# 1    Title Page

2    Title: Does Hemispheric Asymmetry Reduction in Older Adults (HAROLD) in motor cortex reflect

3    compensation?

4    Abbreviated Title: Compensation in sensorimotor HAROLD

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## Abstract

25

26 Older adults tend to display greater brain activation in the non-dominant hemisphere during even

27 basic sensorimotor responses. It is debated whether this Hemispheric Asymmetry Reduction in Older

28 Adults (HAROLD) reflects a compensatory mechanism. Across two independent fMRI experiments

29 involving an adult-lifespan human sample (N = 586 and N = 81; approximately half female) who

30 performed right hand finger responses, we distinguished between these hypotheses using

31 behavioural and multivariate Bayes (MVB) decoding approaches. Standard univariate analyses

32 replicated a HAROLD pattern in motor cortex, but in- and out-of-scanner behavioural results both

33 demonstrated evidence against a compensatory relationship, in that reaction time measures of task

34 performance in older adults did not relate to ipsilateral motor activity. Likewise, MVB showed that

35 this increased ipsilateral activity in older adults did not carry additional information, and if anything,

36 combining ipsilateral with contralateral activity patterns reduced action decoding in older adults (at

37 least in Experiment 1). These results contradict the hypothesis that HAROLD is compensatory, and

38 instead suggest that the age-related, ipsilateral hyper-activation is non-specific, in line with

39 alternative hypotheses about age-related reductions in neural efficiency/differentiation or inter-

40 hemispheric inhibition.

## Significance Statement

41

42 A key goal in the cognitive neuroscience of ageing is to provide a mechanistic explanation of how

43 brain-behaviour relationships change with age. One interpretation of the common finding that task-

44 based hemispheric activity becomes more symmetrical in older adults, is that this shift reflects a

45 compensatory mechanism, with the non-dominant hemisphere needing to "help out" with

46 computations normally performed by the dominant hemisphere. Contrary to this view, our

47 behavioural and brain data indicate that the additional activity in ipsilateral motor cortex in older

48 adults is not reflective of better task performance nor better neural representations of finger

49 actions.

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## Introduction

Functional neuroimaging has established that increased age is linked to weaker task-based neural lateralisation (e.g., Cabeza et al., 1997), with older adults showing increased activation of the non-dominant hemisphere; a pattern summarised as Hemispheric Asymmetry Reduction in Older Adults, or "HAROLD" (Cabeza, 2002). The explanation for this reduced lateralisation is debated. A widely cited idea is that the recruitment of the non-dominant hemisphere reflects compensatory mechanisms (Cabeza et al., 2018). An alternative hypothesis is that this increased activation is non-functional (e.g., Grady et al. 1994), perhaps reflecting inefficient or more dedifferentiated neural processing (Morcom & Johnson, 2015).

Motor responses, such as finger (Mattay et al., 2002; Rowe et al., 2006), wrist (Heuninckx et al., 2005) or grasping (Ward & Frackowiak, 2003; Ward et al., 2008) movements, are sufficient to evoke HAROLD patterns in motor areas. For example, mean activation within the right (ipsilateral) motor cortex increases with age when participants respond with their right hand (Tsvetanov et al., 2015). Brain-behaviour relationships are commonly examined to adjudicate between the compensation and inefficiency hypotheses. If ipsilateral activity is compensatory, averaged activation will be positively related to behavioural performance. Nevertheless, "univariate" activation results are inconclusive: greater ipsilateral motor activation in older adults has been reported to show positive (Mattay et al., 2002; Heuninckx et al., 2008), negative (Langan, et al., 2010; Cassady et al., 2020), or no (Riecker et al., 2006) relationship with kinematics. Multivariate approaches offer an alternative way to test these competing hypotheses. If increased ipsilateral activity is compensatory (rather than non-functional), it should contain task-relevant information. Multivoxel pattern analysis (MVPA) has demonstrated that, in line with de-differentiation, the distinctiveness of information represented within ipsilateral motor areas during finger tapping is reduced in older adults (Carp et al., 2011). However, a stronger assessment of whether ipsilateral motor activity is compensatory requires testing whether task-relevant information in ipsilateral

75    cortex is complementary to that in contralateral cortex. The degree of complementarity could

76    increase with age, even if the total amount of information in ipsilateral cortex decreases with age, as

77    Carp et al. found (i.e., the greater information in young people in ipsilateral cortex could be

78    redundant with that in contralateral cortex). This can be tested by combining voxels across

79    hemispheres and testing whether decoding is improved relative to using voxels from the

80    contralateral hemisphere alone (Morcom & Henson, 2018).

81         Morcom and Henson (2018) used multivariate Bayes (MVB), a model-based MVPA

82    technique, to test whether one model (set of voxels) is more likely than another in predicting

83    experimental conditions (Friston et al., 2008; Morcom & Friston, 2012). They tested a different

84    ageing-related hypothesis (the Posterior-to-Anterior Shift with Age), which claims that increased

85    anterior activity in older people is also compensatory (Davis et al., 2008). They found that, when

86    predicting memory, Bayesian Model Evidence in older adults was more often reduced, rather than

87    increased, for a model with voxels from both anterior and posterior brain regions compared to a

88    model with posterior voxels only. That is, results were more consistent with the hypothesis that age

89    reduces the efficiency/differentiation of neural activity, rather than compensation.

90         Here, we applied the same MVB logic to test HAROLD in the context of motor activity related

91    to simple finger presses across two motor fMRI experiments in the "Cam-CAN" population-derived

92    adult lifespan sample (www.cam-can.org; Shafto et al., 2014). In Experiment 1, participants (N=586)

93    pressed a button with their right index finger whenever they saw/heard a visual/auditory stimulus.

94    In Experiment 2, participants (N=81) were cued to press the button under one of four fingers of their

95    right hand (Figure 1). First, we assessed whether greater mean ipsilateral sensorimotor cortex

96    activation was associated with improved (i.e., shorter/less variable) reaction times (RTs) for older

97    adults during the scanner task, and in separate tasks run outside the scanner. Second, we used MVB

98    to test whether the model evidence based on action decoding was "boosted" for older adults when

99    models included ipsilateral voxels.
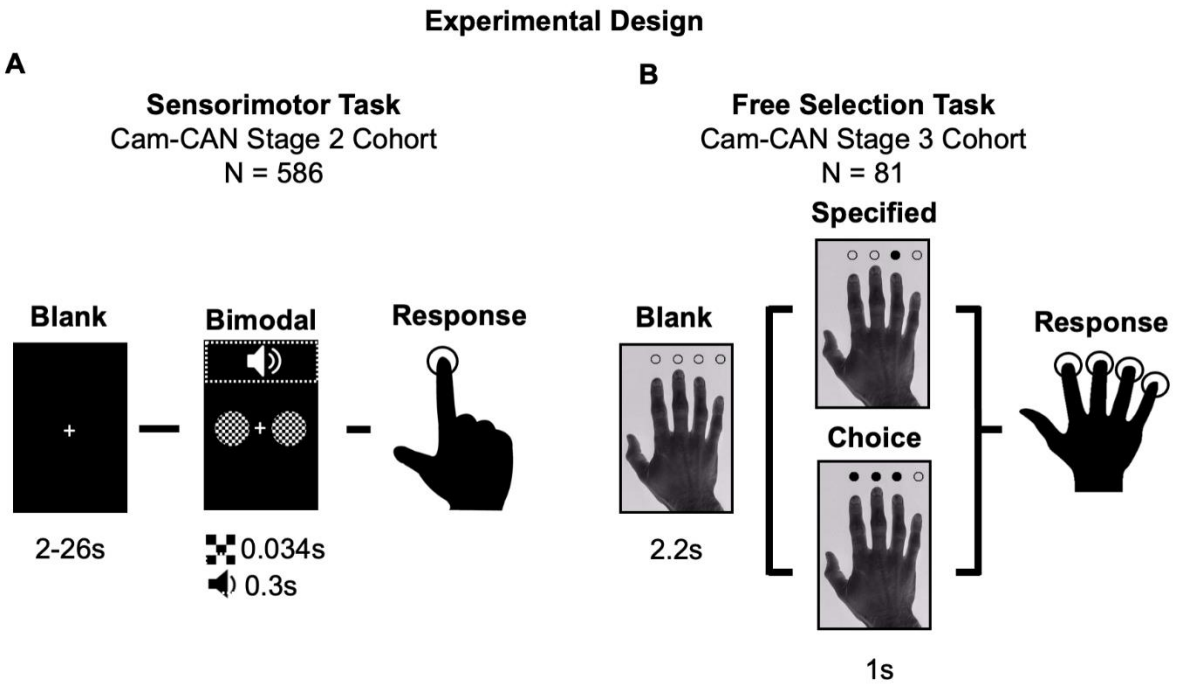
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**Experimental Design**



