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Causal dynamics of memory circuits in mathematical development from childhood to adulthood

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ABSTRACT

Mathematical cognition engages a distributed brain network, but the causal dynamics of information flow within it, particularly how memory circuits interact with other brain regions across development, remain unknown. We examined causal dynamic interactions in typically developing children and adolescents/young adults (AYA) using fMRI during three tasks involving mental arithmetic and symbolic and non-symbolic number comparison. Using multivariate dynamic state-space identification modeling, we found that causal dynamic interactions differed between children and AYA across all three tasks, especially during arithmetic processing. The left medial temporal lobe (MTL) served as a causal signaling hub in AYA across all three tasks, but not in children. The left angular gyrus (AG) maintained consistent hub-like properties during arithmetic task across development. Compared to AYA, children exhibited heightened causal interactions in both the MTL and AG. Moreover, network hub properties of these regions correlated with individual's mathematical achievement specifically during arithmetic processing. Together, we found that the MTL transitioned from heightened, context-dependent, interactions in childhood to a stable causal hub in adulthood, while the AG maintained as a hub during arithmetic processing across development. This dissociation between memory systems, coupled with their task-specific relationship to mathematical abilities, provides novel insights into how brain networks mature to support mathematical cognition.

1. Introduction

Formal mathematical thinking involves multiple cognitive processes that enable us to perform a wide range of tasks, from basic number processing to complex problem solving (Menon, 2016; Menon and Chang, 2021). These mathematical skills are essential for functioning in daily life and professional and academic success (Ritchie and Bates, 2013). While considerable research has focused on the role of parietal and frontal regions in mathematical cognition (Sokolowski, Fias et al., 2017; Arsalidou, Pawliw-Levac et al., 2018; Hawes, Sokolowski et al., 2019), emerging evidence suggests that memory systems also play a crucial role in mathematical processing (Menon, 2016; Peters and Smedt, 2017; Menon and Chang, 2021). Understanding how memory systems interact with other brain regions during mathematical cognition is particularly important because it may reveal how mathematical knowledge is acquired, consolidated, and retrieved – processes that are fundamental to mathematical learning and development. The dynamic interactions between memory systems and other cortical regions involved in numerical cognition across development remain largely unexplored, leaving a critical gap in our understanding of how the brain supports mathematical learning and problem-solving. Investigating these interactions could provide important insights into both typical and atypical mathematical development, potentially informing educational practices and interventions for mathematical learning difficulties.

Recent evidence has revealed the critical involvement of two key memory-related brain systems in mathematical cognition: the medial temporal lobe (MTL) and the angular gyrus (AG). The MTL, traditionally associated with episodic and declarative memory, has emerged as a key component in mathematical processing through converging evidence from multiple methodological approaches and levels of analysis (Chang et al., 2022; Cho et al., 2012; Qin et al., 2014). The AG has long been shown associated with arithmetic processing, especially fact-retrieval

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based arithmetic problem solving (Grabner, Ansari et al., 2009; Grabner, Ansari et al., 2013; Sokolowski, Matejko et al., 2023).

Functional brain imaging studies suggest that the MTL plays a crucial but time-limited role in the early phases of mathematical knowledge acquisition (Menon, 2016; Qin et al., 2014; Rivera et al., 2005), particularly as children transition from procedural strategies to memory-based retrieval strategies in mathematical problem-solving (Cho et al., 2011, 2012). This developmental pattern suggests that a dynamic involvement of the MTL across mathematical skill development. However, the precise mechanisms by which MTL circuits mature and how their role in mathematical cognition evolves across development remain poorly understood.

The involvement of the MTL in mathematical processing extends to fundamental levels of numerical cognition. The activation of this region observed during the mere perception of arithmetic symbols, such as the '+ ' sign, suggests its role in building associations between mathematical operators and problem-solving procedures (Mathieu et al., 2018). This basic-level engagement is complemented by remarkable specificity at the cellular level. Single-neuron recordings in humans have demonstrated that individual MTL neurons can represent both symbolic and non-symbolic numbers with high precision (Kutter et al., 2018) and even discriminate between different arithmetic operations (Kutter et al., 2022). These neurons carry sufficient information to allow statistical classifiers to differentiate between addition and subtraction instructions during mental calculation, suggesting that mathematical operations may rely on neural mechanisms similar to those supporting other forms of memory. While these findings provide crucial insights into the cellular basis of mathematical processing in the MTL, they are inherently limited by their focus on individual brain areas, leaving open questions about how the MTL interacts with broader neural circuits during mathematical cognition.

Beyond investigations of local representations, recent evidence suggests the MTL may serve as a critical hub in the broader mathematical processing network. An intracranial EEG study demonstrated that the MTL functions as a crucial signaling hub during arithmetic problem solving in adults, showing strong outgoing interactions with the intraparietal sulcus (IPS) and ventral temporal occipital cortex (Das and Menon, 2022). However, the generalizability of these findings is constrained by the limited spatial coverage and modest sample sizes inherent in human neurophysiology studies. Moreover, how these causal dynamics might change across diverse mathematical tasks and development in neurotypical populations remains unknown. Understanding such potential task specificity and developmental changes is crucial for building a comprehensive model of how the MTL supports mathematical learning and problem-solving across development.

The AG represents another critical memory-related region implicated in mathematical cognition, particularly in the context of arithmetic fact retrieval (Kadosh and Walsh, 2009). Within the parietal cortex, the AG and IPS have been associated with distinct aspects of numerical cognition: while the IPS has been consistently implicated in the representation and manipulation of quantity and procedural strategy use (Bueti and Walsh, 2009; Menon et al., 2000; Piazza et al., 2007), the AG has been specifically linked to retrieval of arithmetic facts (Grabner et al., 2009; Sokolowski et al., 2023; Tschentscher and Hauk, 2014). However, the precise role of the AG remains debated (Sokolowski et al., 2023). While some studies suggest the AG works in concert with the MTL during fact-retrieval-based arithmetic learning (Fias et al., 2021), others indicate its role during mathematical tasks may be weaker than that of the MTL (Bloechle et al., 2016; Das and Menon, 2022). This discrepancy might reflect the involvement of the AG in broader cognitive functions beyond mathematical processing. Consistent with this view, studies have shown that the AG is involved in various aspects of semantic processing and memory retrieval across multiple cognitive domains (Binder et al., 2009; Kuhnke et al., 2023; Rockland and Graves, 2023), suggesting it may support more general memory retrieval processes than holding a specific role in mathematical cognition.

Considering the interactions of the AG within the larger mathematical processing network may provide critical insights into the specific functional role of this region. While previous studies have examined the activation patterns (Rosenberg-Lee et al., 2011) or functional connectivity (Uddin et al., 2010) of the AG, few have investigated its causal dynamics within the broader network of regions supporting mathematical cognition. Understanding how the AG interacts with other brain regions, particularly the MTL, during mathematical processing could help clarify its specific contribution to mathematical cognition.

By comprehensively examining the dynamic circuits associated with both MTL and AG memory systems in the context of a larger-scale math-related brain network, the current study aimed to clarify our understanding of the roles of these memory systems in mathematical cognition. This approach allows us to directly compare the causal signaling properties of these regions across different mathematical tasks and developmental stages, potentially resolving some of the apparent contradictions in the literature and providing a more nuanced understanding of how different memory systems support mathematical cognition.

To address these gaps in our understanding, we employed a novel multivariate dynamic state-space identification (MDSI) model to examine causal interactions of the MTL and AG within a distributed brain network consistently implicated in mathematical cognition (Fig. 1). The MDSI model provides several key advantages over traditional connectivity analyses: it can estimate directed causal influences between multiple brain regions simultaneously, accounts for the regional differences in hemodynamic response function, and has been rigorously validated using optogenetic stimulation and neuronal simulations (Ryali et al., 2011). This approach allowed us to investigate brain circuits during mathematical processing, overcoming limitations of previous methods. We studied neurotypical children and adolescents/young adults (AYA) using three fMRI tasks: arithmetic verification, which involves math fact retrieval and computation; symbolic number comparison, which requires processing of learned numerical symbols; and non-symbolic number comparison, which engages basic quantity processing. This comprehensive design allowed us to examine how network dynamics differ across fundamental and complex mathematical operations, while also investigating developmental changes in these neural circuits.

Our research goals were fivefold. First, we aimed to examine whether the MTL functions as a causal signaling hub during arithmetic, extending previous iEEG findings to a larger sample and broader network. Second, we investigated whether these dynamics extend to foundational number processing tasks, examining how network interactions vary across different mathematical contexts. Third, we studied developmental changes in network dynamics by comparing school-aged children, who are still acquiring mathematical skills, with AYA who have achieved proficiency. Fourth, we directly compared causal signaling between the MTL and AG across tasks and age groups to understand their differential roles in mathematical cognition. Finally, we examined how the network properties of these regions relate to individual differences in standardized measures of mathematical abilities.

Based on previous findings using intracranial EEG recordings (Das and Menon, 2022), we hypothesized that the MTL would serve as a major causal signaling hub in the mathematical brain network, while the AG might play a relatively limited role. We predicted that network interactions would be modulated by both the type of mathematical knowledge and experience, leading to differences across tasks and age groups. These predictions were based on previous observations of developmental differences in MTL engagement during mathematical processing (Rivera et al., 2005; Peters and Smedt, 2018).

Our study provides novel insights into how memory circuits support mathematical cognition, revealing dynamic and context-specific causal interactions within the mathematical processing brain network. We found that the MTL undergoes a significant developmental shift, transitioning from exhibiting heightened, context-dependent, causal

