 1. A- Experimental set-up. Participants were exposed to a counterclockwise rotation of a texture disk (T) under their right hand or a pneumatic vibration (P) applied on the tendon of their right pollicis longus. Each stimulation could be delivered at 2 intensities: Low or High. **B- Experimental design**. Illustration of the 4 runs, each run consisted of 20 trials, including the 4 stimulation conditions (P_{Low}, P_{High}, T_{Low}, T_{High}) pseudorandomly presented 5 times each. Each trial consisted of a 10 s stimulation followed by a jitter (1.5 ± 0.4 s), 2 s to answer the question "Did you feel the illusion?", and a second jitter (1.5 ± 0.4 s).

to participate in this study. Most of the young participants were students at Aix-Marseille University and the older participants were recruited at the Aix-Marseille Université du Temps Libre or in various senior clubs (hiking, language classes …).

All participants were previously tested in a behavioral study where their ability to discriminate movement velocity of their hand was estimated. The behavioural data were collected two to three weeks before the fMRI session, which included a training session into a mock scanner and the actual MRI acquisition session a few days after. Only one older participant who was unable to complete MRI acquisition was not included in the study. All participants gave their written consent, the study conformed to the Declaration of Helsinki, and the experiment was approved by the local ethics committee (CCP Marseille Sud 1 #RCB, 2010-A00359-30).

2.2. Stimuli

To activate muscle proprioception and touch systems specifically, two kinds of MR-compatible stimulation already used in previous functional magnetic resonance imaging (fMRI) studies (Kavounoudias et al., 2008) were applied to the participant's right hand. In both cases, the proprioceptive and tactile stimuli elicited a clear sensation of hand movement without actual movement (Naito et al., 2007, 2016; Blanchard et al., 2011; Chancel et al., 2018; Landelle et al., 2018).

The muscle proprioceptive stimulation (P) consisted of a pneumatic vibrator (cylinder 3 cm in diameter and 4 cm long) applied to the *pollicis longus* tendon of the participant's right wrist (Fig. 1A). Two constant frequencies of vibration (P_{Low}: 30 Hz or P_{High}: 60 Hz) were obtained by using a SMC ITV2050 air-pressure regulator, driven a 0–10 V analog command. A heavy ceramic spherical mass embedded in the turbine allowed a powerful stimulation, modulated by controlling the air pressure.

The tactile stimulation (T) was delivered by a rotating disk (40 cm in diameter, 7 cm height) covered with cotton twill (8.5 ribs/cm) (Fig. 1A). The disk was driven by a remote motor locked in a faradized box and connected via a rotatory axis to the disk. The disk rotated under the participant's right hand in a counterclockwise direction at two constant velocities (T_{Low}: 10°/s and T_{High}: 30°/s). Motor rotation speed and direction were also driven by a second independent −10/+10 V analog command.

All stimuli lasted for 10 s. The stimulation protocol was implemented using specific software developed for the current study in the LabVIEW environment (National Instruments). The software was synchronized with the MR acquisition using a NI-PXI 6289 multifunction I/O device. A digital input line connected to the TTL (Transistor-Transistor Logic) MR pulses defined the hardware clock source of the whole protocol, which was described in a sequential text script, which included the analog commands of both tactile and proprioceptive stimulation devices. We verified that the tactile and proprioceptive devices did not produce artefacts in the fMRI scans, nor modified the signal-to-noise ratio.

2.3. Procedure

Two to three weeks before the scanning session, all the participants underwent a psychophysical experiment in our laboratory to determinate their ability to discriminate illusion velocity during proprioceptive or tactile stimulation (Landelle et al., 2018). This psychophysical experiment consisted in a two-alternative forced choice task where subjects underwent pairs of proprioceptive or tactile stimuli of various intensities and compared the velocity of two movement illusions. Thus, we obtained individual psychophysical curves, one for muscle proprioception and another for touch, and we extracted the just noticeable difference that reflects the discrimination threshold. The older group exhibited higher values of the proprioceptive and tactile discriminative thresholds, which corresponded to a lower ability to discriminate the velocity of movements in both sensory modalities.

Then, participants underwent a testing session inside a mock scanner a few days before the MRI session that replicated exactly the sequences tested afterwards in the MRI scanner. This allowed participants to be trained (especially older subjects who might have had deficits due to a too long interval between behavioural tests and MRI). In addition, we were able to quantify more precisely the illusions perceived in the lying position during this training session. Indeed, participants were placed in the same position than in the actual 3T MRI scanner, head first and supine. The tactile disk was put on their belly and the participant's hand was placed on the centre of the rotating disk. The vibrator was applied to the *pollicis longus tendon* of the right wrist by an elastic band (Fig. 1A). Both tactile and proprioceptive conditions induced illusory sensations of hand movement rotation in the clockwise direction. Participants were instructed to focus their attention on their right hand and to copy-online the movement sensation perceived using a potentiometer held in their left hand. This latter experimental procedure was then run identically inside the 3T scanner (PRISMA, Siemens), except that participants did not reproduce any movement illusion. They were simply asked to report orally at the end of each stimulation whether or not they felt any illusory movement. MR-compatible microphone (microphone FOMRI-III, Opto-Acoustics) and earplugs (audio system S14, Sensimetrics) were installed to communicate with participants and to record their oral response.

2.4. Experimental design

The scanning session started with a 10 min resting state acquisition, during which participants were instructed to keep their eyes open, fixate on a foveally-presented cross and to not think about anything in particular.

Then, participants were stimulated during 4 successive runs, each comprising 20 stimuli that were of a mixture of two tactile (T_{Low}, T_{High}) and two proprioceptive (P_{Low}, P_{High}) stimuli individually presented randomly, each of them being repeated five times per run (Fig. 1B). To make sure that participants remained awake and followed the instructions to perceive the possible movements of their hand, they were asked to answer 'Yes' at the end of each stimulation if they perceived an illusory movement sensation of their right hand and 'No' if they did not. The interval of response was indicated by two auditory beeps: one delivered on average 1.5 s after the stimulation with a jitter interval of 1.5 ± 0.4 s to prevent from anticipatory response, and the second beep delivered 2 s after the first one to announce the end of the response period followed by a jitter interval of 1.5 ± 0.4 s before the onset of the following stimulation, to ensure random subsampling of the brain relative to each stimulation condition.

2.5. Behavioural data analysis

2.5.1. Movement illusion copy

During all 10 s tactile and proprioceptive stimulation in the mock scanner, participants were asked to copy on-line the illusion perceived in their right hand using a potentiometer hold in their left hand. The angular deviations recorded from the potentiometer were processed using MATLAB R2017 (The Mathworks). We extracted the mean velocity of the illusions (°/s) from the centered angular deviations. The mean velocity of the illusion was calculated from the onset of the illusion (automatically determined at + 2 SD from baseline) up to the maximum angular deviation for each trial. For the two intensities tested in the two modalities, we first calculated the individual mean of the illusion velocity. Then we estimated for each participant the increase in illusion velocity between the high and the low levels of stimulation by computing the rate of velocity increase (RVI; Chancel et al., 2018), as the percentage of velocity increase between the high and low levels of stimulation.

$$RVI = [(Velocity(High) - Velocity(Low)) / Velocity(Low)]*100$$

One young and one old participant were excluded from the

potentiometer analysis because of a technical problem during acquisition. The data did not follow a normal distribution, thus we used non-parametric Mann Whitney tests to compare group differences for tactile and proprioceptive conditions separately, and Wilcoxon tests to compare intra-group differences between the two sensory conditions. Differences were considered statistically significant at a threshold of $p < 0.05$.

2.5.2. Movement illusion occurrence

Based on the responses given by participants after each stimulation during the fMRI session, we calculated the occurrence of illusions for each of the four conditions in the older and younger groups. We verified that the percentage of illusion occurrences was similar during the simulated training session in the mock scanner and the fMRI acquisition session. This suggests that the time interval between sessions did not seem to influence the ability of older people to perceive illusions nor that of younger adults.

2.6. Image acquisition

Data were acquired on a 3-T MRI Scanner (Magnetom-Prisma, Siemens) with an in-built body-coil for radio frequency excitation and the manufacturer's 64-channel phase-array head coil for reception. Blood-oxygen-level-dependant (BOLD) images were acquired with a multi-band sequence (Multi-Band EPI C2P v014) provided by the University of Minnesota (Feinberg et al., 2010; Moeller et al., 2010; Xu et al., 2013). Whole-brain fieldmap images were first acquired with a spin-echo EPI sequence with the same spatial parameters as the BOLD images and acquired twice with opposite phase encode directions along the anterior-posterior axis with the following parameters: TR/TE = 7060/59 ms, voxel size = 2.5 × 2.5 × 2.5 mm^3, slices = 54, FOV (Field of View) = 210 × 210 mm^2, flip angle = 90/180°. BOLD images using a gradient-echo EPI sequence were subsequently acquired with the following parameters: TR = 1224 ms, TE = 30 ms, voxel size = 2.5 × 2.5 × 2.5 mm^3, multiband factor = 3, slices = 54, 284 vol, FOV = 256 × 256 × 204.8 mm^3, flip angle = 65°. Four runs of functionally related-task and a resting-state run were acquired using this BOLD protocol. The scanning session ended with the acquisition of a high-resolution T1-weighted anatomical image (MPRAGE sequence: TR/TI/TE = 2400/1010/2.28 ms, voxel size = 0.8 × 0.8 × 0.8 mm^3, slices = 256, FOV = 256 × 256 × 204.8 mm^3, flip angle = 8°).

2.7. MR image pre-processing

All acquired MR images were converted to nifti format and stored following the Brain Imaging Data Structure standard (http://bids.neuroimaging.io, Gorgolewski et al., 2016). For each participant, all the functional and structural images were pre-processed using SPM12 (Welcome, Department of Imaging Neurosciences, London, UK, http://www.fil.ion.ucl.ac.uk/spm/) running in MATLAB (2017a, Mathworks Natick, Massachusetts, United States). FSL (http://fsl.fmrib.ox.ac.uk/fsl) was used to generate the fieldmap from the two sets of reversed phase encoding SE-EPI using the tool topup.

As the Siemens system (with 3T Prisma) already includes dummy scans that are not stored at the beginning of the acquisition to allow stabilization of magnetization, no images were discarded. For each participant, all functional task-related and resting images were (1) corrected for magnetic field inhomogeneities using fieldmap images, (2) realigned and unwarped to the first image of the time series to correct for head movements between scans, and (3) coregistered to the respective anatomical scan. For all participants, T1-weighted structural images were (4) segmented using DARTEL (Diffeomorphic Anatomical Registration using Exponentiated Lie Algebra) algorithm into grey matter (GW), white matter (WM) and cerebrospinal fluid (CSF) (Ashburner and Friston, 2009). Then, (5) a group-specific template including all younger and older participants' anatomical scans was created using DARTEL algorithm Toolbox. The creation of such a study-specific template allowed to estimate the deformation that best aligned all anatomical images together by iteration and reduced deformation errors that arise when distorting a single subject image into an unusually shaped template. This is relevant when comparing younger and older adults known to have significant structural differences (Hedman et al., 2012). Also, DARTEL is based on a large deformation framework that is more suitable for the older group template generation. Finally, (6) segmented anatomical and functional images were normalized for each participant to the study-specific template using the flow fields containing the individual deformation parameters, (7) normalized to Montreal Neurological Institute (MNI) space, and (8) smoothed with an isotropic three-dimensional Gaussian kernel of 6 mm.

We also computed the total intracranial volume (TIV) of each participant by summing the volumes of white matter, grey matter and LCR before normalization step. This allowed verifying whether differences between groups could be partly explain by brain atrophy occurring with aging.

2.8. Functional task-related image analyses

2.8.1. Subject regression analysis

Task-dependent changes in the BOLD signal were modeled for each subject as boxcar regressors, time-locked to the onsets of the stimulation conditions (P_{Low}, P_{High}, T_{Low}, T_{High}) and the onsets of the answer. These five regressors were convolved with the canonical hemodynamic response function (HRF) of SPM12. Data were high-pass filtered (with a cut-off period of 128 s) to remove low-frequency drifts of the scanner signal. The five regressors corresponding to the four conditions of stimulation and the answer condition were included into a General Linear Model (GLM, Friston, 1995).

