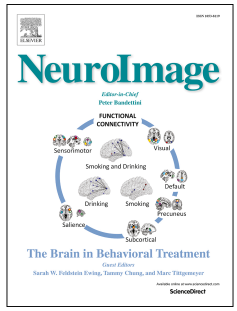

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Interference and problem size effect in multiplication fact solving: Individual differences in brain activations and arithmetic performance

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Abstract

In the development of math ability, a large variability of performance in solving simple arithmetic problems is observed and has not found a compelling explanation yet. One robust effect in simple multiplication facts is the problem size effect, indicating better performance for small problems compared to large ones. Recently, behavioral studies brought to light another effect in multiplication facts, the interference effect. That is, high interfering problems (receiving more proactive interference from previously learned problems) are more difficult to retrieve than low interfering problems (in terms of physical feature overlap, namely the digits, De Visscher & Noël, 2014). At the behavioral level, the sensitivity to the interference effect is shown to explain individual differences in the performance of solving multiplications in children as well as in adults. The aim of the present study was to investigate the individual differences in multiplication ability in relation to the neural interference effect and the neural problem size effect.

To that end, we used a paradigm developed by De Visscher, Berens, et al. (2015) that contrasts the interference effect and the problem size effect in a multiplication verification task, during functional magnetic resonance imaging (fMRI) acquisition. Forty-two healthy adults, who showed high variability in an arithmetic fluency test, participated in our fMRI study. In order to control for the general reasoning level, the IQ was taken into account in the individual differences analyses.

Our findings revealed a neural interference effect linked to individual differences in multiplication in the left inferior frontal gyrus, while controlling for the IQ. This interference effect in the left inferior frontal gyrus showed a negative relation with individual differences in arithmetic fluency, indicating a higher interference effect for low performers compared to high performers. This region is suggested in the literature to be involved in resolution of proactive interference. Besides, no correlation between the neural problem size effect and multiplication performance was found. This study supports the idea that the interference due to similarities/overlap of physical traits (the digits) is crucial in memorizing arithmetic facts and in determining individual differences in arithmetic.

Keywords

Arithmetic fact – interference – numerical cognition – learning – individual differences - mathematics

1. Introduction

The successful development of mathematical competencies requires the acquisition of different types of mathematical knowledge. Among them, arithmetic facts are specifically learned in primary school and constitute a critical foundation for more complex mathematical learning (e.g., Kilpatrick, Swafford, & Findell, 2001). Through the repeated practice of meaningful strategies (McCloskey, Aliminosa, & Sokol, 1991) or through direct memorization, children progressively build an arithmetic facts network permitting them to efficiently retrieve—without relying on a computational procedure—the answers of simple problems, such as 2 × 3 = 6 (Lemaire & Siegler, 1995; Siegler & Shipley, 1995). This arithmetic network enables the retrieval from long-term memory and is mainly composed of multiplication problems (Robinson et al., 2006; Roussel, Fayol, & Barrouillet, 2002; Thevenot, Castel, Danjon, & Fayol, 2015; Thevenot, Castel, Fanget, & Fayol, 2010). Despite long and specific practice at school, the performance in solving simple arithmetic problems shows remarkable individual differences in children as well as adults (e.g., Bailey, Littlefield, & Geary, 2012; De Visscher, Noël, & De Smedt, 2016; Dowker, 2005a, 2015; Geary, Hoard, & Bailey, 2012; Jordan, Hanich, & Kaplan, 2003; Lemaire & Siegler, 1995; Vanbinst, Ceulemans, Ghesquière, & De Smedt, 2015). Some individuals, referred to as individuals with dyscalculia, even show life-long and persistent difficulties in the acquisition of these foundational competencies (Geary, 2004; Geary, Hoard, & Hamson, 1999; Jordan & Montani, 1997; Slade & Russel, 1971). Corroborating these findings, individual differences in brain activity during arithmetic are observed in children (De Smedt, Holloway, & Ansari, 2011) and in adults (Grabner et al., 2007). As described here below, individual differences in arithmetic facts has been recently related to sensitivity to the proactive interference in multiplication, at the cognitive behavioral level (De Visscher & Noël, 2014). However, very little is known about the individual differences in multiplication facts related to the individual sensitivity to interference and to the problem size. The aim of this study is to further our understanding of individual differences in multiplication ability and investigate the correlation of these differences with the sensitivity to the interference and to the size of the problems.

In children as well as in adults, the size of the problem was shown to influence the performance (speed and accuracy), namely that small problems are better performed than large problems (Campbell & Xue, 2001). This problem size effect was largely described and reported as a substantial and robust effect in the literature (e.g. Zbrodoff & Logan 2005; De Brauwer et al. 2006). Recently, another important effect, based on physical similarities (i.e., the visual composition of the problem and its answer) in multiplication facts, has been brought to light–the interference effect. The theoretical principle is that arithmetic facts are associations of operands and answers that repeatedly use the same 10 elements, namely the digits from 0 to 9. More specifically, items that have been memorized can interfere with the process of memorization of a new item if this item is similar to the previously learned ones (proactive interference, Oberauer & Lange, 2008). The more features a problem shares with the previously learned ones, the weaker will be its memory trace. At the neural level, many studies investigated the effect of proactive interference in memory with mainly one paradigm that assesses the proactive interference coming from previous trials (recent-probe task, see Jonides & Nee, 2006). Overall the studies using this task or other tasks measuring proactive interference in memory repeatedly pointed to the left inferior frontal cortex. Based on the proactive interference theory, De Visscher and Noël (2014) developed a parameter assessing the proactive interference that each multiplication problem received throughout the learning of the multiplication tables, from table 2 to table 9. This parameter, based on the feature overlap between multiplications (digits), predicted the performance across multiplications beyond their problem size. In other words, the interference effect explained variance above and beyond the well-known problem size effect, namely that small problems evoke faster reaction times and less errors compared to large problems (Campbell & Xue, 2001; De Brauwer, Verguts, & Fias, 2006a; Zbrodoff & Logan, 2005). More importantly, the individual differences in multiplication was related to the individual sensitivity to this parameter (the individual slope), with lower sensitivity associated to better performance (De Visscher & Noël, 2014; De Visscher et al., 2016). In these studies, the general speed for solving multiplication was related to the sensitivity to the interference parameter in typically developing third grade, fourth grade and fifth grade children as well as in undergraduates. Moreover, hypersensitivity to the interference parameter was related to a certain profile of dyscalculia with circumscribed deficit in arithmetic facts knowledge (De Visscher & Noël, 2014; De Visscher & Noël, 2013; De Visscher, Szmalec, Van Der Linden, & Noël, 2015). Longitudinal data in fourth-grade children with poor or good arithmetic fluencies revealed that the sensitivity to the interference parameter was uniquely predicting the accuracy and speed in multiplication one year later.

In the typical development, the sensitivity to both the interference parameter and the problem size were related to the general speed in multiplication in typically developing children and adults, noting that these two factors explained unique variance (De Visscher & Noël, 2014). In order to better understand the individual differences in multiplication fact performance, the current study aimed at contrasting the sensitivity to these two factors and search for neural evidence in relation with multiplication performance.

