The neural basis of number word processing in children and adults

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ABSTRACT

The ability to map number words to their corresponding quantity representations is a gatekeeper for children's future math success (Spaepen et al., 2018). Without number word knowledge at school entry, children are at greater risk for developing math learning difficulties (Chu et al., 2019). In the present study, we used functional magnetic resonance imaging (fMRI) to examine the neural basis for processing the meaning of spoken number words and its developmental trajectory in 4- to 10-year-old children, and in adults. In a number word-quantity mapping paradigm, participants listened to number words while simultaneously viewing quantities that were congruent or incongruent to the number word they heard. Whole brain analyses revealed that adults showed a neural congruity effect with greater neural activation for incongruent relative to congruent trials in anterior cingulate cortex (ACC) and left intraparietal sulcus (LIPS). In contrast, children did not show a significant neural congruity effect. However, a region of interest analysis in the child sample demonstrated age-related increases in the neural congruity effect, specifically in the LIPS. The positive correlation between neural congruity in LIPS and age was stronger in children who were already attending school, suggesting that developmental changes in LIPS function are experience-dependent.

1. Introduction

Learning number words is the first step in a child's mathematical development. Children slowly learn the correspondence between number words and quantities between the ages of 3.5 and 6 (Le Corre and Carey, 2007; Wynn, 1990, 1992). Children who learn the cardinal principle, that the last number in a count sequence represents the total number of items in a set, before school entry score higher on math assessments when they get to school (Geary et al., 2018). Similarly, children who have yet to master the cardinal principle at school entry are at higher risk for developing persistent math difficulties (Chu et al., 2019).

Despite the importance of number word acquisition in children's early mathematical development, the neural mechanisms that support spoken number word processing are not well characterized in children or adults. Instead, the research on the neural basis of number processing has focused on numerals, quantities, and in some cases written number words. In adults, there is compelling evidence that bilateral intraparietal sulcus (IPS) is involved in the semantic processing of numerals and written number words. IPS is activated during functional magnetic resonance imaging (fMRI) tasks across symbolic (i.e., "3" and "three") and non-symbolic (i.e., three dots) representations of number (e.g.

Arsalidou and Taylor, 2011; Bugden et al., 2019; Cohen Kadosh et al., 2007; Dehaene et al., 2003; Fias et al., 2003; Sokolowski et al., 2017).

A much smaller literature has examined the neural representation of number in children. This work reveals that right and left IPS show different developmental trajectories with right IPS emerging earlier than left IPS and supporting approximate non-symbolic processing. Preverbal infants and preschool children show numerically selective activation in right IPS when passively viewing arrays of dots (Cantlon et al., 2006; Edwards et al., 2016; Kersey & Cantlon, 2016). In contrast, left IPS shows a protracted developmental trajectory that is associated with the acquisition of mathematical skill. In a cross-sectional study with 6- to 14-year-old children, the neural representation of Arabic numerals (i.e., "3") became more precise with age in left IPS, whereas right IPS did not show age-related changes (Vogel et al., 2015). Moreover, in children, improved performance on a numerical discrimination task (i.e., which number is larger, 3 or 5?) was associated with longitudinal task-related changes in activation of left IPS, but not right IPS (Emerson and Cantlon, 2014). Together, these studies suggest that right IPS emerges prior to learning symbolic math and shows stable and consistent recruitment during numerical processing tasks. On the other hand, left IPS emerges later in development and shows greater functional specialization for

processing numerals with age and skill (Bugden et al., 2012; Emerson and Cantlon, 2014; Vogel et al., 2015).

There is some evidence that the increasing specificity of left IPS for processing numerals is driven by children's experience and increasing facility with numbers and math (*e.g.,* Ansari, 2016). For example, concurrent and longitudinal associations have been found between number-related neural activation and performance on measures of numerical and math knowledge in school-aged children when controlling for age (Bugden et al., 2012; Emerson and Cantlon, 2014). Moreover, adult-like neural activation when viewing numerical and mathematical video clips was associated with higher standardized scores of math achievement in 4-to-10-year-old children (Cantlon and Li, 2013). Significant gains in math skills following different numerical and math interventions are accompanied by widespread neural plastic changes including in IPS (Iuculano et al., 2015; Kucian et al., 2011; Michels et al. 2018).

A second pattern that emerges from studies of brain development and number processing is a fronto-parietal shift in activation. Children show greater activation in regions in the prefrontal cortex relative to adults during both symbolic and non-symbolic number processing tasks (e.g., Ansari et al., 2005; Ansari & Dhital, 2006; Cantlon et al., 2008; Rivera et al., 2005). In contrast, activation in bilateral IPS increases across development during number processing. Greater recruitment of the prefrontal cortex in children relative to adults is thought to reflect a greater need for domain general cognitive resources like working memory and attention when children are learning math (Ansari et al., 2005; Cantlon et al., 2008; Lussier and Cantlon, 2017; Nieder, 2009; Rivera et al., 2005).

Despite the fact that children learn the meaning of spoken number words before they learn to use numerals or to read number words, only two prior studies have examined the neural basis of number word processing in children. Pinhas et al. measured event-related potentials (ERP) in 3- to 5-year-old children during a number word-quantity mapping task and found that cardinal principle knowers showed a neural congruity effect; greater signal for incongruent (mismatch between number word and quantity) relative to congruent (number word and quantity matched) trials. Children who have not mastered the cardinal principle did not show a significant neural congruity effect (Pinhas et al., 2014). In a second study, Lussier and Cantlon (2017) used fMRI to examine the neural correlates of visually presented written number words in 8–9-year-old children. Children showed activation in bilateral IPS when making magnitude or parity judgments about the meaning of number words (i.e., "Is eight smaller or larger than fifteen?" or "Is eight odd or even?") over and above size or category judgements of object words.

Behavioral studies, using the Give a Number task, have consistently shown that children can give a puppet 6 or fewer toys accurately by the age of approximately 4.5 years, demonstrating that they have mastered the cardinal principle by this age (CP-knower) (Wynn, 1990, 1992). However, there is considerable evidence that children classified as CP-knowers do not fully comprehend the meaning of number words within their count sequence (e.g., Davidson and Eng & Barner 2012; Le Corre, 2014). For example, despite being able to count to 12 a CP-knower might not know that 12 is more than 11 or that when one is added to a set of 11 the set becomes 12 (e.g., Schneider et al., 2020). Children also show gradual improvement in estimation tasks that require mapping number words onto quantities (e.g., Barth et al., 2009) despite having acquired the cardinal principle (e.g., Le Corre & Carey, 2007; Sullivan & Barner, 2014). These behavioral findings raise the question of whether CP-knowers would show adult-like neural patterns when processing small number words or instead whether a more protracted developmental trajectory tracks increasing automaticity of number word-quantity mapping.