We estimated head motion in the two groups by measuring the frame-wise displacement (FD) which is an indicator that expresses instantaneous head-motion using the three translational and three rotational realignment parameters (Power et al., 2012). We tested the effects of Group (Young, Old) and Run (1,2,3,4) on head movements before and after the preprocessing of the functional images using a 3-way ANOVA for repeated measures. Results showed a significant main effect of Group ($F(1,37) = 15.83$, $p < 0.001$) and Preprocessing ($F(1, 259) = 588$, $p < 0.001$) but no significant Run effect ($F(3, 259) = 0.069$, $p = 0.98$). There was a significant interaction between Group and Preprocessing ($F(1, 259) = 95.4$, $p < 0.001$) but no significant interaction between Group and Run or between Preprocessing and Run (see complete statistical results in Table 1 supplementary data). Tuckey post-hoc revealed that for the 4 functional acquisitions, head movements were significantly higher in the older group (mean FD: 0.33 ± 0.2 mm) compared to the younger group (mean FD: 0.15 ± 0.05 mm) before Preprocessing ($t = 7.06$, $p < 0.001$) (supplementary data Fig. 1A). However, after functional image pre-processing, the difference between the two groups was no longer found ($t = 0.42$, $p = 0.97$) (supplementary data Fig. 1B).

To further account for the complex problem of the nuisance of head motion on the BOLD signal, head movement parameters estimated by the motion realignment procedure were also included in the GLM as covariates of no interest. It has been shown to reduce the effects of motion-related artifact on resting state functional MRI correlations (Power et al., 2012) and it should be thus particularly relevant to prevent age-related differences in BOLD responses from being due to greater head movements that are known in the elderly compared to young adults. Specifically, we used a 24-parameter autoregressive model of motion (Friston et al., 1996), including current (i.e, 3 translations and 3 rotations) and past position (6 head motion parameters one time point before), and the 12 corresponding squared items.

For each individual, we also minimized physiological and other noise sources, which is particularly relevant for the study of healthy aging, to account for physiological confounds, as vascular components that are known to be affected by age (Geerligs et al., 2017). To this end, we modeled nuisance noises present in white matter and CSF using the Tapas

Table 1
Brain activations during a High versus a Low intensity of stimulation in both sensory modalities as evidenced by the positive main effect ($\Delta P + \Delta T) > 0$ in young (A) or older group (B) and the negative main effect ($\Delta P + \Delta T) < 0$ for young (C) and old (D) groups.

A/Young ($\Delta P + \Delta T) > 0$							B/Old ($\Delta P + \Delta T) > 0$					
Areas	*k*	*x*	*y*	*z*	*t*	*d*	*k*	*x*	*y*	*z*	*t*	*d*
L Precentral G (BA 4)	1071	**−30**	**−25**	**55**	**11.18**	**.80**	906	**−35**	**−20**	**50**	**8.73**	**.96**
L Postcentral G (BA 3)		−35	−33	58	9.90			−38	−33	53	7.65	
L Parietal Operc. (S2):	1253						437					
- Ant. (OP4, BA43)		−50	−15	13	6.62			−55	−25	15	6.37	
- Post. (OP1, BA40)		−40	−28	18	6.60			**−48**	**−20**	**20**	**8.03**	**1.3**
L Post. Insula (BA13)		**−40**	**−23**	**0**	**7.55**	**.41**		−33	−33	20	3.91	
L Angular G	76	**−45**	**−68**	**30**	**4.17**	**.23**		–	–	–		
R Parietal Operc. (S2):	736						287					
- Ant. (OP4, BA43)		**58**	**−18**	**13**	**8.06**	**.51**		**50**	**−20**	**20**	**5.90**	**.79**
- Post. (OP1, BA40)		48	−20	13	7.24			48	−20	13	4.89	
R Post. Insula (BA13)		40	−23	15	6.21			–	–	–	–	
R Inf. Parietal Lob.		65	−33	28	4.36		64	**65**	**−25**	**30**	**5.30**	**.66**
R Postcentral G (BA 3b)		–	–	–				53	−18	38	4.68	
L MCC	61	**−8**	**−23**	**45**	**5.79**	**.58**		–	–	–		
L Sup. Frontal G	61	**−13**	**63**	**15**	**5.49**	**.28**		–	–	–		
L Putamen	1253	−25	10	−3	6.66	**.63**	67	**−23**	**5**	**10**	**5.71**	**.50**
R Putamen	179	**25**	**13**	**3**	**5.74**	**.60**	95	**28**	**0**	**13**	**5.00**	**.53**
R Cerebellum (VI)	80	**5**	**−60**	**−18**	**4.62**	**.47**	121	20	−58	−19	3.42	
R Cerebellum (V)		13	−55	−15	4.17			**20**	**−48**	**−25**	**4.63**	**.58**
R Cerebellum (IX)		–	–	–			68	**13**	**−60**	**−48**	**4.90**	**.70**

C/Young ($\Delta P + \Delta T) <0$							D/OLD ($\Delta P + \Delta T) <0$					
Areas	*k*	*x*	*y*	*z*	*t*	*d*	*k*	*x*	*y*	*z*	*t*	*d*
L Paracentral Lob. (BA 4)	598	**−8**	**−28**	**73**	**6.25**	**.74**		–	–	–		
R Paracentral Lob. (BA 4)		8	−28	75	6.12			–	–	–		
L Precuneus (BA 4)		−8	−45	68	6.04			–	–	–		
R Precentral G (BA 4)	254	**40**	**−23**	**63**	**6.51**	**.99**		–	–	–		
R Postcentral G (BA 3)		45	−20	60	5.86							
R IPS (BA 7)	81	**29**	**−51**	**46**	**5.96**	**.88**		–	–	–		
L MO G (BA 19)	569	**−25**	**−90**	**20**	**6.19**	**.90**		–	–	–		
L Precuneus (BA 7)		−13	−73	38	5.69			–	–	–		
L Inf. Occipital G (BA 19)	105	**−45**	**−85**	**−3**	**4.5**	**.51**		–	–	–		
R MO G (BA 19)	410	**28**	**−85**	**25**	**5.67**	**.73**		–	–	–		
R Precuneus (BA 7)		10	−73	45	4.77			–	–	–		
R ACC (BA 32)	254	**10**	**35**	**28**	**5.40**	**.74**		–	–	–		
R Inf. Frontal G (p. Tri)	205	**40**	**23**	**25**	**5.82**	**.67**		–	–	–		
R Inf. Frontal G (BA 45)	66	**45**	**20**	**10**	**4.30**	**.50**		–	–	–		

Brain areas, t-values (t) and Cohen's d values (d) refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels. Note that there were no significant results found for the negative main effect [($\Delta P + \Delta T) < 0$] in the older group. L: left hemisphere, R: right hemisphere, Ant.: anterior, Inf.: inferior, Post.: posterior, Sup.: superior, BA: brodmann area, G: gyrus, lob.: lobule, Operc.: operculum, p. Tri: pars triangularis, ACC: anterior cingular cortex, IPS: intraparietal sulcus, IOG: inferior occipital gyrus, MCC: middle cingular cortex, MOG: middle occipital gyrus, OP: operculum parietal.

PhysiO toolbox (Kasper et al., 2017). Masks of the white matter and CSF were used to extract the specific time series from these regions. In order to eliminate the non-neural aspects of the signal, we used the COMPCOR approach (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2214855/): the mean of the signal and the first 12 principal components of each noise regions (CSF and white matter) were extracted and then included in the regression analyses as explanatory variables of no interest.

To examine brain activations related to proprioceptive and tactile illusions, we created a first level of contrasts between the high and low intensities of stimulation for each sensory modality. For each participant, we defined the contrasts $\mathbf{\Delta P} = (P_{High}\text{-}P_{Low})$ and $\mathbf{\Delta T} = (T_{High}\text{-}T_{Low})$, for the proprioceptive and tactile modalites, respectively. These contrasts allowed us to better control for differences related to our perceptual task

of interest and avoid the problem of the not well-defined baseline (Stark and Squire, 2001). Indeed, it has been well established that increasing the intensity of these kinds of proprioceptive or tactile stimuli results in a velocity increase of the movement illusion, in both young (Blanchard et al., 2011; Chancel et al., 2016) and old adults (Chancel et al., 2018; Landelle et al., 2018), together with an increase in BOLD responses in the whole sensorimotor network in the case of vibration induced illusions in young adults (Romaiguere et al., 2003). Based on our previous findings showing that increasing the intensity of stimulation resulted in smaller increases in the illusion velocity in older adults than in younger adults (Chancel et al., 2018), we investigated between-group differences in these **Δ**P and **Δ**T contrasts.

2.8.2. Group level analysis

To investigate age-related changes in brain activations during illusory movement perception from proprioceptive or tactile origin, the first-level contrast maps (**Δ**P and **Δ**T) were entered into a second-level analysis. The between-group comparisons were implemented in GLM Flex tool (http://mrtools.mgh.harvard.edu/index.php/GLM_Flex) using a 2 × 2 repeated measures ANOVA design including "Group" (Young, Old) as the between-group factor and "Modality" (**Δ**P, **Δ**T) as the within-group factor.

First, we examined the positive main effects of the modality separately in each group, defined as (**Δ**P +**Δ**T) > 0, equivalent to [(P_{High} -P_{Low}) + (T_{High} -T_{Low})] > 0, to reveal the common and specific brain areas involved in hand movement illusion, regardless of the sensory modality. Since the sensorimotor network is known to be modulated by inter-hemispheric inhibitory processes, the negative main effects of modality (**Δ**P +**Δ**T) < 0, equivalent to [(P_{High} - P_{Low}) + (T_{High} - T_{Low})] < 0, were also computed to reveal brain areas relatively more activated (or less deactivated) during a low compared to a high intensity of stimulation in each group.

Then, for each group, differences between proprioceptive or tactile illusions were investigated through the two contrasts: (**Δ**P > **Δ**T) and (**Δ**T > **Δ**P) for both the younger and the older groups.

Finally, we examined for each modality, the differences between the two groups according to the four contrasts: [Young(**Δ**P) > Old(**Δ**P)], [Young(**Δ**P) < Old(**Δ**P)], [Young(**Δ**T) > Old(**Δ**T)] and [Young(**Δ**T) < Old(**Δ**T)].

To account for the problem of multiple comparisons in the statistical analysis of whole brain data, clusterwise significance was always determined at the level of $p < 0.05$ corrected for family-wise error (FWE). For each cluster found significantly activated (deactivated), we plotted the corresponding contrast estimate parameters (based on beta values).

2.8.3. Inter-hemispheric balance analysis

To study the differential activation between homologous regions of the two hemispheres, we calculated, for each subject, the laterality index (LI) and the inter-hemispheric difference value (IHD) for different regions of interests (ROIs). ROIs were defined using a functional benchmark composed of voxels specifically more activated in one group than in the other during proprioceptive or tactile illusions, i.e. in the four contrasts [Young(**Δ**P) > Old(**Δ**P)], [Young(**Δ**P) < Old(**Δ**P)], [Young(**Δ**T) > Old(**Δ**T)] and [Young(**Δ**T) < Old(**Δ**T)]. For each cluster found significantly activated (with cluster-wise FWE correction), we extracted the coordinates of the cluster barycenter and we built a 6 mm radius sphere centered on this peak voxel using MarsBar toolbox in Matlab (http://marsbar.sourceforge.net).

The laterality index ranged between [1;-1] was classically defined by

$$LI = \frac{LH - RH}{|LH| + RH}$$

where LH and RH were defined as the individual mean of the contrast estimate parameters inside the ROIs of the left and right hemispheres, respectively, extracted from the contrasts (**Δ**P > 0) and (**Δ**T > 0). It is generally admitted that a positive laterality index above 0.2 reflects a left hemispheric dominance, a negative value below −0.2 reflects a right hemispheric dominance, while a value ranged between 0.2 and −0.2 indicates a non-dominance between the two hemispheres (Seghier, 2008). We used non-parametric Mann Whitney tests to compare the laterality index between the two groups.

