What's behind a '+' sign? Perceiving an arithmetic operator recruits brain circuits for spatial orienting

Romain Mathieu[1, 2], Justine Epinat-Duclos[1], Monica Sigovan[3], Audrey Breton[1], Anne Cheylus[1], Michel Fayol[4], Catherine Thevenot[5], & Jérôme Prado[1]

[1] Institut des Sciences Cognitives Marc Jeannerod, UMR 5304, Centre National de la Recherche Scientifique (CNRS) & Université Lyon 1, Bron, France

[2] Faculté de Psychologie et des Sciences de l'Education, Université de Genève, 1205 Genève, Switzerland

[3] Laboratoire CREATIS, Université Lyon 1, CNRS/INSERM, INSA-Lyon & HCL, Lyon, France

[4] Université Blaise Pascal, Clermont II & CNRS, UFR de Psychologie, LAPSCO, 63037 Clermont-Ferrand, France

[5] Institut de Psychologie, Université de Lausanne, 1015 Lausanne, Switzerland

Correspondence should be addressed to R.M. (rmathieu@isc.cnrs.fr) or J.P. (jprado@isc.cnrs.fr), Institut des Sciences Cognitives Marc Jeannerod, UMR 5304, Centre National de la Recherche Scientifique (CNRS) & Université Lyon 1, 67 Boulevard Pinel, 69675 Bron cedex, France. Phone: +33 (0)4 37 91 12 65

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Abstract

Do mathematical symbols evoke spatial representations? Although behavioral studies have long demonstrated interactions between space and the processing of Arabic digits, how to interpret these results remains controversial. Here we tested whether activity in regions supporting spatial processing contributes to the processing of symbols conveying fundamental arithmetic concepts -- such as operation signs -- even in the absence of associated digits. Using fMRI, we show that merely perceiving a ‘+’ sign triggers activity in brain regions that support the orienting of spatial attention in adults. Activity in these regions was greater for ‘+’ than ‘×’ signs, indicating that it is modulated by whether an operator reflects an operation that evokes numerical manipulation (rather than rote memorization). Finally, the degree to which subjects activated a spatial region in response to a ‘+’ sign was correlated with the degree to which subjects benefited from being briefly presented with that sign before having to calculate a single-digit addition problem, an effect termed operator-priming. Therefore, not only are some arithmetic operators linked to spatial intuitions, but such intuitions might also have an important role during arithmetic calculation. More generally, our findings support the view that mathematical symbols inherently evoke spatial representations.

Keywords : Attention; Arithmetic; fMRI; Space; Symbol

There is accumulating evidence that math skills relate to spatial skills in both adults and children (Casey *et al.* 1992; Hegarty and Kozhevnikov 1999; Kyttälä and Lehto 2008; Mix and Cheng 2011; Cheng and Mix 2014). To some extent, this may be explained by the fact that many basic mathematical concepts are grounded in space (e.g., measurements). However, it has also long been proposed that mathematical symbols by themselves may rely on spatial representations (Fischer and Shaki 2014). Early support for this idea comes from an effect termed Spatial Numerical Association of Response Codes (SNARC). The SNARC effect refers to the observation that when participants are asked to process Arabic digits (e.g., classify them as even or odd), they respond faster to small numbers with the left hand than with the right hand. The reverse pattern is found for large numbers (Dehaene *et al.* 1993; Wood *et al.* 2008). According to a popular account, the SNARC effect might arise because participants mentally organize numbers of increasing size from left to right along a mental number line (MNL) in long-term memory. The MNL is typically thought to be the manifestation of an evolutionary old approximate number system (ANS), according to which numerical values are represented as a series of partially overlapping Gaussian tuning curves along a mental continuum (Gallistel and Gelman 1992; Dehaene *et al.* 1998; Piazza *et al.* 2004; Nieder and Dehaene, 2009). Further studies have suggested that associations between space and numbers might be so strong that the passive perception of a digit can bias spatial attention (Fischer *et al.* 2003; Ristic *et al.* 2006; Dodd *et al.* 2008). For instance, passively viewing small digits at fixation leads to better detection of subsequent targets in the left visual field, whereas passively viewing large digits facilitates the detection of targets in the right visual field (Fischer *et al.* 2003). Therefore, there is clear evidence of interactions between space and the processing of Arabic digits in the literature.

However, these spatial-numerical interactions may not necessarily indicate that Arabic digits inherently rely on spatial representations. For example, in a series of recent experiments, van Dijck and colleagues have argued that the SNARC effect might be an artifact of the way information is organized in working-memory during task performance (van Dijck and Fias 2011; van Dijck *et al.* 2014; Fias et van Dijck 2016). That is, van Dijck and Fias (2011) showed that when participants are asked to perform a parity judgment task on digits that come from a random sequence previously encoded in working memory (e.g., 7-3-2-9-6), they do not associate smaller and larger numbers to the left and right sides of space (respectively). Instead, numbers at the beginning of the sequence (e.g., 7) are responded faster with the left hand and numbers at the end of the sequence (e.g., 6) are responded faster with the right hand. Thus, the SNARC effect might not reflect the fact that numerical values are represented along a MNL in long-term memory, but rather that information is spatially encoded in working memory during the task (i.e., elements that are early versus late in a sequence are associated with the left versus right side of space). Interestingly, van Dijck, Abrahamse, Majerus & Fias (2013) found that such spatial organization of information in working memory might also account for the attentional SNARC effect observed in Fischer *et al.* (2003). Thus, it is possible that the spatial-numerical interactions observed in behavioral studies arise entirely (or partly, see Huber *et al.* 2016) from working-memory effects. This, of course, casts doubt on the claim that there are long-term associations between space and mathematical symbols such as Arabic digits.