We designed a study to examine the neural correlates of number word to quantity mapping in children and adults. We targeted 4-to-10-year-old CP-knowers and used small number words to ensure that

children had mapped the number words to quantities. The task involved listening to number words while simultaneously viewing quantities that were congruent or incongruent to the number word they heard (Pinhas et al., 2014). The "response-free" nature of this paradigm is optimal for studying neural development across age groups and eliminates the confounds between age and performance intrinsic to tasks that require a behavioral response.

Given that there were no prior fMRI studies showing a neural congruity effect for number word processing in adults, we first identified where neural activation was greater for incongruent relative to congruent trials in a sample of 18- to-44-year-old adults. We hypothesized that adults would exhibit a neural congruity effect in bilateral IPS (e.g., Sokolowski et al., 2017). Then, we tested our pre-registered prediction (https://osf.io/w9dm3) that children would engage regions in the prefrontal cortex and right IPS during the number word-quantity mapping task. We next tested whether there were differences in the neural congruity effect between adults and children. Given the two major developmental trends common to the number processing literature, we hypothesized that we would see a fronto-parietal shift and increasing magnitude of the neural congruity effect, perhaps shifting from a right focused to bilateral IPS locus. To further probe the neural development of number word processing in children, we ran exploratory analyses to test for associations between neural congruity, age, and numerical knowledge and whether brain-behavior associations were stronger in children who attend formal school.

2. Methods

2.1. Participants

The Institutional Review Board at the University of Pennsylvania approved this study. Adult participants and parents of children participants provided informed, written consent. Children younger than age 8 provided verbal assent, and children ages 8 and older provided written assent.

2.1.1. Adult sample

The adult sample was not pre-registered twenty-four adults were recruited from the University of Pennsylvania community. The final sample consisted of 22 participants (18.94 – 44.12 years; M = 25.23 years, SD = 8.20; 64% female). One participant was excluded because they could not hear the number words in the scanner, and one participant did not follow task instructions and made active responses during a passive task. The sample was racially and ethnically diverse (13% Black or African American, 45% White, 32% Asian, 4% Hispanic, 9% other). All participants were fluent English speakers and had normal or corrected-to-normal vision. None of the participants reported any MRI contraindications, neurological or psychiatric illness.

2.1.2. Child sample

The child sample was pre-registered. All pre-registered analyses are reported, and any additional analyses are identified as exploratory. 113 4- to- 10-year-old children were recruited from the Philadelphia region through local preschools, ads on social media and public transportation, or the Penn Child Developmental Labs participant database. Participants were initially screened and excluded if children had diagnosed medical or psychiatric conditions, MRI contraindications like metal implants, or were born prematurely (< 34 weeks). Participants were excluded from the final data analysis for the following reasons: child fell asleep during the scan ($n = 6$); child did not wish to complete the scan ($n = 7$); mean framewise displacement (motion) during the scan was greater than 1 mm ($n = 10$), or greater than 10% of the volumes had composite motion greater than 2 mm ($n = 1$); errors during data acquisition ($n = 2$, 1 child was registered feet first, 1 scanner error related to radiofrequency (RF) coil); image artifacts ($n = 3$, 1 child with signal dropout due to glitter in hair; 1 child with dropout in the frontal lobe; 1 child with a black stripe
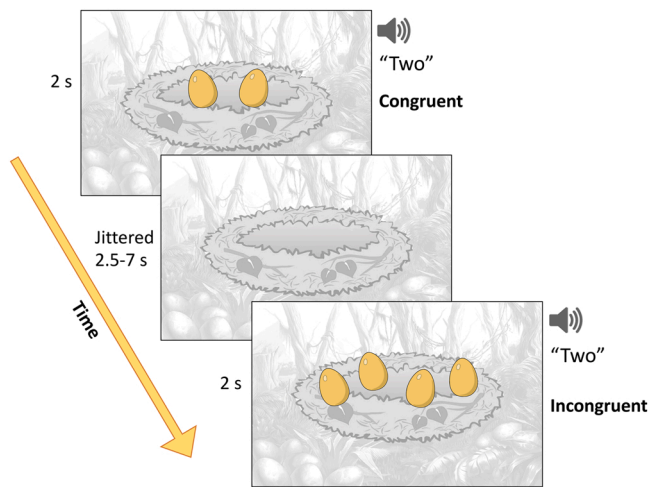
Fig. 1. Example stimuli for number word-quantity mapping task.

across the brain due to motion in the reference images for the multiband sequence). We also excluded participants if no cortical or striatum activation was found across the four planned contrasts (see fMRI pre-processing section), indicating the participant may have been asleep (n = 4).

The final sample consisted of 80 children (4.12–10.59 years; M = 6.23, SD = 1.39; 53% female).[1] All children were fluent in English; 19% of children could speak another language. Demographic information reported here is from 78 of the 80 participants' parents who completed the optional demographic questionnaire. Nine percent of the parents identified as Hispanic, 45% identified as White, 10% identified as Asian, 46% identified as Black or African American, 3% identified as Hawaiian, 3% identified as American Indian, and 5% identified as other. The sample was socioeconomically diverse with a reported median income of $62,500 (participants reported income ranging from $0-$4999 to above $200,000). The median reported parental education level was a bachelor's degree (education reported on a scale ranging from parents having less than a high school degree to having a professional degree (i. e., Ph.D. or M.D)).

2.2. Materials

2.2.1. Behavioral number word-quantity mapping task

Children completed a number word-quantity mapping computer task just before the fMRI scan to encourage active task processing during the passive scan. In this task, children heard a number word while simultaneously seeing a nest of 1–4 eggs on a computer screen. Participants were told that "Dani the Dino likes to show off how many dinosaur eggs she has. She will say a number and show you some eggs, but she doesn't always say the right number." Children were instructed to say "yes" if the number word matched the number of eggs on the screen, and "no" if the number word did not match the number of eggs on the screen. An experimenter recorded their responses. For the congruent trials, the number word they heard matched the number of eggs on the screen, and for the incongruent trials, the number word did not match the number of eggs on the screen. On incongruent trials, the number of eggs differed from the number word by a numerical distance of one or two. The numerical values 1–4 occurred with equal frequency and the numerical distance between the visual and spoken numerical value was 1 or 2 with equal frequency (see Appendix for table of trial list). The stimuli

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remained on the screen until the child made a response. The experimenter initiated each trial by pressing the space bar when the child was judged to be attentive and ready to proceed. Children completed 64 trials (32 incongruent and 32 congruent trials). Data from the behavioral number word-quantity mapping task was available from 72 of the 80 child participants. Twenty-seven children completed an earlier version of the number-word mapping task that required a key press response. Those children were instructed to press "s" if the number word matched the number of eggs on the screen or "l" if the number word did not match the quantity on the screen. A Welch's t-test indicated that children who provided a verbal response were marginally more accurate (M = 95%) than children who responded with a button press (M = 93%), t(58.50) = −1.80, p = .08. Note that the response mode for the behavioral mapping task was switched to make the task easier for younger children (<4 years).