Figure 1. Experimental Design**. (A) Experiment 1.** Sensorimotor task trials began with a blank fixation

screen, followed by a bimodal (i.e., audio and visual) stimulus. Participants made finger press

responses if they sensed either or both types of stimulus (there were also rare unimodal stimuli on

~6% of trials, not shown here nor analysed below, in which only an audio or visual stimulus was

presented, whose purpose was just to ensure that both modalities needed to be attended). **(B)**

**Experiment 2.** Free selection task trials began with a picture of a hand with circles above the index,

middle, ring and little finger. Participants responded with a single finger press that matched one of

the cued digits, where only one digit was cued in the "specified" condition, whereas in the "choice"

condition, participants were free to choose one of the subset of three digits cued. Both experiments

required right-hand responses only.

# Materials & Methods

## Experiment 1: Sensorimotor Task

### Participants

A healthy, population-derived adult lifespan human sample (N=649; ages approximately uniformly distributed from 18 – 87 years; females = 327; 50.4%) was collected as part of the Cam-CAN study (Stage 2 cohort; Shafto et al., 2014). Participants were fluent English speakers in good physical and mental health based on the Cam-CAN cohort's exclusion criteria, which excluded volunteers with a low Mini Mental State Examination (MMSE) score (≤ 24), serious current medical or psychiatric problems or poor hearing or vision, as well as being based on standard MRI safety criteria. From this sample, we excluded participants who had missing behavioural measures from either in-scanner (N=4) or out-of-scanner (N=44). We also excluded participants who responded to <90% of trials either in-scanner (N=10) or out-of-scanner (N=5). Thus, the analysed sample consisted of 586 participants (females = 292; 49.8%). The study was approved by the Cambridgeshire 2 (now East of England–Cambridge Central) Research Ethics Committee. Participants gave informed written consent.

### Materials & Procedure

The sensorimotor task involved 120 bimodal audio/visual trials, as well as eight unimodal trials (four visual and four auditory; Figure 1A) that were included to discourage strategic responding to one modality only. Bimodal trials consisted of visual checkerboards being presented either side of a central fixation (34ms duration) concurrently with a binaural auditory tone (300ms duration). Unimodal trials consisted of either the isolated auditory or visual stimulus. The auditory tones were one of three equiprobable frequencies (300Hz, 600Hz or 1200Hz), which was not relevant to the task or current hypotheses. Participants were instructed to button-press with the right hand index finger when they heard or saw any stimuli. Each trial followed a fixation-only screen with a minimal stimulus onset asynchrony (SOA) of 2 seconds (resulting in SOAs ranging from 2-26 seconds)

136    designed to optimise the estimation of the fMRI impulse response through a sequence of

137    stimulation and null trials (see Shafto et al., 2014).

## Imaging Data Acquisition & Preprocessing

139    The MRI data were collected using a Siemens 3T TIM TRIO system with a 32 channel head-coil. A

140    T2*-weighted echoplanar imaging (EPI) sequence was used to collect 261 volumes, each containing

141    32 axial slices (acquired in descending order) with slice thickness of 3.7mm and an interslice gap of

142    20% (for whole brain coverage including cerebellum; TR = 1970ms; TE = 30ms; flip angle = 78°; FOV =

143    192mm x 192mm; voxel-size 3 x 3 x 4.44mm). Higher resolution (1mm x 1mm x 1mm) T1- and T2-

144    weighted structural images were also acquired (to aid registration across participants).

145    MR data preprocessing and univariate analysis were performed with SPM12 software

146    (Wellcome Department of Imaging Neuroscience, London, www.fil.ion.ucl.ac.uk/spm), release 4537,

147    implemented in the AA 4.0 pipeline (Cusack et al., 2015) described in Taylor et al. (2017). Specifically,

148    structural images were rigid-body registered to an MNI template brain, bias corrected, segmented,

149    and warped to match a grey matter template created from the whole CamCAN Stage 2 sample using

150    DARTEL (Ashburner, 2007; Taylor et al., 2017). This template was subsequently affine transformed to

151    standard Montreal Neurological Institute (MNI) space. The functional images were spatially

152    realigned, interpolated in time to correct for the different slice acquisition times, rigid-body

153    coregistered to the structural image, transformed to MNI space using the warps and affine

154    transforms from the structural image, and resliced to 3mm x 3mm x 3mm voxels.

## Univariate Imaging Analysis

156    To estimate activity for univariate voxelwise contrasts (i.e., to define ROIs), five conditions (i.e., 3

157    bimodal conditions, one per tone frequency, and 2 catch conditions, per audio or visual format)

158    were distinguished within a general linear model (GLM) for each participant using SPM. A regressor

159    for each condition was created from delta functions, aligned to the onset of a stimulus, that were

160    convolved with SPM's canonical hemodynamic response function, plus its temporal and dispersion

161     derivatives, resulting in three regressors per condition. The null events were excluded from the

162     model, and therefore, all regression coefficient were defined relative to this baseline activity. Six

163     additional regressors representing the three rigid body translations and rotations estimated in the

164     realignment stage were included in each GLM to capture residual movement-related artifacts.

165     Finally, the data were scaled to a grand mean of 100 over all voxels and scans within a session, and

166     the model was fit to the data in each voxel. The autocorrelation of the error was estimated using an

167     AR(1)-plus-white-noise model, together with a set of cosines that functioned to high-pass filter the

168     model and data to 1/128 Hz, that were estimated using restricted maximum likelihood. The

169     estimated error autocorrelation was then used to "prewhiten" the model and data, and ordinary

170     least squares used to estimate the model parameters. Contrasts were used to average across the 3

171     tone frequencies in the bimodal trials (i.e., the rarer unimodal trials were not analysed further). This

172     model was used for ROI definition and MVB, whereas for regressions involving univariate data, we

173     used a least squares separate (LSS) approach (Abdulrahman & Henson, 2016) before averaging over

174     voxels.

## Behavioural Measures

176     Reaction time (RT) was the time from stimulus onset to button press onset. RTs were estimated

177     during the fMRI sensorimotor task (i.e., in-scanner RT) and during an independent lab-based simple

178     RT task (i.e., out-of-scanner RT) performed during Stage 1 of the Cam-CAN project. In the out-of-

179     scanner task, participants were presented with the same picture stimulus as the free selection

180     experiment (Figure 1B; see section: Materials & Methods - Experiment 2: Free Selection - Materials

181     & Procedure) where, for each trial (N = 50), a blank circle above an index finger was filled black,

182     cueing a button-press response to be performed as quickly as possible. Upon pressing the button (or

183     after 3s), the circle's fill was cleared and followed by pseudo-random inter-trial interval (see Shafto

184     et al., 2014). Note that, while the out-of-scanner task was speeded, the in-scanner task was

185     unspeeded (so that older participants did not feel too challenged). For each participant, both the

186     mean and standard deviation (variability) of RTs across trials were computed.