Since LH and RH could be opposite in sign, the laterality index was by definition capped at 1 or -1 in several subjects. To examine whether the intensity difference in inter-hemispheric activity was correlated with individual discrimination performance, we therefore calculated the absolute difference in interhemispheric activity as IHD = LH - RH, and tested whether IHD and performances' measures (JND) co-varied in each group and each sensory condition. JND corresponded to the discriminative thresholds required to discriminate the velocity of two movement illusions induced by either a proprioceptive or a tactile stimulation previously established for all the young and old participants of the present study (Landelle et al., 2018). JND was assimilated as a positively skewed continuous variable with a Gamma distribution. Thus, we used generalized linear model (GzLM) to process a linear regression between behavioural data collected independently from the present experiment (JND) and IHD.

2.9. Rs-functional connectivity analyses

The impact of age on the functional connectivity within the sensorimotor network was investigated through resting state networks analysis. The analysis was conducted using the Conn toolbox (https://www.nitrc.org/projects/conn/). After the preprocessing steps performed using SPM12, WM and CSF mask obtained from the segmentation of the individual anatomical image were used as subject-specific noise region of interest. Resting time series of these regions were then entered at the first level of analysis and regressed using the component-based noise correction method (CompCor), to reduce physiological and other noise sources, for each subject (Behzadi et al., 2007). We also applied a high pass filter at 0.01 Hz to reduce physiological noise, without suppressing high-frequency signals, as it has recently been shown that high-frequency signals contain more than just physiological noise, and contribute to functional connectivity. Indeed, compared to band-pass filtering, a 0.01 Hz high pass filter has a better and reliable effect on functional connectivity estimates (Geerligs et al., 2015; Shirer et al., 2015).

We estimated head motion differences between the two groups during resting state acquisitions. A two-way ANOVA was performed on the mean frame-wise displacement included Group and Preprocessing as fixed factors. We found a significant main effect of Group and Preprocessing and a significant interaction between Group and Processing (see complete statistical results in Table 1 supplementary data). Tuckey post-hoc revealed that difference between the two groups was significantly higher in the older group (0.23 ± 0.14 mm) compared to the younger group (0.12 ± 0.05 mm) before Preprocessing ($t = 4.58$, $p = 0.001$). After functional image preprocessing, the difference between the two groups was no longer found ($t = 0.14$, $p = 0.99$) (see supplementary data Fig. 1B).

To prevent age-related differences in functional connectivity from being mainly due to greater head movements by the elderly, we used a 24-parameters autoregressive model of motion (Friston et al., 1996) and movement outliers (i.e. volumes in which scan-to-scan displacement exceeded 2 mm).

Functional ROIs based on the task-related functional results were selected as seed regions. As for the inter-hemispheric difference analysis, we selected functional ROIs based on the clusters of voxels that were found to be specifically more activated in one of the two groups during proprioceptive or tactile illusions: contrasts [Young(**Δ**P) > Old(**Δ**P)] or [Old(**Δ**P) > Young(**Δ**P)] or [Young(**Δ**T) > Old(**Δ**T)] or [Old(**Δ**T) < Young (**Δ**T)]. For each significant cluster (found with cluster-wise FWE correction), we extracted the coordinates of the cluster barycenter and we built a 10 mm radius sphere centered on this voxel using the MarsBar

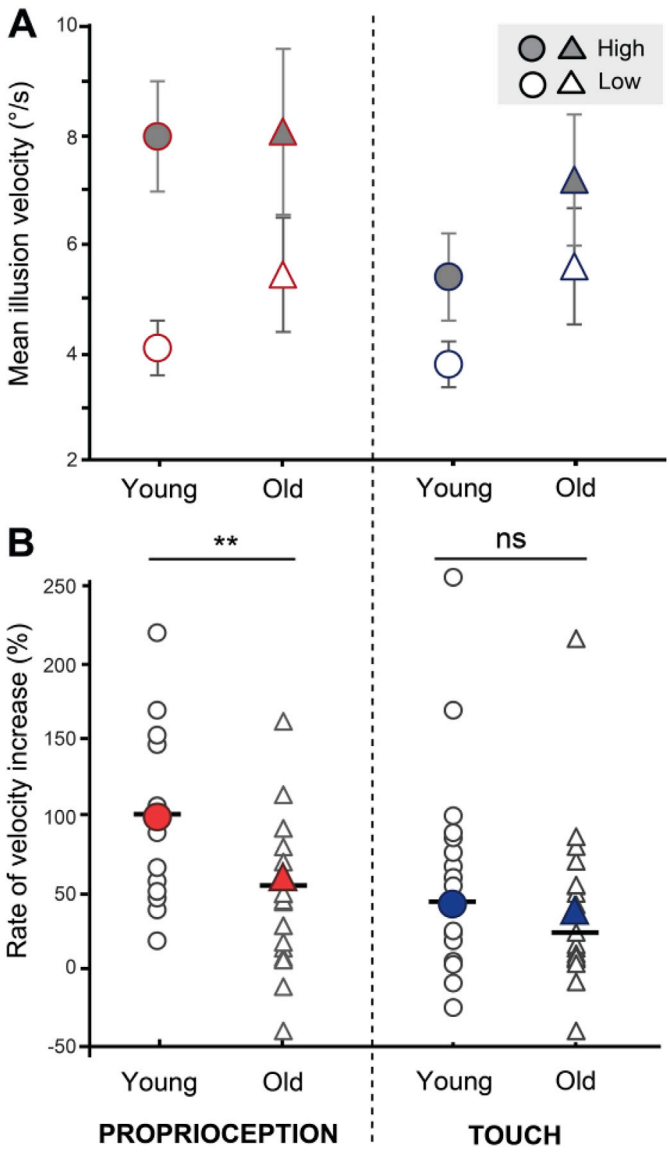


Fig. 2. Comparison of illusion velocities between older and younger participants in the proprioceptive (P, left column, red) and tactile (T, right column, blue) conditions. A) Mean illusion velocity (±SEM) perceived by the younger (circle) and older participants (triangles) in response to a low (unfilled symbols) or a high (grey symbols) intensity of proprioceptive (left column) or tactile (right column) stimulation. B) Individual and mean rate of velocity increase RVI (in percentage %) for the younger (circles) and older (triangles) participants in response to proprioceptive (left column) or tactile (right column) stimulation. Filled symbols are the means of the groups, unfilled symbols are individual values and the horizontal bars are the medians of the groups. ns: no significant; **p < 0.01.

toolbox in Matlab. The sphere was then masked with the thresholded statistical map to include only the significant activated voxels found in the corresponding contrasts.

At the individual level, functional connectivity between the mean resting state BOLD time course for each seed and the BOLD time course throughout the whole brain was estimated using bivariate correlation analyses. Each correlation coefficient was then converted to z-values according to Fisher-transformations. To ensure normality, statistical analyses of the correlation data were performed on these z-values.

Whole brain Fisher-transformed correlation coefficient maps from all the participants were then analyzed at the second level. For each seed, we first examined resting state functional connectivity (rs-FC) within each group using a one sample *t*-test. Second, we compared between-groups rs-FC with a two-sample *t*-test. Finally, to determine whether rs-FC was related to behavioural performance, we included the discrimination performance (1/JND) as a covariate and conducted a regression analysis for each group. All functional connectivity statistical analyses were corrected for multiple comparisons (cluster-wise p-FDR corrected < 0.05).

As effect sizes, we reported Cohen's d for t-tests, which is a standardized measure of the distance between the means of the two groups in standard deviation units [(mean younger group – mean older group)/sd(population)] or the distance from 0 measured in standard deviation units for a single group [mean/sd]. As is commonly assumed, we considered |d| > 0.2–0.5 to be a small effect size, |d| > 0.5–0.8 moderate, and |d| > 0.8 large (Cohen, 1988).

3. Results

3.1. Induced proprioceptive and tactile illusions

3.1.1. Occurrence of illusions

All the participants tested in the present experiment were familiar with the experimental procedure. In fact, they were previously included in a psychophysical study carried out in the laboratory two to three weeks before the MR session, to compare the ability of young and old adults to discriminate the velocity of hand movements, based on proprioceptive or tactile inputs (Landelle et al., 2018).

When tested in a lying position inside the mock scanner, the occurrence of the illusion was always higher than 70% for the two sensory modalities (P_{Young} = 89%, P_{Old} = 77%, T_{Young} = 80%, T_{Old} = 78%), as previously observed in the same participants tested in a seating position at the laboratory (Landelle et al., 2018). During MR recordings inside the 3T scanner, the occurrence of illusions was almost identical to that observed inside the mock scanner (P_{Young} = 88%, P_{Old} = 74%, T_{Young} = 79%, T_{Old} = 74%).

3.1.2. Effect of stimulation intensity on illusion velocity

As shown in Fig. 2A, increasing the intensity of stimulation resulted in an increase in the velocity of the illusion, for both the proprioceptive and tactile stimuli. For the young and old groups, the mean velocities extracted from the on-line copy, made by the participant inside the mock scanner, were higher for the high stimulation intensity, as compared to the low intensity of stimulation as attested by the positive rate of velocity increase (RVI). RVI, which is the percentage of velocity increase between the low and the high intensity of stimulation, significantly differed between the two groups. As shown in Fig. 2B, the RVI was, on average, lower in the older group than in the younger group for the proprioceptive condition (99.4 ± 49% vs 60.1 ± 67%, U = 84, p = 0.0086, d = 0.64, Fig. 2B). By contrast, no significant difference between the younger and older groups was found for the tactile modality (42.5 ± 44% vs. 38.3 ± 54%, U = 167, p = 0.70, d = 0.077). In addition, by comparing the two proprioceptive and tactile conditions, RVI did not significantly differ in the older group (RVI P 62 ± 67% vs. RVI T 38.6 ± 54%, V = 120, p = 0.14, d = 0.35), but the RVI differed in the younger group with a significant higher RVI in the proprioceptive condition (RVI P 99.4 ± 49% vs RVI T 42.5 ± 44%, V = 177, p = 0.001, d = 1.02).

3.2. Brain activation during illusory hand movements

3.2.1. Within-group brain activation during proprioceptive or tactile illusions

In the younger group, the whole sensorimotor network was found to be significantly more activated during a high versus low intensity of stimulation in either proprioceptive or tactile stimulation, as shown by the positive main effect of the modality [(**ΔP** +**ΔT**) > 0], equivalent to [(P_{High} - P_{Low}) + (T_{High} - T_{Low}) > 0]. The activated network included the left primary sensorimotor cortex (left SM1), bilateral, parietal operculum, posterior insula, left angular gyrus, left middle cingular cortex (MCC) and left superior frontal cortex (SFC) as well as subcortical regions