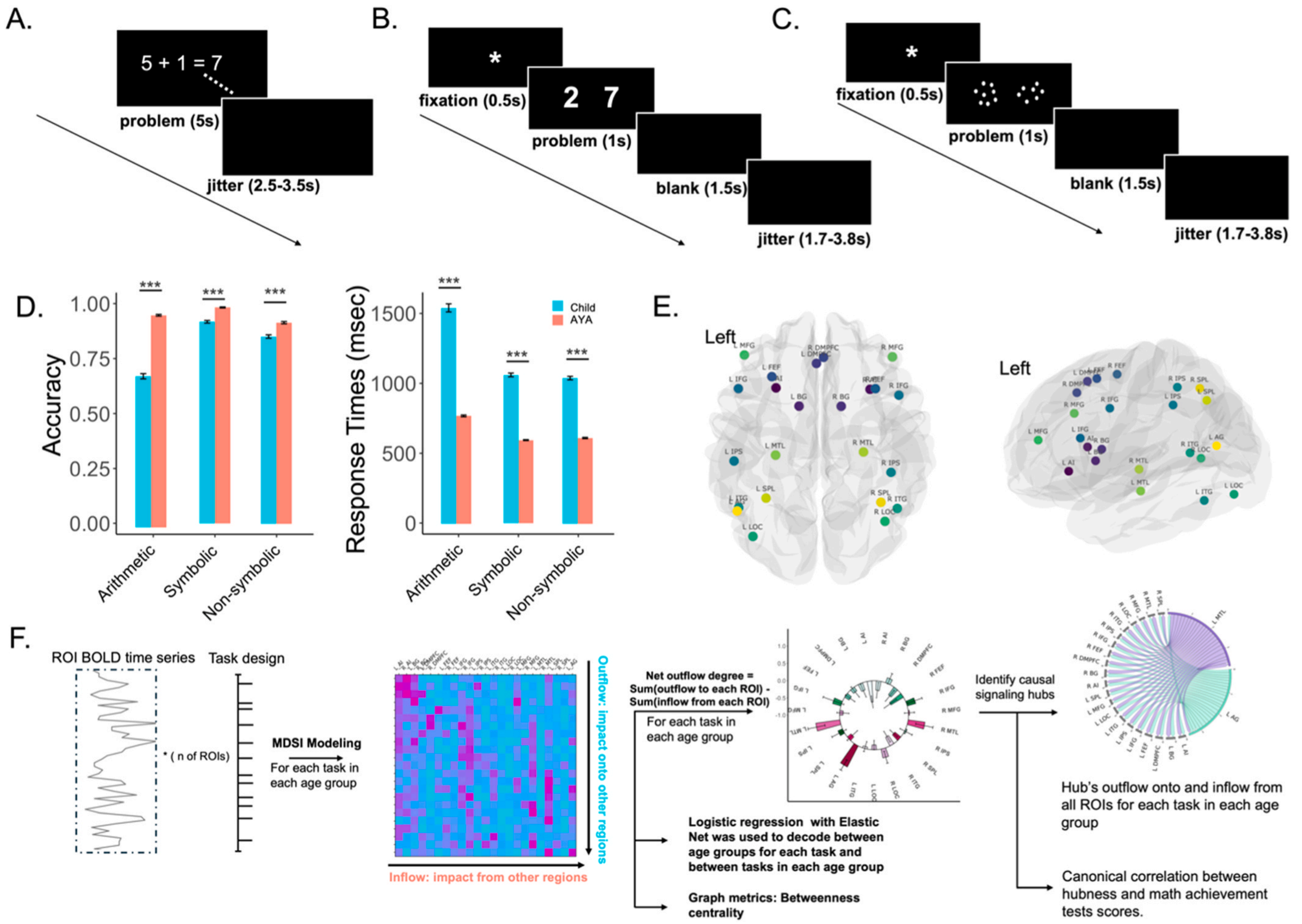

Fig. 1. *Schematic view of task and analysis pipeline.* A. In the arithmetic task, participants were shown an addition equation and were instructed to decide whether the equation was correct or not. Only single digits were used in the equations. B. In the symbolic number comparison task, participants saw a pair of single-digit Arabic numerals and were asked to decide which side had the lager number. The range of numerals was one through nine. C. In the non-symbolic number comparison task, participants saw a pair of dot arrays and decided which side had the larger quantity of dots. The range of dots was from one to nine. The size and total area of the dot arrays were controlled to not correlate with the quantity of dots. D. Behavioral performance of children and adolescents and young adults (AYA) in arithmetic and symbolic and non-symbolic number comparison tasks. Overall, participants were faster and more accurate in number comparison tasks and slower and less accurate in the arithmetic task. AYA performed better than children in all tasks, with the most prominent group difference observed for the arithmetic task. E. An illustration of the 23 regions of interest (ROIs) from a meta-analysis of previous studies on numerical cognition and memory (see details in *Methods*). F. The analysis pipeline of the current study. For each subject in each task, the blood oxygen level dependent (BOLD) time series from each of the 23 ROIs and the task design vector were entered to the multivariate dynamic state-space identification (MDSI) model to estimate the latent dynamic interaction among the 23 ROIs. the MDSI model generated a 23 by 23 causal dynamic matrix with each column indicating the outflow interaction from one ROI to all ROIs and each row indicating the inflow interaction from all ROIs into one ROI. The net outflow degree (NOD) for each ROI was calculated as the difference between the sum of absolute outflow values of each ROI and the sum of absolute inflow values of each ROI. The ROIs with NOD values significantly above zero were defined as the outflow hubs. The outflow and inflow patterns in these hubs and developmental differences were assessed by repeated measures analysis of variance (ANOVA) and paired t-tests. Logistic regression classifiers with Elastic Net were used to determine whether the two age groups were decodable in each task and whether the three tasks were decodable in each age group. Betweenness centrality analysis identified nodes in a network that participated in many shortest paths. Finally, canonical correlation analysis was used to measure the relationship between the NOD of the causal signaling hubs and general math abilities. ***$p < .005$.

interactions in childhood to functioning as a stable causal signaling hub in adulthood. In contrast, the left AG maintained a consistent role as a causal signaling hub specifically during arithmetic processing across development. Our findings suggest that mathematical processing is supported by both specialized numerical systems and general-purpose memory mechanisms, with their relative contributions and interactions changing through development. This integrated view opens new avenues for understanding mathematical learning difficulties and developing targeted interventions and developing targeted interventions that consider both the developmental stage and the specific memory systems involved.

2. Methods

2.1. Participants

Forty-nine children (7–10 years; mean age $= 8.2 \pm 0.7$ years; 27 females) and 48 adolescents and young adults (AYA; 14–21 years; mean age $= 18.3 \pm 1.6$ years; 25 females) participated in the study. Data from 17 child participants and 2 AYA participants were excluded due to excessive head motion during MRI scans (13 children and 2 AYA) or incomplete fMRI task data (4 children). For determining the excessive head motion, we used 3 mm maximum frame-to-frame displacement for children and 1 mm for AYA. The final sample included 32 child participants (7–9 years; mean age $= 8.2 \pm 0.5$ years; 20 females) and 46 AYA participants (14–21 years; mean age $= 18.3 \pm 1.6$ years; 23 females). All participants enrolled in the current study were right-handed. No participants reported neurological, psychiatric, or vision disorders. All adult participants provided written informed consent. For participants under 18 years old, we obtained written informed consents from their parents/legal guardians and assent from the participants. All participants received monetary compensation for their participation. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the institution.

2.2. Tasks

Participants completed three mathematical tasks during fMRI scanning: an arithmetic task, a symbolic number comparison task, and a non-symbolic number comparison task. To maximize data collection, and minimize order effects while maintaining consistency across participants, all participants completed the tasks in the same sequence: arithmetic task run 1, symbolic number comparison task, non-symbolic number comparison task; an additional arithmetic task run 2 was then acquired to ensure that all three tasks had similar number of trials.

2.2.1. Arithmetic task

In the arithmetic task, participants were shown series of addition equations and were instructed to judge whether the equations were correct or not by choosing between two buttons. Each participant completed two runs of the task, with 52 trials in each run and each run lasted 380 s. The task was programmed in Psychopy (Peirce et al., 2019) with a jittered event-related design. In each trial, an equation was presented in a white font at the center of a 1024 × 768 black screen for 5 s and followed by a black blank screen with a duration of either 0, 2.5, or 3.5 s. Participants were allowed to make a response within the 5 s time window. Both operands and the answer in each equation were single-digit Arabic numerals. Within each run, half of the trials were simple problems with one operand being one and the other half were complex problems with both operands greater than one. Half of the trials were presented with the larger operand as the first and the other half with the smaller operand as the first. Moreover, half of the trials were correct equations and the other half were incorrect equations. Finally, the order of the equations was pseudorandomized with each run.

2.2.2. Symbolic number comparison task and non-symbolic number comparison task

In the symbolic number comparison task, participants saw pairs of single-digit Arabic numerals presented side by side and were instructed to pick the side with the larger number by button pressing. Similarly, in the non-symbolic number comparison task, participants viewed pairs of dot arrays presented side by side and needed to judge which side contained more dots by button pressing. The tasks were also programmed in Psychopy (Peirce et al., 2019) with a jittered event-related design. Each comparison task contained one run with 64 trials. In each stimulus, the left number/dot array was always located 40 % away from the left side of the screen and the right number/array was always located 40 % away from the right side. In the non-symbolic number comparison task, the dot size and the total area of the dot array were controlled so neither of the two perceptual dimensions was correlated with the quantity of the dots. The ratio between two numbers or dot arrays varied between 1.125, 1.17, 1.33, 2, 2.25, 2.67, 3.5, 6 across all trials. Each trial started with a green fixation (a "*") for 0.5 s, followed by two numbers or two dot arrays were shown in green color on a 1024 × 768 black screen for 1 s a black blank screen for 1.5 s, and a jitter screen between 1.7 and 3.8 s. Each task lasted for 362 s. In each task, there were 16 unique pairs of quantities and each of them was repeated 4 times, resulting in 64 trials in total.

2.3. MRI data acquisition and preprocessing

Task-based functional MRI data were acquired on a 3 T GE scanner using a T2* weighted gradient echo-spiral in-out pulse sequence (TR=2000 msec, TE=30 msec, FOV = 220 mm^2, matrix size = 64 × 64, pixel size = 3.4375 mm, slice thickness = 4 mm, flip angle = 80 degree). A T1- weighted, high-resolution structural image was acquired for the anatomical co-registration of functional images (slice thickness 1 mm; in-plane resolution: 256 × 256, voxel size = 1.5 × 0.9 × 1.1 mm^3). All functional images were preprocessed using SPM12 (Ashburner et al., 2020). The first five volumes of each time-series were discarded to allow for signal equilibration. The preprocessing pipeline included realignment, slice-timing correction, co-registration to subjects' structural T1 images and normalization to a 2 mm MNI152 template, and smoothing using a 6 mm full-width half-maximum Gaussian kernel to decrease spatial noise. The proportion of volumes with scan-to-scan displacement higher than 0.5 voxel did not exceed 10 % across tasks. Movement did not exceed 3 mm in any rotational and translational axes. Mean scan-to-scan displacement did not exceed 0.5 mm (See ***S1 Table*** for detailed descriptive statistics). To account for potential influences of unmatched head motion between groups, head motion parameters were included as covariates of no interest in fMRI general linear model analysis.

To rule out data quality degradation as a confound, we examined head motion parameters between children and AYA groups across tasks. While children exhibited higher head motion than AYA, motion did not differ across tasks within either group, with no group × task interaction (see ***Supplementary Results).*** We also calculated temporal signal-to-noise ratio (tSNR) (Krüger and Glover, 2001) to assess potential age-related data quality differences. Analysis revealed minimal impact of tSNR on our main findings (see Supplementary Materials); consequently, tSNR was not included as a covariate in main analyses

2.4. ROI selection

Our math-related brain network included 11 bilateral brain regions consistently activated during numerical cognition and learning in children (Butterworth and Walsh, 2011; De Smedt et al., 2011; Cho et al., 2012; Qin et al., 2014; Hannagan et al., 2015; Nieder, 2016; Piazza and Eger, 2016; Arsalidou et al., 2017; Peters and Smedt, 2017), which included 9 bilateral cortical regions identified using Neurosynth (Yarkoni, Poldrack et al., 2011)-based meta-analysis, using term "arithmetic." The cortical regions included: bilateral intraparietal sulcus, superior parietal lobule, anterior insula, middle frontal gyrus, inferior frontal gyrus, dorsal medial prefrontal cortex, frontal eye field, inferior temporal gyrus, and lateral occipital cortex. In addition, bilateral MTL and basal ganglia regions, shown to be important for learning math facts (De Smedt et al., 2011; Cho et al., 2012; Qin et al., 2014; Peters and Smedt, 2017) and procedural knowledge in arithmetic (Geary and Hoard, 2001; Rivera et al., 2005; Supekar et al., 2013) in children, were included. The hippocampus and the caudate, the primary region of the MTL and the basal ganglia (Packard and Knowlton, 2002), respectively, were identified from Neuroquery (Dockes et al., 2020)-based meta-analysis, using terms "declarative memory" and "procedural memory." In addition to these 22 math-related brain regions, we included the left angular gyrus from the most recent meta-analytic work by Sokolowski et al. (2023) to consider its prominent role in number and arithmetic processing.

2.5. MDSI model for estimating causal interactions from fMRI data

MDSI estimates context-dependent causal interactions between multiple brain regions in latent quasi-neuronal states while accounting for variations in hemodynamic responses in these regions. MDSI has been validated using extensive simulations (Ryali et al., 2011; Ryali et al., 2016) and has been successfully applied to our previous studies (Cai et al., 2021; Cho et al., 2012). MDSI models the multivariate fMRI time series by the following state-space equations:

$$\boldsymbol{s}(t) = \sum_{j=1}^{J} v_j(t) C_j \boldsymbol{s}(t-1) + \boldsymbol{w}(t) \tag{1}$$

$$\boldsymbol{x}_m(t) = [\boldsymbol{s}_m(t) \quad \boldsymbol{s}_m(t-1) \ldots \boldsymbol{s}_m(t-L+1)]' \tag{2}$$

$$y_m(t) = b_m \Phi \boldsymbol{x}_m(t) + \boldsymbol{e}_m(t) \tag{3}$$

In Eq. (1), $\boldsymbol{s}(t)$ is a $M \times 1$ vector of latent quasi-neuronal signals at time t of M regions, C_j is an $M \times M$ connection matrix ensued by modulatory input $v_j(t)$, J is the number of modulatory inputs. The non-diagonal elements of C_j represent the coupling of brain regions in the presence of modulatory input $v_j(t)$. $C_j(m,n)$ denotes the strength of causal connection from n-th region to m-th region for j-th type stimulus. Therefore, latent signals $\boldsymbol{s(t)}$ in M regions at time t is a bilinear function of modulatory inputs $v_j(t)$, corresponding to deviant or standard stimulus, and its previous state $\boldsymbol{s(t\text{-}1)}$. $\boldsymbol{w}(t)$ is an $M \times 1$ state noise vector whose distribution is assumed to be Gaussian distributed with covariance matrix $Q(\boldsymbol{w}(t) \sim N(0,Q))$. Additionally, state noise vector at time instances $1,2,\ldots,T(\boldsymbol{w}(1), \boldsymbol{w}(2) \ldots \boldsymbol{w}(T))$ are assumed to be identical and independently distributed (iid). Eq. (1) represents the time evolution of latent signals in M brain regions. More specifically, the latent signals at time t, $\boldsymbol{s}(t)$, is expressed as a linear combination of latent signals at time t-1, external stimulus at time t ($u(t)$), bilinear combination of modulatory inputs $v_j(t), j = 1, 2..J$ and its previous state, and state noise $\boldsymbol{w}(t)$. The latent dynamics modeled in Eq. (1) gives rise to observed fMRI time series represented by Eqs. (2) and (3).