Regarding the development of arithmetic fact knowledge, brain imaging data revealed that during arithmetic tasks younger children showed greater activation in the prefrontal cortex (dorsolateral and ventrolateral) and the anterior cingulate cortex, compared to older children (Rivera, Reiss, Eckert, & Menon, 2005). This was interpreted as higher demands on working memory and attentional resources for younger children. Interestingly, the younger children also showed larger activation in the hippocampus and dorsal basal ganglia, areas related to declarative and procedural memory systems. In particular, the left hippocampus was suggested to be involved in the learning phase of arithmetic facts, where greater activation for small problems compared to large ones, and for addition compared to subtraction, was found in children 10-12 years (De Smedt, Holloway, & Ansari, 2011). Similarly, the increase of the use of retrieval in arithmetic was associated with increase activation in the prefrontal cortices as well as in the hippocampal regions (Cho et al., 2012; Cho, Ryali, Geary, & Menon, 2011), suggesting that these area subserved the learning of arithmetic facts. Finally through development, the left inferior parietal cortex, including the angular gyrus, shows an increase specialization in mental arithmetic (Rivera et al., 2005).

The problem size and the interference effect seem to involve different representations in multiplication solving, namely and respectively the magnitude representation and the physical structure representation (De Visscher et al., 2016; Graham & Campbell, 1992). These effects have indeed been shown to activate distinct areas in a recent brain imaging study. In this study, De Visscher, Berens, Keidel, Noël, and Bird (2015) tested 20 healthy adults who were asked to solve single-digit multiplication problems during fMRI. A 2 × 2 factorial design was used to assess two main effects, namely the interference effect and the problem size effect. Various brain regions were modulated by the two effects, namely bilateral insula lobes, bilateral supplementary motor area and middle cingulate gyri as well as bilateral inferior frontal gyri. Aside from these common areas, the left angular gyrus was found to be specifically modulated by the interference effect, with higher activation for low interfering compared to high interfering problems. The left angular gyrus has been pointed out to subserve the automatic retrieval of arithmetic facts from memory (e.g. Ischebeck et al., 2006). Importantly, the brain activation of this region during multiplication problem solving has been shown to underlie individual differences in arithmetic. For instance, Grabner et al. (2007) reported stronger activation in the left angular gyrus for adults with high mathematical competence compared to those with low mathematical competence, for single-digit as well as for multi-digit multiplication problems. Besides, the problem size effect was modulating the right or bilateral intra-parietal sulcus/i in adults (De Visscher, Berens, et al., 2015; Stanescu-Cosson, Pinel, van de Moortele, et al., 2000) and in children (De Smedt et al., 2011), area known to be involved in magnitude processing (Dehaene, Piazza, Pinel, & Cohen, 2003a; Price, Holloway, Rasanen, Vesterinen, & Ansari, 2007).

The study of De Visscher, Berens, Keidel, Noël, and Bird, (2015) investigated the interference effect and the problem size effect in twenty healthy participants with homogeneous arithmetic fluency. The size and population of their sample did not enable the authors to investigate the individual differences in multiplication performance, which was the aim of the current study. By comparing the neural interference effect and problem size effect and investigate which one accounts best for multiplication performance, the current study aimed to further our understanding of individual differences in multiplication.

To this end, we collected functional activation data from 42 healthy adults who showed high variability in an arithmetic fluency test. Participants were asked to perform a multiplication verification task during fMRI. The multiplication paradigm was based on a 2 × 2 factorial design contrasting the interference level (low *vs* high) and the problem size (small *vs* large), enabling us to investigate the interference effect, the problem size effect, and their interaction. In addition, multiplication fluency was assessed to explore how individual differences in multiplication fluency are related to the neural interference effect and the neural problem size effect. In order to study this relationship and dismiss an explanation in terms of general intelligence factor, a measure of the intellectual quotient was taken into account in the models.

Regarding the problem size effect, one might predict differences of activation in the intraparietal sulci that are thought to sustain magnitude processing and that is modulated by the problem size effect (De Smedt, Holloway, & Ansari, 2011; Dehaene, Piazza, Pinel, & Cohen, 2003; Stanescu-Cosson, Pinel, van De Moortele, et al., 2000). Regarding the interference effect, three hypotheses can be formulated from previous studies. Based on the discussed literature, we expect to find a positive association between the interference effect and individual differences in multiplication in the angular gyrus, where a specific interference effect and individual differences were reported (De Visscher, Berens, Keidel, Noël, & Bird, 2015; Grabner, Ansari, Koschutnig, Reishofer, & Ebner, 2011). Alternatively, the higher interference effect in multiplication could be due to dysfunction of the medial temporal lobe, in particular the hippocampus, that is thought to sustain arithmetic fact learning (De Smedt, Holloway, & Ansari, 2011). Accordingly, a correlation between interference effect and multiplication score is expected in the hippocampus. Finally, as suggested by De Visscher & Noël (2014), individual differences in the interference effect in multiplication might stem from structural or functional differences in the left inferior frontal gyrus, known to be involved in the resolution of proactive interference (e.g. Jonides & Nee, 2006). Accordingly, a correlation between the interference effect in the left inferior frontal gyrus and multiplication performance is expected.

2. Method

2.1 Participants

Participants were 42 healthy right-handed adults (29 females). The participants' age ranged from 18 to 48 years (mean ± SD: 22 ± 5.6). All participants were healthy native German speakers without neurological diseases or learning disorders. They received either EUR 20 or course credit points (in case of psychology students) to compensate for their participation. The study was approved by the Ethics Committee of the Medical University of Graz.

