

Individual Variability in Performance Reflects Selectivity of the Multiple Demand Network among Children and Adults

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Executive function (EF) is essential for humans to effectively engage in cognitively demanding tasks. In adults, EF is subserved by frontoparietal regions in the multiple demand (MD) network, which respond to various cognitively demanding tasks. However, children initially show poor EF and prolonged development. Do children recruit the same network as adults? Is it functionally and connectionally distinct from adjacent language cortex, as in adults? And is this activation or connectivity dependent on age or ability? We examine task-dependent (spatial working memory and passive language tasks) and resting state functional data in 44 adults (18–38 years, 68% female) and 37 children (4–12 years, 35% female). Subject-specific functional ROIs (ss-fROIs) show bilateral MD network activation in children. In both children and adults, these MD ss-fROIs are not recruited for linguistic processing and are connectionally distinct from language ss-fROIs. While MD activation was lower in children than in adults (even in motion- and performance-matched groups), both showed increasing MD activation with better performance, especially in right hemisphere ss-fROIs. We observe this relationship even when controlling for age, cross-sectionally and in a small longitudinal sample of children. These data suggest that the MD network is selective to cognitive demand in children, is distinct from adjacent language cortex, and increases in selectivity as performance improves. These findings show that neural structures subserving domain-general EF emerge early and are sensitive to ability even in children. This research advances understanding of how high-level human cognition emerges and could inform interventions targeting cognitive control.

Key words: cognitive load; development; fMRI; functional connectivity; multiple demand network; spatial working memory

Significance Statement

This study provides evidence that young children already show differentiated brain network organization between regions that process cognitive demand and language. These data support the hypothesis that children recruit a similar network as adults to process cognitive demand; and despite immature characteristics, children's selectivity looks more adult-like as their executive function ability increases. Mapping early stages of network organization furthers our understanding of the functional architecture underlying domain-general executive function. Determining typical variability underlying cognitive processing across developmental periods helps establish a threshold for executive dysfunction. Early markers of dysfunction are necessary for effective early identification, prevention, and intervention efforts for individuals struggling with deficits in processing cognitive demand.

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Introduction

Executive function (EF) is comprised of three distinct, yet intersecting, components (working memory, cognitive shifting, and inhibitory control) that, together, facilitate effective self-regulation (Miyake and Friedman, 2012; Friedman and Miyake, 2017). Children and adolescents, whose impulse control is still developing, perform worse on laboratory measures of EF compared with adults; and their overall EF performance improves with age (Westerberg et al., 2004; Zelazo et al., 2004; Best and Miller, 2010; Anderson and Reidy, 2012; Wiebe and Karbach, 2017). So, do children process cognitively demanding tasks using the same system as adults? Factor analytic studies support a hierarchical

structure of EF in adults, with an overarching “common EF” factor (Friedman and Miyake, 2017). However, developmental studies support a unitary model of EF that only dissociates in mid-to-late childhood (Wiebe et al., 2008, 2011; Brydges et al., 2014; Lerner and Lonigan, 2014). Duncan (2010) proposed that the domain-general multiple demand (MD) network, comprised of frontal, parietal, cingular, and opercular brain regions, subserves this “common EF” factor.

Previous work examined this MD network in adults and showed that it is reliably recruited across a variety of EF tasks (Niendam et al., 2012; Fedorenko et al., 2013; Shashidhara et al., 2020). Fedorenko et al. (2013) identified 10 bilateral regions that show consistent activation in a sample of adults across EF tasks. These MD regions are distinct from the adjacent language network in functional specificity (Fedorenko et al., 2012; Diachek et al., 2020) and resting-state connectivity (Blank et al., 2014). In addition to robust activation for cognitive demand, adults’ activation of the MD network is correlated with behavioral markers, such as reaction time, accuracy, and intelligence (Assem et al., 2020), suggesting that these regions are sensitive to ability. Thus, we expect that activation of children’s MD network would reflect their immature EF ability.

It is possible that neural development of the MD network parallels development of EF performance. In this case, we would expect that, as a child’s performance improves, their MD network activation would look more adult-like. Although similar patterns of activation are observed across EF tasks in children and adults, child studies show more variability in strength and location (Durstun et al., 2002; Vogan et al., 2016; McKenna et al., 2017; Fiske and Holmboe, 2019). Additionally, it remains unclear whether the MD network is functionally and connectionally distinct from adjacent domain-specific language areas in children, as in adults, and whether developmental differences in MD network activation reflect changes in EF ability. To date, no one has looked at neural processing of EF compared with other mental functions, such as language, in a sample of children.

In this study, we investigate the cross-sectional and longitudinal development of the MD network among 4- to 12-year-old children. We collected task-dependent fMRI to localize brain regions that children recruit during a cognitively demanding spatial working memory (SWM) task and during a high-level language processing task. We also collected a resting-state scan. To account for stable individual variability in anatomic and functional network organization (Gratton et al., 2018), which is of increased concern for developmental samples, we generated subject-specific functional ROIs (ss-fROIs) using the Group-Constrained Subject-Specific method (Fedorenko et al., 2010) (<https://web.mit.edu/bcs/nklab/GSS.shtml>). Defining ss-fROIs enhances power and therefore increases the chances of detecting age- and performance-related changes in MD network selectivity. To rule out motion as a confound of developmental differences, we asked a subset of adults to participate in additional “wiggly” scans of the SWM task to compare with child scans. We predicted that (1) children would exhibit a similar but immature pattern of MD network activation as adults, (2) this network would be distinct from the adjacent language network in functional connectivity, and (3) this pattern would look more adult-like in children with better task performance.

Materials and Methods

Participants

We recruited 84 children and 50 adults who completed a battery of fMRI localizer tasks as part of multiple ongoing studies investigating brain development at Ohio State University. Children who did not complete the

Table 1. Demographics and behavioral variables for children and adults included in selectivity analyses

	Children [mean (SD) or %] (<i>n</i> = 37)	Wiggly adults [mean (SD) or %] (<i>n</i> = 16)	Adults [mean (SD) or %] (<i>n</i> = 44)
Age (yr)	8.3 (2.1)	22.9 (4.8)	23.9 (4.9)
Sex (% female)	35%	69%	48%
Race			
White	74%	65%	71%
Black	14%	6%	4%
Asian	3%	14%	11%
Other	9%	15%	14%
Handedness (% right)	89%	100%	93%
Frame-wise displacement	167.3 (77.4)	171.9 (131.8)	49.3 (12.6)

SWM task or had data processing problems (*n* = 16) and those who only completed one run of the SWM task (*n* = 12) were not included in analyses. Seven children and one adult were excluded for excessive head motion (>25% of time points with >1 mm total vector motion or total framewise displacement >3 SDs from the group mean) (Power et al., 2012). Three adults had data processing problems, and two were excluded because of low accuracy (>3 SDs below the group mean). Of the 49 remaining child scans, 8 children participated in multiple scans, leaving a final sample of 37 unique children. Final cross-sectional samples include 44 adults (68% female, mean age = 23.9 years, range = 17.9–38.2 years, SD = 4.9 years) and 37 typically developing children (35% female, mean age = 8.3 years, range = 4.5–12.0 years, SD = 2.1 years). Demographics are reported in Table 1.

We also examine a few subsets of the child and adult samples. We asked 16 adults to complete additional “wiggly” runs of the SWM task, in an attempt to mimic motion in child scans, so that we could compare motion-matched child and adult samples; demographics for this “wiggly” adult group are also reported in Table 1. A subset of 30 children and 29 adults who also completed the language localizer task were included in analyses examining functional and connectivity differences between the MD and language networks. Fourteen children completed the MD and language tasks at multiple time points; however, 6 do not meet our predefined motion cutoffs at both time points. Therefore, we present preliminary longitudinal findings assessing selectivity and resting-state connectivity for the remaining 8 children, each scanned about 1 year apart (75% female, time point 1: mean age = 6.22 years, range = 4.65–7.72 years, SD = 1.12 years, mean time between scans = 1.54 years). Two of these 8 children are missing accuracy data at one time point (because of experimenter/technological error), so only 6 children (83% female, time point 1: mean age = 6.37 years, range = 4.7–7.7 years, SD = 1.4 years, mean time between scans = 1.65) are included in longitudinal analyses assessing the relationship between MD selectivity and SWM performance.

Participants were recruited from the local community around Ohio State University. Participants reported normal vision and no neurologic, neuropsychologic, or developmental diagnoses at the time of recruitment; all participants are fluent in English, as measured by self-report. Informed consent was obtained from all participants or guardians; parental permission and assent were also obtained for child participants. Study protocols were approved by the Institutional Review Board at Ohio State University.