Audio stimuli were spoken by a female experimenter using a SONY ICD PX333 Digital Voice Recorder. Each number word was uttered in a sentence. Noise reduction was performed over the whole recording. The best recorded number word was then extracted from the recorded sentence using Audacity (https://www.audacityteam.org). The audio was cut at onset and offset of speech (using zero crossing). Two hundred and fifty milliseconds of silence were added to the beginning of each file. The files were then normalized so that peak amplitude for all files was the same. And finally, the files were converted from WAV to MP3. The same audio and visual stimuli were shown across incongruent and congruent trials. The number word-quantity mapping task was presented with *Eprime* 2.0 software (Psychological Software Tools, Pittsburg, PA) and administered using a Lenovo 15″ touchscreen laptop.

2.2.2. fMRI paradigm: number word-quantity mapping task

In the scanner, children completed a passive version of the number word-quantity mapping task. Prior to going into the scanner, children were reminded of the task instructions. They were told to pay very close attention to whether Dani says the right number of eggs but not to respond verbally. Undergraduate research assistants observed child participants during the MRI scan to monitor for any signs of inattention given the passive nature of the paradigm. The stimuli were identical across the passive and active versions of the task. A total of 64 trials were administered (32 incongruent and 32 congruent trials) (see Fig. 1).

Functional runs began and ended with a 10-second fixation period. Visual stimuli were presented for two seconds followed by a jittered interstimulus interval (ISI). The ISI was exponentially distributed, ranging between 2.5 and 7 s with a mean of 3.5 s. The timing and order of trial presentation of the task was optimized for timing efficiency using the Optisq2 program (https://surfer.nmr.mgh.harvard.edu/optseq/). The order of presentation was the same across all participants. Children were tested with one 6.13-minute run.

2.2.3. Cardinality knower task

The Give a Number task (GiveN; Wynn, 1990, 1992) was administered to assess children's number word knowledge. In this task, children were presented with a toy dinosaur and a bowl of 15 small apple erasers and asked: "Can you give Dani the Dino *n* apples?" After each trial, the experimenter asked the participant to confirm their response by asking: "Is that n?" If participants gave Dani the correct number of apples, the experimenter then asked them to give Dani n + 1 apples. If participants gave Dani the incorrect number of apples, they were asked to give Dani n-1 apples. The highest number word a child knew was defined as the highest correct number of apples a child could give on two out of three trials. Children who reliably gave Dani six apples were referred to as cardinal principle knowers (CP-knowers). Children older than 7 years of age did not complete the GiveN task.

2.2.4. Standardized assessment of math ability

The Numeration subtest from the Key-Math-3 Diagnostic Assessment (Connolly, 2007) was administered. The Numeration subtest measures

children's general understanding of numbers, covering topics such as identifying numerals, representing and comparing quantities, verbal counting, and ordering numerical sequences. We used the raw score to capture children's math ability, controlling for age.

2.2.5. Standardized assessment of cognitive ability

The Information and Matrix Reasoning subtests from the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV; Wechsler, 2012) were administered to assess acquired knowledge and fluid reasoning skills in children younger than 7 years 8 months. In the Information subtest, children are asked general knowledge questions that assess capacity to acquire, retain, and retrieve factual information (e.g., "Show me your mouth. Touch it" or "What goes in a cup?"). In the Matrix Reasoning subtest, children are presented with a pattern or sequence and children are asked to select one of four possible pictures that fits the sequence. Older children completed the Vocabulary and Matrix Reasoning subtests from the Wechsler Intelligence Scales for Children (WISC- V; Wechsler, 2014). In the Vocabulary subtest, children were asked to define words. Similar to the Matrix Reasoning subtest administered in the WPPSI, children are presented with visual patterns and asked to select the missing image from four possible options. The standardized scores for the Information and Vocabulary subtests were used as a measure of verbal IQ, and the standardized scores for Matrix Reasoning subtests were used as a measure of non-verbal IQ. Four participants did not have valid matrix reasoning scores and three participants did not have valid verbal IQ scores.

2.2.6. Parental questionnaires

Parents were asked to fill out questionnaires about the family demographics, including the annual household income and the highest levels of education obtained by both parents. When available, both parents' years of education was averaged to create a parental education measure. Socioeconomic status (SES) was operationalized as a composite score computed by averaging together z-scored parental education and z-scored total income. An SES score was derived from reported data (1 participant was missing education information from both parents; 12 participants had education information for only one parent, and 7 participants were missing income information). We collected SES to test the specificity of our effects, because prior studies have consistently found an association between SES and numerical knowledge (e.g. Duncan and Magnuson, 2011; Jordan and Levine, 2009), as well as SES and brain measures (e.g. Demir-Lira et al., 2016; Demir et al., 2015; Farah, 2017; Mackey et al., 2015).

2.3. General procedures

2.3.1. Adult sample

Adult participants completed a single 1.5-hour testing session. They completed the consent form and a short demographic questionnaire prior to completing the fMRI scan. The same version of the passive number word-quantity mapping task as used with children was used with adults and each participant completed three 6.13- minute runs in the scanner.

2.3.2. Child sample

Children participated in two test sessions. In one session, children completed a mock MRI scan to acclimate them to the scanning environment. In the mock scanner, children practiced staying still while watching a short video clip and previewed a small part of the number word-quantity mapping task. Following the mock scan, children completed the behavioral version of the number word-quantity mapping task, and then completed the MRI scan. In the other session, children completed the battery of cognitive and academic assessments. Each test session lasted approximately 2–2.5 h in duration.

2.4. fMRI data acquisition

Structural and functional imaging data were collected at the Center for Functional Neuroimaging at the University of Pennsylvania using a Siemens MAGNETOM Prisma 3 T whole-body MRI scanner with a 32-channel head coil. During the child MRI scans, a researcher stayed in the scanner room to reassure the participant, monitor whether they fell asleep during the scan, and provide feedback when they moved by touching the participant's foot. An automated Scout image was acquired to automatically align the scan acquisition window. Then, participants underwent a T1-weighted MPRAGE anatomical scan designed for participants who typically move in the scanner. The volumetric navigator (vNavs) system is inserted in the T1-weighted pulse sequence to monitor head motion during the scan and prospectively correct for motion (Tisdall et al., 2012; 2016). The acquisition parameters are the following: TR = 2530 ms, TE = 1.69 ms/3.55 ms/5.41 ms/7.27 ms, flip angle $= 7°$, voxel size $= 1$ mm^3, isotropic matrix $= 192 \times 192$, 176 sagittal slices, FOV = 192 mm.

T2*functional images were collected using a multi-echo planar imaging sequence (EPI). The functional imaging parameters were the following: slices $= 75$; FOV $= 192$ mm; TR $= 2.0$ s; slice thickness $= 2$ mm; voxel size 2 mm^3; no gap; TE $= 30.20$ ms; multiband acceleration factor $= 3$; flip angle $= 90°$. The first three volumes (6 s) were discarded prior to the start of the run to establish magnetic equilibrium. Participants also completed functional resting state, T2-weighted structural, and diffusion tensor imaging scans that are not analyzed and reported in the present study.

