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A distinct cortical network for mathematical knowledge in the human brain

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ABSTRACT

How does the brain represent and manipulate abstract mathematical concepts? Recent evidence suggests that mathematical processing relies on specific brain areas and dissociates from language. Here, we investigate this dissociation in two fMRI experiments in which professional mathematicians had to judge the truth value of mathematical and nonmathematical spoken statements. Sentences with mathematical content systematically activated bilateral intraparietal sulci and inferior temporal regions, regardless of math domain, problem difficulty, and strategy for judging truth value (memory retrieval, calculation or mental imagery). Second, classical language areas were only involved in the parsing of both nonmathematical and mathematical statements, and their activation correlated with syntactic complexity, not mathematical content. Third, the mere presence, within a sentence, of elementary logical operators such as quantifiers or negation did not suffice to activate math-responsive areas. Instead, quantifiers and negation impacted on activity in right angular gyrus and left inferior frontal gyrus, respectively. Overall, these results support the existence of a distinct, non-linguistic cortical network for mathematical knowledge in the human brain.

1. Introduction

How the human brain represents conceptual knowledge, especially in the domain of mathematics, is a long-debated issue. Brain imaging studies have associated two sets of brain areas with mathematical processing. Number processing and calculation have long been known to activate bilateral intraparietal and prefrontal areas (Dastjerdi et al., 2013; Eger, 2016) in adults, infants and even untrained monkeys (Hyde et al., 2010; Nieder and Dehaene, 2009) and more recently a second number-related activation has been observed in bilateral inferior temporal regions (Daitch et al., 2016; Park et al., 2012; Shum et al., 2013). More recently, these regions have proved to respond to algebraic manipulations in adults (Maruyama et al., 2012; Monti et al., 2012). Activations were also found in bilateral intraparietal sulci and infero-temporal regions when expert mathematicians judged the semantic truth value of mathematical statements, regardless of domain or subjective difficulty level (Amalric and Dehaene, 2016). Interestingly, even when mathematical problems were presented through language, they elicited activation outside of the areas classically described as participating in language semantics, such as the anterior temporal areas and angular gyri (Binder et al., 2009). Instead, those regions were activated by nonmathematical reflection more than by mathematics. The mental representation and manipulation of mathematical concepts thus seems to call upon a distinct set of brain areas, which we refer to using the descriptive term “math-responsive network”, distinct from the brain network for processing sentential meaning.

Such an observation is not isolated, and similar cases of dissociation between math and linguistic processing have already been reported in previous studies in various domains of cognitive sciences. For example, when adult participants were asked to evaluate whether pairs of linguistic or algebraic propositions were either algebraically equivalent or grammatically well-formed (Monti et al., 2012) algebraic equivalence recruited bilateral intraparietal sulci, whereas linguistic equivalence recruited left fronto-temporal perisylvian regions. Another example comes from neuropsychology: Dehaene and Cohen (1997) for instance, described patients with deficits in mathematical skills but preserved language skills, while Klessinger et al. (2007) and Varley et al. (2005) described patients with severe aphasia but preserved mathematical skills

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(indeed, the latter pattern is frequent in progressive degenerative diseases such as semantic dementia; see e.g. (Cappelletti et al., 2012)). Moreover, recent studies conducted in pre-verbal infants, in adults without access to education and with a reduced numerical lexicon, and in a variety of non-human animal species, have revealed a non-verbal capacity to estimate numerosity and to perform simple arithmetical operations over these quantities (Cantlon and Brannon, 2005; Gelman and Butterworth, 2005; Izard et al., 2009; Pica et al., 2004). These results suggest that number comprehension arises independently of language.

One possibility, therefore, is that the domain of mathematical concepts forms a distinct and neurally dissociable semantic subspace. In line with recent studies suggesting that concepts are organized in the brain according to semantic categories (Huth et al., 2016, 2012) such as animate versus inanimate (Caramazza and Shelton, 1998) or concrete versus abstract (Binder et al., 2005) we hypothesize that the math-responsive brain regions may provide domain-specific resources for the mental representation and manipulation of mathematical knowledge, which are not used for non-mathematical knowledge of other semantic domains such as animals, plants, food, history or geography.

This hypothesis, however, must be confronted to several potential alternatives. First, the math-responsive network observed in (Amalric and Dehaene, 2016) overlaps with a "multiple-demand system" active in various effortful domain-general problem-solving tasks (Duncan, 2010; Fedorenko et al., 2013). Could it be that solving math problems intrinsically require more attentional and cognitive resources than solving nonmath problems? Second, which factors determine whether a given problem activates the language-semantics or the math network? Is it solely the semantic content (math versus nonmath) that drives the dissociation? Or are some areas of mathematics, such as algebra, inherently linked to language processing, as might be predicted by Hauser et al.'s (2002) hypothesis that recursive structure lies at the core of both domains? Conversely, would the activation of the math-responsive network be triggered by minimal logical or numerical operators such as numbers, quantifiers or negation, even when they occur in non-mathematical sentences?

To address these issues, we performed two fMRI experiments, building upon the one proposed by Amalric and Dehaene (2016) in which a group of professional mathematicians judged, as quickly as they could, whether simple spoken mathematical and nonmathematical statements were true or false. By varying the content of the statements, we attempted to clarify the factors that drive the activation of the math-responsive network.

2. Experiment 1: simple mathematical facts

In this experiment, we examined whether the math-responsive network would respond whenever subjects judge the truth value of mathematical statements, regardless of their difficulty or content. While our previous work (Amalric and Dehaene, 2016) used complex statements of advanced mathematics, that required several seconds of careful reflection, our purpose here was to select very simple mathematical facts that could be evaluated within one or two seconds, some of which were known by rote or evoked an immediate mental image of the solution.

If our working hypothesis is correct, then all statements of mathematics, even if they are very simple and overlearned, should activate the math-responsive network, whereas equally simple non-math statements should not (Amalric and Dehaene, 2016). Alternatively, if this network forms a "multiple-demand" system that is activated whenever a task calls for the novel, effortful coordination of multiple components under attentional supervision (Duncan, 2010) then some mathematical problems may short-circuit the math-responsive network, for at least two reasons: rote learning or visual imagery.

First, it has been suggested that rote learning of mathematical expressions leads to their storage in verbal memory (Dehaene, 1992) in which case those statements would activate language-related areas rather than the math-responsive network. This hypothesis has plausibility given that some prior fMRI studies, within the domain of arithmetic, have suggested that rote arithmetical problems may rely more on verbal circuitry than novel problems that require an actual calculation. For instance (Ischebeck et al., 2006) showed that arithmetic fact retrieval (trained multiplication) recruited the left angular gyrus whereas arithmetic calculation (subtraction) elicited activation in the intraparietal sulci. Moreover (Delazer et al., 2005) found more activation in the intraparietal sulci when subjects learned to solve a complex and novel arithmetical operation using calculation strategies, while learning by drill induced more activation in the angular gyri.

A second possible factor is mental imagery. If mathematical problems readily evoke a mental image, for instance of the unit circle, that immediately brings to mind the solution of the proposed problem (e.g. $\cos(0) = 1$), then such problems may short-circuit the multiple-demand network and, instead activate visual areas.

To address these issues, experiment 1 included a diversity of mathematical statements, including simple facts that participants knew by heart (e.g. classical algebraic identities) and simple problems that could be solved by visualizing the solution on the trigonometric circle.

2.1. Methods

A group of 14 professional mathematicians, i.e. full-time researchers and/or professors in mathematics participated in this study. Participants were exposed to spoken mathematical and nonmathematical statements and were given 2.5 s to classify each of them as true or false (Fig. 1). They were asked to press a button in their right hand to respond "true" and in their left hand to respond "false". Each trial began with a beep announcing the presentation of the statement and ended with a 7-s resting period.

Five types of mathematical statements were proposed: (1) well-known facts such as classical algebraic identities (e.g. "$(a+b)^2 = a^2+b^2+2\ ab$") or trigonometric formulae ("$\cos(a+b) = \cos(a)\cos(b)-\sin(a)\sin(b)$") called rote facts in Fig. 1, (2) algebraic equations (called algebra in Fig. 1) that consisted in applications of the above identities to specific numbers and symbols (e.g. "$(z-1)^2 = z^2 - 2z + 1$"), (3) trigonometric facts that could be solved by visualizing the solution on the trigonometric circle ("$\sin(x+\pi) = -\sin(x)$"), (4) statements involving complex numbers that strongly elicited visualization of the complex plane (e.g. "the angle between i and $1 + i$ equals $\pi/4$"), or (5) statements concerning geometrical shapes ("Any equilateral triangle can be divided into two right triangles"). These statements were compared to nonmathematical facts about music, painting, literature or movies (e.g. "Pantomime relies on attitude and gesture, without speaking"; see appendix for a complete list of statements). As a low-level control, ascending or descending series of beeps were also presented to probe activation in primary auditory regions. Participants were asked to classify ascending series using the right hand and descending series using the left hand (for more details on stimuli and procedure, see general methods).