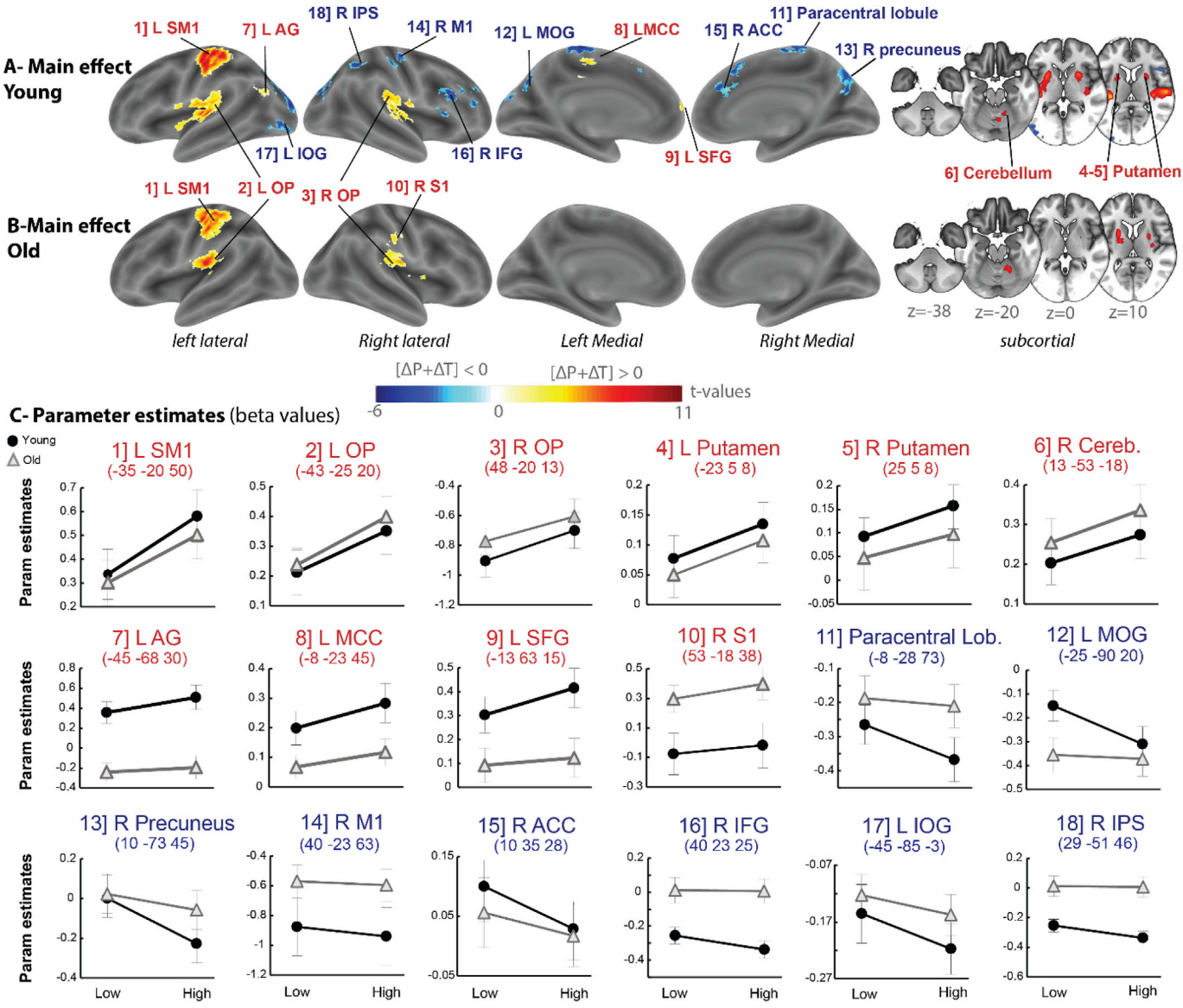


Fig. 3. Comparison of the whole brain networks activated during proprioceptive or tactile stimulation in younger (A) and older (B) adults. A) & B) Main effects of modality in younger (A) and older (B) groups. Positive main effect $[\Delta P + \Delta T] > 0$ in warm colors, equivalent to $[(P_{High}\text{-}P_{Low}) + (T_{High}\text{-}T_{Low})] > 0$, corresponds to brain regions more activated during a high compared to a low intensity of stimulation in both sensory modalities; Negative main effect of modality $[\mathbf{\Delta}P+\mathbf{\Delta}T] < 0$ in cold colors, equivalent to $[(P_{Low} - P_{High}) + (T_{Low} - T_{High})] > 0$ corresponds to brain regions more activated during a low, compared to a high, intensity of stimulation in both sensory modalities. Cortical statistical maps ($p < 0.05$ FWE cluster corrected) are overlaid on inflated brain cortical surface and subcortical maps on axial slices of the mean participants' anatomical image (z coordinates in MNI space). C) For each cluster, a peak coordinate is written in color to indicate whether it corresponds to a positive (red) or a negative (blue) main effect. For a common group activation, the peak was the barycentre of the peaks extracted from the all effect contrasts of the two groups, and for a specific group activation, the peak was extracted from the group main effect. The plots represent the mean parameter estimates (Param estimates, arbitrary units) which is the sum of the beta values [Low = $P_{Low} + T_{Low}$, and High = $P_{High} + T_{High}$] extracted for each subject using a 6 mm sphere around the previously defined peaks for both the younger (dots) and older (triangles) groups. The error bars are the standard errors of the mean. L: left hemisphere, R: right hemisphere, lob.: lobule ACC: anterior cingular cortex, AG: angular gyrus, Cereb: cerebellum, IFG: inferior frontal gyrus, IPS: intraparietal sulcus, IOG: inferior occipital gyrus, M1: primary motor cortex, MCC: middle cingular cortex, MOG: middle occipital gyrus, OP: operculum parietal, SM1: primary sensorimotor area, S1: primary sensory cortex, SFG: superior frontal gyrus.

such as the right cerebellum and bilateral putamen (Fig. 3A in warm colors, Table 1A). As in the younger group, the left SM1, bilateral parietal operculum, right cerebellum and bilateral putamen were also activated in the older group, when testing the positive main effect of the modality based on the contrast of the high and the low intensity of stimulation ($[(\mathbf{\Delta}P + \mathbf{\Delta}T) > 0]$). The older group also exhibited a significant modulation of the BOLD response in the right S1, i.e. the ipsilateral somatosensory cortex (Fig. 3B in warm colors and Table 1B).

When intensities of stimulation were inversely contrasted, corresponding to the negative main effect of modality $[(\mathbf{\Delta}P+\mathbf{\Delta}T) < 0]$, equivalent to $[(P_{Low}\text{-}P_{High})+(T_{Low}\text{-}T_{High})] > 0$, no significant modulation in the BOLD signal was found in the older group (Fig. 3B in cold colors and Table 1D). By contrast, modulation of the BOLD signal in the low versus high intensity contrast was observed for the younger group in brain regions located in the ipsilateral (right) SM1, bilateral paracentral gyrus, right intraparietal sulcus (IPS), occipital brain areas such as bilateral precuneus and middle and inferior occipital gyrus (MOG, IOG), as well as in more frontal regions, including the right anterior cingulate gyrus (ACC), and the inferior frontal gyri (Fig. 3A, in cold colors, and Table 1C). As shown by the contrast estimate parameters plotted in

Fig. 3C (11–18), the significant differences in these regions did not reflect a greater activation during the low intensity of stimulation, but were rather supported by a relative reduction of the contrast estimate parameters for the high stimulation intensity versus the low stimulation intensity. This reduction was less pronounced in the older group and did not reach a significant level (see triangles in Fig. 3C).

3.2.2. Within-group comparison of brain activation during proprioceptive-versus tactile-induced illusions

When comparing brain activations during a high versus a low intensity of stimulation between the two kinds of sensory stimulation, significant differences were observed during proprioceptive stimulation, mainly in the younger group. For the contrast [**ΔP > ΔT**], young participants exhibited greater activations in the left SM1, the bilateral superior temporal gyrus, the right parietal operculum, the right cerebellum, as well as the bilateral putamen (Fig. 4A in warm colors, Table 2A), while only the left SM1 was found more activated in the elderly (Fig. 4B in warm colors, Table 2C).

For the contrast [**ΔT > ΔP**], the left S1, precuneus, and fronto-medial region (posterior medial frontal and anterior cingular cortex) were more

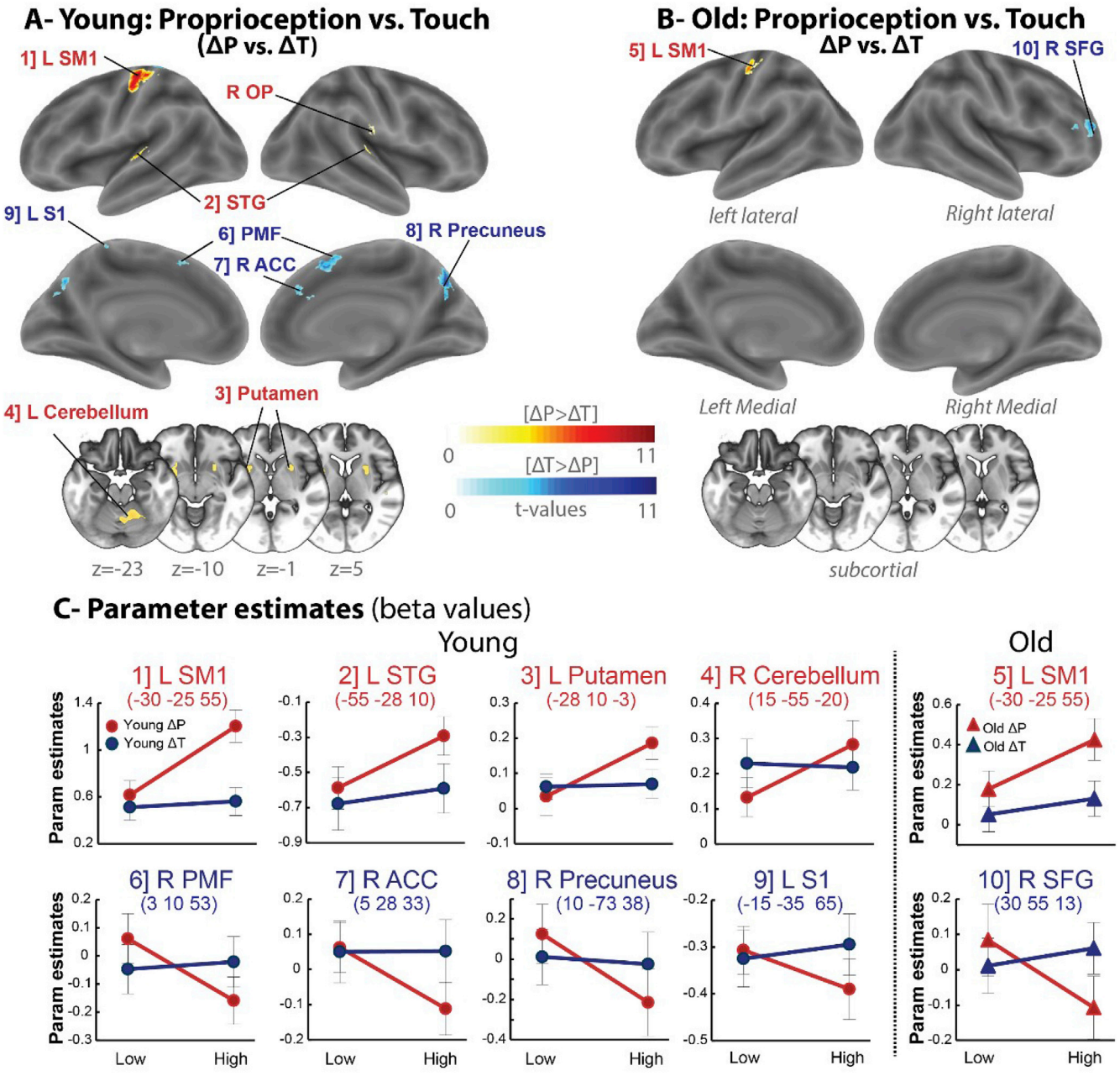


Fig. 4. Modality differences in favor of proprioception (contrast [(ΔP) > (ΔT)], in warm colors) or touch (contrast [(ΔT) > (ΔP)], in cold colors) for the younger group (A) or the older group (B). The two statistical maps corrected for multiple comparisons ($p < 0.05$ FWE cluster corrected) were superimposed on inflated brain cortical surface and subcortical maps on the mean participants' anatomical axial slices (z coordinates in MNI space). **C -** For each significant cluster of activations found, the mean parameter estimates (Param estimates, in arbitrary units) are plotted in red in favor of proprioception [(ΔP) > (ΔT)] or blue in favor of touch [(ΔT) > (ΔP)]. The mean parameter estimates are the mean of the beta values [P_{Low}, T_{Low}, P_{High} and T_{High}] extracted for each subject using a 6 mm sphere around the previously defined peaks for the younger (dots, left panel) and the older (triangles, right panel) groups. The error bars represent the standard errors of the mean. L: left hemisphere, R: right hemisphere, ACC: anterior cingulate cortex, OP: Operculum parietal, PMF: posterior medial frontal, S1: primary sensory area, SM1: primary sensorimotor area, SFG: superior frontal gyrus, STG: superior temporal gyrus.

Table 2
Within-group comparisons of brain activations during proprioceptive versus tactile stimulation according to the contrasts: (A) [Young(ΔP) > Young(ΔT)], (B) [Young(ΔT) > Young(ΔP)] (C) [Old(ΔP) > Old(ΔT)], (D) [Old(ΔT) > Old(ΔP)].