Experimental design

A series of functional localizers were completed by each participant, including an SWM and language localizer task in the fMRI. The full scan protocol collects data for six localizer tasks (including the two we report here), resting-state, T1-, and T2-weighted images during a 90 min scan protocol. Parents completed a battery of parent-report measures about their child and adult participants completed self-report questionnaires.

Functional localizer tasks. An SWM task was used to functionally locate regions that respond to cognitive load, which are associated with the domain-general MD network (Fedorenko et al., 2013) (<https://evlab.mit.edu/funcloc/>). Task difficulty was adjusted by age (low [4–5 years],

medium [6–7 years], and high [8+ years] load); in cases when a child was capable of playing a higher level based on prescan performance, they were given the next level up during the scan. All adults completed the high load version of the task, which is described and depicted by Diachek et al. (2020). Response durations are longer for the low and moderate load versions of the task to give young children one extra second to respond. Intertrial durations are shorter (12 s instead of 14 s) to ensure that the child versions of the task have a similar run time as adults. For each version of the task (low, medium, or high load), each run consisted of six blocks of each condition (Hard and Easy), and each block contained four trials. Hard versus Easy blocks are contrasted to isolate activation selective for cognitive load. Participants view a single grid of 9 (low load) or 12 (medium and high load) squares, some of which are blue. One, two, or three grid patterns with blue squares in new locations appear sequentially. Then, participants are presented with two grid patterns. They must choose which of the two grid patterns matches the sequential presentation of blue squares during that trial and indicate the correct response with a button press. The Hard trials require participants to remember more blue squares than the Easy trials. Each child completed at least one run of this task outside of the scanner to ensure they understood task rules.

A language localizer task was used to functionally locate regions responsive to lexical and structural properties of language (Fedorenko et al., 2010) (<https://evlab.mit.edu/funclloc/>). Participants listened to blocks of English Sentences (Sn), Nonsense sentences (Ns; nonwords lists controlling for prosody but constructed from phonemically intact nonsense words), and Texturized speech (Tx; degraded audio controlling for low-level auditory features) (Scott et al., 2017). Each run consisted of four blocks of each condition and three 14 s fixation blocks. Each block contained three trials (6 s each) followed by a visual cue to press a button.

Data acquisition

Images were acquired on a Siemens Prisma 3T scanner with a 32-channel phase array receiver head coil. Foam padding used for head stabilization and increased comfort for all participants. Anatomical images were acquired with a whole-head, high-resolution T1-weighted MPRAGE scan to facilitate registration of masks to each subject's anatomic space (TR = 1390 ms; TE = 4.6 ms; voxel resolution = $1 \times 1 \times 1 \text{ mm}^3$; flip angle = 12°). Functional images during the SWM task were acquired with similar EPI sequences for all difficulty levels (TR = 1000 ms; TE = 28 ms; voxel resolution = $2 \times 2 \times 3 \text{ mm}^3$; flip angle = 61°); the number of frames differed by difficulty level (low load: 336; medium: 384; high: 400). The language localizer was acquired with the same EPI sequence for both children and adults (TR = 1000 ms; TE = 28 ms; voxel resolution = $2 \times 2 \times 3 \text{ mm}^3$; number of frames = 258; flip angle = 61°). Resting-state functional images were acquired with the same sequence for both children and adults (TR = 1000 ms; TE = 28 ms; voxel resolution = $2 \times 2 \times 3 \text{ mm}^3$; flip angle = 0°); child scans were 5 min and adult scans were 10 min. Participants were instructed to lay still and look at a white fixation cross on a black screen during resting-state image acquisition.

fMRI preprocessing

Anatomical. Data were analyzed with Freesurfer version 6.0.0, FsFast, FSL, and custom MATLAB code. All structural images were preprocessed using a semiautomated processing stream with default parameters (recon-all function in Freesurfer: <https://surfer.nmr.mgh.harvard.edu/fswiki/recon-all/>), including intensity correction, skull stripping, surface coregistration, spatial smoothing, white matter and subcortical segmentation, and cortical parcellation. Cortical gray matter masks for the MD network regions are based on prior literature (Fedorenko et al., 2013) and registered to each subject's native anatomic space.

Task-based fMRI. Functional images were motion-corrected (aligned all time points to the first time point in the scan and regressed out all time points with $>1 \text{ mm}$ total vector motion between consecutive time points). We used bbrregister to register functional data to the subject's anatomic space and resampled to $1 \times 1 \times 1 \text{ mm}^3$. Additional preprocessing steps, including detrending and spatial smoothing (4 mm FWHM kernel for SWM and Language localizers), were applied during volume-

based, first-level GLM analyses. A standard boxcar function (events on/off) was used to convolve the canonical HRF (standard γ function, $d = 2.25$ and $t = 1.25$), and regressors were included for each condition (SWM task: Hard, Easy; Language localizer: Sn, Ns, Tx). Additional nuisance regressors (six orthogonalized motion measures from the preprocessing stage) were applied to the processed images for each task individually. Resulting β estimates and contrast maps (SWM task: Hard $>$ Easy; Language localizer: Sn $>$ Ns) were used for subsequent analyses.

Resting-state fMRI. We preprocessed the resting-state data using Freesurfer's FS-Fast preprocessing pipeline (<https://surfer.nmr.mgh.harvard.edu/fswiki/FsFastAnalysisBySteps>). Framewise displacement was used as a motion regressor. We generated masks of white matter, CSF, and subcortical structures for each subject in their native anatomic space. We performed spatial smoothing, interpolation over motion spikes, bandpass filtering (0.009–0.08 Hz), and denoising using CSF and white matter masks.

Generating a probabilistic map

To quantify the brain areas that respond to cognitive load across child subjects, we generated a probabilistic map from the SWM task significance maps. We smoothed each subject's Hard minus Easy significance map (4 mm FWHM kernel) and registered it to FsAverage space (<https://surfer.nmr.mgh.harvard.edu/fswiki/FsAverage>). We binarized and thresholded each subject's significance map ($-\log_{10}(p) > 2$; or $p < 0.01$) and summed the number of subjects who exhibit significant activation in each voxel.

ss-fROIs

We used the Group-Constrained Subject-Specific method (Fedorenko et al., 2010) to define ss-fROIs. Fedorenko et al. (2013) derived 10 bilateral regions belonging to the MD network based on probabilistic maps of functional activation in a sample of adults. Each region included showed greater functional activation during Hard compared with Easy blocks in at least 60% of subjects across six different cognitively demanding tasks. Each of the masks was registered using Freesurfer's CVS function (Postelnicu et al., 2009) (https://surfer.nmr.mgh.harvard.edu/fswiki/mri_cvs_register) from the CVS atlas MNI152 space to the participant's native anatomic space. We used one run of the first-level GLM analysis to identify each subject's ss-fROIs by assessing subject-specific contrast maps within all 10 bilateral search spaces. Using custom MATLAB scripts, the top 10% of activated voxels during the contrast of interest (i.e., Hard $>$ Easy) were identified as the ss-fROI for each search space. Two sets of MD ss-fROIs were generated for each subject (i.e., from each run of the SWM task). Language ss-fROIs used in resting-state analyses were defined (Sn $>$ Ns contrast) using masks of regions that show activation during high-level language in a previous study in adults (Fedorenko et al., 2010) (<https://evlab.mit.edu/funclloc/>).

Percent signal change (PSC)

Cross-sectional. Custom MATLAB scripts extract PSC for each condition (SWM task: Hard, Easy; Language localizer: Sn, Ns, Tx) within all MD ss-fROIs generated from an independent run of the SWM task (e.g., PSC during Run 1 was extracted within the ss-fROIs generated from Run 2) using the first-level β estimates. ss-fROIs generated from the SWM task were used to extract PSC from the Language localizer task for children and adults who also completed at least one run of the Language localizer task.

Longitudinal. For the subjects who completed two longitudinal scans, we registered ss-fROIs defined at their second time point to the subject's native anatomic space at their first time point using Freesurfer's CVS function (Postelnicu et al., 2009) to assess how more mature/adult-like ss-fROIs are responding at a younger age. We then used the Time point 2 ss-fROIs (that were now in Time point 1's native anatomic space) to extract PSC during the SWM task from Time point 1, so that we could calculate changes in responsiveness to cognitive demand over time. The ss-fROI generated from the first run at Time point 2 was used to extract PSC from the first run at Time point 1; this was repeated for the second run of the SWM task.