2.2. Results

2.2.1. Behavior

Performance (Fig. 2) reached $80.1 \pm 4.6\%$ correct for the math statements, and $86.3 \pm 2.4\%$ for the nonmath statements, a significant difference ($t(13) = 2.20$, $p < 0.05$). The easiest problems were the rote facts, with $90.9 \pm 2.8\%$ correct responses. $85.2 \pm 2.3\%$ of the algebraic equations and $83.3 \pm 4.4\%$ of the problems on complex number properties were correctly classified. Performance on the geometrical statements reached $81.1 \pm 2.4\%$. The trigonometric formulae were the most difficult statements, with an average performance of $59.9 \pm 3.1\%$ correct. Overall, an ANOVA with math problem type as between factor and subject as within factor revealed a significant effect of problem type ($F(4,52) = 14.3$, $p < 0.001$). This effect was mainly due to the trigonometric problems, given that an ANOVA performed on math problems excluding trigonometry did not reveal any significant effect of problem

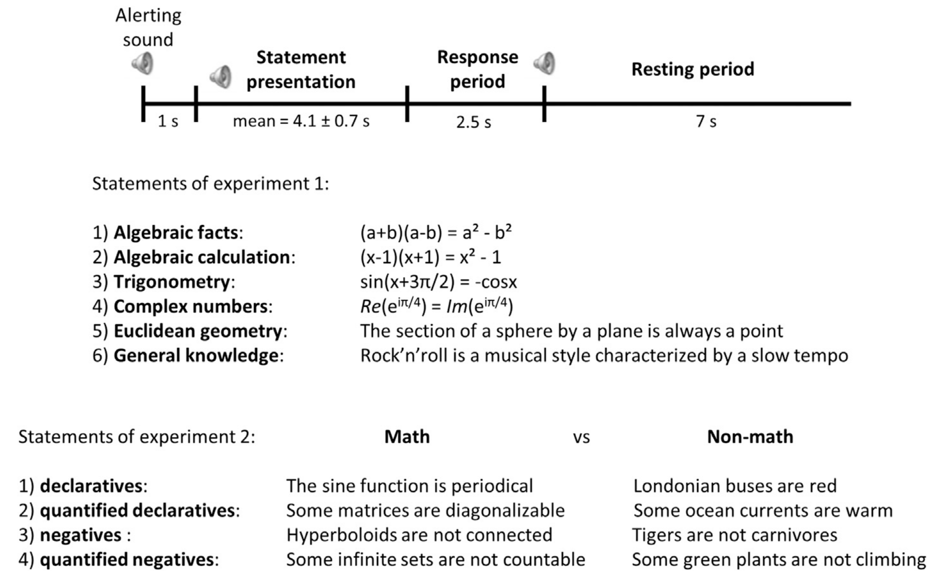

Fig. 1. Experimental paradigm. Subjects listened to a statement announced with a beep, and were asked for a speeded true/false response during a 2.5s period ending with a beep. Exemplar statements from each category are shown.

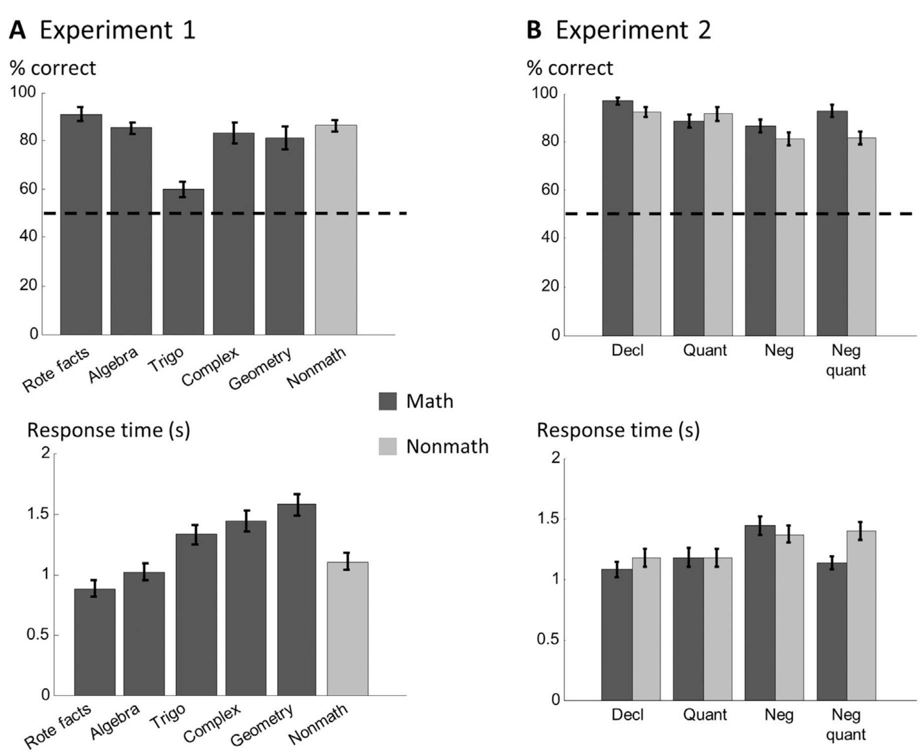

Fig. 2. Behavioral results in experiments 1 and 2. Bars show the percentage of correct responses (top) and mean response times (bottom) per category in both experiment 1 (A) and experiment 2 (B). Error bars equal one standard error of the mean. Dash lines represent the chance level. Dark gray bars stand for mathematical statements and light gray bars for nonmathematical statements.

type ($F(3,39) = 1.66$, $p = 0.19$). Once excluding the trigonometric problems, no difference was found between the math and nonmath problems ($t(13) = 0.41$, $p = 0.69$; $F(4,52) = 1.42$, $p = 0.24$).

On average, participants answered to the mathematical statements in 1.25 ± 0.1s, while the nonmathematical statements were faster, 1.11 ± 0.06s, a significant difference ($t(13) = 36$, $p < 0.001$). Analysis of response time confirmed that the rote facts were the easiest problems, taking only 0.88 ± 0.07s to respond (as measured from sentence ending). The algebraic equations took 1.02 ± 0.07s; the trigonometric problems took 1.33 ± 0.07s; the problems on complex numbers took 1.44 ± 0.08s; and the geometrical problems took 1.57 ± 0.09s. Within mathematical problems, an ANOVA revealed a significant effect of problem type on response time ($F(4,52) = 30.9$, $p < 0.001$). Rote facts were significant faster than nonmath ($t(13) = 2.92$, $p < 0.01$), and trigonometry, complex numbers and geometry were significantly slower than nonmath ($ts(13) > 3.74$, $ps < 0.002$).

2.2.2. *Dissociation between brain activations to math and nonmath reflection*

At the group level, pooling across all types of math, we first searched for activations elicited more by math than nonmath statements. The results revealed extensive activations in bilateral intraparietal sulci, bilateral inferior temporal regions, and bilateral superior, and middle frontal regions (Brodmann areas 9 and 46), at locations similar to Dehaene & Amalric (2016) (Fig. 3). These regions were systematically activated by all five types of math statements, as revealed by significant contrasts of each of them versus nonmath (Fig. S1). The main peaks of each contrast within each math-responsive region were remarkably close (Fig. S1). These findings are summarized in Fig. 3 by a conjunction analysis of each math domain versus nonmath (Fig. 3). Furthermore, plots of the average time course of activation in characteristic math-responsive regions (as independently defined in (Amalric and Dehaene, 2016)), showed that, for all five types of math statements, the BOLD signal rose quickly at the beginning of the trial and remained high until the end of the trial. On the contrary, no activation or even a deactivation was seen for the nonmath statements and the series of beeps.

The converse contrast of nonmath versus math reflection yielded activation all along bilateral superior temporal sulci, in bilateral inferior frontal gyri and mesial orbital gyrus (Fig. 3, areas in yellow). From our previous study (Amalric and Dehaene, 2016) we retrieved the functional regions-of-interests showing activation to general semantics (contrast of meaningful versus meaningless nonmath). Fig. 3 shows the temporal profile of activation in three of these regions. In left anterior middle temporal gyrus (aMTG) and left angular gyrus/posterior superior temporal sulcus (AG/pSTS), the average fMRI signal remained sustained above zero only for the nonmath statements. For the math statements, the activity was either null or transient during statement listening only. Overall, these results fully replicate (Amalric and Dehaene, 2016) and show that these results generalize to simpler facts from 5 different areas of mathematics.

2.2.3. *Effect of difficulty*

Analysis of the participants' accuracy and response time indicated that some math statements were more difficult than others. We thus searched for an effect of difficulty in brain responses. We first used the individual reaction times for each statement and computed their correlation with brain activity within each individual before computing a group-level SPM t-map. This whole-brain approach did not reveal any