A/Young (ΔP) > Young (ΔT)						
Areas	*k*	*x*	*y*	*z*	*t-value*	*d*
L Precentral G (BA 4)	367	**−30**	**−25**	**55**	**9.42**	**1.73**
L Postcentral G (BA 3)		−38	−23	48	7.71	
R Parietal Operc. (BA40)	144	**65**	**−28**	**20**	**5.76**	**0.92**
R Cerebellum (V-VI)	157	**15**	**−55**	**−20**	**5.43**	**1.37**
Cerebellar Vermis (VI)		5	−60	−18	5.20	
L Putamen	96	**−28**	**10**	**−3**	**4.98**	**1.27**
L STG (BA41)	63	**−55**	**−28**	**10**	**5.25**	**1.02**
R Putamen	63	**28**	**8**	**5**	**4.34**	**1.05**
B/Young (ΔT) > Young (ΔP)						
Areas	*k*	*x*	*y*	*z*	*t-value*	
R Post. Medial Frontal	267	**3**	**10**	**53**	**7.13**	**1.43**
R ACC		5	28	33	5.18	
R Precuneus	237	**10**	**−73**	**38**	**6.64**	**1.02**
L Postcentral G (BA 3)	69	**−15**	**−35**	**65**	**5.77**	**1.23**
C/Old (ΔP) > Old (ΔT)						
Areas	*k*	*x*	*y*	*z*	*t-value*	
L Precentral G (BA 4)	367	**−30**	**−25**	**55**	**9.42**	**0.90**
D/Old (ΔT) > Old (ΔP)						
Areas	*k*	*x*	*y*	*z*	*t-value*	
R Sup. Frontal G	95	**30**	**55**	**13**	**5.52**	**1.35**

Brain areas, t-values and Cohen's d values (d) refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels. L: left hemisphere, R: right hemisphere, Post.: posterior, Sup.: superior, G: gyrus, BA: brodmann area, Operc.: Operculum, ACC: anterior cingular cortex, STG: superior temporal gyrus.

activated in the tactile than in the proprioceptive condition, in the younger group (Fig. 4A in cold colors, Table 2C). In the older group only the superior frontal gyrus was found more activated (Fig. 4B in cold colors, Table 2D). As shown by the parameter estimates values (ie. beta values) plotted in Fig. 4C, these latter regions did not actually display a greater activation in the tactile condition, compared to the proprioceptive one, but there was a relative reduction of the parameter estimates in the high versus the low proprioceptive condition, while parameter estimates remained stable and close to zero in the two tactile intensity conditions for both groups.

3.2.3. Between-group analyses of brain activation during high versus low intensity of proprioceptive or tactile stimulation

Common brain regions were found to be activated in young and old participants during tactile or proprioceptive stimulation, but their level of activation was not the same. Between-group statistical analyses revealed significant differences, but only in the proprioceptive condition. In the [Young (**ΔP**) > Old (**ΔP**)] contrast, the left SM1 and left insula were more activated in young, compared to older participants (Fig. 5A in warm colors and Table 3A–B); contrast parameter estimates extracted from this cluster revealed that as the stimulation intensity increased, a higher increase activation occurred in the younger than in the older group (Fig. 5B).

Conversely, in the [Old (ΔP) > Young (ΔP)] contrast, the right S1 and M1, right superior frontal gyrus and right precuneus were found to be relatively more activated in the older group, compared to the younger one (Fig. 5A in warm colors and Table 3C–D). The contrast parameter estimates extracted from these regions revealed that the difference between the two groups was not due to a greater activation in the older group, but rather to a greater decrease of the mean contrast parameter values in the younger group. As shown in the plots in Fig. 5B, parameter estimate values were all negative in these regions during the low and high proprioceptive conditions, compared to baseline, and they decreased as stimulation intensity increased (see black circles in Fig. 5B). On the contrary, the contrast parameter values remained stable, around zero, in the older group (see grey triangles in Fig. 5B).

In addition, we verified that between-group differences were not related to brain atrophy occurring with aging. By comparing the total intracranial volume of all young and old participants, we did not found significant differences between the two groups (TIV: Young (1.46 L ± 0.38) vs Old (1.47 L ± 0.38), $t(37) = -0.037$, $p = 0.97$). Using TIV as a covariate factor, we also found no correlation between TIV and brain activations in the two proprioceptive contrasts ($P_{High} < P_{low}$ and $P_{low} < P_{High}$) for which between-group differences were found.

3.2.4. Interhemispheric balance between the left and the right primary sensorimotor cortices

To further explore the interhemispheric balance of activity between the right and left SM1, the laterality index was computed within the two ROIs obtained in the contrasts [Young (**ΔP**) > Old (**ΔP**)] and [Old (**ΔP**) > Young (**ΔP**)]. This laterality index was found to be very close to 1 in the younger group (LI = 0.80 ± 0.43) reflecting a strong leftward dominance, i.e. contralateral to the stimulation of the right hand during proprioceptive stimulation. By contrast, the laterality index was significantly lower in the older group (LI = 0.00 ± 0.75, $U = 324$ $p < 0.001$, $d = 1.11$) and close to 0, reflecting a loss of lateralization between the two sensorimotor cortex activations. In the tactile condition, the laterality indexes (extracted from the contrasts [Young (**ΔT**) > Old (**ΔT**)] and [Old (**ΔT**) > Young (**ΔT**)]) did not significantly differed ($U = 225$, $p = 0.31$, $d = 0.42$) between the younger (LI = 0.49 ± 0.56) and the older (LI = 0.20 ± 0.76) groups.

Consistently with the laterality index, the intensity difference between the activity of the two sensorimotor cortices extracted from the same ROIs was found to be significantly higher than zero for the younger group in the proprioceptive condition (IHD = 0.54 ± 0.3, $t(19) = 6.71$, $p < 0.001$, $d = 1.22$) (Fig. 6A), reflecting a predominant leftward laterality, while no lateralization of the activations between the two sensorimotor cortices was found in the old group (IHD = 0.06 ± 0.2, $t(18) = 1.11$, $p = 0.27$, $d = 0.25$). Moreover, the younger group had a significant higher inter-hemispheric difference value than the older group ($t = 4.98$, $p < 0.001$, $d = 1.24$) (Fig. 6A). Using GzLM model, we also tested the influence of the inter-hemispheric difference on the ability to discriminate the velocity of proprioceptive- and tactile-induced illusory movements (JND) (Landelle et al., 2018). Fig. 6B shows that in the proprioceptive condition, the fitting curve has a significant negative slope, i.e. the more the inter-hemispheric difference increased, the more participants' JND decrease (corresponding to a better performance) (slope ± SD = −0.84 ± 0.29, $p = 0.0067$). In contrast, no significant regression was found between inter-hemispheric difference value and performance in the tactile condition tested in the same ROIs (slope ± SD = −0.48 ± 0.65, $p = 0.46$) (Fig. 6C).

3.3. Age-related modulation of resting state connectivity within the sensorimotor network

Age-related changes in functional connectivity during resting state (rs-FC) were examined by seed-to-whole-brain analyses using the left and right SM1 cortices as seeds (Fig. 7). More precisely, the two seeds corresponded to the two barycentre of the functionally defined sensorimotor ROIs based on the contrasts [Young (**ΔP**) > Old (**ΔP**)] and [Old (**ΔP**) > Young (**ΔP**)], respectively, as for the interhemispheric difference analysis previously described. As shown in Fig. 7A, the young participants

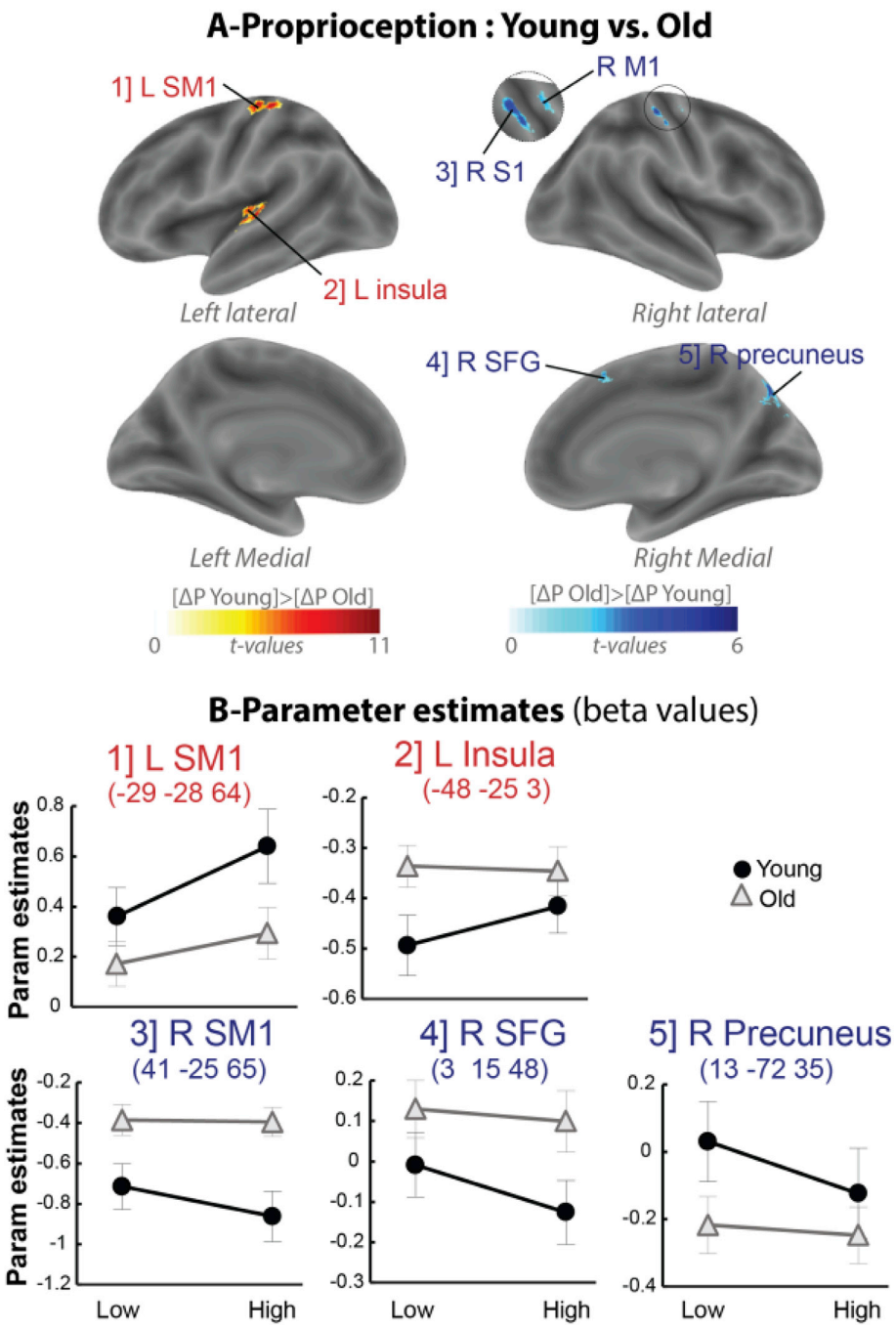


Fig. 5. Group differences contrasting young and old groups in the proprioceptive condition. A-Statistical maps for the contrasts [Young (ΔP) > Old (ΔP)] (in warm colors) and [Old (ΔP) > Young (ΔP)] (in cold colors) in the proprioceptive condition ($p < 0.05$ FWE corrected) were superposed on inflated brain cortical surface. **B-** For each significant cluster of activations found, the mean parameter estimates (Param estimates, in arbitrary units) are the beta values (Low = P_{Low} and High = P_{High}) extracted for each subject using a 6 mm sphere around the barycentre of each cluster and averaged for the younger (black dot) and older (grey triangle) groups. The error bars represent the standard errors. L: left hemisphere, R: right hemisphere, SM1: primary sensorimotor area, S1: primary sensory area, M1: primary motor area, SFG: superior frontal gyrus. No brain region exhibited a significant between-group difference in the tactile condition, neither in the [Young (**ΔT**) > Old (**ΔT**)] contrast nor in the [Young (**ΔT**) < Old (**ΔT**)] contrast.

exhibited an expected significant time course correlation between the two SM1 seeds and the remaining bilateral sensorimotor network, including the pre- and postcentral gyri (M1, S1), premotor cortex, SMA, parietal operculum (S2) and posterior insular cortex as well as subcortical structures, including the ipsilateral cerebellum and thalamus (Table 4A–B). Older adults showed a less extended rs-FC within the sensorimotor network, but additional rs-FC with other networks (Fig. 7B, Table 5A–B). In the elderly, the left and right SM1 seeds were found to be extensively connected with bilateral medio-frontal areas (in the inferior and superior frontal gyrus and posterior-medial frontal gyrus), parietal lobes (superior and inferior parietal lobule, anterior and posterior insula) and the whole superior temporal gyri (Table 5).