## Experiment 2: Free Selection

### Participants

Participants were a subset of the cohort in Experiment 1 who also completed the Free Selection

fMRI experiment during Stage 3 of Cam-CAN data collection (N=87; approximately uniformly

distributed from 19 - 85yrs; females = 38; 43.7%). We excluded 6 participants whose out-of-scanner

RT measures were not collected (all remaining participants responded to >90% of trials, and were

correct for >75% of trials). Therefore, the analysed sample consisted of 81 participants (females =

35).

### Materials & Procedure

The free selection task was adapted from the 3-choice free selection task of Zhang et al. (2012),

which involves a visually-paced right hand button press task that is typically used to examine

executive control and action decisions in ageing. Across 240 trials, participants were presented with

an image of a right hand and pressed a button with one finger in response to a cue (see Figure 1B).

Individual trials involved either one ("specified" condition; N=120, split equally between each of the

four fingers) or three ("choice" condition; remaining 120 trials) of the circles being filled black. In

both cases, participants were instructed to respond as quickly as possible with a single button-press

from a cued digit; thus for choice trials the responding finger could be freely selected. Cues were

pseudorandomly ordered so that participants do not see four or more responses of the same

condition in a row (see Shafto et al., 2014 for more details). A short gap (either 4.2s or 6.2s)

separated blocks of 20 trials.

### Imaging Data Acquisition & Preprocessing

Data acquisition and processing were the same as in Experiment 1 (see section: Methods -

Experiment1: Sensorimotor Task - Imaging Data Acquisition & Preprocessing), aside from an

increased number of volumes being acquired (296) due to a longer session duration.

## Univariate Imaging Analysis

The procedure described for Experiment 1 was repeated here (see section: Materials & Methods - Experiment 1: Sensorimotor Task - Univariate Imaging Analysis), except that only the canonical HRF was used (because the blocked nature of trials prevents reliable estimation of the HRF derivatives; Henson, 2015). For the present analyses, we combined onsets across the specified and choice conditions, leaving four predictors based on which finger was pressed (i.e., index, middle, ring and little). These four conditions were averaged to estimate the mean response versus baseline.

## Behavioural Measures

The same variable definitions and computations were used as described for Experiment 1 (see section: Materials & Methods - Experiment 1 - Sensorimotor Task). Unlike Experiment 1, the out-of-scanner RT variables were measured during a choice RT task that had a design more comparable to the in-scanner free selection task. Specifically, the choice RT task had the same parameters as the simple RT task, but on each trial (N=67) any one of the four circles above the fingers could be filled black, and the participant was instructed to press the corresponding finger as quickly as possible.

## General Methods

## Regions of Interest (ROIs)

A standard group univariate voxelwise approach was used to define a contralateral sensorimotor cortex ROI, based on contrasting all bimodal trials versus baseline in Experiment 1. Specifically, the 70 most significant voxels (based on t-statistic rank) were selected according to the peak closest to the left "hand knob" landmark in the central sulcus (Yousry et al., 1997; Figure 2A; for MNI coordinates see Figure 2A; Table 1). This contralateral ROI was mirror flipped (i.e., x-coordinate reversed in sign) to create the ipsilateral sensorimotor cortex ROI (Figure 2A; Table 1). Note that this ROI selection based on the average response versus baseline is averaged across age (i.e., not biased to show age effects). The same ROIs were applied to Experiment 2 for consistency. Note that images

235     were spatially smoothed (10mm Gaussian kernel) for the purpose of ROI definition only. All ROI

236     analyses used unsmoothed data.

## Multivariate Bayesian Decoding (MVB)

238     A series of MVB decoding models were fit to assess the information about actions represented in

239     each ROI or combination of ROIs. Each MVB decoding model is based on the same design matrix of

240     experimental variables used in the univariate GLM, but the mapping is reversed: many physiological

241     data features (derived from fMRI activity in multiple voxels) are used to predict a psychological

242     target variable (Friston et al., 2008). This target (outcome) variable is specified as a contrast. In both

243     experiments, the outcome was whether an action had been performed (versus baseline), with all

244     covariates apart from those involved in the target contrast (i.e., the null space of the target contrast)

245     removed from both target and predictor variables.

246          Each MVB model was fit using a parametric empirical Bayes approach, in which empirical

247     priors on the data features (voxelwise activity) are specified in terms of spatial patterns over voxel

248     features and the variances of the pattern weights. As in earlier work, we used a "sparse" spatial prior

249     in which patterns are individual voxels. Because these decoding models are normally ill-posed (with

250     more voxels relative to scans, or more precisely, relative to degrees of freedom in the timeseries),

251     these spatial priors on the patterns of voxel weights regularise the solution. MVB also uses an overall

252     sparsity (hyper) prior in pattern space that embodies the expectation that a few patterns make a

253     substantial contribution to the decoding and most make a small contribution.

254          The pattern weights specifying the mapping of data features to the target variable are

255     optimized with a greedy search algorithm using a standard variational scheme, which iterates until

256     the optimum set size is reached (Friston et al., 2007). This is done by maximizing the free energy,

257     which provides an upper bound on the Bayesian log evidence (the marginal probability of the data

258     given that model). The evidence for different models predicting the same psychological variable can

259     then be compared by computing the difference in their log evidences (equivalent to the log of the

260    "Bayes Factor"; Friston et al., 2008; Chadwick et al., 2012; Morcom & Friston, 2012). In this work, the

261    main outcome measures were the log evidence for each model and the spread (standard deviation)

262    of weights across voxels in the ROI (Morcom & Henson, 2018).

263        To test whether ipsilateral activity was compensatory, we used a "boost" measure (Morcom

264    & Henson, 2018) to assess the contribution of the ipsilateral ROI to performing actions. This used

265    Bayesian model comparison within participants to assess whether a combined contralateral-

266    ipsilateral (i.e., bilateral) model boosted prediction of actions relative to a contralateral-only model.

267    The compensatory hypothesis, in which the ipsilateral hemisphere is engaged to a greater degree in

268    older age and improves performance, predicts that a boost will be more often observed with

269    increasing age. The dependent measure was the log model evidence coded categorically for each

270    participant to indicate the outcome of the model comparison. The three possible outcomes were as

271    follows: a boost to model evidence for bilateral relative to contralateral-only models (difference in

272    log evidence > 3), ambiguous evidence for the two models (-3 < difference in log evidence < 3), or a

273    reduction in prediction of action for bilateral relative to contralateral-only (difference in log evidence

274    < -3). These values were chosen because a log difference of 3 corresponds to a Bayes Factor >20

275    which is generally considered strong evidence (Lee & Wagenmakers, 2014).

276        For the across-participant analyses of this MVB "boost", participants were only included if

277    their data allowed reliable decoding by the bilateral model (Morcom & Henson, 2018). To determine

278    this, we contrasted the evidence for the bilateral model with that from models in which the design

279    matrix (and therefore the target variable) was randomly phase-shuffled. One-tailed t-tests were

280    used to compare whether the mean difference between true and shuffled differences in log-

281    evidence was greater than 3 (Morcom & Henson, 2018; Figure 4A), which left a total of 650 and 54

282    participants for Experiment 1 and 2, respectively (i.e., N=4 and N=27 excluded respectively). For

283    additional control analyses, we repeated the MVB boost analysis with models where voxel sizes

284    were equated (see Results section). For one of the control analyses which involved halving the

285    number of voxels in the bilateral model, we repeated this preliminary phase shuffling step (because

286    a different bilateral model was used) which led to excluding four additional participants in

287    Experiment 1 and prevented this particular control analysis for Experiment 2, because there was not

288    evidence that decoding was possible from this ROI ($p$ = 0.12).

