

The Aging Brain and Executive Functions Revisited: Implications from Meta-Analytic and Functional-Connectivity Evidence

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Highlights

- Healthy aging is linked to deterioration in executive functions (EFs)
- ALE meta-analyses examined consistent age differences in brain activity linked to EFs
- In a larger set of EF regions, only left IFJ and (pre)cuneus were sensitive to age
- Advanced age was linked to weaker functional coupling within EF-related networks
- Our findings question earlier meta-analytic findings

Abstract

Healthy aging is associated with changes in cognitive performance including executive functions (EFs) and their associated brain activation patterns. However, it has remained unclear which EF-related brain regions are affected consistently, because the results of pertinent neuroimaging studies and earlier meta-analyses vary considerably. We, therefore, conducted new rigorous meta-analyses of published age differences in EF-related brain activity. Out of a larger set of regions associated with EFs, only left inferior frontal junction (IFJ) and left anterior cuneus/precuneus (aC/PrC) were found to show consistent age differences. To further characterize these two age-sensitive regions, we performed seed-based resting-state functional connectivity (RS-FC) analyses using fMRI data from a large adult sample with a wide age range. We also assessed associations of the two regions' whole-brain RS-FC patterns with age and EF performance. Although functional profiling and RS-FC analyses point towards a domain-general role of left IFJ in EFs, the pattern of individual study contributions to the meta-analytic results suggests process-specific modulations by age. Our analyses further indicate that left aC/PrC is recruited differently by older (compared to younger) adults during EF tasks, potentially reflecting inefficiencies in switching the attentional focus. Overall, our findings question earlier meta-analytic results and suggest a larger heterogeneity of age-related differences in brain activity associated with EFs. Hence, they encourage future research that pays greater attention to replicability, investigates age-related differences in deactivation, and focuses on more narrowly defined EF subprocesses, combining multiple behavioral assessments with multi-modal imaging.

1. Introduction

1.1. Executive Functions

Executive functions (EFs) are a loosely defined set of cognitive control processes that are taken to be critical for goal-directed thought and behavior in complex environments. Despite the lack of a clear formal definition of EFs as well as their ambiguous mapping on typical EF-tasks, there is relative agreement on their importance for regulating human behavior through modulating cognition in a top-down fashion (Diamond, 2013; Jurado & Rosselli, 2007). Different lines of research on how EFs might be best fractionated into subcomponents suggest models that argue for the existence of three core EFs: inhibitory control, working memory, and cognitive set shifting (e.g., Lehto, 1996; Miyake et al., 2000; for reviews see: Alvarez & Emory, 2006; Diamond, 2013). We acknowledge, however, that this differentiation is not undisputed (Baddeley & Hitch, 1974; Engle & Kane, 2004; Norman & Shallice, 1986; Stuss, 2006).

For a long time, it was thought that EFs were exclusively based on frontal lobe functioning as patients with frontal lesions often showed deficits in EFs leading to the interchangeable use of the terms “executive dysfunction” and “frontal lobe dysfunction” (e.g., Duncan, 1986; Owen et al., 1990; Shallice et al., 1982). However, patients with frontal lesions can perform within a normal range on EF tasks (e.g., Eslinger & Damasio, 1985; Shallice & Burgess, 1991) and patients with non-frontal lesions can show similar deficits like patients with frontal lesions (e.g., Anderson et al., 1991; Mountain & Snow, 1993). Years of research led Don Stuss and his collaborators (1995; 2006; 2011) to the assumption that there is a substantial fractionation of frontal lobe functions and that EFs represent only one functional category within the frontal lobes. Previous neuroimaging studies have revealed notable differences in the brain regions involved in EFs, which may be partly due to the elusive conceptualization of EFs (Collette et al., 2006) as well as the wealth of different

perspectives, operationalizations, and traditions in this research, which have resulted in a co-existence of rather diverse labels for the brain networks and regions associated with EFs (Camilleri et al., 2018). Although there are differences between different tasks probing EFs, there also seem to be core regions consistently involved, like left inferior frontal junction (IFJ; e.g., Emery et al., 2008; Milham et al., 2002; Zysset et al., 2007). Duncan and collaborators (Duncan, 2010; Duncan & Owen, 2000; Fedorenko et al., 2013) investigated and defined these core regions and proposed that a “multiple-demand” (MD) brain system was consistently recruited during all kinds of cognitively demanding tasks.

Müller et al. (2015) used a similar approach: They integrated results from three neuroimaging meta-analyses investigating working memory (Rottschy et al., 2012), vigilant attention (Langner & Eickhoff, 2013), and inhibitory control (Cieslik et al., 2015), highly discussed sub-components of EFs (Alvarez & Emory, 2006; Miyake et al., 2000), to define a common core network for EFs. This network was similar to Duncan’s MD system and comprised seven regions: mid-cingulate cortex/supplementary motor area (MCC/SMA), bilateral IFJ/inferior frontal gyrus (IFG), right middle frontal gyrus (MFG), bilateral anterior insula (aIns), right inferior parietal cortex (IPC), and intraparietal sulcus (IPS). Camilleri et al. (2018) went on to propose an extended MD network (eMDN) based on task-dependent and task-independent functional connectivity (FC) analyses seeded from the regions of the meta-analytically defined MD network by Müller and colleagues, to consider the perspective of a more widely distributed network. Camilleri et al. reported 17 regions as part of the eMDN (bilateral IFJ, aIns, SMA/pre-SMA, IPS, putamen, thalamus, MFG extending into the inferior frontal sulcus, dorsal premotor cortex [dPMC], and left inferior temporal gyrus). While the current paper focuses on EF-related activations, for the sake of completeness, we consider it necessary to briefly mention the functional relevance of the default-

mode network (DMN) as it is assumed to be activated during stimulus-independent or spontaneous cognition and deactivated during externally focused cognition. The DMN comprises a network of brain regions that includes the precuneus (PrC)/posterior cingulate cortex (PCC), anterior medial prefrontal cortex (mPFC), and lateral inferior parietal cortex (Shulman et al., 1997; for reviews see: Anticevic et al., 2012; Raichle, 2015). In the interest of space, we did not go into more detail and referred to reviews on this topic.

Taken together, EFs seem to be a macro-construct rather than a single process, which involves distributed networks instead of any particular region, with a core network and more specific regions that are recruited depending on certain task demands (Camilleri et al., 2018; Miyake & Friedman, 2012; Teuber, 1972).

1.2. Healthy Aging

Healthy aging is associated with altered cognitive performance and brain activation patterns in several cognitive domains, especially non-routine tasks that tax executive control processes (Drag & Bieliauskas, 2010; Park et al., 2002; Stuss & Craik, 2019). Although the aging brain faces unfavorable changes, such as the decline of dopaminergic receptors (Li et al., 2001; Yang et al., 2003), volumetric shrinkage of many grey-matter structures (Raz et al., 2005; Resnick et al., 2003; Salat et al., 2004), and reduced white-matter density (Head et al., 2004; Wen & Sachdev, 2004), it also seems to aim for an allostatic maintenance of cognitive functions through functional reorganization. This indicates that the neurobiological substrates of our cognitive system are highly dynamic and adaptive across the lifespan (Greenwood, 2007; Park & Reuter-Lorenz, 2008).

A common finding is the reduced lateralization of brain activation in older adults, which is thought to be compensatory as it is correlated with better performance in older adults (“hemispheric asymmetry reduction in older adults” [HAROLD]; Cabeza, 2002). Furthermore, brain activation shifts from posterior to more anterior brain regions have been observed (“posterior–anterior shift in aging” [PASA]; Davis et al., 2007), which might be caused by older adults’ need for exerting executive control for previously automated operations. Additionally, it has been hypothesized that age-related cognitive and behavioral changes are associated with less specialized brain responses and a decrease in FC with age, in the context of structural and neurobiological changes as well as external experiences (Baltes & Lindenberger, 1997; Goh, 2011; Li & Sikström, 2002; Park et al., 2001; 2004). Reuter-Lorenz and Cappell (2008) postulated that the oft-reported increase in task-related lateral PFC activity with age compensates for less efficient neural circuits (“compensation-related utilization of neural circuits hypothesis” [CRUNCH]). Finally, Park and Reuter-Lorenz (2008) attempted to unite previous theories in their “scaffolding theory of aging and cognition” (STAC). In this context, “scaffolds” describe a supportive framework that helps maintain cognitive and behavioral performance at a relatively high level through advanced age via the strengthening of existing connections, development of new connections, and disuse of connections that have become fragile or deficient. These changes, in turn, are assumed to lead to increased bilateral and/or frontal activation in older adults.

Results from neuroimaging studies on age-related changes in the EF subcomponents working memory, inhibitory control, and cognitive flexibility are rather ambiguous. While some studies reported an increase in bilateral prefrontal activity (e.g., Emery et al., 2008; Madden et al., 1999) and a decrease in occipital activity (e.g., Ansado et al., 2012; Madden et al., 2002, 2010), other studies reported occipital activity increase (e.g., Bloemendaal et al., 2016; Van Impe et al., 2011)

and frontal activity decrease in older adults (e.g., Bloemendaal et al., 2016; Schulte et al., 2011). Moreover, the age-related reduction in hemispheric asymmetry of brain activity is not found consistently (e.g., Carp et al., 2010; Toepper et al., 2014). This large amount of heterogeneous, partly contradictory findings illustrates the need for a quantitative data synthesis by means of meta-analysis in combination with taking a systems-level perspective, which includes identifying the connectional profiles of the identified regions with respect to the rest of the brain.

So far, three quantitative neuroimaging meta-analyses investigating cognitive aging in EFs have been published, each with their own limitations as discussed below: Spreng et al. (2010) performed an analysis across all then available experiments probing EFs in age, such as working memory, task switching, and inhibitory control. The authors found consistent EF-related increases in activity with age in bilateral dorsolateral prefrontal cortex (DLPFC), right posterior MFG/frontal eye field (FEF), left SMA, and left rostrolateral PFC as well as consistent decreases in activity with age in right ventrolateral PFC. Next, Turner and Spreng (2012) conducted separate meta-analyses for the EF subcomponents working memory and inhibition and found domain-specific patterns of across-experiment convergence. For working memory, consistent increases in activity with age were found in bilateral SMA, right MFG, left IFG, and left IPS; consistently lower activity in older adults was found in right IPS, left aIns/frontal operculum, and left FEF. For inhibition-related brain activity, consistent increases in activity with age was found in right MFG/IFG and left superior frontal gyrus, whereas consistent decreases in activity with age was found in right inferior occipital gyrus. Finally, a third meta-analysis by Di et al. (2014) found consistent increases in EF-related activation with age in bilateral IFG, left anterior cerebellum, left fusiform gyrus (FG), right MFG, and right parahippocampal gyrus. Consistently lower EF-related activation with age was found in bilateral Ins, left MFG, left medial frontal gyrus, and right MCC.

Taken together, the picture produced by these meta-analyses is largely inconclusive. This inconsistency across meta-analyses might result from methodological differences, such as the inclusion or exclusion of region-of-interest (ROI) contrasts, the particular selection of tasks included, or the approach to testing for age-related differences. Furthermore, all previous meta-analyses corrected for multiple comparisons by controlling the voxel-level false discovery rate (FDR), which has recently been shown to feature low sensitivity and a high susceptibility for false-positive findings in Activation Likelihood Estimation (ALE) meta-analysis (Eickhoff et al., 2016). In light of these inconsistencies and limitations of earlier efforts as well as the continued growth of the pertinent literature since 2014, a fresh meta-analysis on age-related differences in brain activity associated with EFs appeared much warranted.

1.3. Current Study

In a first step, coordinate-based ALE meta-analysis (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2002, 2012) was used to synthesize results from neuroimaging studies investigating EFs in young and old participants. We started with a meta-analysis of within-group findings, pooling across experimental results obtained in young or old participants, respectively. This approach should test for consistent general EF-related brain activity in our sample of experiments, without regard to age-related differences. It was aimed at replicating previous findings of brain regions involved in EFs. Subsequently, we conducted further meta-analyses of published between-group contrasts, investigating consistent age differences in EF-related brain activity. As a methodological improvement over previous ALE meta-analyses on this topic, we used cluster-level family-wise

error (FWE) correction for multiple comparisons (rather than FDR-based correction) and a minimum number of $n = 17$ experiments per analysis, following the recommendations by Eickhoff et al. (2016).

In a second step, task-independent whole-brain FC patterns of resulting age-sensitive regions were analyzed using resting-state (RS) functional magnetic resonance imaging (fMRI) data of healthy adults. Finally, we assessed the associations of the regions' whole-brain FC with age and performance scores representing EF and its subcomponents in order to gain further insights into the mechanisms underlying cognitive aging.

In summary, this study aimed to investigate (i) which brain regions show consistent age differences in EF-related activity at the meta-analytic level, (ii) the connectional profiles of these age-sensitive regions, and (iii) how the connectivity profiles of these regions are affected by aging and EF-capacity.

2. Methods

2.1. ALE Meta-Analysis

2.1.1. Sample

2.1.1.1. Search for Studies

Pertinent studies were searched for in the databases Web of Science, PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>), PsycINFO (<http://ovidsp.tx.ovid.com>), and Google Scholar (<http://scholar.google.de>) using the following search strings: (1) title: “age” or “aging” or “ageing” or “age-related” or “older adults” or “old adults” or “life-span” or “elderly adults”; and (2) title: “executive functions” or “working memory” or “inhibition” or “cognitive flexibility”; and (3) abstract: “fMRI” or “functional magnetic resonance imaging” or “PET” or “positron emission

tomography” or “neuroimaging” or “cerebral blood flow.” Subsequently, specific EF-related task labels were included in the search string as follows: for working memory, “n-back” or “Sternberg” or “delayed match* to sample” or “delayed simple matching”; for inhibitory control, “Stroop” or “flanker” or “Simon” or “stimulus-response compatibility” or “stop signal” or “go/no-go” or “stimulus detection” or “stimulus discrimination” or “selective attention”; and for cognitive flexibility, “task switching” or “dual task” or “set shifting.” The search criteria were partially motivated by previous meta-analyses regarding aging and EFs (Di et al., 2014; Spreng et al., 2010; Turner & Spreng, 2012). The decision on which tasks to include in the extended search string was made based on Diamond’s (2013) definition of typical tasks for each of the subcategories. Finally, earlier meta-analyses on this topic, reviews, and the reference lists of identified studies were inspected for additional studies to be included.

2.1.1.2. Inclusion and Exclusion Criteria

We included only peer-reviewed publications of fMRI or positron emission tomography (PET) experiments performed in healthy young and old participants without any pharmacological manipulations or other extraneous interventions. Results of group analyses needed to be reported as coordinates of a standard reference space, that is, MNI (Montreal Neurological Institute) or Talairach (Talairach & Tournoux, 1988) space. Studies were only included if the whole brain was covered (i.e. coverage of at least 8 cm in the z-dimension). Consequently, no ROI-based results were included. However, some of the experiments we included reported masking of the between-group contrast with the task-positive main effect to restrict group differences to task-related regions (these studies are marked in Tables A1 and A2). We included results from contrasts between task and sensorimotor control or resting-baseline conditions, contrasts between different levels of task difficulty, as well as correlations between age and task-related activity. Thus, deactivation

data, results from connectivity analyses, or correlations and interactions with other variables (e.g., group $\times$ performance interactions, correlations with reaction time, etc.) were not considered. In case of uncertainty as to any of these criteria, the corresponding author of the given study was contacted for clarification (these studies are marked in Tables A1 and A2).