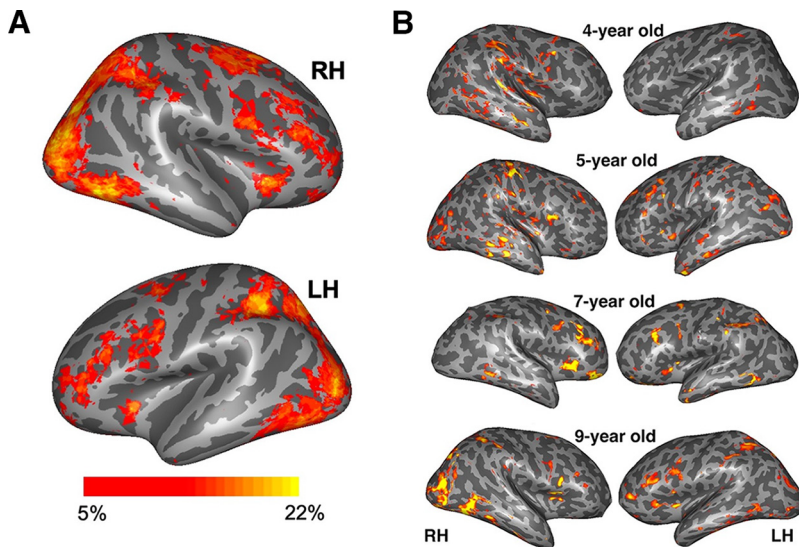


Figure 1. *A*, Probabilistic map showing common activation during a blockwise spatial working memory task ($z > 2.58$; contrast: Hard–Easy) in at least 2 participants and a maximum of 8 participants (22% of participants). *B*, Example significant maps are depicted for 4 participants.

Selectivity indexes

The MD selectivity index quantifies selectivity of MD ss-fROIs for cognitive demand (Eq. 1) (Simmons et al., 2007; Szwed et al., 2011). We examine selectivity indexes, instead of raw PSC, because it normalizes signal contrast relative to general responsiveness of that region. A selectivity index was calculated for each run of a task (SWM or Language) using the PSC values; then the selectivity across both runs was averaged to give each individual one selectivity value per task. The Language selectivity quantifies selectivity of MD ss-fROIs to language (Eq. 2).

$$\text{MD selectivity index} = \frac{\text{PSC.Hard} - \text{PSC.Easy}}{\text{PSC.Hard} + \text{PSC.Easy}} \quad (1)$$

$$\begin{aligned} &\text{Language selectivity index} \\ &= \frac{\text{PSC.Sn} - \text{PSC.Ns}}{\text{PSC.Sn} + \text{PSC.Ns} + \text{PSC.Tx}} \quad (2) \end{aligned}$$

Resting state connectivity

The same ss-fROIs created for the above task-based analysis were used to examine resting-state connectivity in each subject that also completed the resting state scan (child, $n = 34$; adult, $n = 26$). The average time course for each ss-fROI of the MD and language networks was computed from the preprocessed resting-state images. To evaluate interactions between regions, Pearson correlations were generated between ss-fROI time courses. To generate normally distributed values, each functional connectivity value was Fisher z -transformed.

Statistical analyses

Single-sample sign tests were conducted to evaluate if selectivity is >0 because of the negatively skewed distribution of MD selectivity within the child sample; sign tests were also conducted for the adult sample for consistency. We report the dominance statistic (DS), which reflects the proportion of the sample exhibiting selectivity >0 minus the proportion exhibiting selectivity <0 (Mangiafico, 2016), and the nonparametric effect size (Fritz et al., 2012) as measures of effect size for selectivity values. Wilcoxon rank sum tests were conducted to evaluate whether MD selectivity differs between adults and children in the motion- and performance-matched subsamples. Paired-sample sign tests were conducted to evaluate MD selectivity versus language selectivity in MD ss-fROIs, and paired-sample t tests were conducted to evaluate within- versus between-network (with language network

ss-fROIs) resting-state connectivity in children and adults. We corrected for multiple comparisons using Bonferroni-Holm correction (Holm, 1979); each analysis tested for all 10 bilateral ss-fROIs was corrected for three (frontal) or seven (parietal) comparisons.

To assess linear relationships between selectivity, age, and task performance, we conducted Pearson's correlations and multiple linear regressions in the cross-sectional and longitudinal samples to assess associations for individual ss-fROIs. To assess whether the multiple linear regression, including selectivity and age, explains significantly more variance in performance than age or selectivity alone, we conducted stepwise regressions with ANOVAs to compare the linear regressions to the multiple linear regressions, including both variables. To assess how pooled selectivity of the MD network explains variance in performance, we conducted linear mixed effects models, including selectivity from all ss-fROIs (within hemisphere), age, and a random intercept by ss-fROI (lmerTest R package) (Luke, 2017); we refer to these analyses as pooled selectivity throughout. To assess the longitudinal correlation between selectivity and performance, we conducted linear mixed effects models with a random intercept by subject (lmerTest). Last, to assess longitudinal changes in selectivity and performance, we conducted multiple linear regressions to determine the effect of change (i.e., Time point 2 minus Time point 1) in age and change in selectivity on change in accuracy, while controlling for age at Time point 1.

Code accessibility

We used custom scripts in MATLAB for much of the data processing (e.g., generating ss-fROIs and extracting PSC). Scripts are available on request; contact corresponding author (Z.M.S.). We used RStudio version 1.1.331 for statistical analyses examining selectivity and MATLAB version R2020a for statistical analyses examining within- and between-network resting-state connectivity.

Results

Exploratory probabilistic map of the MD network in children

We generated an exploratory probabilistic map of voxels that exhibit significantly greater activation ($z > 2.58$) during Hard versus Easy trials of the SWM task for at least 2 subjects (5% of cross-sectional sample, Fig. 1). The maximum number of subjects who show significant activation in the same voxel is 8 (22% of cross-sectional sample). Despite functional variability, we see a pattern of activation across several frontal and parietal regions that looks similar to the pattern seen in adults (Fedorenko et al., 2013). We also see occipital activations, which likely reflect the fact that the Hard trials show more colored boxes than the Easy trials. Below, we use ss-fROIs defined using each individual's activation map to explore development of the MD network.

Selectivity of the MD network in adults

We considered ss-fROIs to be selective to cognitive demand if their neural responses to Hard trials (on an SWM task) was higher than responses to Easy trials (i.e., if the MD selectivity index [Eq. 1] is significantly >0). Table 2 and Extended Data Table 2-1 show descriptive statistics, effect sizes, and p values for each ss-fROI's MD selectivity index by group. Because of a negatively skewed distribution, we tested selectivity using single-sample, one-tailed, sign tests. As expected, adults show robust selectivity in all bilateral MD ss-fROIs (Table 2, sign tests), which all survive Bonferroni-Holm multiple comparison correction. Because motion is a problem in child neuroimaging and can cause

Table 2. Selectivity of the MD ss-fROIs during an SWM task^a

	Children (<i>n</i> = 37)			Wiggly adults (<i>n</i> = 16)			Adults (<i>n</i> = 44)		
	Median	DS	<i>p</i>	Median	DS	<i>p</i>	Median	DS	<i>p</i>
Right hemisphere									
Posterior parietal	0.15	0.51	$1.28 \times 10^{-3*}$	0.29	1.00	$3.05 \times 10^{-5*}$	0.24	1.00	$5.72 \times 10^{-14*}$
Superior parietal	0.09	0.30	0.045*	0.43	1.00	$2.59 \times 10^{-4*}$	0.27	0.95	$2.56 \times 10^{-12*}$
Inferior parietal	0.22	0.51	$1.28 \times 10^{-3*}$	0.43	1.00	$1.53 \times 10^{-5*}$	0.31	0.95	$5.63 \times 10^{-11*}$
Precentral gyrus	0.14	0.38	0.010	0.46	1.00	$2.59 \times 10^{-4*}$	0.32	0.91	$5.63 \times 10^{-11*}$
Superior frontal sulcus	0.12	0.30	0.040	0.43	0.75	$2.09 \times 10^{-3*}$	0.27	0.91	$2.56 \times 10^{-12*}$
Inferior frontal sulcus	0.11	0.35	0.018	0.61	1.00	$2.59 \times 10^{-4*}$	0.35	0.95	$2.56 \times 10^{-12*}$
Middle frontal gyrus	0.11	0.19	0.155	0.68	1.00	$3.69 \times 10^{-3*}$	0.55	0.91	$5.63 \times 10^{-11*}$
Orbital middle frontal gyrus	0.16	0.14	0.250	0.92	0.75	0.038	0.74	0.95	$2.56 \times 10^{-12*}$
Inferior frontal gyrus	0.28	0.41	0.010	0.67	0.88	$2.09 \times 10^{-3*}$	0.57	1.00	$5.72 \times 10^{-14*}$
Anterior cingulate cortex	0.15	0.24	0.088	0.43	0.88	0.046	0.48	0.95	$2.56 \times 10^{-12*}$
Left hemisphere									
Posterior parietal	0.17	0.43	$4.52 \times 10^{-3*}$	0.35	1.00	$1.53 \times 10^{-5*}$	0.22	1.00	$5.72 \times 10^{-14*}$
Superior parietal	0.30	0.32	0.033*	0.37	1.00	$4.88 \times 10^{-4*}$	0.28	1.00	$5.72 \times 10^{-14*}$
Inferior parietal	0.26	0.38	0.014*	0.33	1.00	$4.88 \times 10^{-4*}$	0.29	1.00	$5.72 \times 10^{-14*}$
Precentral gyrus	0.18	0.54	$2.68 \times 10^{-4*}$	0.35	0.88	$3.69 \times 10^{-3*}$	0.25	0.91	$5.63 \times 10^{-11*}$
Superior frontal sulcus	0.25	0.43	$5.67 \times 10^{-3*}$	0.36	1.00	$2.59 \times 10^{-4*}$	0.31	1.00	$5.72 \times 10^{-14*}$
Inferior frontal sulcus	0.20	0.40	$8.34 \times 10^{-3*}$	0.41	1.00	$3.69 \times 10^{-3*}$	0.37	0.95	$2.56 \times 10^{-12*}$
Middle frontal gyrus	0.30	0.38	0.012*	0.53	1.00	$3.69 \times 10^{-3*}$	0.48	0.95	$2.56 \times 10^{-12*}$
Orbital middle frontal gyrus	0.33	0.38	0.012*	0.65	0.88	0.029	0.76	0.86	$8.09 \times 10^{-10*}$
Inferior frontal gyrus	0.16	0.16	0.203	0.52	1.00	0.029	0.44	0.95	$2.56 \times 10^{-12*}$
Anterior cingulate cortex	0.14	0.32	0.029	0.15	0.88	0.073	0.42	0.91	$5.63 \times 10^{-11*}$