We model the fMRI time series in region *"m"* as a linear convolution of hemodynamic response function (HRF) and latent signal $\boldsymbol{s}_m(t)$ in that region. To represent this linear convolution model as an inner product of two vectors, the past L values of $\boldsymbol{s}_m(t)$ are stored as a vector. $\boldsymbol{x}_m(t)$ in Eq. (2) represents an $L \times 1$ vector with L past values of latent signal at m-th region.

In Eq. (3), $y_m(t)$ is the observed BOLD signal at t of m-th region. Φ is a $p \times L$ matrix whose rows contain bases for HRF. b_m is a $1 \times p$ coefficient vector representing the weights for each basis function in explaining the observed BOLD signal $y_m(t)$. Therefore, the HRF in *m-th* region is represented by the product $b_m \Phi$. The BOLD response in this region is obtained by convolving HRF ($b_m \Phi$) with the L past values of the region's latent signal ($\boldsymbol{x}_m(t)$) and is represented mathematically by the vector inner product $b_m \Phi \boldsymbol{x}_m(t)$. Uncorrelated observation noise $\boldsymbol{e}_m(t)$ with zero mean and variance σ_m^2 is then added to generate the observed signal $y_m(t)$. $\boldsymbol{e}_m(t)$ is also assumed to be uncorrelated with $\boldsymbol{w}(\tau)$, at all t and τ. Eq. (3) represents the linear convolution between the embedded latent signal $\boldsymbol{x}_m(t)$ and the basis vectors for HRF. Here, we use the canonical HRF and its time derivative as bases, as is common in most fMRI studies.

Eqs. (1)–(3) together represent a state-space model for estimating the causal interactions in latent signals based on observed multivariate fMRI time series. Furthermore, the MDSI model also takes into account variations in HRF as well as the influences of modulatory and external stimuli in estimating causal interactions between the brain regions.

Estimating causal interactions between M regions specified in the model is equivalent to estimating the parameters $C_j, j = 1, 2..J$. In order to estimate C_j's, the other unknown parameters Q, $\{b_m\}_{m=1}^{M}$ and $\{\sigma_m^2\}_{m=1}^{M}$ and the latent signal $\{\boldsymbol{s}(t)\}_{t=1}^{T}$ based on the observations $\{y_m^s(t)\}_{m=1,s=1}^{M,S}, t = 1, 2..T$, where T is the total number of time samples and S is number of subjects, needs to be estimated. We use a variational Bayes approach (VB) for estimating the posterior probabilities of the unknown parameters of the MDSI model given fMRI time series observations for S number of subjects. The statistical significance of the parameters is assessed by examining the posterior probabilities of the parameters $C_j, j = 1, 2..J$ at a given level of significance.

2.6. State-space analysis of dynamic causal interactions

To prepare data for MDSI analysis, the fMRI time-series from each ROI and participant were first linearly de-trended and then normalized by its standard deviation. For all ROIs, time-series were extracted using the MarsBar toolbox in SPM12. Spherical ROIs were defined as the sets of voxels contained in 6 mm (diameter) spheres centered on the MNI coordinates of each ROI. MDSI was applied to estimate directed causal interactions among 23 nodes separately in the three tasks (non-symbolic, symbolic, arithmetic) and two groups (children, AYA).

To characterize the causal network interactions generated by MDSI, we first evaluated net causal influences of each node and determined causal outflow from each node in the three tasks and two groups. Specifically, we computed the outflow degree of each node in each task and participant by subtracting averaged inflow weights (all the input connections to a node from all other nodes) from averaged outflow weights (all the output connections from a node to all other nodes). The outflow degree was referred as the net outflow degree (NOD) of each node.

2.7. Graph-theoretical analysis

Additionally, we computed betweenness centrality of each node in each task and participant. Betweenness centrality measures how often a node lies on the shortest path between all pairs of nodes in a network. While a node with high degree has many direction connections, a node with high betweenness centrality acts as a bridge between other nodes in the network (Rubinov and Sporns, 2010).

2.8. Multivariate classification analysis of dynamic causal interactions between groups and between tasks

To determine whether causal networks associated with the three tasks differ between children and AYA during each task, we used the causal network patterns in the two groups. The dynamic causal interaction patterns – MDSI weights of 253 pairs of anatomical regions – were used as the input (features) to a linear logistic regression classifier with Elastic Net. The Elastic Net combined feature elimination from Lasso and feature coefficient reduction from Ridge, and as a result, features with low importance were assigned zero weights. K-fold cross-validation ($K = 4$) was used to measure the performance of the classifier in distinguishing children and AYA. In k-fold, one-fold is used for testing the classifier that is trained using the remaining k-1 folds. This process is repeated K times. These analyses were performed using the scikit-learn package (https://scikit-learn.org/), which is a python-based package for machine learning. Permutation tests (5000 permutations of class labels) were conducted to arrive at p-values associated with classification accuracy.

To examine whether causal networks associated with the three tasks differ in each group, we applied the aforementioned analysis to the MDSI estimated causal networks during the arithmetic, symbolic, and non-symbolic tasks for each group.

2.9. Statistical analysis

To examine how task performance was modulated by group and task, we performed a two-way mixed measures analysis of variance (ANOVA) on accuracy and latency separately, with the between-subject factor Group (Children vs AYA) and within-subject factor Task (Non-symbolic vs Symbolic vs Arithmetic). Upon significant Group by Task interaction, post-hoc paired t-tests and two-sample t-tests were performed.

To identify causal outflow and inflow hubs, we performed a one-sample t-test on causal outflow for each node and results were FDR-corrected. In order to examine how outflow and inflow hubs were modulated by group and task, for each hub region we performed a two-way mixed measures ANOVA with the between-subject factor Group and within-subject factor Task. Upon significant Group by Task interaction, post-hoc paired t-tests and two-sample t-tests were performed.

To examine how betweenness centrality was modulated by group and task, for each hub region we performed a two-way mixed measures ANOVA with the between-subject factor Group and within-subject factor Task. Upon significant Group by Task interaction, post-hoc paired t-tests and two-sample t-tests were performed.

2.10. Canonical correlation analysis (CCA)

We used canonical correlation to examine the relation between the NOD of the causal signaling hubs and children and AYA's math skills. For the math skills, the participants were tested with the Woodcock-Johnson III Test of Cognitive Abilities (WJ III; Schrank, 2011). Specifically, we used the Calculation, Math Fluency, and Applied Problems subtests to test the arithmetic and math problem solving abilities. In the CCA, the NOD of the causal signaling hubs was entered as one set of variables and the three WJ III math subtest scores were entered as the second set of variables. The CCA tries to find the optimal linear combination (variate) of the two sets of variables that can maximize the correlation between the two variables. We set the CCA to estimate two variates for each variable. After the CCA converged, we calculated the Pearson correlation between the first variate of the NOD and the first variate of the math scores to get the CCA correlation coefficients. The CCA was first implemented in each age group and each task respectively. We then tested the slopes of the correlations. Specifically, we used the formula below to test the slope difference between children and AYA in each task respectively.

$$t = \frac{b_1 - b_2}{\sqrt{SE_1^2 + SE_2^2}} \tag{4}$$

In this formula, b_1 and b_2 denote the slope of each correlation. SE_1 and SE_2 denote the standard error of the slopes. The *degree of freedom* was the total sample ($n = 78$) minus 4 (two for the slopes and two for the intercepts), which is 74. We also combined the two age groups and tested the CCA between the NOD of the left MTL and left AG and math scores in all participants.

3. Results

3.1. Behavior

We examined whether children and adolescents and young adults (AYA) performed at different levels on arithmetic and symbolic and non-symbolic number comparison tasks (Fig. 1A-C). In a 2 (age: children, AYA) x 3 (task: arithmetic, symbolic number comparison, non-symbolic number comparison) analysis of variance (ANOVA), the main effect of age and task as well as interaction between age and task were significant for both accuracy and response times (RT) (Fig. 1D). Specifically, children were less accurate and slower than AYA across all tasks (accuracy: $F(1,76) = 111.5$, $p < .001$; RT: $F(1,76) = 71.91$, $p < .001$). Both age groups were most accurate in the symbolic number comparison task ($F(2152) = 17.94$, $p < .001$) and the slowest in the arithmetic task ($F(2152) = 73.76$, $p < .001$). The difference in accuracy or RT between children and AYA was greatest for the arithmetic task (accuracy: $F(2152) = 21.44$, $p < .001$; RT: $F(2152) = 31.15$, $p < .001$). These findings indicate that AYA performed better than children on all tasks, with the most prominent improvements on arithmetic problem solving.

3.2. Developmental changes in causal network interactions in arithmetic and number comparison tasks

To address our main question about whether causal network interactions during math problem solving change across development, we examined whether children and AYA showed different dynamic interaction patterns in the brain network consisted of 23 regions of interest (ROIs) obtained from Neurosynth-based meta-analysis and previous empirical work (De Smedt et al., 2011, Cho et al., 2012, Qin et al., 2014, Arsalidou et al., 2017, Peters and Smedt, 2017, Supekar et al., 2021, Chang et al., 2022, Sokolowski et al., 2023) (see **Methods** and Fig. 1E). We applied a Logistic Regression classifier with the Elastic Net regularization in the multivariate dynamic state-space identification (MDSI) modeling to classify children and AYA in arithmetic, symbolic number comparison, and non-symbolic number comparison tasks (Fig. 1F; Fig. 2A-B, E-F, and I-J). We found that the classification accuracy was the highest in the arithmetic task (*decoding accuracy* = 76.97 %, permutation $p < .001$; Fig. 2C), followed by the non-symbolic number comparison task (*decoding accuracy* = 62.96 %, permutation $p < .001$; Fig. 2K) and the symbolic number comparison task (*decoding accuracy* = 56.45 %, permutation $p < .001$; Fig. 2G). Children and AYA differed more in the dynamic interaction in the math-related brain network for more complex task (arithmetic) and were less distinguishable for simpler tasks (number comparison).

3.3. Causal network dynamics differ between math tasks

We applied Logistic Regression classifier with Elastic Net to examine whether the causal dynamics among the math brain network differed between the three tasks in children and AYA respectively. We found successful between task decoding in children (*decoding accuracy* = 38.54 %, permutation $p < .001$; chance level is 33 %) and AYA (*decoding accuracy* = 46.34 %, permutation $p < .001$; chance level is 33 %), suggesting that causal network dynamics differed between math tasks in both children and AYA. The decoding accuracy seems lower in children than AYA, which might suggest that the network dynamics are less distinguishable when the math skills are premature.

3.4. Causal signaling hubs in the arithmetic task

Our next goal was to examine whether the MTL or any other brain region plays the role of causal signaling hub during arithmetic task performance. Specifically, we measured the causal outflow of each brain region in the MDSI model by estimating the sum of absolute values of causal interactions from the brain region of interest to all other brain regions. Similarly, the causal inflow of each brain region in the model was measured as the sum of absolute values of causal interactions from all other brain regions into the brain region of interest. The net outflow degree (NOD) was estimated as the causal outflow minus the causal inflow. Positive values indicated more outgoing (than incoming) interactions and negative values indicated more incoming (than outgoing) interactions. Here, we defined brain regions with significantly higher than zero NOD as causal signaling hubs.

A repeated measures ANOVA of age (children, AYA) x ROIs showed a significant main effect of ROI on the NOD during the arithmetic task ($F(22, 1672) = 1.93$, $p = .006$; Fig. 3A), which suggests the outflow-inflow profile was different across all regions. No significant main effect of age or age by ROI interaction was observed ($F(1,76) < .001$, $p > .99$).