2.5. Statistical analyses

2.5.1. fMRI preprocessing

Data preprocessing was carried out using fMRI Expert Analysis Tool (FEAT, v6.00, part of the FMRIB software library FSL www.fmrib.ox.ac.uk/fsl). Motion correction was carried out by realigning the time series to the middle volume using MCFLIRT (Jenkinson, 2002). Next, slice-timing correction was applied using Fourier-space phase-shifting aligning to the middle volume (Sladkey et al., 2011). Non-brain voxels were removed using BET (Smith, 2002). Brain images were spatially soothed using a Gaussian kernel of FWHM 6 mm. To remove low frequency drift, high-pass temporal filtering was applied using Gaussian-weighted least-squares straight line fitting with sigma= 50.0 s. The time series was grand-mean intensity normalized by a single multiplicative factor. Functional images were registered to the high-resolution structural image using FMRIB's Linear Registration Tool and normalized to MNI space (FLIRT; Jenkinson, 2001; 2002).

2.5.2. fMRI analyses

Time series statistical analysis was carried out using FMRIB's Improved Linear Model (FILM) with autocorrelation correction (Woolrich, 2001). The design matrix included separate event-related regressors for incongruent and congruent trials. A double-gamma hemodynamic response function was used to model the expected BOLD signal (Friston, Josephs, Rees, & Turner, 1998). The neural signal was modeled as epochs starting with the onset of each trial for a duration of two seconds. Six motion parameters along with the 24 extended parameters (derivatives of motion parameters and the squares of motion parameters and their derivatives) were added as nuisance regressors in the model. Participants were excluded if they had average framewise displacement > 1 mm ($n = 10$), or if 10% of volumes in the run had composite motion greater than 2 mm ($n = 1$). Volumes with composite motion greater than 2 mm were flagged using artifact detection tools (ART, composite motion is the maximum voxel displacement resulting from a combined effect of individual translation and rotation displacement measures: http://www.nitrc.org/projects/artifact_detect). Children included in the final analyses had less than 9.78% of volumes with motion greater than 2 mm within a run (percentage of volume-to-

Table 1
Whole brain analyses that show greater activation for incongruent relative to congruent trials.

Sample	Min Cluster Size	Cluster	Hemisphere	Number of Voxels	z	*p*-value	X	Y	Z
Adults	141	Insula	R	175	4.03	.02	34	20	4
		Anterior Cingulate Cortex	R/L	956	4.32	< 0.001	-6	12	52
		Precuneus/IPS	L	812	4.03	< 0.001	-12	-72	34
Children	185	No significant clusters							
Adults > Children	181	Anterior Cingulate Cortex	R/L	1244	5.23	< 0.001	4	10	60
		Intraparietal sulcus	L	497	4.37	< 0.001	-32	-58	46
Children > Adults	181	No significant clusters							

Note. L = left; R = right; IPS = intraparietal sulcus; coordinates are reported in MNI space; cluster forming threshold set to z > 3.1, and FWE, p < .05. The minimum cluster size when we used a more liberal cluster forming threshold (z > 2.3 and FWE, p < .05) to test neural congruity effect in children was 141 voxels.

volume outliers range between 0% and 9.78%, *M* = 2.84%, *SD* = 2.40%), and had mean framewise displacement *less than* 0.76 mm (mean framewise displacement range between .07–0.76 mm, *M* =.29 mm, *SD* =0.18 mm*)*.

We conducted the following first-level contrasts: congruent > baseline, incongruent > baseline, congruent > incongruent, and incongruent > congruent. First, we tested whether adults showed a neural congruity effect, by conducting an exploratory second-level whole brain analysis using FMRIB's Local Analysis of Mixed Effects (FLAME Stage 1; Woolrich et al., 2004). Only the first of three runs of the number word-quantity mapping task was submitted to this analysis to be comparable to children, who only performed a single run. Second, we ran a whole brain model to test our pre-registered prediction that children who knew the meaning of number words would show a neural congruity effect. Third, we ran an exploratory whole brain model to examine age-related differences between adults and children. This analysis aimed to map out which brain regions showed greater neural signal for incongruent relative to congruent trials in the number word-quantity mapping task in adults compared to children. We also tested for the reverse pattern to examine whether there were brain regions that showed greater neural signal for incongruent relative to congruent trials in children compared to adults. Children showed significantly greater motion (*M*framewise displacement =0.29) during the scan relative to adults (*M*framewise displacement =0.11), *t*(97.93) = 8.33, *p* < .001. Therefore, mean framewise displacement was added as a covariate of no-interest in the group model comparing adults and children. The statistical maps were cluster-corrected for multiple comparisons using Monte Carlo simulation. A cluster-forming threshold was set to z > 3.1 and a family-wise error (FWE) rate of *p* < .05 (Eklund et al., 2016).

Given that our goal was to capture neural activity specific to processing the meaning of number words our pre-registration excluded children who had yet to master the cardinal principle (i.e., subset knowers). However, two of the children tested were not cardinal principle knowers but scored above 75% accuracy on the behavioral number word-quantity mapping task demonstrating that they knew number words one through four. We included them in the analyses but note that the results remain the same when the two children are excluded.

2.5.3. Region of interest analyses

Because prior fMRI studies on numerical processing have found that right and left IPS show different developmental trends, we conducted exploratory regions of interest analyses to test for age-related changes in neural activity for processing number words as a function of numerical knowledge. Bilateral IPS was pre-defined based on a meta-analysis of symbolic and non-symbolic number processing in adults (Sokolowski et al., 2017). The conjunction of the symbolic and non-symbolic activation map was provided by the first author and converted from Talairach to MNI space using a linear transformation (right IPS = 469 voxels, 3752 mm^3; and left IPS = 517 voxels, 4136 mm^3). Mean percent signal change for each participant was extracted from each ROI using Featquery in FSL. Individual participants' neural congruity effect was calculated by subtracting the mean percent signal change for congruent trials from incongruent trials. We tested whether there were any

significant associations between age and the magnitude of the neural congruity effect in the regions of interest. Next, we tested our pre-registered hypotheses that the neural congruity effect is associated with individual differences in numerical knowledge. We conducted regression analyses to test the relationship between neural congruity in our regions of interest with raw scores on the numeration subtest, as well as accuracy on the number word-quantity mapping task, while controlling for age.

We conducted exploratory analyses to examine whether attending formal school increased the strength of the associations between neural congruity in our regions of interest and age and numeration raw scores. Children who attend Kindergarten or grade school were defined as attending formal school, whereas children who attended pre-school, daycare, or remained at home were defined as not attending formal school. We tested whether there was an interaction between formal school attendance and age, as well as an interaction between formal school attendance and Numeration scores in predicting neural congruity in our regions of interest. We tested whether there were significant differences between correlation coefficients using either a Zeiger's (dependent correlations) or Fisher's Z (independent correlations) test. We also tested the specificity of any brain-behavioral associations by including measures for SES, motion, and verbal and non-verbal IQ in our regression models in the supplementary materials. We lastly tested whether the neural congruity effect was associated with verbal and non-verbal IQ. All individual differences analyses were conducted in R (Core Team, 2019), and figures were produced using the ggplot2 package (Wickham, 2016).