^aOne-tailed sign-tests were conducted and medians are reported because of negatively skewed distribution. Subject-specific functional regions of interest (ss-fROIs) are grouped by hemisphere and brain lobe. DS, Dominance statistic. Extended Data Table 2-1 lists the nonparametric effect sizes for each group. Extended Data Table 2-2 lists statistics for comparisons between children and adult groups. Extended Data Table 2-3 lists statistics for language selectivity and repeated-measures comparisons between multiple demand (MD) and language selectivity of MD ss-fROIs for children and adults, separately. Extended Data Table 2-4 lists comparisons of percent signal change for relevant conditions in the spatial working memory (SWM) and language tasks.

*Corrected $p < 0.05$ (Bonferroni-Holm, 3 parietal regions, 7 frontal regions) for each group (e.g., significant selectivity > 0).

spurious correlations (Power et al., 2012), we asked a subset of our adult participants to complete additional runs of the SWM experiment while encouraging them to “wiggle” so that we could compare motion-matched child and adult groups. In the wiggly adult group, most bilateral MD ss-fROIs remain significant (uncorrected $p < 0.05$, sign tests) and survive multiple comparison correction (Bonferroni-Holm-corrected $p < 0.05$; Table 2). This suggests that selectivity of MD ss-fROIs is robust among adults, even in the face of childlike motion, and that any developmental differences we observe among motion-matched samples are likely not driven by motion. Figure 2 depicts mean selectivity by region and group.

Selectivity of the MD network in children

A similar pattern is observed among children. Most MD ss-fROIs show positive selectivity indexes (Fig. 2, light blue bars). Children exhibit significant selectivity in all three bilateral parietal, four right frontal, and six left frontal MD ss-fROIs (uncorrected $p < 0.05$, sign tests) and several survive multiple comparison correction (Table 2). These data show that, in samples of children as young as 4–12 years, we can already see functionally selective activation of the MD network during a cognitive demanding task. Upon visual inspection, all ss-fROIs show greater selectivity in adults than in children, even for the motion-matched adult sample (Fig. 2; Extended Data Fig. 2-1 depicts the average PSC). Surprisingly, only 12 of the 20 ss-fROIs reach statistical significance. Seven of 10 MD ss-fROIs in the right hemisphere show significantly greater selectivity in adults compared with children (uncorrected $p < 0.05$, Wilcoxon rank sum tests; Fig. 2; Extended Data Table 2-2), and all survive multiple comparison correction. In the left hemisphere, only five frontal ss-fROIs show significantly greater selectivity in adults, and all survive multiple comparison correction. Despite robust selectivity in children’s MD ss-fROIs, adults evoke stronger selectivity than children even when matched

on motion. Additionally, in a performance-matched subsample of children ($n = 23$) and adults ($n = 18$), we only see significantly greater MD selectivity for adults among frontal ss-fROIs (Wilcoxon rank sum tests; Extended Data Table 2-2). These data show that, even in young children, the bilateral MD network is engaged during cognitively demanding tasks, just like in adults. However, we see weaker activation in children compared with adults, even in samples controlling for motion and performance on the task. Thus, it is reasonable to attribute these differences to maturation.

Dissociation between MD and adjacent language regions: functional selectivity

We next compared the same participants’ activation on the SWM task to activation on a language task, where participants were asked to listen to meaningful Sentences and Nonsense sentences, as well as Texturized sound. Frontal MD and language regions are often in close proximity, but we know from previous work (Fedorenko et al., 2012, 2013) that these networks are functionally distinct in adults. Do these regions emerge from a common frontal area? If so, we may expect slight sensitivity, or mild selectivity, to language in these MD ss-fROIs in young children.

We conducted single-sample, two-tailed, sign tests to test this hypothesis. We found that no MD ss-fROIs show selectivity to language in either our child or adult samples (i.e., no ss-fROIs show language selectivity significantly > 0 ; $p > 0.05$, two-tailed sign tests, Extended Data Table 2-3). Intriguingly, we observed trends of greater response to the Nonsense sentences condition compared with the Sentences condition (reflected as language selectivity < 0 ; Fig. 2, pink bars; Extended Data Fig. 2-1 depicts the average PSC). Several ss-fROIs show significantly greater PSC during the Nonsense versus Sentences condition in our