A between-group comparison statistically confirmed that rs-FC increased significantly in the younger group within the sensorimotor network, more precisely between each seed and adjacent areas within left and right SM1 (Fig. 7C in purple, Tables 6A and B). By contrast, compared to the younger participants, the left and the right SM1 of the elderly were both found to be more functionally connected to frontal (superior and inferior frontal gyrus), parietal areas (anterior insula, superior temporal gyrus, superior and inferior parietal lobule) and right thalamus (Fig. 7C in yellow, Tables 6C and D).

To investigate the possible link between rs-FC and sensorimotor performance, we conducted regression analyses, including individual discrimination performance, during proprioceptive illusions (1/JND) as a covariate in the seed-to-whole-brain correlation analysis. We found that the connectivity strength between the right and left SM1 seeds and bilateral inferior parietal lobule, bilateral cuneus as well as left cerebellum was higher in older participants who had better discrimination performance during proprioceptive illusions (Fig. 8 and Table 7).

Table 3
Between-group comparisons of brain activations during High versus Low proprioceptive or tactile stimulation according to the contrasts: (A) [Young (ΔP) > Old (ΔP)], (B) [Young (ΔT) > Old (ΔT)], (C) [Old (ΔP) > Young (ΔP)])], (D) [Young (ΔT) > Old (ΔT)].

A/Young(ΔP) > Old(ΔP)							B/Young(ΔT) > Old(ΔT)					
Area	*k*	*x*	*y*	*z*	*t*	*d*	*k*	*x*	*y*	*z*	*t*	*d*
L Precentral G (BA 4)	129	**−28**	**−30**	**75**	**5.56**	**1.05**		–	–	–		
		−29	−28	64	4.57			–	–	–		
L Insula	88	**−48**	**−25**	**3**	**5.67**	**1.12**		–	–	–		
C/Old(ΔP) > Young(ΔP)							D/Old(ΔT) > Young(ΔT)					
Area	*k*	*x*	*y*	*z*	*t*		*k*	*x*	*y*	*z*	*t*	*d*
R Postcentral G (BA 1)	109	**43**	**−35**	**68**	**5.65**	**1.20**		–	–	–		
		41	−25	65	4.70			–	–	–		
R Precuneus	83	**13**	**−73**	**35**	**4.81**	**0.87**		–	–	–		
R Sup. Frontal G (BA32)	60	**3**	**15**	**48**	**5.01**	**1.03**		–	–	–		

Brain areas, t-values (t) and Cohen's d-values (d) refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels. Note that no significant differences between the younger and the older groups were found in the tactile modality L: left hemisphere, R: right hemisphere, G: gyrus, Sup.: superior, BA: brodmann area.

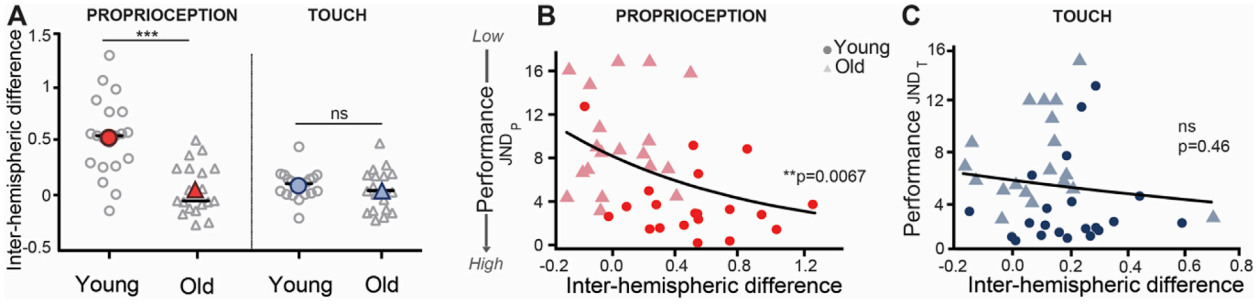


Fig. 6. Interhemispheric balance in the primary sensorimotor cortex of young and old participants during proprioceptive or tactile stimulation. (A) Comparison of inter-hemispheric difference values between the two groups. Individual and mean values of inter-hemispheric difference for the younger (circles) and older (triangles) participants. Inter-hemispheric difference was obtained by subtracting contrast parameter estimates (beta values) of ROIs in the left and right primary sensorimotor areas obtained in the [Young (ΔP) > Old (ΔP)] and [Old (ΔP) > Young (ΔP)] contrast, respectively. Filled symbols are the mean of the groups, unfilled symbols are individual values, and bars are the median of the groups. (B) & (C) Discrimination thresholds (JND) with respect to the inter-hemispheric difference values for the proprioceptive (in red) or tactile condition (in blue). Traces are non-linear regression curves fitting of the JND as function of the inter-hemispheric difference values. Symbols correspond to individual JND as function of the inter-hemispheric difference values for young (circles) and older (triangles) participants. ns: non-significant, $^{**}p < 0.01$; $^{***}p < 0.001$.

4. Discussion

While age-related functional brain changes associated with the decline in motor skills have largely been investigated, little is known on age-related functional changes associated with the perception of body movements. The present study aimed to investigate age-related changes in the central processing of tactile and proprioceptive information of kinesthesia and examine the correlation with hand movement velocity discrimination. We showed that the lower ability to discriminate hand movement velocity exhibited by the elderly correlated with functional brain changes, supporting the hypothesis of a central, rather than peripheral, origin of sensory decline. Using specific sensory stimulation, we found that illusory movement perceptions elicited a pattern of activation, involving a set of common sensorimotor brain regions in young and old participants. However, we found an imbalance between the activation of the two primary sensorimotor cortices in the elderly that could potentially explain the perceptual disability mainly from muscle proprioception origin. In addition, the analysis of rs-FC revealed a decrease within the sensorimotor network and an increase internetwork connectivity in the elderly, compared to young adults. It is noteworthy that some changes in rs-FC appear to be beneficial in older people, as these were positively correlated with their ability to discriminate hand movement velocity. Taken together, these findings provide new insights into the debate on the compensation or dedifferentiation mechanisms that develop with aging.

4.1. Overall functional brain changes in body movement representation with aging

Brain functional changes associated with motor decline have been studied extensively in healthy seniors. However, most studies relied on motor paradigms that do not allow the disentangling motor and sensory components of the movement. The purpose of the current experiment was to study the functional brain changes in the representation of body movements, by inducing illusory sensations of hand movements in participants whose hands were still. In both tactile and proprioceptive stimulation, the increase of the stimulation intensity resulted in an increase of hand movement illusions, as reported by the participants during the mock scanner session. These illusory movements were associated with common brain activations in young and older adults involving sensorimotor areas (left SM1, bilateral parietal operculum, posterior insula, right cerebellum and bilateral putamen), all found more activated during high versus low intensity proprioceptive or tactile stimulation. These regions are part of the sensorimotor brain network classically described in the literature during illusory movements induced by a proprioceptive (Duclos et al., 2007; Naito et al., 2007, 2016; Kavounoudias et al., 2008; Goble et al., 2011) or a tactile stimulation (Kavounoudias et al., 2008) in young adults.

Strikingly, the main differences in brain responses during illusion perception concerned higher deactivations found in the young, but not in the old group. Comparing brain activity during low versus high stimulations [(ΔP +ΔT) <0], we found significant higher deactivation at high

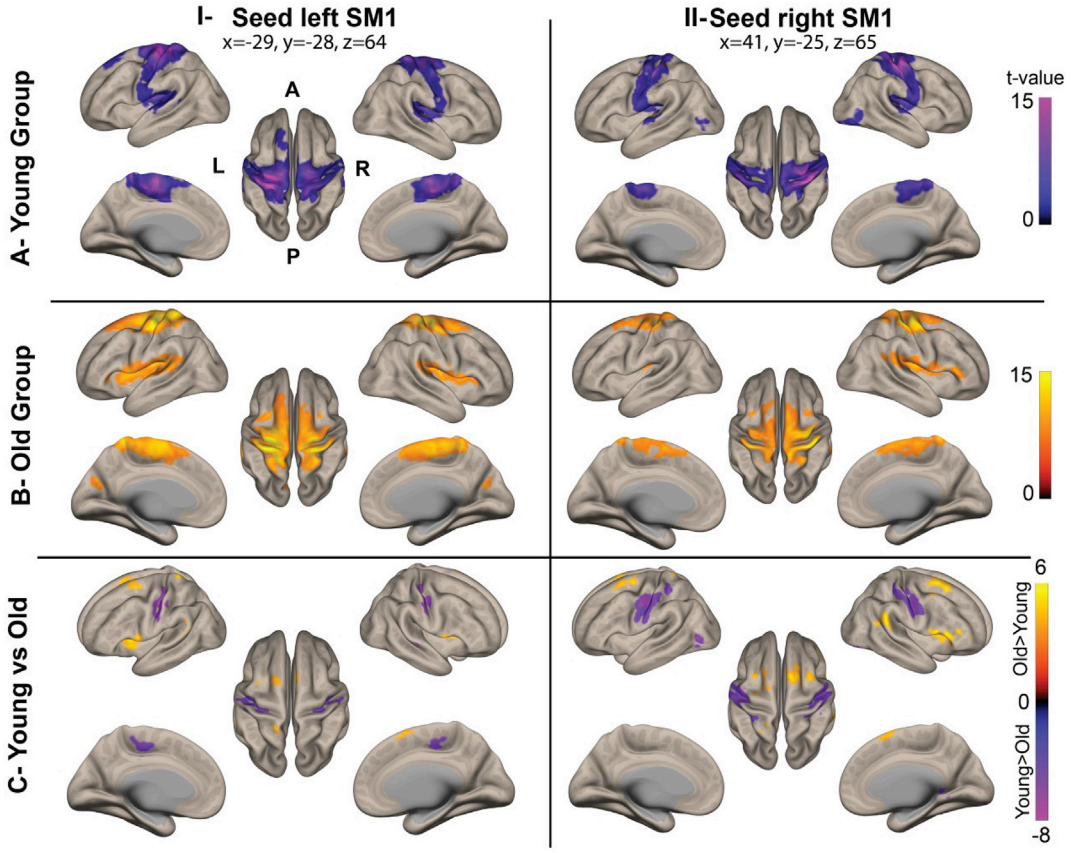


Fig. 7. Resting-state functional connectivity (rs-FC) analyses. Correlation maps ($p < 0.05$ FWE corrected) were computed from two seed regions including the left SM1 ($x = -29$, $y = -28$, $z = 64$) and right SM1 ($x = 41$, $y = -25$, $z = 65$) within the younger group (A), the older group (B), and between the two groups (Young > Old in orange, Old > Young in purple) (C). A: anterior, L: left, P: posterior, R: right.

stimulation intensity in the ipsilateral sensorimotor cortex, right frontal areas (paracentral lobule, anterior cingulate gyrus, inferior frontal gyrus), occipital areas (precuneus, middle and inferior occipital gyrus) and intraparietal sulcus, but only in the younger group. In young adults, deactivations have been already observed during unilateral body stimulation in ipsilateral homologous somatosensory areas, and also in non-stimulated body areas of both hemispheres (Tal et al., 2017) and the precuneus (Kastrup et al., 2008). Also, the precuneus and the cingulate cortex are part of the default mode network, in which activity is expected to be suppressed when a cognitive task is performed (Greicius et al., 2003). The finding that less brain deactivation was found in the older group is consistent with a body of evidence on deficits in inhibitory mechanisms with advancing age. Experiments using transcranial magnetic stimulation have demonstrated decreased excitability of intracortical inhibitory circuits in older people (Peinemann et al., 2001; Sale and Semmler, 2005; Oliviero et al., 2006; Young-Bernier et al., 2012). This decline in inhibitory mechanisms is also consistent with both animal and human studies that have shown a decline in the GABAergic inhibitory system with age (Hua et al., 2008; Gao et al., 2013). Using magnetic resonance spectroscopy, Hermans et al. (2018) recently provided new evidence that age-reduction of GABA levels in sensorimotor regions is associated with impaired motor control processes, such as those usually used to inhibit inappropriate actions in everyday life.