3.4.1. The role of MTL as a causal signaling hub

We next examined the NOD of the MTL in each age group (children and AYA). In children, planned t-test yielded no significant NOD in the left or right MTL during the arithmetic task ($ts < 1.4$, $ps > .16$; Fig. 3A, left panel). In AYA, we found that the left MTL had positive NOD in the math-related brain network during the arithmetic task ($t(45) = 3.12$, $p = .003$; Fig. 3A, middle panel). Additional analysis of the NOD in the right MTL was not significantly greater than zero ($t(45) = 1.63$, $p = .10$). A direct comparison of the NOD between children and AYA showed a significant age difference in the left MTL ($t(1,76) = 3.10$, $p = .003$; Fig. 3A, right panel). These findings suggest developmental changes in the causal dynamic interactions of the left MTL from receiving more interaction in childhood to causal signaling other regions in the math-related brain network in adolescence and young adulthood.

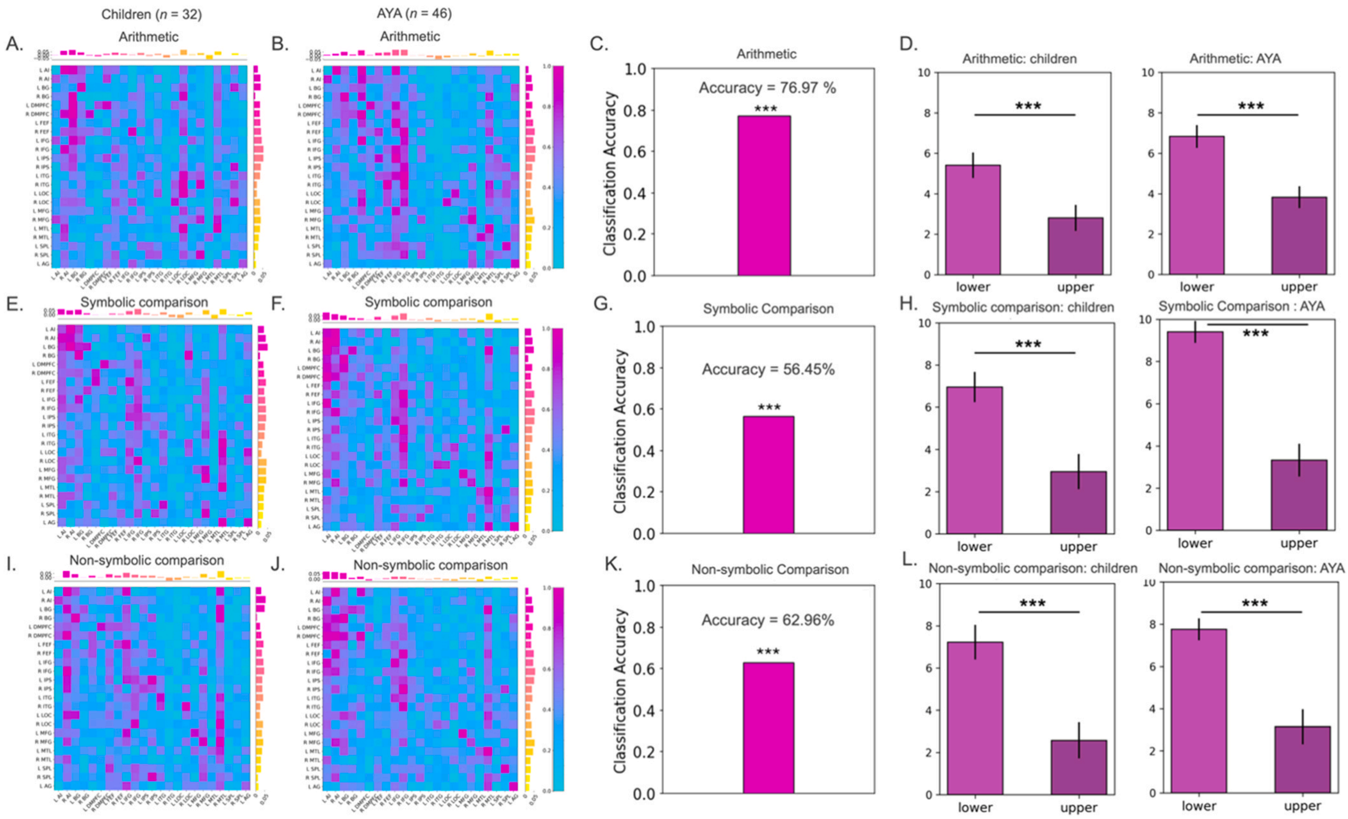

Fig. 2. *Dynamic interactions among the regions in the math brain network in differed between children (left column) and AYA (right column).* In each heatmap, each column represents the outgoing interaction from one region to other regions. Each row represents the incoming interaction from other regions into one region. The bar plots on the top and right side of each heat map show the sum of each column and row. Logistic regression classifications with Elastic Net regularization indicated successful decoding between children and AYA in all tasks. A-B. The MDSI causal dynamic matrix in (A) children and (B) AYA in the arithmetic task. C. The Logistic regression classification accuracy in the arithmetic task. D. The lower triangle of the MDSI causal dynamic matrix has higher summed value than the upper triangle in both children (left panel) and AYA (right panel) in the arithmetic task, indicating asymmetric outgoing and incoming causal interactions. E-F. The MDSI causal dynamic matrix in (E) children and (F) AYA in the symbolic number comparison task. G. The Logistic regression classification accuracy in the symbolic number comparison task. H. The lower triangle of the MDSI causal dynamic matrix has higher summed value than the upper triangle in both children (left panel) and AYA (right panel) in the symbolic number comparison task. I-J. The MDSI causal dynamic matrix in (I) children and (J) AYA in the non-symbolic number comparison task. K. The Logistic regression classification accuracy in the non-symbolic number comparison task. L. The lower triangle of the MDSI causal dynamic matrix has higher summed value than the upper triangle in both children (left panel) and AYA (right panel) in the non-symbolic number comparison task. ***$p < .005$.

3.4.2. The role of AG and other math-related brain regions as causal signaling hubs

While the MTL was found to be a causal signaling hub in AYA, the left AG was a causal signaling hub in both children ($t(31) = 2.38$, $p = .02$; Fig. 3A, left panel) and AYA ($t(45) = 4.06$, $p < .001$; Fig. 3A, middle panel). The NOD in the left AG was not significantly different between children and AYA (t(1,76) = -0.71, $p = 0.48$; Fig. 3A, right panel). No other brain regions were identified as causal signaling hub in either group (*ts*<1.63, FDR corrected *ps* >.32).

These findings suggest that the MTL emerged as a causal signaling hub during arithmetic task performance later in development, whereas the left AG was a stable causal signaling hub across developmental stages.

3.5. Causal signaling hubs in the symbolic number comparison task

Our next goal was to extend the examination of the causal signaling hubs to more fundamental number comparison tasks. We first examined the symbolic number comparison task. In a repeated measures 2 (age: children, AYA) x 23 (23 ROIs) ANOVA, the main effect of ROI on the NOD was significant ($F(22, 1672) = 1.65$, $p = .03$; Fig. 3B). No significant main effect of age or age by ROI interaction was observed (*Fs* < 1.33, *ps* >.14).

3.5.1. The role of MTL as a causal signaling hub

We next examined the NOD of the MTL in each age group and assessed developmental difference. In children, neither the left or right MTL showed the NOD significantly greater than zero during the symbolic number comparison task, though the MTL had positive NOD (*ts* < 1.50, *ps* >.30; Fig. 3B, left panel). In AYA, the left MTL was the causal signaling hub ($t(45) = 3.44$, $p = .001$; Fig. 3B, middle panel). The NOD in the right MTL, while positive, was not greater than zero ($t(45) = 1.71$, $p = .09$). No significant difference between children and AYA was observed in the NOD of either the left or right MTL (*ts* < 1.14, *ps* >.25; Fig. 3B, right panel). These findings suggest a weaker developmental difference in the MTL as the causal signaling hub for the symbolic number comparison, compared to the arithmetic task, which showed a significant developmental difference.

3.5.2. The role of AG and other math-related brain regions as causal signaling hubs

The AG was not identified as causal signaling hub in either group (*ps* >.30). In children, several other brain regions had positive NOD, including the right frontal eye field, right dorsomedial prefrontal cortex, left lateral occipital cortex, and left inferior temporal gyrus. However, the NOD in these regions were not significantly greater than zero (*ts*< 2.01, FDR corrected *ps*>.34). In AYA, we did not find any other causal signaling hub, beyond the left MTL, with significantly greater than zero

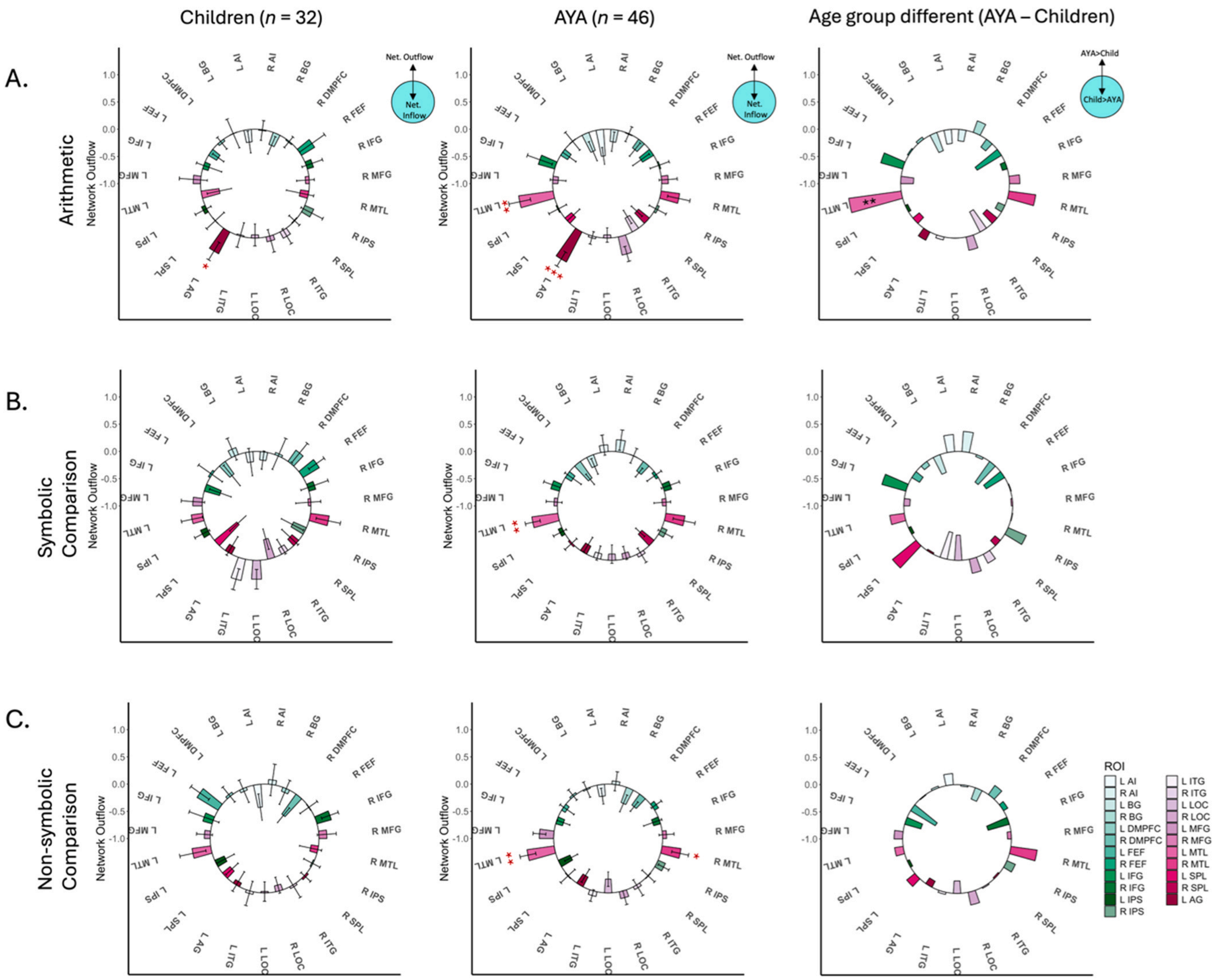

Fig. 3. Net outflow and inflow degree in children and AYA in arithmetic and symbolic and non-symbolic number comparison tasks. A. Net outflow and inflow pattern in children and AYA in the arithmetic task. The left AG had significant net outflow degree (NOD) than other brain regions in children (*left panel*). In AYA, the left MTL and AG were identified as causal signaling hubs (*middle panel*). Significant age difference was observed in the left MTL (*right panel*). B. Net outflow and inflow pattern in children and AYA in the symbolic number comparison task. In children, the outflow causal signaling was distributed across regions in the right MTL, right DMPFC, right FEF, left ITG, and left LOC (*left panel*). However, none of these regions appeared to have NOD significantly higher than zero. The left MTL played a role as an outflow hub in AYA (*middle panel*). No main effect of age or age by ROI interaction was found (*right panel*). C. Net outflow and inflow pattern in children and AYA in the non-symbolic number comparison task. In children, the left FEF, left MTL, and right IFG had relatively greater outflow causal signaling than other regions (*left panel*). However, none of these regions appeared to have NOD significantly higher than zero. The bilateral MTL were the outflow hubs in AYA (*middle panel*). No main effect of age or age by ROI interaction was found (*right panel*). Note: In the left and middle column, bars pointing outside the ring represent outflow and bars pointing inside the ring represent inflow. In the right column, bars pointing outside the ring represent network outflow greater in AYA than children and bars pointing inside the ring represent network outflow greater in children than AYA. AG: angular gyrus. DMPFC: dorsomedial prefrontal cortex. FEF: frontal eye field. IFG: inferior frontal gyrus. ITG: inferior temporal gyrus. LOC: lateral occipital cortex. MTL: medial temporal lobe. $^{*}p < .05$, $^{**}p < .01$.