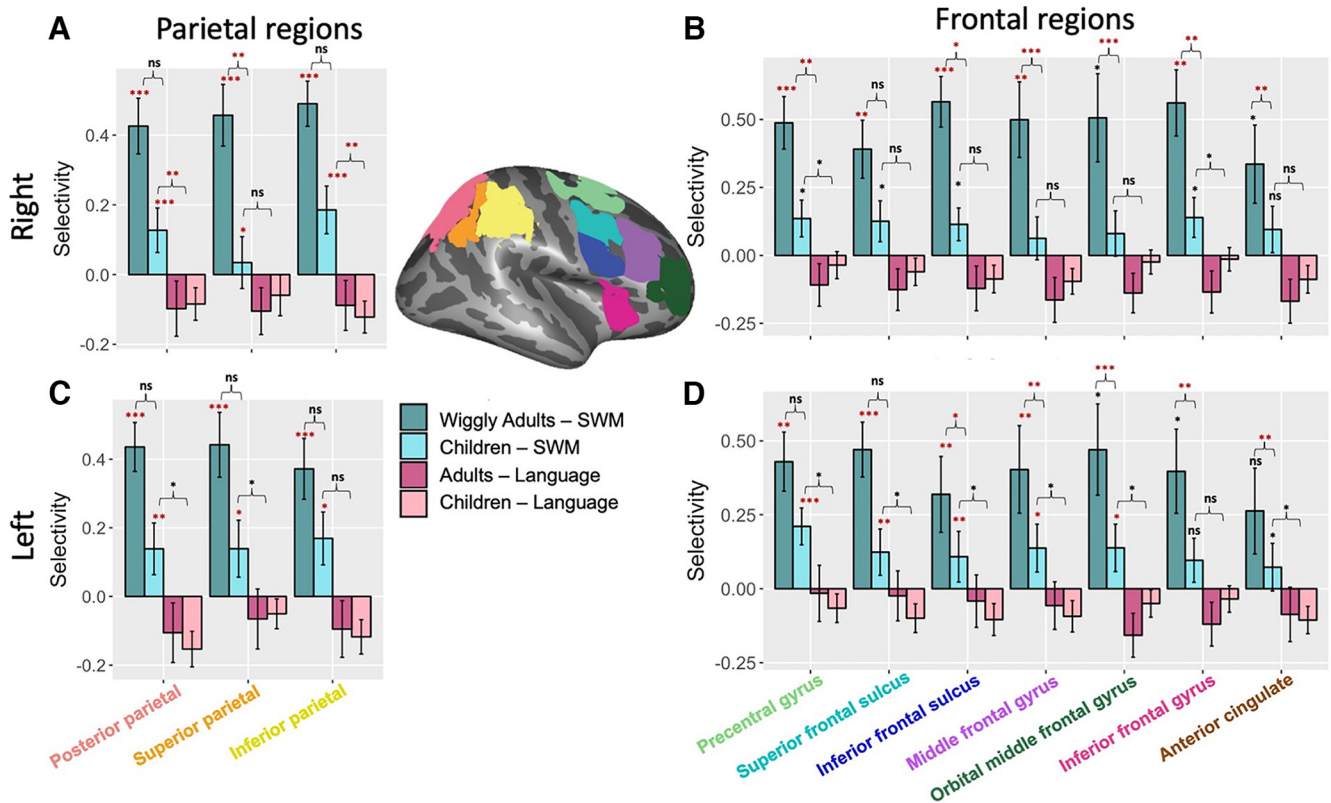


Figure 2. Mean selectivity in the right (**A,B**) and left (**C,D**) multiple demand (MD) network subject-specific functional regions of interest (ss-fROIs) during the spatial working memory (SWM) (blue) and language localizer (pink) tasks for children (lighter colors) and adults (darker colors). One-tailed sign tests were conducted to test whether MD selectivity is significantly >0 . Two-tailed sign tests were conducted to test whether language selectivity is significantly different from zero. Repeated-measures, one-tailed sign tests were conducted to test whether children show greater MD than language selectivity in MD ss-fROIs. Wilcoxon rank sum tests were conducted to test whether adults show greater MD selectivity than children in motion-matched comparison groups. Extended Data Figure 2-1 represents the average percent signal change for each condition, which was used to calculate selectivity. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; strength of significance (uncorrected). Red symbols represent Bonferroni-Holm–corrected $p < 0.05$. Error bars indicate SE.

child and adult samples (uncorrected $p > 0.05$, Wilcoxon rank sum tests; Extended Data Table 2-4). Nonsense sentences may evoke greater functional activation than Sentences in regions associated with cognitive demand as individuals attempt to comprehend the words, effectively engaging in a cognitively demanding task.

We also asked whether children show greater MD selectivity than language selectivity in these ss-fROIs. All but two left hemisphere ss-fROIs show greater MD than language selectivity, and four right hemisphere MD ss-fROIs reach significance for this comparison (uncorrected $p < 0.05$, Extended Data Table 2-3; repeated-measures, one-tailed, sign tests); the right posterior and inferior parietal MD ss-fROIs survive multiple comparison correction. Overall, we see selective activation for SWM in the MD network but no language selectivity within MD ss-fROIs in children. However, it is possible that these two networks are still functionally connected in children. Therefore, we next examined whether these networks are also dissociated in their resting-state connectivity patterns.

Dissociation between MD and adjacent language regions: resting-state connectivity

Previous work shows that in adults, regions of the MD and language networks are also distinct in resting-state functional connectivity (Blank et al., 2014). We investigated whether this pattern is replicated among our sample of adults and whether it is observed among children using their MD ss-fROIs defined for the prior analysis and their language ss-fROIs defined using the

language task. We observe a similar pattern of greater within- than between-network resting-state connectivity in our sample of adults (left: $t_{(25)} = 12.27$, $p = 8.13 \times 10^{-13}$, right: $t_{(25)} = 11.19$, $p = 3.14 \times 10^{-11}$, repeated-measures t test; Fig. 3A). We also see significantly greater within-MD than between-network connectivity in both the left ($t_{(33)} = 3.37$, $p = 1.90 \times 10^{-3}$, repeated-measures t test) and right ($t_{(33)} = 3.28$, $p = 2.5 \times 10^{-3}$, repeated-measures t test) hemispheres for the cross-sectional child sample (Fig. 3B). So, are MD frontal regions also more connected to other MD regions than to language regions that are in closer proximity? When focusing on just the frontal ss-fROIs (which exist in both networks), we also see the same pattern: frontal MD ss-fROIs are more connected to one another than they are to adjacent language ss-fROIs for children (left: $t_{(33)} = 3.46$, $p = 1.90 \times 10^{-3}$, right: $t_{(33)} = 2.87$, $p = 7.1 \times 10^{-3}$, repeated-measures t tests) and adults (left: $t_{(25)} = 9.07$, $p = 2.23 \times 10^{-9}$, right: $t_{(25)} = 8.24$, $p = 1.35 \times 10^{-8}$, repeated-measures t tests).

In our longitudinal sample ($n = 8$), at Time point 1, children show only a trend of greater within- than between-network connectivity in both hemispheres (left: $t_{(8)} = 1.93$, $p = 0.090$; right: $t_{(8)} = 2.16$, $p = 0.063$, repeated-measures t tests; Fig. 3C, top). At Time point 2, within-network connectivity is significantly greater than between-network connectivity in both hemispheres (left: $t_{(8)} = 4.10$, $p = 3.4 \times 10^{-3}$; right: $t_{(8)} = 2.34$, $p = 0.047$, repeated-measures t tests; Fig. 3C, bottom). This suggests that, by early-to-middle childhood, the MD network is already dissociated from the adjacent language network in both function and connectivity.

Development of MD functional selectivity and resting-state connectivity

Next, we explored any developmental changes in selectivity of the MD network in children ages 4–12 years. In the cross-sectional sample, MD selectivity was not significantly associated with age for any MD ss-fROIs ($|R| < 0.31$, p values > 0.05 , Pearson correlations). Analogous correlations in the longitudinal sample also show no significant associations with age ($|t| < 1.83$, p values > 0.05 , linear mixed effects models, random intercept by subject).

When we examined developmental changes in resting-state connectivity, the cross-sectional sample shows no association between age and within-MD network connectivity within the whole network (left: $R = -0.096$, right: $R = -0.094$, p values > 0.05 , Pearson's correlations) or within-MD frontal ss-fROIs (left: $R = -0.106$, right: $R = -0.289$, p values > 0.05 , Pearson's correlations). We also see no association between age and between-network (MD to Language) connectivity for the whole network (left: $R = 0.022$, right: $R = -0.002$, p values > 0.05 , Pearson's correlations) or for the frontal ss-fROIs (left: $R = -0.050$, right: $R = -0.223$, p values > 0.05 , Pearson's correlations). Age is also not related to differences in connectivity across tasks (i.e., within- minus between-network connectivity; left: $R = -0.118$, right: $R = -0.090$, Pearson's correlations). To assess age-related changes in the longitudinal sample, we tested whether change in age between the first and second scan sessions is related to change in connectivity, while controlling for age at first scan. Here, we also see no changes in within-network connectivity (left: $F_{(2,6)} = 0.736$, $p = 0.518$; right: $F_{(2,6)} = 0.255$, $p = 0.783$, multiple linear regressions) or between-network connectivity (left: $F_{(2,6)} = 0.736$, $p = 0.518$; right: $F_{(2,6)} = 0.255$, $p = 0.783$, multiple linear regressions), or difference in connectivity at the whole-network level (left: $F_{(2,6)} = 0.736$, $p = 0.518$; right: $F_{(2,6)} = 0.255$, $p = 0.783$, multiple linear regressions). When looking only at the frontal ss-fROIs (left: $F_{(2,5)} = 2.117$, $p = 0.216$; right: $F_{(2,6)} = 0.209$, $p = 0.817$, multiple linear regressions), we also see no significant relationship. Together, these findings suggest that, during childhood, the MD network is already functionally dissociated from the language network and that changes in functional connectivity and selectivity are not well explained by age alone. Below, we explore how performance on the SWM task relates to age, selectivity, and connectivity of the MD network.

Relationship between age, MD selectivity, and performance on SWM task

Performance by age

In the cross-sectional sample, we only see a significant positive correlation between age and accuracy ($R = 0.44$, $t_{(30)} = 2.67$, $p = 0.012$, Pearson correlation) and a trend of quicker reaction time with age ($R = -0.25$, $t_{(30)} = 1.41$, $p = 0.168$, Pearson correlation; Fig. 4) during

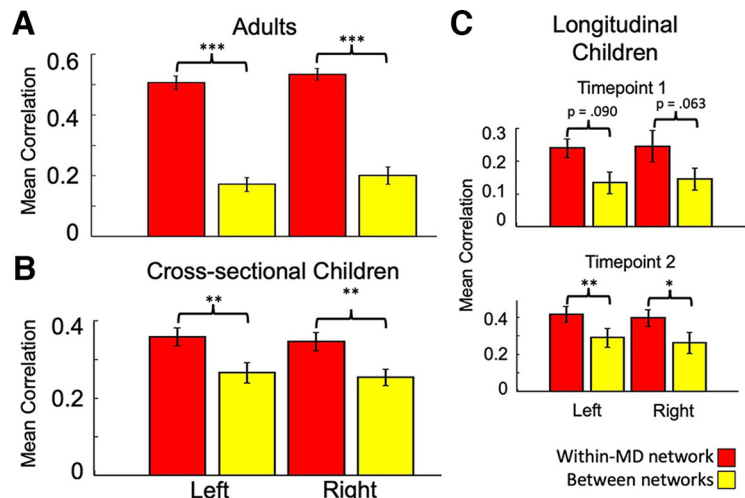


Figure 3. Mean resting-state connectivity of subject-specific functional regions of interest (ss-fROIs) for the multiple demand (MD) and language networks, separated by hemisphere. Group means for the cross-sectional adult (A; $n = 26$) and child (B; $n = 34$), and longitudinal child (C; $n = 8$) samples are depicted. Two-tailed repeated-measures t tests show significantly greater within- than between-network connectivity in both hemispheres. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; strength of significance (uncorrected). Error bars indicate SE.