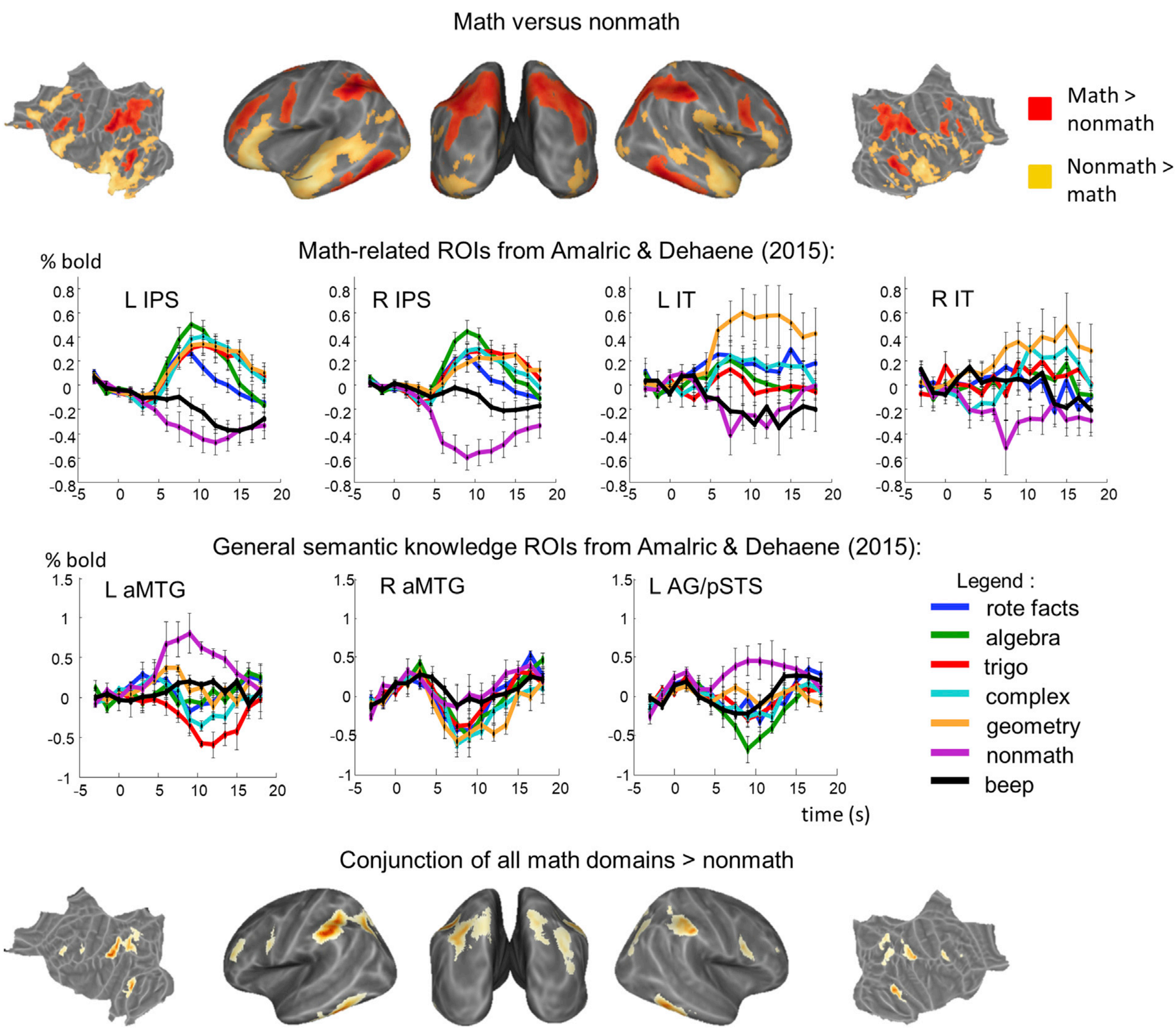

Fig. 3. Dissociation between math and nonmath in experiment 1. (top) Flattened and inflated brain maps showing the contrasts of math > nonmath processing (red) and nonmath > math processing (yellow) (voxelwise $p < 0.001$ uncorrected, clusterwise $p < 0.05$ with FDR correction). (middle) Average time course of BOLD signal for each category of statements in representative regions-of-interest (ROIs) of the networks responsive to math and general-semantics. Left and right intraparietal sulci (IPS), left and right inferior temporal regions (IT), left anterior middle temporal gyrus (L aMTG), left angular gyrus/posterior superior temporal sulcus (L AG/pSTS) and right anterior middle temporal gyrus (R aMTG) were independently determined from Amalric and Dehaene (2016). (bottom) Flattened and inflated brain maps showing the conjunction of the five contrasts of each math category versus nonmath (voxelwise $p < 0.001$ uncorrected, clusterwise $p < 0.05$ with FDR correction, separately for each contrast).

significant cluster in either direction (voxel $p < 0.001$, clusterwise $p < 0.05$, FDR corrected). We then performed a more sensitive analysis to test directly whether problem difficulty has an impact on the activity of math-related parietal regions that presumably overlap with Duncan's multiple-demand system (Duncan, 2010). For each mathematical statement, we extracted the mean beta value from our bilateral intraparietal region of interests, and evaluated whether it correlated with the participants' mean correct rate and response time. No such correlation was found (R(beta, % correct) = 0.074, n.s.; R(beta, RT) = −0.35; n.s.), therefore reaffirming that the math-responsive network activates independently of problem difficulty.

2.2.4. Differences between types of math statements

To test for differences in brain activation between math types in our experiment, we first performed an F-test on all math types. At the whole-brain level, we found differences in the left anterior temporal lobe (temporal pole and anterior superior temporal sulcus), the left inferior frontal gyrus (pars orbitalis, triangularis and opercularis), the right temporal pole, bilateral angular gyri, and a large mesial swath of occipital cortex from the calcarine sulcus to the cuneus (Fig. 4). We then compared each type of math statement against all others. We observed that, in language regions (left IFG, TP, aSTS and pSTS), activation was greater to geometry than other math types. This contrast of geometry > other math also revealed activation in left inferior-temporal regions including the fusiform gyrus (Fig. 4). In the converse contrast, geometry elicited less activation than other types of math statements in a right parietal region (Fig. 4). No significant clusters were found for rote facts or algebra compared to other math statements. Trigonometry, compared with other types of math statements, yielded an extensive activation in the mesial precuneus. Finally, complex numbers induced greater activation in regions alongside the calcarine sulcus and bilateral angular gyri relative to other math statements.

To further investigate the putative impact of the strategy used to solve mathematical problems, we pooled together all statements related to trigonometry and complex numbers, which were designed to elicit mental imagery of the unit circle, and compared them to rote facts and algebra. We observed activation in bilateral angular gyri and at several occipital sites ranging from the calcarine sulcus to more dorsal mesial regions of the cuneus (Fig. 5). Fig. 5 also displays the activation (mean beta) averaged on all voxels of these clusters. Interestingly, while the left calcarine region was specifically activated only by the two types of mathematical statements that involved the unit circle (trigonometry and complex numbers), the right calcarine region was activated for complex numbers but also geometry and nonmath statements. This cluster extended towards more dorsal sites which significantly activated for trigonometry alone. Finally, there was a global deactivation for all kind of statements in the right angular gyrus, and the left angular gyrus activated primarily to complex numbers and geometrical problems, and to a lesser degree to trigonometric problems (Fig. 5).

We also examined the converse contrast of rote facts and algebra (two types of math statements that could be expected to elicit language-like recursive codes for mathematical expressions) versus trigonometry and complex numbers. A single cluster of activation was found, located in the right posterior temporal sulcus (around [65, −37, −4]). Analysis of the betas estimates for each category of statements revealed that this cluster did not activate only for algebra and rote facts, but also for geometrical and nonmath statements and deactivated for trigonometry and complex numbers.

2.2.5. Activation profile in language areas

The above analyses revealed a surprisingly greater activation to geometrical statements in classical language regions. We reasoned that this finding might not indicate a genuine contribution of these regions to geometrical thinking, and instead could be explained by the syntactic complexity of the geometrical statements we used. Indeed, while the statements were matched in length, geometrical statements contained more complex verbs and embedded clauses than other math statements, which all used the expression “is equal to” (e.g. compare “an equilateral triangle can be divided into two right triangles” versus “the cosine of x minus π is equal to the cosine of x”; see appendix for a complete list of

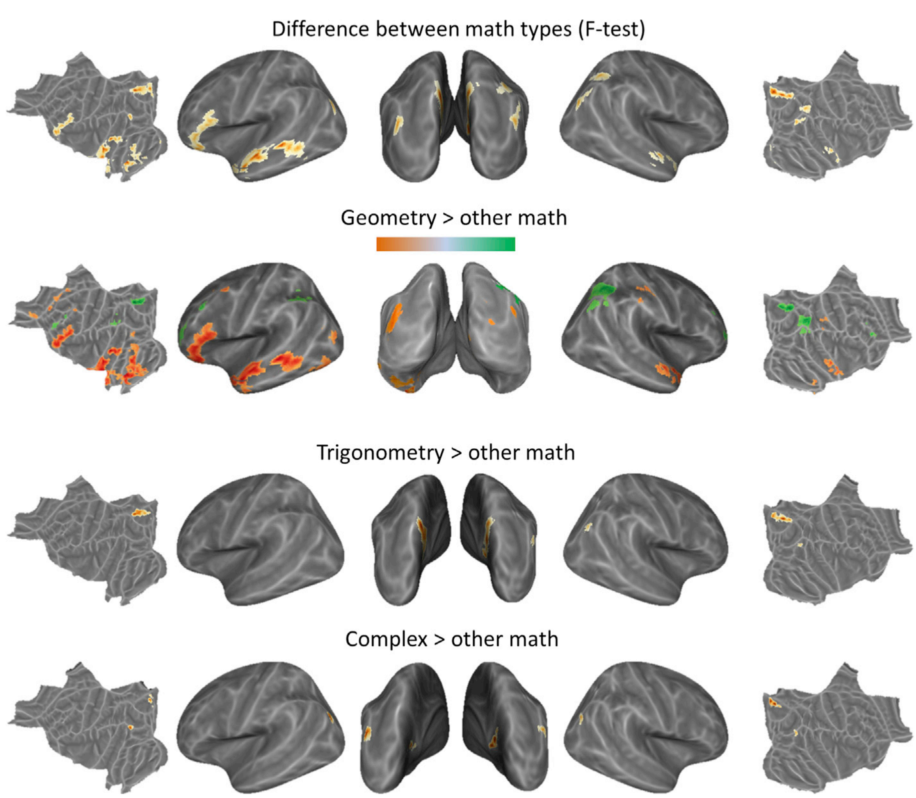

Fig. 4. Activity differences between different domains of mathematics. From top to bottom: flattened and inflated brain maps of (1) the result of a global F-test comparing the five types of math statements in experiment 1; (2) activation elicited more by geometry than other math statements; (3) occipital responses to trigonometry more than other math categories; (4) additional activation in angular gyri for complex numbers compared to other math statements. All maps are threshold at voxelwise $p < 0.001$ uncorrected, clusterwise $p < 0.05$ with FDR correction.

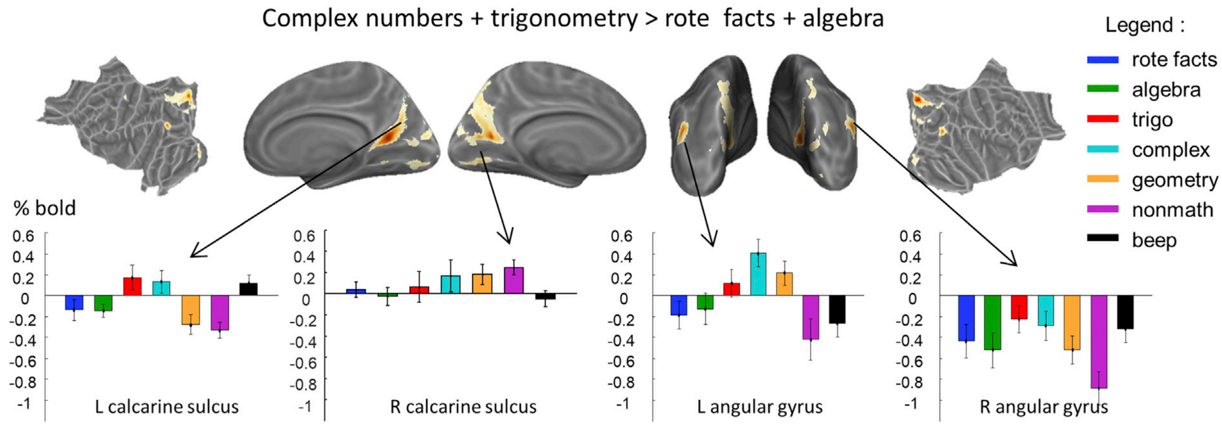

Fig. 5. Occipital regions activated by mathematical statements involving mental imagery of the unit circle. (top) Flattened and inflated brain maps of the contrast complex numbers + trigonometry > rote facts + algebra. (bottom) Mean beta estimates extracted from the principal activated clusters.