To minimize the risk that meta-analytic results were unduly biased by a particular publication, the contribution from any given study was limited to one experiment. If a study reported several experiments eligible for inclusion, their findings (i.e., reported coordinates) were pooled to constitute a single experiment, as suggested by Turkeltaub et al. (2012). Further, if contrasts for both transient and sustained brain activity were available, the contrast reflecting transient activity was chosen as it typically allows for a more process-specific interpretation. For the current approach, coordinates of within-group (i.e., main task effect per group) and between-group (i.e., contrast of task effects between groups: [young > old, old > young]) contrasts as well as correlations between task performance and age were included.

2.1.1.3. Studies Included

After an initial screening of publication abstracts for topicality, 147 studies were retrieved in total. Applying the above criteria left us with 31 eligible studies reporting within-group task effects: 11 for working memory, 12 for inhibition, and 9 for cognitive flexibility. Of note, the study by Townsend et al. (2006) contributed results to two subdomains (inhibition and cognitive flexibility).

In the meta-analyses of age-related differences, 46 eligible studies were included in total: 15 for working memory, 19 for inhibition, 14 for cognitive flexibility, and 1 not clearly assignable to any subdomain. For clarification, not all studies included both within- and between-group contrasts, leading to somewhat different numbers of studies included in the within- and between-group

meta-analyses, respectively. Of note, Eich et al. (2016) and Townsend et al. (2006) were included for inhibition and cognitive flexibility, and Lamar et al. (2004) for inhibition and working memory. Studies reporting different tasks (i.e., experiments that contribute to different subdomains) were pooled by the respective subdomain (vs. by subject group) and may thus contribute with two data points. To make sure that this pooling by subcomponent would not have an effect on the results, we additionally computed the meta-analyses with solely one point of data per study, i.e., pooling by subject group. The results were the same. For the sake of interpretability, we therefore decided to pool the aforementioned studies by subcomponent. See Figure 1 for an overview of the different analysis steps conducted.

For further information about the studies included, please see Tables A1 and A2. A checklist for neuroimaging meta-analyses as recommended by Müller et al. (2018) can be found in Table A3.

2.1.2. Activation Likelihood Estimation

2.1.2.1. ALE Algorithm

All meta-analyses were conducted using the revised version of the ALE algorithm for coordinate-based meta-analysis of neuroimaging results (Eickhoff et al., 2009, 2012; Turkeltaub et al., 2002, 2012) implemented as in-house MATLAB tools. This algorithm aims to identify areas with across-experiment convergence of activity foci that is higher than expected from random spatial association. Before analysis, any coordinates reported in Talairach space were transformed into MNI space (Lancaster et al., 2007). Because the standard brain templates used in SPM (statistical parametric mapping) since version SPM96 and in FSL (FMRIB Software Library) are given in MNI space, reported results from analyses using SPM or FSL were treated as MNI coordinates

unless the authors explicitly mentioned a transformation from MNI to Talairach space or the use of an alternative brain template.

In a first step, important content of the included studies was coded and recorded. In a second step, the reported coordinates of each experiment's peak activations ("foci") were projected on a brain template, acknowledging the spatial uncertainty associated with each coordinate by modeling Gaussian probability distributions around each focus. Third, the probability distributions of all activation foci were combined for each voxel, resulting in a modeled activation map. The union of these modeled activation maps then yielded voxel-wise ALE scores, which were compared to a null distribution reflecting a random spatial association between experiments. The p -value of a "true" ALE score was then given by the proportion of equal or higher values obtained under the null distribution. The resulting non-parametric p values for each meta-analysis were cut off at a threshold of $p < .05$ (family-wise error corrected at cluster level; cluster inclusion threshold at voxel level: $p < .001$).

2.1.2.2. Meta-Analyses Conducted

First, a meta-analysis pooling across within-group task effects (i.e., main task effects for both age groups) was conducted on all experiments to examine the main effect of performing EF tasks on brain activity independent of age. Second, for examining age-related effects, we performed three different meta-analyses of between-group contrasts: (1) pooled, (2) old > young, and (3) young > old. We also aimed to conduct separate meta-analyses for each EF subcomponent, but only for inhibition more than 17 experiments were found to be eligible. Hence, a comparison between EF subcomponents was not possible. The results of the inhibition-specific meta-analyses can be found in Tables A5 and A6.

Pooled analyses search for consistent group differences in EF-related brain activity, independent of the direction of the between-group effect. For neuroimaging findings, pooled meta-analyses may provide the best summary because the directions of group differences in individual experiments depend on how exactly these differences were calculated, which varies widely between studies: Some authors compute task versus control contrasts at the individual-subject level, which are then compared between old and young adults at group level, whereas others compute group (old versus young) by task (task versus control or baseline) interactions at the second level. As control conditions strongly vary between experiments (from resting baseline to high-level control tasks), effects of between-group activation differences in these control conditions may influence the overall direction of group differences unpredictably (Müller et al., 2017).

2.2. *Resting-State Functional Connectivity*

To further characterize EF-related brain regions consistently affected by aging (i.e., regions with significant convergence in the pooled age-related meta-analysis), we investigated their RS-FC patterns. Therefore, whole-brain RS-FC analyses were conducted. RS-fMRI images of 413 healthy adults were obtained from the publicly available enhanced Nathan Kline Institute - Rockland Sample (eNKI-RS; Nooner et al., 2012; age range = 18 – 80; mean age = 44.85; SD = 18.51; 272 females). The re-analysis of the data was approved by the local ethics committee of the Heinrich Heine University Düsseldorf. Images were obtained with a Siemens TimTrio 3T scanner using BOLD (blood-oxygen-level-dependent) contrast [gradient-echo EPI (echo planar imaging) pulse sequence, TR = 1.4 s, TE = 30 ms, flip angle = 65°, voxel size = $2.0 \times 2.0 \times 2.0$ mm³, 64 slices]. 404 volumes were acquired. Participants were instructed to keep their eyes open and maintain fixation on a central dot. Physiological and movement artifacts were removed from RS data by

using FIX (FMRIB's ICA-based Xnoiseifier, version 1.061 as implemented in FSL 5.0.9; Griffanti et al., 2014; Salimi-Khorshidi et al., 2014), which decomposes the data into independent components and identifies noise components using a large number of distinct spatial and temporal features via pattern classification. Unique variance related to the identified artifactual components is then regressed from the data. Data were further preprocessed using SPM12 (Wellcome Trust Centre Neuroimaging, London) and in-house Matlab scripts. After removing the first four dummy scans of each time series, the remaining EPI volumes were then corrected for head movement by a two-pass affine registration procedure: first, images were aligned to the initial volume and, subsequently, to the mean of all volumes. The mean EPI image was then co-registered to the gray-matter probability map provided by SPM12 using normalized mutual information and keeping all EPI volumes aligned. Next, the mean EPI image of each subject was spatially normalized to MNI-152 space using the “unified segmentation” approach (Ashburner & Friston, 2000). The resulting deformation parameters were then applied to all other EPI volumes. Finally, data were spatially smoothed with a 5-mm FWHM (full width at half maximum) Gaussian kernel to improve the signal-to-noise ratio and to compensate for residual anatomic variations.

The BOLD signal time-courses of all voxels within each seed region, expressed as the first eigenvariate, were extracted for each subject. To reduce spurious correlations, variance explained by the mean white-matter and cerebrospinal-fluid signal were removed from the time series together with 24 movement parameters (including derivatives and 2nd-order effects; cf. Satterthwaite et al., 2013), which was subsequently band-pass filtered with the cut-off frequencies of .01 and .08 Hz. Linear (Pearson) correlations between the time series of the seed regions and all other grey-matter voxels in the brain were computed to quantify RS-FC. The resulting voxel-wise correlation coef-

ficients were then transformed into Fisher's Z-scores and entered in a group-level analysis of variance. The results of this random-effects analysis were masked with the subjects' mean Z-scores $\geq .1$ and thresholded at a voxel-level FWE-corrected threshold of one-sided $p < .05$. Here, we chose one-sided testing, as our hypotheses were directed (i.e., we were only interested in the positive coupling between our seed regions and the rest of the brain). An additional extent threshold of 10 contiguous voxels was applied to exclude smaller, potentially spurious clusters.

2.3. *Association of RS-FC with Age and EF Abilities*

In the same sample of 413 adults, we also examined the association of the seed region's whole-brain RS-FC with age as well as EF abilities using analysis of covariance (ANCOVA). For assessing EF abilities, we computed four compound scores: a total score and three subscores, each representing a particular EF subcomponent (i.e., working memory, inhibitory control, and cognitive flexibility). The cognitive tasks used were also obtained from the eNKI-RS. Performance raw scores were z-transformed - outliers $> |3|$ standard deviations were removed - and added up to calculate EF subcomponent scores as follows: The working memory compound score consisted of reaction time (RT) and error rate (ER) of the 2-back and 1-back conditions of the Short Letter-N-Back Test, which is part of Penn's Computerized Neurocognitive Battery (CNB; Gur et al., 2010). The inhibition compound score consisted of (i) the conflict effect of the Attention Network Task (ANT; Fan et al., 2002), (ii) RT and ER of the Color-Word Interference Test, which is part of the Delis-Kaplan Executive Function System (D-KEFS; Delis et al., 2004), and (iii) RT and ER of the Short Penn Continuous Performance Test (Number and Letter Versions), which is also part of Penn's CNB. The cognitive flexibility compound score consisted of RT of the Trail Making Test, which is part of the D-KEFS, as well as of RT and ER of the Penn Conditional Exclusion Task,

part of Penn's CNB. Finally, for the total EF score, all single scores were added up and divided by the absolute number of scores. All compound scores were multiplied by -1. Hence, higher scores represent higher performance. The results of the ANCOVA were masked with the RS-FC map of the respective seed region (as described above, see section 2.2.) and thresholded at a voxel-level FWE-corrected threshold of two-sided $p < .00625$ (additional extent threshold of 10 contiguous voxels). The p -value was adjusted for multiple comparisons as we tested four models, and adjusted for two-sided testing as recommended by Chen et al. (2018). All results were anatomically labeled by reference to probabilistic cytoarchitectonic maps of the human brain using the SPM Anatomy Toolbox version 3 (Eickhoff et al., 2005, 2007) and visualized with the BrainNet Viewer (Xia et al., 2013).

3. Results

3.1. Meta-Analyses

3.1.1. Analysis of EF-related Effects Across Age

A meta-analysis across both age groups and all experiments (reflecting all three EF sub-components) was conducted to examine the general main effect of taxing EFs on regional brain activity. Significant convergence across experiments was found in left IFJ, left pre-SMA, left IPS/SPL, left mid-FG, left central Ins, and right frontal pole/MFG (see Table 1 and Figure 2).

3.1.2. Analyses of Age-related Differences

We performed three different meta-analyses of contrasts between age groups: (1) pooled, (2) old > young, and (3) young > old. The pooled meta-analysis, which included all experiments

($n = 49$) that probed age differences in EF-related brain activity irrespective of the contrast's direction, revealed only two regions with significant convergence of such age differences: left IFJ and left anterior cuneus/precuneus (aC/PrC; see Table 1 and Figure 3A). Convergence in left IFJ was almost equally driven by experiments probing working memory (32.95%), inhibition (28.54%), and cognitive flexibility (38.41%). Furthermore, it was more strongly driven by experiments contrasting old > young (60.24%) than by experiments contrasting young > old (39.7%). Convergent activity in left aC/PrC was also driven by experiments on working memory (24.9%), inhibition (41.91%), and cognitive flexibility (32.45%). In contrast to left IFJ, however, it was almost exclusively driven by old > young contrasts (91.68%). Please see Table A4 for a full overview of the study contributions.

The meta-analysis testing for consistently lower brain activity across EF experiments in older (vs. younger) adults ($n = 31$) did not yield any significant convergence. Conversely, the meta-analysis testing for consistently higher activity across EFs experiments in older (vs. younger) adults ($n = 42$) revealed significant convergence in left aC/PrC (see Table 1 and Figure 3B).

We also aimed to conduct separate meta-analyses for each EF subcomponent, but only for inhibition more than 17 experiments were found to be eligible. The results of the inhibition-specific meta-analyses can be found in Tables A5 and A6.

3.2. *Connectional Characterization*

The two age-sensitive regions resulting from the pooled meta-analysis (i.e., left IFJ and left aC/PrC) were connectionally characterized by conducting whole-brain RS-FC analyses. The RS-FC map obtained for left IFJ comprised 14 clusters of significant coupling: the seed region extending into DLPFC, MFG, FEF, dPMC, SMA/pre-SMA, frontal pole, and aIns; left caudate nucleus;

left IPS extending into FG and SPL; two clusters in left cerebellum VII; right IFJ extending into DLPFC, FEF, dPMC, and frontal pole; right cerebellum VI and VII; right IPS/angular gyrus; right FG extending into Wernicke's region; right SMA/pre-SMA; right aIns, right primary somatosensory cortex (S1); and bilateral anterior cingulate cortex (ACC; see Table 2 and Figure 4A).

The RS-FC analysis of left aC/PrC yielded 13 clusters: the seed region extending into bilateral PCC, FG, subiculum, calcarine gyrus, and left IPL; left frontal pole extending into subgenual area, FEF, and bilateral frontopolar cortex; left posterior Insula (pIns) extending into parietal operculum; left cerebellum VII; two clusters in right cerebellum IX and VII; bilateral temporoparietal junction (TPJ); and four clusters in bilateral IFG pars orbitalis (see Table 2 and Figure 4B).

3.3. *Association of RS-FC with Age and EF Abilities*

3.3.1. *Age*

An ANCOVA was performed to examine the association between the seed regions' RS-FC patterns and age. We observed significant negative associations with age for RS-FC between left IFJ and 10 clusters: left aIns, left FEF, left TPJ, bilateral IFJ/DLPFC, bilateral FG, and bilateral aCC (see Table 3 and Figure 5A).

Age was also significantly negatively associated with RS-FC between left aC/PrC and 5 regions: the seed region extending into bilateral visual cortex, left Heschl's gyrus extending into planum temporale, left SPL, left S1, and left thalamus (see Table 3 and Figure 5B). Finally, age was significantly positively associated with RS-FC between left aC/PrC and 3 regions: left IPL, left PrC, and left TPJ (see Table 3 and Figure 6).

3.3.2. *EF Abilities*

Finally, we performed an ANCOVA to assess the association between the seed regions' RS-FC patterns and EF abilities. RS-FC between left aC/PrC and the seed region extending into bilateral visual cortices was significantly positively associated with the total EF score (see Table 4 and Figure 7).

We found a significant negative association of the cognitive flexibility score with RS-FC between left aC/PrC and 3 regions: bilateral IPL and right middle temporal gyrus (MTG; see Table 4 and Figure 8A), whereas RS-FC between left aC/PrC and the seed region extending into bilateral visual cortices was significantly positively associated with the cognitive flexibility score (see Table 4 and Figure 8B).