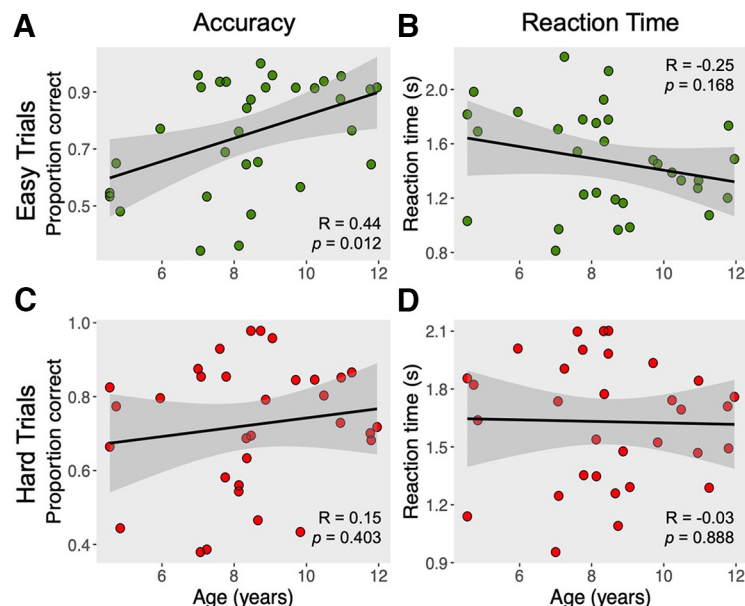


Figure 4. Pearson correlations for age and behavioral metrics during the spatial working memory (SWM) task in the cross-sectional child sample. Accuracy (A,C) and reaction time (B,D) during Easy (A,B) and Hard (C,D) trials are reported separately.

Easy trials. There is no relationship between age and accuracy or reaction time for Hard trials (p values > 0.05 ; Fig. 4). In the longitudinal sample, we also see a positive association between age and accuracy for both conditions (Hard: $t_{(9,6)} = 2.85$, $p = 0.018$; Easy: $t_{(6,8)} = 4.38$, $p = 3.53 \times 10^{-3}$, linear mixed effects model with random intercept by subject). They show no significant associations for reaction time (p values > 0.05). Next, we investigate whether MD selectivity or connectivity reflect a child's ability to process cognitive demand.

Performance by MD selectivity

Pearson's correlations between accuracy and selectivity of several MD ss-fROIs show a significant relationship during both Hard

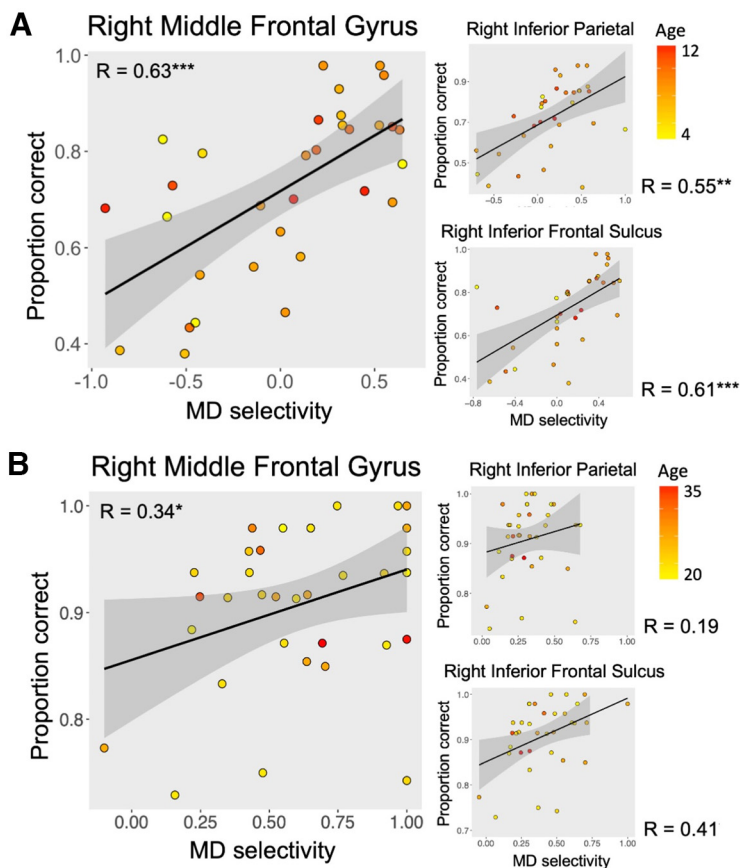


Figure 5. Pearson correlations between neural selectivity of multiple demand (MD) subject-specific functional regions of interest (ss-fROIs) and behavioral accuracy during Hard trials of the spatial working memory task in children (**A**) and adults (**B**); stronger selectivity was related to better task performance regardless of age. $^*p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$; strength of significance (uncorrected). A full list of statistics by individual ss-fROIs is reported in Extended Data Table 3-1 for children and Extended Data Table 3-2 for adults.

and Easy trials among children (uncorrected $p < 0.05$, Pearson correlations; Extended Data Table 3-1). The majority of the ss-fROIs that show increasing MD selectivity with performance on Hard trials are in the right hemisphere. When assessing pooled selectivity, selectivity of ss-fROIs in both hemispheres is related to accuracy (linear mixed effects model with random intercepts by ss-fROI; Extended Data Table 3-1). Figure 5A depicts three correlations of the most robust selectivity by performance associations among children, namely, in right middle frontal gyrus, right inferior parietal, and right inferior frontal sulcus. Similar to children, we see a positive trend in the relationships between adult accuracy on Hard trials and selectivity for several MD ss-fROIs, although only five ss-fROIs are statistically significant (uncorrected $p < 0.05$, Pearson correlations; Extended Data Table 3-2). Figure 5B depicts the association between selectivity and adult performance during Hard trials in the same three ss-fROIs as depicted for children. This association remains significant for adults when pooled within hemisphere (linear mixed effects model with random intercepts by ss-fROI; Extended Data Table 3-2). For accuracy during Easy trials, children (Extended Data Table 3-1), but not adults (Extended Data Table 3-2), show significant associations between MD selectivity and accuracy.

Performance by MD selectivity while controlling for age

Then, we explored the unique effect of MD selectivity on accuracy, while accounting for variability associated with age. During

Hard trials, five right ss-fROIs and one left ss-fROI remain significantly related to accuracy (multiple linear regressions; Table 3); three of the right ss-fROIs (inferior frontal sulcus, middle frontal gyrus, inferior parietal) survive multiple comparison correction (Bonferroni-Holm-corrected $p < 0.05$; Table 3). Pooled selectivity across all ss-fROIs in each hemisphere (to assess selectivity of the MD network as a whole) show significant main effects of selectivity, but not age, in both hemispheres (linear mixed effects models with random intercepts by ss-fROI; Table 3). During Easy trials, age remains robustly associated with accuracy in all models controlling for variance explained by MD selectivity (Extended Data Table 3-3). The association between accuracy and pooled selectivity in both hemispheres remains significant when framewise displacement is controlled for in the model for both Hard (left: $B = 0.10$, $t_{(316)} = 5.59$, $p = 4.81 \times 10^{-8}$, right: $B = 0.15$, $t_{(316)} = 7.91$, $p = 4.35 \times 10^{-14}$, linear mixed effects models with random intercepts by ss-fROI) and Easy (left: $B = 0.09$, $t_{(316)} = 4.55$, $p = 7.80 \times 10^{-6}$, right: $B = 0.12$, $t_{(316)} = 6.22$, $p = 1.54 \times 10^{-9}$, linear mixed effects models with random intercepts by ss-fROI) trials.