It could be argued that higher brain activations found in the young adults compared to the older ones may simply be due to the deterioration of cutaneous and muscle spindle receptors that occurred with aging (Ribeiro and Oliveira, 2007; Shaffer and Harrison, 2007), leading to a lower recruitment of central brain structures during sensory stimulation. However, the fact that brain regions were found relatively less deactivated in old compared to young participants fails to support this hypothesis. In addition, using the vibration stimulation applied on the arm muscles, a previous study (Quoniam et al., 1995) explored the integrity of the proprioceptive reflex pathways in elderly. The latter authors did not found any differences in the tonic vibration reflexes elicited in young and old participants (60–86 years old), suggesting that the efficiency of spinal sensorimotor pathways as evidenced by joint muscle vibration seems unaffected in elderly. Therefore, the decrease in brain level activations and deactivations observed in elderly mainly in the proprioceptive condition may not be fully explained by a decrease in the efficiency of the vibration stimulation, with respect to muscle spindle and afferent fibres known to deteriorate with aging.

4.2. Representations of body movements from muscle proprioception are more altered with aging than those from touch

Specific tactile and proprioceptive sensory stimulation allowed us to investigate the neural substrates of age-related kinesthetic alteration from these two distinct sensory sources. Between-group comparisons showed that age-related changes in kinesthesia seemed to depend on the sensory source involved. At the perceptual level, increasing the intensity of stimulation had a lower impact on the elderly, as shown by a reduced rate of velocity increase in the older group, but only for the proprioceptive stimulation. In line with our previous studies, this alteration was not observed for the tactile stimulation, suggesting that impairment of muscle proprioception may be more pronounced with age than touch alteration for kinesthetic purpose (Chancel et al., 2018). Keeping in mind these behavioural results, brain responses differed only in the proprioceptive condition between the two groups. When the high and low intensities of tactile stimulation were contrasted, brain activations did not significantly differ between old and young participants.

Table 4
Seeds to whole brain functional analysis during resting state in the younger group. List of brain regions displaying significant functional connectivity with the two seeds placed in the primary sensorimotor cortex (SM1) left (A) or right (B).

A/Young: seed SM1 left							B/Young: seed SM1 right					
Area	*k*	*x*	*y*	*z*	*t*	*d*	*k*	*x*	*y*	*z*	*t*	*d*
L Precentral G (BA 4)	9761	**−28**	**−28**	**63**	**46.94**	**2.45**	7779	−23	−30	68	8.48	
L Postcentral G (BA 3)		−45	−23	63	14.84			−45	−23	45	8.72	
L Paracentral (BA 6)		−15	−20	70	12.44			−13	−38	70	8.04	
Paracentral (BA 6)		−3	−18	63	14.17			13	−13	63	9.21	
R Precentral G (BA 4)		28	−20	63	10.38			**40**	**−28**	**65**	**37.68**	**2.42**
R Postcentral G (BA 3)		18	−40	68	10.59			18	−40	68	7.58	
L Insula (BA 13)		−35	−20	13	10.50			−35	−24	−23	6.74	
L Operc. Parietal (BA41)		−43	−23	15	9.68			−38	−32	25	5.63	
R Operc Parietal (BA41)		38	−23	18	8.66			48	−20	18	12.58	
R Insula (BA 13)		43	−10	13	8.04			36	−17	21	8.87	
R Cerebellum (VI)	407	**28**	**−45**	**−30**	**6.53**	**1.40**		–	–	–		
R Cerebellum (IV–V)		18	−53	−20	5.90			–	–	–		
R Thalamus	108	**13**	**−23**	**15**	**7.53**	**1.98**	169	**28**	**3**	**−30**	**8.43**	**1.12**
L Thalamus	77	−13	−23	5	5.99	**1.30**		–	–	–		
R ITG		–	–	–			240	**53**	**−77**	**5**	**6.28**	**1.58**
L Cerebellum (IV–V)		–	–	–			196	**−18**	**−53**	**−20**	**7.46**	**1.48**
L ITG		–	–	–			77	**−48**	**−78**	**−3**	**5.69**	**1.32**
L Cerebellum (VIII)		–	–	–			48	**−23**	**−55**	**−53**	**4.91**	**1.16**

Brain areas and t-values refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels, t: t-value and d: Cohen's d. L: left hemisphere, R:right hemisphere, G: gyrus, BA: brodmann area, Operc: operculum, ITG: inferior temporal gyrus.

Table 5
Seeds to whole brain functional analysis during resting state in the older group. List of brain regions displaying significant functional connectivity with the two seeds placed in the primary sensorimotor cortex (SM1) left (A) or right (B).

A/Old: seed SM1 left							B/Old: seed SM1 right					
Area	*k*	*x*	*y*	*z*	*t*	*d*	*k*	*x*	*y*	*z*	*t*	*d*
L Precentral G (BA 4)	7373	**−28**	**−28**	**−63**	**41.11**	**2.50**		−33	−18	63	10.68	
R Postcentral G (BA 3)		28	−35	65	15.38			29	−49	70	7.34	
L Postcentral G		−45	−23	63	14.84			−40	−30	65	10.26	
R Precentral G (BA 4)		28	−23	65	14.16		5372	**43**	**−28**	**65**	**28.17**	**2.32**
L SPL (BA 7)		−20	−45	68	13.60			−20	45	68	13.60	
L Sup. Frontal G		−25	−10	60	11.18			−25	−10	60	5.99	
L Paracentral Lob (BA 6)		−8	−28	63	10.82			−8	−28	63	**3.65**	
PMF		0	15	58	6.32			−3	0	63	6.37	
R Inf. Frontal G		–	–	–				58	30	5	6.76	
L Operc. parietal	4709	**−53**	**−35**	**18**	**10.85**	**2.39**	59	**−40**	**−23**	**18**	**4.49**	**1.97**
L Insula		−35	−20	13	10.50			−35	−23	18	4.42	
L Sup. temporal G		−65	−25	10	10.13			-	-	-		
R Operc. parietal							2013	40	−23	18	5.80	
R Insula (BA 13)		38	−23	18	8.66			**28**	**−35**	**20**	**8.13**	**1.17**
R Thalamus		13	−23	15	7.53			13	−25	15	6.73	
L Thalamus		−18	−20	13	6.60			–	–	–		
R Sup. Temporal G		50	−25	13	6.3			50	−25	13	4.22	
R Inf. Parietal Lob.		68	−30	20	7.53			65	−33	18	6.44	
R Calcarine G (V2)	76	**15**	**−70**	**20**	**5.64**	**1.15**		–	–	–		
R Cerebellum (IX)	62	**−5**	**−53**	**−33**	**5.70**	**1.53**		–	–	–		

Brain areas and t-values refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels, t: t-value and d: Cohen's d. L: left hemisphere, R: right hemisphere, G: gyrus, BA: brodmann area, Lob.: lobule, Operc.: operculum, PMF: posterior medial frontal area, SPL: superior parietal lobule.

These results strongly support the previous observations that kinesthetic deterioration with aging seems to occur through a more pronounced degradation of the muscle proprioception than the cutaneous one. They also suggest that despite the peripheral and central alteration of the somatosensory structures, the kinesthetic function based on tactile information does not seem to be severely affected in healthy older people, at least in the 60–75 age range and within the velocity range of the movements presently tested. Indeed, when the proprioceptive condition

Table 6

Age-related changes in resting state functional connectivity. List of brain regions showing significant increase in functional connectivity in the younger compared to older group (A & B; Young > Old) or in the older compared to younger group (C & D; Old > Young) regarding the two regions of interests SM1 left (A&C) or SM1 right (B&D) as seeds.

A/Young > Old: seed SM1 left							B/Young > Old: seed SM1 Right					
	k	*x*	*y*	*z*	*t*	*d*	k	*x*	*y*	*z*	*t*	*d*
L Postcentral G (BA 3)	459	**−28**	**−23**	**48**	**6.36**	**1.27**	962	**−43**	**−15**	**40**	**7.54**	**1.33**
L Precentral G (BA 6)		−48	−20	45	5.74			−53	−8	40	6.60	
R Postcentral G (BA3)	242	**28**	**−23**	**50**	**5.56**	**1.36**	826	**43**	**15**	**40**	**6.67**	**1.46**
R Precentral G (BA 6)		43	−15	45	4.52			60	−3	38	5.53	
L Paracentral lob (BA 6)	226	**−3**	**−23**	**50**	**6.43**	**1.47**		-	-	-		
R Paracentral lob (BA 6)		13	−20	48	5.20			-	-	-		
R Mid. Temporal G	93	**68**	**−10**	**−10**	**4.67**	**1.30**	243	**15**	**−13**	**33**	**7.84**	**1.41**
R Sup. Temporal G		70	−10	3	4.57							
Cerebellum (vermis 3)		-	-	-			208	**3**	**−43**	**−5**	**6.49**	**1.31**
Cerebellum (curs 1)		-	-	-			139	**45**	**−78**	**−18**	**4.51**	**1.15**
L Mid. Occipital G		-	-	-			77	**−40**	**−70**	**0**	**6.35**	**1.23**
C/Old > Young: seed SM1 left							D/Old > Young: seed SM1 Right					
	k	*x*	*y*	*z*	*t*	*d*	k	*x*	*y*	*z*	*t*	*d*
L Ant. Insula	597	**−33**	**13**	**5**	**4.91**	**1.10**		-	-	-		
L Inf. Frontal G		−50	8	8	4.82			-	-	-		
R Ant. Insula (BA 13)	369	**33**	**13**	**10**	**5.64**	**1.38**		34	13	6	4.03	
R Inf. Frontal G		53	10	3	4.45		644	**60**	**15**	**13**	**5.50**	**1.20**
L Precentral G	300	**−25**	**−3**	**60**	**5.70**	**1.32**						
L Precentral G		−45	0	60	4.55							
L Sup. Frontal G		–	–	–			283	**−28**	**13**	**55**	**4.87**	**1.30**
L SPL (BA 5)	187	**−23**	**−45**	**70**	**5.93**	**1.30**	77	**−23**	**−50**	**70**	**5.28**	**1.37**
R Sup. Frontal G (BA 6)	137	**5**	**13**	**63**	**5.11**	**130**		-	-	-		
R Sup. Frontal G (BA 8)		0	18	55	4.84			-	-	-		
R Sup. Frontal G	112	**38**	**0**	**60**	**5.05**	**1.23**	725	**33**	**10**	**63**	**5.64**	**1.34**
R Sup. Frontal G		25	4	65	3.39			23	10	65	5.06	
R Thalamus	77	**5**	**−28**	**15**	**5.27**	**1.37**	119	**20**	**−10**	**10**	**4.90**	**1.21**
L Inf. Parietal Lob.	76	**−65**	**−45**	**23**	**4.85**	**1.29**		-	-	-		
R Sup. Temporal G		-	-	-			332	**65**	**−33**	**20**	**5.15**	**1.32**
R Inf. Parietal Lob.		-	-	-				65	−43	30	5.02	
R Postcentral G (BA 1)		-	-	-			67	**25**	**−48**	**75**	**5.35**	**1.29**

Brain areas and t-values refer to peaks of statistically significant activation after correction for multiple comparison at the cluster level (FWE $p < 0.05$). Coordinates of local maxima are denoted by x, y, z in millimetres (MNI space). k represents the number of voxels, t: t-value and d: Cohen's d. L: left hemisphere, R: right hemisphere, Ant.: anterior, Mid.: middle, Inf.: inferior, Sup.: superior, G: gyrus, Lob: lobule, BA: brodmann area, SPL: superior parietal lobule.

was compared to the tactile condition, greater sensorimotor brain activations were found in the younger group including the contralateral (left) sensorimotor cortex (SM1), right operculum parietal (S2), bilateral putamen, and right cerebellum. This result can be partly explained by a differential magnitude of perceived effect as a function of stimulation intensity. Indeed, the increase in illusion velocity reported by the young participants in the high versus low proprioceptive conditions was higher than the perceived increase in tactile conditions (Rate of velocity increase RVI P > RVI T). However, while stimulation intensities were the same for the older group, only the contralateral (left) SM1 was found to be more activated in the proprioceptive compared to the tactile condition. It would be thus easier for the elderly to reach the performance of the young adults in the tactile condition, since it required a lower brain activation compared to the proprioceptive condition. This is in line with the general view that older adults use more neural resources to achieve cognitive performance equivalent to that of young adults. As a task becomes more complex, the maximum level of resources available would be reached in older adults while young adults could continue to increase their brain activity (see the CRUNCH model by Reuter-Lorenz and Cappell, 2008).

