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Gray matter volume in left intraparietal sulcus predicts longitudinal gains in subtraction skill in elementary school

Macarena Suárez-Pellicioni[a,*], **Firat Soylu**[a], **James R. Booth**[b]

[a]Department of Educational Studies in Psychology, Research Methodology, and Counseling, University of Alabama, 270 Kilgore Ln, Tuscaloosa, AL 35401, USA

[b]Department of Psychology and Human Development, Vanderbilt University, Nashville, TN, USA

Abstract

Although behavioral studies show large improvements in arithmetic skills in elementary school, we do not know how brain structure supports math gains in typically developing children. While some correlational studies have investigated the concurrent association between math performance and brain structure, such as gray matter volume (GMV), longitudinal studies are needed to infer if there is a causal relation. Although discrepancies in the literature on the relation between GMV and math performance have been attributed to the different demands on quantity vs. retrieval mechanisms, no study has experimentally tested this assumption. We defined regions of interests (ROIs) associated with quantity representations in the bilateral intraparietal sulcus (IPS) and associated with the storage of arithmetic facts in long-term memory in the left middle and superior temporal gyri (MTG/STG), and studied associations between GMV in these ROIs and children's performance on operations having greater demands on quantity vs. retrieval mechanisms, namely subtraction vs. multiplication. The aims of this study were threefold: First, to study concurrent associations between GMV and math performance, second, to investigate the role of GMV at the first time-point (T1) in predicting longitudinal gains in math skill to the second time-point (T2), and third, to study whether changes in GMV over time were associated with gains in math skill. Results showed no concurrent association between GMV in IPS and math performance, but a concurrent association between GMV in left MTG/STG and multiplication skill at T1. This association showed that the higher the GMV in this ROI, the higher the children's multiplication skill. Results also revealed that GMV in left IPS and left MTG/STG predicted longitudinal gains

*Corresponding author. mspellicioni@ua.edu (M. Suárez-Pellicioni).

Credit authorship contribution statement

Macarena Suárez-Pellicioni: Investigation, Formal analysis, Writing – review & editing. **Firat Soylu:** Formal analysis, Writing – review & editing. **James R. Booth:** Conceptualization, Project administration, Data curation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Compliance with ethical standards

Written assent was obtained from the children and consent from their parents or guardians. All experimental procedures were approved by the Institutional Review Board at Northwestern University.

Data and code availability statement

The dataset used in this study is available in OpenNeuro (10.18112/openneuro.ds001486.v1.1.0).

For the analyses we used the codes generated by Statistical Parametric Mapping (SPM) 12 (Wellcome Trust Centre for Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm) and Computational Anatomy Toolbox (CAT12; http://dbm.neuro.uni-jena.de/cat12/) segmentation tool.

in subtraction skill only for younger children (approximately 10 years old). Whereas higher levels of GMV in left IPS at T1 predicted larger subtraction gains, higher levels of GMV in left MTG/STG predicted smaller gains. GMV in left MTG/STG did not predict longitudinal gains in multiplication skill. No significant association was found between changes in GMV over time and longitudinal gains in math. Our findings support the early importance of brain structure in the IPS for mathematical skills that rely on quantity mechanisms.

Keywords

gray matter volume; math; children; fMRI; longitudinal

1. Introduction

Successful arithmetic learning is of critical importance not only for everyday life, but for academic achievement (Duncan et al., 2007), professional development (Gross et al., 2009), future economic success (Ritchie and Bates, 2013; Rose, 2006), and general quality of life (Reyna and Brainerd, 2007; Rivera-Batiz, 1992). Functional Magnetic Resonance Imaging (fMRI) research has investigated how children learn mathematics by measuring differences in brain activation while participants solve math tasks inside the scanner (e.g. Peters and De Smedt, 2018). Measuring fMRI brain activation patterns are strongly task-dependent, but the study of structural integrity is independent of paradigm design and participants' performance (Rotzer et al., 2008). Despite the potential of research on brain structure in explaining differences in math performance, these studies are scarce. One of the most widely used analyses of brain structure is voxel-based morphometry (VBM), which provides measures of regionally specific gray matter volume (GMV), for each participant, allowing researchers to correlate these volumetric measures with cognitive measures of interest (Ashburner and Friston, 2000).

Some evidence for the relationship between brain structure and math skill comes from adults with exceptionally high math abilities (Aydin et al., 2007; Popescu et al., 2019). These studies have provided some contradictory results, reporting both higher (Aydin et al., 2007; bilateral inferior parietal lobule; IPL) and lower (Popescu et al., 2019; intraparietal sulcus; IPS) GMV in parietal cortex in mathematicians as compared to controls. Evidence from mathematician's brains, and from adult brains in general, are the consequence of undergoing extensive training in mathematics, being the result of education and enculturation. For this reason, results from adults may not generalize to children, and we should study children to understand how structural brain features are causally related to mathematics learning (Karmiloff-Smith, 2010).

A number of studies investigating the relationship between brain structure and math skill in children have focused on children with developmental dyscalculia. The main conclusion from these studies is that children with dyscalculia show lower GMV in the left IPS (Isaacs, 2001), right IPS (Cappelletti and Price, 2014; Rotzer et al., 2008; Rykhlevskaia et al., 2009), right IPL (Ranpura et al., 2013), and in frontal structures including the middle and inferior frontal gyri (MFG; IFG; Rotzer et al., 2008). Given that some have suggested dyscalculia is a qualitatively distinct population rather than the tail of a normal distribution (Mazzocco et al., 2011), it is not clear whether these findings generalize to math learning for typically developing children.

The current literature on the relationship between brain structure and math skill in typically developing children is still limited. Lubin and colleagues studied this relationship in 10-year-old children and found that children with lower proficiency levels had lower GMV in the left IPS as compared to those with high proficiency (Lubin et al., 2013). Li et al. (2013) also found a positive correlation between GMV in the left IPS and children's arithmetic achievement. Other studies, however, have not found an association between math skill and GMV in this region. Studying children from 3rd to 8th grade, Wilkey et al. (2016) found that GMV in the bilateral hippocampus and right IFG was associated with higher math performance, but they found no association with IPS. Polspoel et al. (2020) found that GMV in the right fusiform gyrus showed a positive correlation with arithmetic fluency in 4th graders, whereas GMV in IPS played no significant role.

These studies, however, were correlational, meaning that no directionality can be established, leaving unanswered the question of whether the effects found in the brain are the cause or the consequence of math learning. Another limitation of previous correlational studies with children is the inclusion of participants from a wide age range. Given that children's brain structure changes over development (Toga et al., 2006), these studies can fail to detect or falsely suggest changes over time (Casey et al., 2005). The optimal solution to avoid these confounds is to use longitudinal studies (Geary, 2011; Karmiloff-Smith, 2010) with relatively narrow age groups.

Only three studies have addressed the role of GMV at time 1 (T1) in predicting longitudinal gains in math skill. Supekar et al. (2013) studied the neural predictors of response to an eight-week one-to-one math tutoring in 3rd graders and found that GMV in the right hippocampus was related to performance gains, whereas GMV in the IPS did not show any associations. Evans et al. (2015) measured GMV in 8-year-old children and used those measures to predict longitudinal gains in numerical skill. They found that GMV in left IPS and left dorsolateral prefrontal cortex (DLPFC) at age 8 predicted gains in numeric skill 6 years later. Price et al. (2016) studied concurrent and longitudinal associations between GMV and math skill in 1st and 2nd graders and found that GMV in the left IPS was the only region showing an association with math competence at the end of 1st grade and that GMV in this region at the end of 1st grade was associated with math competence at the end of 2nd grade.

It has been suggested that the discrepancies in the literature on the association between GMV and math skill could be attributed to the different nature of the tests used to measure math performance (Price et al., 2016; Wilkey et al., 2016). The studies that found an association between GMV in regions associated with retrieval, but not in IPS, and math performance or math gains have in common that they used measures emphasizing fluency and efficiency. Polspoel et al. (2020) used an arithmetic fluency test, Wilkey et al. (2016) used an in-school math test requiring memory encoding and retrieval, and Supekar et al. (2013) calculated a combined score including accuracy and response times. The studies that found an association between GMV in IPS and math performance, on the other hand, have in common that they measured math performance with tasks that relied more on quantity mechanisms or involved calculation. Lubin et al. (2013) measured math performance by asking children to transcode from the analog system (i.e. dot comparison) to the symbolic system and back, Li et al. (2013) used a test requiring numerical reasoning and the ability to solve arithmetic problems, Price et al. (2016) used a composite measure of math performance including calculation and problem resolution, and Evans et al. (2015) asked participants to solve calculation for all four operations.

Previous brain structure studies focusing on arithmetic performance have not taken into account the evidence from fMRI studies suggesting that different mechanisms are involved in solving different operations (Arsalidou and Taylor, 2011; Rosenberg-Lee et al., 2011) depending on the degree of retrieval or calculation they require (Polspoel et al., 2017). Probably the clearest difference between operations is shown between subtraction and multiplication, with subtraction relying on calculation and activating quantity mechanisms in the parietal cortex (particularly the intraparietal sulcus (IPS); Prado et al., 2011, 2014; Suárez-Pellicioni et al., 2020) and multiplication relying on retrieval of solutions from long-term memory and considered not to involve quantity mechanisms in IPS (Prado et al., 2011, 2014; Suárez-Pellicioni et al., 2018, 2019).

The main objective of this study is to fill these gaps in the literature by studying the association of GMV in regions of the brain important for representing quantity and for the storage of arithmetic facts in long-term memory with gains in two operations known to have a different engagement of these mechanisms: subtraction and multiplication. To this aim, we used an ROI approach, focusing on the brain regions that have been reported to be functionally related to children's subtraction gains (Suárez-Pellicioni et al., 2020) and that are considered to be crucial for quantity representation (Dehaene et al., 2003): the bilateral IPS (Arsalidou et al., 2018; Arsalidou and Taylor, 2011; Battista et al., 2018) and regions that are considered to store the representation of arithmetic facts in a verbal code in long-term memory, the left MTG/STG (Prado et al., 2011, 2014; Suárez-Pellicioni et al., 2018, 2019) Given that most of the cross-sectional and longitudinal studies described above found the effects in the left IPS, we studied hemispheric differences by using separate ROIs for the left and right IPS.

Although it is important to investigate whether brain structure predicts gains in math skill, it is also informative to determine whether *changes* in GMV are related to *changes* in math performance. Changes over time can be reflected in the loss of GMV due to the synaptic pruning to improve neural efficiency (Gogtay et al., 2004), or the increase of GMV with the formation of new connections over learning, through synaptogenesis (Kanai and Rees, 2011). Synaptic pruning and synaptogenesis, therefore, have opposite effects on brain structure over development. Evidence from adults has shown that better performance through training and practice led to increases in GMV in task-related regions of the brain for mirror reading (Ilg et al., 2008), playing video games (Kühn et al., 2014), learning to juggle (Boyke et al., 2008; Draganski et al., 2004), or learning in medical students (Ceccarelli et al., 2009; Draganski et al., 2006; Koch et al., 2016). Only one study has attempted to answer this question in the field of math. Price et al. (2016) looked at the association between changes in GMV from 1st to 2nd grade with math performance in 2nd grade. However, given that they did not measure math performance at T1 (i.e. 1st grade), they were unable to calculate changes in performance over time, leaving unanswered the question about the association between the two changes measures.