It is thus interesting to note that spatial associations do not appear to be restricted to Arabic digits. They can also be observed with non-numerical symbols that convey fundamental arithmetic concepts, such as operation signs (e.g., ‘+’) (Marghetis *et al.* 2014; Pinhas *et al.* 2014). For instance, Pinhas and colleagues (2014) asked participants to classify ‘+’ and ‘-’ signs with right-hand or left-hand response keys. They found that ‘+’ signs were responded faster with the right key, whereas ‘-’ signs were responded faster with the left key. Unlike the SNARC effect, this “operation sign spatial association” (OSSA) effect is more easily explained by positing long-term associations between space and numbers than by working-memory effects. For instance, if numbers are organized from left to right along a MNL, the OSSA may originate from the experience of always activating results that are larger than the operands when adding and results that are smaller than the operands when subtracting. It is also possible that adding or subtracting numbers resemble rightward and leftward movements along the MNL, such that ‘+’ and ‘-’ signs themselves might become progressively associated with a rightward or leftward shift of attention (McCrink *et al.* 2007; Knops, Viarouge *et al.* 2009b; Masson and Pesenti 2014, 2016; Masson *et al.* 2016; Mathieu *et al.* 2016). The existence of such movements along the MNL during arithmetic calculation is suggested by recent findings from Knops, Thirion, Hubbard, Michel, and Dehaene (2009a). The authors measured fMRI activity of adult participants while they (i) performed saccades towards targets presented in the left and right visual field and (ii) calculated the results of multi-digit subtraction and addition problems. The study not only revealed that brain activity in the posterior superior parietal lobule (PSPL) could distinguish between leftward and rightward saccades, but also that this classification could be used to distinguish between subtraction and addition. In other words, patterns of brain activity for eye movements resemble patterns of brain activity for arithmetic calculation in the PSPL, in line with the idea that subtracting or adding quantities is somewhat similar to moving to the left or right of a MNL. The perception of an arithmetic sign might thus prime such movements, giving rise to the OSSA (note that this hypothesis remains speculative because Knops *et al.* did not use actual arithmetic signs in their study, but rather the letters A and S for 'adding' and 'subtracting').

Regardless of the factor at the source of the spatial intuitions underlying the OSSA, there are reasons to posit that such intuitions may critically contribute to mental arithmetic. This is suggested by a study showing that the mere presentation of a '+' sign 150 ms before a single-digit addition problem facilitates problem-solving, an effect that can be termed *operator-priming* (Roussel *et al.* 2002; Fayol and Thevenot 2012). Interestingly, this *operator-priming effect* appears to be specific to '+' (as well as '-') signs because it is not observed for '×' signs and multiplication problems. This suggests that perceiving multiplication signs might not elicit any type of intuition that contributes to problem-solving. This may be due to the fact that associations between operands and multiplicative answers are explicitly learned by rote in school, such that the mere presentation of a '×' sign may not by itself evoke a MNL. Together, the OSSA and the *operator-priming effect* thus suggest that some arithmetic operators (e.g., '+') might be associated with stronger spatial intuitions than others ('×'), and that these intuitions might have an important role in mental arithmetic.

Here we set out to test this hypothesis using fMRI. Specifically, we tested (i) whether the mere perception of a '+' sign triggers activity in brain regions that are associated with the orienting of spatial attention (to a greater extent than '×' signs), and (ii) whether this activity contributes to the *operator-priming effect*. In the scanner, adult participants were first asked to perform an overt spatial attention task in which they moved their eyes towards horizontal targets. This task, adapted from Knops *et al.* (2009a), allowed us to precisely localize the brain regions involved in the orienting of spatial attention. Within these brain regions, we then measured brain activity while participants were presented with trials in which a ‘+’ sign was displayed without any operands (hereafter addition *sign-only* trials) (see **Fig. 1**). Tight control for the perception of that ‘+’ sign was provided by trials in which a ‘×’ sign was displayed without any operands (hereafter multiplication *sign-only* trials). Both ‘+’ and ‘×’ signs have similar conceptual and perceptual features. However, ‘×’ signs do not elicit any *operator-priming effect* and therefore should not be associated with any automatic processing (see above). To provide a context for the perception of these signs and disguise the goal of the fMRI experiment, *sign-only* trials were also interspersed with filler trials in which the ‘+’ or ‘×’ was immediately followed by operands (hereafter *sign-plus-operand* trials), prompting subjects to solve the arithmetic problem. Finally, outside of the scanner, the size of the *operator-priming effect* was measured for each participant using a version of the operator-priming task employed by Fayol and Thevenot (2012).

Materials and Methods

Participants

Twenty-nine native French-speaking volunteers with no prior history of neurological disease, mental disorders or attention deficits participated in the study. Following the selection criteria of Fayol and Thevenot (2012), subjects were included in the study only if they scored above 70 on the addition and subtraction-multiplication subtests of the French Kit to ensure that they were all proficient in arithmetic (French *et al.* 1963). The French Kit is a non-standardized test of arithmetic abilities that is widely used in behavioral research (Campbell and Xue 2001; Imbo *et al.* 2007; Fayol and Thevenot 2012). Each of its subtests (i.e., addition and subtraction-multiplication) consists of two pages of 60 problems. The addition subtest involves addition problems with three numbers of either one or two digits (e.g., 63 + 99 + 5). The subtraction-multiplication subtest involves subtraction problems with two-digit operands (e.g., 51 - 28) and multiplication problems with both two-digit and one-digit operands (e.g., 73 × 8). All participants were given 2 min per page and were instructed to solve the problems as fast and accurately as possible. The number of problems correctly solved on each of the addition and subtraction–multiplication tests were summed up to yield a total arithmetic score. Scores ranged from 70 to 144 (mean = 92) across subjects. All subjects included in the study were also right-handed, as measured by the Edinburgh Handedness Inventory. Data from 2 subjects were excluded because of excessive head-movement in the scanner (i.e., greater than 3mm, $n = 1$) and poor whole-brain coverage (i.e. insufficient coverage of the temporal and the occipital lobes, $n = 1$). Therefore, the final sample consisted of 27 participants (13 males) aged from 18 to 27 years (mean age = 22.7 years). All participants provided written informed consent to participate in the study, which was approved by the local ethics committee (CPP Sud-Est II, Lyon). Across the two sessions, the total duration of the experiment was about three hours. Subjects were paid 80 € for their participation in the study.