Neither for working memory nor for inhibitory control was there any significant association between performance (compound scores) and RS-FC of either seed region with the rest of the brain.

4. Discussion

Coordinate-based ALE meta-analyses were used to synthesize the neural correlates of age-related changes in EFs. In particular, we first ran a meta-analysis across all age groups and all three EF subcomponents followed by a pooled and two directed meta-analyses examining age differences in EF-related brain activity. The initial global analysis corroborated a set of regions well-known for being involved in EFs. Consistent activation differences between young and old adults, however, were restricted to left IFJ and left aC/PrC. Subsequently, we assessed the connectional profiles of these two age-sensitive regions and how their RS-FC profiles are modulated by age and EF abilities. Left IFJ was found to be linked to regions involved in executive functioning, whereas left aC/PrC was connectionally linked to regions involved in attentional processes and the DMN.

Furthermore, RS-FC between left IFJ and EF-related regions decreased with increasing age. Similarly, RS-FC between left aC/PrC and regions involved in perceptual processes decreased with increasing age, while RS-FC between left aC/PrC and DMN-related regions increased with age. Finally, only very few associations of seed-based RS-FC with EF abilities were observed: RS-FC between left aC/PrC and bilateral visual cortex was positively associated with the total EF score and cognitive flexibility, whereas RS-FC between left aC/PrC and DMN-related regions was inversely associated with cognitive flexibility.

4.1. Comparison to Previous Meta-Analyses

The current results of between-group contrasts deviate quite noticeably from previous meta-analyses of age differences in EF-related brain activity (Di et al., 2014; Spreng et al., 2010; Turner & Spreng, 2012). The only two regions consistently found across these earlier meta-analyses are left IFJ and pre-SMA. Thus, there is substantial disagreement between all meta-analyses devoted to this topic.

These discrepancies might be explained by several methodological differences: First, all previous meta-analyses included several reports of ROI analyses, which biases ALE whole-brain tests for significance towards convergence in the given ROIs (Müller et al., 2017). The null distribution in ALE reflects a random spatial association between findings across the entire brain assuming that each voxel has the same a priori chance of being activated (Eickhoff et al., 2012). The inclusion of ROI analyses would obviously violate this assumption, leading to inflated significance estimations for regions supported by ROI analyses (Müller et al., 2017). Second, all previous meta-analyses attempted to correct for multiple comparisons by controlling the voxel-level FDR, which is considered invalid for topographic inference on smoothed data (Chumbley & Friston, 2009),

features low sensitivity, and leads to inflated positive findings (Eickhoff et al., 2016). FWE correction for ALE meta-analyses on the other hand provides good sensitivity and low susceptibility to false positives. Third, previous meta-analyses were partly based on rather small samples, rendering them prone to yielding clusters of “convergence” driven by very few or even single experiments (Eickhoff et al., 2016). Fourth, earlier analyses included some tasks that, according to our definition, would not constitute clear-cut operationalizations of EFs (e.g., sentence comprehension or word generation tasks). Taken together, the inclusion of ROI studies, heterogeneity in the tasks included, limited sample sizes, and FDR-corrected thresholding may have rendered previous meta-analyses very liberal, leading to more widespread but potentially spurious convergence across published results.

4.2. *Left IFJ*

The pooled meta-analysis of age differences in EF-related brain activity yielded convergence in left IFJ. Our data indicate that left IFJ is recruited to a different degree by younger versus older adults. The sign of this difference, however, appears to depend on the type of task: For tasks taxing working memory, many studies report an age-related decrease in IFJ activation (e.g., Bäckman et al., 2011; Podell et al., 2012; Prakash et al., 2012). Podell et al. (2012) argued that deficits in working memory updating in older adults are accompanied by a reduced utilization of efficient neurocognitive strategies, relative to younger adults. This is in line with the dedifferentiation hypothesis of cognitive aging, stating that brain regions showing specialized responses to specific cognitive tasks become less specialized with increasing age (Baltes & Lindenberger, 1997; Goh, 2011; Li & Sikström, 2002; Park et al., 2001; 2004). In the context of inhibitory control and attention shifting, however, studies report an age-related increase in left IFJ activity (e.g., Korsch et al.,

2014; Townsend et al., 2006; Zysset et al., 2007). According to Townsend et al. (2006), the more extensive activation patterns observed in older adults may be due to (i) the failure of within-channel inhibition of irrelevant visual information, or (ii) compensatory neural recruitment caused by the attempt to increase relevant and decrease irrelevant information processing. This is in line with Korsch et al.'s (2014) conclusion that increased age-related IFJ activation is caused by the use of different strategies when irrelevant information interferes with correct response selection. Looking at the individual study contributions to our cluster, our results support these findings. For experiments on cognitive flexibility or inhibition that contributed to the cluster, convergence in left IFJ was mainly driven by the contrast old > young (rather than young > old). In contradistinction, for experiments on working memory, convergence was mainly driven by the contrast young > old (rather than old > young; see Table A4). These findings, although purely descriptive, point to a shared cognitive mechanism in the context of inhibition and cognitive flexibility, possibly leading to the observed similar aging effects on IFJ activity.

In the literature, there also is a well-established link between left IFJ and task switching, set shifting, or updating task representations (Brass & Cramon, 2004; Derrfuss et al., 2005; Worringer et al., 2019), that is, processes that allow adjusting behavior to new external demands in a top-down fashion (i.e., cognitive flexibility). This notion is also supported by repetitive transcranial magnetic stimulation studies (Higo et al., 2011; Zanto et al., 2011), pointing to IFJ's causal participation in updating task representations and regulating neural excitability in visual areas according to the task goal. Supporting the broad involvement of left IFJ across EF domains, Derrfuss et al. (2004) mapped the activity from experiments investigating working memory, task switching, and inhibitory control and found a significant overlap in IFJ for all task types. The almost equal contribution of working memory, inhibition, and cognitive flexibility experiments to the IFJ cluster

in the pooled EF meta-analysis also points to its importance for all EF subcomponents. Further indirect evidence is provided by IFJ's location at the junction of the inferior frontal and inferior precentral sulci, and thus at the intersection of three functional neuroanatomical domains: premotor, language, and working memory. Although our study cannot clarify the precise functional role of left IFJ, this region may integrate information from these three domains (Brass et al., 2005). In particular, it is thought to (re)activate and implement relevant stimulus–response mappings, connecting stimulus information with motor output according to behavioral goals (Hartstra et al., 2012; Worringer et al., 2019).

Our RS-FC results further stress left IFJ's important role in EFs, as its RS-FC map is highly overlapping with Camilleri et al.'s (2018) eMDN, the proposed neural correlate of EFs and with the frontoparietal control network (FPCN; Cole & Schneider, 2007), that is, bilateral ACC/pre-SMA, DLPFC, IFJ, aIns, dPMC, PPC. The negative association between RS-FC of left IFJ and age (see Figure 5A) indicates that age-related connectivity changes are not regionally specific (e.g. prefrontal) but rather wide-spread, including the dorsal attention network (DAN), the FPCN as well as the eMDN. An age-related RS-FC decline in these networks has been reported previously (Campbell et al., 2012; He et al., 2014). The frequently reported age-related decline in EF performance might thus be associated with decreased FC between regions and networks important for executive functioning. Through its functional role, that is, stimulus–response mapping and its importance for all EF subcomponents, left IFJ seems to be operating as a key node for executive functioning and thus showing domain-general recruitment as well as intrinsic correlations to multiple task positive networks.

Summing up, our meta-analytic and connectional findings suggest a pivotal role of left IFJ in EFs. While its involvement in EFs may mostly be domain-general, its recruitment appears to

change with age depending on the type of task. As older adults seem to rely more on left IFJ in the context of cognitive flexibility and inhibition, younger adults recruit it more strongly in the context of working memory. Decreased RS-FC with age of left IFJ and regions associated with different task positive networks points to (i) generalized age-related changes across the brain rather than degradation in a particular region, as well as (ii) a possible underlying neural correlate for EF performance decline with age.

4.3. *Left anterior Cuneus/Precuneus*

Convergence in left aC/PrC was found in the meta-analyses EF pooled and EF old > young. To account for the difficulties in accurately comparing anatomical locations across individuals and studies due to individual differences as well as differences in spatial processing and brain templates (Brett et al., 2002) we chose to label the region of convergence aC/PrC instead of deciding on just one region and thus neglecting important functional implications. Taking the contribution of our region into account, convergence in the pooled meta-analysis was mainly driven by the contrast old > young. Consequently, consistent increased activation in aC/PrC was specific to older compared to younger adults. Furthermore, it has been associated with initiating shifts of attentional focus (Bzdok et al., 2015; Langner & Eickhoff, 2013; Worringer et al., 2019). This is in accordance with our finding of activity convergence in left aC/PrC being driven by the subcomponents inhibition and cognitive flexibility, where shifting the attentional focus and thus inhibiting irrelevant input plays a key role (see Table A4). Previous studies (DiGirolamo et al., 2001; Kuptsova et al., 2016; Townsend et al., 2006) testing age-related differences in attention shifting suggest that younger and older adults relied on the same regions during shift conditions, that is, frontoparietal

regions including PrC. Older adults, however, also recruited these regions during the control condition, (i.e. attentional focusing). The authors suggested that older adults relied more on executive networks, even in the non-shift task condition, to compensate for reduced efficiency of sensory and cognitive processing. Another explanation might be that older adults had difficulties inhibiting the alternate task even during the non-shift condition. By inspecting the study contributions to the left aC/PrC cluster in the pooled EF meta-analysis, one can see that 92% of the studies leading to a convergence in left aC/PrC result from the contrast old > young. 83% of these studies did not report any inclusive masking with a task-positive effect, and 68% tested against an active control condition, rather than rest. While we did not directly investigate deactivations – due to the lack of studies available that matched our inclusion criteria – one could argue, based on these numbers, that convergence in left aC/PrC might be mainly driven by consistently greater aC/PrC deactivation in older adults during the control (vs. task) condition and/or consistently greater deactivation in younger adults during the experimental (vs. control) task, rather than a higher task-induced aC/PrC activation in older adults. A greater age-related deactivation during control (vs. task) and deactivation difficulties (compared to younger adults) in task (vs. control) could lead to inefficiencies in attentional switching in older adults. Together with PCC, PrC is assumed to be one of the central and specialized hubs of the DMN, being intrinsically connected to the DMN as well as to attentional networks, in line with our RS-FC findings (see Figure 4B). Its role might be controlling the dynamic interaction between these networks for an efficient distribution of attention (Leech et al., 2011). Furthermore, PrC appears to be in a special position within the DMN as it is coupled with the DMN at rest, and with task positive networks during task performance (Leech et al., 2011; Utevsky et al., 2014). Its widespread FC pattern, involving higher association regions, corroborates

an important role in integrating internally and externally driven stimulus processing (Cavanna & Trimble, 2006).

While PrC's RS-FC with sensorimotor regions decreased in older adults, its RS-FC with regions associated with the DMN and DAN increased with age. Previous studies found that older adults failed to deactivate the DMN during a range of cognitive tasks (e.g., Grady et al., 2006; Lustig et al., 2003; Park et al., 2010; Persson et al., 2007). Spreng and Schacter (2011) assumed that this is due to a reduction of large-scale network flexibility in the context of changing task demands. These differences might also be due to differences during fixation, as older adults have a reduced susceptibility to mind wandering (Giambra, 1989; Jackson & Balota, 2012). Furthermore, it might be more difficult for older adults to fixate the cross, possibly explaining an age-related RS-FC increase of left PrC with the DAN. Additionally, it has been proposed that functional networks become less specific with age (Geerligs, Maurits, et al., 2014; Geerligs, Renken, et al., 2014). Thus, there might be a dedifferentiation in activation patterns – in accordance with the aforementioned dedifferentiation hypothesis of neural aging – and a compensatory recruitment of further brain regions. The latter has also been proposed by the cognitive aging theories CRUNCH (Reuter-Lorenz & Cappell, 2008) and STAC (Park & Reuter-Lorenz, 2008), which state that in older adults, to maintain cognitive and behavioral performance, connections that have become fragile or deficient are weakened, existing connections are strengthened, and new connections are developed.

RS-FC between left aC/PrC and bilateral visual cortices showed a positive association with the total EF and cognitive flexibility score, whereas RS-FC between left aC/PrC and both bilateral IPL and right MTG revealed negative associations with the latter score. While larger RS-FC of PrC and visual areas seems to support cognitive flexibility, RS-FC of PrC and regions associated

with the DMN and DAN is linked to worse performance in cognitive flexibility tasks. Taking our previous findings into account, a similar RS-FC map was positively associated with age, which could be because of a dedifferentiation in activation patterns as proposed in the dedifferentiation theory of neural aging (Baltes & Lindenberger, 1997; Goh, 2011; Li & Sikström, 2002; Park et al., 2001; 2004) or compensatory activations as postulated in CRUNCH (Reuter-Lorenz & Cappell, 2008), and STAC (Park & Reuter-Lorenz, 2008). However, given the nature of the available data and the methods applied, we cannot draw firmer and more theory-specific conclusions.

Summing up, our findings suggest that left aC/PrC is specifically recruited by older (vs. younger) adults, possibly to compensate for difficulties in shifting their attentional focus. Conversely, our results indicate an age-related increase in relative aC/PrC deactivation during the control task and/or an age-related decrease in relative aC/PrC deactivation during the experimental task, rising an alternative hypothesis for the higher task-induced aC/PrC activation in older adults. Left aC/PrC's intrinsic coupling with the DMN and DAN supports its proposed role as a specialized hub, involved in internally as well as externally oriented information processing. The age-related decrease in RS-FC between aC/PrC and sensorimotor networks suggests some decoupling with age that is detrimental to action-related, externally oriented processing; the concurrent increase in RS-FC between DMN and DAN, in turn, suggests age-related difficulties in decoupling aC/PrC from the DMN during task states and from DAN-related regions during rest. Taking left aC/PrC's often reported covariation with left IFJ during rest into account which was not found in the current study, our findings might reflect (and possibly contribute to) a dedifferentiation in functional network patterns in older adults, potentially undermining the special role this region plays in shifting between internally and externally directed attention.

4.4. *Limitations and Outlook*

Although ALE is a well validated and widely used coordinate-based meta-analytic approach, it stands to reason that image-based meta-analyses may have provided greater sensitivity (Salimi-Khorshidi et al., 2009). However, as imaging data have previously been rarely shared, it would have been difficult to impossible to find a sufficient number of experiments with whole-brain images of effect estimates and standard errors.