The specific aims of this study were threefold: First, to study concurrent associations between GMV and math performance at T1 and at Time 2 (T2; see red arrows in Fig. 1). Second, to investigate the role of GMV at T1 in predicting longitudinal gains in subtraction and multiplication skill (see cyan arrow and lines in Fig. 1). Third, to study the changes in GMV over time associated with longitudinal gains in subtraction and multiplication skill (see violet arrows and lines in Fig. 1). Given the relatively wide age range of children in our study (i.e. 8 to 14 years old at T1), we included age at T1 as one of the predictors in all the regression analyses.

2. Methods

2.1. Participants

2.1.1. Whole sample—Sixty-five 3rd to 8th graders were recruited from schools in the Chicago metropolitan area to participate in the study. This dataset has been deposited in OpenNeuro (10.18112/openneuro.ds001486.v1.1.0) and a detailed description of the dataset is provided in Suárez-Pellicioni et al. (2019). Time-point 1 of this dataset is the basis of other publications including Berteletti and Booth (2015, 2015), Berteletti et al. (2014), Demir-Lira et al. (2019), Demir et al. (2014, 2015) and Prado et al. (2014). The longitudinal data of this dataset is the basis of other publications including Demir-Lira et al. (2016), Suárez-Pellicioni and Booth (2018), and Suárez-Pellicioni et al. (2018, 2019, 2020). None of these studies have looked at the role of gray matter volume in predicting gains in subtraction or multiplication skill, which constitutes the objective of this study.

All participants were native English speakers, right-handed, were free of past and present psychiatric disorders including Attention Deficit Hyperactivity Disorder (ADHD), neurological disease, or epilepsy. According to parental report, no participant had hearing impairments, uncorrected visual impairment, was born prematurely (less than 36 weeks), was taking medication affecting the central nervous system, or had any contraindication for being scanned, such as having braces. Participants had no history of intellectual deficits, all of them scoring 85 standard score (hereinafter, SS) or above on the full IQ scale of the Wechsler Abbreviated Scale of Intelligence – WASI (Weschler, 1999). Participants showed no reading deficits, all of them scoring 85 SS or above on the average of word attack and word identification subtests of the Woodcock-Johnson III Test of Achievement (WJ-III; Woodcock et al., 2001). Children and their parents or guardians provided written consent to participate in the study. Parents were compensated $20 per hour for their time. All experimental procedures were approved by the Institutional Review Board at Northwestern University. One participant was excluded for being left-handed, another one for having insufficient coverage of the parietal area, two for having low IQ, two for having low reading skill, and three for having missing data at T2. The final sample consisted of 56 participants who were tested longitudinally, with sessions being approximately 2 years apart. More detailed information about the sample is given in Table 1.

2.1.2. Groups based on children's age at T1—
In order to explore the role of age at T1 in explaining concurrent associations (aim 1), and longitudinal gains (aims 2 and 3) in subtraction and multiplication skill, two groups were created based on the median-split of children's age at T1 (hereinafter, age groups T1): the younger group (n=28) and the older group (n=28). As expected, age groups differed in age at T1 ($t(54) = -11.25$, $p < .001$). Groups also differed in age at T2 ($t(54) = -10.77$, $p < .001$), but not in time between sessions ($t(54) = -1.26$, $p = .21$). Younger and older children did not differ in working memory at T1 ($t(52)$[1] $= 1.15$, $p = .26$), total intracranial volume (TIV) at T1 ($t(54) = -0.65$, $p = .52$) or at T2 ($t(54) = -0.41$, $p = .68$), in sex distribution ($X^2 = 2.58$, $p = .11$), or in full IQ ($t(54) = 1.41$, $p = .16$). Age groups also differed in subtraction ($t(54) = -2.71$, $p = .009$) and multiplication ($t(54) = -3.15$, $p = .003$) skill at T1, but not in subtraction ($t(54) = -0.42$, $p = .67$) and multiplication ($t(54) = 0.07$, $p = .95$) skill at T2. Younger and older children differed in GMV in the left MTG/STG ($t(54) = 2.22$, $p = .03$), but not in GMV in the left IPS ($t(54) = 1.95$, $p = .06$) or right IPS ($t(54) = 0.68$, $p = .50$) at T1. See Section 2.2 for details on the materials used to measure these constructs. More detailed information about these age groups is given in Table 1.

2.2. Standardized measures

2.2.1. Math skill: subtraction performance—
The subtraction subtest of the Comprehensive Mathematical Abilities Test (CMAT; Hresko et al., 2003) was used to measure subtraction skill. This untimed test includes 23 subtraction problems that are solved in paper-and-pencil format. It has a wide range of difficulty, including single-digit subtractions, multi-digit subtractions, subtraction of decimals, and subtraction of fractions. This test was administered outside the scanner, both at T1 and at T2. Raw scores of this test at T1 and at T2 were used as the dependent measures in the analyses to address aim 1. Raw scores of this test both at T1 and at T2 were used to calculate longitudinal gains in subtraction skill, which were used as the dependent measures in the analyses to address aims 2 and 3.

2.2.2. Math skill: multiplication performance—
The multiplication subtest of the Comprehensive Mathematical Abilities Test (CMAT; Hresko et al., 2003) was used to measure children's multiplication skill. This untimed test includes 26 multiplication problems that are solved in paper and pencil format. The test has a wide range of problems difficulty, including single-digit multiplications, multi-digit multiplications, multiplications of decimals, and multiplication of fractions. This test was administered both at T1 and at T2, outside the scanner. Raw scores of this test at T1 and at T2 were used as the dependent measures in the analyses to address aim 1. Raw scores of this test both at T1 and at T2 were used to calculate longitudinal gains in multiplication skill, which were used as the dependent measures in the analyses to address aims 2 and 3.

2.2.3. Reading skill—
Reading skill was measured at T1 by the word identification and word attack subtest from the Woodcock-Johnson III Test of Achievement (WJ-III; Woodcock et al., 2001), which requires pronouncing words and non-words, respectively. The

[1]Degrees of freedom is smaller for this analysis because one participant had missing data for this measure.

average of the two tests was used to ensure that the participants included in our final sample did not show reading deficits (for more details see Section 2.1.1).

2.2.4. Working memory—Verbal working memory (WM) was measured by the listening recall subtest of the Automated Working Memory Assessment (AWMA; Alloway et al., 2007). This subtest involves simultaneous storage and processing of verbal information. It requires children to decide whether a sentence is true or false, for example, "*Bananas live in water*", and also to remember the final word of the sentence, that is "*water*". The number of sentences per item increases as children proceed through the test, increasing the number of final words they had to hold in memory to later retrieve.

Visuo-spatial WM was measured with the spatial recall subtest of the AWMA (Alloway et al., 2007). In this test, children view pictures of two shapes where the shape on the right has a red dot near it and they need to identify whether the shape on the right is the same as the shape on the left when rotated in two dimensions, or whether it is the mirror image. At the end of the trial, individuals are asked to remember the position of the red dot and to answer by pointing to a picture with three possible positions marked. The number of shape pairs to be compared increases as children proceed through the test, and participants must recall the correct position of all the red dots in the correct temporal order.

This test was administered both at T1 and at T2. The average of the verbal and visuo-spatial standard scores was used as a global measure of working memory

2.2.5. Intelligence—Intelligence was measured with the Wechsler Abbreviated Scale of Intelligence – WASI (Wechsler, 1999), which comprises verbal and performance IQ scales. The verbal IQ scale includes the vocabulary and similarities subtests. In the vocabulary subtest, the participant has to define words, while in the similarities test the participants are presented with two words that represent common objects or concepts and they have to describe how they are similar. Performance IQ was measured with the block design and matrix reasoning subtests of the WASI. The block design requires the participants to use red-and-white blocks to re-create, within a specified time limit, a model design. In the matrix reasoning subtest, participants view an incomplete series or matrix and select the response option that completes it logically. This test was administered both at T1 and at T2.

2.3. Experimental protocol

In the first visit to the lab, informed consent was obtained from children and their parents or guardians, and standardized tests were administered. In the scanning session, which took place within a week of the first visit, a high-resolution structural MRI was obtained for each participant. Participants came back to the laboratory approximately 2 years later. In this session, another high-resolution structural MRI was obtained, and some of the standardized tests previously administered at T1 were collected again. For more details about the experimental protocol see Suárez-Pellicioni et al. (2019).

2.4. MRI data acquisition

Images were collected using a Siemens 3 T TIM Trio MRI scanner (Siemens Healthcare, Erlangen, Germany) at CAMRI, Northwestern University's Center for Advanced MRI. A high resolution T1 weighted 3D structural image was acquired for each participant, with the following parameters: TR = 2300 ms, TE = 3.36 ms, matrix size = 256×256, field of view = 240 mm, slice thickness = 1 mm, number of slices = 160.

2.5. MRI data analysis

2.5.1. MRI preprocessing—First, a customized age- and sex-matched Tissue Probability Map (i.e. TPM) was generated across time-points using the Template-O-Matic toolbox (Wilke, Holland, Altaye, and Gaser, 2008). Then, T1-weighted images were segmented into GMV and WMV using the Computational Anatomy Toolbox (CAT12; http://dbm.neuro.uni-jena.de/cat12/) segmentation tool on SPM12 (Wellcome Trust Centre for Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm). The custom TPM generated in the previous step was used for segmentation. Third, a custom DARTEL template was created using the segmented images. The segmented images were then warped to the custom DARTEL template and normalized to the Montreal Neurological Institute (MNI) template with 1.5 mm isotropic voxels and an 8 mm^3 Gaussian kernel for smoothing.

Data quality was checked using the "Display one slice for all images" function and considering the image quality ratings (IQR) generated by CAT12, which factors in both noise (e.g., motion) and spatial resolution. The visual inspection revealed no issues and the IQR for all images was above the "satisfactory" threshold (i.e. C; 0.75).

The "Estimate mean values inside ROI " function was used to extract GMV values from the regions of interest (see Section 2.5.2 for more information on the ROIs), for each participant and for each time-point. Finally, the total intracranial volume (TIV) for each participant for each time-point, was extracted using the "Estimate TIV" function.

2.5.2. Regions of interest (ROIs)—The regions of interest in this study comprised the left and right intraparietal sulci (IPS) and the left middle and superior temporal gyri (MTG/STG). These regions were anatomically defined using the anatomical automatic labeling template. Given previous evidence showing an association between GMV in the left IPS and math performance (e.g. Li et al., 2013; Lubin et al., 2013; Price et al., 2016) or math gains (e.g. Evans et al., 2015; Price et al., 2016), we studied hemispheric differences in this region by having separate ROIs of the left and the right IPS, shown in green and violet in Fig. 2A and 2B, respectively. Given that the IPS is located between the inferior and superior parietal lobules, we dilated these two areas with the WFU PickAtlas tool (http://www.nitrc.org/projects/wfu_pickatlas; 2D dilatation of 2) and selected the intersection of them using MarsBar (http://marsbar.sourceforge.net/). Given the evidence suggesting that GMV in IPS is not involved in tasks that rely on the retrieval of the solution from long-term memory (Polspoel et al., 2020; Superkar et al., 2013; Wilkey et al., 2016), we also extracted GMV from the left MTG/STG, shown in Fig. 2C, which is considered to store the representation of arithmetic facts in a verbal code in long-term memory (Prado et al., 2011, 2014; Suárez-Pellicioni et al., 2018, 2019).