Psychometric assessment

Because the French kit is not a standardized test, participants' arithmetic skill with respect to the general population was further assessed with the Math Fluency subtest of the Woodcock-Johnson III Tests of Achievement (Woodcock *et al.* 2001). The Math Fluency is a standardized test in which participants solve simple addition, subtraction and multiplication problems within a 3-min time limit. The test consists of two pages of 80 problems involving operands from 0 to 10. Addition, subtraction and multiplication problems are intermixed, but multiplication problems are only introduced after Item 60. Standardized scores ranged from 100 to 128 (mean = 111), indicating that participants had average to high arithmetic skills. Scores on the French kit and on the Math Fluency were highly correlated across subjects ($r = 0.56$, $p = 0.0025$, $BF_{10} = 18.15$; see below for details on Bayes Factor).

Behavioral session

During a first behavioral session, each participant performed a version of the operator-priming task used by Fayol and Thevenot (2012) and Roussel *et al.*(2002). Stimuli were single-digit addition and multiplication problems. Problems were composed of pairs of operand between 2 and 9, presented in both commutative orders (e.g., 7+2 and 2+7). Tie problems (e.g., 2+2) were excluded. Thus, there were 56 addition problems and 56 multiplication problems.

In each trial, a problem was presented in its entirety, with the two operands, the operator sign (+ or ×), the equal sign and the answer (**Fig. 4a**). The answer could be valid or invalid. Invalid answers were obtained by adding or subtracting 1 to or from the valid answer (see **Table S2** for a full list of problems and answers). For both operations, the arithmetic sign was presented either 150 ms before (negative Stimulus Onset Asynchrony or SOA), or at the same time as the operands (null SOA). Therefore, there were 448 trials [i.e., 56 pairs of operands × 2 operations (addition/multiplication) × 2 SOA (negative/null) × 2 answers (valid/invalid)]. Trials were distributed across 4 successive blocks of 112 trials each. In each block, trials were pseudorandomly ordered so that no more than three problems of the same type could appear consecutively. The order of blocks was counter-balanced between subjects. The experiment started with 8 practice trials. These practice trials included tie problems (e.g., 2 + 2), problems involving 0 (e.g., 5 × 0) and problems involving 1 (e.g., 3 + 1). The whole behavioral session lasted about 30 minutes.

Stimulus presentation was controlled by Presentation software (Neurobehavioral Systems, Albany, CA). Problems were displayed in white Arial 60-point font on a black background (single-digit operands size: 1.5°; arithmetic sign size: 1°). Problems were presented left-to-right (e.g., 3 × 4 = 12) with the center of the screen corresponding to the arithmetic operator. All trials started with the presentation of a white central fixation dot for 1,500 ms, immediately followed by a red central fixation dot for 1,000 ms signaling that the problem was about to be presented. The content of the next screen varied as a function of the SOA condition. In the negative SOA condition, the arithmetic sign (+ or ×) appeared alone for 150 ms and was immediately followed by the operands, the operator, the equal sign and the answer (**Fig. 4a**). In the null SOA condition, the whole problem appeared directly after the red central fixation dot (**Fig. 4a**). The subjects had to indicate whether the answer was valid or invalid as quickly as possible by pressing one of two keys on the computer keyboard. Participants had a maximum of 4,000 ms to give their response. Response time (RT) corresponded to the time between the presentation of the whole problem and the button press.

fMRI session

Ten days on average after the behavioral session (and no longer than 2 months after), subjects participated in the fMRI session. Participants performed two different tasks in the scanner: an overt spatial attention task and an arithmetic task (**Fig. 1**). Participants practiced both tasks before entering into the scanner. Visual stimuli were generated using Presentation software and projected onto a screen at the front of the scanner that was viewed by the participants through a mirror attached to the head coil.

The overt spatial attention task was adapted from Knops *et al.* (2009a) and consisted in alternating blocks of saccades and fixation. During saccade blocks (9 blocks), participants were asked to make saccades towards several successive target dots. Each saccade block contained 16 target dots (width and height, 0.2° visual angle) that appeared at random positions with an eccentricity of 3°, 3.5°, 4°, 4.5°, 5° or 5.5° in the left or right visual field (up to ±0.42° jitter in y) for an average of 800 ms (with a jitter of ±200 ms). During fixation blocks (9 blocks), participants were asked to maintain fixation on a central dot for 12,800 ms. Block order was counterbalanced across participants. The total duration of the task was 4 min.

In the arithmetic task, participants were presented with *sign-only* and *sign-plus-operands* versions of addition and multiplication trials. At the beginning of each trial, a sign was presented at the center of the screen for 150 ms. The sign was '+' in addition trials and '×' in multiplication trials (**Fig. 1**). In *sign-only* trials (30 trials each), the trial ended with the presentation of the sign and was simply followed by the inter-trial period of fixation (see below). This allowed us to isolate neural activity due to the presentation of the sign alone. In *sign-plus-operands* addition and multiplication trials (50 trials each), the '+' or '×' sign was immediately followed by a single-digit addition or multiplication problem (respectively) presented with an answer. Those trials were used as fillers and required participants to evaluate whether the answer of the problem was true or false. Problems were constructed using the exact same criteria as in the behavioral session (see above and see **Table S2** for a full list of problems and answers). The answer was valid in half of the trials (e.g., 4 + 3 = 7; 4 × 3 = 12) and invalid in the other half (e.g., 4 + 3 = 6; 4 × 3 = 13). The baseline consisted of trials in which an abstract '◊' sign replaced the '+' or '×' sign. There were 30 baseline *sign-only* trials (in which the '◊' sign was not followed by any operands) and 50 baseline *sign-plus-operands* trials (in which the '◊' sign was immediately followed by a string of three letters), prompting participants to indicate whether one of the letters presented was a B. In all *sign-plus-operands* trials, the problem remained on the screen for 4,000 ms or until the participants gave an answer. All trials were followed by a variable period of fixation ranging from 3,000 ms to 3,800 ms. A red central fixation dot appearing between trials signaled that the next trial was about to begin in 1,000 ms. As in the behavioral session, problems were displayed in white Arial font on a black background (single-digit operands size: 1.5°; arithmetic sign size: 1°). Problems were presented left-to-right (e.g., 3 × 4 = 12) with the center of the screen corresponding to the arithmetic operator. The arithmetic task was decomposed in four functional runs of about 5 minutes each. The timing and order of trial presentation within each run was optimized for estimation efficiency using optseq2 (http://surfer.nmr.mgh.harvard.edu/optseq/). Behavioral responses were recorded using an MR-compatible response device placed in each hand. In *sign-plus-operands* trials, participants responded with their right thumb if the problem was valid and with their left thumb if the problem was invalid. RT corresponded to the time between the presentation of the whole problem and the button press. No response was required for *sign-only* trials.