2.2 Materials and procedure

2.2.1 Psychometric test session

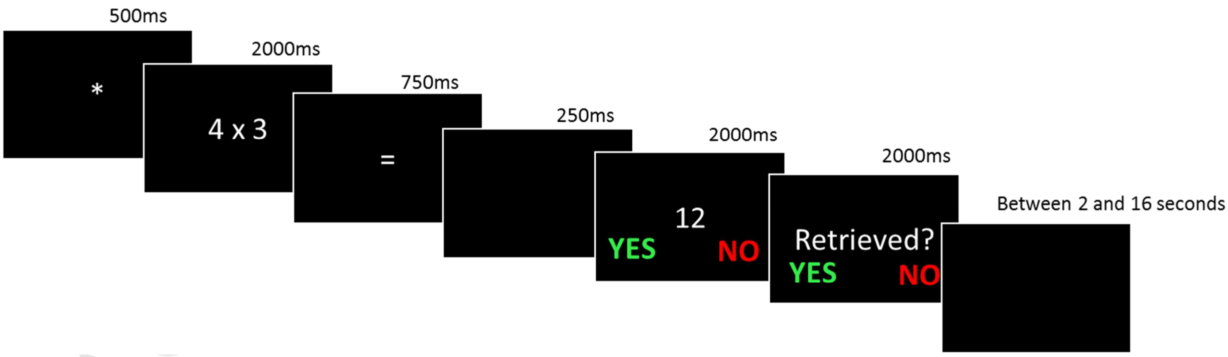
All participants were recruited from a large pool of participants who had been screened some months before the present study. Participants performed several psychometric tests. Among these tests were an Arithmetic Fluency Test and an Intelligence test, which are directly relevant for the present study. The Arithmetic Fluency Test was developed by the Educational Neuroscience Laboratory at the University of Graz (Vogel et al., 2017) based on the French Kit Test (French, Ekstrom & Price, 1963). The test was designed to measure the fluency with which individuals can solve arithmetic problems, including multiplications, subtractions and additions. For this, arithmetic problems were grouped by operation on separate sheets. Participants had to solve as many problems as possible on each sheet within a given time limit. Overall, 64 single-digit multiplications (e.g., 5 x 7), 128 single-digit additions (e.g., 4 + 7) and 128 subtractions with a minuend between 4-20 and a single-digit subtrahend (e.g., 16 - 8) were included. Participants were given 90 seconds for each of the three sheets/operations. In the present study, we focused on arithmetic fluency in multiplication as the single-digit multiplication problems are typically solved through fact retrieval operations (Campbell & Xue, 2001; Robinson et al., 2006; Roussel et al., 2002; Thevenot et al., 2015, 2010).

For assessing general intelligence, a short version of the Berlin Intelligence Structure Test (BIS-T; Jäger, Süß, & Beauducel, 1997) was administered. This test draws on three content components of intelligence (verbal, figural, and numerical) and, within the three content components, on four operational abilities (processing speed, memory, reasoning, and creativity). The applied short version of the BIS-T comprised 16 subscales, which were then aggregated to a score of general intelligence (IQ).

From the participant pool, a sample of 42 participants was selected who revealed a large variability in arithmetic fluency but whose general intelligence score was within the average range (between 90 and 110).

2.2.2 fMRI test session

The fMRI design and procedure of the present study were similar to that used by De Visscher et al. (2015). In the scanner, participants had to perform a multiplication verification task (see Figure 1). Each trial started with a fixation asterisk for half a second followed by a multiplication problem displayed for 2 seconds. After an equal sign and a black screen (lasting 1 sec altogether) the potential answer of the problem was displayed for 2 seconds. Participants were instructed to calculate the problem before seeing the target. When the target answer was displayed, participants had to decide whether the answer was correct (by pressing the left response button) or incorrect (by pressing the right response button). In addition to the displayed answer, two tags remained on the screen in order to remind the participant of the key responses (a green/red "yes"/"no" was on the left/right bottom side of the screen). After each target, participants were prompted to answer the question of whether they retrieved the answer to the problem from memory or not. Participants affirmed this question by pressing the left response button, or denied it (if they used calculation strategies) by pressing the right response button. The inter-trial interval was jittered exactly as in De Visscher et al. (2015) and lasted between 2 and 16 seconds (mean ± SD: 6.34s ± 3.88s).



<u>Figure 1:</u> Time-course of one trial of the multiplication verification task inside of the scanner.

The experimental design was a 2 × 2 factorial design using the two variables of interest: proactive interference (i.e., interference parameters: high vs. low) and problem size (i.e., products: large vs. small). The stimuli sets, order of presentation, inter-trial intervals and procedure were the same as in De Visscher et al. (2015). Multiplication problems were distributed into four conditions: small-low interfering, large-low interfering, small-high interfering and large-high interfering. From the 36 multiplication problem with operands from 2 to 9 (without the commutative pairs), all problems that permit to adhere to an orthogonal design were selected. The final set of problems consisted of 6 items per condition (24 in total). This orthogonal design enabled us to investigate the unique contribution of each variable separately. Problems with 0 or 1 as operand were not included because they are known to be solved by rule-based strategies (Campbell & Xue, 2001). The stimuli list with the measure of the proactive interference weight (interference parameter) and the problem size (products) is provided in Supplementary material. The stimuli presentation followed a rapid event-related design. A script included in the AFNI package (Cox, 1996) was used to select an optimal combination of stimulus order and inter-trial interval (i.e. the one with the smallest amount of un-modeled variance, from the 10 000 potential designs generated). Each problem was presented 6 times, resulting in 36 trials per condition and 144 trials in total. Three out of the six presentations were associated with the correct answer and three were associated with an operand-related incorrect answer (see Supplementary material). The order of the operands (large *vs* small operand first) was counterbalanced within and between runs, and across the six presentations of each stimulus.

Functional data collection was carried out in one functional run (34 minutes). The experimental task was broken down into 6 blocks, with a short break in-between the blocks. Before participants were positioned in the scanner, they were familiarized with the task demands and asked to perform 5 practice trials. The practice trials did not contain any of the problems presented during the fMRI test session. Inside the scanner, a structural scan taking 5 min was acquired before the beginning of the experimental task.

2.2.3 MRI acquisition

All images were acquired on a 3T Siemens Magnetom Prisma Fit scanner, using a 64-channel phased-array head coil. Functional images were acquired using a T2-weighted gradient-echo EPI sequence (TR = 2050 ms, TE = 25.0 ms, flip angle = 90°, FOV = 192 × 192 mm, matrix = 64 x 64). Each functional volume corresponded to 41 contiguous axial slices of 3 mm of thickness, acquired in a descending order. The voxel size of the functional volumes was 3 mm^3. For purposes of co-registration and standardization to a template brain, a high-resolution (1 mm^3) T1-weighted whole brain anatomical volume was collected using a Generalized Autocalibrating Partially Parallel Acquisitions (GRAPPA) sequence.

2.3 fMRI-Data analyses

The preprocessing and statistical analyses of MRI data were carried out using SPM8 (Wellcome Department of Imaging Neuroscience, London, UK). Individual functional data sets were slice-time corrected, then spatially realigned to the first volume and corrected for distortions in order to adjust for field inhomogeneity of the scanner (using the Realign and Unwarp function in SPM). The resulting volumes were registered to the anatomical scan and standardized through the application of the calculated transform between the MNI template brain and the anatomical scan using the DARTEL toolbox (Ashburner, 2007). The Echo-Planar Imaging (EPI) images were eventually smoothed with an 8 mm Full Width at Half Maximum (FWHM) Gaussian kernel. In order to remove low frequency modulations, a 128 seconds high-pass filter was applied. The structural scans were normalized to produce a mean image that is used to display statistical data with group level statistics (using DARTEL toolbox). The Juelich atlas from the Anatomy Toolbox in SPM (Eickhoff et al., 2005) was used to assign anatomical labels to significant brain regions.

A first-level model of the fMRI data was calculated in accordance with the general linear model (GLM) principles, grouping the correctly verified problems into the four experimental conditions. Seven additional regressors of no interest were modeled, including the 6 rigid-body movement parameters derived from the image realignment procedure and the error trials of the arithmetic task. The HRF amplitude as well as the temporal and dispersion derivatives were calculated on a voxel-wise basis. The window of interest corresponded to the time window during which participants were actively computing/retrieving the answer of the problem, namely from the onset of the problem presentation until the proposed answer. Following the procedure of De Visscher et al. (2015), this period of interest was specified as a 3 sec long boxcar function, and was convolved with SPM's canonical hemodynamic response function (HRF).