3. Analyses

3.1. Analyses to address aim 1: concurrent associations between GMV and math skill at T1 and at T2

The first step was to study the association between GMV in the bilateral IPS and left MTG/STG and concurrent subtraction and multiplication performance both at T1 and at T2 (see red arrows in Fig. 1). Analyses were performed using SPSS 22 (IBM, SPSS Statistics, IBM Corporation, NY, United States).

Age at T1 was of special relevance given previous studies showing that the association between GMV and math skill seems to be limited to younger children (Wilkey et al., 2016). Total intracranial volume (TIV), which is a measure of variation in head size, is an important variable to control for in volumetric analyses (Malone et al., 2015). For these reasons, age at T1 and TIV at T1 were entered as predictors in the first step of the regressions. GMV in left IPS, right IPS, and left MTG/STG at T1 were entered as predictors in step 2 of the regressions. The decision of introducing predictors in two steps was made in order to be able to assess how much additional variance GMV in the three ROIs could explain over and above the factors entered in the first step. The dependent measure was subtraction skill at T1 (see Fig. 3A). All measures were continuous.

The exact same analysis was performed for multiplication, including multiplication skill at T1 as the dependent measure instead of subtraction skill (see Fig. 3B).

Two more regression analyses were carried out to study concurrent associations at T2. The only difference with the above-mentioned regressions is that all the predictors were measured at T2, and the dependent measures were subtraction (Fig. 3C) and multiplication (Fig. 3D) performance at T2, respectively.

3.2. Analyses to address aim 2: the role of GMV at T1 in predicting longitudinal gains in math skill

Two regression analyses were performed to address the role of GMV in bilateral IPS and left MTG/STG in explaining longitudinal gains in arithmetic. In the first regression, age at T1 and TIV at T1 were entered as predictors in the first step, and GMV in left IPS, right IPS, and left MTG/STG were entered as predictors in the second step. The dependent measure, in this case, was the longitudinal gains in subtraction skill (Fig. 3E) calculated as the difference score between performance in the test at T2 as compared to T1 (T2–T1). All measures were continuous.

The same regression analysis was carried out for multiplication, which was as described above but included longitudinal gains in multiplication skill (i.e. T2–T1) as the dependent measure (Fig. 3F).

3.3. Analyses to address aim 3: association between changes in GMV over time and longitudinal gains in math skill

As shown in Fig. 3G, we carried out a regression analysis including age at T1 and TIV at T1 as predictors in the first step, and changes in GMV over time (T2–T1) in left IPS, right IPS, and left MTG/STG as predictors in the second step of the regression. The dependent measure was longitudinal gains in subtraction skill (T2–T1). All measures were continuous.

The counterpart analysis for multiplication was exactly as described above, but included longitudinal gains in multiplication skill (T2–T1) as the dependent measure (Fig. 3H).

4. Results

4.1. Behavioral results: longitudinal gains in subtraction and multiplication skill

First, we analyzed the longitudinal gains in subtraction and multiplication skill for the whole sample by calculating a repeated-measures ANOVA, including operation (subtraction; multiplication) and time (T1; T2) as the within-subject variables and age groups at T1 (younger; older) as the between-subjects measure. The main effect of time ($F(1,54) = 16.95$, $p < .001$, partial $\eta^2 = 0.24$), and operation ($F(1,54) = 60.41$, $p < .001$, partial $\eta^2 = 0.53$) were significant, but the main effect of age groups ($F(1,54) = 3.29$, $p = .08$, partial $\eta^2 = 0.06$) was not. The main effect of operation showed overall higher subtraction (mean = 15.71; SD = 4.10) than multiplication performance (mean = 12.68; SD = 4.93) across time-points ($t(55) = 7.84$, $p < .001$).

The interaction between operation, time, and age groups ($F(1,55) = 1.72$, $p = .20$, partial $\eta^2 = 0.03$), between operation and age groups ($F(1,54) = 1.65$, $p = .20$, partial $\eta^2 = 0.03$), and between operation and time ($F(1,54) = 0.10$, $p = .75$, partial $\eta^2 = 0.002$) were not significant. The interaction between time and age groups was significant ($F(1,54) = 12.73$, $p = .001$, partial $\eta^2 = 0.19$), and showed significant gains over time in subtraction ($t(27) = -5.70$, $p < .001$) and multiplication ($t(27) = -4.35$, $p < .001$) for the younger group, but not for the older group[2] (subtraction: ($t(27) = -1.28$, $p = .21$); multiplication: ($t(27) = 0.22$, $p = .82$)[3]. For more details about gains in arithmetic skill for the whole sample and for the age groups see Table 1.

4.2. Aim 1: No concurrent associations between GMV and subtraction performance at T1 or T2

As shown in Table 2, the regression analyses exploring concurrent associations between GMV in the bilateral IPS and left MTG/STG and subtraction skill at T1 (Fig. 3A) showed

[2]We do not think this lack of improvement for the older group is due to a ceiling effect. Ceiling effects are found when participants show very high performance (i.e. usually for easy tests/conditions), which prevent distinguishing participants in terms of their skill level. In this study, older children showed mean raw scores of 13.8 and 16.6 for the multiplication and subtraction tests, respectively, at time 2. Those tests include 26 and 23 items, respectively, indicating that children had room to grow. It is worth mentioning that the items that the older children did not solve at time 2 required the subtraction or multiplication of multi-digit numbers with different numbers of decimals (e.g. 435.2 – 78.376; 8.6 × 0.46), the subtraction and multiplication of fractions with different denominators (e.g. 1/2 – 1/4; 12/15 × 3/16) and the subtraction and multiplication of a combination of whole numbers and fractions (e.g. 13 1/2 – 9 9/11; 6 2/7 × 3 2/11). Given that the test was untimed, we cannot attribute this lack of completion to lack of time. It is possible that even for older kids at time 2 some of these items were too challenging. An analysis of scores for older children (Shapiro-Wilk test) showed that the distribution of subtraction ($W(28) = 0.97$, $p = .54$) and multiplication ($W(28) = 0.95$, $p = .15$) scores at T2 did not differ from a normal distribution, so they were not negatively skewed. Consistent results were found if a Kolmogorov-Smirnov test was calculated instead.

[3]Although this group of older children did not show significant changes over time in the CMAT subtraction and multiplication tests, this group showed improvement in the Math fluency subtest of the Woodcock–Johnson III (Woodcock et al., 2001) ($t(27) = -7.64$, $p < .001$), which requires the rapid calculation of single-digit addition, subtraction and multiplication facts within a 3-min time limit. This group also showed improvement in the Numeracy subtest of the KeyMath-3 test (Connolly, 2007) ($t(27) = -2.73$, $p = .01$).

that age at T1 and TIV at T1 were concurrently associated with subtraction performance, whereas no relation was shown for GMV in any of the ROIs.

In order to understand the role of age at T1 in explaining the association between GMV and subtraction performance at T1, regression analyses were carried out separately for younger and older children (for more details about age groups see Section 2.1.2). These analyses were exactly as shown in Fig. 3A, but included only TIV as a predictor in the first step of the regression, but not age at T1. As shown in Table 3, these regression analyses revealed that TIV at T1 was concurrently associated with subtraction performance at T1 for younger children, whereas GMV in bilateral IPS or left MTG/STG showed no significant association. No variable was concurrently associated with subtraction performance at T1 for older children.

As for the concurrent association at T2 (Fig. 3C), and as shown in Table 2, this analysis revealed that none of the predictors were concurrently associated with subtraction skill at T2. Given that age at T1 was not a significant predictor in the model for the concurrent associations at T2, no follow-up regressions were calculated separately for younger and older children.

4.3. Aim 1: GMV in left MTG/STG is concurrently associated with multiplication skill at T1 for the whole sample

As shown in Table 2, the regression analyses exploring concurrent associations between GMV in the bilateral IPS and left MTG/STG and multiplication skill at T1 (Fig. 3B) showed that age at T1, TIV at T1, and GMV in left MTG/STG were concurrently associated with multiplication skill at T1. The scatterplot in Fig. 4 shows the positive association between multiplication performance at T1 and the residuals of GMV in left MTG/STG at T1 after accounting for the variables entered in previous steps (i.e. age, TIV, GMV in left and right IPS at T1) to mirror the regression analysis. The scatterplot shows that the higher the GMV in the left MTG/STG, which is considered to store the representation of arithmetic facts in long-term memory (Prado et al., 2011, 2014; Suárez-Pellicioni et al., 2018, 2019), the better performance on a standardized test of multiplication skill.

Given that age was also a significant predictor, we performed separate regression analyses for younger and older children (for more details about age groups see Section 2.1.2). These analyses were as shown in Fig. 3B, but included only TIV as a predictor in the first step of the regression, and not age at T1. No factor showed association with multiplication skill when the analysis was carried out separately for each age group.

As for the concurrent association at T2 (Fig. 3C), and as shown in Table 2, this analysis showed that none of the predictors were concurrently associated with multiplication skill at this time point. No follow-up regressions were calculated separately for each age group because age was not significantly associated with multiplication skill at this time point.

4.4. Aim 2: GMV in left IPS is associated with longitudinal gains in subtraction skill only for younger children

In order to address aim 2, we studied the role of GMV in the bilateral IPS and left MTG/STG in predicting longitudinal gains in subtraction skill (Fig. 3E). As shown in Table 4, the regression analysis showed that age at T1 and GMV in left MTG/STG were significant predictors of longitudinal gains in this operation. In order to further explore the role of age in explaining the association between GMV and subtraction skill, separate regression analyses were performed for younger and older children (for more details on age groups see Section 2.1.2). These analyses were exactly as shown in Fig. 3E, but included only TIV as a predictor in the first step of the regression, but not age at T1. The results of these regression analyses for the two age groups are shown in Table 5. As shown in Table 5, GMV in left IPS at T1 and left MTG/STG at T1 were significant predictors of longitudinal gains in subtraction skill for younger children[4]. While the model including TIV at T1 was not significant, adding GMV in these two ROIs as predictors in the second step explained a significant amount of variance in the model. No variable explained the gains in this operation for older children.

The scatterplot in Fig. 5 shows the association between longitudinal gains in subtraction skill and GMV in left IPS (Fig. 5A) and left MTG/STG (Fig. 5C) at T1 for younger children. Although these effects were not significant for the older group, the association between subtraction gains and GMV in left IPS (Fig. 5B) and left MTG/STG (Fig. 5D) is shown for the older group for comparison purposes. These scatterplots show that, the higher the GMV in left IPS at T1 and the smaller the GMV in left MTG/STG at T1, the greater the longitudinal gains in subtraction skill experienced by younger children.