Behavioral analyses

RT data were logarithmically transformed to reduce skew of the RT distributions and improve the conformity of the data to the standard assumptions of parametric testing (Howell 2011). Mean RT was calculated based on valid problems that were responded correctly. Following Fayol and Thevenot (2012), mean RT during the operator-priming task was analyzed using planned comparisons generated by a within-subject ANOVA with the factors Operation (Addition, Multiplication) and SOA (Negative, Null). Standard statistics are reported for all effects, as well as Bayes factors (BF_{10}) indicating the strength of evidence for the alternative hypothesis (H1) relative to the null hypothesis

(H0) (Jeffreys 1961; Dienes 2011). Bayes factors were calculated using JASP (https://jasp-stats.org). A BF_{10} greater than 3 is typically suggestive of substantial evidence in favor of the alternative hypothesis (Jeffreys 1961; Dienes 2011).

fMRI data acquisition

Images were collected with a Philips Achieva 3T MRI scanner (Philips Medical Systems, Best, The Netherlands). The fMRI blood oxygenation level dependent (BOLD) signal was measured with a susceptibility weighted single-shot echo planar imaging (EPI) sequence. Imaging parameters were as follows: time repetition (TR) = 2,200 ms, time echo (TE) = 30 ms, flip angle = 90°, matrix size = 128 × 128, field of view = 220 mm, slice thickness = 3.5 mm (0.5 mm gap), number of slices = 25, voxel size = $2 \times 2 \times 4$ mm^3. About 118 volumes (SD = 2) were obtained during each run of the arithmetic task and 119 volumes were obtained during the spatial attention task. A high-resolution T1-weighted whole-brain anatomical volume was also collected for each participant. Parameters were as follows: TR= 6.59 ms, TE= 2.96 ms, flip angle = 8°, matrix size = 512 × 512, field of view = 240 mm, slice thickness = 1 mm, number of slices = 188.

fMRI data preprocessing

Data analysis was performed using the Statistical Parametric Mapping software (SPM12; Functional Imaging Laboratory, UCL, London, UK, http://www.fil.ion.ucl.ac.uk/spm). Each fMRI run started with five dummy scans to allow for magnetization equilibration effects. The functional images were corrected for slice acquisition delays and spatially realigned to the first image of the first run to correct for head-movements. The realigned functional images and the anatomical scans for each subject were then normalized into the standard Montreal Neurological Institute (MNI) space. This was done in two steps. First, after co-registration with the functional data, the structural image was segmented into gray matter, white matter and cerebrospinal fluid by using a unified segmentation algorithm (Ashburner and Friston 2005). Second, the functional data were normalized to the MNI space by using the normalization parameters estimated during unified segmentation (normalized voxel size, 2 × 2 × 4 mm^3). Finally, the functional images were spatially smoothed with a Gaussian filter equal to twice the voxel size (4 × 4 × 8 mm^3 full width at half-maximum).

fMRI data processing

Saccades and fixation blocks in the overt spatial attention task were modeled as epochs and the hemodynamic response function (HRF) was convolved with a boxcar function corresponding to the epoch duration (about 12.8s). Six regressors of no interest reflecting head motion were also included in the model, and the time series data from each run were high-pass filtered (1/128 Hz). Finally, serial correlations were corrected using an autoregressive AR (1) model. For each subject, the fMRI response for saccades blocks was compared to the fMRI response for fixation blocks. These subject-specific contrasts were subsequently entered into a random effect (RFX) one-sample t-test across subjects. A whole-brain family-wise error (FWE) corrected cluster-level threshold of $p < 0.05$ was applied to that contrast map (voxel height threshold: $p < 0.005$). This cluster-level threshold was calculated by (i) estimating the group smoothness using the group residuals from the general linear model and (ii) using this information as input in whole-brain Monte Carlo simulations (10,000 iterations calculated with the 3dClustSim program - Compile date = Jul 8 2016, http://afni.nimh.nih.gov/afni/).

Following prior fMRI studies involving fast-rate attention cueing paradigms with cue-only trials (Weissman *et al.* 2005; Orr and Weissman 2009; Griffis *et al.* 2015), *sign-only* trials of the arithmetic tasks were analyzed using a finite impulse response (FIR) model. Therefore, no assumption was made regarding the shape of the fMRI response for addition ('+') and multiplication ('×') *sign-only* trials, which was estimated with respect to baseline *sign-only* trials ('◊').We modeled 8 time points with an interval of 2.2 s (corresponding to one TR) ranging from the onset of the sign to 17.6 s after the sign. The magnitude of the fMRI response for each type of *sign-only* trial was calculated by subtracting activity at the onset of the sign (i.e., 1st bin, or 0 s after the onset) from the peak activity (i.e., 3rd bin, or ~6.6 s after the onset). Six regressors of no interest reflecting head motion were also included in the model. The time series data from each run were high-pass filtered (1/128 Hz), and serial correlations were corrected using an autoregressive AR (1) model. To ensure that our model was adapted to capture the BOLD response associated with our stimuli, we plotted the hemodynamic time-series in all activated clusters (see below and **Fig. 2b**). For each subject, the magnitude of the fMRI responses for addition *sign-only* trials was contrasted against the magnitude of the fMRI responses for multiplication *sign-only* trials. Subject-specific contrasts were then submitted to a RFX one-sample t-test that was restricted to the voxels identified in the contrast of saccades versus fixation of the spatial orienting task. Using 3dClustSim and the procedure described above, a FWE corrected cluster-level threshold of $p < 0.05$ was applied to that contrast map (voxel height threshold: $p < 0.005$). All coordinates are reported in MNI space and cytoarchitectonic areas are identified by referencing to the Jüelich atlas from the SPM Anatomy toolbox (Eickhoff *et al.* 2005). Complementary analyses of filler *sign-plus-operand* trials are described in **Supplementary Data**.

