

RESEARCH ARTICLE

The same, but different: Preserved distractor suppression in old age is implemented through an age-specific reactive ventral fronto-parietal network

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Abstract

Previous studies have shown age-related impairments in the ability to suppress salient distractors. One possibility is that this is mediated by age-related impairments in the recruitment of the left intraparietal sulcus (Left IPS), which has been shown to mediate the suppression of salient distractors in healthy, young participants. Alternatively, this effect may be due to a shift in engagement from proactive control to reactive control, possibly to compensate for age-related impairments in proactive control. Another possibility is that this is due to changes in the functional specificity of brain regions that mediate salience suppression, expressed in changes in spontaneous connectivity of these regions. We assessed these possibilities by having participants engage in a proactive distractor suppression task while in an fMRI scanner. Although we did not find any age-related differences in behavior, the young ($N = 15$) and older ($N = 15$) cohorts engaged qualitatively distinctive brain networks to complete the task. Younger participants engaged the predicted proactive control network, including the Left IPS. On the other hand, older participants simultaneously engaged both a proactive and a reactive network, but this was not a consequence of reduced network specificity as resting state functional connectivity was largely comparable in both age groups. Furthermore, improved behavioral performance for older adults was associated with increased resting state functional connectivity between these two networks. Overall, the results of this study suggest that age-related differences in the recruitment of a left lateralized ventral fronto-parietal network likely reflect the specific recruitment of reactive control mechanisms for distractor inhibition.

KEYWORDS

cognitive control, distractor suppression, fronto-parietal network, healthy aging, proactive inhibition, reactive inhibition, resting state functional connectivity

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1 | INTRODUCTION

Healthy aging has been associated with reduced cognitive control—especially in the ability to resolve competition from distractors through suppression mechanisms (Hasher, Stoltzfus, Zacks, & Rypma, 1991; Lustig, Hasher, & Zacks, 2007). These effects have been documented in various behavioral contexts including memory retrieval (e.g., Healey, Hasher, & Campbell, 2013; Wais, Martin, & Gazzaley, 2012), and perceptual competition (e.g., Dey & Sommers, 2015; Mevorach, Spaniol, Soden, & Galea, 2016; Quigley & Müller, 2014) where the presence of task-irrelevant distractors, especially when it is salient (Tsvetanov, Mevorach, Allen, & Humphreys, 2013) can sometime exert a more pronounced effect on older participants. Brain imaging studies have also supported this conjecture by showing reduced suppression of distractors in old age, such that the BOLD response to a specific stimulus was not diminished in response to an instruction to ignore it (e.g., Gazzaley, Cooney, Rissman, & D'Esposito, 2005; Schmitz, Cheng, & Rosa, 2010).

One possible cause for these changes is that the brain mechanisms that trigger suppression (Chadick & Gazzaley, 2011) are generally modulated by age. Indeed, previous studies (Campbell, Grady, Ng, & Hasher, 2012; Chadick, Zanto, & Gazzaley, 2014) have found an age-related reduction in suppression-related activity across a fronto-parietal network, which notably correlated with behavioral performance. The notion that salience suppression in old age is linked to possible age-mediated changes in a suppression-related fronto-parietal network is supported by a series of studies that highlighted the contribution of the left intraparietal sulcus (IPS) to salience suppression in young adults (Mevorach, Allen, Hodson, Shalev, & Humphreys, 2010; Mevorach, Hodson, Allen, Shalev, & Humphreys, 2010; Mevorach, Humphreys, & Shalev, 2006; Mevorach, Shalev, Allen, & Humphreys, 2008). These studies showed that inhibiting the Left IPS in young adults using brain stimulation (through transcranial magnetic stimulation; TMS) led to increased interference from salient distractors, establishing a causal relationship between the Left IPS and salient distractor suppression. In particular, the Left IPS was shown to apply a suppression signal to the occipital cluster that reduced the processing of salient distracting stimuli. TMS to the Left IPS disrupted this signal, leading to an increase in processing of distracting stimuli (Mevorach, Allen, et al., 2010; Mevorach, Hodson, et al., 2010). Interestingly, the behavioral performance of older adults in the same task (Tsvetanov et al., 2013) appears to mimic the effects of Left IPS inhibition in young adults—older participants showed increased interference from salient (but task-irrelevant) distractors (relative to young participants). Thus, it is plausible that salience suppression in old age is linked to difficulties in the recruitment of the Left IPS.

Another possibility relates to the contribution of different control modes in old versus young adults (Braver, 2012) rather than a general impairment of suppression control networks. Several studies have suggested that older adults tend to engage reactive distractor inhibition (inhibiting distractors only after they have appeared), while young adults tend to rely more on proactive distractor inhibition (inhibiting, or preparing to inhibit, distractors before they have appeared; Braver, 2012; Braver, Paxton, Locke, & Barch, 2009; Braver, Satpute, Rush, Racine, & Barch, 2005). Brain imaging studies have also found

evidence for an age-related temporal delay in the recruitment of cognitive control-related regions such as the dorso-lateral prefrontal cortex (DLPFC; Grady, 2012; Jimura & Braver, 2010; Paxton, Barch, Racine, & Braver, 2008). This supports the notion that older participants tend to engage a reactive (temporally late) control mode, whereas younger participants tend to engage a proactive (temporally early) control mode. A shift toward reactive control mode in old age would also fit with older adults' performance in the salience suppression task that was employed in Tsvetanov et al. (2013) as engagement of the Left IPS is thought to mediate proactive suppression in these tasks. Mevorach, Humphreys, and Shalev (2009) found with young adults that TMS inhibition of the Left IPS only affected young participants' ability to suppress salient distractors when it was applied prior to stimulus onset. Thus, when young adults were prevented from utilizing proactive control through the Left IPS their performance resembled the behavior of older adults (Mevorach et al., 2009). While the Left IPS is thought to be involved in proactive salience suppression, other left lateralized fronto-parietal regions have been associated with reactive control in young adults. Specifically, DiQuattro and Geng (2011) showed, in young adults, that when a distractor was first selected before being reactively and rapidly rejected, a left lateralized ventral fronto-parietal network, focused on the left temporoparietal junction (TPJ) and left inferior frontal gyrus (IFG), was engaged. Thus, it is possible that performance in distractor suppression task in old age is associated with a shift from engaging proactive suppression mechanisms (in the Left IPS) to reactive suppression mechanisms (in the Left TPJ and IFG).

A third possibility for the underlying causes of changes in distractor suppression in old age, and the possible change in brain activation old age entails in such tasks, is the age-mediated reduced functional specificity (known as dedifferentiation) of brain networks (Dennis & Cabeza, 2011; Goh, 2011). Network specificity is usually tested through resting state functional connectivity (RSFC), which reflects the intrinsic connectivity between brain regions irrespective of a task and has been shown to be an effective marker of both functional and structural connectivity (Biswal, Zerrin Yetkin, Haughton, & Hyde, 1995; Cordes et al., 2001; Greicius, Supekar, Menon, & Dougherty, 2009; Khalsa, Mayhew, Chechlacz, Bagary, & Bagshaw, 2014; Straathof, Sinke, Dijkhuizen, & Otte, 2019). Previous studies have examined the RSFC of a wide-range of brain regions across the lifespan (Chen et al., 2016; Damoiseaux et al., 2008; Ferreira & Busatto, 2013; Goldstone et al., 2016; Onoda, Ishihara, & Yamaguchi, 2012; Salami, Wählin, Kaboodvand, Lundquist, & Nyberg, 2016; Tomasi & Volkow, 2012; Toussaint et al., 2014; Tsvetanov et al., 2016; Zhang, Andreano, Dickerson, Touroutoglou, & Barrett, 2019). Typically, an increase in between network connectivity in aging populations has been reported (Betzel et al., 2014; Geerligs, Maurits, Renken, & Lorist, 2014; Geerligs, Saliasi, Maurits, Renken, & Lorist, 2014; Goldstone et al., 2016; Salami et al., 2016). Reduced within network connectivity in older participants, for example, within the Default Mode Network (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008; Ferreira & Busatto, 2013; Goh, 2011) is also reported, although with less consistency in the literature (Chen et al., 2016; Onoda et al., 2012; Toussaint et al., 2014; Tsvetanov et al., 2016). These findings point to reduced network

specificity and dedifferentiation (Andrews-Hanna et al., 2007; Cabeza, 2001; Dennis & Cabeza, 2011; Geerligs, Maurits, et al., 2014; Grady et al., 2010; Madden et al., 2010; Park et al., 2004), where brain networks become less specialized over time. Consequently, Geerligs and Tsvetanov (2016; though see Campbell & Schacter, 2016 for an alternative view) have argued that integration of structural and functional measures of brain activity is essential in the study of aging populations. In the context of salient distractor suppression in aging, reduced network specificity (measured through RSFC) may affect the recruitment of separate proactive and reactive networks in old age, in turn mediating salience suppression in this age group. Importantly, however, the brain activation signature during task performance in this case may resemble a scenario in which participants engage both proactive and reactive networks so it is important to assess whether such engagement is related to a shift of control mode or a consequence of loss of network specificity.