Further, we were not able to conduct domain-specific meta-analyses for working memory and cognitive flexibility, since too few experiments were eligible for inclusion. More individual fMRI studies would be necessary to separately investigate the three EF subcomponents. The inclusion of more experiments would furthermore allow for testing a domain-specific account of EFs by directly contrasting the subcomponents with each other and testing additional or different EF subdivisions including even more fine-grained EF subprocesses. As previously discussed in the context of left IFJ and left aC/PrC, it seems that there is a process-specific sensitivity to aging. This process specificity may strongly contribute to the observed small to nonexistent across-experiment convergence of age differences in regional EF-related brain activity. In the context of inhibitory control, Korsch et al. (2014) found different age effects for different conflict tasks. In particular, there was overlap in brain activation during a flanker task between the two age groups and additional age-related activity in parietal and frontal regions. In contrast, during a stimulus–response compatibility task, no overlap in brain activation between the two groups was observed. Hence, age differences in EF-related brain activity appear to be task-specific to a substantial degree. This, in turn, would then lead to a heterogeneous distribution of age-related effects across studies, even within EF subdomains, which severely limits the chances for meta-analytic convergence and would argue for changing the focus of future research away from attempting to localize

common, (sub)domain-general activation differences between age groups toward identifying process-specific mechanisms of age-related activity modulations. As discussed earlier, another explanation could be age-related regional changes in grey-matter volume (i.e. atrophy). Thus, we recommend that future studies on this topic investigate (i) domains and even subdomains, (ii) compare age-related differences in EFs across different modalities, and (iii) incorporate computational cognitive modeling (Kriegeskorte & Douglas, 2018).

Additionally, due to the small number of studies that reported deactivations, we were only able to investigate activation effects. As our results indicate age-related difficulties in deactivating left aC/PrC in the context of EF-tasks, we call for future studies investigating both directions of task-induced brain activity changes.

Somewhat surprisingly, no significant correlations between the two seeds' whole-brain RS-FC patterns and the EF subcomponents working memory and inhibition were found. As there is ample evidence for RS-FC correlations with EF abilities in the literature (e.g., Hampson et al., 2006; Markett et al., 2013), a possible explanation could be that the tests used to assess EF domain-related abilities (via compound scores) were not sufficiently representative of the rather broad EF subdomains to yield a valid assessment of individual abilities or, the breadth of the subdomains prevented the scores from sufficiently reflecting particular subprocesses and age modulations thereof. The latter notion is supported by the fact that age correlated only moderately with the combined EF score ($r = -.44, p < .001$), the cognitive flexibility score ($r = -.41, p < .001$), and the inhibitory control score ($r = -.31, p < .001$). It did only weakly correlate with the working memory score ($r = -.15, p < .05$). For future studies on these questions it may be beneficial to incorporate various psychometric assessments of a particular cognitive function, which would allow isolating

function- and test- specific variance in order to elucidate brain–behavior relationships (and their changes across the lifespan) at a more commensurate level of “granularity”.

Comparing our results to those of earlier neuroimaging meta-analyses of age-related differences in EFs underlines the importance of (i) transparently reporting the analysis choices made, (ii) providing a detailed description of inclusion and exclusion criteria and their motivation, and (iii) precisely reporting the papers and contrasts included as well as whether further information was received from the authors of the original study (for guidelines see Müller et al., 2018). Otherwise, even meta-analyses lack comparability and reproducibility.

4.5. *Conclusion*

The current study suggests that left IFJ and left aC/PrC play an important role in age-related differences in EFs as they were found the only two brain regions that showed consistent age differences in their recruitment during EF tasks across three major domains (working memory, inhibitory control, and cognitive flexibility). Although RS-FC analyses point towards a domain-general role of left IFJ in EFs, the pattern of contributions to the meta-analytic results also suggests process-specific modulations by age. In particular, older adults appear to rely more on left IFJ in the context of cognitive flexibility and inhibition, whereas younger adults recruited it more strongly in the context of working memory. Our findings further indicate that left aC/PrC is specifically recruited by older adults during EF tasks, potentially reflecting inefficiencies in switching the attentional focus. Overall, our results question earlier meta-analytic findings that suggested different and more comprehensive sets of brain regions as showing consistent age modulations of their EF-related activity. Rather, our findings attest to the substantial heterogeneity of such age-related differences and call for research that pays more attention to replicability and focuses on

more narrowly and precisely defined EF subprocesses by combining multiple behavioral assessments, computational cognitive modelling, and multi-modal imaging.

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9. Appendix

Table A1

Overview of All Studies Included in the Meta-Analysis of Within-Group Contrasts Comprising Information About the Mean Age, Number of Activation Foci for Each Age Group, Masking with Task-Positive Effect, and Correction

Study #	First author	Year	n	Age Young ^a	Foci Young	Page #	Age Old ^a	Foci Old	Page #	Task	Masking	Correction
Working Memory												
1	Anguera	2011	16	21.1 (2.5)	-	-	71.4 (4.2)	13	p. 19 table 3	Spatial WM	masked	uncorrected
2	Bäckman	2011	20	25.2 (22-30)	4	p. 1852, text 3.3	70.3 (65-75)	-	-	Spatial Delayed Matching	unmasked	uncorrected
3	Emery ^b	2008	10	21.9 (2.6)	5	p. 1582 table 1	71.2 (6.2)	11	p. 1582 table 1	Letter-Number Sequencing	unmasked	corrected
4	Grady	1998	13	25 (3)	8	p. 413, table 2	66 (4)	12	p. 413, table 2	Delayed Match-to-sample	unmasked	uncorrected
5	Haut	2005	8	23.3 (1.6)	6	p. 222, table 3	67.3 (10.4)	5	p. 222, table 3	Number-Letter Sequencing	unmasked	uncorrected
6	Madden	1999	12	23.17 (2.86)	5	p. 126, table 2	71 (4.67)	13	p. 126, table 2	Recognition Memory	unmasked	uncorrected
7	Oren	2017	22	29 (3.7)	10	p. 96, table 2	71.8 (4.6)	4	p. 96, table 2	n-back	unmasked	corrected
8	Piefke	2012	14	23.6 (3.3)	18	p. 1291 table 3b, p. 1293 table 4b	65.1 (6.3)	26	p. 1291 table 3b, p. 1293 table 4b	n-back, Delayed Match to Sample	unmasked	uncorrected
9	Raye	2008	14	20 (18-26)	2	p. 857 table 1D	75 (70-83)	2	p. 857 table 1E	Refreshing	unmasked	uncorrected

10	Smith	2001	12	22.9 (18-29)	2	p. 2098, table 1c	66.6 (65-72)	3	p. 2099, table 2c	Operation Span	unmasked	corrected
11	Vellage	2016	38	25.7 (21-32)	8	p. 7 table 2	65.8 (58-74)	18	p. 7 table 2	Filter and Storage	unmasked	uncorrected
Inhibition												
1	Ansado	2012	16	23.31 (3.42)	24	p. 17, table 2 and 3, p. 18, table 4	67.82 (3.21)	22	p. 17, table 2 and 3, p. 18, table 4	Letter-name matching	unmasked	uncorrected
2	Chee	2006	17	21 (20-24)	4	p. 500, table 2	67 (60-75)	-	-	Object Processing	unmasked	uncorrected
3	Colcombe	2005	20	23.5 (19-28)	2	p. 369, table 3	67.5 (52-87)	3	p. 369, table 3	Flanker Task	masked	corrected
4	Huang ^b	2012	15	25.53 (3.48)	31	-	66.07 (4.15)	27	-	Stroop like	unmasked	uncorrected
5	Korsch	2014	19	22.95 (2.72)	9	p. 5, table 2	70.26 (3.49)	15	p. 5, table 2	Mixed Flanker-Stimulus-Response-Conflict	masked	uncorrected
6	Lamar	2004	16	27.9 (5.6)	9	p. 1371, table 3	69.1 (5.6)	14	p. 1372, table 4	Delayed Non-match to Sample	unmasked	uncorrected
7	Lee	2006	9	29.8 (6.2)	-	-	65.2 (4.2)	9	p. 174, table 2	Response Regulation	unmasked	uncorrected
8	Madden	2002	7	23 (2.13)	12	p. 30, table 2	66.5 (4.96)	19	p. 30, table 2	Visual Search	masked	corrected
9	Milham	2002	10	23	7	p. 10, table 2	68	10	p. 11, table 3	Stroop	unmasked	uncorrected
10	O'Connell ^b	2012	14	22 (3.3)	5	-	70.6 (4.2)	20	-	Oddball	unmasked	corrected
11	Townsend	2006a	10	27.9 (18-41)	-	-	70.7 (65-89)	4	p. 8/9 text	Sustained Attention	masked	corrected
12	Zhu	2010	22	20 (17-23)	8	p. 18, table 2	74 (68-80)	9	p. 18, table 2	Flanker Task	unmasked	corrected

Cogni- tive Flex- ibility												
1	Anderson	2000	12	24.4 (3.0)	5	p. 783, table 5	68.5 (4.0)	5	p. 783, table 5	Divided Attention	unmasked	uncorrected
2	Chmielewski	2014	14	24.37 (2.89)	16	p.5, table 2	60.51 (3.34)	33	p. 5, table 2	Dual-Tasking	unmasked	uncorrected
3	DiGirolamo	2001	8	25 (20- 30)	17	p. 2069, ta- ble 2	69 (63-75)	22	p. 2069, table 2	Task Switching	unmasked	uncorrected
4	Eich	2016	62	25.82 (20-30)	2	p. 217, table 1	64.84 (60-70)	3	p. 217, table 1	Task Switching	unmasked	uncorrected
5	Kuptsova ^b	2016	19	20-30	11	-	51-65	4	-	Task Switching	unmasked	corrected
6	Madden	1997	12	24.33 (2.01)	9	p. 400, table 2	65.5 (5.2)	13	p. 400, table 2	Visual Search	unmasked	uncorrected
7	Meinzer	2009	16	26.1 (3.7)	10	p. 20, table 2	69.3 (5.6)	10	p. 20, table 2	Verbal Fluency	unmasked	corrected
8	Townsend	2006b	10	27.9 (18-41)	15	p. 17, table 1	70.7 (65-89)	3	p. 17, table 1	Attention Shifting	masked	corrected
9	Van Impe	2011	20	25.2 (3)	-	-	68 (4.19)	19	p. 2405 table 5	Dual-Tasking	unmasked	corrected

Note. # = number, n = number of subjects for the smaller group, which is used in ALE to model the Gaussian kernel.

^aAge in mean and standard deviation as retrieved from the original study. ^bFurther material was derived from the author of the original study.

Table A2

Overview of All Studies Included in the Meta-Analyses of Between-Group Contrasts Comprising Information About the Mean Age, Number of Activation Foci for Each Age Group, Masking with Task-Positive Effect, and Correction

Study #	First author	Year	n	Age Young ^a	Foci Y>O	Page #	Age Old ^a	Foci O>Y	Page #	Task	Masking	Correction
Working Memory												
1	Anguera	2011	16	21.1 (2.5)	1	p. 20 table 5	71.4 (4.2)	10	p. 20 table 5	Spatial WM	masked	uncorrected
2	Bäckman	2011	20	25.2 (22-30)	3	p. 1852 text 3.3	70.3 (65-75)	4	p. 1852 text 3.3	Spatial De- layed Matching	unmasked	uncorrected
3	Bennett	2013	20	21.8 (2.5)	1	supplementary table 3	65.3 (5.3)	3	supplementary table 2	Delayed Item Recognition	masked	corrected
4	Emery ^b	2008	10	21.9 (2.6)	-	-	71.2 (6.2)	37	supplementary table 1	Letter-Number Sequencing	unmasked	corrected
5	Fakhri	2012	16	21 (3.7)	5	p. 358 table 3	68 (7.9)	5	p. 358 table 3	Probe Recogni- tion	unmasked	corrected
6	Grady	1998	13	25 (3)	4	p. 413 table 2, p. 418 figure 4C, p. 419 table 4	66 (4)	2	p. 413 table 2, p. 418 figure 5C	Delayed Match-to-sam- ple	unmasked	uncorrected
7	Grady	2007	16	26.1 (3.7)	-	-	65.8 (4.5)	8	p. 196 table 4	N-back	unmasked	uncorrected
8	Haut	2005	8	23.3 (1.6)	1	p. 222 table 4	67.3 (10.4)	-	-	Number-Letter Sequencing	unmasked	uncorrected
9	Kurth	2016	20	23.4 (8.7)	2	p. 89 table 4	74.4 (5.6)	10	p. 89 table 4, p. 90 table 5	Probe Recogni- tion	unmasked	corrected
10	Lamar	2004a	16	27.9 (5.6)	13	p. 1372 table 5	69.1 (5.6)	4	p. 1372 table 5	Delayed Match-to-sam- ple	unmasked	uncorrected

11	LeCouvey	2015	34	46.79 (18.82)	3	p. 7 table 4A	46.79 (18.82)	-	-	Binding Task	masked	uncorrected
12	Paxton ^b	2007a	20	22.8 (3.7)	9	p. 34 table 2, supplementary table 2b	73 (5.7)	22	p. 34 table 2, supplementary table 2b	AX-CPT	unmasked	uncorrected
13	Podell	2012	11	< 35	16	supplementary table 2	> 65	-	-	Updating WM	masked	corrected
14	Prakash	2012	25	23.4 (3.3)	4	p. 195 table 2	72.16 (4.6)	-	-	N-back	masked	corrected
15	Raye	2008	14	20 (18- 26)	2	p. 857 table 1D	75 (70- 83)	2	p. 857 table 1E	Refreshing	unmasked	uncorrected
Inhibition												
1	Ansado	2012	16	23.31 (3.42)	4	p. 17 table 3 and 4	67.82 (3.21)	9	p. 17 table 2 and 3	Letter-name matching	unmasked	uncorrected
2	Bloemen- daal	2016	23	22.7 (0.6)	2	supplementary figure 7	67.6 (0.7)	9	supplementary table 5	Load Depend- ent Stop-signal Anticipation	unmasked	uncorrected
3	Dørum	2016	21	24.42 (5.06)	6	p. 7 table 2	64.67 (7.44)	-	-	Multiple Ob- ject Tracking	unmasked	corrected
4	Eich	2016a	62	25.82 (20-30)	-	-	64.84 (60-70)	6	p. 218 table 3, p. 219 table 4	Task switching with go/no-go component	unmasked	uncorrected
5	Grady	2010	10	25 (3)	10	p. 173 table 3	66 (4)	18	p. 173 table 3	Face Discrimi- nation	unmasked	uncorrected
6	Huang	2012	15	25.53 (3.48)	-	-	66.07 (4.15)	16	p. 26 table 4	Stroop like	unmasked	uncorrected
7	Korsch	2014	19	22.95 (2.72)	1	p. 7 table 3	70.26 (3.49)	3	p. 7 table 3	Mixed Flanker- Stimulus-Re- sponse-Con- flict	masked	uncorrected