Do the longitudinal analyses mirror the cross-sectional results? Two subjects were missing accuracy data at one time point, so these analyses only include 6 children with two data points each. Even in this small sample, we see that change in selectivity is significantly related to change in accuracy during Hard trials when pooling across ss-fROIs within hemisphere, even while controlling for change in age and age at first scan (Table 4, linear mixed effects models with random intercept by ss-fROI); however, this effect is not observed in individual ss-fROIs (Table 4, linear regressions). Because of the small sample size, to further examine these results, we assessed reliability of the variables of interest. We see that selectivity indexes ($R = 0.29$, $p = 4.49 \times 10^{-8}$, Pearson's correlation) and accuracy during Easy ($R = 0.79$, $p = 3.21 \times 10^{-8}$, Pearson's correlation) and Hard ($R = 0.78$, $p = 9.01 \times 10^{-8}$, Pearson's correlation) trials are correlated across runs within time point. These longitudinal results replicate the association between performance and MD selectivity observed in the cross-sectional sample, suggesting that children's neural responses reflect their EF ability and look increasingly adult-like as their ability improves across time.

Model comparisons

Does MD selectivity explain more variance in performance than variance explained by age? We compare models of both age and selectivity (multiple linear regression) to models of either age or selectivity alone (linear regressions) using stepwise regression. All significant multiple linear regressions (Table 3) explain significantly more variance in performance during Hard trials than linear regressions including age alone (Extended Data Table 5-1, ANOVAs). Notably, these multiple linear regressions do not explain more variance than linear regressions with selectivity alone (Extended Data Table 5-1, ANOVAs). We see this same pattern for pooled selectivity in both hemispheres (Table 5, linear mixed effects model). This suggests that selectivity of MD regions

Table 3. Main effect of selectivity of MD ss-fROIs on accuracy during hard trials of the spatial working memory task in the cross-sectional child sample ($n = 32$)^a

Accuracy: hard trials	Selectivity (B)	Selectivity (t)	Age (B)	Age (t)	Full model (F)	Adjusted R^2
Right hemisphere						
Posterior parietal	0.17	1.98	2.20×10^{-2}	1.47	2.35	0.08
Superior parietal	0.13	2.10*	1.21×10^{-2}	0.86	2.60	0.09
Inferior parietal	0.24	3.63**	1.46×10^{-2}	1.17	7.10**	0.28 ^b
Precentral gyrus	0.21	3.10**	7.69×10^{-3}	0.59	5.25*	0.22
Superior frontal sulcus	0.16	2.64*	8.75×10^{-3}	0.64	3.92*	0.16
Inferior frontal sulcus	0.28	4.01***	-1.12×10^{-4}	-0.01	8.56**	0.33 ^b
Middle frontal gyrus	0.23	4.21***	2.16×10^{-3}	0.18	9.43***	0.35 ^b
Orbital middle frontal gyrus	0.10	1.62	5.51×10^{-3}	0.37	1.69	0.04
Inferior frontal gyrus	0.08	1.06	1.02×10^{-2}	0.68	0.92	-5.36×10^{-3}
Anterior cingulate cortex	0.12	1.98	8.76×10^{-5}	0.01	2.35	0.08
Pooled selectivity	0.16	7.97***	8.19×10^{-3}	1.95	NA	NA
Left hemisphere						
Posterior parietal	0.20	2.87**	1.85×10^{-2}	1.37	4.58*	0.19
Superior parietal	0.14	2.38*	1.14×10^{-2}	0.83	3.25	0.13
Inferior parietal	0.11	1.74	8.48×10^{-3}	0.58	1.90	0.06
Precentral gyrus	0.09	1.07	1.34×10^{-2}	0.90	0.93	-4.47×10^{-3}
Superior frontal sulcus	0.12	2.05	8.41×10^{-3}	0.59	2.49	0.09
Inferior frontal sulcus	0.08	1.36	5.11×10^{-3}	0.33	1.30	0.02
Middle frontal gyrus	0.10	1.61	7.75×10^{-3}	0.53	1.67	0.04
Orbital middle frontal gyrus	0.03	0.47	1.07×10^{-2}	0.69	0.46	-0.04
Inferior frontal gyrus	0.07	0.92	6.73×10^{-3}	0.42	0.78	-0.01
Anterior cingulate cortex	0.11	1.76	2.91×10^{-3}	0.19	1.93	0.06
Pooled selectivity	0.10	5.15***	8.42×10^{-3}	1.89	NA	NA

^aTo examine individual subject-specific functional regions of interest (ss-fROIs), multiple linear regressions ($df = 2,29$) were conducted to account for variability associated with age. To examine the whole network within hemisphere, linear mixed effects models ($df = 317$) estimate the effect of selectivity and age on accuracy, with random intercepts by ss-fROI.

^bBonferroni-Holm indicates full model corrected $p < 0.05$ (corrected for 3 parietal or 7 frontal regions). Extended Data Tables 3-1 and 3-2 list the Pearson correlations between accuracy and selectivity of multiple demand (MD) ss-fROIs for children and adults, respectively. Extended Data Table 3-3 lists the main effects of selectivity and age for multiple linear regressions estimating accuracy during easy trials among children.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; strength of significance (uncorrected).

adequately explains variance in performance during Hard trials, regardless of age, for children ages 4–12 years.

Finally, we assess whether the relationship between selectivity and performance differs by group. For all right hemisphere MD ss-fROIs and all but three left hemisphere MD ss-fROIs, we see a significant main effect of group (i.e., adults have higher accuracy than children) and selectivity (i.e., both adults and children who have higher accuracy have higher selectivity), but no ss-fROIs show a significant interaction between group and selectivity (Extended Data Table 5-2). Pooled selectivity within both hemispheres shows a significant interaction between group and selectivity, such that the relationship between selectivity and performance is stronger among children than adults (Extended Data Table 5-2). The main effect of group and the interaction effect (selectivity by group) are also observed in a performance-matched subsample of children ($n = 23$) and adults ($n = 18$; Extended Data Table 5-3) for pooled selectivity within the left hemisphere; only a group main effect is observed for pooled selectivity within the right hemisphere. This result mirrors those reported above regarding the performance by selectivity associations in each group separately (Fig. 4) and the between-group tests of greater selectivity in adults (Extended Data Table 2-2). Thus, MD selectivity seems to reflect individual differences in working memory performance in both children and adults.

Performance by connectivity

In the cross-sectional sample, we observed no correlations between resting-state connectivity (of either hemisphere) and performance (during Hard and Easy trials) for within- ($|R| < 0.26$, p values > 0.05 , Pearson's correlations) or between-network ($|R| < 0.16$, p values > 0.05 , Pearson's correlations) connectivity. In the longitudinal sample, change in connectivity does not explain change in performance, even when accounting for variance explained by

change in age and age at Time point 1 (within-network: $|t| < 0.83$, p values > 0.05 ; between-network: $|t| < 1.16$, p values > 0.05 , multiple linear regressions).

Discussion

Do children process cognitively demanding tasks using the same neural system as adults? As evidenced with visual inspection of our novel probabilistic atlas of children's MD network and with quantitative analysis of MD selectivity within ss-fROIs, we show that children recruit similar regions to adults while engaged in a cognitively demanding task. Although many MD regions already show positive selectivity, we see group differences between motion- and performance-matched child and adult groups, likely reflecting children's immature EF ability. Among children, individual differences in performance are more accurately explained by models, including both age and MD selectivity, than models with age alone. Although we still see a relationship between performance and selectivity among adults, this relationship is weaker, suggesting that neural activation is more reflective of EF ability during childhood, than once individuals are fully matured.

When evaluating resting-state connectivity of ss-fROIs, we observed expected dissociation of the MD and language networks in both children and adults. Although adults show significantly greater within- than between-network connectivity, replicating prior literature (Blank et al., 2014; Malik-Moraleda et al., 2022); we also observe higher within- and between-network connectivity than was observed in these studies. We speculate that global differences (i.e., greater connectivity overall) are because of methodological differences, like instructing participants to fixate on a cross (as we do here) instead of closing their eyes, which produces higher connectivity values (Van Dijk et al., 2010). Additionally, we observed no age effects in connectivity

Table 4. Longitudinal change in selectivity and change in age explaining change in accuracy during hard trials of an SWM task in a subsample of children scanned twice, about 1 year apart ($n = 6$)^a

Accuracy: hard trials	Change in selectivity (t)	Change in age (t)	Age at first scan (t)	Full model (F)
Right hemisphere				
Posterior parietal	0.83	0.84	−0.23	0.50
Superior parietal	0.69	0.70	0.54	0.04
Inferior parietal	3.63	3.48	2.59	1.01
Precentral gyrus	−0.96	−0.38	0.53	0.13
Superior frontal sulcus	−0.20	−0.05	−0.07	0.04
Inferior frontal sulcus	0.30	0.40	−0.08	2.04
Middle frontal gyrus	1.47	1.03	−0.60	0.41
Orbital middle frontal gyrus	0.08	0.29	0.17	0.34
Inferior frontal gyrus	0.41	0.49	0.32	0.03
Anterior cingulate cortex	2.05	2.03	1.70	1.47
Pooled selectivity	1.55	2.04*	1.10	NA
Left hemisphere				
Posterior parietal	1.18	0.62	−0.42	0.27
Superior parietal	0.24	0.36	0.25	0.19
Inferior parietal	1.69	−0.74	−1.30	4.57
Precentral gyrus	−0.54	−0.42	0.33	0.34
Superior frontal sulcus	0.23	0.35	0.26	0.04
Inferior frontal sulcus	2.41	2.13	1.88	0.06
Middle frontal gyrus	1.06	−0.62	−0.77	0.78
Orbital middle frontal gyrus	0.95	0.63	−0.02	0.03
Inferior frontal gyrus	−0.01	0.23	0.16	0.08
Anterior cingulate cortex	0.20	0.38	0.10	0.04
Pooled selectivity	2.12*	1.95	0.53	NA

^aTo examine selectivity of individual ss-fROIs, multiple linear regressions were conducted ($df = 3,2$). To examine pooled selectivity within hemisphere, linear mixed effects models with random intercepts by ss-fROI were conducted.