It is therefore possible that salient distractor inhibition in old age may be mediated by impaired top-down proactive suppression (e.g., in the Left IPS) or by a shift toward reactive suppression (e.g., engagement of Left TPJ and IFG). Or it could also be that changes in the engagement of separate brain regions in old compared to young adults result from reduced network specificity and dedifferentiation (reflected in decreased within-network and increased between-network RSFC)—this implies that performance in old age is not associated with reactive rather than proactive control but rather that distractor suppression is less efficient or specific. To test these possibilities, we used functional MRI to compare brain activity between young and old participants that performed the salience-based selection task from Tsvetanov et al. (2013). Specifically, we focus on three a priori questions: (a) Do old adults exhibit altered patterns of activation in the Left IPS, reflecting impaired proactive distractor suppression? (b) Do older adults rely more on a specific left ventral network (incorporating Left TPJ and Left IFG) reflecting reactive suppression processes? and (c) Do older adults exhibit dedifferentiation that may explain differential pattern of activation in the dorsal and ventral areas (for proactive and reactive suppression, respectively)? While we report clear differences in BOLD activations in the dorsal and ventral regions as a function of age, we found no evidence of dedifferentiation in our two age groups. Consequently, in an exploratory analysis we test whether increased RSFC between the dorsal and ventral regions is beneficial for distractor suppression in the young and old adults. Surprisingly, we found that increased RSFC between the Left IPS and a ventral fronto-parietal network was associated with more salience suppression for the older adults, but less salience suppression for the younger adults. This supports the notion that engagement of ventral regions is specific and reflects a relevant cognitive function for successful task performance.

2 | METHODS

2.1 | Participants

Fifteen young participants (mean age: 22.67 years, *SEM* of age: .85, age range: 18–30; 13 females) and 15 older participants (mean age:

66.07 years, *SEM* of age: 1.26, age range: 59–77 years; 7 females) took part in the study. Young participants were recruited from the undergraduate population of the University of Birmingham, United Kingdom. They were compensated for their participation with course credits. The older participants were recruited from a volunteer pool maintained by the School of Psychology at the University of Birmingham. They were compensated for their time with a single payment of £25. Participants were screened for MRI contraindications and were healthy with no history of head injury, mental health issues or neurological disorders. The old participants were screened for decline in cognitive functions using the Montreal Cognitive Assessment (MoCA). All of the older participants scored within the normal range (greater than or equal to 26; mean score: 28.2, *SEM* of score: .312). The study was approved by the institutional ethics committee at the University of Birmingham and conformed with the Declaration of Helsinki. All participants gave informed consent prior to taking part in the study.

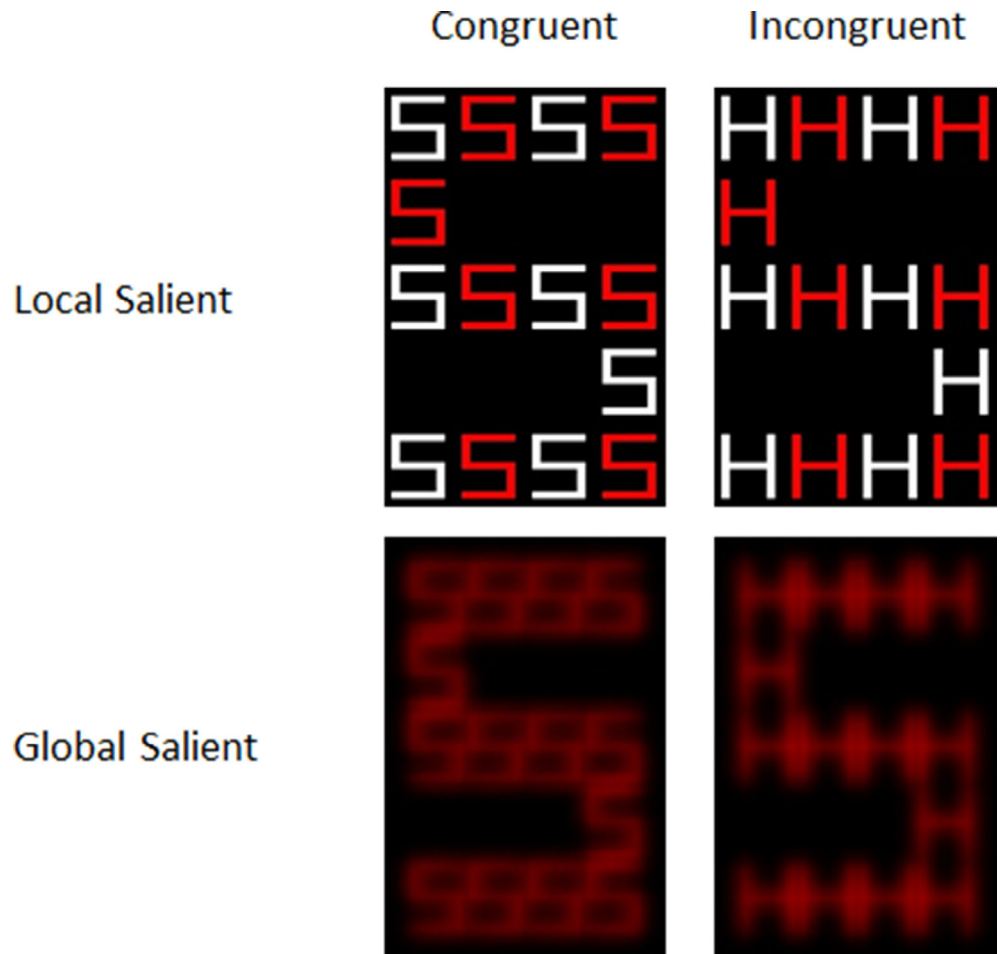
2.2 | Global/local task

The Global/Local task used here utilized hierarchical letters (Navon, 1977) similar to Mevorach et al., 2016). In this task an array of small (local) letters constitutes a single, large (global) letter (Figure 1). In different blocks of trials participants are required to identify either the local or the global letter (referred to as target) and to ignore the other (either global or local; referred to as distractor). In addition, the relative saliency of the local or global levels is orthogonally manipulated in relation to which level participants should report. Thus, in some blocks the target level (e.g., global) is the salient aspect of the compound letter (when the display is globally salient) while in others the distractor level (e.g., local) is the salient aspect (when the display is locally salient). Consequently, the task included two block types in which the target level is more salient (Target Salient): identify global in Global Salient displays and identify local in Local Salient displays; and two block types in which the distractor is more salient (Distractor Salient): identify global in Local Salient displays and identify local in Global Salient displays. Previously we have shown with a similar task that the Left IPS is critical for Distractor Salient blocks (e.g., Mevorach, Allen, et al., 2010; Mevorach, Hodsoll, et al., 2010) and that older adults demonstrate a specific impairment in those blocks (Tsvetanov et al., 2013).

2.3 | Stimuli

The stimuli were presented using MATLAB (MathWorks, Natick, MA) and the Psychophysics toolbox. All stimuli appeared against a black background. The relative saliency of the global and local elements was manipulated using two sets of displays representing high global saliency and high local saliency. In both sets the hierarchical letters were created from the orthogonal combinations of the letters H and S (Figure 1). For the displays with a relatively high local saliency the local elements alternated colors (white and red; Figure 1). Each local

FIGURE 1 Example stimuli. In each trial only one such hierarchical letter was presented and participants had to identify either the local or the global letter according to the current block instruction. The top row shows examples of where the local letters are more salient than the global letter. The bottom row shows examples where the global letter is more salient than the local letter. The left column shows examples where the global and local letters have the same identity (congruent), whereas the right column shows examples where they have a different identity (incongruent). In these examples, the global form is always an “S,” but in the study it could also be an “H”



letter subtended $.933^\circ \times 1.17^\circ$ of visual angle (in width and height, respectively) with the global letter subtending $4.43^\circ \times 6.756^\circ$ of visual angle (in width and height, respectively). The inter-item distance was 0.32° in visual angle. For the display with relative global salience the local stimuli consisted of red only letters (Figure 1, bottom row). The width and height of the local letters were the same as reported previously. These images were additionally blurred in MATLAB using a Gaussian low-pass filter (with a Gaussian kernel of full width at half-maximum of 1.56 mm), resulting in a global letter subtending $3.96^\circ \times 6.29^\circ$ of visual angle (in width and height, respectively). Due to the blurring effect, the adjacent local letters blend into each other, albeit on a gradient, so there is no clear inter-letter distance for these stimuli. To reduce strategic focusing on a local area of the screen and to encourage a diffuse attentional state, the stimuli appeared centrally at a location either 1.098° above or below the center of the screen (Grice et al, 1983).

2.4 | Global/local task procedure

Inside the MRI scanner, stimuli were projected onto a screen ~ 620 mm from the participant's eyes and viewed through a mirror mounted on the MRI head coil. In different blocks of trials, participants were

instructed to identify either the global (large letter formed of the small letters) or local (small letters that form the larger figure) letter while ignoring the letter on the other level (Figure 1). Each block represented one of four possible conditions: identify global in Global Salient displays; identify global in Local Salient displays; identify local in Global Salient displays and identify local in Local Salient displays. Each block was repeated three times to form a series of 12 blocks randomly ordered. A 2 s visual instruction (“GLOBAL”/“LOCAL”) indicating which level of shape participants will need to identify preceded each block. The blocks themselves were comprised of 12 consecutive trials, half of which contained congruent displays (the same letter features in the local and global levels) and the other half incongruent ones (the letters in the local and global levels differed), randomly distributed. Participants were required to identify the target letter using a two-button response box by pressing the “left” or “right” button using their index or middle fingers (with “left” representing the letter S and “right” representing the letter H). Both accuracy and speed were emphasized. Prior to the first block of each experimental scan, participants were presented with a fixation cross for 6 s to allow them to adapt to the lower lighting. Each experimental trial began with the presentation of the compound letter stimuli for 250 ms, followed by a fixation period in which a central fixation cross (a plus sign) was displayed for 1,750 ms. Participants could make a response anytime between the initial presentation of the stimulus and

the end of the fixation period. The next trial would begin immediately after the fixation period ended. Each block lasted for 26 s (2 s of instruction and 24 s of the task; 2 s per trial). After each block, there was a 2,000 ms instruction screen that centrally presented the word "REST" followed by a 24 s rest period in which only a fixation cross was present.