8	Lamar	2004 b	16	27.9 (5.6)	6	p. 1372 table 5	69.1 (5.6)	8	p. 1372 table 5	Delayed Non- match to Sam- ple	unmasked	uncorrected
9	Langeneck er	2004	13	26.3 (5.5)	-	-	71.1 (5.4)	22	p. 196 table 4 and 5	Stroop	unmasked	corrected
10	Lee	2006	9	29.8 (6.2)	-	-	65.2 (4.2)	3	p. 174 table 2	Response Reg- ulation	unmasked	uncorrected
11	Madden	2002	7	23 (2.13)	5	p. 30 table 2	66.5 (4.96)	-	-	Visual Search	masked	corrected
12	Milham	2002	10	23	6	p. 10 table 2	68	4	p. 11 table 3	Stroop	unmasked	uncorrected
13	O'Connell	2012	14	22 (3.3)	-	-	70.6 (4.2)	2	p. 9 table 4	Oddball	unmasked	corrected
14	Paxton ^b	2007 b	16	21.56 (3.14)	1	supplemen- tary table 5b	72.38 (6.51)	29	p. 36 table 3, supplementary table 5b	AX-CPT	unmasked	uncorrected
15	Persson ^b	2007	28	21.7 (2.5)	-	-	68.1 (5.8)	4	received from author	Verb Genera- tion	masked	corrected
16	Schulte	2011	14	23.6 (19-30)	9	p. 2083 table 2, p. 2084 ta- ble 3	71 (58- 85)	16	p. 2083 table 2, p. 2084 ta- ble 3	Stroop Match- to-sample	unmasked	uncorrected
17	Sebastian	2013	49	39.96 (17.14)	8	p. 2188 table 3	39.96 (17.14)	12	p. 2188 table 3		masked	corrected
18	Townsend	2006a	10	27.9 (18-41)	-	-	70.7 (65-89)	4	p. 9 text	Sustained At- tention	masked	corrected
19	Zysset	2007	23	26.6 (3.6)	-	-	57.1 (6.49)	7	p. 941 table 2	Stroop	unmasked	uncorrected
Cognitive Flexibil- ity												
1	Chmielew- ski	2014	14	24.37 (2.89)	-	-	60.51 (3.34)	2	p. 193 text	Dual-Tasking	unmasked	uncorrected

2	Eich	2016 b	62	25.82 (20-30)	7	p. 217 table 1	64.84 (60-70)	21	p. 217 table 1	Task Switching	unmasked	uncorrected
3	Fernandes	2006	11	26.33 (3.36)	2	p. 2459 table 5	71.18 (4.07)	8	p. 2459 table 5	Divided Atten- tion	masked	uncorrected
4	Hubert	2009	12	22.4 (2.5)	-	-	65 (4.5)	6	p. 15 table 5	Task of To- ronto	masked	uncorrected
5	Kunimi	2016	20	23.85 (5.43)	-	-	67.35 (4.27)	22	p. 23 table 2	Task Switching	unmasked	corrected
6	Kuptsova	2016	19	20-30	-	-	51-65	29	p. 367 table 3	Task Switching	unmasked	corrected
7	Madden	1997	12	24.33 (2.01)	5	p. 400 and 401 table 2	65.5 (5.2)	5	p. 400 and 401 table 2	Visual Search	unmasked	uncorrected
8	Madden	2010	20	22.4 (2.5)	1	p. 36 table 3	69.6 (6.05)	17	p. 36 table 3	Task Switching	masked	uncorrected
9	Meinzer	2009	16	26.1 (3.7)	-	-	69.3 (5.6)	5	p. 8 text	Verbal Fluency	unmasked	corrected
10	Steffener ^b	2016	63	25.79 (2.7)	-	-	65.47 (2.89)	13	received from author	Task Switching	masked	uncorrected
11	Townsend	2006 b	10	27.9 (18-41)	3	p. 18 table 2	70.7 (65-89)	20	p. 18 table 2	Attention Shifting	masked	corrected
12	Van Impe	201 1	20	25.2 (3)	-	-	68 (4.19)	19	p. 2405 table 5	Dual-Tasking	unmasked	corrected
13	Zhu	201 6	28	32 (3.8)	-	-	68.4 (5.4)	18	p. 141 table 3	Task Switching	unmasked	corrected
14	Worthy	201 6	18	23.61 (18-31)	6	p. 18 table 2	67 (61- 79)	-	-	Decision Mak- ing	unmasked	corrected
Mis- callene- ous												
1	Esposito	199 9	41	45.5 (19.7)	13	p. 969 table 1, p.970 table 2	45.5 (19.7)	11	p. 969 table 1, p.970 table 2	WCST, RPM	unmasked	uncorrected

Note. # = number, n = number of subjects for the smaller group, which is used in ALE to model the uncertainty of coordinates, Y>O = young > old, O>Y = old > young.

^aAge in mean and standard deviation as retrieved from the original study. ^bFurther material was obtained from the authors of the original study.

Table A3

Checklist for Neuroimaging Meta-Analyses by Müller et al. (2018)

The research question was specifically defined	YES, and it included the following contrasts: 1) Within-group contrasts for young 2) Within-group contrasts for old 3) Between-group contrasts young > old 4) Between-group contrasts for old > young The specific contrasts are reports in Tables 1 and 2
The literature search was systematic	YES, it included the following keywords in the following databases: 1) (1) title: “age” or “aging” or “ageing” or “age-related” or “older adults” or “old adults” or “life-span” or “elderly adults”; and (2) title: “executive functions” or “working memory” or “inhibition” or “cognitive flexibility”; and (3) abstract: “fMRI” or “functional magnetic resonance imaging” or “PET” or “positron emission tomography” or “neuroimaging” or “cerebral blood flow” 2) For working memory “n-back” or “sternberg” or “delayed match to sample” or “delayed simple matching” or “stimulus-response-compatibility”; for inhibition “stroop” or “flanker” or “simon” or “stop signal” or “go/no-go” or “stimulus detection” or “stimulus discrimination” or “selective attention”; for cognitive flexibility “task switching” or “dual task” or “set shifting” 3) Databases: Web of Science (http://apps.webofknowledge.com), PubMed (https://www.ncbi.nlm.nih.gov/pubmed/), PsycINFO (http://ovidsp.tx.ovid.com), and Google Scholar (http://scholar.google.de)
Detailed inclusion and exclusion criteria were applied	YES, and reasons of non-standard criteria were: Inclusion of:

	- fMRI and PET studies - Healthy young and old participants without any pharmacological manipulations - Masking of the between-group contrast with task-positive effect - Activation data - For meta-analysis of within-group contrast: main task effect per group - For meta-analysis of between-group contrast: group comparison, positive correlation with age (old > young), negative correlation with age (young > old) - No correlation or interaction with other variables (e.g., RT) - Task > sensorimotor control, task > resting-baseline, task difficult > task easy - The difficult task condition was included, if contrasts representing easy and difficult conditions were available - The contrast reflecting transient brain activity was included when contrasts for sustained and transient activity were available
Sample overlap was taken into account	YES, using the following method: - Contribution from a study was limited to one experiment per study - If a study reported several experiments eligible for inclusion, the reported coordinates were pooled to constitute a single experiment
All experiments used the same search coverage (state how brain coverage was assessed and how small volume corrections and conjunctions were taken into account)	YES, the search coverage was the following: - Only whole-brain coverage - Exclusion of ROI studies - Inclusion of masking of the between-group contrast with task-positive effect
Studies are converted to a common reference space	YES, using the following conversion(s): - Coordinates reported in Talairach space were converted to MNI space (Lancaster et al., 2007).

Data extraction was conducted by two investigators (ideal case) or double-checked by the same investigator (state how double-checking was performed)	YES, the following authors: - Marisa Heckner, Edna Cieslik, and Robert Langner checked inclusion criteria - Marisa Heckner extracted coordinates - Marisa Heckner extracted other info: Number and age of subjects included, task, contrast, space, modality, masking of between-group contrast with task-positive effect, level of performance between age groups, correction of results - Edna Cieslik double-checked the following data: Coordinates extracted, number and age of subjects included, task, contrast, space, modality, masking of between-group contrast with task-positive effect, level of performance between age groups, correction of results
The paper includes a table with at least the references, basic study description (e.g., for fMRI tasks, stimuli), contrasts and basic sample descriptions (e.g., size, mean age and gender distribution, specific characteristics) of the included studies, source of information (e.g., contact with authors), reference space	YES, and also the following data: - If further information was received by the authors - How coordinates were treated (MNI or Talairach) when space was not clearly specified in original study - If the between-group contrast was masked with the task-positive effect - If results were corrected for multiple comparisons - Level of performance between age groups
The study protocol and all analyses was planned beforehand, including the methods and parameters used for inference, correction for multiple testing, etc.	YES: 1) No non-planned or post-hoc analyses. 2) The meta-analysis used the default methods and parameters of our group.
The paper includes meta-analytic diagnostics	Contributions from individual experiments to each cluster of significant convergence were provided for each meta-analysis performed.

Table A4

Single Experiments Contributing to the Clusters of Convergence

Analysis	Studies	Contribution in %
Executive Functions		
<i>within-group</i>		
across age		
L occipital FG	Emery 2008	2.40
	Grady 1998	10.24
	Madden 2002	12.63
	Ansado 2012	0.11
	Madden 1997	5.77
	Townsend 2006	12.62
	Van Impe 2011	0.17
	Korsch 2014	7.26
	Madden 1999	1.40
	Smith 2001	12.81
	Zhu 2010	12.42
	DiGirolamo 2001	8.96
	Chee 2006	5.83
	Huang 2012	0.31
	Kuptsova 2016	7.06
L Ins	Grady 1998	8.95
	Madden 2002	11.84
	Ansado 2012	13.77
	Townsend 2006	2.11
	Madden 1999	10.27
	Oren 2017	11.38
	DiGirolamo 2001	6.88
	Anderson 2000	0.15
	Lee 2006	4.26
	Anguera 2011	6.76
	Huang 2012	9.13
	O'Connell 2012	14.49
R frontal pole	Emery 2008	6.48
	Milham 2002	10.69
	Grady 1998	0.16
	Madden 2002	10.17
	Van Impe 2011	7.14
	Chmielewski 2014	0.51
	Oren 2017	11.84
	Haut 2005	0.99
	Lamar 2004	15.66
	Anguera 2011	9.60
	Huang 2012	13.39
	Kuptsova 2016	13.22
L IFJ	Emery 2008	7.26

	Milham 2002	4.53
	Grady 1998	6.19
	Ansado 2012	0.08
	Madden 1997	9.13
	Townsend 2006a	2.20
	Townsend 2006b	4.43
	Chmielewski 2014	3.98
	Smith 2001	2.07
	Oren 2017	2.10
	DiGirolamo 2001	6.25
	Bäckman 2011	1.21
	Piefke 2012	7.66
	Anguera 2011	8.26
	Meinzer 2009	8.34
	Huang 2012	11.72
	Kuptsova 2016	7.48
	Colcombe 2005	7.09
L pre-SMA	Milham 2002	4.66
	Madden 2002	3.45
	Ansado 2012	12.54
	Madden 1997	9.64
	Korsch 2014	8.72
	Madden 1999	4.19
	DiGirolamo 2001	11.33
	Lee 2006	0.11
	Piefke 2012	7.20
	Meinzer 2009	11.28
	Huang 2012	16.81
	Kuptsova 2016	7.87
	Colcombe 2005	2.19
L IPS/lateral occipital cortex	Grady 1998	3.40
	Madden 2002	11.20
	Ansado 2012	8.15
	Madden 1997	9.77
	Townsend 2006b	2.78
	Van Impe 2011	6.10
	Korsch 2014	8.16
	Madden 1999	0.36
	Smith 2001	5.94
	Oren 2017	0.23
	DiGirolamo 2001	5.98
	Haut 2005	1.28
	Piefke 2012	9.52
	Anguera 2011	3.11
	Meinzer 2009	8.64
	Huang 2012	8.35
	Kuptsova 2016	6.93
<i>between-group</i>		
pooled		

L aC/PrC	Emery 2008	0.63
	Paxton 2007b	10.36
	Anguera 2011	8.87
	Zysset 2007	4.39
	Fakhri 2012	7.81
	Kunimi 2016	5.35
	Madden 2010	8.00
	Lamar 2004b	14.05
	Lamar 2004a	0.46
	Schulte 2011	7.53
	Eich 2016b	8.11
	Eich 2016a	2.92
	Kuptsova 2016	10.99
	Bäckman 2011	7.12
	Grady 2010	2.65
	Esposito 1999	0.71
L IFJ	Emery 2008	7.43
	Milham 2002	14.73
	Zysset 2007	4.48
	Grady 1998	0.95
	Madden 1997	6.77
	Townsend 2006b	7.08
	Fernandes 2006	0.33
	Prakash 2012	19.03
	Madden 2010	0.16
	Langenecker 2004	1.41
	Korsch 2014	7.61
	Zhu 2015	13.46
	Kuptsova 2016	10.61
	Podell 2012	4.63
	Bäckman 2011	0.87
	Grady 2010	0.28
	Esposito 1999	0.11
old > young		
L aC/PrC	Emery 2008	1.08
	Paxton 2007b	10.80
	Anguera 2011	10.05
	Zysset 2007	5.27
	Kunimi 2016	6.95
	Madden 2010	6.74
	Lamar 2004b	14.43
	Schulte 2011	8.24
	Eich 2016b	10.86
	Eich 2016a	3.22
	Kuptsova 2016	10.33
	Bäckman 2011	7.65
	Grady 2010	3.58
	Esposito 1999	0.78

Table A5

Brain Regions Showing Significant Convergence of Activity in Inhibition

ALE-Analysis	Cluster	Voxel	MNI Coordinates			$Z_{\max}$	Cytoarchitecture (Overlap in %)
			x	y	z		
pooled	L aC/PrC	113	-16	-70	12	4.35	Area hOc6 (V6; 72.1)
							Area hOc3d (V3d; 13.8)
							Area hOc2 (V2; 3.5)
							Area hOc1 (V1; 1.3)
			-6	-66	10	3.92	Area hOc1 (V1; 35.7)
old > young	L aC/PrC	138					Area hOc2 (V2; 18.9)
			-16	-70	12	4.53	Area hOc6 (V6; 72.1)
							Area hOc3d (V3d; 13.8)
							Area hOc2 (V2; 3.5)
							Area hOc1 (V1; 1.3)
			-6	-66	10	4.1	Area hOc1 (V1; 35.7)
							Area hOc2 (V2; 18.9)

Note. L = left hemisphere, R = right hemisphere. $Z_{\max}$ = maximum z-score of the local maxima.

Table A6
Single Experiments Contributing to the Inhibition Cluster of Convergence

Analysis	Studies	Contribution in %
pooled		
L aC/PrC	Paxton 2007b	20.97
	Zysset 2007	18.65
	Lamar 2004b	30.08
	Schulte 2011	14.39
	Eich 2016a	15.90
old > young		
L aC/PrC	Paxton 2007b	21.83
	Zysset 2007	17.01
	Lamar 2004b	29.46
	Schulte 2011	16.32
	Eich 2016a	15.37

Table 1

Brain Regions Showing Significant Convergence of Activity in Executive Functions

ALE-Analysis	Cluster	Voxel	MNI Coordinates			Z _{max}	Cytoarchitecture (Overlap in %)
			x	y	z		
Executive Functions							
<i>Within-Group</i>							
Across Age	L IFJ	355	-46	8	28	5.15	Area 44 (46.6)
			-48	6	34	4.96	Area 44 (39.7)
	L pre-SMA	333	-4	20	46	4.74	Area 6mr/pre-SMA (1.2)
			-2	30	38	4.08	-
			6	26	36	3.75	-
			6	26	38	3.75	-
			-6	32	28	3.32	-
			-6	26	32	3.21	-
	L IPS	335	-26	-62	46	5.66	Area hIP3 (IPS; 32.5)
							Area hIP6(IPS; 3.9)
			-18	-70	46	4.50	Area hIP8 (IPS; 57.6)
							Area 7A (SPL; 38.5)
			-22	-64	58	3.99	Area 7A (SPL; 63.3)
	L FG	285					Area hIP3 (IPS; 10.5)
			-34	-84	-4	4.84	Area hOc41a (39.9]
							Area hOc4v (V4(v); 29.6)
							Area hOc41p (19.2)
							Area FG1 (10.6)
			-38	-72	-14	4.41	Area FG2 (52.9)
							Area FG1 (40.1)
							Area hOc4v (V4(v); 1.9)
							Area hOc41a (1.3)
							Area Id7 (97.2)
	L aIns	173	-34	22	2	4.30	-
	R frontal pole	137	44	38	28	4.28	-
<i>Between-Group</i>							
Pooled	L aC/PrC	198	-8	-66	12	4.45	Area hOc2 (V2; 7.7)
							Area hOc1 (V1; 5.9)
			-4	-58	30	3.76	-
			-6	-58	26	3.52	-
	L IFJ	119	-6	-56	26	3.52	-
			-44	18	28	4.15	Area 45 (3.9)
	L aC/PrC	225	-8	-66	10	4.61	Area hOc1 (V1; 34.8)
							Area hOc2 (V2; 12.5)
			-4	-58	30	3.97	-
			-6	-56	26	3.78	-

Note. L = left hemisphere, R = right hemisphere, $Z_{\max}$ = maximum z-score of the local maxima.