There were no significant correlations between framewise displacement during the functional scan and age, *r*(75) = .07, *p* = .56, 95% CI = [− 0.16,.29]) or numeration scores, *r*(72) = −.03, *p* = .78, 95% CI = [− 0.20,.26]), suggesting that brain-behavioral associations are not confounded by motion. Outliers were defined as scores that were twice the interquartile range below the first quartile or above the third quartile. Two outliers based on numeration scores (both raw scores = 37) and three outliers based on neural congruity in LIPS were removed from their respective correlation analyses. We removed one data point as an outlier for neural congruity in a LIPS cluster pre-defined based on the meta-analysis (Sokolowski et al., 2017) (neural congruity data point below −0.33) and two data points as outliers for neural congruity in LIPS$_{IPL}$, defined based on the whole brain analysis showing greater neural congruity in adults relative to children (one neural congruity data point below –0.33 and one neural congruity points above .30). No other outliers were identified in the other ROIs.

3. Results

3.1. Behavioral results of the number word-quantity mapping task in children

Mean accuracy on the number word-quantity mapping task ranged between 75% and 100% with 19% percent of children scoring 100% (*M* = 94.2%, *SD* =0.06, Skewness = −1.38, Shapiro-Wilk normality test =0.84, *p* < .001).

A. Neural congruity in Adults > Children

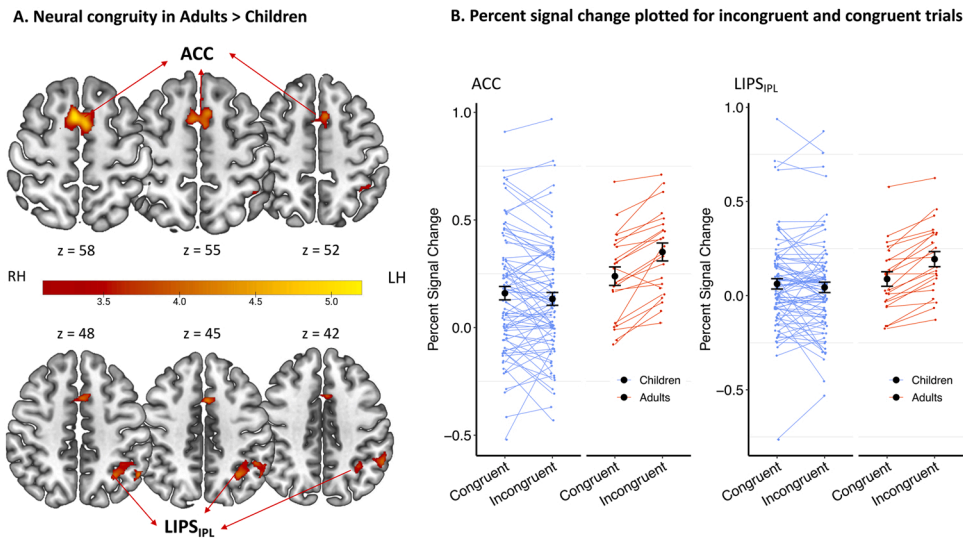**B. Percent signal change plotted for incongruent and congruent trials**

Fig. 2. Whole brain analysis showing a larger neural congruity effect in anterior cingulate cortex and left intraparietal sulcus in adults relative to children. *Note.* A.) Brain regions that show greater activation for incongruent relative to congruent trials during a number word-quantity mapping task in adults compared to children. No regions showed a neural congruity effect in children. Activation in anterior cingulate cortex and the left IPS extending into the inferior parietal lobule overlaid on horizontal slices using MRIcroGL (https://www.nitrc.org/projects/mricrogl). RH = Right hemisphere; LH = Left hemisphere. (B.) Mean percent signal change were extracted for incongruent>baseline and congruent>baseline from LIPS$_{IPL}$ and ACC in adults (orange) and children (blue) for visualization purposes. Error bars are one standard error from the mean. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

A. Regions of interest displayed on sagittal and coronal slices

B. Interaction between formal school and age in predicting neural congruity in both LIPS clusters
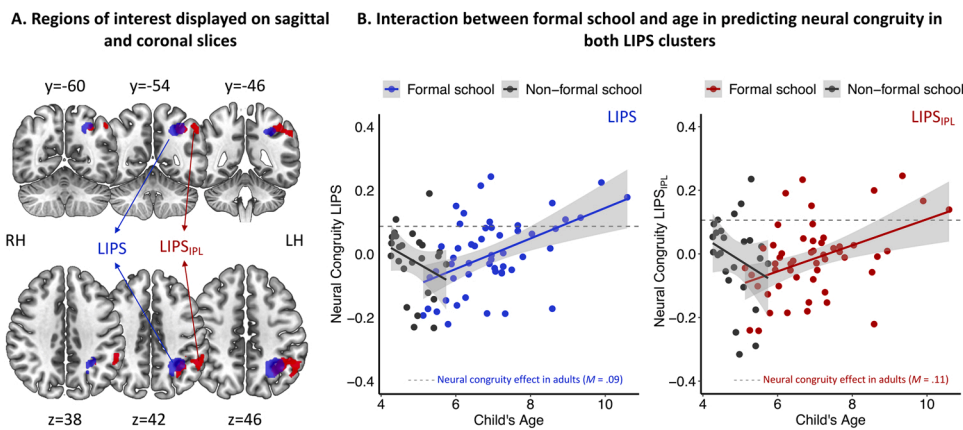

Fig. 3. Children in formal school show a strong relationship between age and neural congruity effect in both LIPS clusters. *Note.* Significant interaction between neural congruity and formal school attendance in predicting age. Children who attended formal school showed a positive correlation between age and the neural congruity in both left intraparietal sulcus clusters (A) Regions of interest are displayed on coronal and axial slices using MRIcroGL (https://www.nitrc.org/projects/mricrogl).
The LIPS$_{IPL}$ in red was defined based on whole brain analysis showing greater neural signal for incongruent relative to congruent trials in adults. Left IPS in blue was defined based on a previous meta-analysis (Sokolowski et al., 2017). The overlap between both clusters is shown in purple (165 voxels, 1320 mm^3). (B) Neural congruity was calculated by subtracting the percent signal change for congruent trials

from incongruent trials. Neural congruity in LIPS (left side) and LIPS$_{IPL}$ (right side) are plotted against age separately for children who attend formal school (in color) and who do not attend formal school (in black). The dashed lines indicate the mean neural congruity effect found in adults (LIPS, M =0.09; LIPS$_{IPL}$, M =0.11). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.2. Whole brain analyses

In adults, we first ran a whole brain analysis to search for brain regions that showed a significant difference between incongruent and congruent conditions during the number word-quantity mapping task. We found a significant neural congruity effect in right insula, anterior cingulate cortex, and a cluster in left precuneus that extends through IPS and inferior parietal lobule*) (see* Table 1*)*. We ran a follow up whole brain analysis with young adults (n = 17), excluding older adults (>35 years-old), and found a similar pattern of results, suggesting that the wide age range we obtained in adults did not impact the group results (see Supplemental Fig. S1 and Supplemental Table 1*)*.