NOD ($ts < 1.70$, FDR corrected $ps > .43$).

These findings suggest that the MTL was as a causal signaling hub during symbolic number comparison later in development. However, direct comparison between age groups indicated that developmental changes in the MTL was not significant.

3.6. Causal signaling hubs in the non-symbolic number comparison task

Finally, we investigated the causal signaling hubs in the non-symbolic number comparison task. The 2 (age: children, AYA) x 23 (23 ROIs) repeated measures ANOVA yielded a main effect of ROI on the weighted causal outflow ($F(22,1672) = 1.94$, $p = .005$; Fig. 3C). No significant main effect of age or age by ROI interaction was observed ($Fs < 0.85$, $ps > .66$).

3.6.1. The role of MTL as a causal signaling hub

We next examined the NOD of the MTL in each age group and assessed developmental difference. In children, the NOD in the left MTL, while positive, was not significantly higher than zero ($t(31) = 1.39$, $p = .17$). The NOD in the right MTL was also not significantly higher than zero ($t(31) = -.65$, $p = .51$). In AYA, bilateral MTL were found as the causal signaling hubs (left MTL: $t(45) = 3.37$, $p = .002$; right MTL: $t(45) = 2.21$, $p = .03$; Fig. 3C, middle panel). The NOD in bilateral MTL was not significantly different between children and AYA ($ts < 1.89$, $ps > .06$; Fig. 3C, right panel). These findings suggest a weaker developmental difference in the MTL as the causal signaling hub for the non-symbolic number comparison, compared to the arithmetic task, which showed a significant developmental difference.

3.6.2. The role of AG and other math-related brain regions as causal signaling hubs

The AG was not identified as causal signaling hub in either group (*ps* >.40) in the non-symbolic number comparison task. No other brain regions had significantly higher than zero NOD in either children or AYA (ts< 2.23, FDR corrected ps>.19). No significant difference between groups was observed for the NOD in the rest of the ROIs (ts<2.07, FDR corrected ps>.73).

Together, our causal signaling hub analysis shows that the left MTL was a stable causal signaling hub in AYA across arithmetic and symbolic and non-symbolic number comparison tasks. The right MTL was identified as the causal signaling hub in AYA only in the non-symbolic number comparison task. In children, the NOD in the bilateral MTL was not significantly higher than zero in any of the tasks. The developmental difference in the NOD of the MTL was significant in the arithmetic task but not in the symbolic or non-symbolic number comparison task, which suggests the differential role of the MTL across development was context dependent. Moreover, we observed that the left AG was a major causal signaling hub in the arithmetic task but not in symbolic or non-symbolic comparison tasks in both children and AYA, which is consistent with findings of the involvement of AG in arithmetic tasks (Grabner et al., 2009; Sokolowski et al., 2023).

3.7. Outflow and inflow in the left MTL during arithmetic and number comparison tasks in children and AYA

Our next series of analyses examined the level of outflow and inflow for each task in each age group in the left MTL, which was consistently shown as the causal signaling hub across arithmetic and number comparison tasks in AYA. We calculated the outgoing and incoming dynamic interaction in the MTL and examined whether the outflow/inflow pattern differed between age groups in the three tasks (Figs. 4 and 5).

3.7.1. Outflow in the left MTL

We found a significant age difference between children and AYA across the tasks for the outflow in the left MTL ($F(1,76) = 7.28$, $p = .008$). No significant main effect of task ($F(2152) = .37$, $p > .05$) or task by age interaction ($F(2152) = .38$, $p > .05$) was found. Follow-up *t*-test showed a significant developmental difference in the arithmetic verification task ($t(1,76) = 2.53$, $p = .01$). Children had higher outflow in the left MTL than AYA in the arithmetic task (Fig. 4D). The developmental differences in the symbolic and non-symbolic number comparison tasks did not reach significance (*ts* <1.65, *ps* >.10).

3.7.2. Inflow in the left MTL

For the inflow in the left MTL, a significant main effect of age was observed ($F(1,76) = 22.79$, $p < .001$). We also found an age by task interaction ($F(2152) = 3.97$, $p = .02$). The age difference was larger in the arithmetic verification task than in symbolic or non-symbolic number comparison tasks. No significant main effect of task ($F(2.152) = 1.13$, $p > .05$) was observed. Follow-up *t*-tests showed significant developmental differences in all three tasks (*ts* > 2.13, *ps* <.04). Children had higher inflow than AYA in the left MTL in all three tasks (Fig. 5D).

Combining with the finding that the NOD (i.e. outflow – inflow) in the left MTL was lower in children than in AYA, especially in the arithmetic task, these results suggest that both outflow and inflow are enhanced in children, leading to diminished net outflow in the left MTL.

3.8. Outflow and inflow in the left AG during arithmetic and number comparison tasks in children and AYA

As the left AG was identified as the outflow hub in the arithmetic task in both age groups, we examined the levels of outflow and inflow in the left AG in both age groups in each task.

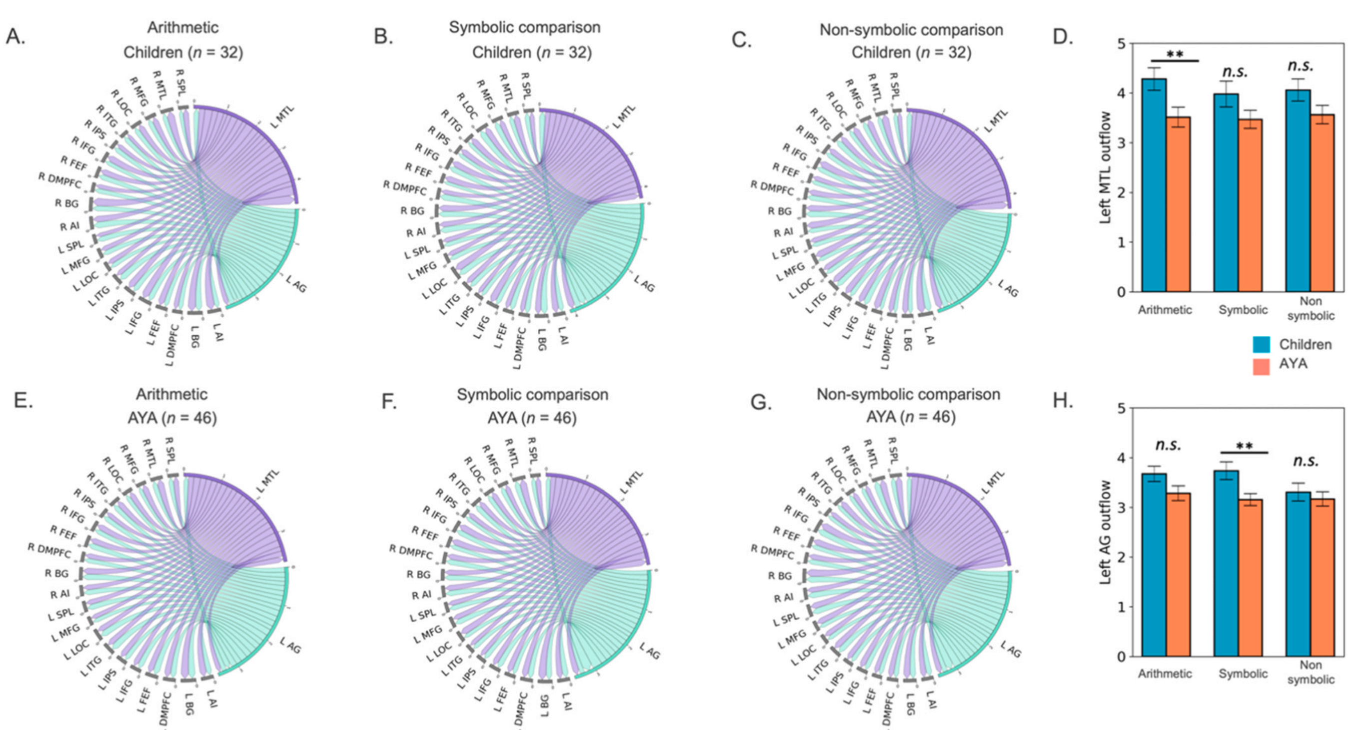

Fig. 4. Outflow causal signaling from all the regions of interest into the left MTL (purple) and left AG (mint green). A-C. The outflow causal signaling in the left MTL and left AG in (A) arithmetic, (B) symbolic number comparison, and (C) non-symbolic number comparison tasks in children. D. Children had significantly higher outflow than AYA in the left MTL in the arithmetic task. E-G. The outflow causal signaling in the left MTL and left AG in (E) arithmetic, (F) symbolic number comparison, and (G) non-symbolic number comparison tasks in AYA. H. Children had significantly higher outflow than AYA in the symbolic number comparison task. *p < .05, **$p < .01$, *n.s.*, not significant, $p > .05$.

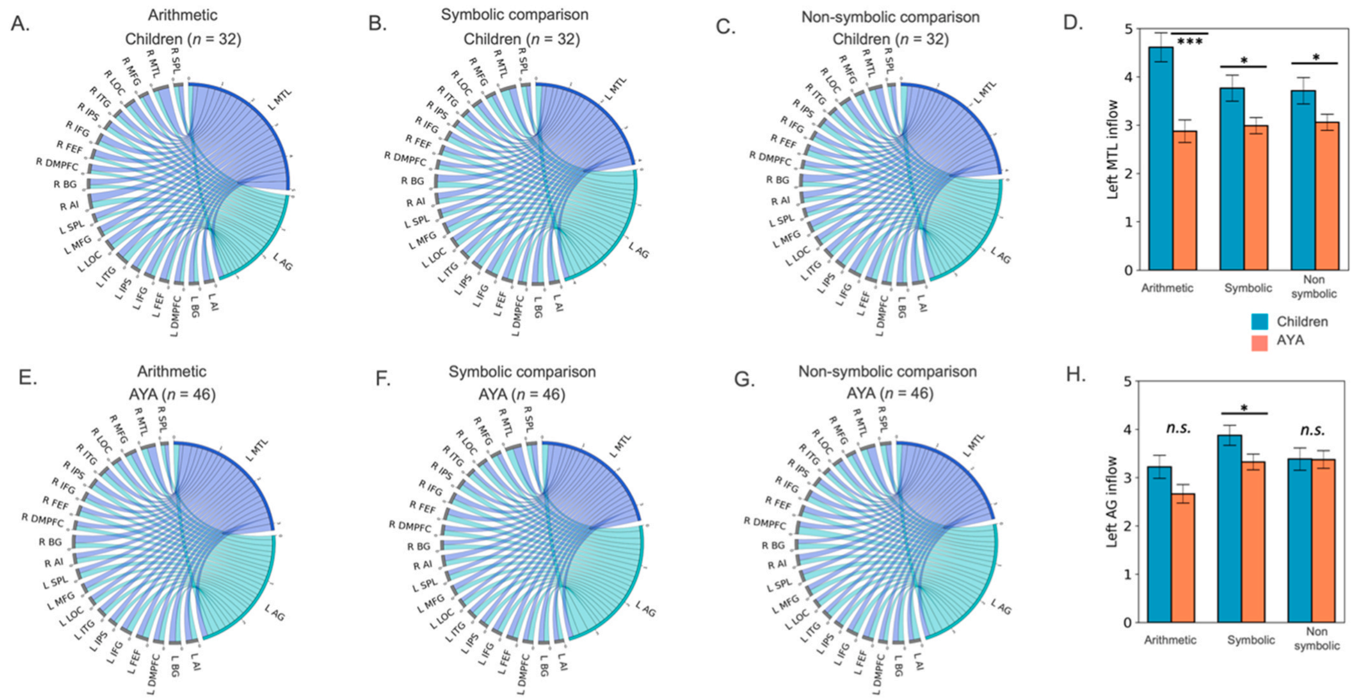

Fig. 5. Inflow causal signaling from all the regions of interest into the left MTL (blue) and left AG (mint green). A-C. The inflow causal signaling in the left MTL and left AG in (A) arithmetic, (B) symbolic number comparison, and (C) non-symbolic number comparison tasks in children. D. On average, children had higher inflow in the left MTL than AYA across all three tasks. E-G. The inflow causal signaling in in the left MTL and left AG in (E) arithmetic, (F) symbolic number comparison, and (G) non-symbolic number comparison tasks in AYA. H. On average, children had higher inflow than AYA in the symbolic number comparison task. *p < .05, **p < .01, ***p < .005, *n.s.*, not significant, p > .05.