Table 2

RS-FC Analyses

Seed	Cluster	Voxel	MNI Coordinates			T	Cytoarchitecture (Overlap in %)
			x	y	z		
L IFJ	L IFJ/DLPFC	9071	-46	16	28	104.00	Area 44 (20.9)
							Area 45 (17.9)
			-50	10	32	48.90	Area 44 (40.8)
			-42	46	-4	40.10	-
			-46	42	2	39.60	Area 45 (2.4)
			-40	2	56	34.90	-
			-4	20	48	34.80	Area 6mr/preSMA (4.8)
			-4	30	42	34.70	-
			-42	4	54	34.70	-
			-44	6	52	34.50	-
			-30	22	-4	32.90	Id7 (11.9)
			-32	-60	42	36.20	Area hIP3 (IPS; 55.2)
	L IPS	8083					Area hIP1 (IPS; 23.1)
							Area hIP6 (IPS; 21.6)
			-44	-46	44	33.10	Area hIP2 (IPS; 44.0)
							Area hIP1 (IPS; 34.6)
							Area hIP3 (IPS; 18.6)
			-54	-56	-18	33.19	Area FG4 (14.3)
							Area FG2 (4.0)
			-60	-50	-12	30.60	-
			-24	-76	48	18.60	Area hIP8 (IPS; 35.8)
							Area hIP5 (IPS; 26.3)
							Area hPO1 (IPS; 12.5)
							Area 7A (SPL; 8.3)
			-22	-72	50	17.50	-
			-40	-50	56	16.60	Area hIP3 (IPS; 38.4)
							Area 7A (SPL; 23.7)
							Area 7PC (SPL; 21.5)
							Area PGa (IPL; 7.6)
							Area hIP2 (IPS; 7.0)
			-24	-70	56	16.50	Area hIP6 (IPS; 45.9)
							Area 7A (SPL; 40.4)
			-34	-40	-22	15.10	Area FG3 (61.3)
							Area FG4 (1.4)
			-46	-50	16	13.70	-
	R IFJ/DLPFC	3429	46	18	28	36.70	Area 45 (21.0)
			46	32	18	32.50	Area 45 (48.8)
			30	36	-14	17.60	Area Fo3 (24.5)
			34	38	-14	17.60	Area Fo3 (10.6)
			30	12	50	16.50	Area 6d3 (39.0)
			48	46	-14	15.30	-
			52	38	-14	14.70	-
			38	6	62	14.50	-
			50	8	48	13.70	-
			46	12	50	12.50	-
	R cerebellum	1477	12	-76	-28	34.50	-
			30	-72	-50	30.30	-

			28	-64	-32	28.80	-
R IPS	1439	34	-60	42	24.00	Area hIP6 (IPS; 39.1)	
						Area hIP3 (IPS; 2.0)	
		46	-38	42	16.30	Area hIP2 (IPS; 56.0)	
						Area hIP1 (IPS; 8.5)	
R FG	750	62	-48	-16	22.20	-	
		70	-36	-8	14.50	-	
		70	-22	4	12.10	Area TE 3 (65.1)	
R SMA/pre-SMA	303	4	26	46	20.40	-	
		4	32	44	19.80	-	
R aIns	129	30	24	-4	22.30	Area Id7 (3.1)	
L caudate	40	-12	10	6	19.70	-	
		-14	6	12	18.90	-	
L cerebellum	36	-10	-76	-30	19.40	-	
L cerebellum	33	-32	-70	-50	18.00	-	
L aCC	23	-4	4	28	24.90	Area 33 (18.4)	
R aCC	21	6	6	28	22.60	Area 33 (42.6)	
R S1	20	68	-8	22	12.50	Area 1 (15.0)	
						Area OP4 (PV; 12.3)	
						Area 3b (2.6)	
						Area PFop (IPL; 1.9)	
		66	-4	28	10.60	Area 1 (22.7)	
						Area 3b (2.0)	
L aC/PrC	L aC/PrC/pCC	29870	-6	-64	16	68.00	-
			-8	-60	12	67.20	-
			8	-58	14	56.40	-
			2	-66	24	50.70	-
			-24	-42	-12	35.50	Subiculum (10.7)
							CA1 (Hippocampus; 4.5)
			24	-38	-14	32.80	CA1 (Hippocampus; 5.9)
							Subiculum (5.2)
			-2	-58	42	32.30	-
			-44	-72	30	30.00	Area PGp (IPL; 58.9)
							Area PGa (IPL; 23.1)
			-18	-16	-26	28.50	CA1 (Hippocampus; 42.7)
							Subiculum (17.4)
							Entorhinal Cortex (13.2)
							DG (Hippocampus; 11.5)
							HATA Region (3.0)
			-20	-18	-24	28.40	CA1 (Hippocampus; 38.0)
							Subiculum (32.0)
							DG (Hippocampus; 22.5)
							Entorhinal Cortex (7.2)
L frontal pole	6434	-4	50	-14	32.60	Area Fp2 (46.3)	
							Area p32 (24.2)
		4	54	-14	31.90	Area Fp2 (56.3)	
		4	46	-16	31.30	Area p32 (21.4)	
							Area Fp2 (16.5)
							Area s32 (12.8)
		-2	10	-10	24.60	Area 25 (53.4)	
							Area 33 (46.6)
		4	24	-14	23.00	Area s24 (74.6)	
							Area s32 (25.1)
		-22	30	40	22.60	-	

		4	8	-12	21.60	Area 33 (29.7) Area 25 (27.7) BF (Ch 1-3; 4.1)
		-4	54	6	21.40	Area p32 (70.8) Area Fp2 (5.7)
		2	8	-8	21.20	Area 33 (46.8) Area 25 (13.8) BF (Ch 1-3; 12.3)
		6	58	8	21.10	Area p32 (51.8) Area Fp2 (44.0)
R TPJ	2392	58	-8	-22	24.20	-
		42	18	-36	18.00	-
		36	-22	16	17.60	Area OP2 (PIVC; 50.3) Area Ig1 (16.3) Area OP1 (SII; 16.1) Area OP3 (VS; 11.1) Area Ig2 (4.1)
		50	10	-34	15.30	-
		50	-20	8	14.20	Area TE 1.0 (21.4) Area OP1 (SII; 11.0) Area TE 1.1 (1.3)
		42	-32	16	11.60	Area PFcm (IPL; 41.1) Area OP1 (SII; 8.8) Area TE 1.1 (5.5)
		70	-18	4	8.93	Area TE 3 (69.9)
		70	-22	0	8.20	Area TE 3 (59.5)
L TPJ	2190	-62	-10	-18	25.30	-
		-38	16	-32	15.70	-
		-40	14	-40	15.50	-
		-36	20	-38	15.10	-
		-50	8	-34	13.50	-
R FEF	754	24	32	42	22.50	-
L pIns	719	-36	-20	18	17.50	Area OP2 (PIVC; 36.8) Area OP3 (VS; 31.2) Area Ig2 (3.7)
		-32	-24	12	17.10	Area Ig1 (52.2) Area OP2 (PIVC; 1.6)
		-42	-28	10	16.40	Area TE 1.1 (64.4) Area TE 1.0 (34.6)
R cerebellum	403	8	-52	-46	26.20	-
		2	-58	-46	26.10	-
R cerebellum	67	12	-84	-42	17.80	-
L IFG pars orbitalis	47	-28	12	-22	17.60	Area Fo3 (27.2)
L IFG pars orbitalis	44	-30	28	-18	13.90	Area Fo3 (79.9)
R IFG pars orbitalis	38	30	30	-16	14.60	Area Fo3 (37.3)
R IFG pars orbitalis	22	28	14	-22	15.60	Area Fo3 (16.8)
L cerebellum	21	-10	-84	-42	15.20	-

Note. L = left hemisphere, R = right hemisphere.

Table 3
Association of RS-FC and Age

	Cluster	Voxel	MNI Coordinates			T	Cytoarchitecture (Overlap in %)
			x	y	z		
L IFJ -	R IFJ/DLPFC	392	48	18	24	7.80	Area 45 (26.0)
							Area 44 (6.5)
			56	32	18	6.82	Area 45 (69.9)
			52	18	34	6.81	Area 45 (36.6)
							Area 44 (29.0)
			54	36	12	6.61	Area 45 (53.7)
			50	36	4	6.39	Area 45 (43.3)
			54	38	6	6.27	Area 45 (39.5)
			56	36	4	6.18	Area 45 (41.6)
			50	24	16	5.63	Area 45 (35.9)
	L IFJ/DLPFC	206					Area 44 (1.1)
			-52	16	28	9.53	Area 45 (39.7)
							Area 44 (36.4)
			-44	20	20	7.51	Area 44 (2.5)
							Area 45 (1.9)
			-54	26	24	6.39	Area 45 (59.4)
			-50	14	34	6.22	Area 44 (7.6)
	L TPJ	168	-54	-28	0	6.95	-
			-62	-30	4	6.68	-
			-52	-40	6	6.60	-
			-58	-42	10	6.49	-
			-32	24	-4	7.42	Area Id7 (43.5)
	L aIns	65	-36	24	-8	6.16	Area Id7 (9.5)
			-38	-44	-22	5.97	Area FG4 (56.3)
	L FG	33					Area FG3 (43.7)
			-46	-44	-20	5.85	Area FG4 (80.5)
			-40	-46	-20	5.75	Area FG4 (66.3)
							Area FG3 (33.3)
							Area 33 (42.6)
	R aCC	21	6	6	28	9.12	Area FG4 (29.3)
	R FG	20	50	-56	-18	5.84	Area FG2 (19.1)
	L aCC	18	-4	6	28	7.67	Area 33 (18.9)
	R STG	12	70	-24	4	5.80	Area TE 3 (64.4)
	L FEF	10	-32	8	36	5.67	-
L aC/PrC -	L aC/PrC	8267	-4	-64	4	10.60	Area hOc1 (V1; 55.0)
			-16	-68	10	9.63	Area hOc2 (V2; 52.0)
							Area hOc6 (V6; 52.0)
							Area hOc1 (V1; 4.7)
			8	-62	10	9.20	Area hOc1 (V1; 29.9)
							Area hOc2 (V2; 15.7)
			20	-44	-6	9.10	CA1 (Hippocampus; 1.3)
			-14	-44	-6	8.83	Subiculum (28.2)
			14	-46	-4	8.82	Subiculum (10.1)
			12	-68	16	8.79	hOc6 (3V6; 52.4)
							hOc2 (V2; 16.7)
							hOc1 (V1; 11.9)
							hOc3d (V3d; 2.9)

			-8	-78	2	8.70	Area hOc1 (V1; 52.5) Area hOc2 (V2; 44.2) Area hOc3v (V3v; 2.9)
			-6	-82	6	8.69	Area hOc1 (V1; 71.5)
			-20	-48	-6	8.69	-
L Heschl's gyrus	27		-44	-28	6	6.19	Area TE 1.1 (40.4) Area TE 1.0 (15.5)
L SPL	21		-12	-42	48	6.49	Area 5M (SPL; 32.8) Area 5Ci (SPL; 23.5)
L thalamus	12		-16	-30	-4	6.01	-
L S1	10		-20	-32	60	5.84	Area 4p (26.2) Area 4p (22.7) Area 4a (21.9)
L aC/PrC + L IPL	49		-48	-68	28	5.71	Area PGp (IPL; 34.3) Area PFm (IPL; 21.7) Area PGa (IPL; 17.4)
			-50	-64	24	5.65	Area PGp (IPL; 30.0) Area PFm (IPL; 28.6) Area PGa (IPL; 12.5)
L TPJ	21		-62	-22	-28	6.70	-
			-64	-30	-24	6.23	-
			-66	-32	-22	6.22	-
L PrC	10		-4	-56	30	5.87	-

Note. L = left hemisphere, R = right hemisphere, - negative association with age, + positive association with age.

Table 4

*Association of RS-FC and Combined Total Executive Functions and Cognitive Flexibility**Compound Scores*

	Cluster	Voxel	MNI Coordinates			T	Cytoarchitecture (Overlap in %)
			x	y	z		
<i>Executive Functions</i>							
L aC/PrC +	L aC/PrC	121	-8	-66	12	6.65	Area hOc2 (V2; 7.7)
							Area hOc1 (V1; 5.9)
			-18	-72	12	6.02	Area hOc6 (V6; 72.8)
							Area hOc1 (V1; 13.2)
						Area hOc2 (V2; 1.1)	
<i>Cognitive Flexibility</i>							
L aC/PrC -	R IPL	81	50	-68	22	6.37	Area PGp (IPL; 54.0)
							Area hOc4la (11.7)
			46	-70	30	5.86	Area PGp (IPL; 51.1)
							Area PGa (IPL; 4.5)
	L IPL	79	48	-72	32	5.77	Area hIP5 (IPS; 1.7)
			-36	-82	34	6.23	Area PGp (IPL; 69.6)
							Area hIP5 (IPS; 36.6)
							Area PGp (IPL; 26.6)
							Area PGa (IPL; 8.5)
							Area hIP4 (IPS; 5.0)
			-46	-80	28	5.92	Area PGp (IPL; 57.1)
							Area PGa (IPL; 12.0)
	R MTG	20	52	-12	-26	6.75	-
L aC/PrC +	L+R visual corti- ces	834	-10	-68	10	7.15	Area hOc2 (V2; 32.1)
							Area hOc1 (V1; 30.4)
			-2	-70	12	6.73	Area hOc1 (V1; 20.3)
							Area hOc2 (V2; 7.6)
			22	-64	2	6.72	Area hOc1 (V1; 74.8)
			2	-70	10	6.61	Area hOc1 (V1; 40.7)
							Area hOc2 (V2; 20.6)
			12	-70	8	5.93	Area hOc1 (V1; 69.8)
							Area hOc2 (V2; 19.7)
			-14	-70	-6	5.92	Area hOc3v (V3v; 53.4)
							Area hOc4v (V4(v); 24.0)
							Area hOc2 (V2; 22.6)
			-8	-68	-4	5.91	Area hOc2 (V2; 46.4)
				Area hOc3v (V3v; 31.3)			
				Area hOc4v (V4(v); 17.2)			
				Area hOc1 (V1; 5.0)			
-12	-68	-4	5.91	Area hOc3v (V3v; 43.0)			
				Area hOc2 (V2; 41.2)			
				Area hOc4v (V4(v); 14.6)			
				Area hOc1 (V1; 1.1)			

-8	-76	-12	5.81	Area hOc3v (V3v; 10.7) Area hOc4v (V4(v); 2.5)
-6	-78	-10	5.76	Area hOc3v (V3v; 35.8) Area hOc1 (V1; 32.0) Area hOc4v (V4(v); 1.8) Area hOc2 (V2; 1.2)

Note. L = left hemisphere, R = right hemisphere, - negative association with age, + positive association with age.