289    ## Experimental Design & Statistical Analysis

290    Age effects on continuous univariate, behavioural and multivariate measures were tested using

291    robust regression in R [version: 3.6.1] with the *rlm* function (package: MASS [version: 7.3-51.4]), in

292    order to down-weight extreme values (Venables & Ripley, 2002). These regression analyses used

293    standardised linear and quadratic age predictors. Two-tailed robust F-tests (Wald tests) were used to

294    test the significance of regression coefficients: we first tested for general age effects (linear and/or

295    quadratic), and if significant (α level of 0.05), we performed post-hoc Wald tests on linear and

296    quadratic age predictors separately. Analysis of the categorical outcomes for the between-region

297    MVB model comparison (Figure 4B) used ordinal regression. When all three categorical outcomes

298    were observed, this was implemented with the *polr* function (package: MASS; as in Henson &

299    Morcom, 2018; Table 4), whereas *glm* (package: stats [version: 3.61]) was used in binary cases (i.e.,

300    when 'reduction' was not observed for any participant; Figure 4B). For ordinal regression, the results

301    are reported from a model containing only the linear age term, due to the categorical nature of the

302    data (though the same pattern of findings were observed with the full quadratic model; see Table 4

303    with chi-square tests for general age effects).

304        When important, null-hypothesis significance tests were supplemented with Bayes factors

305    (Wagenmakers, 2007; Rouder et al., 2009). For continuous outcomes, we used the *lmbf* (package:

306    BayesFactor [version: 0.9.12-4.2]) with default parameters (Rouder, et al., 2012) to contrast models

307    with/out the effect predicted by compensation accounts. For categorical outcomes (i.e., MVB model

308    comparison), we used the *brm* function (package: brms [version: 2.10.0]) with the Bernoulli family

309    function to test for the absence of the hypothesis predicted by compensation (i.e., age effect > 0). A

310     Student's t distribution prior was used, based on 7 degrees of freedom, a mean of 0, and a scale

311     factor of 10 and 1 for the intercept and slope, respectively (e.g., Wagenmakers et al., 2010). The

312     Bayes Factors were interpreted according to criteria set out by Jeffreys (1961; cited from Jarosz &

313     Wiley, 2014), where a $BF_{01}$ between 1-3, 3-10 and >10 indicates 'anecdotal', 'substantial' and 'strong'

314     evidence in favour of the null, respectively.

## Data Availability

316     Raw and minimally pre-processed MRI (i.e., from automatic analysis; Taylor et al., 2017) and

317     behavioural data are available by submitting a data request to Cam-CAN (https://camcan-

318     archive.mrc-cbu.cam.ac.uk/dataaccess/). The univariate and multivariate ROI data, and behavioural

319     data, can be downloaded from the Open Science Framework alongside analysis code

320     (https://osf.io/seuz5/).

## Results

### HAROLD univariate effect

323     The univariate voxel-wise contrast of key press versus baseline during the sensorimotor task

324     (Experiment 1), averaged across participants, showed strong contralateral activation throughout

325     fronto-parietal cortex (red voxels in Figure 2A, left). The x-coordinates of a contralateral motor

326     cortex ROI that spanned suprathreshold voxels in the pre-central gyrus were flipped to define an

327     ipsilateral motor cortex ROI (Figure 2A gold voxels; Table 1; see Methods - General Methods - ROIs).

328             Consistent with HAROLD's predictions, when averaging over voxels within the ipsilateral ROI,

329     there was a significant effect of age on univariate activity, with an increase in activation that

330     flattened off in old age (Figure 2B, left), in line with significant linear and quadratic components (see

331     Table 1). In fact, although the ROI was defined independently of age, it entirely overlapped

332     voxelwise results from a positive t-contrast on the (linear) effect of age (green voxels in Figure 2A,

333     left). The significant age effect for the contralateral ROI was in the opposite direction, with mean

334     activity decreasing linearly as a function of age (Figure 2B, left; Table 1).

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335    When applying these ROIs defined in Experiment 1 to Experiment 2, we replicated this

336    HAROLD effect, where greater age was associated with greater ipsilateral sensorimotor cortex

337    activation; an age effect that again decelerated in later life (Figure 2B, right; Table 1). Unlike

338    Experiment 1, no suprathreshold age effect was observed when repeating the voxelwise linear

339    contrast, possibly owing to the lower statistical power than in Experiment 1 (Figure 2A, right). Again,

340    the trend for the age effect in the contralateral ROI was in the opposite direction, though only the

341    quadratic term was significant when tested independently (Table 1).

342

343    Table 1. Age effects on mean univariate and spread of multivariate action effects.

| Experiment | Measure/ROI | | Age Effect | | Linear | | Quadratic | |
|---|---|---|---|---|---|---|---|---|
| | | | F | p | t | p | t | p |
| Sensorimotor | | | | | | | | |
| | Univariate Mean | | | | | | | |
| | | Contralateral | **31.7** | **<.0001** | **-7.95** | **<.0001** | -0.3 | 0.76 |
| | | Ipsilateral | **18.2** | **<.0001** | **5.26** | **<.0001** | **-3.11** | **.002** |
| | Multivariate Spread | | | | | | | |
| | | Contralateral | **4.82** | **.008** | **2.31** | **.021** | **-2.08** | **.038** |
| | | Ipsilateral | 2.97 | .052 | - | - | - | - |
| Free Selection | | | | | | | | |
| | Univariate Mean | | | | | | | |
| | | Contralateral | **4.49** | **.014** | 1.88 | .067 | **-2.32** | **.025** |
| | | Ipsilateral | **9.31** | **.0002** | **3.66** | **.0004** | **0.900** | **.032** |
| | Multivariate Spread | | | | | | | |
| | | Contralateral | 2.83 | .065 | - | - | - | - |
| | | Ipsilateral | 2.02 | .14 | - | - | - | - |