2.5 | fMRI data acquisition

Experiments were conducted at the Birmingham University Imaging Center (BUIC) using a 3T Philips Achieva with a 32-channel head coil. Each scanning session consisted of five scans, four functional scans and a T1-weighted anatomical scan (image resolution = 1 mm isotropic, TR \approx 7.4 ms [shortest], TE = 3.5 ms, flip angle = 7°, slice orientation = Sagittal, inversion time = 1,100 ms, bandwidth = 191.5 Hz). During functional scans BOLD fMRI data were acquired using gradient-echo EPI (TR = 2,000 ms, TE = 35 ms, voxel dimensions = 3 × 3 × 4 mm, 32 slices, flip angle = 80°, SENSE = 2). Three experimental runs of the behavioral task were acquired. These scans lasted for 10 min 24 s each (306 volumes). Finally, a resting state fMRI scan was acquired where participants were instructed to relax, lie still and keep their eyes open. The resting state scan acquisition parameters were identical to the functional scans. The screen was turned off for this scan and there was nothing specific for the participants to fixate on. This scan lasted 12 min 12 s. MRI compatible glasses were provided for any participants who required them.

2.6 | fMRI data analysis

fMRI analysis was performed using the general linear model (GLM) in FEAT version 6.00 (FMRI Expert Analysis Tool), which is part of FSL version 5.09 (www.fmrib.ox.ac.uk/fsl). A first-level analysis was conducted individually on each experimental run (three per subject). The first three volumes of each scan (6 s) were removed to reduce the transient magnetization effects and to allow the BOLD signal to stabilize. The individual scan data was then pre-processed prior to further analysis. A regular-up slice-timing correction using Fourier-space time-series phase-shifting was applied. Head movements were corrected using MCFLIRT motion correction (Jenkinson, Bannister, Brady, & Smith, 2002). The skull and other nonbrain matter were removed using BET (Smith, 2002). Images were then spatially smoothed using an isotropic Gaussian kernel of full width at half-maximum of 5 mm and all volumes within a scan were mean-based intensity normalized using the grand mean for the time series. Signals within the scan were then high-pass temporally filtered (Gaussian-weighted least-squares straight line fitting, with $\sigma = 52$ s). Each participant's whole-head EPI image was registered to their individual (brain-extracted) T1 anatomical image using FLIRT with 7° of freedom (Jenkinson et al., 2002; Jenkinson & Smith, 2001), the anatomical was separately registered to Montreal Neurological Institute space using FLIRT with 12° of freedom (Jenkinson et al., 2002; Jenkinson & Smith, 2001) and the transform

applied to the functional data, consistent with prior aging literature (Bachmann et al., 2018; van der Thiel, Rodriguez, Van De Ville, Giannakopoulos, & Haller, 2019). We also note that although research has shown that non-linear algorithms (such as FSL's FNIRT) can produce empirically better registrations (Klein et al., 2009), Churchill et al. (2017, Supporting Information Text 2) has shown that linear algorithms (such as FSL's FLIRT) can produce similar results. In this study, FLIRT was sufficient to produce high quality registrations (See Figures S7 and S8 for representative examples of registration quality).

BOLD responses to each of the four conditions of the behavioral task were separately modeled by custom waveform regressors defined by the onset and duration of the experimental blocks (26 s; 12 active blocks per experimental run). Each waveform was convolved with a gamma haemodynamic response function (Phase: 0, SD: 3, Mean lag: 6). The design matrix consisted of four regressors (described above) for each of the four block types in the behavioral task: Respond Global/Global Salient, Respond Global/Local Salient, Respond Local/Global Salient, and Respond Local/Local Salient. The temporal derivatives of each regressor were also included and the same temporal filtering was applied to the design matrix as was applied to the data. Four contrasts were calculated to compare BOLD signal change between different task blocks: Global Salient > Local Salient, Local Salient > Global Salient, Distractor Salient > Target Salient and Target Salient > Distractor Salient. The main contrast of interest is Distractor Salient > Target Salient as this is the contrast in which previous research has highlighted Left IPS activation in young participants (Mevorach, Allen, et al., 2010; Mevorach, Hodsoll, et al., 2010; Mevorach, Shalev, Allen, & Humphreys, 2008); moreover, it is a contrast that is designed to reveal a top-down control signal associated with the need to suppress salient distractors. However, see the Supporting Information for peak voxels and activation maps for Local Salient > Global Salient contrast (Figure S2 and Table S2).

Second-level analyses were performed to calculate the mean fMRI responses for each individual subject by combining the three first-level analyses using fixed-effects. BOLD Z-statistic images were thresholded using clusters determined by a $Z > 2.3$ and cluster corrected significance of $p < .05$.

Separate third-level analyses were then conducted to obtain the mean fMRI response for each of the four lower-level contrasts. A mixed effect analysis was performed to obtain the activity within (Flame 1) and between (Flame 1 + 2; Smith et al., 2004; Woolrich et al., 2009) each age group for each contrast. The analyses included 1 s-level analysis for each subject as input ($N = 15$ for the two within group analyses and $N = 30$ for the between group analysis). BOLD Z-statistic images were thresholded using clusters determined by a $Z > 2.3$ and cluster corrected significance of $p < .05$.

In addition, for the between group analysis, resting state fluctuation amplitude (RSFA; Kannurpatti & Biswal, 2008) was calculated for each voxel using resting state data (see below for details of resting state pre-processing). Voxel-wise matrices for each subject were mean subtracted across subjects and then concatenated to make an additional group-level confound regressor which was included in the third-level model. To account for three young participants that did not have resting state data (see below), zeros were added to the

covariate matrix. The RSFA regressor models between-subject variability in voxel responsiveness, as a means of accounting for and ultimately minimizing variability between different groups due to intrinsic vascular reactivity. RSFA has been shown to be an especially effective regressor for this purpose in the analysis of age-related BOLD data (Kannurpatti, Motes, Rypma, & Biswal, 2011; Tsvetanov et al., 2015).

2.7 | ROI definitions

The Left IPS and Left TPJ/Left IFG appear to mediate proactive and reactive distractor suppression, respectively. Therefore, we used these regions as proxies to assess proactive and reactive suppression related activity. Three ROI masks were created based on coordinates of relevant fMRI activation that were reported in previous studies. Masks were created by generating a sphere (using *fsmaths*) with a diameter of 5 mm centered on the relevant MNI coordinate. A Left IPS mask was created around the coordinates reported in Mevorach et al. (2008); Mevorach, Allen, et al., 2010; Mevorach, Hodson, et al., 2010) for brain activation associated with proactive suppression of salient distractors (MNI Coordinates: $-30, -68, 34$; peak activation). A Left TPJ and Left IFG mask were created around the coordinates reported in DiQuattro and Geng (2011; Figure 4; peak activation) which were associated with a reactive control network (MNI coordinates: $-46, 50, 34$, and $-50, 30, 8$, for Left TPJ and Left IFG, respectively). For each participant, mean BOLD activity (% signal change) was extracted for each of the three masks during Target Salient and Distractor Salient blocks using FEATQUERY. Although we focus here on the blocks related to the contrast of interest (Distractor Salient > Target Salient).

Three relevant networks were identified that have been associated with visuospatial processing, executive control, and salience processing and that correspond to the dorsal (IPS) and ventral (TPJ, IFG) regions of interest (see Figure S3 for an overlay of the three networks and the three ROIs defined above): a visuospatial network (including IPS and FEF), an executive control network (spanning mostly DLPFC and parietal regions and including TPJ and IFG), and a salience network (including insula and dACC; see Shirer, Ryali, Rykhlevskaia, Menon, and Greicius (2012) and the Supporting Information for a full list of nodes). MNI space ROIs for the whole networks and their individual nodes were obtained from the Stanford FIND lab (Shirer et al., 2012; http://findlab.stanford.edu/functional_ROIs.html).