For the second level analyses, each individual's HRF amplitude estimates from the four experimental conditions were entered into a 2 (interference: high vs. low) × 2 (problem size: small vs. large) repeated measures ANOVA, permitting to examine group-wide BOLD differences as a function of interference level and problem size. In order to explore individual differences, regression models were carried out separately on the problem size effect and the interference effect, with the multiplication fluency measure. For the group effect analyses, we report effects that survived whole-brain family wise error (FWE) corrected thresholds at the peak level ($p < .05$). For the individual differences analyses, no cluster survived whole-brain FWE corrected thresholds at the peak level ($p < .05$). We therefore used an initial uncorrected ($p<.001$) threshold and report effect that survived whole-brain FWE corrected threshold of $p < .05$ at the cluster level, which is a more liberal but acceptable threshold that effectively controls for a 5% rate of false positives (see Eklund, Nichols, & Knutsson, 2016).

Subsequently, we calculated Bayes factors in the areas modulated by the interference effect or by the problem size effect in order to test the specificity of these areas for each effect. While investigating the areas modulated by the interference effect, the absence of problem size effect in the area was the null hypothesis. In contrary, while investigating the areas modulated by the problem size effect, the absence of interference effect in the area was the null hypothesis. The rationale used for interpreting the Bayes factors followed that of Dienes (2011b), considering a Bayes factor above 3 as substantial evidence for the null hypothesis.

3. Results

3.1 Behavioral data of the psychometric test session

The descriptive statistics for the psychometric tests are described in Table 1.

Table 1. Descriptive statistics of the behavioral measures.

N = 42	Minimum	Maximum	Mean	SD
Multiplication fluency	15	64	43.71	14.77
General intelligence (IQ)	91.53	109.60	100.55	4.41

3.2 Behavioral data of the fMRI task

3.2.1 Effects of interference and problem size

The average accuracy on the multiplication verification task was 97% (SD = 2.9). During the task, participants reported a retrieval strategy in 83% (SD = 17.9) of the trials. The average percentage of correct responses (%CR) for each condition is displayed in Figure 2.

A repeated-measures ANOVA with the within-subjects variables Interference level (low *vs* high) and Problem size (small *vs* large) was run on the %CR. A main effect of Interference level revealed higher performance for low interfering (M = 98.45, SD = 2.67) problems than for high interfering problems (M = 95.97, SD = 5.58; $F(1,41) = 14.640$, $p < .001$, $\eta_p^2 = .263$). A main effect of Problem size was shown, with higher performance for small (M = 98.45, SD = 2.77) compared to large problems (M = 95.97, SD = 5.53; $F(1,41) = 20.560$, $p < .001$, $\eta_p^2 = .334$). In addition, a significant interaction was found ($F(1,41) = 9.797$, $p = .003$, $\eta_p^2 = .193$), indicating a higher interference effect for large problems than for small ones (see Figure 2).

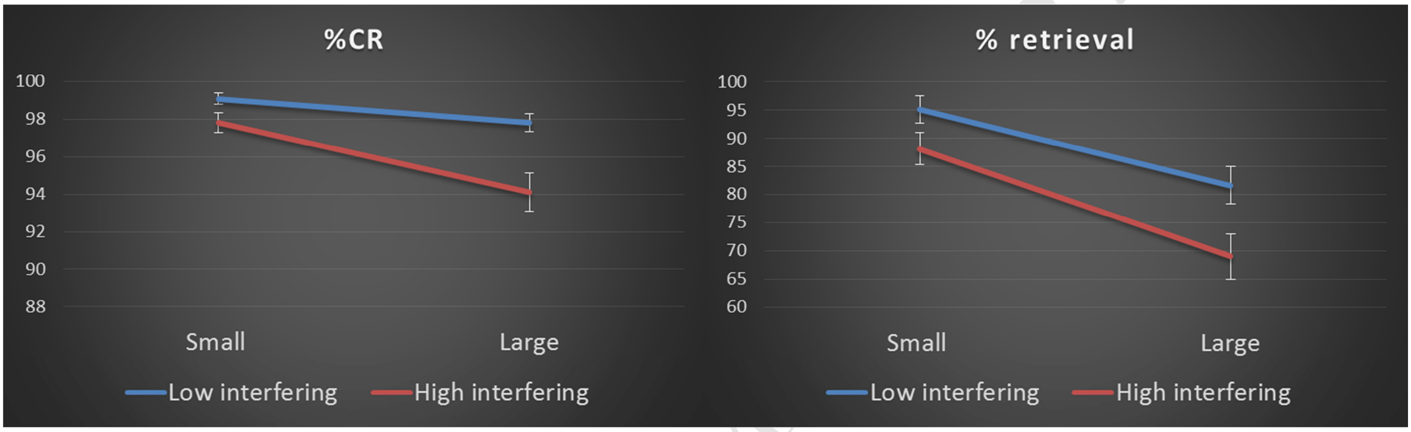


Figure 2: Left graph: Mean percentage of correct responses in the multiplication verification task according to the conditions, contrasting the interference level (low *vs* high) and the problem size (small *vs* large). Right graph: Mean percentage of retrieval for each condition, contrasting the level of interference (low vs high) and the size of the problem (small vs large).

Regarding the percentage of retrieval, the same repeated-measures ANOVA as above was run and revealed a main effect of Interference, indicating more retrieval for low interfering problems (M = 88.33, SD = 20.00) than for high interfering problems (M = 78.54, SD = 24.37, $F(1,41) = 28.549$, $p < .001$, $\eta_p^2 = .410$). Similarly, a main effect of Problem size emerged, with higher retrieval rate for small (M = 91.57, SD = 17.20) compared to large problems (M = 75.30, SD = 24.74, $F(1,41) = 39.080$, $p < .001$, $\eta_p^2 = .488$). Finally, a significant interaction showed a larger interference effect on retrieval frequency in large problems compared to small problems ($F(1,41) = 11.041$, $p = .002$, $\eta_p^2 = .212$). The average percentage of retrieval per condition is displayed in Figure 2.

3.3 Imaging data

Using the same paradigm, De Visscher et al. (2015) reported that the problem size effect was specifically modulating the right intra-parietal sulcus in typical adults, area known to be involved in magnitude processing (Dehaene et al., 2003a; Price et al., 2007). Aside from the problem size effect, the interference effect was specifically modulating the left angular gyrus, which has been suggested to be related to automatic retrieval (Grabner et al., 2011). In order to investigate whether the current data replicate the previous findings of De Visscher et al., (2015), we first explored the data at the group level, assessing the interference effect, the problem size effect and their interaction, by means of a 2 (Interference level: high vs low) × 2 (Problem size: large vs small) ANOVA (see Figure 3). We report effects that survived whole-brain family wise error (FWE) corrected thresholds at the peak level ($p < .05$). The exact same model on the retrieved correct trials only reached the same conclusions, and is reported in the Supplemental material.