4.5. Aim 2: GMV in left IPS predicts subtraction skill at T2 over and above subtraction skill at T1

An important question that arises when identifying the neurocognitive mechanisms explaining longitudinal gains in mathematics is whether these brain measures can predict later math performance over and above initial levels of math performance. We answered this question by performing a regression analysis including subtraction skill at T1 and TIV at T1, which were entered as predictors in step 1, and GMV in left IPS and in left MTG/STG (i.e. the two factors being significant in Table 5), which were entered in step 2. The dependent measure was subtraction skill at T2.

As shown in Table 6, GMV in left IPS at T1 predicted subtraction skill at T2 over and above initial levels of subtraction skill, TIV, and GMV in left MTG/STG. As expected, this was specific to younger children. For older children, subtraction skill at T1 was a significant predictor of later subtraction performance, but GMV in left IPS or left MTG/STG were not.

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[4]Intelligence is also believed to influence cortical gray matter distribution (Aydin et al., 2007). GMV in left IPS ($\beta = 0.72$, $t = 2.94$, $p = .007$) and left MTG/STG ($\beta = -0.50$, $t = -2.36$, $p = 0.03$) at T1 was also a significant predictor of longitudinal gains for younger children if full IQ at T1 was entered in the first step of the regression instead of TIV at T1.

4.6. Aim 2: GMV in left MTG/STG did not predict longitudinal gains in multiplication skill

In order to address aim 2, we studied the role of GMV in the bilateral IPS and left MTG/STG in predicting longitudinal gains in multiplication skill (Fig. 3F). As shown in Table 4, the regression analysis showed that age at T1 was a significant predictor of multiplication gains. We carried out separate regression analyses for younger and older children (for more details about age groups see Section 2.1.2), which were the same as in Fig. 3F but included only TIV at T1 as a predictor in the first step of the regression, and not age at T1. As shown in Table 5, the regression analyses carried out separately for younger and older children revealed no significant predictor of multiplication gains. Of particular interest, although GMV in left MTG/STG was concurrently associated with multiplication skill at T1 (Table 2), it did not predict longitudinal gains in this operation.

4.7. Aim 3: No association between changes in GMV and longitudinal gains in math skill

The analyses to address aim 3 studied the association between changes in GMV in the bilateral IPS and left MTG/STG and longitudinal gains in subtraction (Fig. 3G) and multiplication (Fig. 3H) skills. As shown in Table 7, these analyses revealed that age at T1 was the only significant predictor of longitudinal gains in both operations. In order to explore the role of age at T1 in explaining the association between changes in GMV in the three ROIs and longitudinal gains in math skills, separate regression analyses were carried out for younger and older children (for more details about age groups see Section 2.1.2). These regression analyses were exactly as described in Fig. 3G and H, but included only TIV at T1 as a predictor in step 1, and not age at T1.

As shown in Table 8, none of the factors were associated with longitudinal gains in subtraction or multiplication skills either for younger or for older children.

4.8. Whole-brain results

The whole-brain analysis complements the region of interest analysis. Because age showed co-linearity (correlation) with TIV, based on the results of “check design orthogonality” procedure, the structural data was proportionally scaled according to individual TIV values, an alternative procedure to using TIV values as a nuisance variable. An absolute threshold mask of 0.1 was used to exclude voxels outside of the brain. AFNI 3dFWHMx (https://afni.nimh.nih.gov) was used to estimate noise smoothness values for the design specification using the “- acf” (spatial autocorrelation function) option, and the ResMS (estimated residual variance image) file as the input. The ACF values were used as inputs for 3dClustSim to calculate clusters for significance at the whole-brain level, using Monte Carlo simulations, separately for each contrast, at uncorrected (voxel-wise) $p < .005$ and $p < .05$ corrected (cluster-wise) thresholds. ROIs (i.e. bilateral IPS and left MTG/STG) were excluded from the whole-brain analyses using an exclusive mask of these regions.

Four F-tests were conducted to address Aim 1, using the factorial design specification option in SPM12. We aimed to address the relationship between GMV and math skill at each time point, and whether this association depended on children’s age. Specifically, the analysis studied the: 1) Interaction between subtraction skill and age at T1 for GMV data at T1, 2) Interaction between multiplication skill and age at T1 for GMV data at T1, 3) Interaction between subtraction skill and age at T2 for GMV data at T2, and 4) Interaction between multiplication skill and age at T2 for GMV data at T2. None of these interactions showed significant clusters.

As for Aim 2, two *F*-tests were conducted using the factorial design specification option in SPM12 to study the relationship between GMV at T1 and longitudinal gains in math, and whether this depended on children's age. Specifically, the analyses addressed the: 1) Interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for GMV data (T1); 2) Interaction between longitudinal gains in multiplication skill (T2–T1) and age (T1) for GMV data (T1). Only the former interaction, involving gains in subtraction skill, produced a significant cluster, which was located in the left precuneus (See Table A2 in the Appendix and Fig. A1-A). Follow-up tests, looking at the correlation between subtraction gains and GMV at T1, were conducted separately for the younger and older children (see Section 2.1.2 for a detailed description of these groups). Seven clusters showed a positive correlation with subtraction gains for the younger children, whereas none reached significance for the older children. These clusters were located in the bilateral parietal cortex and in the frontal cortex, as well as in the precuneus, which overlapped the main interaction cluster in that region (See Table A2-Follow-ups for the younger children). The results show that while GMV at T1 is associated with longitudinal subtraction gains, no such association exists for longitudinal multiplication gains, paralleling the results from our ROI analysis.

As for Aim 3, following the recommendation for longitudinal VBM analysis in the CAT 12 manual, two F-tests were conducted using the flexible factorial design in order to study the relationship between GMV changes (T2–T1) and longitudinal gains in math (T2–T1), and whether this depended on children's age (T1). Specifically, the analysis studied the: 1) Interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for the changes in GMV (T2–T1), and 2) Interaction between longitudinal gains in multiplication skill (T2–T1) and age (T1) for the changes in GMV (T2–T1). The interaction involving subtraction gains produced a single cluster in the left superior parietal area (see Table A3 in the Appendix and Fig. A1-B). Follow-up tests looking at the interaction between longitudinal gains in subtraction and changes in GMV over time were conducted separately for the younger and older children.

For the younger children, the interaction produced two significant clusters located in the bilateral superior frontal cortices, which did not overlap the main interaction cluster in parietal cortex (i.e. $K = 4224$; See Table A3-Follow-ups for the younger children). Separate tests for positive and negative correlations showed a left superior frontal cluster overlapping with the higher-level interaction cluster (i.e. K=1667), where the increase in GMV positively correlated with gains in subtraction skill (See Table A3-Follow-ups for the younger children). There were no negative correlations.

For the older children, the interaction produced three clusters; two in the bilateral superior frontal lobes and one in the left superior parietal cortex, with the latter cluster overlapping the main interaction cluster in parietal cortex (i.e. K=4224; Table A3-Follow-ups for the older children). The separate tests for positive and negative correlations did not show any clusters where subtraction gains were associated with GMV changes, not providing further evidence on the nature of this interaction.

The analysis corresponding to Aim 3 for the multiplication task, looking at the interaction between longitudinal gains in multiplication skill (T2–T1) and age (T1) for the changes in GMV (T2–T1) revealed two significant clusters, one in the left superior parietal and another in the right superior frontal (see Table A4 in the Appendix and Fig. A1-C). Follow-up tests looking at the interaction between longitudinal gains in multiplication and changes in GMV over time were conducted separately for the younger and older children.

For the younger children, this analysis revealed a significant interaction in the bilateral superior frontal cortex (left-centered peak; including precentral and supplementary motor areas bilaterally) (Table A4-Follow-ups for the younger children). This cluster did not overlap the higher-level interaction cluster in right superior frontal cortex (i.e. K=772). Separate tests for positive and negative correlations showed a bilateral superior frontal cluster overlapping with the interaction cluster (i.e. K=5982) and with the same peak coordinates. Increases in GMV over time in these clusters was positively correlated with gains in multiplication skill (Table A4-Follow-ups for the younger children). There were no negative correlations.

As for the older children, the interaction revealed two significant clusters, one in the left superior parietal and the other in the left inferior occipital cortex (Table A4-Follow-ups for the older children). The cluster in left superior parietal did overlap the higher-level interaction cluster involving the same anatomical region (i.e. K=3479). Separate tests for positive and negative correlation did not show any significant cluster where multiplication gains were associated with changes in GMV, not providing further evidence on the nature of this interaction.

5. Discussion

Acquiring proficient math skills is critical for academic success and is foundational for the science, technology, and engineering disciplines. Elementary school children show large behavioral gains in arithmetic skills (De Brauwer and Fias, 2009), which are foundational for the development of more advanced skills. Unraveling the neurocognitive mechanisms underlying arithmetic is important not only to prevent children from falling behind but to potentially maximize the benefits that children can obtain from math instruction. While important efforts have been made to understand children’s math processing by investigating differences in brain activation while children solve math tasks inside the scanner (e.g. Peters and De Smedt, 2018), little is known about the role that brain structure plays in the development of math skill.

Only a small number of studies have examined the role of brain structure in math skill in typically developing children (e.g. Li et al., 2013; Lubin et al., 2013; Polspoel et al., 2020; Wilkey et al., 2016). The studies using longitudinal designs, which are crucial for addressing developmental questions (Geary, 2011; Karmiloff-Smith, 2010), are even scarcer (e.g. Evans et al., 2015; Price et al., 2016; Supekar et al., 2013). These longitudinal studies have looked at the effect of GMV in predicting math gains using tests that included a wide range of skills. Some suggested that discrepancies in the literature may be attributed to the diverse nature of the tests used to measure skill (e.g. Price et al., 2016; Wilkey et al., 2016), with GMV in the IPS predicting gains in tests involving calculation (i.e. Li et al., 2013; Lubin et al., 2013; Evans et al., 2015; Price et al., 2016) but not in tests that involved retrieval of the solutions from long-term memory (Polspoel et al., 2020; Supekar et al., 2013; Wilkey et al., 2016). However, no study to date has tested this hypothesis by comparing the role that GMV in bilateral IPS and left MTG/STG play in explaining math skill in tasks that tap differently into calculation and retrieval, which constituted the main objective of this study.[5]

We obtained structural images from children when they were approximately 11 years old (i.e. T1) and once again when they were approximately 13 years old (i.e. T2). We then studied the relation of GMV in bilateral IPS and left MTG/STG, considered to be crucial for quantity processing and to store the representation of arithmetic facts in long-term memory, respectively, to subtraction and multiplication skills. We expected relations of GMV in left and/or right IPS with subtraction, believed to rely more on quantity processing and calculation, and of GMV in left MTG/STG with multiplication, considered to rely more on the retrieval of the solution from long-term memory. The specific aims of this study were threefold: First, to study the concurrent associations of GMV with subtraction and multiplication skill at T1 and at T2. Second, to investigate the role of GMV at T1 in predicting longitudinal gains in subtraction and multiplication skills (T2–T1). Third, to examine the role of changes over time (T2–T1) in GMV in predicting longitudinal gains in subtraction and multiplication skills (T2–T1). Given the relatively wide age range of children in our sample, we included age at T1 as a predictor in all the regression analyses.