The visuospatial network was selected because it includes the Left IPS coordinates from Mevorach et al. (2008; Figure 2a) and the Left IFG coordinates from DiQuattro and Geng (2011; Figure 2c). The executive control network was selected because it overlaps with the Left TPJ and Left IFG coordinates from DiQuattro and Geng (2011; Figure 2b,c). However, DiQuattro and Geng (2011) only identified activity in these regions in a young cohort. It is possible that activity is right lateralized or even bilateral in elderly populations, as aging has been associated with both spatial reorganization of networks (Cabeza, Anderson, Locantore, & McIntosh, 2002) and reductions in hemispheric specialization (Cabeza, 2001). Therefore, we considered the

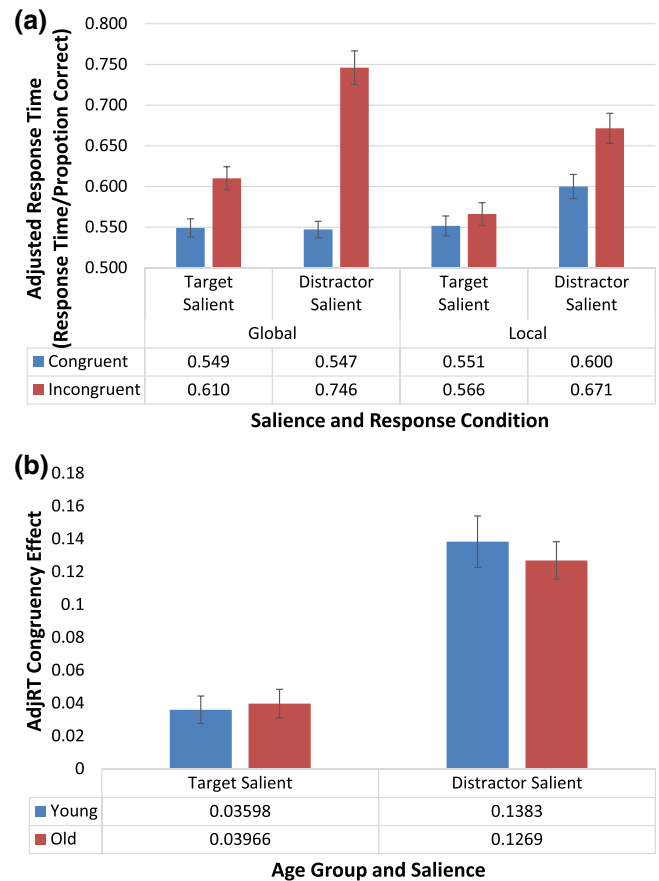


FIGURE 2 Behavioral performance in the global/local task. (a) Mean adjRT combined across both age groups. Data is presented as a function of the three task parameters (response level, salience and congruency). (b) Mean congruency effect (interference) as a function of salience (Target Salient vs. Distractor Salient) for the two age groups. Error bars represent SEM

FIND labs' (Shirer et al., 2012) "Left Executive Control Network" and "Right Executive Control Network" as a single amalgamated network in our analysis consisting of the individual clusters from both networks. The salience network was chosen because we are interested in, and are using a paradigm known to elicit (Tsvetanov et al., 2013), age-related differences in salience suppression. Assessing RSFC in this network will help to determine if aging effects are due to differences in attentional control or salience processing. For the same reasons as before, we considered the FIND labs' "Posterior Salience Network" and "Anterior Salience Network" as a single amalgamated network.

2.8 | RSFC analysis

To assess the possibility that age-related behavioral deficits are associated with changes in the functional connectivity of proactive or reactive suppression-related brain regions, or through an interaction between the engagement of these brain regions and their functional connectivity, seed-based correlation analysis was used to estimate seed-specific, within-network RSFC and between network RSFC for

the three predefined networks (Visuo-spatial, Executive and Saliency; Damoiseaux & Greicius, 2009; van den Heuvel & Hulshoff Pol, 2010; van den Heuvel, Mandl, Kahn, & Hulshoff Pol, 2009). Resting state data were pre-processed prior to analysis (Fox et al., 2005; Goldstone et al., 2016; Wilson et al., 2015). Data were motion corrected, spatially smoothed (5 mm) and temporally band-pass filtered ($0.009 < \text{Hz} < 0.08$). White matter and cerebrospinal fluid signals, the global brain signal, and motion parameters were calculated and then removed from the data using linear regression. To calculate FC, the mean resting-state BOLD signal time course was extracted from all voxels in a seed ROI. The Pearson's correlation between that seed timecourse and the timecourse of every other voxel in the brain was then computed. The mean R value across all voxels in a target ROI was then used to define a measure of FC. This is consistent with prior literature (Goldstone et al., 2016; Wilson et al., 2015, 2019).

Due to technical difficulties, the resting state scans of 3 of the 15 young participants were unusable. The following procedures were applied to the data for each remaining subject. Given the heterogeneity in RSFC throughout individual networks (Braga, Van Dijk, Polimeni, Eldaief, & Buckner, 2019; Dixon et al., 2018; Kernbach et al., 2018) and the exploratory nature of our RSFC analyses, we elected to calculate "seed-specific" within network connectivity measure to restrict our analysis to specific hypotheses regarding our primary regions of interest (Left IPS, Left TPJ and Left IFG), within the bounds of the standardized FIND lab networks. To calculate seed-specific within network connectivity, an individual ROI from each network was chosen as the seed and seed based temporal correlations were calculated between that seed and every other ROI within the network. There are no established conventions for which region to use as a seed hub. For this analysis, seed-selection is crucial since different seeds will produce different results even for ROI's within the same network. Gong et al. (2009); Menon & Uddin, 2010) identified the insula and posterior cingulate gyrus as centrally connected regions, independent of age and sex, which suggests ROI's in these regions would be appropriate choices. Furthermore, as we were specifically interested in left lateralized ROI's (i.e., Left IPS, Left TPJ, Left IFG) we selected seed ROI's in the left hemisphere. In each network, only one node matched both criteria (left lateralized and in the posterior cingulate/insula region). The seed ROI for the executive control network was the left angular gyrus, the seed for the saliency network was the left precuneus, and the seed for the visuospatial network was the left superior parietal lobe. Within each network we calculated the RSFC for every possible pairwise connection involving the seed ROI (if ROI A was the seed region: ROI A \rightarrow ROI B; ROI B \rightarrow ROI A; ROI A \rightarrow ROI C; ROI C \rightarrow ROI A; and so on) and averaged them together creating one FC measure per network. This value was interpreted to reflect seed-specific within network connectivity. This connectivity metric was calculated individually for every participant. Finally, three independent samples *t* tests, one for each network, were performed to determine if the averaged seed-specific network connectivity was different between age groups.

To assess between-network connectivity, combinations of the FIND lab whole network ROI's (executive control, saliency, and visuospatial network) were set as both seeds and targets. Note that our

method of calculating functional connectivity does not directly correlate the time series between two regions, but rather calculates the correlation between the seed region and every voxel in the brain and then averages the R values across the voxels in the target region. Although they are highly similar, the average R values are different depending on which of two regions is the seed and which is the target because there is variance in the correlations with individual voxels. Therefore, for each combination, two versions of the analyses were performed such that each network was the seed and the target. Then we took the mean Pearson R values of the two analyses for each participant. For example, to assess connectivity between the executive control and the visuospatial networks, we calculated RSFC where the executive control network was the seed region and the visuospatial network was the target and vice versa. This was repeated for the between network connectivity for the visuospatial network and the saliency network, and for the between network connectivity for the executive control network and the saliency network. This procedure was done to obtain unbiased functional connectivity measures not affected by the seed definition. Independent samples *t* tests were performed to determine if the between network connectivity was different across age groups. All *t* tests on RSFC were subjected to a Benjamini-Hochberg correction for multiple comparisons (Benjamini & Hochberg, 1995, 2000; Benjamini & Yekutieli, 2001; Thissen et al, 2002; Verhoeven et al, 2005; Glickman et al, 2014). Details of the correction procedure are documented in the Supporting Information (also see Table S3). Any reported significant *p*-values were significant relative to the corrected cutoff score for that test.

3 | RESULTS

3.1 | Power analysis

An a priori statistical power analysis for a repeated measures ANOVA was performed for sample size estimation, based on data from Tsvetanov et al. (2013). In this study, they found that older participants had higher congruency costs in the Distractor Salient condition than young participants, defined by a three-way interaction between Age, Saliency, and Congruency. This interaction was significant when the data was transformed into efficiency scores (RT/Accuracy) to account for speed accuracy trade-offs ($p = .008$, Partial Eta Squared = .158). The partial eta squared from this analysis converted to an effect size $f(U)$ of 0.433. The other parameters of the analysis were set as the following: Alpha = .05, Power = 0.95, Number of Groups = 2, Number of Measurements = 6, Nonsphericity Correction = 1. Based on this, the total projected sample size (across all groups) needed to detect this three-way interaction with an effect size of .433 (GPower 3.1.9.2; Faul, Erdfelder, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007; Lakens, 2013; Figure S6) is 26 for a repeated measures ANOVA with a within-between subjects interaction. Thus, an ideal study would include 13 participants per group to have a power of .966 (Appendix A). In our study, there are 15 young and 15 older participants (Total $N = 30$ a priori Power = .986; Figure S6).

3.2 | Behavioral analysis

Response time in milliseconds (RT) and accuracy rate (i.e., proportion of correct responses) were measured as dependent variables. For each participant, RTs that were more than 2 SDs from the mean (calculated for each task condition separately), within a given experimental run (3 per participant corresponding to each task-related fMRI scan) were excluded. On average, this resulted in the loss of 5.5% ($SEM = .2\%$) and 5.1% ($SEM = .2\%$) of the RT data for the young and old participants, respectively, with no significant difference between groups ($t[88] = -1.55$, $p = .124$). Additionally, to account for speed/accuracy trade-offs, which are often present in aging data, the data was converted to adjusted response time (AdjRT; sometimes referred to as an inefficiency measure; Townsend and Ashby, 1983) by dividing the participants' response time by their proportion correct (similarly to Tsvetanov et al., 2013). Indeed, this control was necessary as older participants did have generally slower RTs (Mean RT; Younger = 533 ± 16 ms; Older = 633 ± 14 ms; $t[28] = 4.56$, $p < .001$, $d = 1.67$) and more accurate responses (Proportion Correct; Younger = $.95 \pm .08$; Older = $.98 \pm .03$; $t[28] = 3.73$, $p < .001$, $d = 1.36$). All values are reported as mean \pm standard error of the mean.