3.3.1 Effects of interference and problem size: group level analyses

Main effect of interference

Regarding the interference effect, we report both the contrasts high > low interfering and low > high interfering (see Table 2). The main effect of interference is represented in red in Figure 3. High interfering problems showed higher BOLD response than low interfering problems in a large cluster comprising the right/left superior medial gyri, posterior-medial frontal cortex, middle frontal gyri, anterior and middle cingulate cortex. The same contrast revealed modulation of BOLD response bilaterally in the insula lobes, inferior frontal gyri, caudate nuclei, left intraparietal sulcus, right superior orbital gyrus, and left middle frontal gyrus. The reverse contrast (low > high) showed higher BOLD response for low interfering problems compared to high interfering problems in the right inferior parietal lobule, left/right mid orbital gyri, and right angular gyrus.

We investigated the specificity of the areas modulated by the interference effect, by calculating Bayes factors with the null hypothesis being the absence of problem size effect in these areas. All brain areas that showed higher BOLD response to high interfering problems compared to low interfering ones also exhibited substantial evidence in favor of a problem size effect (all Bayes factors < 0.001), except for the right AG. In contrast, the cluster in the right angular gyrus that showed higher BOLD response for low compared to high interfering problems, showed no evidence of a problem size effect (Bayes factor of 3.64, which is 3.64 times in favor of the null hypothesis (Dienes, 2011a)).

Table 2.

Main effect of Interference (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	BA	*k*	*t*	*Z*
Contrast High > Low					
Left/right superior medial gyri Left/right posterior-medial frontal cortices Left/right middle frontal gyri Left/right anterior and middle cingulate cortices	[0, 21, 45]	R 8	714	10.00	Inf
Left insula lobe (area 44)	[-30, 24, 0]	L 13	306	9.19	Inf
Right insula lobe	[33, 24, 0]	R 13	146	8.50	7.72
Left inferior frontal gyrus (area 44/45)	[-42, 21, 27]	L 9	458	7.06	6.58
Right caudate nucleus	[15, 9, 9]	R 48	62	6.29	5.95
Left caudate nucleus	[-9, 9, 6]	L 48	57	6.03	5.72
Left intraparietal sulcus (hIP3/hIP1/hIP2)	[-39, -45, 42]	L 40	123	5.84	5.56
Right superior orbital gyrus (area Fo3)	[24, 42, -15]	R 11	15	5.75	5.48
Left middle frontal gyrus (area Fp1)	[-33, 54, 12]	L 10	61	5.44	5.21
Right inferior frontal gyrus	[45, 30, 24]	R 9	40	5.33	5.11
Left intraparietal sulcus (hIP3)	[-27, -69, 39]	L 39	18	5.06	5.06
Contrast Low > High					
Right inferior parietal lobule (area PFt, PFop, PF, PFcm)	[60, -27, 27]	R 40	164	6.60	6.20
Left/right mid orbital gyri (area s24, s32)	[6, 27, -9]	R 32	87	6.19	5.86
Right angular gyrus (area PGa (IPL))	[60, -54, 9]	R 37	69	6.03	5.72

Main effect of problem size

The main effect of problem size is represented in green in Figure 3 and in Table 3. Similarly to interference effect (high > low), higher BOLD response was found for large problems compared to small ones in a large cluster comprising the right/left superior medial gyri, posterior-medial frontal cortex, middle frontal gyri, anterior and middle cingulate cortex. Also similar to high > low contrast, the large > small contrast modulated the BOLD response bilaterally in the insula lobes, in the right inferior frontal gyrus, left caudate nucleus, left intraparietal sulcus, and left middle frontal gyrus. Aside from these common areas, the problem size contrast revealed a modulation of the BOLD response in the right intraparietal sulcus, in the left and right cerebelli, left inferior temporal gyrus, left/right superior frontal gyrus, right superior orbital gyrus and right posterior medial frontal cortex.

The reverse contrast, with higher BOLD response for small problems compared to large problems, was found only in the right mid orbital gyrus.

We investigated the specificity of the areas modulated by the problem size effect, by calculating Bayes factors with the null hypothesis being the absence of interference effect in these areas. None of these areas showed strong evidence in favor of the specificity of the problem size effect (all Bayes factors < 0.12, one cluster in the left inferior temporal gyrus with Bayes factor = 1.04, and one cluster in right superior orbital gyrus Bayes factor = 1.50, which are anecdotal evidence in favor of the null hypothesis).

Table 3.

Main effect of Problem size (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	BA	*k*	*t*	*Z*
Contrast Large > Small					
Left/right superior medial gyrus	[-3, 24, 42]	L 8	497	8.47	7.70
Left/right posterior-medial frontal cortices					
Left/right middle frontal gyrus					
Left/right anterior and middle cingulate cortices					
Left insula lobe (area 45,44)	[-30, 21, -3]	L 13	874	7.96	7.31
Right insula lobe	[30, 24, 0]	R 13	153	7.46	6.91
Left intraparietal sulcus (hIP1/hIP3)	[-36, -57, 45]	L 39	854	7.39	6.86
Right inferior frontal gyrus	[45, 27, 27]	R 9	289	7.17	6.68

Left caudate nucleus, thalamus	[-12, 3, 12]	L 48	296	7.04	6.57
Right intraparietal sulcus (hIP3/hIP1/hIP2)	[36, -54, 45]	R 39	341	6.35	5.99
Left middle frontal gyrus (Area Fp1)	[-39, 54, 9]	L 10	171	6.33	5.98
Right cerebellum (lobule VI, lobule VIIa Crus I)/left lobule VI	[9, -81, -27]	-	96	6.28	5.94
Left inferior temporal gyrus (area FG4, FG2)	[-51, -54, -12]	L 37	44	5.86	5.58
Left cerebellum (lobule VIIa Crus I, lobule VI, area FG2)	[-33, -63, -27]	-	28	5.15	4.95
Left superior frontal gyrus	[-18, 15, 66]	L 6	19	5.09	4.90
Right superior frontal gyrus	[30, 12, 63]	R 6	8	4.96	4.78
Right superior orbital gyrus (FP1)	[24, 63, -3]	R 10	5	4.93	4.76
Right posterior medial frontal cortex	[15, 12, 66]	R 6	6	4.92	4.75
Contrast Small > Large					
Right mid orbital gyrus (area s32, Fp2, s24, left area s32)	[6, 39, -12]	R 11	33	5.34	5.12