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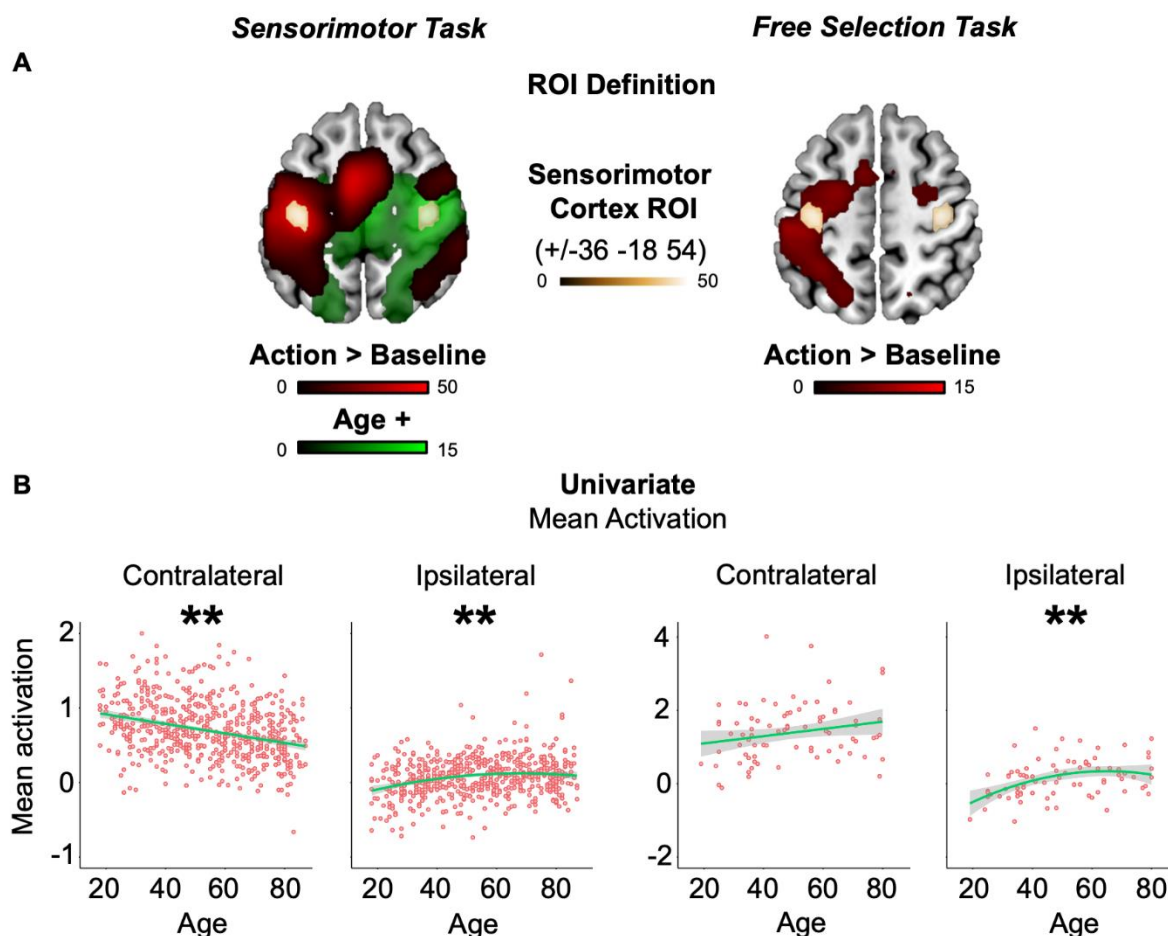
Figure 2. ROI definitions and responses. **(A) ROI Definitions.** Univariate whole-brain voxelwise T-tests are displayed on a standard template brain for all actions > baseline (red map) and for positive (linear) effect of age (green map). Color depth indicates T-statistic value. The actions > baseline contrast from Experiment 1 was used to define the functional ROI in sensorimotor cortex (gold map), which was mirror-flipped across hemispheres for unbiased analysis of age effects in both experiments (see section: Methods - General Methods - ROIs). **(B) Univariate ROI Responses.** Consistent with HAROLD, increased age predicted increased univariate activation of the ipsilateral ROI in both experiments, accompanied by the opposite pattern in the contralateral ROI. Green lines represent robust-fitted regression lines (with a second polynomial expansion in cases where a significant quadratic component was observed) and shaded areas show 95% confidence intervals. [* = p < 0.05, ** = p < 0.01].

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## Testing Compensation: Behavioural

359   If the increased univariate activity in ipsilateral sensorimotor cortex is compensatory, it might be

360   expected to benefit task performance. We measured task performance using the variability (Table 2)

361   and mean (Table 3) of RTs for both the in-scanner and out-of-scanner motor tasks. First, we tested

362   whether there was a main effect of age on RT (Figure 3A). For variability of simple RTs in Experiment

363   1, significant effects were found for RTs recorded both in-scanner and out-of-scanner, where higher

364   ages were linearly associated with increased variability, that is, worse performance (Table 2; Figure

365   3A left). These significant age effects were replicated in the choice RTs of Experiment 2, both in-

366   scanner and out-of-scanner, where, again, a linear positive change in RT variability was predicted by

367   increased age (Table 2; Figure 3A right). For the out-of-scanner measure in Experiment 1, the

368   quadratic component was also significant, such that the increase in RT variability actually

369   accelerated in old age (Figure 3A). For mean simple RTs, there was no significant effect of age for the

370   in-scanner measure during Experiment 1 (Table 3; Figure 3A left), most likely because this version of

371   the task was not speeded. However, there was an age effect on the speeded out-of-scanner task,

372   with, like for RT variability, significant linear and quadratic components, indicating that worse

373   performance accelerated in old age (Table 3; Figure 3A left). For Experiment 2, the results for mean

374   RT were similar to those reported for RT variability (i.e., there was a positive linear effect of age;

375   Figure 3A right).

376      Having established age effects on task performance, the critical question was whether this

377   age-related variance was related to ipsilateral motor activation, with compensation predicting that

378   higher activation in older people would relate to better (i.e., faster and less variable) RTs. To assess

379   this, we used multiple regression to test whether age, ipsilateral activation and their interaction

380   predicted RT variabilty. If ipsilateral activity is compensatory and has an overall benefit to

381   performance, then one would expect a significant interaction between age and ipsilateral activity,

382   whereby the tendency for higher ipsilateral activation to be associated with reduced RT variability

383   would increase with age. However, contrary to this prediction, no significant interaction between

384    ipsilateral activity and age was observed when predicting RT variability (Table 2; Figure 3B top row)

385    or mean RT (Table 3; Figure 3B bottom row) either in- or out-of-scanner for Experiment 1 or

386    Experiment 2. In fact, Bayes Factors presented consistent evidence in favour of no interaction for all

387    measures with a significant age effect in Experiment 1 (Figure 3B left) and three of the four

388    measures in Experiment 2 (Figure 3B right) (see Table 2, 3).
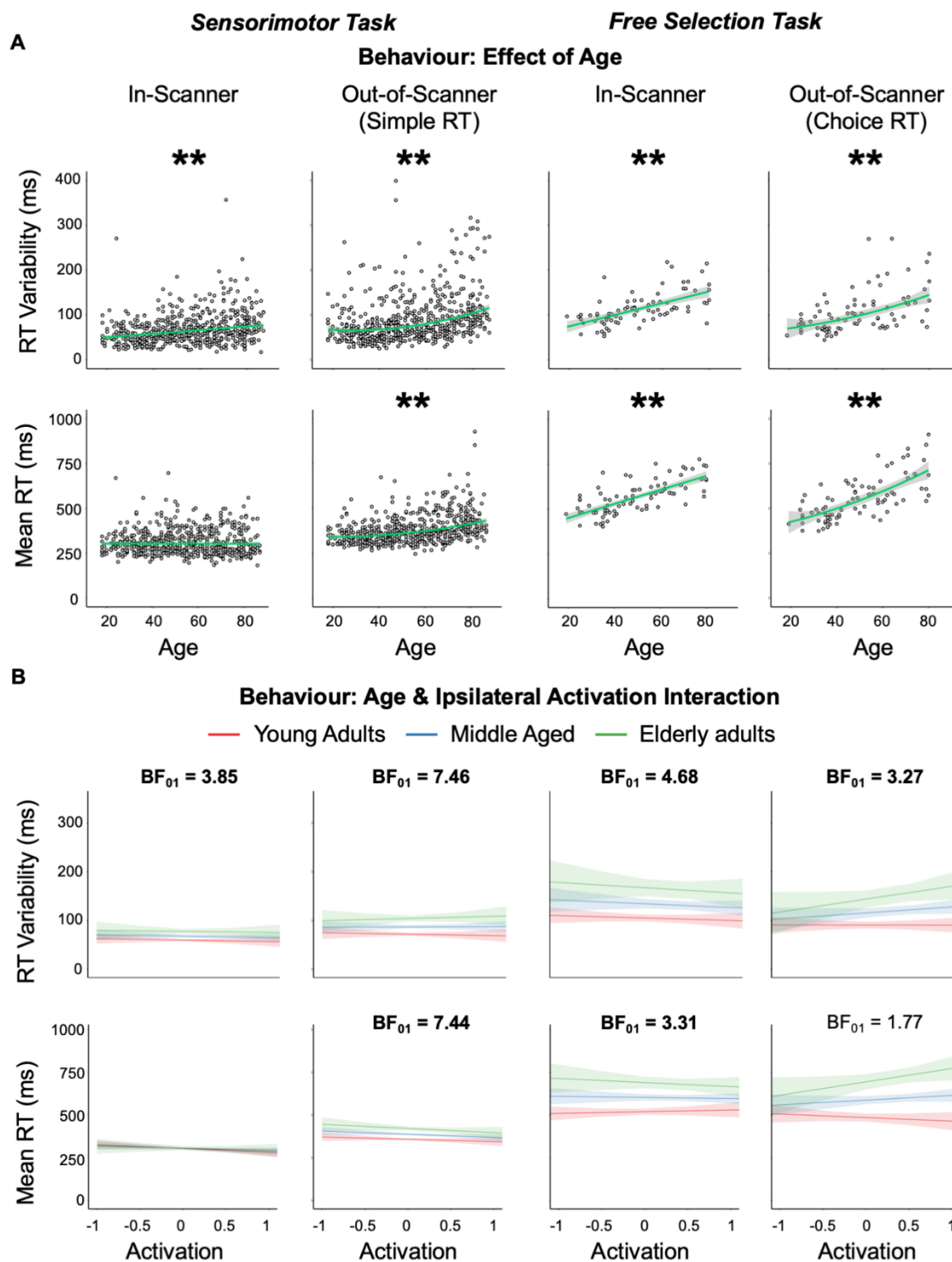
Figure 3. Behavioural results for RT variability and mean RT. **(A) Effect of age.** Increased age