In children, we ran a second whole brain model and contrary to our prediction, we failed to find a significant neural congruity effect in any region of the brain (with a cluster-forming threshold set to $z > 3.1$, and FWE, $p < .05$). The null result remained when we used a more liberal cluster-forming threshold ($z > 2.3$, and FWE, $p < .05$).

We next examined the differences in the neural signal for incongruent relative to congruent conditions in adults compared to children. We found age-related differences in the anterior cingulate cortex (ACC), as well as left intraparietal sulcus extending into the inferior parietal

lobule (LIPS$_{IPL}$). As shown in Fig. 2(a), adults showed greater neural signal for incongruent relative to congruent trials compared to children in both the ACC and LIPS$_{IPL}$. Fig. 2(b) shows that there was a significant difference in the BOLD signal for incongruent and congruent trials in adults but not in children.

3.3. Relationship between neural congruity and age in children

Although children did not exhibit a neural congruity effect at the group-level, we hypothesized that children might show age-related associations with the neural congruity effect in right and left IPS as a function of increasing number knowledge. We tested this hypothesis in both the pre-defined right and left IPS regions of interest and in the regions that showed a significantly greater neural congruity effect in adults relative to children (LIPS$_{IPL}$ and ACC; see Fig. 2a). As seen in Fig. 3 (a), there are 165 voxels (1320 mm^3) that are shared between LIPS defined based on the meta-analysis (LIPS; Sokolowski et al., 2017) and LIPS$_{IPL}$ found in the whole brain analysis showing a larger neural congruity for adults compared to children. The neural congruity in each of our ROIs did not significantly violate assumptions of normality (Shapiro-Wilk p-values >0.15).

Table 2
Correlation matrix.

			1	2	3	4	5
1	Age	r	–	.19†	.09	.32**	.12
		95% CI		-.04,.40	-.14,.30	.11,.51	-.11,.33
2	Neural congruity LIPS$_{IPL}$	r		–	.32**	.81***	.56***
		95% CI			.11,.51	.72,.88	.39,.70
3	Neural congruity ACC	r			–	.24*	.21†
		95% CI				.02,.44	-.01,.42
4	Neural congruity LIPS	r				–	.71***
		95% CI					.58,.81
5	Neural congruity RIPS	r					–
		95% CI					

Note.
$^\dagger = p < .10$,
$* = p < .05$,
$** = p < .01$,
$*** = p < .001$, CI = confidence interval,
LIPS$_{IPL}$ = left intraparietal sulcus extending into the inferior parietal lobule, ACC = anterior cingulate cortex, LIPS = left intraparietal sulcus, RIPS = right intraparietal sulcus (LIPS$_{IPL}$ and ACC were defined based on whole brain analysis showing greater neural congruity in adults relative to children. LIPS and RIPS defined based on previously conducted meta-analysis (Sokolowski et al., 2017)).

There was a significant positive association between age and magnitude of the neural congruity effect in LIPS in the child sample (blue region in Fig. 3a) (see Table 2). The association between age and neural congruity in LIPS remained significant when mean framewise displacement, SES, verbal IQ, and non-verbal IQ standard scores were added to the model (see Supplemental Table 2). A median split analysis on age is consistent with the positive correlation found between neural congruity in LIPS and age (additional details of analysis are provided in supplemental materials). We did not find significant correlations between age and the size of the neural congruity effect in LIPS$_{IPL}$, RIPS, and ACC (see Table 2). A Zeiger's test revealed that the relationship between neural congruity in LIPS and age was significantly stronger than the relationship between neural congruity in LIPS$_{IPL}$ and age, $z = 1.96$, $p = .03$; RIPS and age, $z = 2.43$, $p = .009$; and between ACC and age, $z = 1.73$, $p = .04$.

3.4. Experience-dependent associations in neural congruity effect in children

We further explored whether the positive relationship between age and neural congruity in left IPS was associated with school experience. Children enrolled in Kindergarten or grade school were defined as attending formal school having school attendance ($n = 52$, $M_{age} = 6.96$ years, $SD = 1.19$, Age range: 5.13 – 10.59 years) whereas children who attended preschool, daycare, or remained at home were defined as not attending formal school ($n = 25$, $M_{age} = 4.87$ years, $SD = 0.46$, Age range: 4.26 – 5.74 years). Multiple regression analysis revealed that there was a significant interaction between formal school attendance and age in predicting neural congruity in LIPS$_{IPL}$ (see Table 3). The interaction between formal school attendance and age in predicting neural congruity in both LIPS clusters were significant when mean framewise displacement, SES, verbal, and non-verbal IQ standard scores were added to the model (see Supplemental Table 3).

There was a significantly stronger positive correlation between age and neural congruity in LIPS$_{IPL}$, $r(50) = 0.43$, $p = .002$, 95% CI = [.17,.63] and LIPS, $r(50) = 0.49$, $p < .001$, 95% CI = [.25,.67] in children who attended *formal* school relative to children who had not yet attended *formal* school (LIPS$_{IPL}$: $r(23) - 0.25$, $p = .22$, 95% CI = [− 0.59,.16]; LIPS: $r(23) = -0.29$, $p = .16$, 95% CI = [− 0.62,.12])

Table 3
Multiple regression analysis showing a significant interaction between age and formal school experience in predicting neural congruity effect in LIPS.

Variable	Neural Congruity LIPS$_{IPL}$		
	B	SEβ	β
Intercept	-.06*	.03	
Age	.002	.02	.04
Formal School	.07	.08	.28
Age x Formal School	.12*	.05	.64*
R^2	.14		
F(df)	3.84 (3, 73)*		
Neural congruity in ACC			
	B	SEβ	β
Intercept	-0.07*	.03	
Age	-0.01	.02	-.12
Formal School	.09	.08	.34
Age x Formal School	.08	.06	.44
R^2	.04		
F(df)	.91 (3, 73)^{ns}		
Neural congruity in LIPS			
	B	SEβ	β
Intercept	-0.06*	.02	
Age	.01	.02	.13
Formal School	.08	.07	.35
Age x Formal School	.12*	.05	.68*
R^2	.20		
F(df)	6.24 (3, 73)**		
Neural congruity in RIPS			
	B	SEβ	β
Intercept	-0.06*	.03	
Age	-0.02	.02	-.25
Formal School	.14†	.07	.62†
Age x Formal School	.12*	05	.75*
R^2	.10		
F(df)	2.55 (3, 73)†		

Note.
$^\dagger = p < .10$,
$* = p < .05$,
$** = p < .01$,
$*** = p < .001$,
NC = neural congruity effect, LIPS$_{IPL}$ = left intraparietal sulcus extending into inferior parietal lobule, ACC = anterior cingulate cortex, LIPS = left intraparietal sulcus, RIPS = right intraparietal sulcus (LIPS$_{IPL}$ and ACC were defined based on whole brain analysis showing greater neural congruity in adults relative to children. LIPS and RIPS defined based on previously conducted meta-analysis (Sokolowski et al., 2017)).
There is a strong positive correlation between age and formal school attendance in our current sample, rpb . = 0.70, p < .001†. Collinearity statistics indicate that there is evidence for multicollinearity, but that VIF values < 10 and condition indices < 10 suggests it is not a serious concern across regression models (Belsley et al., 1990; Hair et al., 1995; Marquardt, 1970) (Age, Tolerance =0.24, VIF = 4.13; Formal School, Tolerance =0.13, VIF = 7.80, and Age x Formal school interaction, Tolerance =0.25, VIF =4.05; Condition Indices range from 1 to 6.46).