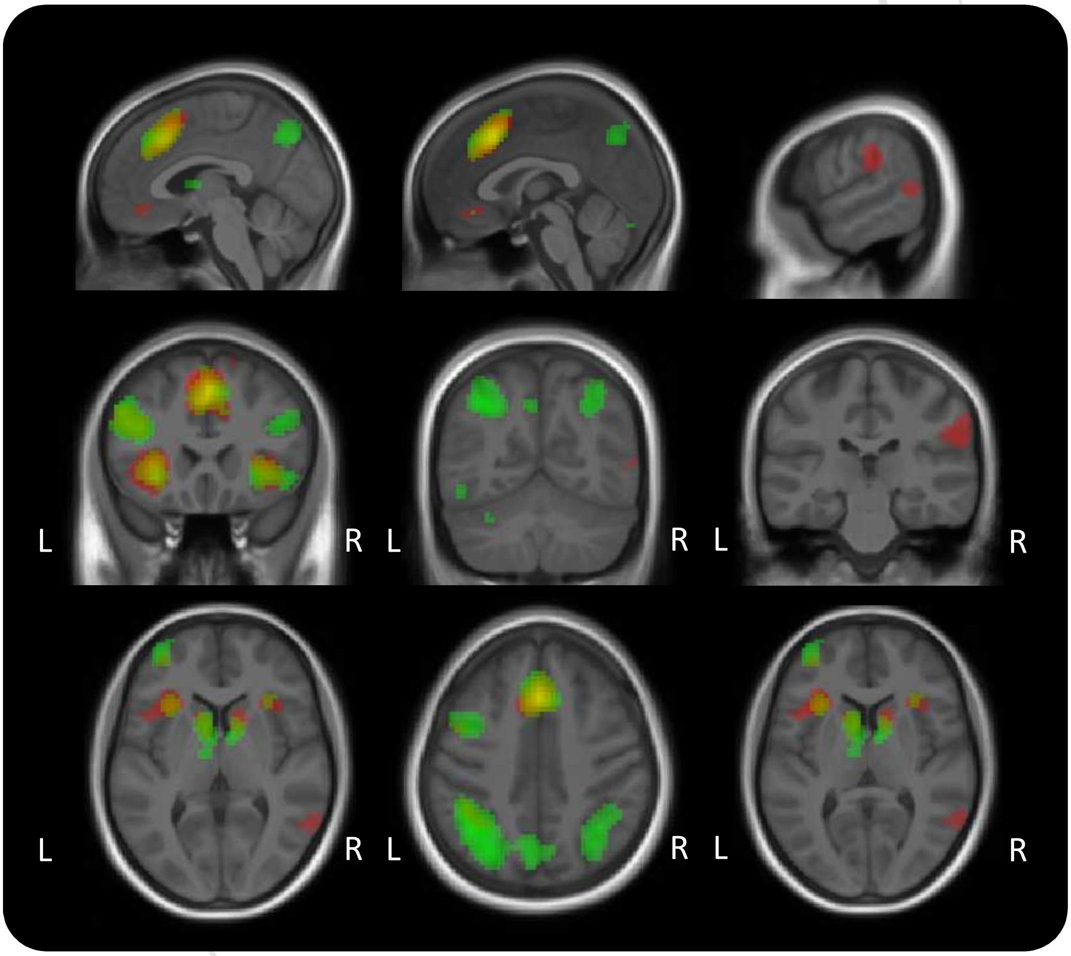


***Figure 3**: Main effect of interference (red blobs), main effect of problem size (green blobs) and overlap (yellow blobs) on the mean structural scan of the group (irrespective of the direction). From left to right, the MNI coordinates of the corresponding brain section are [-1.6, 19.6, 5.6], [0.8, -59.5, 44.4], [60.6, -29.2, 4.8].*

Interaction between interference and problem size

There was no significant interaction between Interference and Problem size at the predefined FWE correction $p < .05$ threshold at peak level—even at a lowered threshold of $p < .001$ (uncorrected) with FWE correction at cluster level.

3.3.2 Individual differences

3.3.2.1 Interference effect

In order to investigate how individual differences in arithmetic fluency were related to the neural interference effect, a whole-brain regression model on the low versus high interfering contrast was computed with the multiplication fluency and the IQ score (regressor of no interest) as covariates. With a FWE corrected threshold ($p < .05$) at the peak-level, the analyses revealed no area. Subsequently we ran the same model with an initial uncorrected threshold $p < .001$, and reported clusters surviving FWE corrected $p < .05$ threshold, which is a more liberal but acceptable threshold that effectively controls for a 5% rate of false positives (see Eklund, Nichols, & Knutsson, 2016). This analysis revealed only one significant cluster, the left inferior frontal gyrus, extending to the left precentral gyrus (MNI [-45, 24, 21], $k = 212$, $t = 4.68$, $Z = 4.14$, see Figure 4). The data show that the adults with higher arithmetic knowledge show less neural interference effect within the left inferior frontal gyrus (see Figure 4).

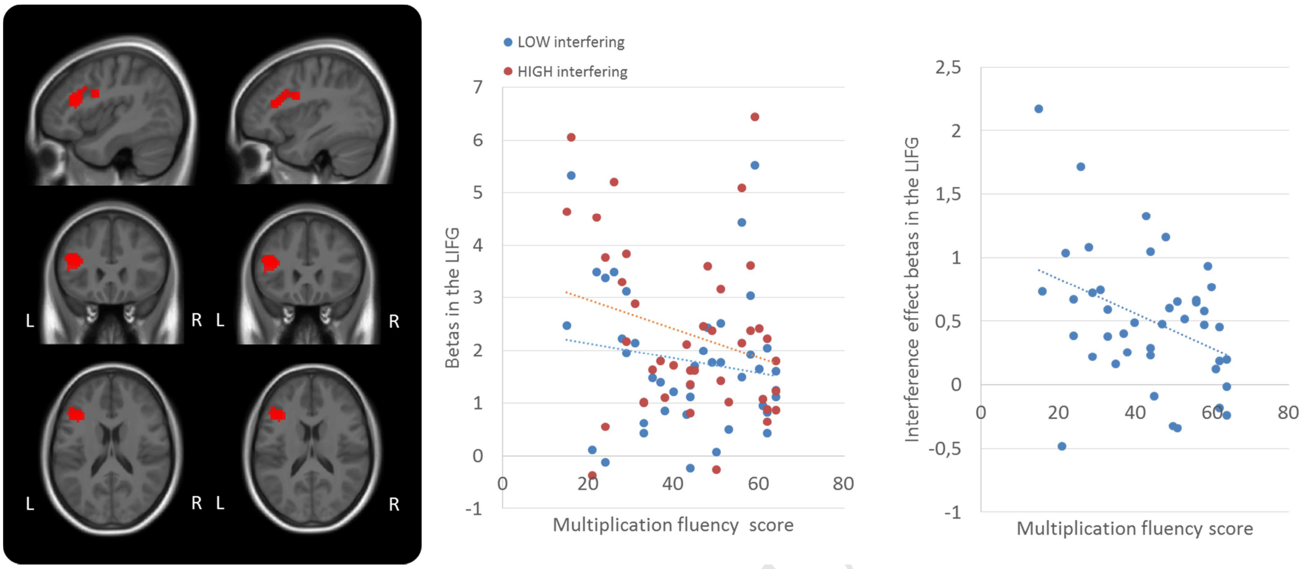


Figure 4: Left: Individual interference effect correlation with simple arithmetic performance, in the left inferior frontal gyrus, extending to the precentral cortex. The MNI coordinates of the corresponding brain section are [-40.1, 24.1, 18.0] and [-36.1, 27.0, 17.7]. Middle: Individual betas in the left inferior frontal gyrus for low and high interfering conditions according to the multiplication fluency score. Right: Interference effect (high minus low interfering betas) in the left inferior frontal gyrus according to the multiplication fluency score.