Region of interests (ROIs) analyses

Brain activity in clusters showing a greater response to addition than multiplication *sign-only* trials within the brain network for spatial orienting was extracted using the SPM toolbox Marsbar (http://marsbar.sourceforge.net/). Regions of Interest (ROIs) included all significant voxels within a 6-mm radius of each coordinate of interest, so as to ensure that plots would represent activity around the peak of each cluster. For each participant and ROI, we calculated the average response for (i) addition *sign-only* trials (versus baseline) and (ii) multiplication *sign-only* trials (versus baseline). Hemodynamic time-series were plotted for visualization purpose.

Two analyses were performed with the ROIs. First, we assessed the functional coupling between ROIs during addition and multiplication *sign-only* trials (versus baseline) by performing across-subject correlations between contrast estimates in each pair of ROI. This was done separately for addition *sign-only* trials and multiplication *sign-only* trials, yielding a $n \times n-1$ correlation matrix (where n is the number of ROIs) in each case. *P* values were corrected for multiple comparisons using the Bonferroni procedure. Second, we correlated the contrast estimates associated with addition *sign-only* trials (versus baseline) to the operator-priming effect calculated in the behavioral session for addition problems in each ROI. *P* values were corrected for multiple comparisons using the Bonferroni procedure. Bayes factor are reported for each t-test and correlation.

Control experiment

In a control experiment outside of the scanner, 15 participants (mean age = 24.33 years, 6 males) performed a version of the fMRI task while their eye movements were continuously measured using a Tobii X120 eye-tracker (temporal resolution: 60 Hz, spatial resolution: 0.5 degree of visual angle). This experiment was composed of *sign-only* trials (15 addition, 15 multiplication, 15 baseline) and *sign-plus-operands* trials (25 addition, 25 multiplication, 25 baseline), which were randomized across two separate runs. Participants were seated at 80 cm from a computer screen with their head stabilized by a chin rest and forehead rest to minimize head movements, as in the MRI scanner (operands size: 1.5°; arithmetic sign size: 1°). We measured the proportion of time spent at fixating the arithmetic sign for each *sign-only* trial. First we defined a 3° square area of interest (AOI) around the center of the screen. Second, we divided the time spent in this AOI by the total time elapsed between the onset of the sign and the end of the trial (i.e., a period of 2-s of white central fixation).

Results

'+' signs elicit responses in several brain regions underlying the orienting of spatial attention

We first identified the voxels that were involved in the orienting of spatial attention using the contrast of saccades versus fixation in the spatial attention task. This contrast was associated with activity in several regions of a dorsal fronto-parieto-occipital network, including the bilateral superior and middle frontal gyri extending to the precentral gyrus, the bilateral inferior and middle occipital gyri and the bilateral superior and inferior parietal lobules (see orange outlines in **Fig. 2a and Table 1)**. We then tested whether there were any voxels in this spatial orienting network in which the magnitude of the response to addition *sign-only* trials was greater than the magnitude of the response to multiplication *sign-only* trials. This was the case in 3 regions: the right Posterior Superior Parietal Lobule (PSPL), the right Frontal Eye Field (FEF), and the right Middle Occipital Gyrus (MOG) (see red clusters in **Fig. 2a** and **Table 2**). FMRI time courses in each of these regions (hereafter regions of interest or ROIs) are plotted in **Figure 2b** for visualization purpose. Thus, the mere presentation of a '+' sign (compared to a '×' sign) triggered activity in several brain regions that were also involved in the orienting of spatial attention.

Sign-related activity in the FEF is coupled with sign-related activity in the PSPL across subjects

Brain regions underlying spatial attention are often conceptualized as components of a functionally coherent network (Corbetta *et al.* 1998; Corbetta and Shulman 2002; Grosbras *et al.* 2005). Therefore, we investigated whether any pairs of ROIs that were more responsive to addition than multiplication *sign-only* trials were functionally coupled during addition *sign-only* trials (across subjects). Specifically, we calculated the across-subjects correlations between each pair of ROI, separately for addition *sign-only* trials and multiplication *sign-only* trials. All p values were corrected for multiple comparisons (see **Methods**). For addition *sign-only* trials, we found a significant correlation between the FEF and the PSPL ($r= 0.57$, $p = 0.012$) (see **Fig. 3a**). No such correlation was found for multiplication *sign-only* trials ($r= 0.13$, $p = 1$; see **Fig. 3b**). Bayes Factor analysis indicated substantial evidence for a coupling between the FEF and PSPL during addition *sign-only* trials ($BF_{10} = 20.97$), but no evidence for such a coupling during multiplication *sign-only* trials ($BF_{10} = 0.29$). Therefore, across subjects, the FEF and PSPL were functionally coupled with each other in addition but not multiplication *sign-only* trials.

Responses to '+' signs in the FEF relate to the operator-priming effect

We then asked whether inter-individual variability in the degree to which ROIs responded to the '+' sign was related to inter-individual variability in the size of the *operator-priming effect* (i.e., a facilitation of addition problem-solving when the operator is presented 150 ms before the problem). To this aim, we asked all participants to perform a version of the operator-priming task (Fayol and Thevenot 2012) outside of the scanner (see **Methods** and **Fig. 4a**). First, we sought to replicate the results of Fayol and Thevenot (2012), who obtained a priming effect for addition but not multiplication signs. In line with their results, planned comparisons confirmed that addition problems were solved faster when the operator was presented 150 ms before the problem (negative SOA trials) than when it was presented at the same time (null SOA trials) (968 ms vs 988 ms; $F(1, 26) = 9.02$, $p = 0.006$), whereas no difference was observed for multiplication problems (910 ms vs 920 ms; $F(1, 26) = 1.50$, $p = 0.23$). Bayes Factor analysis indicated substantial evidence for an operator-priming effect with addition problems ($BF_{10} = 7.37$), but no evidence for an operator-priming effect with multiplication problems ($BF_{10} = 0.40$). Second, for each ROI, we calculated the inter-individual correlation between the size of the *operator-priming effect* for addition problems and the magnitude of the fMRI response to addition *sign-only* trials. We found a significant correlation in the FEF ($r=0.53$, $p = 0.004$), surviving Bonferroni correction for multiple comparisons across all 3 ROIs ($p_{\mathrm{corr}} = 0.024$). Bayes Factor analysis indicated substantial evidence for this correlation ($BF_{10} = 11.08$). In other words, subjects who show greater responses to '+' signs in the FEF are those who show larger operator-priming effects with addition problems (see **Fig. 4b**). No such correlation was found between the size of the *operator-priming effect* for multiplication problems and the magnitude of the fMRI response to addition *sign-only* trials in the FEF ($r=0.06$, $p = 0.76$, $p_{\mathrm{corr}} = 1$; see **Fig. 4c**). Bayes Factor analysis also indicated no evidence for such a correlation ($BF_{10} = 0.25$). Finally, there was no significant (and anecdotal evidence for a) correlation between the operator-priming effect for addition problems and the fMRI response to multiplication *sign-only* trials in any ROIs (all rs < 0.33, all ps > 0.60, all $BF_{10} < 0.87$).