(Fishers z- test for LIPS$_{IPL}$ and LIPS respectively, $z = 2.79$, $p = .005$; $z = 3.27$, $p = .001$) (see Fig. 2b).

3.5. Associations between neural congruity and behavioral measures

We next examined whether neural congruity in any regions of interest was associated with numeration raw scores or behavioral performance on the number word-quantity mapping task while controlling for age. Contrary to our prediction, accuracy on the number word-quantity mapping task did not account for significant unique variance in neural congruity in any regions of interest. Given the uniformly high performance and therefore low variance on the behavioral mapping task ($M = 94.2\%$, $SD = 0.06$) the lack of correlations is uninformative (additional details on analyses are in Supplemental materials). However, the numeration subtest, which did not suffer from a ceiling effect, also did not account for significant variance in neural congruity in LIPS$_{IPL}$, LIPS, RIPS, or ACC (see regression models in Table 4). In regression

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Table 4
Multiple regression analysis examining the relationship between numeration performance and neural congruity.

Variable	Neural Congruity LIPS$_{IPL}$		
	B	$SE\beta$	β
Intercept	-.13	.07	
Age	.02	.01	.26
Numeration Raw Scores	-.002	.003	-0.08
R^2	.04		
F(df)	1.52 (2, 71)^{ns}		
	Neural congruity in ACC		
	B	$SE\beta$	β
Intercept	-0.01	.08	
Age	-0.01	.02	-.13
Numeration Raw Scores	.006	.004	.25
R^2	.03		
F(df)	1.03 (2, 71)^{ns}		
	Neural congruity in LIPS		
	B	$SE\beta$	β
Intercept	-0.19**	.07	
Age	.03*	.01	.41*
Numeration Raw Scores	-0.002	.003	-.12
R^2	.11		
F(df)	4.34 (2, 71)*		
	Neural congruity in RIPS		
	B	$SE\beta$	β
Intercept	-0.10	.07	
Age	.03†	.01	.33†
Numeration Raw Scores	-0.006	.003	-.30
R^2	.05		
F(df)	1.78 (2, 71)^{ns}		

Note.
† $= p < .10$,
* $= p < .05$,
** $= p < .01$,
*** $= p < .001$,
LIPS$_{IPL}$ = left intraparietal sulcus extending into the inferior parietal lobule, ACC = anterior cingulate cortex, LIPS = left intraparietal sulcus, RIPS = right intraparietal sulcus (LIPS$_{IPL}$ and ACC were defined based on whole brain analysis showing greater neural congruity in adults relative to children. LIPS and RIPS defined based on previously conducted meta-analysis (Sokolowski et al., 2017)).

models that tested whether school attendance interacted with numeration performance to predict neural congruity, we found a significant interaction specifically in LIPS$_{IPL}$ (β=.41, SE =0.008, p=.02, F(4,69) =2.94, p=.03, R^2 =.15). However, when accounting for age in the regression model, the association between numeration performance and neural congruity in LIPS$_{IPL}$ was not significant in children who attended formal school (β=.05, SE =.004, p=.75, F(2, 46) =4.99, p=.04, R^2 =.18),

or who did not attend formal school (β=-.30, SE =.01, p=.20, F(2, 22) =1.71, p=.20, R^2 =.14) (see Fig. 4; see Supplemental Fig. 2 for a plot of the residuals when neural congruity and numeration scores are regressed on age). No significant interaction was found between school attendance and performance on the Numeration subtest when predicting neural congruity in LIPS (β=.27, SE =.007, p=.12, F(4, 69) =3.48, p=.01, R^2 =.17), RIPS (β=.28, SE=.007, p=.12, F(4, 69)=1.52, p=.21, R^2 =.08), or ACC (β= −0.04, SE =.009, p=.83, F(4, 69) =0.51, p=.73, R^2 =.03) (see Supplemental Table 4 and Table 5 for full interaction regression models).

We further tested whether age-related changes in neural congruity were correlated with domain general cognitive processes. No significant correlations were found between neural congruity in any region of interest and verbal or non-verbal IQ (all p-values >0.16) (see Supplemental Table 6).

4. Discussion

The present study was the first to use fMRI to study the development of neural activation during spoken number word mapping in young children and adults. While adults showed a robust neural congruity effect in left intraparietal sulcus (LIPS$_{IPL}$) and anterior cingulate cortex (ACC), children did not show a significant neural congruity effect at the group-level. We did however find age-related increases in neural

Table A1
Number word mapping task trial list.

Verbal Number Word	Visual Quantity	Distance	Condition
one	2	1	Incongruent
one	3	2	Incongruent
two	1	1	Incongruent
two	4	2	Incongruent
three	1	1	Incongruent
three	4	2	Incongruent
four	2	1	Incongruent
four	3	2	Incongruent
one	1	0	Congruent
one	1	0	Congruent
two	2	0	Congruent
two	2	0	Congruent
three	3	0	Congruent
three	3	0	Congruent
four	4	0	Congruent
four	4	0	Congruent

Note1). Each trial was administered four times for a total of 64 trials (32 incongruent, 32 congruent trials)
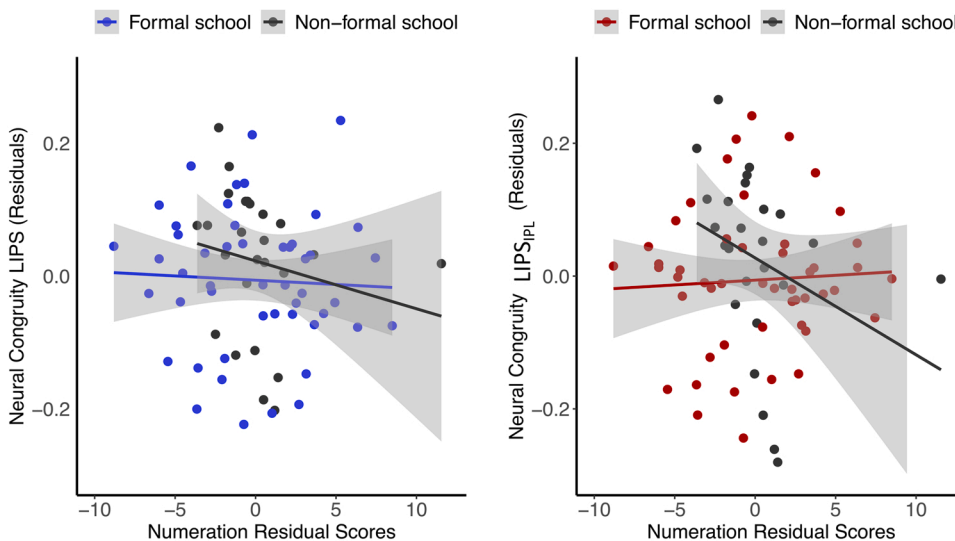