statements). To further investigate the relation of math statements to language, we performed a sensitive analysis in 7 regions of interest associated with syntactical processing in previous studies: temporal pole (TP), anterior and posterior superior temporal sulcus (aSTS and pSTS), temporo-parietal junction (TPJ), inferior frontal gyrus pars orbitalis and triangularis (IFGorb and IFGtri) and Brodmann area 44 (BA 44) (Fedorenko et al., 2011; Pallier et al., 2011). We used an independent language localizer (see the general methods section for more details) to identify subject-specific peaks of activation to spoken sentences relative to rest and tested the contribution of those language voxels to math reflection. Fig. 6 shows the average beta for each type of statements in each region on interest. Three different patterns of activation can be seen. First, TP, TPJ and IFGorb exhibited no significant activation for rote facts, algebra, trigonometry and complex numbers, significantly more activation for geometry (except in TPJ, all *p*s < 0.02 with Bonferroni correction for multiple comparisons over the 7 regions of interest), and even significantly more activation to nonmath than to all types of math (except in TP for nonmath > geometry, all *p*s < 0.02 with Bonferroni correction). Second, in aSTS, pSTS and IFGtri, all categories exhibited a significant activation (all *p*s $< 10^{-6}$ with Bonferroni correction), but geometry elicited systematically more activation than other math types (except for complex numbers in aSTS, all *p*s < 0.04 with Bonferroni correction) and was not significantly different from nonmath. Finally, BA 44 exhibited a radically different pattern of activation: geometrical statements induced significantly greater activation than any other category except complex numbers (all *p*s < 0.015 with Bonferroni correction), and no difference

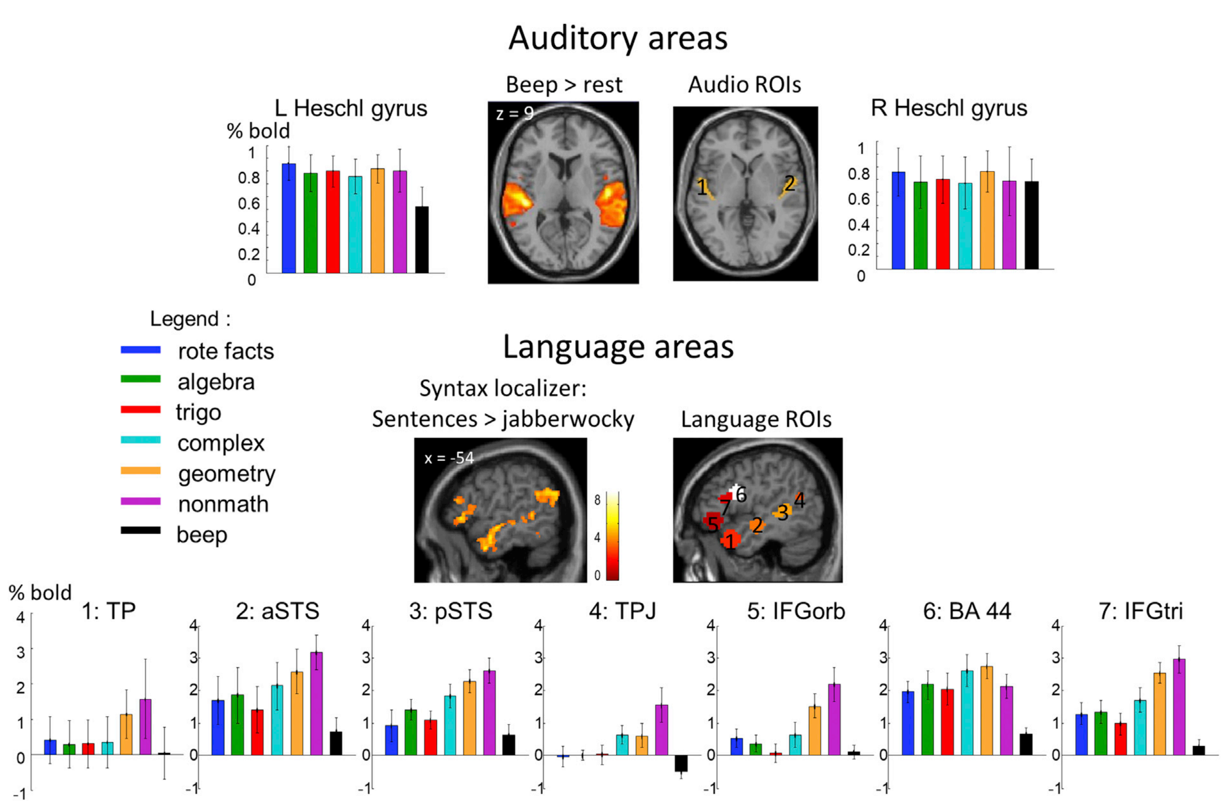

Fig. 6. Activation profile in auditory and language ROIs in experiment 1. (top) Axial slices showing activation in superior temporal auditory areas for series of beeps versus rest (left) and anatomical a-priori regions of interest in Heschl's gyrus (right) from which beta estimates of each category were extracted (bar plots). (bottom) Sagittal slices showing activation for sentences versus jabberwocky (grammatical sentences with meaningless pseudo-words) in the language localizer (left) and the 7 language regions of interest defined by Pallier et al. (2011) (right), from which beta estimates of each category were extracted (bar plots).

was found between other math types and nonmath ($F(4,44) = 1.6$, n.s.).

Interestingly, this analysis suggests that certain types of mathematical statements, such as rote facts, algebra or trigonometry, even when presented as spoken formulas, make virtually no use of the language areas TP, TPJ and IFGorb. As a control, we first verified that the activation differences between categories of stimuli were not due to low-level auditory differences. We thus probed activation to each category in bilateral Heschl gyri (Fig. 6). In both hemispheres, no difference was found between sentence categories (left: $F(5,55) = 1.23$, $p = 0.31$, right: $F(5,45) = 1.51$, $p = 0.21$; Note that degrees of freedom may vary because, for some ROIs, some participants did not exhibit a single activated voxel in the localizer contrast of sentences > jabberwocky). This finding indicated that the audio recordings of the statements were well matched. Second, to examine whether some intrinsic characteristics of the statements could explain our findings, we examined the activation elicited by each individual statement by averaging over the 7 language areas TP, aSTS, pSTS, TPJ, IFGorb, IFGtri and BA 44. Fig. S2 shows the mean betas over these 6 regions for each statement, sorted in ascending order. We notably observed that statements were grouped per category: notably, the strongest activation was to nonmath statements, immediately followed by the vast majority of geometrical statements, then the group of statements related to complex numbers, the other math statements, and finally the non-linguistic beep control. This ordering was well predicted by the number of grammatical morphemes present in the statement (i.e. grammatical markers such as verb endings, plural markers, etc): $R = 0.64$, $p = 2.10^{-9}$. Importantly, in language regions exhibiting significant activation to math statements (aSTS, pSTS, IFGtri and BA44), activation was again strongly correlated with the number of grammatical morphemes present in the math statement ($R = 0.55$, $p = 6.10^{-6}$). These results suggest that the differential activation of language areas, and in particular their strong activation to geometrical statements, could be due to differences in syntactical complexity among categories of statements.

2.2.6. Activation profile in math-responsive areas

We conducted a similar analysis of activation to each individual statement in math-responsive regions (left and right IPS, left and right IT, again a priori defined from (Amalric and Dehaene, 2016). This revealed a completely different ordering (see Fig. S3). Nonmath statements and series of beeps systematically deactivated these regions, while math statements systematically activated these regions regardless of their content. This finding was so reproducible that each of the 12 nonmath statements yielded a negative beta (deactivation), while every single of the 60 math statements yielded a positive beta (activation). Each region exhibited a significant activation for all categories of math (except for geometry in right IPS, all $ps < 0.015$ with Bonferroni correction for multiple comparisons over 4 regions of interest). Conversely, nonmath statements systematically deactivated all of these math-responsive regions (all $ps < 0.05$ corrected). Moreover, in the left and right IT, activation to all math categories was similar (left: $F(4,48) = 1.44$, n.s.; right: $F(4,48) = 0.74$, n.s.). In the left and right IPS, rote facts, algebra, trigonometry and complex numbers elicited similar activation (left: $F(3, 36) = 1.85$, n.s.; right: $F(3,36) = 1.51$, n.s.), and elicited more activation than geometry (left: $ps < 0.015$ corrected for algebra and complex numbers > geometry; right: all $ps < 0.004$ corrected). These results may suggest that while IT activates regardless of statements format, IPS is sensitive to their surface form. Indeed, the amount of activation in right IPS was negatively correlated with the number of grammatical morphemes in the math statements ($r = -0.35$, $p = 0.0057$).

2.3. Discussion

Experiment 1 indicates that the math-responsive network found in our previous study (Amalric and Dehaene, 2016) is highly reproducible and can be activated even by simple and well-known mathematical facts. This network was more activated by any of the five types of math statements than by the nonmath statements. This finding indicates that there is a core neural substrate for math processing, independent of content and difficulty.

In addition to this core finding, we also found some support for the idea that math statements differ in the strategy deployed. Our first hypothesis was confirmed: statements that required visual imagery of the unit circle in order to visualize the properties of trigonometric functions or complex numbers yielded more activation of mesial visual areas, compatible with a contribution of mental imagery (Albers et al., 2013; Klein et al., 2006; Kosslyn, 2005). The results, however, disconfirmed our second hypothesis, derived from Hauser et al's (2002) recursion hypothesis, according to which rote algebraic facts and algebra problems would cause a great activation of language areas than other problems. In fact, even though they were presented in spoken form, these statements induced no activation of language areas TP, TPJ and IFGorb, thereby confirming the strict role of these regions in combinatorial semantics and general non-mathematical semantic knowledge (Amalric and Dehaene, 2016; Binder et al., 2009; Fedorenko and Thompson-Schill, 2014; Pallier et al., 2011; Price et al., 2015). Even in areas pSTS, aSTS, BA44 and IFGtri, which have been hypothesized to participate in a core network for the constituent structure of language (Pallier et al., 2011) activation was lesser for rote algebraic facts, algebraic and trigonometric calculation, or complex numbers than for geometrical and nonmath statements. We could explain this result by examining the syntactic content of our statements: the geometrical and nonmathematical sentences, which caused the highest activation, were of greater syntactic complexity than the others, as measured by the number of grammatical morphemes. The results concur with previous brain-imaging and neuropsychological studies of algebraic processing in suggesting that "naked" expressions such as a^2-b^2, which are devoid of lexical or referential elements, put little or no emphasis on language areas (Klessinger et al., 2007; Maruyama et al., 2012; Monti et al., 2012).