Control analyses

Our main analyses revealed differences in activity between the perception of a '+' sign and that of a '×' sign in the brain system for spatial orienting. However, it is important to ensure that this finding is not driven by any confounding factors. First, across all subjects, multiplication *sign-plus-operand* trials were solved faster than addition *sign-plus-operand* trials (1,009 ms versus 1,075 ms; t_{26}

$= 3.27$, $p = 0.003$; $BF_{10} = 12.91$). Therefore, greater overall difficulty for solving addition problems (as compared to solving multiplication problems) might have led participants to engage more attentional resources when perceiving a '+' sign in comparison to a '×' sign, explaining differences in activity between the signs. To discard this hypothesis, we performed an additional analysis in which we included the mean RT difference between addition and multiplication *sign-plus-operands* trials as nuisance covariate. This analysis revealed that, over and above differences in RT between the two operations, the exact set of brain regions (FEF, PSPL and MOG) that were activated in our main analyses was still significantly more activated for '+' than '×' signs. Thus, differences in activity between addition and multiplication *sign-only* trials do not appear to have been driven by differences in behavioral performance between addition and multiplication *sign-plus-operands* trials.

Second, even though participants were explicitly told to keep fixation throughout the entire experiment, it could be argued that differences in activity between addition and multiplication *sign-only* trials might have been driven by differences in the rate of eye movements associated with the perception of '+' and '×' signs (i.e., there could have been more eye movement in addition than multiplication *sign-only* trials). To test whether eye movements differed between those trials, we asked fifteen new participants to perform a version of the fMRI task outside of the scanner while their eye movements were recorded on-line (see **Methods**). We did not find any difference in the proportion of time spent at fixating the arithmetic sign between addition and multiplication *sign-only* trials ($t_{14} = 0.07$, $p = 0.95$, $BF_{10} = 0.26$), indicating that participants did not make more eye movements in addition than multiplication *sign-only* trials. Therefore, greater activity in the FEF, PSPL, and MOG in addition than multiplication *sign-only* trials is not due to more eye movements when perceiving '+' than '×' signs.

Discussion

It has long been claimed that mathematical symbols may rely on spatial representations (Fischer and Shaki 2014). Much evidence for that claim comes from behavioral studies demonstrating interactions between space and the processing of Arabic digits (Dehaene *et al.* 1993; Fischer *et al.* 2003). However, recent studies have challenged this idea by showing that such interactions could be an artifact of the organization of information in working-memory during task execution (van Dijck and Fias 2011; van Dijck *et al.* 2013). Here we used fMRI to test whether the brain mechanisms for space contribute to the processing of fundamental arithmetic symbols, i.e., operation signs, even when these signs are not associated with digits. We show that the mere perception of a '+' sign (compared to a '×' sign) triggers activity in several brain regions that also underlie the orienting of spatial attention. We further show that such activity contributes to the operator-priming effect, whereby addition problem-solving is facilitated by the preview of a '+' sign. Our findings demonstrate that at least some arithmetic symbols evoke spatial intuitions in adults, and that such intuitions might play a role in arithmetic calculation.

The mere perception of a '+' sign recruits several brain regions that are involved in the orienting of spatial attention

Our main finding is that the mere presentation of a '+' sign elicits enhanced fMRI activity in 3 regions that support the orienting of spatial attention (as identified by an independent overt spatial attention task): the PSPL, the FEF and the MOG. Because the PSPL and the FEF were found to be coupled with each other during the processing of a '+' sign across subjects, both of these regions are likely components of a functionally coherent network. This network is often thought to support the orientation of covert and overt spatial attention (Corbetta *et al.* 1998; Corbetta and Shulman 2002; Grosbras *et al.* 2005). For example, the FEF is a key region for the planning and execution of eye movements (Grosbras *et al.* 2005). Both the FEF and the PSPL have also been shown to be associated with covert shifts of attention (i.e., rapidly orienting attention without moving the eyes) and the updating of spatial information (Simon *et al.* 2002; Grosbras *et al.* 2005). In the present study, participants were explicitly told to keep fixation in the scanner and we did not find additional eye movements during the perception of '+' than '×' signs in a control eye-tracking experiment (see **Results**). Thus, the recruitment of such a network in response to a '+' sign suggests that the perception of this sign may automatically deploy covert spatial attention.

It is interesting to speculate about the potential explanations for such a deployment. One possibility is that, with experience, educated adults might have associated '+' signs with the activation of a result that is necessarily larger than any of the operands (e.g., a form of plausibility check that cannot be used for multiplication problems, whose results can be smaller than or equal to an operand) (Marghetis *et al.* 2014). The rightward associations that large numbers have might thus cause automatic shifts of attention to the right side of space in adults. Another possibility is that calculating the result of an addition problem *per se* might involve moving rightward along the MNL, thereby increasing number size (McCrink *et al.* 2007). This is in keeping with the proposal that spatial updating mechanisms in the FEF and PSPL may be co-opted for arithmetic calculation (Knops *et al.* 2009a). For example, it has been shown that the pattern of activation in the PSPL during addition problem-solving is correlated to the pattern of activation during right saccadic movements, suggesting that subjects use the same neural mechanisms when moving their eyes to the right and adding numbers (Knops *et al.* 2009a). It is possible that these movements (which would be largely absent for multiplication problems because these are mostly learned by rote) might have been progressively associated with the addition sign itself with practice, and be triggered by the mere presentation of that sign in adults.