Fig. 4. No significant interaction between performance on the numeration subtest and formal school attendance in predicting neural congruity in both LIPS clusters. *Note.* Neural congruity was calculated by subtracting the mean percent signal change for congruent trials from incongruent trials. Neural congruity in LIPS (left side in blue) and LIPS$_{IPL}$ (right side in red) and are plotted against numeration raw scores separately for children who attend school (in color) and who do not attend school (in black). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

congruity specifically in LIPS in children and this association was driven by children who attend school. Thus, the neural basis of number-word processing exhibits a protracted developmental trajectory.

Despite the fact that the children in our sample demonstrated comprehension of the number words 1–4, children did not show an adult-like neural congruity effect when presented with incongruent visual arrays and spoken number words. This is analogous to findings on the neural bases of reading and letter-sound integration which show a protracted neural development of the visual word form area (VWFA) well after children have learned to read (e.g., Blackburne et al., 2014). For example, the VWFA showed less specificity, or ability to differentiate printed words versus line drawings of nameable objects, in children compared to adults (Centanni, et al., 2017). Contrasts between words and pseudowords do not reach an adult-like pattern until adolescence even though much younger children can differentiate words from pseudowords (Brem et al., 2006; Maurer et al., 2005, 2006). ERP patterns for letter speech processing develop approximately four years into formal reading instruction (Froyen et al., 2009). Similarly, ERPs that differentiate letters and numbers in adults (Park et al., 2014) do not emerge until sometime between 10 and 15 years of age despite behavioral evidence that much younger children can differentiate between letters and numbers (Park et al., 2018). Thus, our results add to the more general finding that brain measures often show continued developmental changes even when they accompany discriminations that are at ceiling levels of performance.

An interesting question is whether the emergence of the neural congruity effect for number words with age reflects maturational processes or is driven by specific experience with number words. The relationship between age and neural congruity was strong in children who attended school which may suggest that exposure to number words in school drove the emergence of the neural congruity effect. However, our results cannot cleanly differentiate between these possibilities given that school attendance and age were confounded. In fact, we also observed a trend whereby neural congruity in bilateral IPS was negatively associated with age and numeration raw scores in children who do not attend formal school. These correlations were not significant and likely artefactual. Future studies with large sample sizes would be necessary to identify whether there are qualitative differences in brain-behavioral correlations in children prior to and after starting formal school. It is important to note that the correlation between age and neural congruity in LIPS was significantly stronger than the correlation between age and neural congruity in RIPS or ACC. Thus, an age-related increase in neural congruity in LIPS for number word processing may reflect increasingly automatic mappings between number words and their underlying representations with age or with number-word exposure in school or both. These findings are consistent with the suggestion that LIPS becomes a functionally specialized region for processing symbolic numerals (Bugden et al., 2012; Emerson & Cantlon, 2014; Matejko et al., 2019; Vogel et al., 2015).

Alternatively, the strong association found between neural congruity in LIPS and age could reflect children's developing attentional systems and thus reflect more domain general processes. Children who attend school have greater experience attending to task events and filtering out irrelevant information. With age and experience, children are better able to attend to task relevant information while in the scanner. Although the domain general attention explanation cannot be ruled-out, it is likely that the neural changes in LIPS reflect both domain general and domain specific processes such that neural systems for attending to numerical information are becoming more refined (Wilkey et al., 2020; Wilkey and Price, 2019). Again, the fact that age-related associations were specific to LIPS, not the RIPS or ACC, and that they do not correlate with measures of non-verbal and verbal IQ suggests that the increase in neural congruity with age in children who attend school may at least in part reflect increasing automaticity in mapping number words to semantic representations of number.

Our finding that adults showed a greater neural congruity in ACC,

while children did not, is consistent with studies reporting that adults show greater activation in ACC relative to both children and adolescents when performing a wide variety of tasks that are specifically designed to assess conflict resolution (Adleman et al., 2002; Bunge and Wright, 2007; Engelhardt et al., 2019; Rubia et al., 2006). The recruitment of ACC in adults during the number word-quantity mapping task may indicate that our mapping task elicits more domain general conflict processing in adults compared to children.

Contrary to our prediction, we did not find a correlation between neural congruity and either of the behavioral measures of numerical competence. This may have been due to the specific numerical performance measures we chose. The behavioral version of the matching task elicited close to ceiling levels of performance and the Numeration subtest from KeyMath is an assessment of general numerical concepts most appropriate for our youngest children. Future research should include a wider range of age-appropriate math measures. Another limitation of our study is that it cannot disambiguate between domain-specific and/or domain-general mechanisms or even experiential and/or maturational processes that underlie age-related associations found in LIPS. Although we found that children who attend formal school showed a stronger relationship between age and neural congruity in LIPS, age and school attendance were highly correlated in our sample.

Longitudinal studies designed to track neural changes that accompany the acquisition of the cardinal principle and more nuanced aspects of number word learning should be important for understanding how math learning differences emerge early in development. Specifically, tracking the neural changes in older children should uncover when the neural congruity effect first emerges and whether its emergence interacts with other neurodevelopmental trends, such as the fronto-parietal shift *(*e.g., Ansari et al., 2005; Ansari & Dhital, 2006; Cantlon et al., 2008; Rivera et al., 2005*)*, or the right-to-bilateral IPS localization (e.g. Edwards et al., 2016; Kersey and Cantlon, 2016; Sokolowski et al., 2017). Studying individual differences in brain development as children are acquiring the cardinal principle might prove useful for optimizing interventions (Gabrieli et al., 2015). Future studies could test the hypothesis that greater exposure and experience with tasks that strengthen number word to quantity mapping would induce adult-like patterns of neural activation for number words in children.

4.1. Conclusions

Despite behavioral evidence that young children know the meanings of number words, an adult-like pattern of neural activation to number words is slow to develop. Whereas adults showed a robust neural congruity effect in a number word-quantity mapping paradigm in both LIPS and ACC, children showed no effect at the group level. We found an association between age and neural congruity in LIPS in children that was stronger for children who attended school. Given that forming strong number word-quantity mappings is a predictor of future math success, characterizing the associated individual differences in developing brain systems and how they are shaped by experience, has the potential to inform optimal learning pathways early in development.

CRediT authorship contribution statement

The behavioral data and brain measures extracted from the regions of interest that support the findings in this study is available on open science framework https://osf.io/c36ms/. The whole brain data are available upon request to the corresponding author (SB).

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.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2021.101011.

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