A repeated measures ANOVA was conducted on the AdjRT data with salience (Target Salient vs. Distractor Salient), response level (global vs. local) and congruency (congruent vs. incongruent) as within-subjects variables and age group (young vs. older) as a between-subjects variable. As expected, congruent displays (562 ± 11 ms) were responded to faster than incongruent displays (648 ± 13 ms; $F(1, 28) = 180.75$, $p < .001$, $\eta_p^2 = .866$) and overall younger participants were quicker (566 ± 16 ms) than older ones (644 ± 16 ms; $F(1, 28) = 11.370$, $p = .002$, $\eta_p^2 = .289$). This suggests that even after accounting for speed-accuracy trade-offs, older participants are still slower to respond than younger participants.

Importantly, there was a significant interaction between salience and congruency, ($F(1, 28) = 20.497$, $p < .001$, $\eta_p^2 = .423$), indicating that the congruency effect (adjRT incongruent–adjRT congruent) differed according to salience, with participants finding it harder to ignore the distractor in the Distractor Salient (136 ms) compared with the Target Salient (38 ms) displays ($t[29] = -8.365$, $p < .001$, $d = -1.527$; One-way paired samples t test; Figure 2a). However, there were no significant interactions with age group (all F 's $< .960$; all p 's $> .336$; Figure 2b; Table S1). This suggests that aside from a generalized slowing in the older participants, there were no significant differences in performance in this task between the young and old participants and therefore no indication of behaviorally measurable impaired distractor inhibition as a function of age in this cohort (for the full behavioral analysis see Supporting Information).

3.3 | fMRI analysis

Although our cohort of older participants did not exhibit the expected impairment in suppressing salient distractors previously reported (Tsvetanov et al., 2013) we assessed whether the brain activation in the two age groups represents a relatively different engagement of

attention control mechanisms. To do this we focused our analysis on age-related differences during Target Salient versus Distractor Salient trials as this is the behavioral manipulation intended to assess the ability to suppress salient information and is therefore of greatest interest. Furthermore, age did not interact with congruency or response level. Although this is also true for salience, we have theoretically driven, a priori hypotheses regarding brain activity with respect to salience which justifies our focus on this variable.

3.4 | Regions of interest analysis

As previous studies documented a behavioral detriment in old age (Tsvetanov et al., 2013) that was comparable to the effect of brain stimulation over the Left IPS of younger participants (Mevorach et al., 2009), we first assessed the size of activation in this predefined Left IPS region (using MNI coordinates from Mevorach et al., 2008), in a ROI analysis. A repeated measures ANOVA on the mean BOLD signal change in the Left IPS with salience (Target Salient vs. Distractor Salient) as a within subjects variable, and age group as a between subjects variable revealed main effects of salience ($F[1, 28] = 16.590$, $p < .001$, $\eta_p^2 = .372$) and of age group ($F[1, 28] = 10.049$, $p = .004$, $\eta_p^2 = .264$; Figure 3a). Importantly however, the interaction was not significant, ($F(1, 28) = 1.120$, $p = .299$). Thus, it appears that for both old and young participants the Left IPS was engaged more during Distractor Salient trials ($.463 \pm .072\%$ signal change) compared to Target Salient trials ($.348 \pm .066$). However, overall activation was higher in old participants ($.619\% \pm .095$) than in young participants ($.192\% \pm .095$). This shows that both old and young participants recruit the Left IPS during the global/local task when salient distractors need to be ignored.

Second, to assess whether a reactive control network is being engaged in old age, a similar ROI analysis was conducted with the two regions previously identified as important for reactive control—the Left TPJ and the Left IFG (DiQuattro & Geng, 2011). A repeated measures ANOVA on the mean BOLD signal change in the Left TPJ (Figure 3b) with salience (Target Salient vs. Distractor Salient) as a within subjects variable, and age group as a between subjects variable did not find a significant main effect of salience ($F[1, 28] = 2.106$, $p = .158$) but the overall group difference was significant, ($F[1, 28] = 10.708$, $p = .003$, $\eta_p^2 = .277$) with older participants again showing increased activation ($.238 \pm .071$) compared to young participants ($-.089 \pm .071$). The interaction was not significant ($F(1,28) = .581$, $p = .452$). Similarly, a repeated measures ANOVA on the mean BOLD signal change in the Left IFG (Figure 3c) with salience (Target Salient vs. Distractor Salient) as a within subjects variable, and age group as a between subjects variable also showed an overall group difference ($F[1, 28] = 4.531$, $p = .042$, $\eta_p^2 = .139$) with older adults showing limited activity ($.061 \pm .111$) and young participants ($-.274 \pm .111$) showing deactivation. Again, the interaction was not significant ($F[1, 28] = .299$, $p = .589$) but this time the main effect of salience approached significance levels ($F[1, 28] = 4.012$, $p = .055$). These findings fit with the idea that older participants generally favor reactive control as the Left TPJ is more heavily engaged in older adults, though it does not show

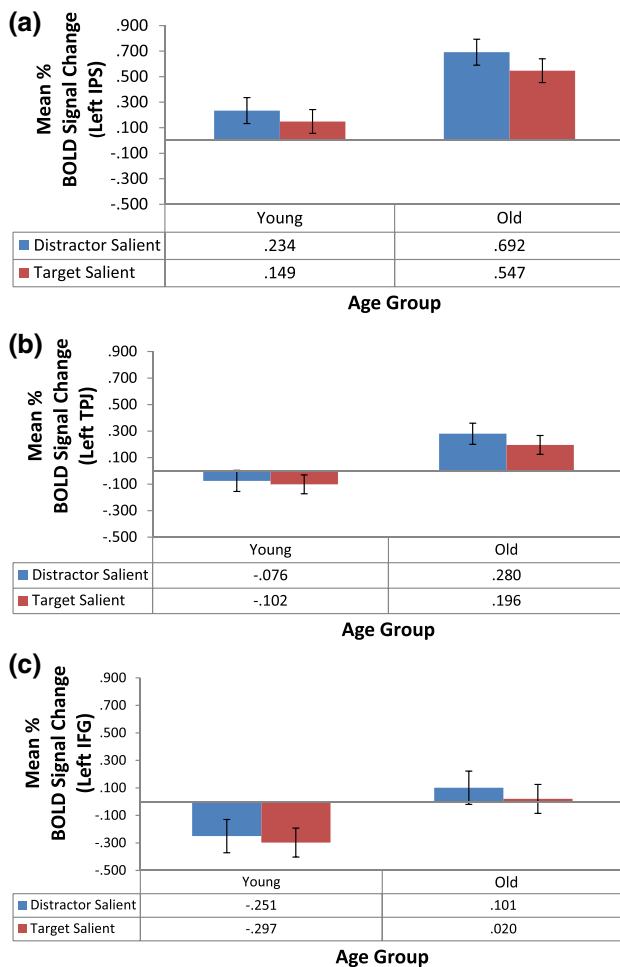


FIGURE 3 Mean % BOLD signal change (\pm SEM) within the Left IPS (a), Left TPJ (b), and Left IFG (c) masks as a function of relative salience and age group. IFG, inferior frontal gyrus; IPS, intraparietal sulcus

sensitivity to the salience condition. They also fit with the notion that younger participants favor proactive control since younger participants seem to exhibit either deactivation (Left IFG) or reduced engagement (Left TPJ) of parts of the reactive control network. The tendency of the activations in the Left IFG for both groups to be sensitive to salience can also fit with the notion that salient distractors are more likely (at least on some trials) to capture attention in both groups and therefore require reactive control to be engaged, even though on a group level, younger adults are less likely to do so.

3.5 | Whole-Brain GLM analysis

The ROI analysis supports the notion that older participants are using additional reactive control brain mechanisms, but this may also reflect a general increase in the recruitment of brain regions which is not specific to reactive regions (which could also relate to dedifferentiation and reduced network specificity). This is also possible given that the activity of the left ventral regions does not appear sensitive to the

increase in the demand for reactive control when a salient distractor needs to be ignored (i.e., little to no difference in activity in left ventral regions between Target and Distractor Salient trials). To test this further we performed a whole-brain analysis comparing brain activation for Distractor Salient and Target Salient displays between the two age groups.

For young participants, the Distractor Salient > Target Salient contrast revealed extensive bilateral activity (Table 1 and Figure 4a) throughout dorsal fronto-parietal regions, as well as occipital regions. For the old participants, the same contrast revealed an even more extensive network of bilateral fronto-parietal activations, extending more ventrally (Table 1 and Figure 4b). For both groups these activations overlapped with the left parietal activity that was previously reported for similar tasks (Mevorach et al., 2008; Mevorach et al., 2010b). Notably, contrasting these activation maps between the age groups revealed unique activation in the Left TPJ as well as the left inferior/middle frontal regions (including in the Left IFG) in the older group (Figure 4c), whereas the young adults show no significant BOLD response in these areas. This suggests that the left-lateralized ventral fronto-parietal activation, and the engagement of the mechanisms they subserves, is unique to the older participants and is scaled with the increase in demand for distractor inhibition (in the Distractor Salient condition), while the more dorsal activations appear to be shared across both groups. Importantly, these age-related differences in the fronto-parietal areas appear to be specific rather than general (e.g., there are no apparent differences in visual cortex), supporting the notion that this activity reflects a specific cognitive effect and not a mere increased BOLD response throughout.

3.6 | RSFC analysis

The unique left ventral fronto-parietal activations we have documented in the old participants appear to highlight specific reactive control areas and therefore suggest a change in the way older participants perform the task compared to young ones, irrespective of similar behavioral results. However, it could still be the case that these activations, although seemingly specific, are a result of reduced network specificity in old age (Andrews-Hanna et al., 2007; Cabeza, 2001; Dennis & Cabeza, 2011; Geerligs, Maurits, et al., 2014; Geerligs, Saliassi, et al., 2014; Grady et al., 2010; Madden et al., 2010; Park et al., 2004) so that multiple networks are working excessively together. To further test this potential explanation, we have assessed the spontaneous RSFC between networks relevant to our task (the three pre-defined FIND lab networks, the Left IPS mask, and the task defined left ventral reactive network). If the unique activation in the left ventral network is a consequence of reduced network specificity, we expect to record higher RSFC between these networks in old compared with young participants. Here we report the most relevant results but see the Supporting Information for the complete set of analyses (Figures S3 and S4).