Spatial intuitions are relevant for simple arithmetic

Our results further indicate that activity related to a '+' sign in the spatial orienting network may be functionally relevant for simple addition problem-solving. That is, inter-individual differences of activity in the FEF were related to inter-individual differences in the size of the *operator-priming* *effect* measured outside of the scanner. Thus, participants for whom the FEF responded the most to a '+' sign were the participants who benefited the most for having a '+' sign presented 150 ms before the operands. This might be because individuals who deploy their attention the most upon viewing a '+' sign may the most prepared for a rightward shift of attention that is relevant for either intuitively checking the plausibility of the result (which should be larger than any of the operands) (Marghetis *et al.* 2014) or calculating that results by moving to the right of the MNL (Mathieu *et al.* 2016). Although future studies might disentangle between these possibilities, this brain-behavior correlation demonstrates that a selective deployment of spatial attention in response to the arithmetic operator contributes to the *operator-priming effect*.

Our findings are also generally consistent with several recent studies showing interactions between arithmetic processing and spatial attention (Fischer and Shaki 2014; Masson and Pesenti 2014, 2016; Mathieu *et al.* 2016). For example, we recently found evidence for rapid shifts of spatial attention during simple problem-solving in adults. Specifically, we asked adults to solve single-digit addition and subtraction problems while each constituent was presented sequentially (Mathieu *et al.* 2016). Whereas the first operand and the arithmetic sign were presented at the center of the screen, the second operand was presented either on the left or the right visual field. Participants were faster to solve an addition problem when the second operand was presented in the right visual field, whereas they were faster to solve a subtraction problem when the second operand was presented in the left visual field. Such a result, along with several other consistent reports (Fischer and Shaki 2014; Masson and Pesenti 2014, 2016), indicates that even very simple arithmetic problem-solving in adults may be associated with spatial intuitions.

It might be argued that the claim that spatial intuitions contribute to simple arithmetic is at odds with the consensual view that results of simple arithmetic problems (including addition) are typically not calculated but simply retrieved from memory in adults (Campbell and Xue 2001). We see at least two possible explanations for such an apparent inconsistency. First, as proposed by Marghetis and colleagues (2014), it is possible that spatial intuitions complement memory-based strategies by providing 'an intuitive check on rote or algorithmic calculation, supplying a rough sense of expected magnitude against which the algorithmically derived solution can be compared' (p. 1,591). According to this view, the fact that arithmetic is associated with spatial intuitions does not negate the fact that simple problems may still be solved by retrieving results from long-term memory. Rather, it may provide a mechanism for limiting errors (e.g., when the result of an addition is smaller than the operands). Second, it is also possible that memory-based strategies are not as prevalent as typically thought, and in several cases supplanted by procedures that may be spatial in nature (Baroody 1983; Roussel *et al.* 2002; Fayol and Thevenot 2012; Barrouillet and Thevenot 2013; Mathieu *et al.* 2016; Thevenot *et al.* 2016; Uittenhove *et al.* 2016). For example, although adults typically report retrieving results of most frequent addition problems, the time it takes to solve these problems is not constant (as would be predicted by a systematic use of retrieval). Rather, it increases linearly with the distance between the original operand and the sum (e.g., adults take 20ms longer to solve 1 + 3 than 1 + 2 or 1 + 4 than 1 + 3) (Groen and Parkman 1972; Barrouillet and Thevenot 2013; Uittenhove *et al.* 2016). Therefore, it is possible that adults might unconsciously solve these problems by rapidly moving to the right of a MNL (solving time would then depend on the distance between the original operand and the target sum to be reached) (Barrouillet and Thevenot 2013). Future studies are needed to test between these possibilities.

The '×' sign as a control condition

In the present study, brain activity elicited by '+' signs was compared to that elicited by '×' signs. The '×' sign was chosen as a control condition because (i) it is not associated with any automatic processing as demonstrated by a lack of *operator-priming effect* in Fayol and Thevenot (2012) and in the present study, (ii) it is as familiar as a '+' sign, and (iii) it is perceptually very similar to a '+' sign. Thus, we reasoned that such signs might act as excellent controls for the purpose of the present study. However, it could be argued that these symbols may differ in terms of mathematical or non-mathematical meanings. This, rather than the idea that addition signs evoke spatial intuitions, may have driven the observed differences. For instance, although the '+' sign is relatively unambiguously associated to the concept of addition, the '×' sign may be used to describe the concept of multiplication but also the alphabetic letter 'x' or the concept of 'unknown' in algebra. We think that it is very unlikely that participants may have interpreted the '×' sign with such meanings in the present study for two reasons. First, our experiment was clearly not ambiguous concerning the potential meaning of the signs that were presented on the screen. Participants were explicitly told at the beginning that they will be presented with simple arithmetic problems along with arithmetic signs during the task. *Sign-only* trials were also intermixed with *sign-plus-operands* trials that clearly and unambiguously reinforced a context of addition and multiplication problem-solving. Second, no participant reported having interpreted the '×' sign as a letter or anything else than a multiplication sign after the fMRI session. This was supported by an exploratory whole-brain analysis in which we did not find any more activity for '×' than '+' signs in brain regions that are involved in the visual recognition of letters such as the fusiform gyrus (McCandliss *et al.* 2003). Therefore, we believe that the perception of a '×' sign is an excellent control for the perception of a '+' sign in the context of the present study.

Relevance of the current findings to the debate about the link between mathematical symbols and space

Overall, our results are in keeping with a long line of studies showing interactions between space and the processing of mathematical symbols (Fischer and Shaki 2014). However, most prior studies have demonstrated such interactions with Arabic digits, for example in the context of the SNARC effect (Dehaene *et al.* 1993; Fischer *et al.* 2003). It has been recently argued, however, that the SNARC effect may not provide definitive evidence that mathematical symbols rely on spatial representations. This is because the effect may be related to the spatial coding of numbers in working-memory during task execution rather than to a long-term organization of numbers along a MNL (van Dijck and Fias 2011; van Dijck *et al.* 2013). Our findings are relevant to this debate because, together with a previous behavioral study also showing associations between space and arithmetic signs (Pinhas *et al.* 2014), they demonstrate that associations between space and mathematical symbols can occur even in the absence of numerical information. This is more readily explained by positing that numbers may indeed be organized from left to right along a MNL (such that arithmetic signs might prime shifts of attention along that MNL) than by a working-memory account. Of course, this does not mean in any way that the SNARC effect cannot be accounted for by a purely working-memory account. Rather, our findings may be more consistent with the proposal that "long-term memory associations between number and space exist independent of temporary associations or ordinal positions in working memory" (Huber *et al.*, p. 12).