Still, the presence of syntactical differences between the stimuli in experiment 1 led us to perform a second experiment in which we fully controlled for syntax. In experiment 2, mathematicians listened to mathematical and nonmathematical statements that had the same exact syntactic structure, involving a minimal copula relationship (x *is* y).

3. Experiment 2: effect of minimal combinatorial operations such as quantifiers and negation

Experiment 2 had two goals. First, we examined whether the math-responsive network continued to respond when extremely simple declarative statements were presented (e.g. "the sine function is periodical") and contrasted with syntactically similar statements outside the mathematical domain (e.g. "London buses are red"). Second, we examined whether this network responds to the logical form of sentences, independently of its math or nonmath content. This question is motivated by prior studies indicating that activation of the math-responsive network can be elicited by a wide range of problem-solving tasks (Duncan, 2010) and in particular some simple logical reasoning tasks, even outside a strictly mathematical context (Goel, 2004; Goel and Dolan, 2001; Monti et al., 2007). For example (Goel, 2004) suggested that the evaluation of logical deductions such as "No humans can get osteoporosis; Some humans are men; Some men cannot get osteoporosis", relative to the integration of two related and a third unrelated statements, induced activations in bilateral superior parietal cortex. These results may therefore suggest that, under some conditions, logical reasoning over nonmath contents may activate the math-responsive network. Could logical reasoning, rather than mathematical content, explain our earlier results (Amalric and Dehaene, 2016; and the present experiment 1)?

An important characteristic of logical reasoning is the presence of logical operators such as negation, conjunction or quantifiers. Some recent neuroimaging studies have demonstrated a parietal activation in response to quantifiers (Hubbard et al., 2008; McMillan et al., 2005; Troiani et al., 2009; Wei et al., 2014). For example, bilateral intraparietal sulci activate to written sentences containing numerical quantifiers ("at least three", "more than two", etc …) according to (Troiani et al., 2009). While this result might simply be due to the presence of numbers in those statements, McMillan et al. (2005) suggested that all types of quantifiers, including non-numerical ones ("some", "every", "more than", etc …) induce a shared activation in inferior parietal cortex.

Experiment 2 therefore used a 2 × 2 x 2 factorial design in which we independently manipulated (1) the math or nonmath content of the statements; (2) the presence of a negation; (3) the presence of the quantifier "some". If the math-responsive network genuinely encodes mathematical concepts and their relationships, then it should show an effect of the first factor (math content), over and above any influence of the other two factors (negation and quantification). If, on the contrary, previous results are due to the greater need for logical reasoning for math than for nonmath statements, then we should see main effects of negation and quantification, regardless of the mathematical or nonmathematical nature of the content.

3.1. Methods

The same participants as in experiment 1 were exposed to a set of spoken true or false mathematical and non-mathematical statements (Fig. 1), following the same procedure. These statements were either declarative sentences ("The sine function is periodical"; "Londonian buses are red"), sentences with a quantifier *some* ("Some matrices are diagonalizable"; "Some ocean currents are warm"), a negation ("Hyperboloids are not connected"; "Orange blossom is not perfumed"), or both quantifier and negation ("Some order relations are not transitive"; "Some green plants are not climbing"). Math and nonmath statements were carefully matched for syntax within each category. Indeed, they were paired with the same number of words and the same grammatical categories (for more detailed stimuli and procedure see general methods and appendix).

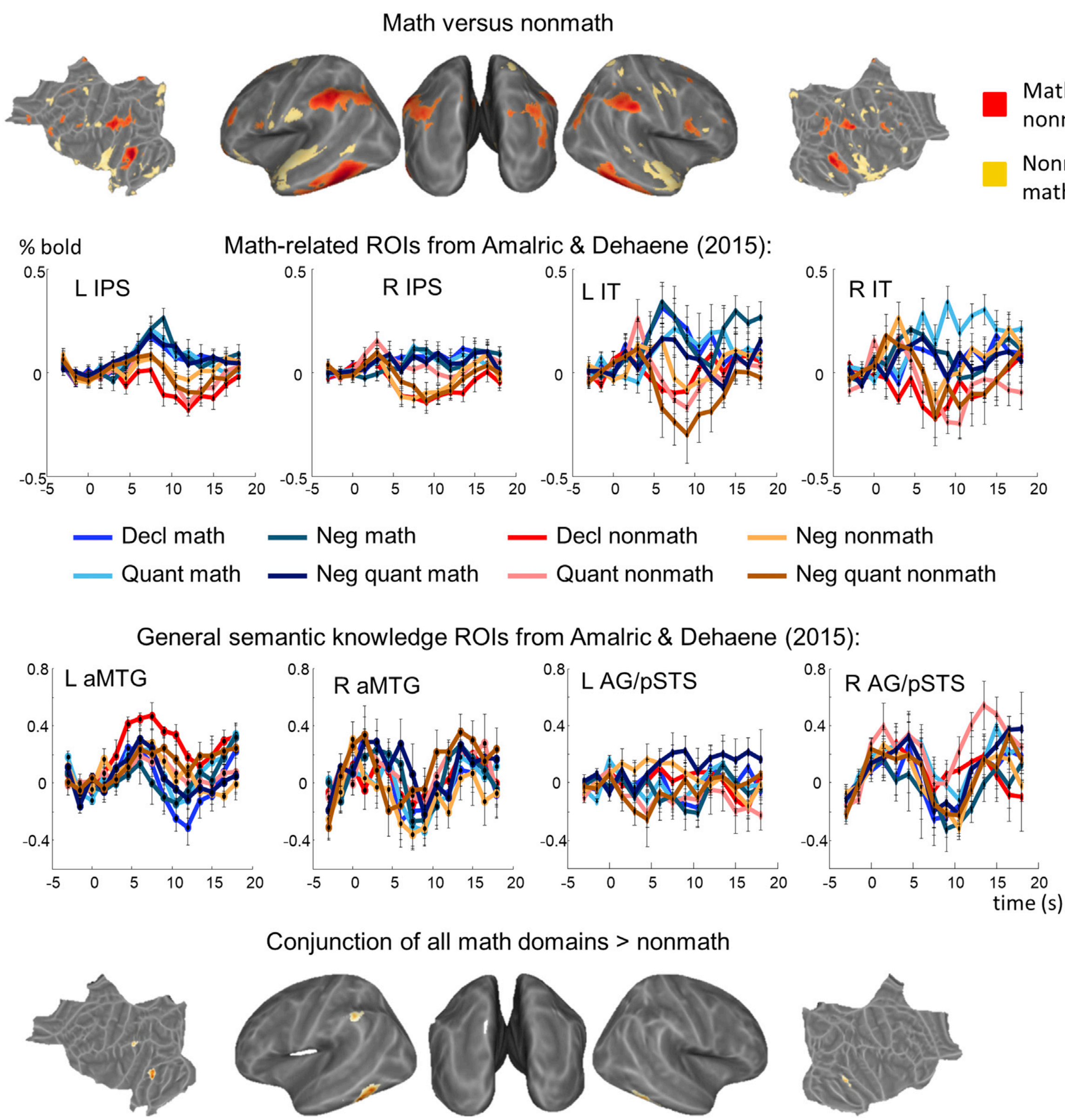

Fig. 7. Dissociation between math and nonmath in experiment 2. (top) Flattened and inflated brain maps showing the contrasts of math > nonmath (red) and nonmath > math (yellow). (middle) Time course of bold signal for each category of statements in representative brain areas of the networks responsive to math and general-semantics. (bottom) Flattened and inflated brain maps showing the conjunction of the four contrasts of math > nonmath within each condition.

3.2. Results

3.2.1. Behavior

Overall performance (Fig. 2) was 82.9 ± 5.5% correct (math: 90.4 ± 1.6% correct; nonmath: 86.2 ± 2.0% correct; no significant difference). A 2 × 2 x 2 factorial ANOVA confirmed that the content (math/nonmath) did not have any significant effect, and revealed only a significant effect of negation ($F(1,88) = 4.40$, $p < 0.05$), but not of quantifiers. Furthermore, no significant interaction between the factors was found.

Participants answered in average in 1.25 ± 0.05s (math: 1.21 ± 0.08s; nonmath: 1.28 ± 0.08s; no significant difference; Fig. 2.2). The presence of negation significantly lengthened the response time ($F(1,88) = 12.65$; $p < 0.001$), while no effect of quantifier was found. Within each condition, no difference was found between math and nonmath response times, except for quantified negation ($t(11) = 2.52$, $p < 0.05$; interaction between content, negation and quantifier: $F(1,88) = 4.11$, $p < 0.05$).

3.2.2. Math versus nonmath dissociation

We first searched for regions exhibiting more activation to math than to nonmath statements, and again found the math-responsive network: bilateral IPS and IT, as well as weaker superior and middle frontal activations (Fig. 7). Similar results were found within each condition (declarative, negative, quantified declarative and quantified negative) for the contrast of math versus nonmath (Fig. S4). Furthermore, the conjunction of math > nonmath contrasts in all four categories again revealed activation in bilateral inferior-temporal regions and the left intraparietal sulcus, although right IPS and dorsal frontal cortex no longer reached significance (Fig. 7). Plots of the time course of activation within a-priori math-related regions from Amalric and Dehaene (2016) revealed a systematic activation to mathematical statements and, contrariwise, a systematic deactivation to nonmath statements (Fig. 7). Examination of the mean activation induced by each individual statement, averaged over the four main math-related regions (i.e. bilateral IPS and IT), confirmed this result (see Fig. S6). Indeed, virtually all non-math statements (43/48) had negative betas while the majority of math statements (27/48) yielded a positive activation, and a 2 × 2 × 2 ANOVA on beta estimates with content, negation and quantifier as factors revealed that only the content (math/nonmath) had a significant effect ($F(1,88) = 28.8$, $p < 0.001$).