3.8.1. *Outflow in the left AG*

Similar to the left MTL, we found a significant age difference between children and AYA across all tasks for the outflow in the left AG ($F(1,76) = 5.60$, $p = .02$; Fig. 4H). No significant main effect of task ($F(2152) = 1.53$, $p > .05$) or task by age interaction ($F(2152) = 1.40$, $p > .05$) was found. Follow-up *t*-tests showed a significant developmental difference in the symbolic number comparison task ($t(1,76) = 2.75$, $p = .007$). No significant developmental difference was observed in the arithmetic or non-symbolic number comparison tasks ($t(1,76) = .60$, $p > .05$).

3.8.2. *Inflow in the left AG*

For the inflow in the left AG, we found a significant main effect of task ($F(2152) = 7.72$, $p < .005$; Fig. 5H). The inflow in the left AG was lower in the arithmetic task than in number comparison tasks. No significant age effect ($F(1,76) = 3.47$, $p = .07$) or age by task interaction was found ($F(2152) = 1.58$, $p > .05$). Follow-up *t*-tests indicated a significant developmental difference in the symbolic number comparison task ($t(1,76) = 2.11$, $p = .04$). No significant developmental difference was observed in the non-symbolic number comparison task ($t(1,76) = .04$, $p > .05$) or the arithmetic task ($t(1,76) = 1.85$, $p = .07$).

These findings suggest enhanced outflow and inflow in the left AG in children than AYA, especially for the symbolic number comparison task.

3.9. *Comparison of causal signaling of MTL and AG*

As described above, the left MTL was a stable causal signaling hub in AYA in all three tasks (Fig. 3A-C, middle panel) and the left AG was a causal signaling hub in both children and AYA in the arithmetic verification task (Fig. 3A, left and middle panel). For the left MTL, children and AYA had different NOD in the arithmetic task (Fig. 3A, right panel) but not in the other two tasks. For the left AG, there was no significant difference between children and AYA regarding the NOD across the three tasks. To further examine these findings, we compared the NOD of the two regions in the two age groups across the three tasks (Fig. 6A & B).

A repeated measures ANOVA of task (arithmetic, symbolic number comparison, non-symbolic number comparison) x age (children, AYA) x ROIs (MTL, AG) yielded a significant age by ROI interaction ($F(2455) = 7.62$, $p < .001$). Specifically, the left MTL, but not the left AG, had higher NOD in AYA than in children across tasks (Fig. 6C). A significant task by ROI interaction ($F(1, 456) = 4.64$, $p = .03$) indicated that the left MTL had higher NOD than the left AG in the number comparison tasks but not in the arithmetic task across groups (Fig. 6D). There was also a significant main effect of ROI ($F(1, 456) = 6.49$, $p = .01$): The left MTL had overall higher NOD than the left AG (Fig. 6E). Finally, a significant main effect of task ($F(2455) = 2.98$, $p = .052$) indicated that the NOD across the left MTL and AG was overall highest in the arithmetic task (Fig. 6F).

Together, these findings suggest the developmental changes in the NOD occurred in the left MTL but not in the left AG. Furthermore, across age groups, the left MTL had higher NOD than the left AG, particularly for symbolic and non-symbolic number comparison tasks. Moreover, the role of the left AG as a hub in the arithmetic task regardless of age seems to suggest its domain specificity in arithmetic.

3.10. *Comparison of MTL and AG node centrality*

To further probe the differential network roles of the MTL and AG, we examined betweenness centrality of the left MTL and AG in children and AYA in arithmetic and symbolic and non-symbolic number comparison tasks. Node betweenness centrality is a measure used in network analysis to quantify the importance of a node within a network (Newman, 2005). It is measured as the fraction of all shortest paths in the brain network that contain a certain region. Regions with high level of betweenness centrality means they are in many shortest paths.

We conducted a repeated measures ANOVA of task (arithmetic, symbolic number comparison, non-symbolic number comparison) x age

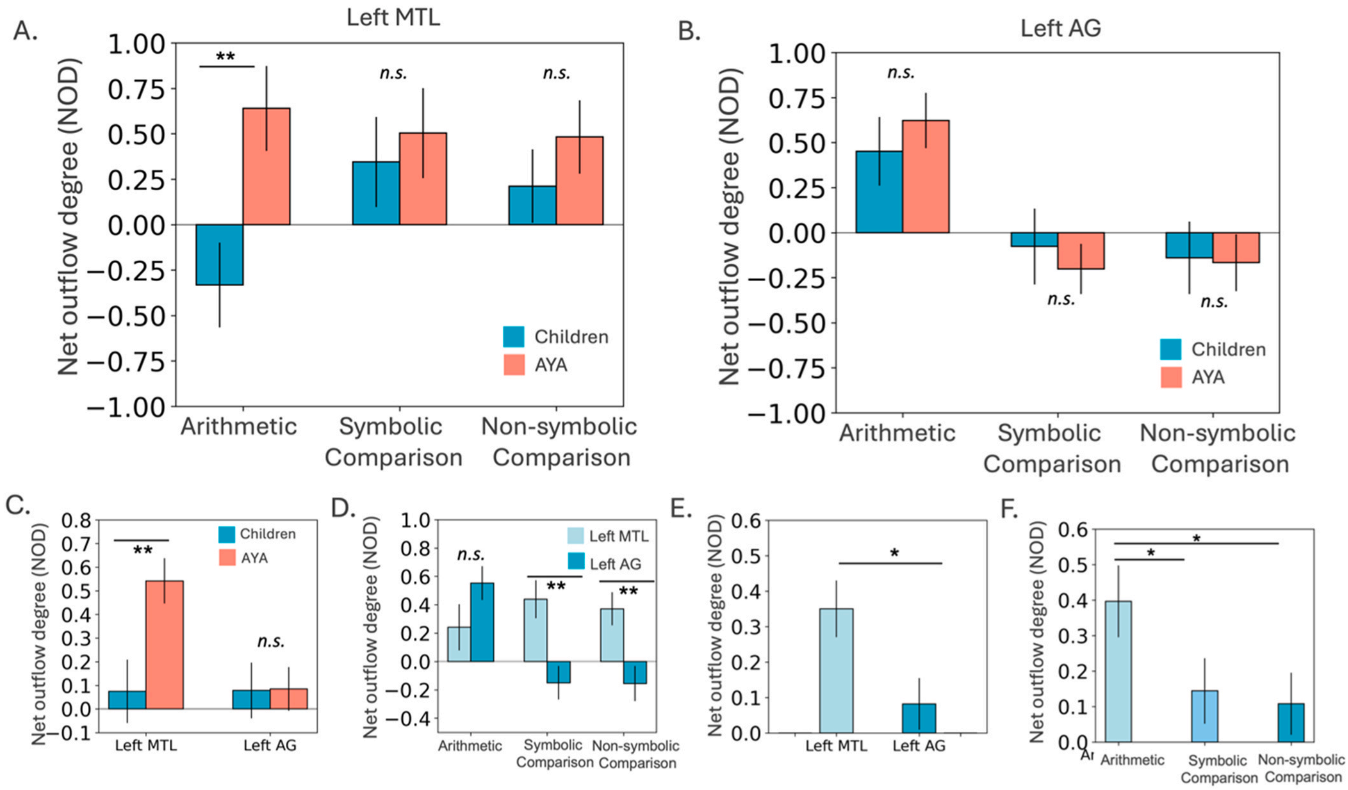

Fig. 6. The left MTL is a stable causal hub across tasks while the left AG is a causal hub in the arithmetic task in AYA. A. Net outflow degree (NOD) of the left MTL was significantly greater in AYA than children for the arithmetic task. Furthermore, AYA had consistently positive NOD in all three tasks, whereas children had overall negative NOD for the arithmetic task. B. The NOD of the left AG was not significantly different between children and AYA for any task. C. Across the three tasks, the left MTL had higher NOD in AYA than in children. No significant difference was observed between children and AYA for the NOD in the left AG. D. The difference in NOD between the left MTL and AG was significant for symbolic and non-symbolic number comparison tasks. E. The left MTL overall had higher NOD than the left AG across tasks and age groups. F. Overall NOD across the left AG and MTL was higher in the arithmetic task than the two number comparison tasks. *$p < .05$, **$p < .01$, *n.s.*, not significant, $p > .05$.

(children, AYA) x ROIs (MTL, AG), which revealed a significant age by ROI interaction ($F(2455) = 4.50$, $p = .03$; Fig. 7C) and a significant task by ROI interaction ($F(2455) = 3.45$, $p = .03$; Fig. 7D). Specifically, the left MTL, but not the left AG, had higher centrality in children than AYA across tasks (Fig. 7C). The left MTL had higher centrality than the left AG in the arithmetic task but not in number comparison tasks. In addition, we found a significant main effect of ROI ($F(1456) = 19.21$, $p < .001$; Fig. 7E), with left MTL having overall higher centrality than left AG. Finally, there was also a significant main effect of age ($F(1456) = 7.59$, $p = .006$; Fig. 7F), with children having higher overall centrality than AYA. Together, these results suggest a relatively stronger central role of the left MTL compared to the left AG across children and AYA and the developmental difference in the centrality of the left MTL, especially in the arithmetic task.

It is noteworthy that high levels of centrality in the left MTL were observed during arithmetic task for children, despite their low levels of NOD, compared to AYA. Combined with the observation of enhanced inflow and outflow in the left MTL in children, compared to AYA, during arithmetic task, these findings suggest that the MTL may play a central role in bidirectional causal interactions with the math-related brain network during arithmetic task performance in early childhood.

3.11. Causal signaling in the left MTL and AG correlate with standardized measures of math abilities

Finally, we examined whether NOD of the left MTL and AG during mathematical tasks are correlated with individual differences in standardized measures of mathematical abilities. Mathematical achievement was assessed using the Calculation, Math Fluency, and Applied Problem subtests from the Woodcock Johnson III Tests of Achievement (Schrank, 2011). Using canonical correlation analysis (CCA), we investigated the relationship between NOD measures and mathematical achievement scores separately for each age group and task.

In children, we found significant positive correlations between NOD and math achievement scores across all three tasks (*Pearson rs* $>.38$, $p < .03$). In contrast, these correlations were not significant in AYA (*Pearson rs* $<.29$, *ps* $>.05$). Although the correlation strengths appeared different between age groups, formal comparison of correlation slopes revealed no significant differences across the three tasks (*ts* $<.46$, *ps* $>.65$; see *Methods*).

When analyzing the combined sample, we found a significant positive correlation between NOD and math achievement scores specifically in the arithmetic task (*Pearson* $r = .31$, $p = .006$; Fig. 8A). No significant correlations emerged for either the symbolic or non-symbolic number comparison tasks (*Peason rs* $<.13$, *ps* $>.10$; Fig. 8B & C). Analyses revealed that the significant correlation between combined hub properties and mathematical achievement was primarily driven by the left MTL (left MTL: *Pearson* $r = .25$, $p = .02$) rather than the left AG (*Pearson* $r = .20$, $p = .08$; *S4 Figure*).