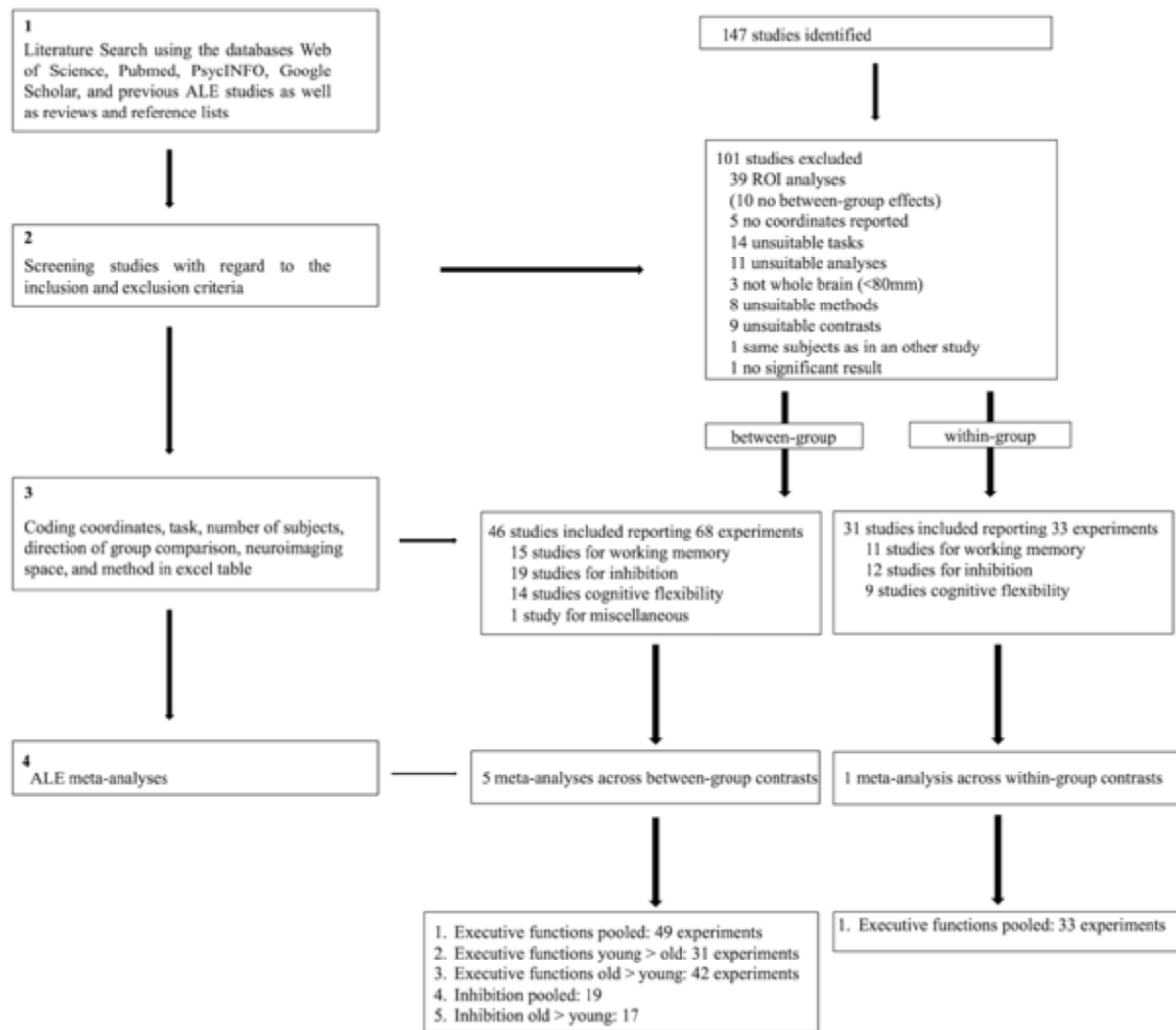


Figure 1. Flowchart of the meta-analysis steps conducted.

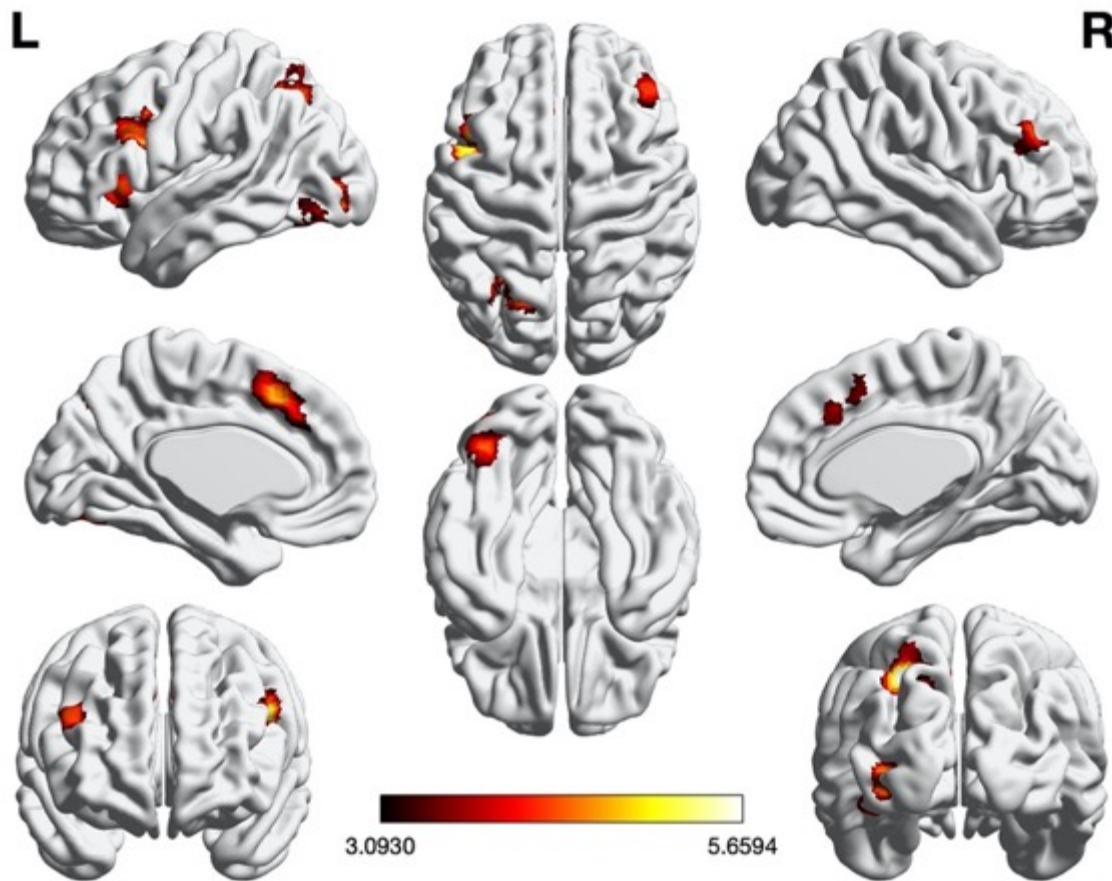


Figure 2. Foci of brain activity showing significant convergence of activity for EFs across age (cluster-level $p < .05$, family-wise error-corrected for multiple comparisons, cluster-forming threshold at voxel level: $p < .001$). The scale bar reflects the maximum z-score of the local maxima.

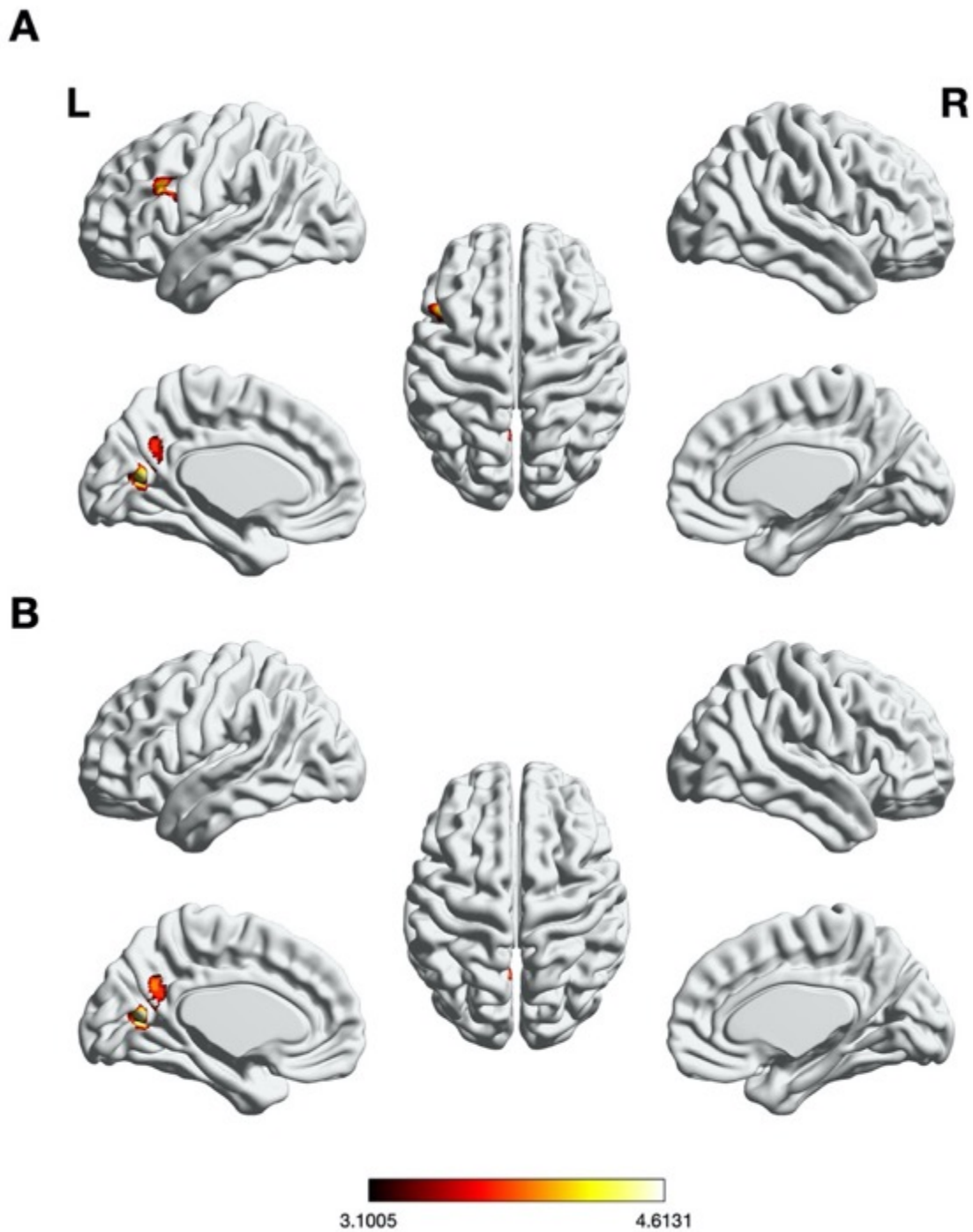


Figure 3. Foci of brain activity showing significant convergence of activity for (A) EFs pooled, (B) EFs old > young (cluster-level $p < .05$, family-wise error-corrected for multiple comparisons, cluster-forming threshold at voxel level: $p < .001$). The scale bar reflects the maximum z-score of the local maxima.

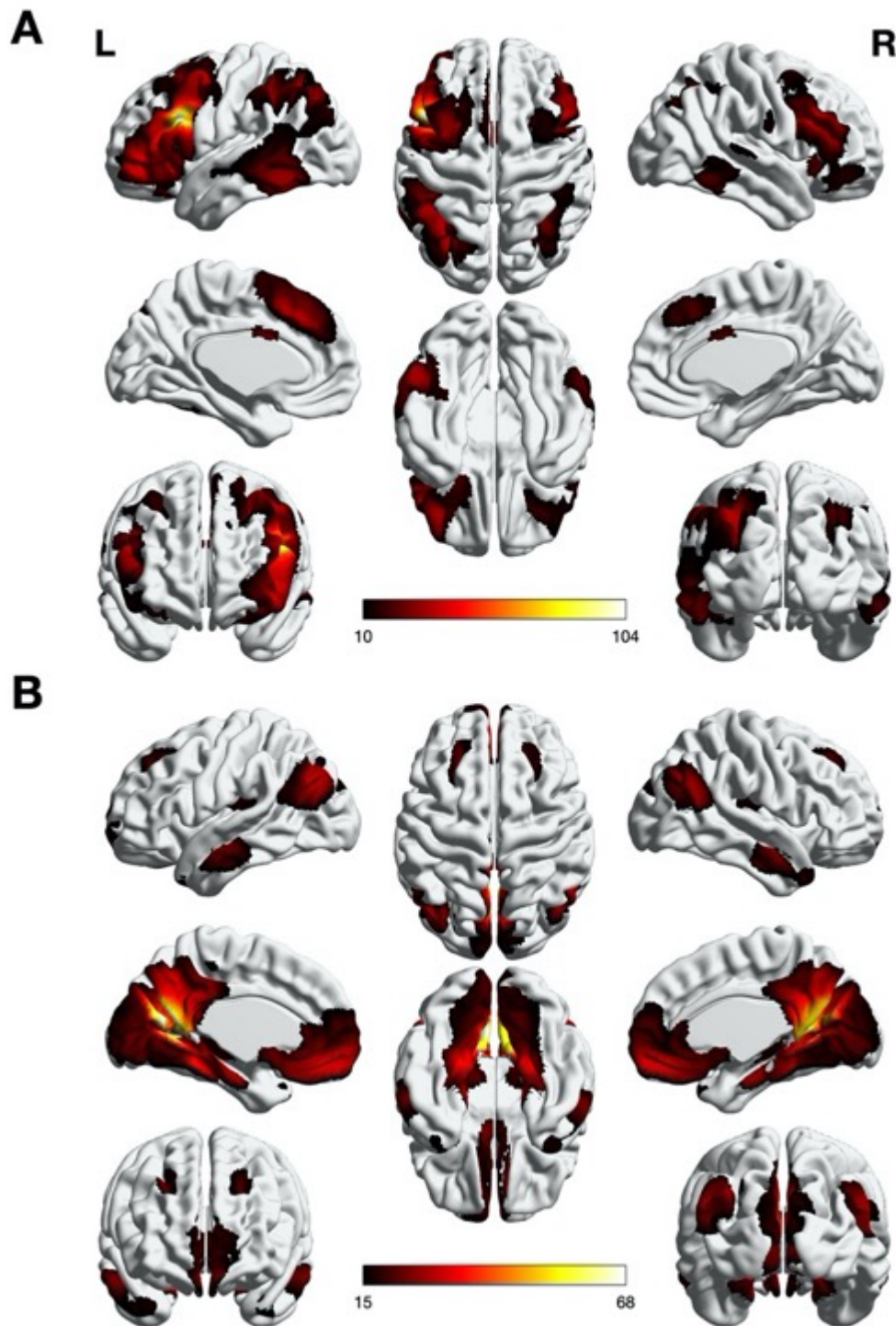


Figure 4. Whole-brain RS-FC analyses of (A) left IFJ and (B) left aC/PrC (voxel-level family-wise error corrected threshold of one-sided $p < .05$, extent threshold = 20, masked with the subjects' mean Z-scores $\geq .1$). The scale bar reflects t-scores.