4.3. Reduced lateralization between primary sensorimotor cortices in the elderly during a proprioceptively-induced illusion

On the contrary to previous studies focusing on motor skills (Hutchinson, 2002; Mattay et al., 2002; Ward and Frackowiak, 2003) or on superficial stimulation applied to the skin (Kalisch et al., 2009; Brodoehl et al., 2013), we did not find an overall contralateral increase in brain

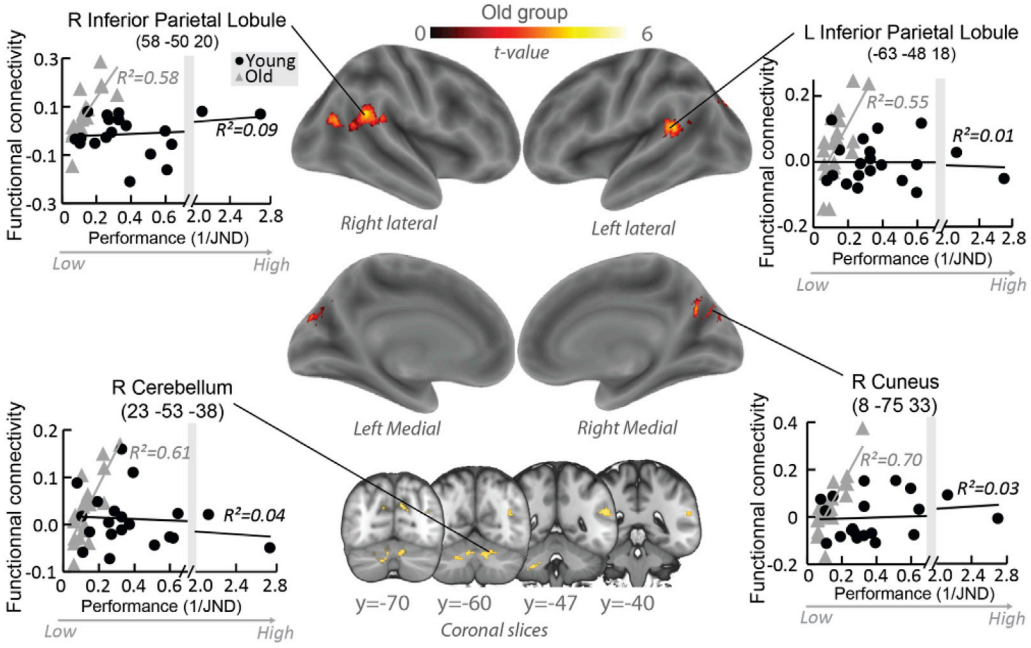


Fig. 8. Resting state functional connectivity (rs-FC) within the sensorimotor network linked to the discrimination performance in the older group. Individual discrimination thresholds (1/JND) were regressed as co-variates in the seed-to-whole-brain analyses with the two SM1 seed regions: left SM1 (x = −29, y = −28, z = 64) and right SM1 (x = 41, y = −25, z = 65). Statistical brain maps ($p < 0.05$ FDR cluster corrected) are overlaid on inflated brain cortical surface and on coronal slices of the mean participants' anatomical image (y coordinates in MNI space). Individual correlation values are plotted for Old (grey triangles) and Young (black circles) participants. No significant correlation was found in the younger group. L: left hemisphere, R: right hemisphere.

Table 7
Brain regions showing significant increase in functional connectivity during resting state according to the discriminative level of performance in older adults in the main effect seed-to whole brain analysis between SM1 left (x = −29, y = −28, z = 64) and SM1 right (x = 41, y = −25, z = 65) as seeds, and any other voxel in the brain.

	k	*x*	*y*	*z*	*t*	*d*
R Cerebellum (VI)	759	**23**	**−53**	**−38**	**5.12**	**0.43**
L Cerebellum (VIII)		−25	−50	−43	4.67	
R Cuneus (BA 7)	370	**8**	**−75**	**33**	**6.37**	**0.54**
L Cuneus		−8	−80	35	3.76	
R IPL (BA 40)	245	**58**	**−50**	**20**	**4.83**	**0.74**
L IPL (BA 40)	245	**−63**	**−48**	**18**	**4.53**	**0.87**

Brain areas refer to statistically significant peaks after correction for multiple comparison at the cluster level (FDR $p < 0.05$). Coordinates of local maxima are denoted by x,y,z in millimetres (MNI space). t: t-value and d: Cohen's d and k represents the number of voxels. L: left hemisphere, R: right hemisphere, BA: brodmann area, IPL: inferior parietal lobule.

activation in the elderly compared to young adults. By contrast, a between-group comparison revealed a lower activation in the contralateral SM1 and left insula in older participants compared to younger ones, especially in the proprioceptive condition. In line with Ward et al. (2008), who found that the contralateral activation of M1 co-varied positively with increasing the force produced by one hand in younger, but less in older participants, we also found a significant increase in the contralateral SM1 by increasing the stimulation intensity in both groups, but to a lesser extend in the older group for the proprioceptive stimulation.

In addition to a significant decrease in the contralateral (left) SM1 activation, we also found a lower deactivation of the homologous ipsilateral (right) SM1, with respect to the baseline level in the older group, compared to the younger group. In young adults, a decrease in the BOLD signal below the baseline level, also termed negative BOLD response, has classically been observed in the ipsilateral sensorimotor cortex following a unilateral motor task (Allison et al., 2000; Hamzei et al., 2002; Newton et al., 2005) or somatosensory stimulation (Kastrup et al., 2008). This ipsilateral negative BOLD response was found to be stimulation intensity dependent, as its magnitude increased with the intensity of tactile stimulation (Klingner et al., 2010; Mayhew et al., 2016). Even if the exact physiological origin of negative BOLD response has not yet been fully demonstrated, it is thought to reflect an increase in ipsilateral cortical inhibition leading to the lateralization of brain activity toward the contralateral side, commonly found in unimanual tasks (Kastrup et al., 2008; Klingner et al., 2010, 2015; Gröschel et al., 2013; Mayhew et al., 2016). In this line, we found in the young adult group a higher ipsilateral SM1 deactivation during the high versus low intensity of proprioceptive stimulation. In the elderly, the ipsilateral SM1deactivation was lower than that of young adults, which has already been reported during unilateral motor tasks (Ward and Frackowiak, 2003; Naccarato et al., 2006; Riecker et al., 2006; Ward et al., 2008). Our data extend these findings, providing additional insights into the field of self-body motion perception.

Taken together, the lower contralateral activation of SM1 and the lower deactivation of ispilateral SM1, clearly observed here, resulted in a strong alteration of the interhemispheric balance between the primary sensorimotor cortices, as shown by the higher inter-hemispheric difference value in the young, compared to the older, group. The lack of lateralized brain activation found in the older adults raises the general issue of whether this is through a compensatory or a dedifferenciation mechanism. The engagement of broader neural circuitry leading to reduced brain activation lateralization has been shown to be positively correlated with overall performance levels in the elderly, suggesting a compensatory process (see the HAROLD model by Cabeza et al., 2002; Hutchinson, 2002; Mattay et al., 2002; Ward and Frackowiak, 2003). Conversely, in the present experiment, changes in interhemispheric activity between the primary sensorimotor cortices (reflected by a lower inter-hemispheric difference value) correlated with declining individual performance in perceiving illusion velocity induced by tendon vibration. In other words, participants were found to be more performant in discriminating the velocity of their illusions, as the activation of the sensorimotor cortices was more lateralized in favor of the contralateral side, while the poorest discriminative performance was found in participants who exhibited a reduced imbalance between the bilateral sensorimotor activations (reflected by a lower inter-hemispheric difference valuelaterality index). Our results are consistent with previous findings in the motor domain showing a reduction of interhemispheric inhibition in the primary motor

cortex of the elderly (Talelli et al., 2008) and a laterality decrease in activation of the motor cortices, which was also found associated with poorer motor task performance (Langan et al., 2010).

The present findings suggest that an imbalance between the primary sensorimotor cortices might cause difficulty in the precise encoding of kinematic parameters of hand movements, which in turn would lead to an impairment of movement velocity discrimination. As the interhemispheric balance between the primary sensorimotor cortices did not differ between young and old adults in the tactile condition and they perceived the same increase of velocity during a high versus a low intensity of stimulation further supports this hypothesis. This should account for the fact that movement discrimination, based on tactile information, was less affected in the elderly than that based on muscle proprioception, at least for the relatively slow movement range tested in the present study.

The deactivation of the ipsilateral SM1 is thought to take place through transcallosal inhibition. A reduction of the size of the corpus callosum with age (Sullivan et al., 2002), confirmed by white matter degradation revealed by diffusion tensor imaging (Lebel et al., 2012), could be responsible for a disruption of the interhemispheric balance, resulting in a disinhibition of the ipsilateral hemisphere. However, additional studies coupling structural and functional brain approaches are needed in order to further substantiate these findings.

4.4. Decrease in intra- and increase in inter-network functional connectivity in the elderly

With regard to the rs-FC within the sensorimotor network, previous studies reported contradictory results with some studies showing an age-related decrease (Wu et al., 2007; Bo et al., 2014) or an age-related increase (Fling et al., 2011; Tomasi and Volkow, 2012; Solesio-Jofre et al., 2014; Seidler et al., 2015), as well as no difference (Geerligs et al., 2015) in connectivity strength. These discrepancies could be partly due to methodological differences across these studies and to the fact that the different seeds chosen corresponded to different body part representations. In the present study, functional connectivity between the two sensorimotor cortices around the two seeds were found to be decreased in older adults, while the premotor frontal regions were more connected than in younger adults. However, the age-related increase in rs-FC within the sensorimotor network was not correlated with better discrimination performance, like they were not found to be correlated with better motor performances in the study by King et al. (2017) (King et al., 2017).

Seed-to-whole-brain analyses, using the right and left SM1 as seeds, showed an extension of functional connections with frontal (superior and inferior frontal gyrus) and parietal (anterior insula, superior and inferior parietal lobule) regions among older participants, as compared to younger ones. Conversely, rs-FC was found to be limited to regions traditionally belonging to the sensorimotor network among the young adults. These results further support the large body of studies that have consistently shown an increase in internetwork functional connectivity in old, compared to young adults (Chan et al., 2014; Song et al., 2014; Ferreira et al., 2016; Grady et al., 2016; Geerligs et al., 2017; King et al., 2017). Although it may first be assumed that the spread of rs-FC in the elderly results from the non-selective recruitment of irrelevant regions due to a dedifferentiation process, the elderly might take advantage of some extended connections. In fact, the connectivity strength between the right and left SM1 seeds with the bilateral inferior parietal lobule, cuneus, and bilateral cerebellum was found to be related to better discrimination performance during proprioceptive illusions. A recent study consistently found that greater rs-FC between the motor cortex and the cerebellum, in elderly was found positively linked to better manual motor performance (Seidler et al., 2015). Moreover, inferior fronto-parietal regions including inferior parietal lobule are known to be particularly involved in human body representation (Naito et al., 2016) and has been shown to be activated during a kinesthetic illusion perception (Naito et al., 2007; Kavounoudias et al., 2008). It is thus not surprising that a stronger rs-FC between these regions and the motor cortex was associated with better movement discrimination performance in older participants.

5. Conclusion

The present work provides new insights into the central origin of the alteration of hand movement perception with advancing age and suggests that this might be caused by an alteration of the interhemispheric balance between the sensorimotor cortices occurring as early as 65 years old. The kinesthetic function of touch seems less affected, as it may rely less on the sensorimotor interhemispheric balance. Despite the structural and functional degradation of the brain with aging, the spreading of functional connectivity between different brain networks observed at rest can ultimately have a positive impact on kinesthesia, as it involves body representation brain areas.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Caroline Landelle: Investigation, Writing - original draft, Writing - review & editing, Visualization. **Jean-Luc Anton:** Formal analysis, Writing - review & editing. **Bruno Nazarian:** Methodology, Writing - review & editing. **Julien Sein:** Software, Writing - review & editing. **Ali Gharbi:** Methodology. **Olivier Felician:** Investigation, Writing - review & editing. **Anne Kavounoudias:** Conceptualization, Methodology, Writing - original draft, Writing - review & editing, Supervision, Funding acquisition.

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Appendix A. Supplementary data

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