As for the first aim, we did not find any concurrent association between GMV in any of the ROIs and subtraction skill at T1 or at T2. GMV in bilateral IPS or left MTG/STG was not concurrently associated with subtraction performance even when the regression analyses were carried out separately for younger and older children. Despite the lack of a concurrent association between GMV and subtraction skill at T1, we found that GMV in the left IPS predicted longitudinal gains in subtraction skill for the younger group. More specifically, the higher the GMV in left IPS at T1, the more children gained in subtraction skill over time. GMV in left MTG/STG was also a significant predictor of subtraction gains for the younger group but in the opposite direction. Whereas the higher the GMV in left IPS at T1 the *more* they gained in subtraction skill, the higher the GMV in the left MTG/STG at T1 the *less* they gained in this operation. This finding suggests that structural integrity of quantity representation regions in the brain is what explains improvement in this operation, whereas the structural integrity of verbal representation regions, which potentially could have facilitated the use of the retrieval strategy, seems to be detrimental to improvement in this operation (Suárez-Pellicioni et al., 2020).

[5]Some functional MRI studies have studied brain activation associated with the strategy that children reported using while solving multiplication and subtraction problems instead of comparing brain activation between the two operations. They have found strategy-related differences in brain activation, but not operation-related differences (Polspoel et al., 2017). Future studies should address the same question using GMV in order to disentangle operation-related from strategy-related effects.

Early math performance is the largest predictor of later math achievement (Watts et al., 2014), so it is important to determine the utility of neuroimaging measures in predicting longitudinal gains in math skill over and above initial levels of math performance. Our regression analysis showed that initial levels of subtraction skill was a significant predictor of later skill (T2), suggesting that the extent of the gains over time is dependent on children's initial skill (i.e. T1 achievement). GMV in left IPS also significantly contributed to explain changes from T1 to T2, suggesting that a combination of behavioral and neuroimaging variables is an effective way to predict longitudinal improvement in math (Dumontheil and Klingberg, 2012), as has been shown in other domains (Hoeft et al., 2007).

The role of GMV in left IPS in predicting gains was specific to younger children[6]. This finding is consistent with Wilkey et al. (2016) that showed an association between GMV and math skill for children in their younger but not older group, who were about the same age as our participants in the younger and older groups (i.e. approximately 10 and 12 years old at T1, respectively). This is also consistent with studies finding concurrent associations between GMV in IPS and math performance in children with mean ages of 10 (Lubin et al., 2013), 10.5 (Li et al., 2013), and 7.4 (Price et al., 2016). The finding of this association only for younger children may suggest that brain structure of the left IPS is important early on because children rely more on quantity-based calculation strategies, whereas older children tend to retrieve the solution from long-term memory. Using fMRI, a previous study showed no evidence for such a shift, with no involvement of retrieval-related brain regions predicting subtraction gains (Suárez-Pellicioni et al., 2020). Our results are more likely due to the younger group relying on quantity mechanisms to compute the calculations required to solve the subtraction test, while older children may have automatized these procedures (Fayol and Thevenot, 2012; LeFevre et al., 2006). An alternative explanation is that the predictive effect was found only for younger children because only they showed significant longitudinal gains in subtraction skill.

As expected, the predictive effects were specific to the left hemisphere, which is consistent with several cross-sectional (Lubin et al., 2013; Li et al., 2013) and longitudinal (Evans et al., 2015; Price et al., 2016) studies finding effects for the left, but not right, IPS[7]. While the IPS responds to both non-symbolic (i.e. approximate number system (ANS); Ansari et al., 2006; Ansari and Dhital, 2006) and symbolic comparisons (Ansari et al., 2005; Pinel et al., 2001), studies have shown evidence of early specialization of the right IPS for non-symbolic magnitude processing (Cantlon et al., 2006; Hyde et al., 2010; Izard et al., 2008), whereas the left IPS has been reported to show a progressive specialization in symbolic magnitude processing (Emerson and Cantlon, 2015; Vogel et al., 2015). The fact that we found the predictive effects only for the left IPS questions the role of ANS in explaining longitudinal gains in math (Matejko and Ansari, 2016; Mussolin et al., 2014; Suárez-Pellicioni and Booth, 2018), pointing to the importance of symbolic number processing in explaining gains in math skill (De Smedt et al., 2013) and supports studies showing the importance of

[6]Note that it is possible that these results, being based on half the sample (i.e. 28 younger participants), may be low on statistical power.

[7]Note, however, that whole-brain analyses showed that, for younger children, GMV at T1 in a cluster located in the right superior parietal cortex showed a positive correlation with longitudinal gains in subtraction skill (see Table A1 in the Appendix).

activation in the left IPS by symbolic numbers in determining math success (Bugden et al., 2012).

Our results were not only specific to younger children, but also to operation. As expected, we found that GMV in IPS longitudinally predicted gains in subtraction skill, but not multiplication.[8] This finding constitutes the first evidence supporting previous suggestions that the diversity in the findings in the literature about GMV and math skill could be due to the different demands of the tests used to measure math performance or gains (e.g. Price et al., 2016; Wilkey et al., 2016). By comparing two operations, we were able to show that GMV in left IPS is exclusively associated with the operation that has consistently been shown to rely on quantity representations (i.e. subtractions; e.g. Prado et al., 2011, 2014; Suarez-Pellicioni et al., 2020), but not on those that rely on the retrieval of the solution from long-term memory (i.e. multiplications; e.g. Prado et al., 2011, 2014; Suarez-Pellicioni et al., 2018, 2019).

Multiplication skill at T1, on the other hand, showed a concurrent association with GMV in left MTG/STG for the whole sample, which confirms previous predictions about the differential role of GMV in different brain regions depending on the calculation and retrieval demands of the tasks used to measure math skill (e.g. Price et al., 2016; Wilkey et al., 2016). This concurrent association showed that the higher the GMV in left MTG/STG at T1, the higher the level of multiplication skill at T1. This effect was found only at T1, but did not depend on children’s age. This suggests that structural integrity in left MTG/STG plays an important role in explaining children’s ability to solve multiplications when kids are relatively young. The lack of concurrent association at T2, together with the fact that GMV in left MTG/STG at T1 did not predict longitudinal gains in multiplication skill, suggests a time-limited role of the GMV in these temporal regions in explaining multiplication achievement. It could be that structural integrity in these regions explains gains in earlier stages of multiplication learning, so future studies should investigate younger children.

The third aim of this study was to investigate changes in GMV associated with longitudinal gains in math performance. Only Price and colleagues (2016) tried to address this question before. While they found no association between GMV changes and math performance in the 2nd grade (T2), they were not able to calculate changes in math skill because they did not measure math performance in the 1st grade (at T1). Despite this limitation, Price et al. (2016) interpreted their lack of finding for the changes in IPS as suggesting a stable role of left IPS in skill development. Our results showed no significant association between changes in GMV and longitudinal gains in subtraction skill. It is hard to interpret a null result because they can be attributed to a lack of power or other methodological limitations. It is possible that the amount of experience needed to alter GMV is substantial, so the changes in subtraction performance shown by children in our sample might not have been big enough to show detectable GMV increases. It is also possible that the 2 years separating the two time-points in our study may have contributed to maturation-related decreases in GMV, making the learning-related effects in GMV (Kanai and Rees, 2011) harder to detect. Future studies

[8]The results from our whole-brain analyses revealed consistent results, with no cluster showing a significant interaction between GMV at T1, age at T1, and longitudinal gains in multiplication skill.

should address these issues with training studies or with longitudinal studies with closer time-points.

Some studies have provided mixed evidence regarding the concurrent and longitudinal association between GMV in frontal regions and math skill. Wilkey et al. (2016) found an association between math scores and GMV in right IFG, and Evans et al. (2015) found that GMV in dorsolateral and ventrolateral prefrontal cortices, among other regions, predicted gains in math performance (Evans et al., 2015). On the other hand, other studies using whole-brain analyses have found that GMV in frontal cortex did not correlate with (Lubin et al., 2013) or longitudinally predict (Price et al., 2016; Supekar et al., 2013) math performance. In our study, whole-brain analyses revealed that GMV at T1 in two clusters located in bilateral superior frontal cortices showed a positive correlation with longitudinal gains in subtraction skill for younger children (see Table A1 in the Appendix), supporting previous claims that regions in the frontal cortex play an important role in magnitude representations (Sokolowski et al., 2017), and should therefore be expected to be involved in operations such as subtraction. While in this study we focused on the role of GMV in quantity (bilateral IPS) and verbal (left MTG/STG) representation areas in explaining subtraction and multiplication improvement, future studies should be carried out to explore the role of GMV in frontal regions in predicting longitudinal gains in math skill in order to clarify the discrepancies in the literature.

Our findings are consistent with functional MRI correlational evidence showing that subtractions engage the IPS as compared to multiplications and multiplications engages the left temporal cortex as compared to subtractions (Prado et al., 2011) and that children increase their reliance on parietal cortex to solve subtractions and their reliance on temporal cortex to solve multiplications with more years of math instruction (Prado et al., 2014). Our findings are also consistent with longitudinal fMRI evidence showing that the storage of phonological representations in temporal cortex is a significant predictor of multiplication gains (Suárez-Pellicioni et al., 2019) and that the neural problem size effect in bilateral IPS at T1, but not in temporal cortex, predicted longitudinal gains in subtraction fluency (Suárez-Pellicioni et al., 2020). Together, this work suggests the early importance of brain structure in the IPS for the successful development of mathematical skills that rely on quantity mechanisms. Future studies should investigate the relation between brain structure and brain activation in the IPS to constrain the role of this crucial brain region in the development of math skill.

Acknowledgments

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Appendix

Table A1

List of participants included in the study.

Participant number	Participant number (continuation)	Participant number (continuation)
5	35	67
6	36	69
7	40	70
8	44	71
9	45	73
10	46	75
11	47	76
12	48	77
13	49	83
14	50	86
16	53	88
18	54	89
20	55	90
22	56	93
23	57	95
24	60	96
27	61	103
29	65	106
34	66	

Table A2

Results of the whole-brain analysis for subtraction gains corresponding to Aim 2. Cluster size (*K*) , MNI coordinates of the peaks, *Z* values, and approximate Brodmann areas (~BA) for the clusters showing significance for the interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for GMV at T1.

K	MNI (*x*, *y*, *z*)	*Z*-score	~BA	Anatomical region
Interaction between longitudinal gains in subtraction skill and age for GMV at T1				
581	−12 −60 45	4.46	7	left precuneus
Follow-up effects for the younger children				
Positive correlation between longitudinal gains in subtraction skill and GMV at T1				
1577	−12 −62 45	4.48	7	left precuneus
1898	36 −28 56	4.16	7	right superior parietal
520	−15 52 26	3.98	9	left superior frontal
486	−12 −16 63	3.79	4	left precentral
4064	27 −81 – 12	3.77	17	right inferior occipital
588	12 44 36	3.57	8	right superior frontal
1116	−24 −51 −9	3.51	19	left lingual

Table A3

Results of the whole-brain analysis for subtraction gains corresponding to Aim 3. Cluster size (K), MNI coordinates of the peaks, *Z* values, and approximate Brodmann areas (~BA) for the clusters showing significance for the interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for the changes in GMV (T2–T1).