In the converse contrast, the brain regions exhibiting greater activation for nonmath than math statements were the bilateral superior temporal sulci and the left IFGOrb. Similar clusters of activation were found in bilateral superior temporal poles for nonmath > math reflection when restricting to declarative or quantified statements. For negative statements, only a small difference between nonmath and math statements in the left temporal pole was observed, and no such difference was seen for quantified negative statements. Note that the main contrast of nonmath versus math statements elicited less extended activation in semantic-related regions than the equivalent contrast in experiment 1 (Fig. S5). In particular, no activation in bilateral angular gyri was found. Examination of temporal activation in regions-of-interest extracted from the nonmath > math contrast in our previous study (Amalric and Dehaene, 2016) revealed noisy signals (Fig. 7), suggesting that the simpler nonmath statements used in the present experiment activated slightly more dorsal regions. Only in the left anterior superior temporal

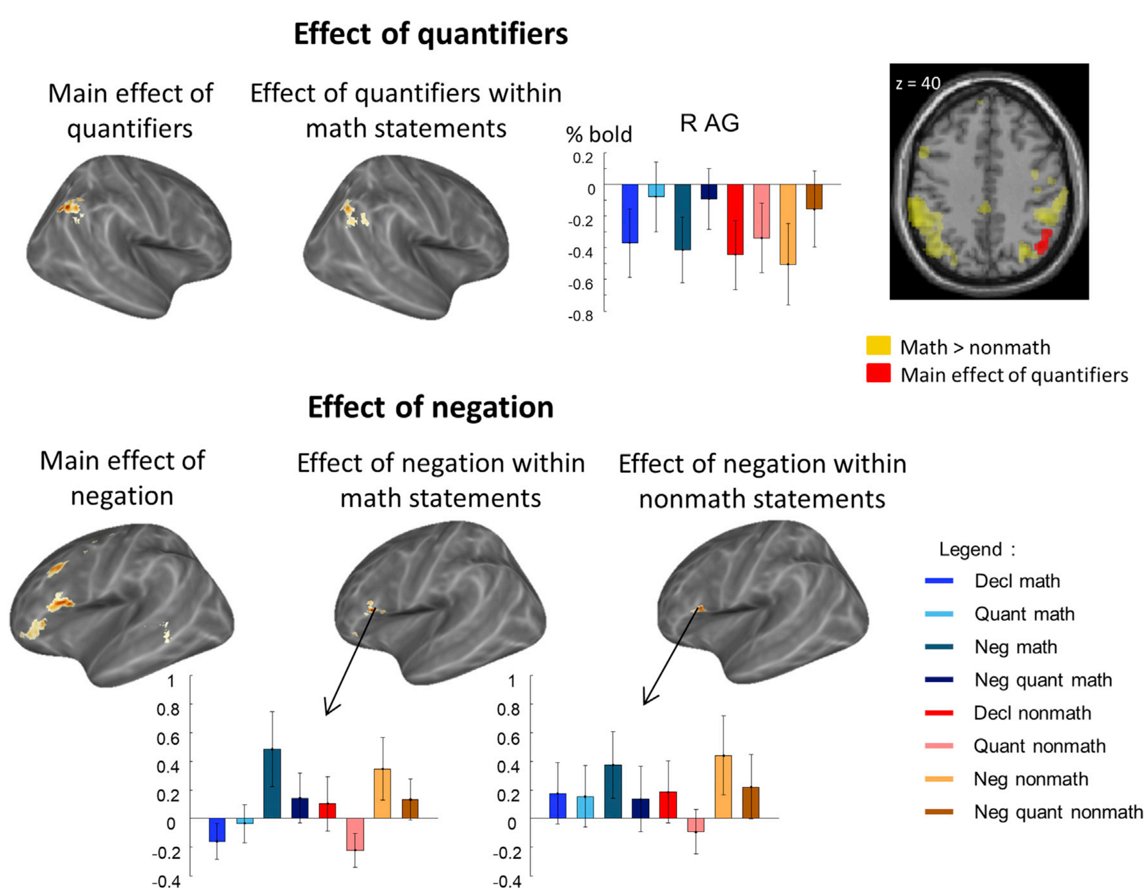

Fig. 8. Main effects of quantifiers and negation. (top) Inflated brain maps showing the main effect of presence or absence of the quantifier "some", pooled over both math and nonmath statements, and the effect of quantifiers within math statements only. The bar plot displays the mean beta values in the right angular gyrus cluster of activation. (top right) Axial slice showing the relative locations of the activations induced by the main effect of quantifiers (red) and by math more than nonmath statements (yellow). (bottom) Inflated brain maps showing the main effect of negation, pooled over math and nonmath statements (left) and within math and nonmath statements separately. Bar plots display the mean activation in left IFG clusters found in the two latter maps.

sulcus did activation to the nonmath statements remain sustained until the end of the trial, especially for the declaratives, while the math statements induced only a transient activation followed by a systematic deactivation (Fig. 7).

3.2.3. Effect of quantifiers

We studied the main effect of quantification by comparing all statements that contained a quantifier (i.e. quantified plus negative quantified math and nonmath statements) to all other statements. This contrast revealed a cluster of activation in the right angular gyrus (Fig. 8). Interestingly, this activation totally spared math-related regions, as suggested by the brain map at the top right of Fig. 8, showing the non-overlap of the math > nonmath contrast and the main effect of quantifiers. A similar activation was found when restricting to math statements, although no significant effect of quantifiers was found within the non-math statements. Plots of average betas in this cluster revealed that the quantified statements induced a lesser deactivation than simple declaratives or negatives (Fig. 8).

3.2.4. Effect of negation

We searched for regions where activity was modulated by the presence of negation, regardless of the math/nonmath distinction. The comparison of all negative statements (math and nonmath, quantified or not) versus all other statements revealed activation in the left inferior frontal gyrus, in the three pars triangularis (peak at [-44 26 -1], t = 5,85), Opercularis (peak at ([-56 16 16], t = 5,37) and Orbitalis (peak at [-51 26 -7], t = 4,90) (Fig. 8). When restricting to math, resp. to nonmath statements, a common activation was found in IFG triangularis (around [-56 16 9]). The effect of negation within math statement induced additional activation in IFG Orbitalis (peak at [-51 20 -5], t = 4,29). Nevertheless, there was no whole-brain interaction between negation and content (math vs nonmath), and the profiles of activation (Fig. 8) indicated that both sites tended to show a higher activation whenever a statement contained a negation.

3.2.5. Activation in auditory and language ROIs

We first checked whether auditory responses differed between categories in Heschl gyri, and found similar responses to all statements in the right hemisphere ($F(7,70) = 0.44$, n.s), and very small but significant differences in the left hemisphere ($F(7,84) = 2.70$, $p = 0.03$ with Bonferroni correction over 2 regions, Fig. 9. We then performed an ROI analysis in the 7 language-related ROIs that were used in experiment 1 (i.e. TP, aSTS, pSTS, TPJ, IFGorb, BA44 and IFGtri). Fig. 9 shows the average activation elicited by each statement type within the subject-specific voxels identified by the language localizer within each region. All categories elicited significant activation in all 7 regions, with the sole exception of TPJ (all $ps < 0.04$ corrected for multiple comparisons over 7 regions of interest), and ANOVAs performed in each region revealed no significant differences between categories.

Finally, this result was confirmed by examining the activation elicited by each individual statement, averaged over all 7 language areas. Once sorted in ascending order, no clear segregation appeared (Fig. S6) and neither the math/nonmath content nor the presence of a negation or a quantifier showed a significant effect on beta estimates (main effects and interactions in a 2 × 2 × 2 ANOVA: all $Fs(1.88) < 1.32$, n.s.).

3.2.6. Effect of word abstractness

One could argue that non-math statements comprise more concrete words than math statements, and that this difference, rather than the math content, could explain our results. This is unlikely at face value given that previous studies of abstract versus concrete words have not observed effects in math-responsive areas (Wang et al., 2010). Rather, a meta-analysis of 19 fMRI studies assessing the difference in brain activation elicited by abstract versus concrete nouns revealed that “abstract concepts elicit greater activity in the inferior frontal gyrus and middle temporal gyrus compared to concrete concepts, while concrete concepts elicit greater activity in the posterior cingulate, precuneus, fusiform gyrus, and parahippocampal gyrus compared to abstract concepts” (Wang et al., 2010). Nevertheless, to evaluate this possibility in the current context, we examined the effect of word abstractness on brain activation. We asked a professional mathematician to rate the level of concreteness of words used in math and non-math statements respectively on a scale from 0 (= very abstract) to 5 (= very concrete). We then used the abstractness rating of each statement as a predictor of brain activity, separately for math- and language-responsive regions. No significant correlation was found between the activity of math-responsive regions and the degree of abstractness, neither for math nor for non-math concepts. Only a small positive correlation was found between the level of abstractness of non-math concepts and the activity of the left inferior frontal region ($R = 0.31$, $p < 0.03$, uncorrected for multiple ROIs). As word concreteness is often related to mental imagery, we also examined whether the activity elicited by math and nonmath statements differed in the primary visual cortex. No significant difference between math and non-math statements was found.