These findings indicate that the hub-like properties of the left MTL and AG correlated with individual differences in mathematical abilities. Notably, this brain-behavior relationship was most prominent during arithmetic processing, suggesting that network organization during more complex mathematical operations may be particularly important for mathematical competence.

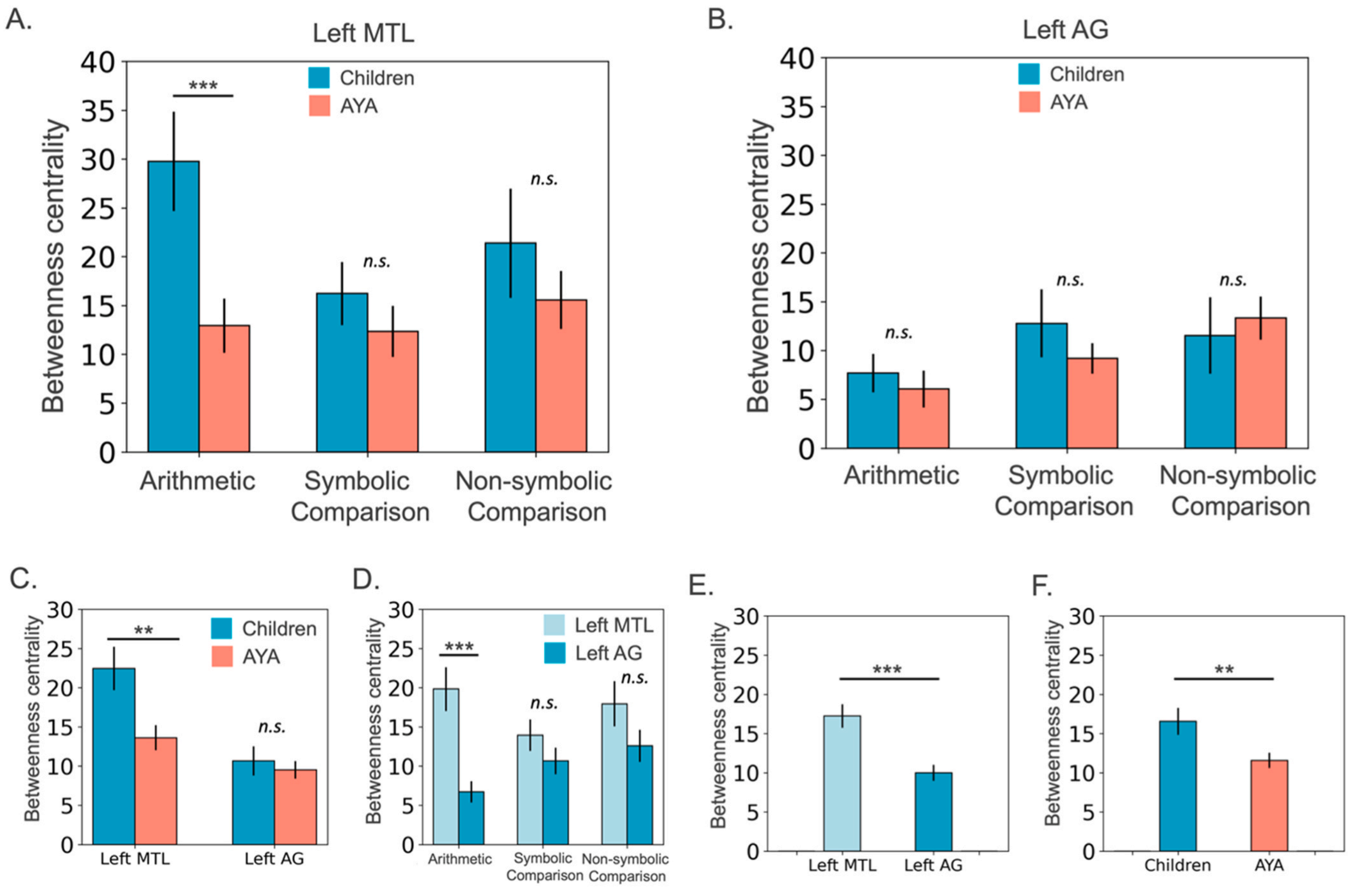

Fig. 7. The left MTL showed developmental difference in betweenness centrality in the network of regions of interest in the arithmetic task. A. The betweenness centrality of the left MTL was significantly higher in children than AYA in the arithmetic task. B. The left AG showed no significant difference in betweenness centrality between children and AYA in all three tasks. C. Children and AYA differed in betweenness centrality in the left MTL across the three tasks. Such age difference was not seen in the left AG. D. The left MTL showed higher betweenness centrality than the left AG in the arithmetic task. E. The left MTL overall had higher betweenness centrality than the left AG across tasks and age groups. F. Overall betweenness centrality across the left MTL and AG was higher in children than AYA. $^{**}p < .01$, $^{***}p < .005$, n.s., not significant, $p > .05$.

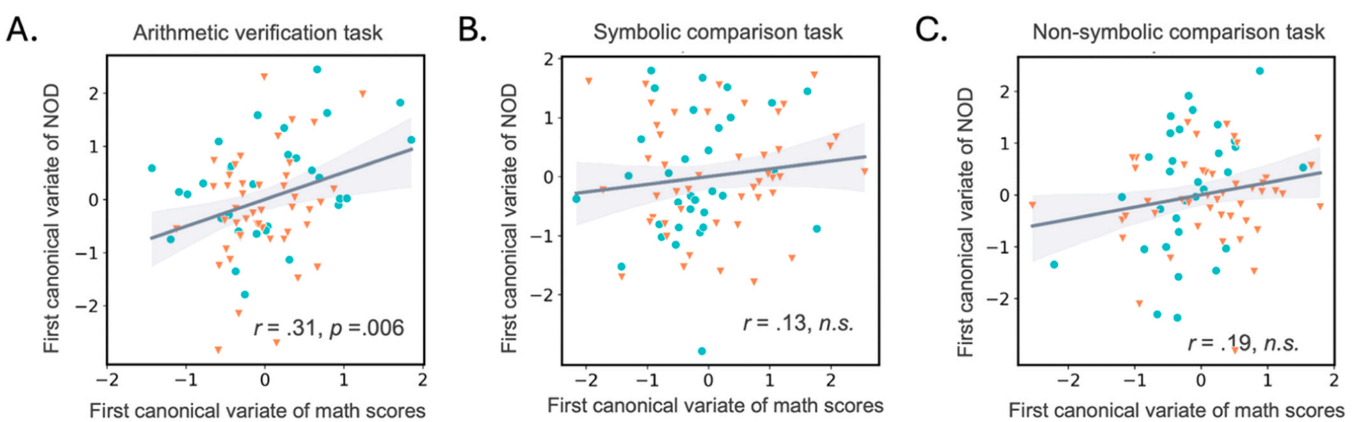

Fig. 8. Network hub properties predict mathematical achievement during arithmetic processing. Canonical correlation analysis between network outflow degree (NOD) of the left MTL and AG and standardized mathematical achievement scores. A. Significant positive correlation between NOD and mathematical achievement in the arithmetic verification task. B. No significant correlation between NOD and mathematical achievement in the symbolic number comparison task. C. No significant correlation between NOD and mathematical achievement in the non-symbolic number comparison task. NOD reflects the difference between outgoing and incoming causal interactions for each region (see Fig. 1 and *Methods*). Mathematical achievement was assessed using the Calculation, Math Fluency, and Applied Problems subtests from the Woodcock Johnson III Tests of Achievement. Children are represented by circles, AYA by triangles. *n.s.*, not significant, $p > .05$.

4. Discussion

We examined causal dynamics of memory circuits within a distributed brain network implicated in mathematical cognition and compared signaling patterns between children and adolescents and young adults (AYA). Our findings reveal novel insights into how mathematical cognition emerges through dynamic interactions between multiple brain systems, with memory circuits in the MTL and AG playing distinct developmental roles. The MTL undergoes a significant developmental shift, transitioning from exhibiting heightened, context-dependent, interactions in childhood to serving as a stable causal hub in adulthood across multiple mathematical tasks. In contrast, the AG maintains consistent hub-like properties specifically during arithmetic processing throughout development, suggesting early specialization for fact retrieval. These contrasting developmental trajectories indicate that different memory systems mature along distinct timelines to support mathematical processing.

Notably, both regions show heightened bidirectional interactions in childhood, particularly during arithmetic processing, suggesting less efficient network organization early in development. These patterns of interaction become more refined with age, with the MTL emerging as a domain-general hub for mathematical processing while the AG maintains its specialized role in arithmetic. Furthermore, the strength of these network properties correlates with individual differences in mathematical abilities, especially in arithmetic problem solving, highlighting their particular importance during mathematical skill acquisition.

These results challenge traditional views of mathematical cognition by demonstrating that memory systems play crucial but distinct roles in mathematical processing, with their contributions evolving significantly across development. This new understanding suggests that mathematical cognition relies on the coordinated maturation of multiple memory systems, each supporting different aspects of mathematical thinking at different developmental stages.

4.1. Developmental changes in causal network dynamics are task dependent

To quantify developmental changes in network dynamics, we conducted a classification analysis of network patterns between children and AYA across the three tasks. Our analysis revealed that the classification accuracy of network dynamics between children and AYA was highest in the arithmetic task (76.97 %), followed by the non-symbolic number comparison task (62.96 %), and lowest in the symbolic number comparison task (56.45 %).

The observed differences in network dynamics across tasks (arithmetic > non-symbolic > symbolic comparison) underscore the importance of considering task demands when studying mathematical cognition. The arithmetic task, which relies more heavily on fact retrieval and procedural knowledge, elicited the greatest differences between age groups. This finding supports the idea that brain network organization becomes more specialized and efficient with development and experience (Menon, 2013; Supekar et al., 2013). The lower classification accuracy in symbolic and non-symbolic number comparison tasks suggests that the neural processes underlying these more basic numerical skills may mature earlier or require less extensive network reorganization. The gradient of developmental differences across tasks highlights the dynamic nature of brain network development in mathematical cognition and emphasizes the value of examining multiple aspects of mathematical cognition to gain a comprehensive understanding of the developing mathematical brain.

Our study also demonstrates the utility and power of the multivariate dynamic state-space identification model in estimating causal interactions between distributed brain regions involved in math cognition. This advanced analysis approach allowed us to examine large-scale network dynamics, significantly extending beyond the limitations of our previous intracranial EEG study (Das and Menon, 2022), which were constrained by small sample sizes and limited spatial coverage. Our state-space model provides a more comprehensive understanding of how different brain regions interact during mathematical processing and how these interactions evolve with development. By capturing the directional flow of information between brain regions, this method offers a unique window into the causal architecture of the mathematical brain network.

4.2. MTL is a causal network hub in adolescents and young adults (AYA) but not in children

Next, we examined the role of the MTL as a causal signaling hub across different age groups and tasks. Our findings confirm and extend previous evidence from intracranial EEG studies suggesting that the hippocampus serves as a major causal signaling hub in arithmetic processing (Das and Menon, 2022). These effects were observed only in AYA but not in children. We observed that the left MTL consistently showed strong outflow across all three tasks in AYA, indicating its role as a general causal signaling hub in numerical processing.

In contrast to the left MTL, the right MTL showed stronger outflow only in the non-symbolic number comparison task, suggesting potential domain specificity of the right MTL. Non-symbolic number comparison involves spatial representations of quantity, which has been associated with the right hemisphere processes (Holloway et al., 2010). This hemispheric also aligns with the general observation that symbolic processing may engage the left MTL more prominently (Hocking et al., 2009; Price, 2012; Whitney et al., 2009). The verbal component in the arithmetic and symbolic number comparison tasks may engage the left MTL more consistently across participants, whereas both hemispheres may be similarly engaged in the non-symbolic task without a language component. This lateralization could reflect the dominant role of the left hemisphere in language processing and symbolic representation, which are crucial for arithmetic and symbolic number processing. This finding advances our understanding of how different aspects of numerical cognition may engage distinct MTL neural circuits.

4.3. Developmental changes in MTL causal network dynamics

We next compared the MTL network dynamics between children and AYA. We first focused on direct comparison of net outflow (outflow – inflow) reflecting a causal signaling hub between the two groups and then compared outflow and inflow separately between the groups. A striking finding of our study is the developmental change observed in the MTL. In children, we did not find net causal outflow signaling in the MTL to be significant in any of the three tasks. Moreover, the direction of net outflow in the MTL changed across tasks, suggesting unstable and context-dependent causal signaling in childhood.