K	MNI (*x*, *y*, *z*)	*Z*-score	~BA	Anatomical region
Interaction between longitudinal gains in subtraction skill and age for change in GMV				
4224	−14 −81 51	3.55	7	left superior parietal
Follow-up effects for the younger children				
Interaction between longitudinal gains in subtraction skill and changes in GMV over time				
1667	−15 −8 75	3.98	6	left superior frontal
911	18 −6 74	3.51	6	right superior frontal
Positive correlation between longitudinal gains in subtraction skill and change in GMV				
4564	−15 −8 75	4.14	6	left superior frontal
Follow-up effects for the older children				
Interaction between longitudinal gains in subtraction skill and change in GMV over time				
1956	−18 54 −12	3.33	11	left superior frontal
6597	−12 −82 50	3.25	7	left superior parietal
601	12 57 −14	2.89	11	right superior frontal

Table A4

Results of the whole-brain analysis for multiplication gains corresponding to Aim 3. Cluster size (K), MNI coordinates of the peaks, *Z* values, and approximate Brodmann areas (~BA) for the clusters showing significance for the interaction between longitudinal gains in multiplication skill (T2–T1) and age (T1) for the changes in GMV (T2–T1).

K	MNI (*x*, *y*, *z*)	*Z*-score	~BA	Anatomical region
Interaction between longitudinal gains in multiplication skill and age for change in GMV				
3479	−22 −80 54	3.47	7	left superior parietal
772	26 51 15	3.39	11	right superior frontal
Follow-up effects for the younger children				
Interaction between longitudinal gains in multiplication and change in GMV over time				
5982	−15 −9 75	3.97	6	bilateral superior frontal
Positive correlation between longitudinal gains in multiplication skill and change in GMV				
9567	−15 −9 75	4.13	6	bilateral superior frontal
Follow-up effects for the older children				
Interaction between longitudinal gains in multiplication and change in GMV				
8658	−14 −80 48	4.06	7	left superior parietal
565	−28 −78 −10	3.48	18	left inferior occipital

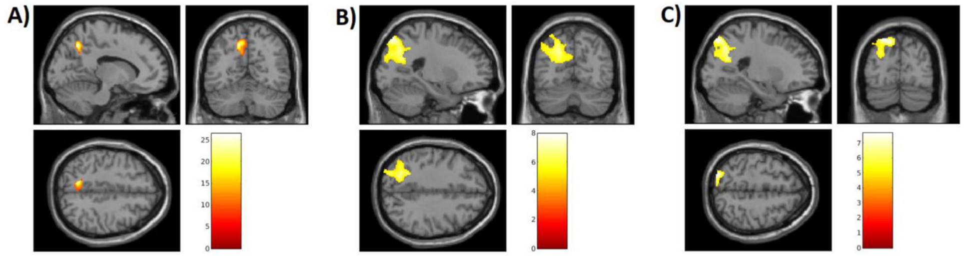

Fig. A1. Whole brain results.

(A) Cluster in left precuneus showing an interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for GMV at T1; (B) Cluster in left superior parietal cortex showing an interaction between longitudinal gains in subtraction skill (T2–T1) and age (T1) for changes in GMV (T2–T1); (C) Cluster in left superior parietal and right superior frontal cortices showing an interaction between longitudinal gains in multiplication skill (T2–T1) and age (T1) for changes in GMV (T2–T1).

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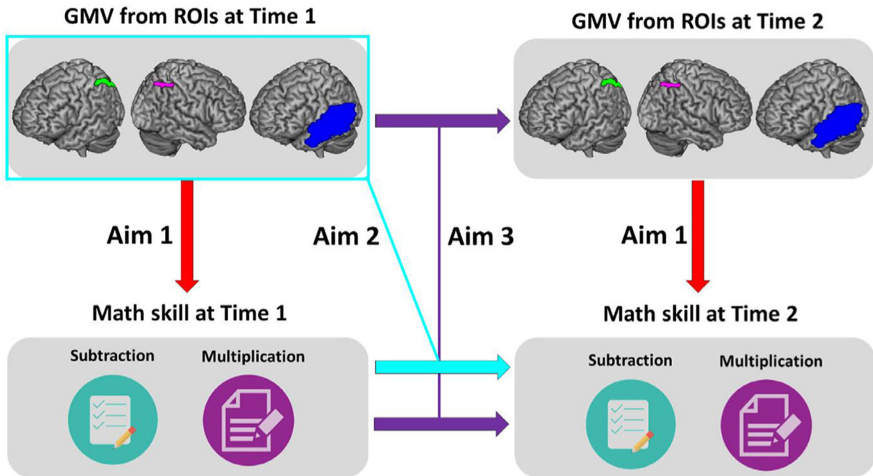

Fig. 1.

Illustration of the three main aims of the study. Illustration of the three aims of this study, consisting of investigating the role of GMV in the bilateral IPS and left MTG/STG in explaining concurrent subtraction and multiplication performance at T1 and at T2 (i.e. aim 1; arrows in red); the role of GMV in the bilateral IPS and left MTG/STG at T1 in predicting longitudinal gains in subtraction and multiplication skills (i.e. T2–T1; aim 2; arrow and line in cyan), and the role of the changes over time (T2–T1) in the GMV in the bilateral IPS and left MTG/STG in predicting longitudinal gains in subtraction and multiplication skills (i.e. aim 3; arrows and line in violet).

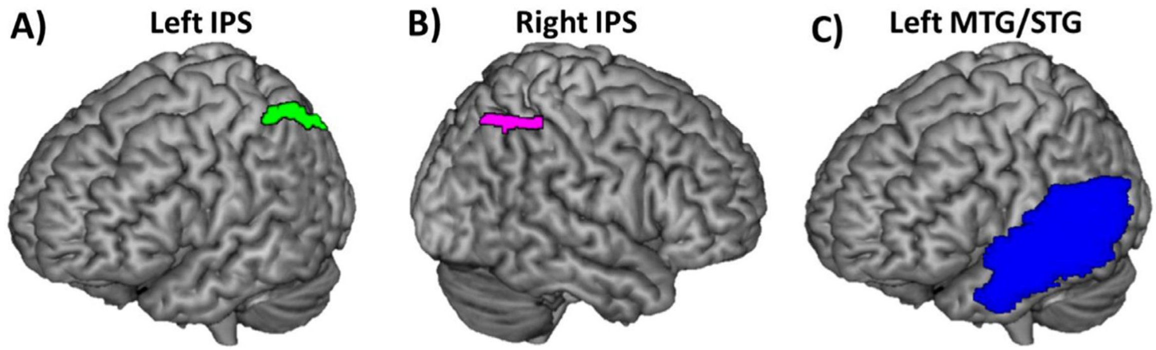

Fig. 2.
Regions of interest (ROIs). ROIs were anatomically defined in the (A) left intraparietal sulcus (IPS), (B) right intraparietal sulcus (IPS), and (C) left middle and superior temporal gyri (MTG/STG).

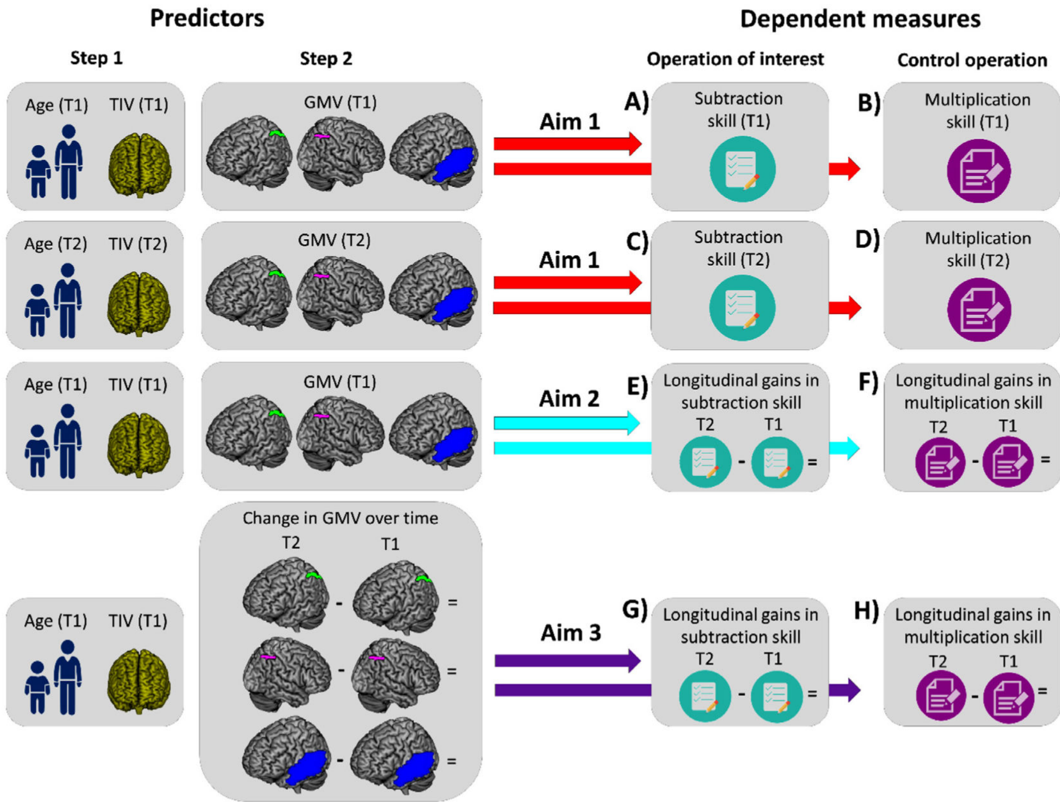

Fig. 3.

Illustration of the predictors and dependent measures included in the regression analyses performed for the whole sample (*n*=56). Illustration of the eight regression analyses carried out to address: Aim 1, looking at concurrent associations between GMV in the bilateral IPS and left MTG/STG at T1 and (A) subtraction and (B) multiplication skills at T1, and looking at concurrent associations between GMV in the bilateral IPS and left MTG/STG at T2 and (C) subtraction and (D) multiplication skills at T2; Aim 2, looking at the role of GMV in the bilateral IPS and left MTG/STG at T1 in predicting longitudinal gains in (E) subtraction and (F) multiplication skills; Aim 3, looking at the role of changes in GMV in the bilateral IPS and left MTG/STG over time (T2–T1) in predicting longitudinal gains in (G) subtraction and (H) multiplication skills. All measures were continuous.