predicted worse performance (greater RT variability/mean) across Experiments 1 (left) and 2 (right)

whether measures were acquired in- or out-of-scanner. For asterisk and regression line conventions,

see Figure 2**. (B) Interaction between age and ipsilateral univariate activation.** No significant

interactions between age and ipsilateral mean activation were observed across experiments,

395 regardless of whether measures were acquired in-or out-of-scanner. Bayes Factors for the null ($BF_{01}$)

396 that had substantial evidence for this lack of interaction are in bold. Though the interaction was

397 tested in a continuous fashion, tertile splits were used to define age groups (red, blue, green lines)

398 for purposes of illustration.

399 Table 2. Age and mean univariate effects from behavioural multiple regression with RT variability.

400 Degrees of freedom for Experiment 1: full model $F(5,580)$, age effect $F(2,580)$ and $t(580)$; Experiment

401 2: full model $F(5,75)$, age effect $F(2,75)$ and $t(75)$. Bold text indicates $p < 0.05$.

| Experiment | Measure/Coefficient | Effect | | | Linear | | Quadratic | | $BF_{01}$ |
|---|---|---|---|---|---|---|---|---|---|
| | | F | t | p | t | p | t | p | |
| Sensori-motor | In-Scanner | | | | | | | | |
| | Full Model | **9.44** | - | **<.0001** | - | - | - | - | - |
| | Ipsilateral | - | -0.53 | .596 | - | - | - | - | - |
| | Age | **22.87** | - | **<.0001** | **6.66** | **<.0001** | 0.67 | .5 | - |
| | Ipsilateral * Age | 0.07 | - | .932 | - | - | - | - | **3.85** |
| | Out-of-Scanner | | | | | | | | |
| | Full Model | **20.7** | - | **<.0001** | - | - | - | - | - |
| | Ipsilateral | - | 0.16 | .873 | - | - | - | - | - |
| | Age | **49.62** | - | **<.0001** | **9.37** | **<.0001** | **3.18** | **.002** | - |
| | Ipsilateral * Age | 0.49 | - | .612 | - | - | - | - | **7.4** |
| Free Selection | In-Scanner | | | | | | | | |
| | Full Model | **11.32** | - | **<.0001** | - | - | - | - | - |
| | Ipsilateral | - | -0.75 | .457 | - | - | - | - | - |
| | Age | **22.46** | - | **<.0001** | **6.59** | **<.0001** | 1.02 | .319 | - |
| | Ipsilateral * Age | 0.36 | - | .698 | - | - | - | - | **4.68** |
| | Out-of-Scanner | | | | | | | | |
| | Full Model | 6.95 | - | **<.0001** | - | - | - | - | - |
| | Ipsilateral | - | 0.65 | .512 | - | - | - | - | - |
| | Age | **10.42** | - | **.0001** | **4.4** | **<.0001** | 0.47 | .641 | - |
| | Ipsilateral * Age | 1.15 | - | .321 | - | - | - | - | **3.27** |

402

403     Table 3. Age and mean univariate effects from behavioural multiple regression with mean RT. See

404     Table 2 for degrees of freedom and conventions.

405

| Experiment | Measure/Coefficient | | Effect | | | Linear | | Quadratic | | BF$_{01}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | F | t | p | t | p | t | p | |
| Sensori-motor | In-Scanner | | | | | | | | | |
| | | Full Model | 2.03 | - | .074 | - | - | - | - | - |
| | | Ipsilateral | - | - | - | - | - | - | - | - |
| | | Age | - | - | - | - | - | - | - | - |
| | | Ipsilateral * Age | - | - | - | - | - | - | - | - |
| | Out-of-Scanner | | | | | | | | | |
| | | Full Model | **22.27** | - | **<.0001** | - | - | - | - | - |
| | | Ipsilateral | - | -1.14 | .258 | - | - | - | - | - |
| | | Age | **54.38** | - | **<.0001** | **10.03** | **<.0001** | **2.43** | **.015** | - |
| | | Ipsilateral * Age | 1.81 | - | .165 | - | - | - | - | **7.44** |
| Free Selection | In-Scanner | | | | | | | | | |
| | | Full Model | **17.97** | - | **<.0001** | - | - | - | - | - |
| | | Ipsilateral | - | 0.4 | .693 | - | - | - | - | - |
| | | Age | **33.37** | - | **<.0001** | **7.64** | **<.0001** | **2.07** | **.044** | - |
| | | Ipsilateral * Age | 1.96 | - | .149 | - | - | - | - | **3.31** |
| | Out-of-Scanner | | | | | | | | | |
| | | Full Model | 16.23 | - | **<.0001** | - | - | - | - | - |
| | | Ipsilateral | - | -0.57 | .565 | - | - | - | - | - |
| | | Age | **23.38** | - | **<.0001** | **6.68** | **<.0001** | 0.52 | .608 | - |
| | | Ipsilateral * Age | 2.96 | - | .058 | - | - | - | - | 1.77 |

406       Lastly, we tested the possibility that ipsilateral recruitment in later life partially compensates

407    for reduced contralateral function. Although compensatory recruitment may have a net benefit to

408    performance, compensation can also function like a walking stick, being engaged to a greater degree

409    by people with a greater need for it (Backman, 1985). In such cases, compensatory brain activity may

410    correlate negatively with individual performance in older adults (i.e., only partially, rather than fully,

411    compensating relative to younger people (e.g., Daselaar & Cabeza, 2005; de Chastelaine et al., 2011;

412    Morcom & Johnson, 2015)). We therefore used multiple regression to ask whether ipsilateral

413    activation would relate positively to performance once effects of contralateral impairment were

414    taken into account by including contralteral mean activity (i.e., degree of impairment) as a predictor.

415    We expected that ipislateral activation would be associated with better performance only in people

416    with low contralateral activity, not in people with maintained (high) contralateral activity, who did

417    not need to compensate. This type of compensatory account therefore predicts an interaction

418    between contralateral and ipsilateral activity in relation to RT performance. To test this, we repeated

419    analyses replacing the age predictor with contralateral mean activity. In neither experiment was

420    there a signficant interaction between ipsilateral activity and contralateral activity (all *p's* ≥ 0.074).