We first compared RSFC between the executive control and visuospatial whole network ROI's across the age groups (roughly

TABLE 1 MNI coordinates of peak voxels and activated brain regions for significant clusters obtained from the third level between group general linear model analysis (Figure 4)

Contrast	Voxels	<i>p</i>	Peak voxel Z	Peak voxel x	Peak voxel y	Peak voxel z	Activated brain regions
Distractor Salient > Target Salient Old only	214,597	0.00E+00	7.88	-26	-71	39	Both bands of the left intra-parietal sulcus (Left IPS), including superior and inferior parietal lobe
	54,591	7.73E-19	6.74	-41	12	28	Left lateral prefrontal cortex, including the left inferior frontal gyrus (IFG) and left middle frontal gyrus.
	37,275	2.30E-14	6.57	57	13	24	Right lateral prefrontal cortex, including the right IFG and right middle frontal gyrus
	12,450	2.38E-06	6.43	6	22	40	Bilateral medial prefrontal cortex, including the paracingulate gyrus
	3,488	4.13E-02	3.75	16	9	6	Right caudate nucleus
Distractor Salient > Target Salient Young Only	101,567	4.72E-29	5.89	-46	-76	-7	Left lateral occipital cortex, extending toward the parietal cortex. Both bands of the Left IPS, including the superior and inferior parietal lobe.
	5,993	1.74E-03	5.14	46	7	35	Left lateral prefrontal cortex, including the Left IFG and left middle frontal gyrus,
	3,972	2.15E-02	4.18	-48	8	31	Right lateral prefrontal cortex, including the right IFG and right middle frontal gyrus
Distractor Salient > Target Salient Old > Young	11,101	8.34E-06	4.72	-45	-46	38	Left TPJ, inferior parietal cortex, extending posteriorly to the inferior bank of the IPS, supramarginal gyrus
	10,847	1.06E-05	4.37	-48	11	14	Left IFG, insular cortex, frontal orbital, frontal operculum, middle frontal gyrus
	4,183	1.63E-02	3.92	-4	-63	-14	Cerebellum

corresponding to the ventral and dorsal activations we report in Figures 3 and 4). We found a significant difference but with the old participants (.0113 ± .010) showing reduced rather than increased RSFC relative to young adults (.0605 ± .011; $t[25] = -3.234$, $p = .00342$, $d = -1.252$). Second and to have a more direct test of the network connectivity between the groups we also calculated the RSFC between the brain regions that are shown to be active in our task. Thus, for each age group we calculated RSFC between the Left IPS mask (which have shown sensitivity to the distractor inhibition demand in both age groups) and the ventral reactive network activation (uniquely activated in the older participants; Figure 4c). However, even here we found no evidence for increased RSFC as both groups exhibited similar connectivity metrics (.2901 ± .014; and .2807 ± .020, for the old and young participants, respectively; $t[25] = -.398$, $p = .694$). It should be noted that there is some limited overlap between the Left IPS mask and the task defined ventral reactive network, suggesting this analysis may reflect a within network, rather than a between network, analysis. Regardless, given the lack of a difference in RSFC, this distinction does not affect our interpretation of the results. We found no other statistically significant group difference in RSFC either between or within networks (for a full description of both between and within network connectivity analysis across the two age groups see Supporting Information), although the seed-specific within network connectivity in the visuo-spatial network tended to be lower for older participants (Figure S4).

3.7 | Analyzing the link between RSFC, BOLD activity, and behavior

The RSFC analysis suggests that the stronger recruitment of the left ventral fronto-parietal network in the old participants is not likely a consequence of blurring of the roles these networks play (so that they are recruited together to implement a similar function) but rather that the two independent networks are interacting in order to enable older participants to perform well in this specific task. If that is indeed the case, then we would expect the resting functional connectivity between the networks to contribute to efficient task performance in old (but not necessarily in young) participants. To assess the contribution of the RSFC to performance we conducted a backwards elimination regression analyses in which we included both the BOLD activity in the critical dorsal and ventral regions and the RSFC between them as predictors for performance (AdjRT) in the Distractor Salient condition of the task. We focused on the Distractor Salient condition because it is the behavioral measure of greatest interest. Furthermore, the main fMRI contrast in this study, that defined the task-activated ventral reactive network, identified greater activity during the Distractor Salient trials compared to the Target Salient trials. Therefore, this analysis would not be valid for other behavioral conditions. For each participant, we calculated the congruency effect during Distractor Salient trials as the outcome measure. The congruency effect

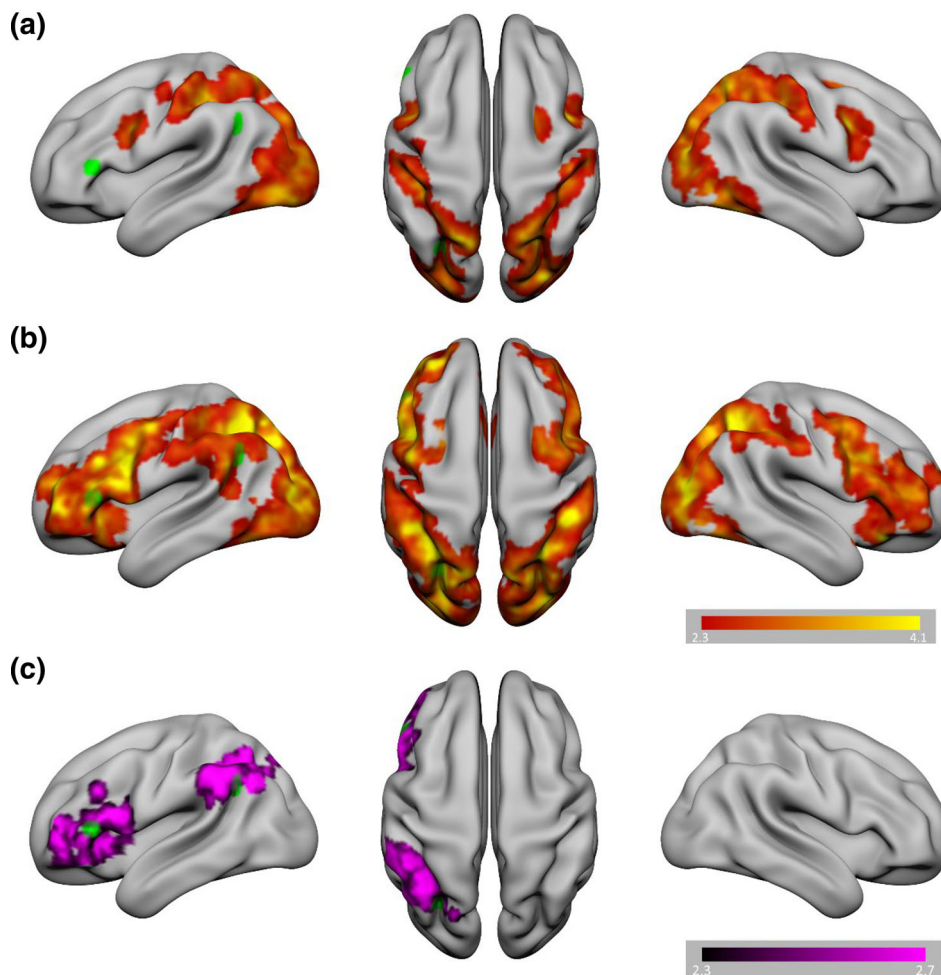


FIGURE 4 Significant group-level BOLD responses for the Distractor Salient > Target Salient contrast for young (a) and old (b) participants. Activation maps are superimposed on a standard brain mesh taken from BrainNet Viewer (Xia et al, 2013; <http://www.nitrc.org/projects/bnv/>); (c) Presents the statistically different activation maps for (b) > (a). That is larger activations in old versus young adults. Green masks mark the three ROIs in the Left IFG, Left TPJ and Left IPS (the latter is only visible in the superior view). IFG, inferior frontal gyrus; IPS, intraparietal sulcus

is a behavioral measure of distractor inhibition. With respect to the Distractor Salient condition, it reflects the magnitude of inhibition applied to a salient distractor. The differences in BOLD activity (mean % signal change, averaged across the entire mask or network ROI's) between Distractor Salient and Target Salient trials (i.e., the suppression specific activation) in the Left IPS mask (which we showed was sensitive to the distractor's salience in both age groups) and in the ventral fronto-parietal network (which was only sensitive to distractor salience in older participants) were entered as predictors in the model together with the RSFC between the two regions.