Surprisingly, additional analysis revealed that with outflow and inflow measures taken separately, both outflow and inflow were enhanced in children, leading to diminished net outflow degree (i.e., outflow - inflow) in all three tasks. For the outflow measure, the largest developmental difference was observed in the arithmetic task (effect size $d = .77$), followed by the symbolic ($d = .51$) and non-symbolic ($d = .49$) number comparison tasks. The inflow followed the same trend, where the largest developmental difference was seen in the arithmetic task ($d = 1.74$), followed by symbolic ($d = .78$) and non-symbolic ($d = .65$) number comparison tasks. These results suggest that causal signaling both from and to the MTL may be undergoing maturation in children, exhibiting a profile of hyper-causal signaling in both outflow and inflow directions, leading to reduced hub-like properties when compared to AYA.

The hyper-signaling observed in the MTL in children, characterized by increased bidirectional causal interactions, may reflect a less efficient, more diffuse pattern of information processing. This could be indicative of a developmental stage where the MTL may be highly plastic and responsive, but not yet optimized for efficient mathematical performance. The greatest developmental difference observed in the arithmetic task suggests that this potential developmental change is particularly pronounced for more complex mathematical operations that may rely more on memory retrieval.

Our findings align with previous studies (Qin et al., 2014; Rivera et al., 2005), which found higher hippocampal activity in arithmetic tasks in children compared to adults. The gradual transition from this heightened bidirectional interaction state in childhood to a more directed, efficient causal signaling hub in adolescence and adulthood may represent a key aspect of mathematical skill development. This shift could reflect the refinement of distributed neural circuits leading to more specialized and efficient information flow within the mathematical cognition network.

4.4. AG serves as a causal network hub only during arithmetic processing

Given the extant literature implicating the AG in mathematical cognition, we examined its role as a potential causal signaling hub across our three tasks and two age groups. Analysis of net outflow degree (i.e. outflow – inflow) revealed that the left AG functions as a strong causal signaling hub in both children and AYA specifically during arithmetic, but not during symbolic or non-symbolic number comparison tasks. This task specificity aligns with previous research showing AG involvement in arithmetic processing in both children and adults (Polspoel et al., 2017; Grabner et al., 2013), suggesting its specialized role in more complex mathematical operations that rely on fact retrieval and semantic memory processing.

Notably, while the net outflow in the AG showed no developmental differences, suggesting early establishment of its hub-like properties in arithmetic processing, the pattern of interactions revealed interesting developmental changes. Children exhibited higher levels of both outflow and inflow in the left AG compared to AYA during arithmetic and symbolic number comparison tasks, but not during non-symbolic number comparison. This pattern of selective difference between age groups suggests that developmental changes in AG may be specifically related to symbolic information processing. The increased bidirectional causal interactions observed in children might reflect less efficient, more diffuse processing, paralleling our observations in the MTL.

4.5. Comparing developmental changes in network dynamics of the MTL and AG

Our analysis revealed that both the left MTL and left AG function as causal signaling hubs, but with distinct developmental trajectories and task specificities. We additionally compared NOD and betweenness centrality in these regions, collapsed across age groups and tasks. The results revealed a striking dissociation: while the left MTL showed strong developmental differences in both NOD and centrality measures, the left AG maintained consistent network properties in all tasks across development (Fig. 6C and Fig. 7C).

The developmental differences in the left MTL were particularly pronounced during arithmetic but not during symbolic or non-symbolic number comparison tasks (Fig. 6A and Fig. 7A). This task-specific pattern provides compelling evidence that the maturation of MTL function in mathematical processing is context-dependent. Specifically, the MTL appears to undergo more substantial developmental changes in its network role during complex mathematical operations that require fact retrieval and computation, compared to basic numerical comparison tasks.

This dissociation between the MTL and AG suggests different developmental trajectories for distinct memory systems supporting mathematical cognition. While the AG appears to establish its role in arithmetic early and maintain it through development, the MTL shows a more complex pattern of maturation, particularly in its support of advanced mathematical operations.

4.6. Relation between causal network dynamics and mathematical abilities

Canonical correlation analysis revealed distinct patterns in how network properties relate to mathematical abilities across development and task contexts. In children, we found significant correlations between the NOD of the left MTL and AG and performance on standardized measures of calculation, arithmetic fluency, and applied mathematical problem solving across all tasks. In contrast, AYA showed no significant correlations between these network properties and mathematical achievement. Although the correlation patterns appeared differently between age groups, formal comparison of correlation slopes revealed no significant developmental differences.

When analyzing the combined sample, we found that NOD correlated with mathematical achievement specifically during arithmetic verification, but not during symbolic or non-symbolic number comparison. Moreover, the NOD of the left MTL showed strong correlations with standardized measures of math ability. These findings extend previous research on the relationship between MTL and AG structure, function, and mathematical abilities, with a stronger emphasis on the importance of the left MTL (Abreu-Mendoza et al., 2022; De Smedt et al., 2011; Grabner et al., 2009a,b; Supekar et al., 2013; Wilkey et al., 2018). The task-specific nature of these relationships aligns with evidence that symbolic arithmetic processing is particularly predictive of formal mathematical skills (Brankaer et al., 2014; Fazio et al., 2014; Lyons et al., 2014; Menon and Chang, 2021).

These brain-behavior relationships suggest that the transition from heightened interactions in childhood to more stable, efficient configurations in adulthood may represent a key mechanism in mathematical development (Abreu-Mendoza et al., 2022; Jolles et al., 2016; Menon and Chang, 2021; Price et al., 2018; Qin et al., 2014; Rosenberg-Lee et al., 2015). Understanding these task-specific and developmental changes in brain-behavior relationships could have important implications for identifying and supporting individuals with mathematical learning difficulties.

4.7. Role of MTL and AG memory circuits in mathematical cognition

Our findings advance understanding of the role of the MTL in mathematical processing in several ways. First, they provide causal evidence for the involvement of the MTL across a range of numerical tasks, from basic number comparisons to more complex arithmetic operations, supporting its proposed role as a general hub in mathematical cognition. Second, the presence of the MTL as a hub in AYA across all tasks, but not in children, suggests its role becomes more generalized with development. Third, the developmental pattern of enhanced bidirectional interactions in children, coupled with the emergence of net outflow in the MTL in AYA, suggests a significant directional refinement of MTL function with development. The transition from heightened bidirectional interactions in childhood to more focused, unidirectional outflow in AYA suggests a developmental shift towards more efficient information processing in this region. This could reflect the maturation of the MTL as a stable, task-independent hub for mathematical processing may occur later in development, through enhanced directed connectivity with task-relevant regions.

Our results also advance our understanding of the role of the AG in arithmetic processing in several ways. First, they provide causal evidence for the involvement of the AG specifically in arithmetic, supporting its proposed role in fact retrieval. The absence of the AG as a hub in number comparison tasks suggests that its role may be limited to more complex mathematical operations that rely on semantic memory or procedural knowledge. Second, they reveal that the net influence of the AG during arithmetic remains stable across development, which suggests its task-specificity may be established early in development. Third, the reduction in bidirectional interactions from childhood to adolescence suggests a refinement of AG function across development, potentially reflecting increased efficiency in interaction with task-relevant regions.

Our findings also have implications for understanding the differential roles of the MTL and AG in mathematical cognition. While both regions showed higher bidirectional interactions in children, the AG maintained its hub status across development in arithmetic tasks, unlike the MTL. This suggests that the AG may play a more stable, task-specific role in arithmetic processing, while the MTL's function appears to undergo more substantial developmental changes across various numerical tasks. These findings converge with reports from training studies that point toward a central role of the hippocampus and other MTL structures in the acquisition and consolidation of a broad range of mathematical knowledge, and not just arithmetic facts (Bloechle et al., 2016; Kutter et al., 2018, 2022; Üstün et al., 2021).

4.8. Implications for understanding the role of memory systems in mathematical cognition

Our findings further highlight the crucial role of memory systems in mathematical cognition, particularly emphasizing the dynamic involvement of the MTL in development. The MTL, traditionally associated with declarative memory, emerged as a key player in numerical processing across various tasks in adolescence and young adulthood, suggesting that memory processes are integral to mathematical cognition even in tasks that may not rely on fact retrieval. The maturation of the MTL to a more refined, unidirectional signaling hub in adolescence and adulthood suggests that increased efficiency of the MTL memory system may support mathematical processing later in development.

These findings provide new insights into how different memory systems contribute to mathematical cognition. Rather than viewing mathematical processing as solely dependent on abstract symbol manipulation, our results reveal the dynamic involvement of multiple memory systems. The MTL's engagement across both basic numerical and complex arithmetic tasks suggests that its memory-related computations may support multiple aspects of mathematical processing, from forming symbol-quantity associations to storing and retrieving arithmetic facts. The AG's specific involvement during arithmetic, but not comparison tasks, indicates a more specialized role, potentially in semantic retrieval processes that support arithmetic fact recall.

The developmental changes observed in both the MTL and AG imply that maturation of multiple memory systems contribute to the development of mathematical skills. This has important implications for educational approaches, suggesting that strategies targeting the enhancement of these memory systems could be beneficial for improving mathematical abilities. Moreover, the distinct developmental trajectories of the MTL and AG suggest that different aspects of memory might be targeted at different developmental stages to optimize mathematical learning.

4.9. Developmental changes in network dynamics may reflect excitatory/inhibitory balance maturation

Finally, we consider potential neurophysiological bases of our findings. The pattern of heightened bidirectional interactions observed in children likely reflects developmental changes in excitatory/inhibitory (E/I) balance over the course of brain maturation. While we do not have direct evidence for E/I developmental changes in this numerical cognition domain, substantial evidence from developmental neuroscience indicates that E/I balance undergoes significant maturation from childhood to adulthood (Saberi et al., 2025; Zhang et al., 2024; Zhang et al., 2011). During early development, excitatory connections are more prevalent and are gradually refined through inhibitory circuit maturation and synaptic pruning (Caballero et al., 2021; Chechik et al., 1999). This developmental trajectory is consistent with our observation of heightened bidirectional interactions in children that become more focused and efficient in adults.

Supporting this interpretation, previous research has shown that children with mathematical learning disabilities exhibit hyperactivity and hyperconnectivity compared to matched controls (Jolles et al., 2016; Rosenberg-Lee et al., 2015), suggesting that disrupted E/I ratios may be associated with less efficient cognitive processing. Our finding that children with stronger bidirectional interactions show better correlations with mathematical abilities may indicate that some degree of elevated E/I activity during development is beneficial for mathematical skill acquisition. However, the maturation toward more balanced and selective signaling appears necessary for optimal adult-level performance.

This developmental perspective suggests that the transition from diffuse, bidirectional signaling in childhood to more focused, hub-like organization in adulthood reflects fundamental maturation of cortical circuits supporting mathematical cognition. Understanding these E/I developmental changes may provide insights into both typical mathematical development and potential targets for intervention in mathematical learning difficulties.

5. Conclusion

Our study provides novel insights into the development of brain networks involved in mathematical processing, revealing dynamic changes in causal interactions and signaling hubs from childhood to adulthood. We found that the MTL in the left hemisphere undergoes a significant developmental shift, transitioning from hyper-signaling and context-dependent causal interactions in childhood to serving as a stable causal signaling hub in numerical processing in adolescence and young adulthood. In contrast, the left AG maintained consistent hub-like properties across development specifically during arithmetic processing. These patterns of findings highlight distinct developmental trajectories for different memory systems supporting mathematical cognition. Our findings reveal that the network dynamics of the MTL may undergo a global developmental shift, reflecting the maturation of declarative memory systems that support efficient mathematical processing across multiple domains, from basic number processing to complex arithmetic.

By elucidating the causal dynamics of memory circuits within the math brain network and how they change with development, our study contributes to the growing body of knowledge on the neurodevelopmental basis of mathematical cognition. These insights open new avenues for research into the intersection of memory and mathematical cognition, potentially leading to more effective, developmentally appropriate strategies for mathematics education and interventions for mathematical learning difficulties.

Data statement

The research data, including the de-identified behavioral data and functional MRI data necessary to reproduce study findings, will be made available upon request.

CRediT authorship contribution statement

Ruizhe Liu: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Yuan Zhang:** Writing – review & editing, Methodology, Formal analysis. **Hyesang Chang:** Writing – review & editing, Conceptualization. **Vinod Menon:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare no usage of generative AI in the writing process.

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Declaration of Competing interest

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

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2025.101628.

Data availability

Data will be made available on request.

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