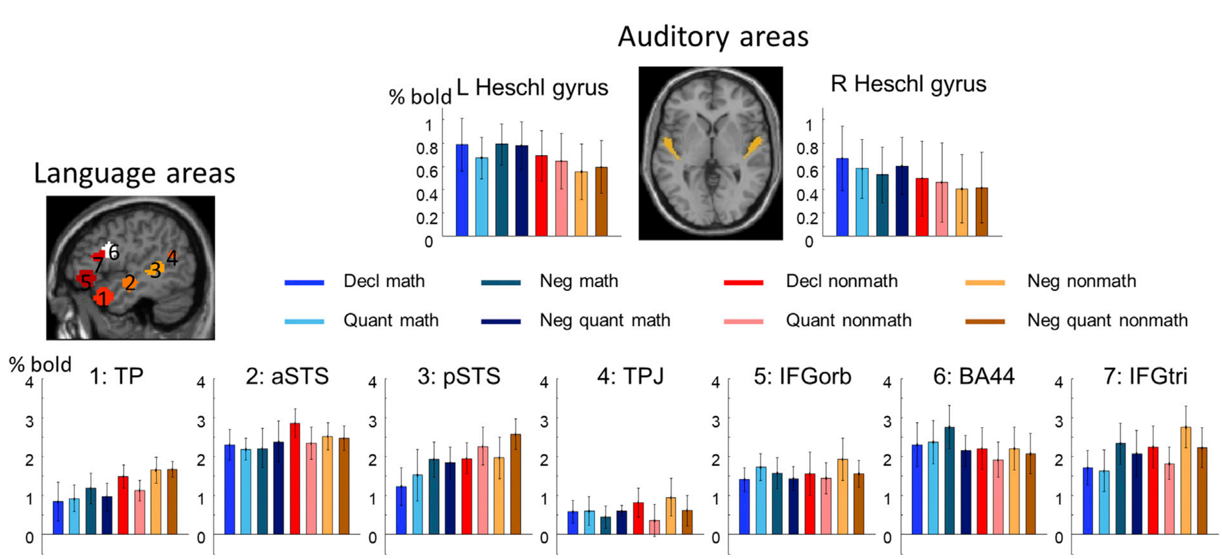

Fig. 9. Activation profile in auditory and language areas in experiment 2. (top) Axial slices showing auditory anatomical regions of interest, i.e. Heschl gyri, from which beta estimates of activation evoked by each category of statements were extracted (bar plots). (bottom) Sagittal slice showing the 7 language regions of interest used to extract beta estimates represented in bar plots.

3.3. Discussion

In experiment 2, all statements were extremely simple declarative copular sentences (x is y). As a consequence, they were well matched in syntactic complexity, and we verified that they elicited indistinguishable activations in classical language areas. Nevertheless, we again replicated a main effect of semantic content: the math statements, relative to nonmath statements, again activated bilateral intraparietal and inferior temporal regions. This result therefore reinforces the idea that there is a math-responsive network in the brain constituted of bilateral IPS and IT regions that systematically processes math-related semantic content.

We verified that the observed dissociation was not driven by a difference in the level of abstractness between math and nonmath concepts. Math-responsive regions were not modulated by the degree abstractness of either math or non-math statements, and only the abstractness of nonmath statements led to a small increase in left IFG activation, i.e. outside the math-responsive network. This conclusion fits with the results of many studies investigating the difference between activation elicited by abstract versus concrete words (Wang et al., 2010) and which again found that these contrasts modulated activity outside of the typical math- and semantic-related brain networks. In fact, it is likely that, for an expert mathematician, the subjective degree of concreteness of math and nonmath concepts may not even differ. In the study led by (Amalric and Dehaene, 2016) participants' ratings of statements "imageability" revealed that, if anything, math concepts yielded more mental imagery than nonmath concepts in mathematicians.

Finally, the presence of logical operators such as quantifiers and negation was insufficient to drive any change in activation in the math-responsive regions. Negation correlated with activation in the left IFG, suggesting a syntactical complexity effect. Quantifiers correlated with less deactivation in the right angular gyrus, the same region previously found by (McMillan et al., 2005). Crucially, however, our design revealed that this quantification site did not overlap with the parietal activation associated with mathematical reflection.

4. General discussion

We start by summarizing our main findings. In two fMRI experiments with professional mathematicians, we replicated, with simpler math statements, the dissociation that was previously observed between brain circuits involved in math and nonmath reflection (Amalric and Dehaene, 2016). As we simplified the statements, this dissociation became even more drastic in the case of rote algebraic facts or algebraic calculation statements, since those problems elicited virtually no activation in language areas TP, pSTS and IFGorb, but continued to induce unchanged activity in bilateral parietal and inferior temporal math-responsive areas. Indeed, the activation of the math-responsive network was common to all mathematical domains, although trigonometry and complex numbers, which induced mental imagery, evoked additional activation in the occipital cortex. Conversely, nonmath problems did not engage the math-responsive regions, even when they contained logical operators such as quantifiers or negation. Instead, main effects of quantifiers and negation were respectively observed in the right angular gyrus and the left IFG. We now discuss those findings in turn.

Our findings support the hypothesis that mathematical concepts form a domain-specific area of knowledge with a distinct cortical substrate. This conclusion is similar to the specializations that have been previously reported in the literature, for instance for semantic knowledge of animate vs inanimate categories (Huth et al., 2016; Mahon and Caramazza, 2009). The intraparietal sulci and bilateral lateral inferior temporal regions appear to constitute a core network for mathematical knowledge which activates whenever we access concepts of mathematics, regardless of domain or problem difficulty. Indeed, whether mathematical problems were easy or difficult, retrieved from memory, resulting from calculation or visualized, these four brain regions were systematically activated. This finding concurs with previous evidence for activation of these regions by the mere presentation of numbers, in adults without any advanced mathematical training (Daitch et al., 2016; Dehaene et al., 2003; Eger, 2016; Pinheiro-Chagas et al., submitted) and even in preschoolers watching Sesame Street numeracy programs (Cantlon and Li, 2013). Furthermore, intracranial recordings (Dastjerdi et al., 2013) and an fMRI study of semantic networks (Huth et al., 2016) have suggested that merely listening to sentences that contain number words or words referring to units of measure, positions and distances suffices to activate bilateral parietal, inferior frontal and inferior temporal regions.

In our previous research (Amalric and Dehaene, 2016) we had used complex mathematical statements that required several seconds of reflection and found additional intense and bilateral activations in dorsal prefrontal cortex. With the much simpler facts used in the present experiments, including mere definitional properties that could be responded to in $\sim$1 s (e.g. "the sine function is periodical"), this frontal activation was strongly reduced (experiment 1) or even disappeared (experiment 2), while the activation in bilateral intraparietal and inferior temporal regions remained. Our findings therefore suggest that the latter region play a core role in representing mathematical concepts, whereas prefrontal areas may be additionally recruited when active manipulation of those concepts is needed. Further research should determine whether IT and IPS make distinct contributions to mathematical knowledge, since the present experimental manipulations were only very modestly successful in dissociating them. Examination of response profiles in bilateral IT did not reveal any significant differences between categories of math statements, while bilateral IPS, particularly in the right hemisphere, responded less to geometrical statements, perhaps because they involved a greater linguistic complexity. We also studied problems that predictably require mental imagery (complex numbers and trigonometry, which call for a mental image of the unit circle). This factor did not modulate the main math-responsive network, but increased activation in mesial occipital cortex.

The various controls that we used revealed that math-related regions appeared to be exclusively used for mathematical thinking in our experiments, and remained silent when processing nonmathematical statements, even when such statements contained minimal logical operators. Instead, the presence of a negation induced more activation in the left IFG (Broca's area). This result suggests that negation acted primarily by increasing the syntactical or semantic complexity of sentences. This finding may not be surprising given that negation, at least in French, necessarily increases the number of words in a sentence compared to simple or quantified declaratives.

Statements using the quantifier "some", in turn, caused a greater activation (or more accurately, a lesser deactivation) than other statements in the right inferior parietal cortex. While this finding replicates what was reported by McMillan et al. (2005) we observed two major differences compared to their findings. First, inspection of the beta estimates in this region revealed no activation for statements that contained a quantifier, but a strong deactivation for declarative and negative statements. Second, McMillan and colleagues interpreted the finding of a quantifier-related activation in the inferior parietal lobule as reflecting the existence of a shared cortical circuit for numbers and quantifiers. However, the activation that they labeled as belonging to the "inferior parietal lobule" actually falls closer to the angular gyrus than to the intraparietal sulcus. Our results indicate that this inferior parietal region showing a main effect of quantifiers does not overlap with the math-responsive network. Altogether, these observations question the idea that the mere presence of a quantifier such as "some", in an otherwise non-mathematical sentence, suffices to call upon numerical processes.

The present study confirms that mathematical reflection does not call upon the classical areas involved in word- and sentence-level semantics, namely the most anterior, polar part of the superior and middle temporal sulcus, and the temporo-parietal junction/angular gyrus (Binder et al., 2009). We did observe bilateral anterior temporal activations during the processing of non-mathematical statements in the present experiments and in our previous study (Amalric and Dehaene, 2016) but these regions activated much more to nonmath than to math statements. In fact, a sensitive analysis in language-related regions of interest extracted from a previous study by (Pallier et al., 2011) revealed that statements of algebra, trigonometry and complex numbers, even though they were presented verbally, led to virtually no activation of left TP, TPJ and IFGOrb in the first experiment of the present study.

We also note in passing that while Ischebeck et al. (2006) found that the retrieval of rote arithmetic facts, compared to arithmetic calculation, involved the bilateral angular gyri, this result was not replicated here, as we found that even rote algebraic facts, such as knowledge that a^2-b^2=(a-b)(a+b), activated the math-responsive network. This result suggests that routinized algebraic expressions are not stored in rote verbal form (unlike, say, multiplication tables), but involve an actual manipulation of mathematical concepts – as indeed supported by the previous finding that they engage IT and IPS areas (Maruyama et al., 2012).

Naturally, mathematics and language are not completely disconnected in the brain. Since both mathematical and non-mathematical statements were presented as spoken sentences, we expected that the core areas for language processing would be jointly activated. Indeed, in experiment 1, listening to math statements activated a core set of language areas (aSTS, pSTS, IFGTri) to an extent proportional to their syntactical complexity. Moreover, in experiment 2, ROI analysis indicated that the activation in language areas did not differ between math and nonmath statements, thus reflecting their similar syntactical construction. It is therefore only within areas that have been labeled as playing a semantic role (TP, AG) that a massive difference between math and nonmath statements is found.

Altogether, our findings indicate a major dissociation between the brain networks for mathematical and nonmathematical semantics. They confirm and extend previously reported dissociations between the recognition of letters versus numbers in the ventral visual pathway (Abboud et al., 2015; Park et al., 2012; Shum et al., 2013) between algebraic versus linguistic processing in brain-lesioned patients and brain-imaging studies (Klessinger et al., 2007; Maruyama et al., 2012; Monti et al., 2012) and between advanced mathematical versus semantic processing in professional mathematicians (Amalric and Dehaene, 2016). Mathematics in the broadest sense of the term (including elementary numerical and spatial processing) may thus constitute a distinct subsystem within the realm of human conceptual knowledge.