3.3.2.2 Problem size effect

In order to investigate how individual differences in arithmetic fluency are related to the neural problem size effect, a whole-brain regression model on the small versus large interfering contrast was computed with the multiplication fluency and the IQ score (regressor of no interest) as covariates. With a voxel-wise threshold of $p < .05$ FWE corrected, results did not show any significant area for this model. Using a more liberal but acceptable threshold (initial uncorrected threshold $p < .001$, FWE corrected $p < .05$ cluster-wise threshold), no significant area was found.

4. Discussion

In the typical and atypical development of math ability, a large variability of performance in solving simple arithmetic problems is observed and has not found a compelling explanation yet. Thus far, most of behavioral and neuroimaging studies focused on the global performance in arithmetic fluency, mainly contrasting different arithmetic operations, different problem-solving strategies, or different problem sizes (De Smedt et al., 2011; Grabner et al., 2011; Grabner et al., 2009; Menon, 2014b; Peters & De Smedt, 2017). However, behavioral studies showed that the performance is also influenced by the proactive interference created during the arithmetic fact learning (in terms of physical feature overlap, namely the digits, (De Visscher & Noël, 2014; De Visscher et al., 2016)). At the neural level, both the problem size and the proactive interference level were distinguished as two separate effects in multiplication facts, taking place respectively in the right intraparietal sulcus and in the left angular gyrus (De Visscher et al., 2015). In this previous study, the individual differences in multiplication related to both the interference and problem size effect was not investigated given the small and homogeneous sample used. The aim of the present work was therefore to investigate the individual differences in multiplication ability related to neural mechanisms of the sensitivity to interference and problem size.

To that aim, we used a paradigm developed by De Visscher, Berens, et al. (2015) that contrasts the interference effect and the well-known problem size effect in a multiplication verification task. The behavioral data of our participants confirmed both the interference effect and the problem size effect, namely that larger problems and high interfering problems were more error-prone than the small and the low interfering problems. These results corroborates the findings of De Visscher and Noël (2014) showing a robust interference and problem size effect in third and fifth graders as well as undergraduates.

When addressing the question of individual differences, the left inferior frontal gyrus showed a modulation of activation due to the interference effect related to multiplication fluency, with higher neural interference effect in that region for lower performers compared to higher performers. Importantly in the current study, the general reasoning ability was taken into account and controlled for in the analyses. Our results are in line with findings showing individual differences in arithmetic fluency related to modulation of the left inferior frontal gyrus (Berteletti, Prado, & Booth, 2014). While the left inferior frontal gyrus was commonly seen as part of the classical language areas of the left hemisphere on which the arithmetic fact retrieval rely (Dehaene & Cohen, 1995), this region is also known to be involved in proactive interference resolution (Jonides & Nee, 2006). For instance, a patient with a circumscribed lesion in the left inferior frontal gyrus showed heightened sensitivity to proactive interference compared to other patients with other frontal lesions (Thompson-Schill et al., 2002). More precisely, the left inferior frontal gyrus is suggested to be involved in resisting proactive interference stemming from previous trials (Jonides & Nee, 2006; Thompson-Schill et al., 2002). The sensitivity to the inference effect in multiplication leads to lower multiplication performance, and this relation is observed in the region involved in interference resolution and selection of the relevant information. Nonetheless, the current study do not permit to directly test the idea that sensitivity-to-interference in memory provoke difficulties in memorizing items that have a high level of similarity between them, as multiplication facts do. Further studies are required to address that hypothesis with a behavioral measure of sensitivity-to-interference in memory.

Importantly, in the present study no individual differences in the neural problem size effect were related to arithmetic fluency. While the problem size effect is robust and well-recognized, its potential for explaining individual differences at the neural level seems to be low. It has to be noted that the way problem size is defined varies a lot across studies and depends on the arithmetic operation (Campbell & Xue, 2001; De Brauwer et al., 2006a; Zbrodoff & Logan, 2005). In the current study, the size is determined by the products of the problem (small products for small problems versus large products for large problems). Very few studies investigated the problem size and its link with individual differences in arithmetic. One brain imaging study in 10-12-year-old-children by De Smedt et al. (2011) showed higher activation of the intraparietal sulci in children with low arithmetic fluency for small problems compared to children with high arithmetic fluency. In this study, problems were defined as small when the product of the operands was below or equal to 25, and as large when the product of the operands was above 25. Additions and subtractions were used, and subtraction size was determined by the reverse relation with additions. It is therefore difficult to compare our results to these or other results since arithmetic operations are different, the problem size is defined differently, and any of these studies took the interference effect into account together with the problem size effect.

At the behavioral level, De Visscher & Noël (2014b) showed that both the problem size and the interference effect predicted the performance across multiplications but that mainly the sensitivity to the interference effect was related to impairment in solving multiplication while the sensitivity to the problem size was not. As supported by the behavioral study of De Visscher et al. (2016), the interference effect is more related to retrieval and memory issue, while the problem size could stem from many different reasons (the frequency, the magnitude of the answers or the distribution of answers, the strategy used, the neighboring consistency; (Ashcraft & Christy, 1995; Campbell, 1995; LeFevre, Sadesky, & Bisanz, 1996; Siegler, 1988; Verguts & Fias, 2005).

The group level analyses are overall in line with the results of De Visscher, Berens, Keidel, Noël, and Bird (2015). Increased BOLD response for low interfering problems compared to high interfering ones was found in the right angular gyrus, and this area did not show modulation by the problem size effect. This is partly corroborating the results of De Visscher, Berens, et al., (2015), in which this contrast revealed the left angular gyrus in the main model that was including all trials. It has to be noted that the right angular gyrus also showed specific modulation by the interference effect in the model including the retrieved trials only (see Appendix C in De Visscher, Berens, Keidel, Noël, & Bird, 2015, Bayes factor of 2.30 which is close to substantial evidence in favor of the null hypothesis (absence of problem size effect). This Bayes factor was computed after publication). The left angular gyrus is commonly thought to be involved in verbally-mediated process and to contribute to arithmetic retrieval (Dehaene et al., 2003a). In opposition with our predictions, the left angular gyrus was not significantly modulated by the interference level. Nonetheless, the right angular gyrus was modulated by the interference effect, area that is suggested to contribute to visuo-spatial fact retrieval (Arsalidou & Taylor, 2011). Despite less attention for the right angular gyrus, both angular gyri are known to be related to retrieval of arithmetic problems, in adults with more activation for trained than for untrained problems, (Grabner et al., 2009) and in children for retrieval compared to procedural strategies based on verbal report (Polspoel, Peters, Vandermosten, & De Smedt, 2017; Tschentscher & Hauk, 2014).