421    This remained the case even if we added age as a third predictor. Indeed, there was substantial

422    Bayesian evidence against this effect for all measures (with or without age) in Experiment 1 ($BF_{01}$'s ≥

423    3.19) and, in Experiment 2, for the in-scanner RT variability measure (3 predictor model: $BF_{01}$ = 4.04;

424    all other $BF_{01}$'s ≤ 2.98).

### Testing Compensation: Multivariate

We further tested the compensation account of HAROLD using a multivariate approach. If the increasing ipsilateral activation with age reflected compensation, then multivoxel analyses should show that this increased activity carries additional information about actions, over and above that provided by the contralateral hemisphere. Note that this could happen even if the mean response across voxels did not relate to behavioural performance, as in the previous section (e.g., Morcom & Henson, 2018).

To test this, we first applied MVB to the combination of contra- and ipsilateral motor ROIs (i.e., 138 voxels in total), to check classification of an action was above chance, by comparing real versus phase-shuffled fMRI data. Results showed that the difference in log model evidence was greater than 3 on average across participants in both Experiment 1 ($t$(585) = 44.27, $p < 0.0001$) and Experiment 2 ($t$(80) = 4.57, $p < 0.0001$). Figure 4A shows that decoding was possible for the majority of participants. There was also a significant linear effect of age on the probability that model evidence was (or was not) greater than 3 for Experiment 2 where successful decoding was more likely to occur for older ages ($z$(80) = 3.11, $p = 0.005$). In Experiment 1, this was not examined due to the rarity (N=4) that the difference in model evidence was less than 3 (Figure 4A).

Having shown that MVB decoding was possible, one measure of multivariate information is the spread (e.g., standard deviation) of voxel classification weights (Morcom & Henson, 2018). This measure indexes the absolute magnitude of unique voxel contributions to the task. We therefore calculated spread for MVB models applied to each ROI separately. The results are shown in Figure 4B. In Experiment 2, no significant effect of age was observed on the spread of either the contralateral or ipsilateral weights (Figure 4B right; Table 1). However, in Experiment 1, there was a significant effect of age on spread for the contralateral ROI, in which the linear and quadratic components were significant, indicating that decodable information about a right finger press increased with age (in a decelerating fashion) in contralateral sensorimotor cortex (Figure 4B left;

24

450    Table 1). The effect of age on weight spread was not significant for the ipsilateral hemisphere,

451    though there was a trend in the same direction (Figure 4B left; Table 1). Thus, unlike in Morcom &

452    Henson (2018), it might be that multivariate information about a right finger press increases with

453    age in ipsilateral motor cortex, the region that is proposed to compensate. However, even if this

454    age-related increase occurs for both ipsilateral and contralateral ROIs, it is possible that the same

455    information is being represented in each hemisphere. That is, any age-related increase in

456    information in the ipsilateral ROI could be redundant with that in the contralateral ROI, rather than

457    being unique (i.e., compensatory).

458    Therefore the crucial test was whether the information in the ipsilateral ROI improved action

459    prediction compared to that in the contralateral ROI. Using MVB in Experiment 1, the proportion of

460    participants showing such an ipsilateral "boost" actually decreased, rather than increased, with age

461    (linear, $z(580) = -2.86$, $p = 0.004$) (Figure 4C). In other words, contrary to a compensatory account,

462    the odds that model evidence was boosted by including ipsilateral with contralateral activity for

463    older adults was 0.61 times that for younger adults. Indeed, the Bayes Factor provided strong

464    evidence in favour of accepting the null over the compensatory hypothesis ($BF_{01} = 21.99$). For

465    Experiment 2, no significant effect of age was found ($z(52) = -0.88$, $p = 0.38$) (Figure 4C) though, in

466    line with Experiment 1, there was substantial Bayesian evidence against the compensatory

467    hypothesis ($BF_{01} = 4.87$).

468    We performed a final check where we explicitly matched the number of voxels in the

469    combined versus contralateral models. Regardless of whether we halved the number of voxels in the

470    combined model (from 140 to 70), or doubled the number of voxels in the contralateral model (from

471    70 to 140), the significant linear negative effect of age in Experiment 1 and non-significant effect in

472    Experiment 2 were replicated (after halving: Experiment 1: $t(575) = -10.02$, $p < 0.0001$; after

473    doubling: Experiment 1: $t(579) = -14.13$, $p < 0.0001$; Experiment 2: $p = 0.29$). All findings were of the

25

474     same pattern across experiments when models contained both the linear and quadratic age terms

475     (see Table 4).

Figure 4. MVB results. **(A) Multivariate Mapping.** For the target outcome being decoded (i.e.,

performing an action), the difference in log model evidence was significantly higher than 3 (dashed

line) when using real (as opposed to phase-shuffled) action onsets, indicating reliable decoding

across both experiments (left and right; dotted line indicates a difference of 0). **(B) Multivariate ROI**

**Responses.** The spread of voxel weights showed an increase with age in the contralateral ROI in

482     Experiment 1, plus a similar trend in Experiment 2, and for the ipsilateral ROI in Experiment 1, but

483     not in Experiment 2. **(C) Model Comparison.** For Experiment 1 (left) results showed that, contrary to

484     a compensatory account, increased age actually led to a reduction in the likelihood of a boost when

485     including ipsilateral voxels. For the free selection task (right), the effect of age was in the same

486     direction but did not reach significance.

487

488     Table 4. Age effects from ordinal regression during the MVB boost analyses.

| Experiment | Measure | Age Effect | Linear | | | Quadratic | | |
|---|---|---|---|---|---|---|---|---|
| | | p (X2) | t | z | p | t | z | p |
| Sensorimotor | | | | | | | | |
| | Bilateral - Contralateral-only | **.021** | - | **-2.7** | **.007** | - | 0.55 | .582 |
| | Control: Halve Bilateral | **<.0001** | **-7.21** | - | **<.0001** | -0.21 | - | .84 |
| | Control: Double Contralateral | **<.0001** | **-6.1** | - | **<.0001** | -1.43 | - | .151 |
| Free Selection | | | | | | | | |
| | Bilateral - Contralateral-only | .597 | - | - | - | - | - | - |
| | Control: Halve Bilateral | - | - | - | - | - | - | - |
| | Control: Double Contralateral | .49 | - | - | - | - | - | - |

489
490

## Discussion

491

492    After replicating univariate HAROLD effects in motor cortex (e.g., Naccarato et al., 2006; Tsvetanov

493    et al., 2015) across two finger movement fMRI experiments in a large lifespan sample, we tested if

494    the additional ipsilateral activation in older adults reflected a compensatory mechanism. None of the

495    behavioural or multivariate measures, in either experiment, showed age effects that would be

496    predicted by a compensation account of HAROLD. In fact, Bayes Factors demonstrated substantial

497    evidence against compensatory interactions between age and ipsilateral mean activation for all

498    behavioural analyses in Experiment 1 as well as for many in Experiment 2. Likewise, the Bayes

499    Factors for the MVB boost analysis were strongly against any age effect, where a compensation

500    account would predict an age-related boost for action decoding with additional ipsilateral voxels. In

501    fact, for Experiment 1, an age effect was observed in the opposite direction: as age increased, adding

502    the additionally activated voxels was found to be *less* likely to improve action decoding.

503        Previous tests of age-related compensatory accounts have been inconclusive (Ward, 2006).

504    Some of this uncertainty in the literature might owe to differences in sample size, task and/or

505    analysis. At least for finger presses, we believe that our sensorimotor results are more conclusive

506    because: (1) they come from a relatively large and more population-representative samples, (2) they

507    simultaneously model age, behaviour and (ispi- and contra-lateral) activation, and (3) include a

508    Multivariate Bayesian approach that tests not only whether there is multivoxel information about

509    actions in ipsilateral cortex, but also whether this information is distinct (i.e., non-redundant) from

510    that in contralateral cortex.