Overall, there were two BOLD activity measures and one RSFC measure as continuous predictors, and age group as a categorical predictor in the model. We used the MATLAB function “stepwiselm” and set the starting model to one which included all main effects and interactions between the predictors. Then we set “penter = 0” so that terms could only be removed from the model. Starting with the highest order interaction, the function tests the null hypothesis that the term has a coefficient of zero. If the null hypothesis cannot be rejected, it removes the term from the model. This continues until only terms with non-zero coefficients remain (but not necessarily a p-value less than .05). The model with all non-zero coefficients was a 5 term model (Ordinary $R^2 = .62$; Adjusted $R^2 = .53$) including a significant main effect of age group ($\beta = -.42$, $t = -4.16$, $p = .0002$)

and RSFC ($\beta = -.96$, $t = -3.26$, $p = .0038$), and a non-significant main effect of Left IPS suppression specific BOLD activity ($\beta = -.67$, $t = -1.77$, $p = .09$). It also included significant interactions between age group and RSFC ($\beta = 1.55$, $t = 4.48$, $p = .0002$), and Left IPS suppression specific BOLD activity and RSFC ($\beta = 3.15$, $t = 2.31$, $p = .0309$). We conducted two sensitivity analyses (See Figures S9a and S9b) calculating both the leverage and cooks d. However, no participant was considered an outlier based on both measures, so we did not exclude participants based on these metrics. The code and necessary files to generate the full set of regression analysis details in MATLAB is available on the OSF page for this study (doi: 10.17605/OSF.IO/EC3DH).

Here, we interpret the higher order interactions. First, the interaction between age group and the RSFC between the Left IPS and the ventral fronto-parietal network suggests that young and older participants exhibit different directional link between the RSFC and successful inhibition of distractors (measured through the congruency effect). Figure 5 illustrates a scatter plot of the RSFC plotted against the fitted congruency effect in the Distractor Salient condition derived from the regression analysis (but see Figure S10 for a scatterplot of the raw data). These results suggest that for older participants successful inhibition of salient distractors is predicted to be better as a function of increased RSFC between the Left IPS and the ventral fronto-parietal network, but for younger participants it is predicted to be better as a

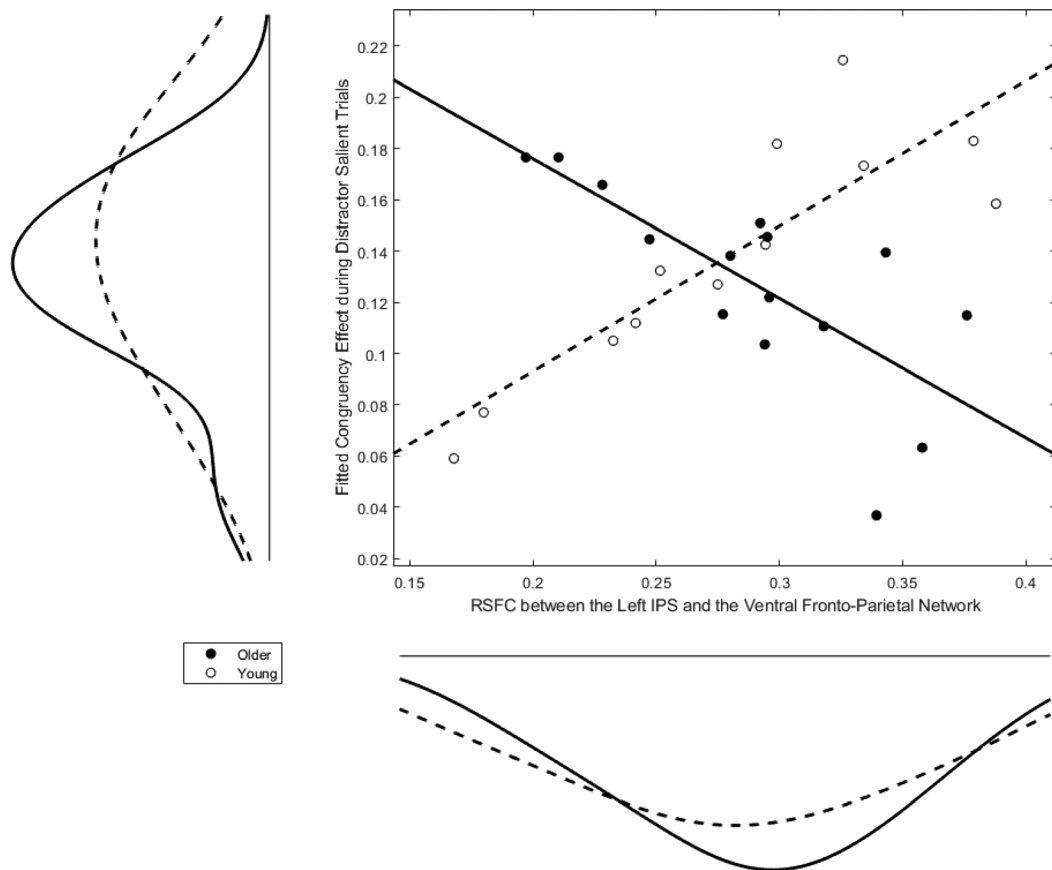


FIGURE 5 Fitted data scatterplot of young (open circles and dashed lines) and old (solid circles and lines) participants' performance (congruency effect in the Distractor Salient condition) as a function of the RSFC between the Left IPS and the ventral fronto-parietal network. The RSFC values reflect the raw data input into the regression analysis and the congruency effect values reflect the fitted Y-values per participant derived from the regression analysis. For both age group RSFC between the Left IPS and the ventral fronto-parietal network predicted performance, the effect is diametrical where increased connectivity for young participants results with increased interference while the opposite is apparent for older participants (increased connectivity leads to reduced interference). Marginal histograms are reported and displayed as kernel density plots. IPS, intraparietal sulcus; RSFC, resting state functional connectivity

function of decreased RSFC between the Left IPS and the ventral fronto-parietal network. In other words, this suggests that increased RSFC between these regions is associated with less interference from salient distractors for older participants and more interference for younger participants (Figure 5). This result supports the notion that the recruitment of the two networks in older adults is functionally specific rather than a consequence of reduced network specificity.

The interaction between the Left IPS suppression specific BOLD activity and the RSFC between the Left IPS and the ventral fronto-parietal network is more complicated to tease apart. In Figure 6, we used the beta parameters to simulate the predicted congruency effect during Distractor Salient trials for a range of RSFC and BOLD activity across both age groups. This graph makes the interaction more apparent. At low connectivity, greater suppression specific BOLD activation is associated with lower congruency effects (and therefore more effective suppression), but at high connectivity, greater suppression specific BOLD is associated with higher congruency effects (and therefore less effective suppression). Although age does not significantly interact with these factors in the same term in the regression,

the magnitude of this effect appears strong for the simulated young participants and attenuated in the older participants and should be investigated further in the future. More generally, it suggests that there is a functionally relevant (i.e., related to behavior) association between RSFC and suppression specific BOLD activity in this study.

4 | DISCUSSION

The present fMRI study attempted to identify the brain mechanisms underlying the difficulty in inhibiting salient distractors often experienced during old age. Specifically, we asked whether the Left IPS region, that has been previously shown to play a critical role in salience suppression in young adults in proactive suppression, differs in its task-activation in older adults; whether the Left TPJ and left IFG regions, that have been previously associated with reactive control, show increased task-activation for the older adults; and whether altered RSFC, specifically of the fronto-parietal networks of interest (including Left TPJ, Left IFG and Left IPS), indicates reduced network

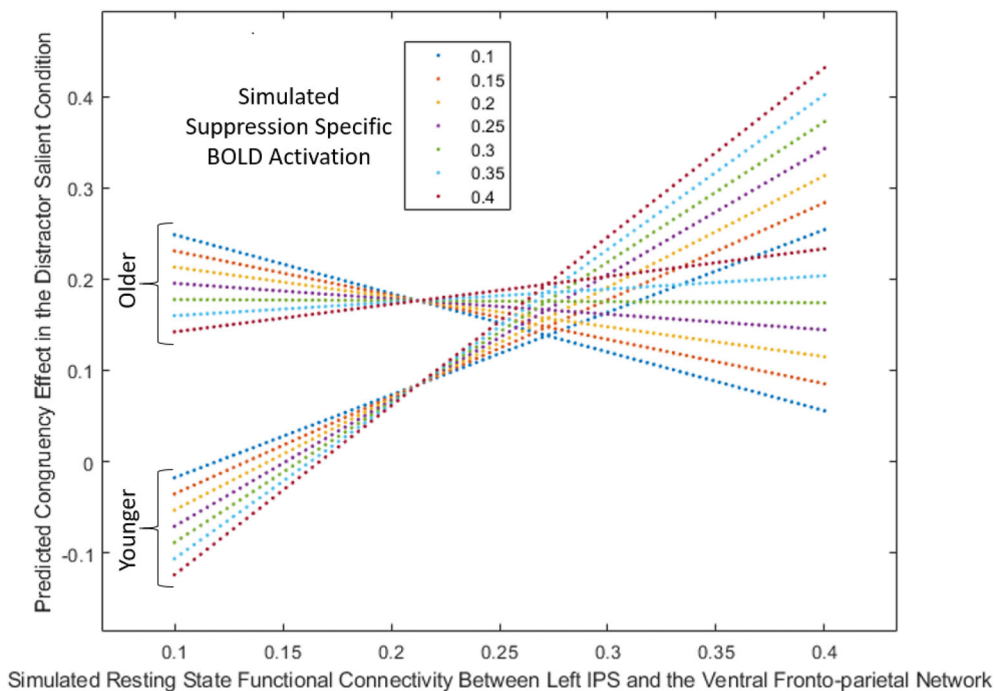


FIGURE 6 Simulation of Distractor Salient congruency effect as a function of RSFC and Left IPS bold activity. Beta parameters from the regression analysis were used to simulate the predicted congruency effect during Distractor Salient trials for a range of RSFC and BOLD activity across both age groups. IPS, intraparietal sulcus; RSFC, resting state functional connectivity

specificity in the older age group that could underlie changes in task activations. In contrast to previous studies (Mevorach et al., 2016; Tsvetanov et al., 2013), older participants did not exhibit an exaggerated behavioral effect of salient distractors compared with younger participants. The congruency effect, when the distractor was salient relative to when the target was salient, was equivalent across young and old participants (even though, overall performance was slower for older compared with younger adults). We note however, that our old participants were slightly younger than those participating in the two previous studies (the mean age and age range was 74, 65–84 in Tsvetanov et al. (2013); 71, 63–85, in Mevorach et al. (2016); and 66, 59–77, in the present study) which may have contributed to this preserved performance. Despite this, there was strong evidence that the old participants in our study used a qualitatively different brain network compared with younger participants to perform the task.