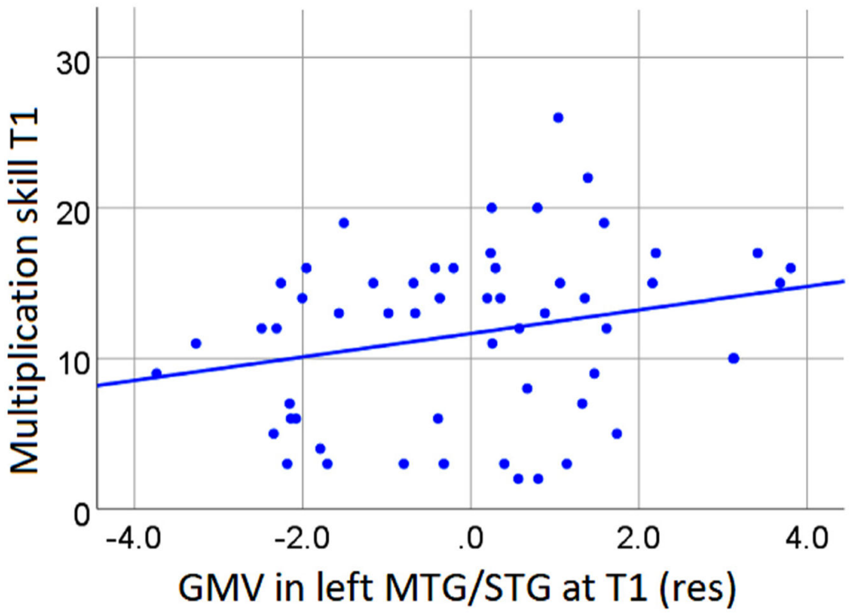

Fig. 4.

Association between multiplication skill and GMV in left MTG/STG at T1. Scatterplot showing a positive association between multiplication skill at T1 and GMV in left MTG/STG at T1 after accounting for predictors previously entered in the regression analysis (i.e. age, TIV, GMV in left and right IPS at T1) for the whole sample (n = 56).

Note. No outliers were identified in this data. Outliers were defined as data points 2.2 interquartile ranges (IQRs) below the first quartile (Q1) or above the third quartile (Q3) (Hoaglin and Iglewicz, 1987).

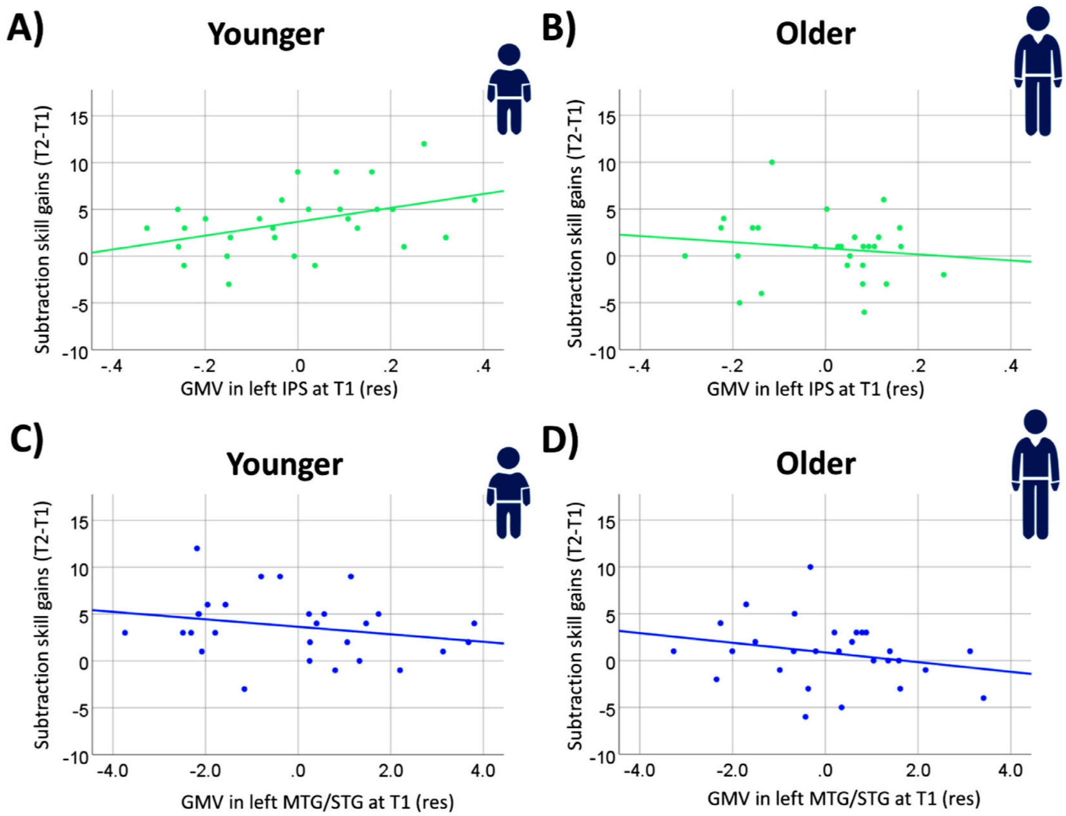

Fig. 5.

Association between longitudinal gains in subtraction skill and GMV in left IPS and left MTG/STG at T1. Scatterplots showing the association between longitudinal gains in subtraction skill and GMV in left IPS (5A) and GMV in left MTG/STG (5C) for younger children, the group for which these two factors showed a significant effect in the regression analysis (Table 5). Scatterplots showing the association between subtraction gains and GMV in left IPS (5B) and left MTG/STG (5D) at T1, just for comparison purposes.

Note. In order to more closely mirror the regression results, GMV in left IPS at T1 shows the residuals after the other variables entered in the regression model (i.e. age, TIV, GMV in right IPS, and GMV in left MTG/STG) have been accounted for. GMV in left MTG/STG at T1 shows the residuals after the other variables in the model (i.e. age, TIV, GMV in left and right IPS) have been accounted for. No outliers were identified in this data. Outliers were defined as data points 2.2 interquartile ranges (IQRs) below the first quartile (Q1) or above the third quartile (Q3) (Hoaglin and Iglewicz, 1987).

Table 1

Demographic information. Demographic characteristics and standard scores for the whole sample and for the age groups at T1 created to further explore the role of age in the association between GMV and math skill.

	Whole sample (*n*=56)	Age group (T1)	
		Younger (*n*=28)	Older (*n*=28)
Age at T1[a]	11.2 (1.5)	10.0 (0.6)	12.4 (1.0)
Age at T2[a]	13.5 (1.5)	12.2 (0.6)	14.7 (1.1)
Time between sessions[a]	2.3 (0.3)	2.3 (0.2)	2.4 (0.3)
Female/male ratio	26/30	10/18	16/12
Working memory T1[b]	104.3 (10.5)	106.0 (9.8)	102.7 (11.1)
Working memory T2[b]	108.2 (15.1)	110.0 (15.2)	107.1 (15.2)
Full IQ T1[b]	112.0 (15.0)	114.8 (14.6)	109.2 (15.2)
Full IQ T2[b]	110.7 (15.9)	114.1 (16.0)	107.3 (15.3)
Subtraction skill T1[c]	14.6 (4.8)	12.9 (4.9)	16.3 (4.2)
Subtraction skill T2[c]	16.8 (4.1)	16.6 (4.7)	17.1 (3.5)
Subtraction gains (T2–T1)[c]	2.2 (3.7)	3.7 (3.4)	0.8 (3.4)
Multiplication skill T1[c]	11.7 (5.7)	9.4 (5.5)	13.9 (5.1)
Multiplication skill T2[c]	13.7 (5.8)	13.8 (5.3)	13.6 (6.4)
Multiplication gains (T2–T1)[c]	2.0 (6.0)	4.4 (5.3)	−0.3 (6.0)
GMV in L IPS T1[d]	2.27 (0.27)	2.34 (0.28)	2.20 (0.26)
GMV in L IPS T2[d]	2.15 (0.24)	2.22 (0.24)	2.08 (0.23)
Changes in L IPS (T2–T1)[d]	−0.12 (0.15)	−0.12 (0.15)	−0.12 (0.15)
GMV in R IPS T1[d]	0.78 (0.09)	0.78 (0.09)	0.77 (0.09)
GMV in R IPS T2[d]	0.75 (0.07)	0.76 (0.07)	0.73 (0.07)
Changes in R IPS (T2–T1)[d]	−0.03 (0.06)	−0.02 (0.05)	−0.04 (0.07)

	Whole sample (n=56)	Age group (T1)	
		Younger (n=28)	Older (n=28)
GMV in L MTG/STG T1[d]	36.52 (2.26)	37.20 (2.53)	35.90 (1.76)
GMV in L MTG/STG T2[d]	35.50 (2.14)	36.05 (2.37)	34.86 (1.71)
Changes in L MTG/STG (T2–T1)[d]	−1.02 (1.26)	−1.15 (1.42)	−1.04 (1.10)
TIV T1[d]	1413 (161)	1398 (136)	1427 (184)
TIV T2[d]	1420 (167)	1411 (139)	1429 (192)

Note. T1: Time 1; T2: Time 2.

[a] In years.

[b] Standard scores.

[c] Raw scores.

[d] In mm^3. R IPS: right intraparietal sulcus; L IPS: left intraparietal sulcus; L MTG/STG: left middle temporal gyrus/superior temporal gyrus. TIV: Total intracranial volume.

Table 2

Aim 1 regression results for the whole sample. Results of the regression analyses carried out for the whole sample (*n*=56) in order to study the role of age, TIV, and GMV in the bilateral IPS and left MGT/STG at T1 and T2 in explaining concurrent performance in subtraction and multiplication at each time-point.

Step	Predictor	β	t	R^2	ΔR^2	F	ΔF
			Dependent measure: subtraction skill at T1				
1	Age T1	0.318	2.628^{*}	0.224	0.224	7.639^{***}	7.639^{***}
	TIV T1	0.335	2.762^{*}				
2	Age T1	0.369	2.701^{*}	0.292	0.068	4.115^{***}	1.595
	TIV T1	0.305	2.406^{*}				
	GMV L IPS T1	−0.229	−1.228				
	GMV R IPS T1	0.021	0.111				
	GMV L MTG/STG T1	0.295	1.990				
			Dependent measure: multiplication skill at T1				
1	Age T1	0.445	3.807^{***}	0.279	0.279	10.247^{***}	10.247^{***}
	TIV T1	0.264	2.261^{*}				
2	Age T1	0.509	3.898^{***}	0.352	0.074	5.443^{***}	1.894
	TIV T1	0.252	2.083^{*}				
	GMV L IPS T1	−0.215	−1.206				
	GMV R IPS T1	0.081	0.454				
	GMV L MTG/STG T1	0.307	2.167^{*}				
			Dependent measure: subtraction skill at T2				
1	Age T2	−0.014	−0.107	0.066	0.066	1.874	1.874
	TIV T2	0.257	1.935				
2	Age T2	−0.002	−0.016	0.080	0.014	0.864	0.244
	TIV T2	0.284	1.963				
	GMV L IPS T2	−0.064	−0.324				
	GMV R IPS T2	0.126	0.633				
	GMV L MTG/STG T2	0.053	0.332				
			Dependent measure: multiplication skill at T2				

	Predictor	β	t	R^2	ΔR^2	F	ΔF
1	Age T2	−0.031	−0.228	0.048	0.048	1.328	1.328
	TIV T2	0.217	1.618				
2	Age T2	−0.095	−0.612	0.075	0.028	0.814	0.496
	TIV T2	0.187	1.290				
	GMV L IPS T2	−0.188	−0.958				
	GMV R IPS T2	0.029	0.145				
	GMV L MTG/STG T2	−0.026	−0.159				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; TIV: total intracranial volume; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2 : change in R^2 . ΔF: Change in *F*. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 2.45 for the analyses at T1 and between 1.00 and 2.17 at T2.