511        Another reason for the lack of agreement in the literature is that compensation may take

512    more than one form, and is difficult to test with small samples (for reviews, see Scheller et al., 2014;

513    Morcom & Johnson, 2015). Compensation may not always give rise to a positive relationship

514    between the compensatory activation and behaviour. Instead, it might only be partially successful,

515    analogous to a walking stick that helps older people walk faster than without it, but still not as fast

516    as they would in the absence of any age-related decline (Daselaar & Cabeza, 2005; de Chastelaine et

517    al., 2011). In the present case, if performance declines with age due to reduced contralateral motor

518    function, this may be only partially offset by compensatory ipsilateral activation, giving rise to a net

519    negative association between ipsilateral activity and performance in older people. We therefore

520    tested for this 'partial compensation' in additional behavioural analyses that used contralateral

521    activity as a surrogate for the degree of age-related motor impairment. However, there was

522    evidence against the predicted interaction of contralateral and ipsilateral activity on performance.

523    Moreover, partial compensation is inconsistent with our MVB results, where multivariate

524    information was more likely to be unchanged or reduced with the purported compensatory

525    mechanism (i.e., ipsilateral activity) with increasing age.

526            Thus our multivariate (MVB) analyses arguably provide the strongest evidence against

527    compensation (Figure 4C). This result is consistent with the only other multivariate experiment, to

528    our knowledge, to examine this in the motor system, where MVPA demonstrated less distinctive

529    ipsilateral motor cortex activity with age (Carp et al., 2011). However, our results strengthen that

530    finding in a crucial way. While age could reduce the information in ipsilateral motor cortex, it might

531    also reduce information in contralateral motor cortex to a greater extent, such that ipsilateral cortex

532    still provides compensatory (non-redundant) information. This question of redundant information

533    can only be tested by combining voxels across hemispheres, as enabled by MVB. Indeed, the voxel

534    weight spread measure from MVB in Experiment 1 hinted that older age might be associated with

535    increased multivariate spread across hemispheres (Figure 4B left). Considered in isolation, this might

536    support a compensatory role of ipsilateral motor cortex (contrary to Carp et al., 2011). However,

537    MVB model comparison showed that adding these voxels did not lead to an age-related

538    improvement in action decoding (i.e., this information was redundant to task performance, because

539    it was already represented by the contralateral hemisphere). This illustrates the unique strength of

540    an MVB approach, going beyond MVPA.

541    If the HAROLD pattern does not reflect compensation, what does the age-related hyper-

542    activation of ipsilateral sensorimotor cortex reflect? One possible explanation is neural inefficiency,

543    where older adults simply require greater neural and/or haemodynamic activity for the same

544    computation (for review, see Barulli & Stern, 2013). Alternatively, there is growing evidence of

545    neural dedifferentiation, whereby the functional specificity of brain regions reduces with age, such

546    that additional areas (e.g., in the case of HAROLD, those that are ipsilateral) become involved in

547    tasks that were not required when younger (for review, see Koen et al., 2020). Related to both ideas

548    is the notion of task difficulty, illustrated by studies showing that younger adults activate similar

549    areas to older adults, but only for higher demands (Reuter-Lorenz & Cappell, 2008). Task difficulty

550    indeed influences ipsilateral motor cortex activity differently with age (e.g., Seidler et al., 2004;

551    Verstynen et al., 2005). The fact that we observed the inverse age effect during the boost analysis in

552    Experiment 1 (i.e., a simple detection task) but not Experiment 2 (i.e., a more demanding, decision-

553    making task) might be relevant, but this remains purely speculative because the difference could

554    simply be attributed to power, given that Experiment 2's sample was an order of magnitude smaller.

555    Another non-compensatory account of HAROLD is motor disinhibition. Transcranial

556    Magnetic Stimulation (TMS) approaches have shown that movement-related motor cortex activity

557    inhibits ipsilateral motor areas (Schambra et al., 2003; Lee et al., 2003; Sohn et al., 2003; Kobayashi

558    et al., 2004; Vercauteren et al., 2008) and, crucially, that these mechanisms attenuate (Peinemann et

559    al., 2001), or even reverse (Rowe et al., 2006; Talelli et al., 2008b), with age. In other words,

560    increased ipsilateral activation could be the result of reduced interhemispheric/transcallosal

561    inhibition (Ferbert et al., 1992; Lee et al., 2003; Plewnia et al., 2003; Naccarato et al., 2006; Talelli et

562    al., 2008a; Langan et al., 2010; McGregor et al., 2011; Wang et al., 2016; Burianová et al., 2020). This

563    is consistent with age-related disruption of corpus callosum integrity (e.g., Ota et al., 2006; Giorgio

564    et al., 2010; Langan et al., 2010; also see Lenzi et al., 2007; Cox et al., 2015) and of functional

565    connectivity between left and right motor cortices (Langan et al., 2010), as well as their

566    concentrations of glutamate (Kaiser et al., 2005). Comparable inhibitory mechanisms have been

567    proposed for memory (e.g., Logan et al., 2002; Gazzaley et., 2005; de Chastelaine et al., 2011) and,

568    for motor control, this provides plausible explanations of why older adults commit unintended

569    mirror movements more often than younger adults (e.g., Koerte et al., 2010). This hypothesis could

570    be examined by testing inter-hemispheric structural and functional connectivity in samples like Cam-

571    CAN.

572         Finally, note that our results are limited to finger key-presses (whether simple or choice),

573    and it is possible that better evidence for compensation within the HAROLD framework would come

574    from more complex motor tasks (e.g., grasping; Knights et al., 2021). Another important limitation to

575    consider (which also applies to, but is rarely addressed by, prior studies) is the degree to which age-

576    related effects could be driven by increased noise in the fMRI data, for example due to greater

577    (uncorrectable) head motion (e.g., Geerligs et al., 2017) or age-related changes in neurovascular

578    coupling (e.g., D'Esposito, et al., 2003). While the simple explanation that some of our results are

579    driven by noisier data in older adults might weaken the classical power to detect significant age

580    effects, this would not explain the high Bayes Factors we found for the null hypothesis that age does

581    not interact with ipsilateral activation in predicting behaviour (Figure 4B). Likewise, if estimates were

582    noisier in older adults, then successful decoding should have been less common for these

583    participants, yet successful decoding was found for almost every participant in Experiment 1, while

584    Experiment 2 showed the opposite pattern, where the likelihood of successful decoding increased

585    with age. It is possible that the age effects we found in ipsilateral sensorimotor cortex were purely

586    vascular (e.g., owing to a weaker neurovascular coupling, a form of the "inefficiency" hypothesis

587    discussed above), rather than neural. However, when adjusting task-activations for resting-state

588    fluctuation amplitudes (RSFA), which are assumed to capture vascular reactivity, Tsvetanov et al.

589    (2015) found that the increase of ipsilateral motor cortex with age in the same Cam-CAN data used

590    for Experiment 1 was one of few age-related effects to survive adjustment, suggesting it is not solely

591    a vascular effect. Another limitation of the present study is that the sample was cross-sectional,

592    which limits inferences to individual differences in birth year (and associated potential generational

32

593    differences), rather than about the specific longitudinal changes that occur with age (e.g., Anstey et

594    al., 2003). Future longitudinal studies could address this.

595        In conclusion, our behavioural and multivariate approaches both contradicted the

596    hypothesis that HAROLD is compensatory. Instead, results suggested that, at least in the case of

597    ipsilateral motor cortex activity evoked by finger movements, this activation in older adults is non-

598    specific, perhaps reflecting neural inefficiency or motor disinhibition.

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