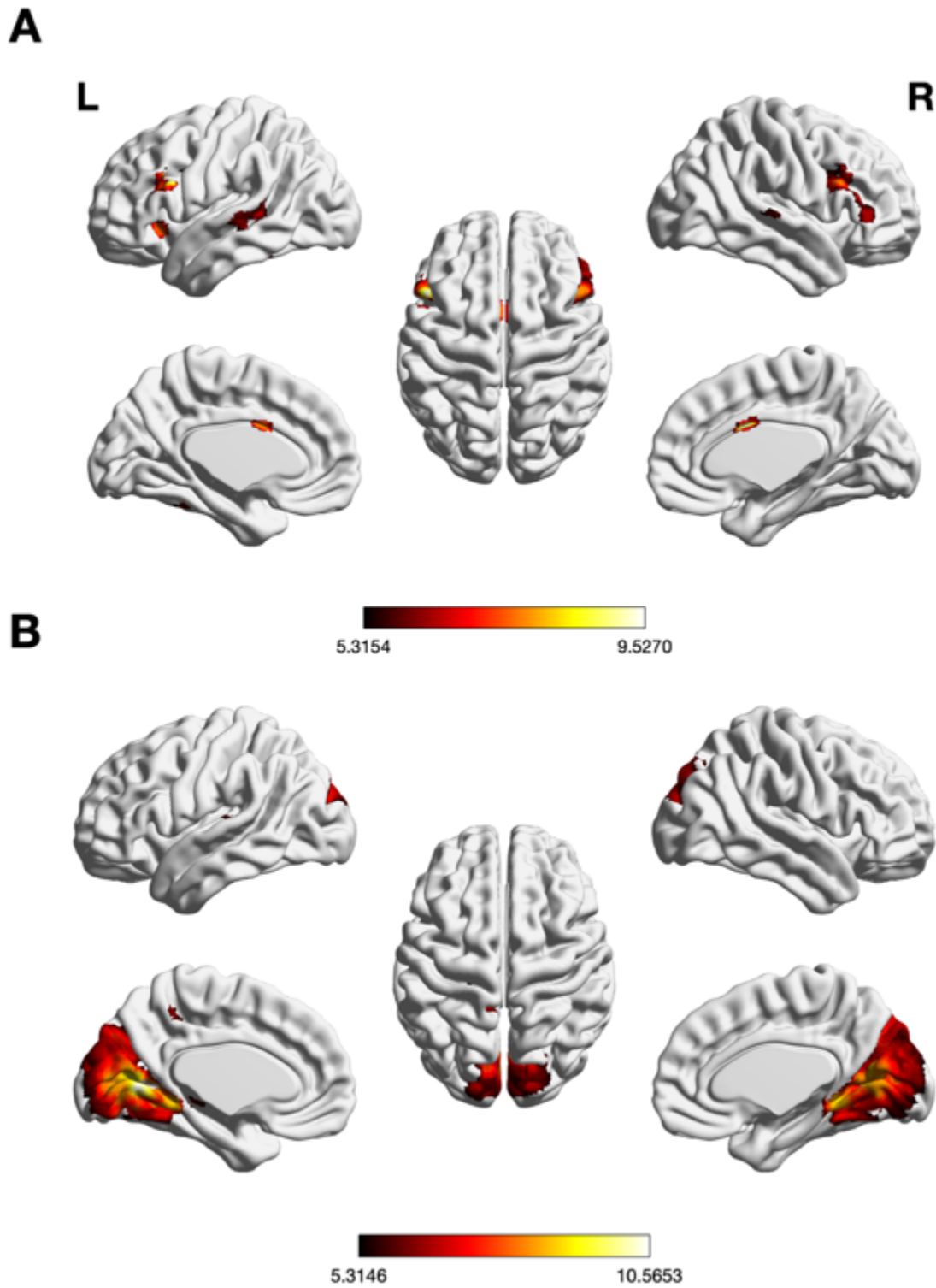


Figure 5. Significant negative association between whole-brain RS-FC of (A) left IFJ and age and (B) aC/PrC and age, (voxel-level family-wise error-corrected threshold of two-sided $p < .00625$, extent threshold = 10, masked with RS-FC map of left IFJ and aC/PrC, respectively). The scale bar reflects t-scores.

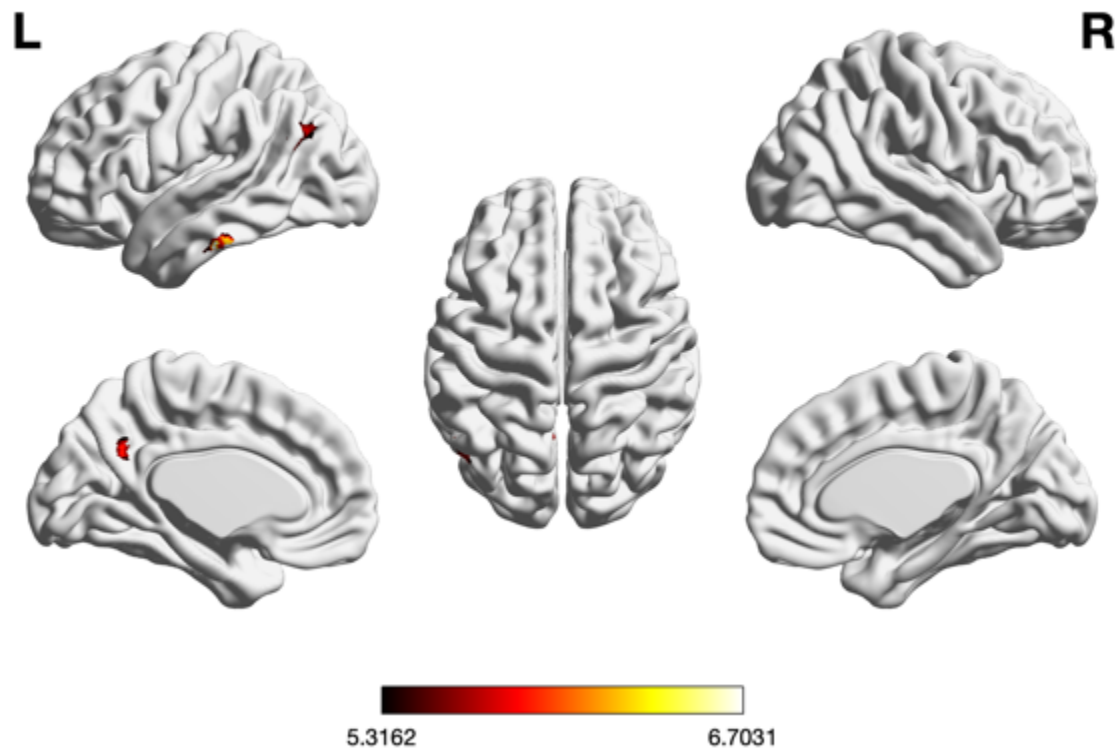


Figure 6. Significant positive association between whole-brain RS-FC of left aC/PrC and age, (voxel-level family-wise error-corrected threshold of two-sided $p < .00625$, extent threshold = 20, masked with RS-FC map of left aC/PrC). The scale bar reflects t-scores.

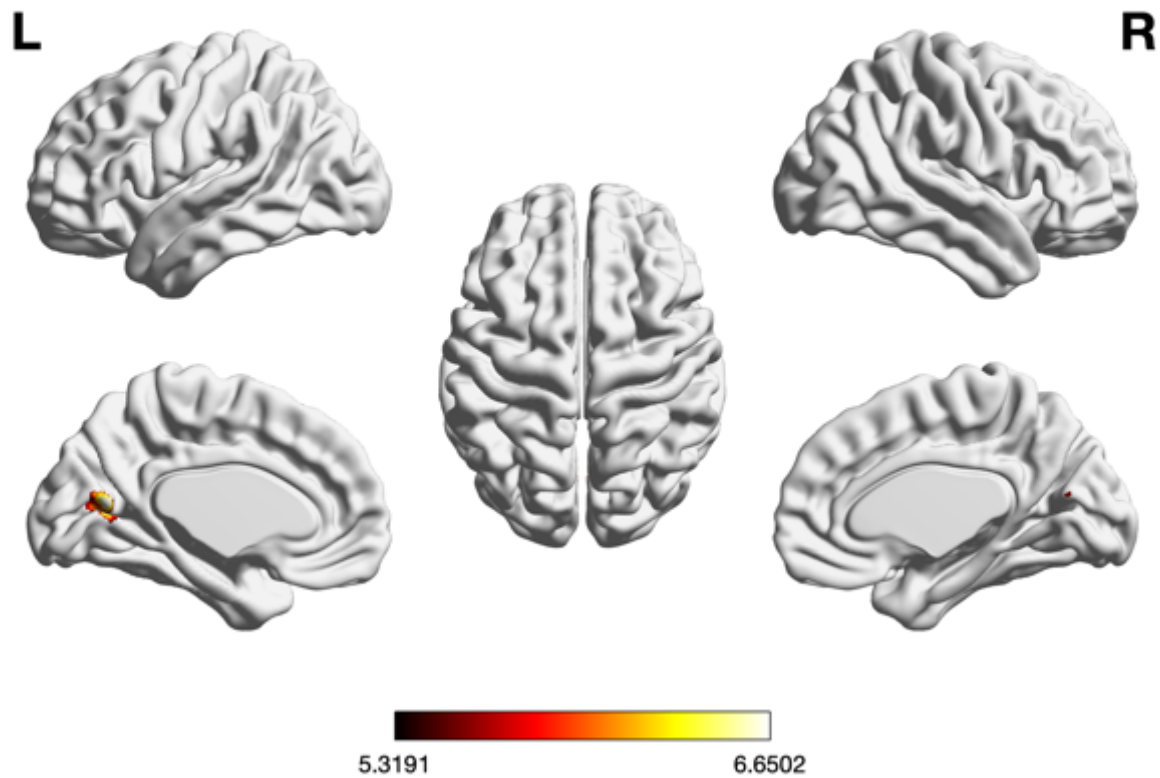


Figure 7. Significant positive association between whole-brain RS-FC of left aC/PrC and executive functions, (voxel-level family-wise error-corrected threshold at two-sided $p < .00625$, extent threshold = 10, masked with RS-FC map of left aC/PrC). The scale bar reflects t-scores.

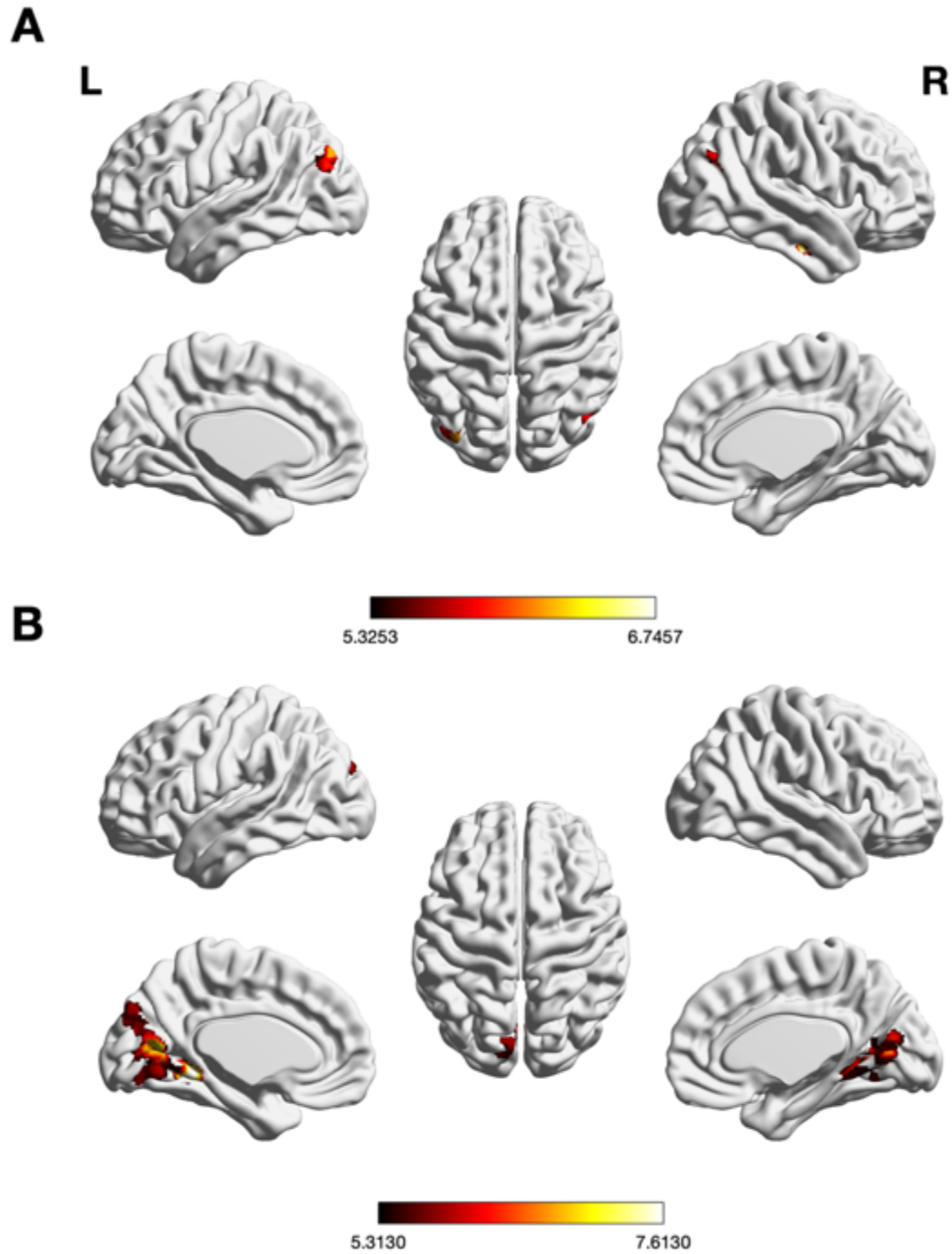


Figure 8. (A) Significant negative and (B) positive association between whole-brain RS-FC of left aC/PrC and cognitive flexibility, (voxel-level family-wise error-corrected threshold at two-sided $p < .00625$, extent threshold = 10, masked with RS-FC map of left aC/PrC). The scale bar reflects t-scores.