* $p < 0.05$; strength of significance (uncorrected).

for either sample of children, which deviates from prior neurodevelopmental literature (for review, see Power et al., 2010). This study uses ss-fROIs, which account for individual variability and capture a more personalized evaluation of network connectivity than studies that average activity within larger search-spaces; this may explain differences between our findings and existing literature on the relationship between age and connectivity. Our findings suggest that, in 4- to 12-year-old children, dissociation between MD and language networks is already functionally distinct. These data do not preclude the possibility that larger age effects exist in samples younger than 4 years or across broader age ranges.

Interestingly, although we see differences between children and adults in both hemispheres, the most robust associations between selectivity of MD ss-fROIs and performance (i.e., accuracy) are observed during Hard trials in right MD regions. This may reflect right lateralization during visuospatial processing in adults (Jiang and Kanwisher, 2003; de Schotten et al., 2011; Crittenden and Duncan, 2014). We did not formally assess lateralization in this study and speculate that right lateralization may develop later in development as performance improves, which is consistent with observations of right lateralization in adolescents, but not children (Houdé et al., 2010).

Researchers observe age-related changes in working memory behavioral metrics (i.e., accuracy, reaction time) between children, adolescents, and young adults, such that response time and accuracy show linear negative and positive associations, respectively, with chronological age (Gathercole et al., 2004; Linares et al., 2016). We also observed age-related changes in accuracy and reaction time in the child sample and, therefore, controlled for age when assessing relationships between performance and MD

Table 5. ANOVAs comparing linear mixed effects models (with a random intercept by ss-fROI) that explain variance in accuracy from age or pooled selectivity (within hemisphere) alone to similar linear mixed effects models, including both age and pooled selectivity as explanatory variables^a

Comparison model	Hard trials		Easy trials	
	Age (χ^2)	Selectivity (χ^2)	Age (χ^2)	Selectivity (χ^2)
Right hemisphere				
Pooled selectivity	25.70**	3.60	37.96***	63.08***
Left hemisphere				
Pooled selectivity	58.38***	3.83	16.39**	59.22***

^aSignificant χ^2 reflects that models with age and selectivity explain significantly more variance than models with age or selectivity alone. Extended Data Table 5-1 lists ANOVA results comparing linear regressions and multiple linear regressions for individual ss-fROIs that show a significant multiple linear regression model in Table 3 or Extended Data Table 3-3. Extended Data Tables 5-2 and 5-3 list the main effects of selectivity and age group (child and adult), and the interaction effect, explaining accuracy during hard trials for the full child and adult samples (Extended Data Table 5-2) and for a performance-matched subsample (Extended Data Table 5-3).

** $p < 0.01$; *** $p < 0.001$; strength of significance.

selectivity and connectivity. We found that variability in working memory performance was best explained by models, including both age- and task-dependent neural selectivity, suggesting that neural activity provides additional information about individual differences in EF ability among 4- to 12-year-old children. The relationship between pooled selectivity within hemisphere and accuracy holds in our longitudinal sample; however, we acknowledge that this is a small sample and results should be interpreted with caution.

We also see performance-related increases in selectivity in the adult sample, primarily in right frontal regions. This replicates studies showing an association between individual differences in EF and MD activation in adults (Assem et al., 2020; Mitchell et al., 2022) and is consistent with studies showing that damage to MD regions is linked to cognitive deficits (Warren et al., 2014; Woolgar et al., 2018). In a sample of older children, adolescents, and young adults, Satterthwaite et al. (2013) show a stronger relationship between working memory performance and MD activation than between working memory performance and age. Here we show that this relationship between selectivity to cognitive demand and task performance is also observed in a younger cross-sectional sample and a small longitudinal sample of young children and that selectivity explains variance in performance, beyond that explained by age alone. These results suggest that functional selectivity of the MD network is a potential neural mechanism underlying EF improvement throughout development.

Of note, some studies have found age-related activation changes, but not performance-related changes (e.g., in a sample of 7-22-year-olds engaging in a working memory task) (Kwon et al., 2002) and meta-analytic work including 4- to 17-year-olds engaging in various EF tasks (Houdé et al., 2010). These studies included a wider age range than the current sample, so our findings do not contradict age-related changes when including older participants. Age-related changes across developmental periods are consistent with observed group main effects (i.e., greater adult MD selectivity than children) in our study. Because variability in performance decreases with age (Buczylowska and Petermann, 2018), it is possible that age may account for more variability when including samples spanning developmental periods. Evidence so far suggests that during middle childhood, age may not be the best marker for neural development of cognitive control. We show that MD network selectivity seems an adequate marker of task performance, a proxy for EF ability, during childhood.

Last, we explored whether MD ss-fROIs are already functionally distinct from the adjacent language network. In adults, the MD and language networks are differentiated in both function (Fedorenko et al., 2012, 2013) and resting-state connectivity (Blank et al., 2014). We replicate these findings in adults and extend prior work in children (Satterthwaite et al., 2013), to explore whether this distinction is evident in children. We see greater selectivity for cognitive load than for language in regions functionally localized using the SWM task (i.e., MD ss-fROIs), and we see greater within- than between-network resting-state connectivity for these same MD ss-fROIs compared with ss-fROIs functionally localized using the language task. Both approaches show that, even in young children, we see functional distinction between brain regions recruited for processing cognitive load versus language, suggesting that these networks are already dissociated in childhood, despite ongoing functional reorganization (Power et al., 2010).

Strengths of this study include using two fMRI localizer tasks to define ss-fROIs, which increase power by accounting for individual variability in functional organization. We also analyzed cross-sectional and longitudinal samples of children so that we could evaluate these relationships using different approaches, compare, and draw conclusions based on consistent findings between different designs and statistical tests. Further, we used strict motion-cutoffs, and compare motion- and performance-matched child and adult subgroups to rule out motion and performance as potential confounds, respectively.

Some limitations should be noted. First, we did not assess the association of MD selectivity with out-of-scanner working memory performance. Therefore, our findings may be limited in generalizability because of influences of the scanning environment, as the neural selectivity observed in this study may not accurately represent neural function in more naturalistic situations. Second, substantial motion is observed in child samples, which can produce spurious correlations in fMRI (Power et al., 2012). Because of strict motion cutoffs and comparing motion-matched samples, we believe that observed differences between children and adults are because of maturational differences, and not a motion artifact. However, these findings may not generalize to children who move more during scanning. Third, our child sample engaged in age-appropriate versions of the SWM task, it is possible that group differences are driven by task difficulty. We see similar accuracy (during Hard trials) across age in our child sample (i.e., difficulty of the tasks appropriately engages younger children), suggesting that difficulty does not drive group effects. Fourth, we acknowledge that our longitudinal sample is small and may show low power because of noise; we include them here to offer additional insight to the cross-sectional findings. Last, it is possible that non-MD network regions show selectivity to cognitive demand and could be related to performance (Feilong et al., 2021); future studies can explore other regions and resting-state networks, such as the default mode network, and their selectivity to cognitive demand and dissociation from the MD network.

In conclusion, this study provides evidence that a common neural network underlies processing cognitive demand in children and adults. Although children 4–12 years of age do not yet exhibit fully mature selectivity of the MD network, they show adult-like patterns and performance-related increases in selectivity. These findings further our understanding about neural development underlying improvements in EF. Future studies should explore how recruitment of MD ss-fROIs changes over time in a larger sample that allows evaluation of moderating and

mediating variables. Identifying functional architecture that supports EF across development furthers our understanding of how the human brain processes cognitive demand and how that is related to variability in behavioral performance across developmental periods.

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