Conclusion

To summarize, the present study shows that the simple perception of a '+' sign in adults triggers a specific response in several brain regions that are also involved in the orienting of spatial attention. We further demonstrate that this sign-related activity is linked to the *operator-priming effect*, whereby the preview of a '+' sign before a problem facilitates problem-solving. Thus, our findings not only show that some arithmetic signs evoke spatial intuitions in educated adults, but also that these intuitions relate to arithmetic performance. More generally, our study lends support for the idea that mathematical symbols inherently evoke spatial representations. It is also consistent with the growing body of research showing associations between space and the processing of symbolic and non-symbolic magnitudes in a variety of tasks (Fischer and Shaki, 2014). It has been recently suggested that such association may have an ancient evolutionary origin (Rugani *et al.* 2015; Adachi, 2014) and might be intimately related to the ANS (Brannon and Merritt, 2011). Future studies may thus explore to what extent these associations are related to measures of the ANS acuity in adults, and how they emerge over development and learning in children.

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Tables

Table 1. Brain regions that were activated during the overt spatial attention task.

Anatomical location	*Cluster size in mm^3 (number of voxels)*	*MNI coordinates*			*Z-score*
		X	*Y*	*Z*	
L. Middle Occipital Gyrus	5392 (337)	42	-64	6	6.42
L. Calcarine (17)	30800 (1925)	-10	-76	6	6.23
R. Calcarine (17)	-	14	-80	10	5.89
L. Lingual (17)	-	-12	-66	2	5.35
R. Lingual (18)	-	10	-70	2	5.34
R. Superior Occipital Gyrus (18)	-	22	-92	10	4.74
R. Middle Occipital Gyrus	-	28	-70	26	4.60
L. Frontal Eye Field (6)	18784 (1174)	-24	-6	46	6.21
L. Precentral Gyrus (6)	-	-44	-4	50	5.86
L. Supplementary Motor Area (6)	-	-6	0	62	4.90
R. Supplementary Motor Area (6)	-	4	6	62	3.78
R. Precentral Gyrus (6)	11088 (693)	56	8	42	5.71
R. Frontal Eye Field (6)	-	26	-6	50	4.91
L. Posterior Superior Parietal Lobule (7A)	14032 (877)	-24	-58	62	5.23
L. Inferior Parietal Lobule (7PC)	-	-34	-46	54	5.09
L. Precuneus (7A)	-	-14	-66	58	4.77
R. Superior Temporal Gyrus (PF)	3568 (223)	66	-36	22	5.22
R. Posterior Superior Parietal Lobule (hIP3)	7456 (466)	28	-58	54	4.65
R. Inferior Parietal Lobule (7PC)	-	32	-46	50	3.56
R. Precuneus (7P)	-	14	-70	62	3.20
L. Putamen	1888 (118)	-22	6	6	4.40

L. = left; R. = right; MNI = Montreal Neurological Institute; Cytoarchitectonic areas were found with SPM Anatomy toolbox (Eickhoff et al., 2005) and are shown in parenthesis.

Table 2. Brain regions involved in the orienting of spatial attention that were more activated for addition than multiplication *sign-only* trials.

Anatomical location	*Cluster size in mm³ (number of voxels)*	*MNI coordinates*			*Z-score*
		X	*Y*	*Z*	
R. Frontal Eye Field (6)	512 (32)	26	-4	50	4.03
R. Middle Occipital Gyrus	704 (44)	34	-84	26	3.52
R. Posterior Superior Parietal Lobule (7A)	624 (39)	24	-58	62	3.48

L. = left; R. = right; MNI = Montreal Neurological Institute; Cytoarchitectonic areas were found with SPM Anatomy toolbox (Eickhoff et al., 2005) and are shown in parenthesis.

Figure Captions

Figure 1. fMRI experimental design

In the scanner, participants (*n*=27) were presented with *sign-only* and *sign-plus-operands* versions of addition and multiplication trials. At the beginning of each trial, a sign was presented at the center of the screen for 150 ms. The sign was '+' in addition trials and '×' in multiplication trials. In *sign-only* trials (left), the trial ended with the presentation of the sign and was simply followed by the inter-trial period of fixation. In *sign-plus-operands* trials (right), the '+' or '×' sign was immediately followed by a single-digit addition or multiplication problem presented along with an answer. In those cases, participants were asked to evaluate whether the answer of the problem was true or false.

Figure 2. Neural activity associated with the perception of a '+' sign in the brain network for spatial attention

(a) Brain regions showing greater activation for addition than multiplication *sign-only* trials. Orange outlines delineate regions that were more activated during saccades than fixation in the overt spatial attention task. (b) FMRI time courses in each activated clusters, with respect to baseline (for visualization only). Activations are overlaid on a 3D rendering of the MNI-normalized anatomical brain. FEF, Frontal Eye Field; PSPL, Posterior Superior Parietal Lobule and MOG, Middle Occipital Gyrus.

Figure 3. Functional coupling between FEF and PSPL across subjects

Across-subject (*n*=27) correlation between the FEF and the PSPL during addition *sign-only* trials (a) and multiplication *sign-only* trials (b). *r* represents the Pearson correlation coefficient.

Figure 4. Brain-behavior correlation

(a) During the behavioral session, participants (*n*=27) were asked to evaluate the result of single-digit addition and multiplication problems. For both operations, the arithmetic sign was presented either 150 ms before (negative SOA trials), or at the same time as the operands (null SOA trials). (b) Activity in the right Frontal Eye Field (R. FEF) in response to '+' signs as a function of the *operator-priming effect* calculated in the behavioral session for addition problems (b) and multiplication problems (c). *r* represents the Pearson correlation coefficient.