Table 3

Aim 1 regression results for age groups at T1. Results of the regression analyses performed to study the role of TIV and GMV in the bilateral IPS and left MTG/STG at T1 in explaining concurrent performance in subtraction and multiplication at T1, separately for younger (*n*=28) and older (*n*=28) children.

		Younger children						Older children					
	Predictor	**β**	***t***	R^2	ΔR^2)	***F***	ΔF	**β**	***t***	R^2	ΔR^2	***F***	ΔF
		Dependent measure: subtraction skill at T1											
1	TIV T1	0.475	2.755 *	0.226	0.226	7.589 *	7.589 *	0.243	1.279	0.059	0.059	1.635	1.635
2	TIV T1	0.473	2.638 *	0.283	0.057	2.269	0.609	0.149	0.681	0.158	0.099	1.083	0.905
	GMV L IPS T1	−0.288	−1.162					−0.169	−0.513				
	GMV R IPS T1	0.128	0.522					−0.131	−0.373				
	GMV L MTG/STG T1	0.219	0.942					0.253	1.272				
		Dependent measure: multiplication skill at T1											
1	TIV T1	0.351	1.913	0.123	0.123	3.659	3.659	0.221	1.156	0.049	0.049	1.337	1.337
2	TIV T1	0.343	1.764	0.155	0.032	1.057	0.290	0.286	1.344	0.199	0.150	1.431	1.440
	GMV L IPS T1	−0.156	−0.580					−0.586	−1.829				
	GMV R IPS T1	0.051	0.193					0.447	1.300				
	GMV L MTG/STG T1	0.202	0.802					0.236	1.217				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; TIV: total intracranial volume; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2: change in R^2. ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 1.97 for the regression analyses with younger children and from 1.00 to 3.39 for the regression analyses with older children.

Table 4

Aim 2 regression results for the whole sample. Results of the regression analyses carried out for the whole sample (*n*=56) in order to study the role of age, TIV, and GMV in the bilateral IPS and left MTG/STG at T1 in predicting longitudinal gains in subtraction and multiplication skill (T2–T1).

	Predictor	β	t	R^2	ΔR^2	F	ΔF
Step	**Dependent measure: longitudinal gains in subtraction skill (T2–T1)**						
1	Age T1	−0.421	−3.456 ***	0.215	0.215	7.252 ***	7.252 ***
	TIV T1	−0.174	−1.429				
2	Age T1	−0.452	−3.431 ***	0.341	0.126	5.171 ***	3.185 *
	TIV T1	−0.080	−0.654				
	GMV L IPS T1	0.242	1.350				
	GMV R IPS T1	0.203	1.131				
	GMV L MTG/STG T1	−0.300	−2.097 *				
	Dependent measure: longitudinal gains in multiplication skill (T2–T1)						
1	Age T1	−0.439	−3.575 ***	0.203	0.203	6.738 ***	6.738 ***
	TIV T1	−0.081	−0.661				
2	Age T1	−0.528	−3.800 ***	0.267	0.064	3.639 *	1.457
	TIV T1	−0.094	−0.730				
	GMV L IPS T1	0.063	0.332				
	GMV R IPS T1	−0.099	−0.522				
	GMV L MTG/STG T1	−0.249	-−1.650				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; TIV: total intracranial volume; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2 : change in R^2. ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 2.45.

Table 5

Aim 2 regression results for age groups at T1. Results of the regression analyses performed to study the role of TIV and GMV in the bilateral IPS and left MTG/STG at T1 in predicting longitudinal gains in subtraction and multiplication skills (T2–T1), separately for younger (n=28) and older (n= 28) children.

		Younger children						Older children					
	Predictor	**β**	**t**	**R^2**	**ΔR^2**	**F**	**ΔF**	**β**	**t**	**R^2**	**ΔR^2**	**F**	**ΔF**
	Dependent measure: longitudinal gains in subtraction skill (T2–T1)												
1	TIV T1	−0.209	−1.088	0.044	0.044	1.184	1.184	−0.153	−0.787	0.023	0.023	0.620	0.620
2	TIV T1	−0.161	−0.995	0.413	0.370	4.052 *	4.833 *	−0.023	−0.103	0.090	0.067	0.568	0.562
	GMV L IPS T1	0.650	2.902 *					−0.105	−0.307				
	GMV R IPS T1	0.184	0.827					0.350	0.954				
	GMV L MTG/STG T1	−0.459	−2.188 *					−0.151	−0.731				
	Dependent measure: longitudinal gains in multiplication skill (T2–T1)												
1	TIV T1	−0.154	−0.795	0.024	0.024	0.632	0.632	−0.023	−0.115	0.001	0.001	0.013	0.013
2	TIV T1	−0.132	−0.667	0.125	0.101	0.823	0.889	−0.137	−0.588	0.048	0.047	0.290	0.382
	GMV L IPS T1	0.212	0.774					0.182	0.520				
	GMV R IPS T1	−0.026	−0.094					−0.358	−0.955				
	GMV L MTG/STG T1	−0.386	−1.505					−0.031	−0.148				

Note.

(*) $p < .05$;

(**) $p < .01$,

(***) $p < .005$. β: Standardized; TIV: total intracranial volume; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2 : change in R^2. ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 1.97 for the regression analyses with younger children and from 1.00 to 3.39 for the regression analyses with older children.

Table 6

GMV in left IPS predicting subtraction skill at T2 over and above skill at T1. Results for the regression analyses performed to study the role of GMV in left IPS and left MTG/STG at T1 (entered in step 2) in predicting subtraction skill at T2, over and above subtraction skill at T1 and TIV at T1 (entered in step 1), separately for younger (n=28) and older (n=28) children.

		Younger children						Older children					
Step	**Predictor**	**β**	**t**	**R^2**	**ΔR^2**	**F**	**ΔF**	**β**	**t**	**R^2**	**ΔR^2**	**F**	**ΔF**
							Dependent measure: subtraction skill at T2						
1	Subtraction skill at T1	0.751	4.974***	0.559	0.559	15.837***	15.837***	0.628	3.906***	0.392	0.392	8.069***	8.069***
	TIV T1	−0.007	−0.048					−0.007	−0.041				
2	Subtraction skill at T1	0.836	6.354***	0.711	0.152	14.148***	6.055**	0.625	3.536***	0.392	0.000	3.713**	0.002
	TIV T1	−0.031	−0.244					−0.008	−0.045				
	GMV L IPS T1	0.489	3.434***					−0.008	−0.045				
	GMV L MTG/STG T1	−0.239	−1.663					0.008	0.048				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; L IPS: left intraparietal sulcus; L MTG/STG: left middle and superior temporal gyri. ΔR^2 : change in R^2. ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.01 to 1.64 for the regression analysis with younger children and ranging from 1.01 to 1.21 for the regression analysis for older children.

Table 7

Aim 3 regression results for the whole sample. Results of the regression analyses carried out for the whole sample (n=56) in order to investigate the role of age, TIV at T1, and changes in GMV in the bilateral IPS and left MTG/STG over time (T2–T1) in explaining longitudinal gains in subtraction and multiplication skill (T2–T1).

Step	Predictor	β	t	R^2	ΔR^2	F	ΔF
		Dependent measure: longitudinal gains in subtraction skill (T2–T1)					
1	Age T1	−0.421	−3.4562 ***	0.215	0.215	7.252 ***	7.252 ***
	TIV T1	−0.174	−1.429				
2	Age T1	−0.421	−3.363 ***	0.229	0.014	2.974 *	0.310
	TIV T1	−0.148	−1.128				
	Change in GMV in L IPS	0.089	0.305				
	Change in GMV in R IPS	−0.186	−0.745				
	Change in GMV in L MTG/STG	0.024	0.145				
		Dependent measure: longitudinal gains in multiplication skill (T2–T1)					
1	Age T1	−0.439	−3.575 ***	0.203	0.203	6.738 ***	6.738 ***
	TIV T1	−0.081	−0.661				
2	Age T1	−0.450	−3.613 ***	0.238	0.035	3.119 *	0.765
	TIV T1	−0.100	−0.763				
	Change in GMV in L IPS	−0.062	−0.212				
	Change in GMV in R IPS	0.203	0.821				
	Change in GMV in L MTG/STG	0.077	0.469				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2: change in R^2. ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 5.51.

Table 8

Aim 3 regression results for age groups at T1. Results of the regression analyses performed to study the role of TIV at T1 and changes in GMV in the bilateral IPS and left MTG/STG over time (T2–T1) in explaining longitudinal gains in subtraction and multiplication skills (T2–T1), separately for younger (n=28) and older (n=28) children.

		Younger children						Older children					
Step	**Predictor**	β	t	R^2	ΔR^2	F	ΔF	β	t	R^2	ΔR^2	F	ΔF
		Dependent measure: longitudinal gains in subtraction skill (T2–T1)											
1	TIV T1	− 0.209	−1.088	0.044	0.044	1.184	1.184	−0.153	−0.787	0.023	0.023	0.620	0.620
2	TIV T1	− 0.234	−1.133	0.132	0.088	0.871	0.777	−0.119	−0.536	0.035	0.012	0.208	0.092
	Change in GMV L IPS	− 0.018	−0.044					0.123	0.216				
	Change in GMV R IPS	− 0.303	−0.924					−0.186	−0.361				
	Change in GMV L MTG/STG	0.155	0.592					−0.061	−0.226				
		Dependent measure: longitudinal gains in multiplication skill (T2–T1)											
1	TIV T1	− 0.154	−0.795	0.024	0.024	0.632	0.434	−0.023	−0.115	0.001	0.001	0.013	0.013
2	TIV T1	− 0.175	−0.828	0.085	0.061	0.533	0.678	−0.093	−0.432	0.085	0.084	0.532	0.705
	Change in GMV L IPS	− 0.227	−0.541					0.004	0.007				
	Change in GMV R IPS	0.000	0.000					0.318	0.633				
	Change in GMV L MTG/STG	0.317	1.177					−0.099	−0.378				

Note.

(*) $p < .05$.

(**) $p < .01$.

(***) $p < .005$. β: Standardized; L IPS: left intraparietal sulcus; R IPS: right intraparietal sulcus. L MTG/STG: left middle and superior temporal gyri. ΔR^2 : change in R^2 . ΔF: Change in F. No multicollinearity was found in these analyses, with the VIF values ranging from 1.00 to 4.41 for the regression analyses with younger children and from 1.00 to 7.70 for the regression analyses with older children.