Similarly to De Visscher, Berens, et al. (2015), higher BOLD responses for large problems compared to small ones were found in bilateral intraparietal sulci, however the specificity of the right intraparietal sulcus was not confirmed in the current study (no strong evidence from the Bayes factors in favor of the null hypothesis regarding the interference effect in these regions). These slight discrepancies might due to the differences in the sample selection that included participants with different levels of arithmetic fluency in this current study compared to a more homogeneous sample in De Visscher, Berens, et al. (2015). Also, cultural differences in the educational system or language differences might have slightly influenced the results. However, the overall main effects are similar and constitute a replication of the differences between the problem size and the interference effect at the brain modulation level.

Other brain areas were similarly modulated by both the interference and problem size effect. Higher BOLD response for the high interfering problems and large problems were found compared to the low interference and small ones respectively. These common brain areas are frequently reported in the literature on arithmetic (e.g., Arsalidou & Taylor, 2011): superior medial gyri, posterior-medial frontal cortices, middle frontal gyri, anterior and middle cingulate cortices, insula lobes, caudate nuclei, inferior parietal lobes, superior or mid orbital gyri. All these areas were also found in De Visscher et al. (2015), except the caudate nuclei. Most of these areas have been previously associated with domain-general (e.g., task difficulty) rather than with domain-specific processing mechanisms (e.g., numerical processing, Fox et al., 2005; Sunaert, Van Hecke, Marchal, & Orban, 2000).

In conclusion, our findings bring new understanding on individual differences in multiplication ability, related to the neural sensitivity to the interference effect and to the problem size effect. Our results revealed a neural interference effect linked to individual differences in multiplication in the left inferior frontal gyrus, while controlling for the IQ. This interference effect in multiplication found in the left inferior frontal gyrus showed a negative relation with individual differences in arithmetic fluency, indicating a higher interference effect for low performers compared to high performers. This region is known to be involved in resolution of proactive interference. Besides, no correlation between the neural problem size effect and multiplication ability was found. Our results support the idea that the interference due to similarities/overlap of physical traits (the digits) is crucial in memorizing arithmetic facts and in determining individual differences in arithmetic.

5. Supplementary material

Appendix A. Stimuli list of the multiplication verification task.

	LOW INTERFERING				HIGH INTERFERING			
	Problem	Problem size (product)	Interference level	False answer (distance with the correct answer)	Problem	Problem size (product)	Interference level	False answer (distance with the correct answer)
SMALL	2 × 7 =	14	4	12 (2)	3 × 6 =	18	8	15 (3)
	9 × 2 =	18	7	16 (2)	5 × 4 =	20	8	16 (4)
	5 × 5 =	25	3	30 (5)	4 × 3 =	12	10	15 (5)
	4 × 4 =	16	5	20 (4)	4 × 6 =	24	12	28 (4)
	2 × 8 =	16	7	18 (2)	3 × 7 =	21	13	24 (3)
	2 × 6 =	12	3	10 (2)	8 × 3 =	24	13	21 (3)
LARGE	6 × 6 =	36	4	30 (6)	3 × 9 =	27	9	24 (3)
	6 × 5 =	30	6	36 (6)	9 × 4 =	36	9	32 (4)
	5 × 9 =	45	6	40 (5)	8 × 5 =	40	9	45 (5)
	9 × 9 =	81	6	72 (9)	7 × 8 =	56	9	63 (7)
	5 × 7 =	35	7	40 (5)	6 × 7 =	42	22	48 (4)
	7 × 7 =	49	7	56 (7)	4 × 8 =	32	25	28 (4)

Appendix B. 2x2 factorial analyses on retrieved correct trials only

The same model has been run on the retrieved trials only, with the same threshold (FWE corrected, p < .05 voxel-wise).

Main effect of interference

Main effect of Interference (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	BA	*k*	*t*	*Z*
Contrast High > Low					
Left/right superior medial gyrus	[0, 21, 45]	R 8	331	8.39	7.62
Left/right posterior-medial frontal cortices					
Left/right middle frontal gyrus					
Left/right anterior and middle cingulate cortices					
Left insula lobe (area 44)	[-33, 21, 0]	L 13	186	7.91	7.26
Right insula lobe	[33, 24, 0]	R 13	36	6.57	6.17
Left inferior frontal and precentral gyri (area 45/44)	[-45, 9, 33]	L 8	263	5.80	5.52
Right caudate nucleus	[12, 15, 3]	R 48	12	5.51	5.27
Right superior orbital gyrus (area Fo3)	[24, 42, -15]	R 11	6	5.05	4.86
Contrast Low > High					
Right inferior parietal lobule (area PFt, PFop, PF, PFcm)	[60, -27, 27]	R 40	99	5.99	5.68
Left/right mid orbital gyrus (area s24, s32)	[3, 33, -9]	R 11	45	5.97	5.67

Right angular gyrus (area PGa (IPL))	[63, -51, 9]	R 37	30	5.30	5.08

Main effect of problem size

Main effect of Problem size (*pFWE[peak]* < .05, *k* > 4)	*Peak voxel MNI Coordinates [x,y,z]*	BA	*k*	*t*	*Z*
Contrast Large > Small					
Left/right superior medial gyrus Left/right posterior-medial frontal cortices Left/right middle frontal gyrus Left/right anterior and middle cingulate cortices	[3, 21, 45]	R 8	191	7.10	6.61
Left insula lobe (area 45,44)	[-30, 21, -3]	L 13	63	6.58	6.18
Right insula lobe	[30, 24, 0]	R 13	42	6.07	5.75
Left intraparietal sulcus (hIP1/hIP3)	[-39, -54, 48]	L 39	269	5.83	5.54
Left inferior frontal and precentral gyri (area 45, 44)	[-48 ,21, 30]	L 9	242	5.78	5.50
Left caudate nucleus, thalamus	[-12, 3, 15]	L 48	48	5.76	5.48
Right middle frontal gyrus	[48, 33, 21]	R 9	75	5.44	5.21
Left middle frontal gyrus (Area Fp1)	[-39, 54, 12]	L 10	21	5.36	5.13
Left precuneus (area 7P, 7A)	[-6, -66, 45]	L 7	27	5.30	5.08
Right intraparietal sulcus (hIP3/hIP1, hIP2)	[33, -66, 45]	R 39	105	5.24	5.02
Right caudate nucleus	[9, -81, -27]	-	15	5.17	4.96
Right cerebellum (lobule VI, lobule VIIa Crus I)	[9, 3, 6]	-	15	5.07	4.88
Contrast Small > Large					
Right mid orbital gyrus (area s32, s24, left area s24, s32)	[3, 33, -9]	R 11	16	5.04	4.85

Interaction between interference and problem size

Similarly to the full model, there was no interaction between Interference and Problem size.

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