With respect to the Left IPS contribution, older participants appeared to rely on its engagement similarly to young participants in conditions where salient distractors had to be inhibited. Both the ROI and the whole brain analyses revealed the Left IPS to be sensitive to the salience of the distractors across the age groups, with increased BOLD responses when salient distractors (compared to low-salience ones) had to be ignored. As we did not find group differences in behavioral measures, this may simply suggest that both young and old adults are able to recruit a dorsal fronto-parietal network (including the Left IPS) in order to successfully ignore salient distractors. However, there were three indications that this is not likely the case. First, overall activation in the Left IPS mask was higher for older compared to younger participants, after correcting for differences in vascular reactivity. Second, we note that the seed specific within-network connectivity of the visuospatial network (comprising dorsal fronto-parietal-occipital regions including the Left IPS) tended to be reduced

for old compared to young participants (although this did not reach statistical significance levels). Third, our regression analysis suggested that increased recruitment of the Left IPS in old age (but not in young age) corresponded to increased difficulty in inhibiting the salient distractors. Thus, the Left IPS appears to be engaged slightly differently in old compared to young adults within a network whose resting activity appears to be less well synchronized.

Perhaps more importantly, we found clear group differences in the role played by ventral regions. The ROI analyses with the Left TPJ and IFG, gave initial support to this notion, with overall activation levels in the Left TPJ for older participants exceeding those of younger participants and with more pronounced IFG deactivations in younger participants than for the older participants. This was then further corroborated by the whole brain GLM analysis, which contrasted directly the brain activations for distractor and Target Salient displays between the two age groups. This analysis revealed unique activations in the older participants that were focused on the left lateralized ventral fronto-parietal network of interest (including the Left TPJ and Left IFG). Thus, whereas dorsal fronto-parietal regions were engaged in both young and old participants when they had to inhibit salient distractors, Left TPJ and IFG regions were uniquely engaged in old participants. Taken together, our findings suggest that the parietal contribution to salience suppression is modulated by age, with the ventral fronto-parietal network engaged in addition to a dorsal network (rather than supplant it). Such a pattern of brain dynamics may result from two alternative causes—dedifferentiation or a shift in control mode, which we will now consider.

Previous research has suggested that brain dynamics in old age represent reduced network specificity (or dedifferentiation), which is indexed by reduced within-network and increased between-network RSFC in aging populations (Betzel et al., 2014; Geerligs,

Maurits, et al., 2014; Geerligs, Saliassi, et al., 2014). In the context of the present study it is possible that older participants use both dorsal and ventral fronto-parietal networks because the two networks lose their specificity and are recruited together. However, our data points to a different explanation, particularly as we found no compelling evidence for reduced network specificity in the older participants. While there was some indication for reduced seed-specific within network connectivity (in the visuospatial network with the seed in the left superior parietal lobe) there was no indication of increased between-network connectivity. In fact, the only statistically significant group difference in RSFC highlighted a reduced connectivity in old age between the Executive and visuospatial networks. Furthermore, the increased task activation in older participants seems to be most pronounced in the left ventral fronto-parietal regions, whereas an account of increased global engagement would have predicted more widespread brain activation in this age group. Reduced network specificity would have likely also resulted with reduced sensitivity to the distractor salience (Distractor Salient vs. Target Salient displays), which is the opposite effect to what we have found.

Furthermore, previous studies have also specifically linked increased between network connectivity in old age with a poor cognitive profile (Tsvetanov et al., 2016). Interestingly, Tsvetanov et al. (2016), have documented a similar relation in younger age group (but the effect was more pronounced in old age). Thus, if the brain dynamics we reported for older participants here are a consequence of reduced network specificity, we expect that increased between network connectivity in this age group will correlate with poor performance. While this was the effect in young participants (in the regression analysis the between network connectivity was positively predicting increased distractor interference) we found the exact opposite effect in older participants, where increased between network connectivity predicted decreased distractor interference. This further supports the notion that the involvement of the ventral network in old age served a specific functional purpose rather than indicated a blurring of network boundaries.

The ventral activations in old age we report here, as well as the apparent contribution of their RSFC with the Left IPS to distractor inhibition, fits better with the notion that older participants rely on reactive control to suppress salient distractors while younger participants utilize preparatory (or proactive) control processes (Braver, 2012). The Left TPJ and IFG contribution in DiQuattro and Geng (2011) was specifically associated with an event in which a salient distractor might first capture attention before control processes in these regions can trigger a shift of attention away from the distractor, which will then be implemented through the dorsal attention network. We therefore suspect that the left lateralized ventral network here is engaged for a similar purpose following attention capture by a salient distractor. It may also be the case that the differences in dorsal activation in old age (a general increase in the levels of activation) is a result of later-triggered shift of attention selection away from the distractor (which does not take place in younger participants). This conjecture points to testable predictions. For instance, we would expect the left ventral network in old age (but not in young age) to precede (or direct) the contribution of the dorsal network.

We would also expect old participants (even when they do not show increased congruency effects) to process the salient distractor to a greater extent compared to young participants (e.g., to experience neural adaptation to repeating distractors or implicit memory; compare, Schmitz et al., 2010).

4.1 | Limitations

One limitation of this study is that we cannot rule out that our comparisons between young and older responses are affected by sex imbalance in our young sample. Previous literature has established that some cognitive control mechanisms exhibit sex differences, particularly response inhibition. In a stop-signal task, Li, Huang, Constable, and Sinha (2006) and Li et al. (2009) found significantly greater activation across a range of cortical and subcortical regions in men compared to women associated with stop successes and greater activation in women in the posterior cingulate cortex during stop errors. Although response inhibition falls under the heading of "cognitive control", it is a distinct process compared to salience suppression. We did not find any studies that explicitly tested for sex differences in proactive or reactive cognitive control, or in salience suppression, therefore it is difficult to say whether our female biased sample could have either under- or overestimated the mean response of the young group. However, if women did exhibit greater activation than men in posterior regions associated with the suppression of salience (similar to Li et al., 2006, 2009), it would have worked against our primary findings of greater activation in the older cohort. Therefore, it is possible that older participants engage even more brain regions (or engage the detected regions more strongly) than we were able to detect in this study. Nevertheless, accounting for sex differences will be an important goal for future studies of salience suppression and cognitive control.

Another limitation is that our findings cannot distinguish between a scenario in which proactive control through the dorsal attention network is impaired in old age and a scenario in which reactive processes are simply preferred in this age group. The tendency toward reduced seed-specific within network connectivity in the visuospatial network (with the seed in the left superior parietal lobe) may point toward the former but previous studies have also argued for the latter. For instance, Grady (2012), suggested that the shift toward favoring reactive control in old age may reflect a change in the time required to engage proactive control due to the need to accumulate greater neural resources in older participants (though see Ashinoff, Geng, & Mevorach, 2019, for evidence that reactive distractor suppression is also delayed in older populations). It therefore remains to be seen whether the changes in brain activity we have documented here are a result of impaired proactive processing or a strategic shift toward reactive control that is mediated through the left ventral fronto-parietal network in old age. Whichever is the case, our findings point to a specific change in old age where a left lateralized ventral fronto-parietal network becomes functionally relevant for distractor inhibition, most likely through generating reactive control signals that are

implemented in the dorsal attention network. Importantly, these changes in brain functionality are seen even as behavioral differences are not evident.

5 | CONCLUSIONS

Despite exhibiting equivalent performance in a task designed to encourage proactive inhibition, the older participants in this study engaged a qualitatively different network of brain regions than younger participants. Older participants exhibited both increased BOLD activation in the Left IPS (in contrast to our hypotheses regarding impaired recruitment of proactive control mechanisms), and in Left TPJ and Left IFG (consistent with our hypotheses regarding recruitment of reactive control mechanisms). Furthermore, an exploratory analysis revealed that increased RSFC between the Left IPS and a ventral fronto-parietal network was associated with improved salience suppression for older participants, but impaired salience suppression for the younger participants. This supports the notion that the age-related BOLD differences were specific and functional, rather than a consequence of dedifferentiation. These findings also fit with a recent report on aging effects in a stop-signal task (Hu, Job, Jenks, Chao, & Li, 2019) where connectivity (derived from a granger causality analysis) between proactive and reactive-associated regions in a left-fronto parietal network correlated with proactive inhibition (more connectivity = more inhibition) in older participants. Although the two studies are fundamentally different in a number of ways (including in some of the processes they reference) they highlight a similar picture whereby a distinctive network engaged by older participants likely represents a compensation mechanism for the frequently reported age-related deficits in proactive inhibition. This also raises the possibility that previous reports of intact proactive control in older participants may be driven by extra reliance on reactive control processes as well as effective functional connectivity in the aging brain.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

All raw behavioral data and experimental code for this study are publicly available on the Open Science Framework (OSF): DOI 10.17605/OSF.IO/EC3DH. Raw fMRI data is available upon request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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