5. General methods

5.1. Ethics statement

All experiments were approved by the regional ethical committee for biomedical research, and subjects gave informed consent after they read consent information.

5.2. Stimuli

All statements were recorded using Audacity software by a female native French speaker who was familiar with mathematical concepts. Within each experiment, the math and nonmath statements from the different categories were matched in duration (Experiment 1: math: 4.15 ± 0.46s; nonmath: 3.98 ± 0.45s; no significant difference; Experiment 2: math: 4.47 ± 0.57s; nonmath: 4.48 ± 0.36s; no significant difference). A complete list of stimuli can be found in appendix.

5.3. Procedure

In both experiments, a white fixation cross was presented on a black background, which participants had to fixate continuously. Each trial started with a beep and a color change of the fixation cross (which turned to red), announcing the onset of the statement. Participants were then asked to answer as quickly as they could, and within 2.5 s of sentence ending. This response period ended with a beep, and was signaled by the fixation cross turning to green. Subjects gave their evaluation of the sentence (true, false) by pressing a button held in the right hand for true, and in the left hand for false. Each trial ended with a 7-s resting period (Fig. 2.1).

Experiment 1 was divided into 7 runs of 12 statements each, including at least one exemplar of each category (rote facts, algebra, trigonometry, complex numbers, geometry, nonmath and beeps), randomly picked among all possible statements. Experiment 2 was divided into 3 runs of 32 statements each, including exactly two exemplars of each subcategory (math/nonmath x true/false x declarative/quantified/negative/negative quantified), again randomly picked among all statements.

5.4. Language localizer

At the end of the fMRI exam, participants performed a language localizer. In a unique run of 14 min, participants listened to correct sentences, jabberwocky sentences (i.e. sentences composed of pseudowords with preserved grammatical markers), and jabberwocky in random order (i.e. pseudo-sentences with degraded grammatical structure). At the beginning of each trial, they heard a target word or pseudoword, and had to decide whether the following sentence or pseudosentence contained this target. Trials ended with a 7-s resting period. When present (90% of trials), targets always appeared in the last third of sentences in order to maintain participants' concentration until the end of the trial. Sentences and pseudo-sentences contained 14 words and used complex syntax, including relative clauses. They were all recorded using Audacity software, and were matched in duration (sentences: 4.84 ± 0.54s; jabberwocky: 5.16 ± 0.50s; random order: 5.11 ± 0.44s; $F(2,57) = 2.44$; n.s.).

5.5. fMRI data acquisition and analysis

We used two 3-Tesla whole body systems (Trio and Prisma) with high-resolution multiband imaging sequences developed by the Center for Magnetic Resonance Research (CMRR) (Xu et al., 2013) (multiband factor = 4, Grappa factor = 2, 80 interleaved axial slices, 1.5 mm thickness and 1.5 mm isotropic in-plane resolution, matrix = 128×128, TR = 1500 ms, TE = 32 ms), with 64 channel head-coil.

Using SPM8 software, functional images were first corrected for slice timing, realigned, normalized to the standard MNI brain space, and spatially smoothed with an isotropic Gaussian filter of 2 mm FMWH. A two-level analysis was then implemented in SPM8. For each participant, fMRI images were high-pass filtered at 128s. Then, time series from experiment 1 and experiment 2 were modelled separately. For both experiments, time series was modelled using a single regressor per statement, with a kernel corresponding to statement presentation plus the mean reaction time for that subject. We then defined subject-specific contrasts by comparing the activation evoked by two subsets of sentences during the reflection period. Regressors of non-interest included the six movement parameters for each run. Within each auditory run, additional regressors of non-interest were added to model activation to the auditory beeps and to the button presses.

For the second-level group analysis, individual contrast images for each of the experimental conditions relative to rest were smoothed with an isotropic Gaussian filter of 5 mm FWHM, and entered into a second-level whole-brain ANOVA with stimulus category as within-subject factor. All brain activation results are reported with a clusterwise threshold of $p < 0.05$, corrected with false-detection-rate (FDR) for multiple comparisons across the whole brain, using an uncorrected voxelwise threshold of $p < 0.001$.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2019.01.001.

References

Abboud, S., Maidenbaum, S., Dehaene, S., Amedi, A., 2015. A number-form area in the blind. Nat. Commun. 6, 6026. https://doi.org/10.1038/ncomms7026.
Albers, A.M., Kok, P., Toni, I., Dijkerman, H.C., de Lange, F.P., 2013. Shared representations for working memory and mental imagery in early visual cortex. Curr. Biol. 23, 1427–1431. https://doi.org/10.1016/j.cub.2013.05.065.
Amalric, M., Dehaene, S., 2016. Origins of the brain networks for advanced mathematics in expert mathematicians. Proc. Natl. Acad. Sci. Unit. States Am. 201603205. https://doi.org/10.1073/pnas.1603205113.
Binder, J.R., Desai, R.H., Graves, W.W., Conant, L.L., 2009. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. Cerebr. Cortex 19, 2767–2796. https://doi.org/10.1093/cercor/bhp055.
Binder, J.R., Westbury, C.F., McKiernan, K.A., Possing, E.T., Medler, D.A., 2005. Distinct brain systems for processing concrete and abstract concepts. J. Cognit. Neurosci. 17, 905–917. https://doi.org/10.1162/0898929054021102.
Cantlon, J.F., Brannon, E.M., 2005. Semantic congruity affects numerical judgments similarly in monkeys and humans. Proc. Natl. Acad. Sci. U. S. A. 102, 16507–16511. https://doi.org/10.1073/pnas.0506463102.
Cantlon, J.F., Li, R., 2013. Neural Activity during Natural Viewing of Sesame Street Statistically Predicts Test Scores in Early Childhood. PLoS Biol. 11, e1001462. https://doi.org/10.1371/journal.pbio.1001462.
Cappelletti, M., Butterworth, B., Kopelman, M., 2012. Numeracy skills in patients with degenerative disorders and focal brain lesions. Neuropsychology 26, 1–19. https://doi.org/10.1037/a0026328.
Caramazza, A., Shelton, J.R., 1998. Domain-specific knowledge systems in the brain: the animate-inanimate distinction. J. Cognit. Neurosci. 10, 1–34. https://doi.org/10.1162/089892998563752.
Daitch, A.L., Foster, B.L., Schrouff, J., Rangarajan, V., Kaşikçi, I., Gattas, S., Parvizi, J., 2016. Mapping human temporal and parietal neuronal population activity and functional coupling during mathematical cognition. Proc. Natl. Acad. Sci. Unit. States Am. 113, E7277–E7286. https://doi.org/10.1073/pnas.1608434113.
Dastjerdi, M., Ozker, M., Foster, B.L., Rangarajan, V., Parvizi, J., 2013. Numerical processing in the human parietal cortex during experimental and natural conditions. Nat. Commun. 4, ncomms3528. https://doi.org/10.1038/ncomms3528.
Dehaene, S., 1992. Varieties of numerical abilities. Cognition, Numerical Cognition 44, 1–42. https://doi.org/10.1016/0010-0277(92)90049-N.
Dehaene, S., Cohen, L., 1997. Cerebral pathways for calculation: Double dissociation between rote verbal and quantitative knowledge of arithmetic. Cortex 33, 219–250.
Dehaene, S., Piazza, M., Pinel, P., Cohen, L., 2003. Three parietal circuits for number processing. Cogn. Neuropsychol. 20, 487–506. https://doi.org/10.1080/02643290244000239.
Delazer, M., Ischebeck, A., Domahs, F., Zamarian, L., Koppelstaetter, F., Siedentopf, C.M., Kaufmann, L., Benke, T., Felber, S., 2005. Learning by strategies and learning by drill—evidence from an fMRI study. NeuroImage 25, 838–849. https://doi.org/10.1016/j.neuroimage.2004.12.009.
Duncan, J., 2010. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. Trends Cognit. Sci. 14, 172–179. https://doi.org/10.1016/j.tics.2010.01.004.
Eger, E., 2016. Neuronal foundations of human numerical representations. Prog. Brain Res., The Mathematical Brain Across the Lifespan 227, 1–27. https://doi.org/10.1016/bs.pbr.2016.04.015.
Fedorenko, E., Behr, M.K., Kanwisher, N., 2011. Functional specificity for high-level linguistic processing in the human brain. Proc. Natl. Acad. Sci. Unit. States Am. 108, 16428–16433. https://doi.org/10.1073/pnas.1112937108.
Fedorenko, E., Duncan, J., Kanwisher, N., 2013. Broad domain generality in focal regions of frontal and parietal cortex. Proc. Natl. Acad. Sci. Unit. States Am. 110, 16616–16621. https://doi.org/10.1073/pnas.1315235110.
Fedorenko, E., Thompson-Schill, S.L., 2014. Reworking the language network. Trends Cognit. Sci. 18, 120–126. https://doi.org/10.1016/j.tics.2013.12.006.
Gelman, R., Butterworth, B., 2005. Number and language: how are they related? Trends Cognit. Sci. 9, 6–10. https://doi.org/10.1016/j.tics.2004.11.004.
Goel, V., 2004. Differential involvement of left prefrontal cortexin inductive and deductive reasoning. Cognition 93, B109–B121. https://doi.org/10.1016/j.cognition.2004.03.001.
Goel, V., Dolan, R.J., 2001. Functional neuroanatomy of three-term relational reasoning. Neuropsychologia 39, 901–909. https://doi.org/10.1016/S0028-3932(01)00024-0.
Hubbard, E.M., Diester, I., Cantlon, J.F., Ansari, D., van Opstal, F., Troiani, V., 2008. The evolution of numerical cognition: from number neurons to linguistic quantifiers. J. Neurosci. 28, 11819–11824. https://doi.org/10.1523/JNEUROSCI.3808-08.2008.
Hauser, M.D., Chomsky, N., Fitch, W.T., 2002. The faculty of language: what is it, who has it, and how did it evolve? Science 298, 1569–1579. https://doi.org/10.1126/science.298.5598.1569.
Huth, A.G., de Heer, W.A., Griffiths, T.L., Theunissen, F.E., Gallant, J.L., 2016. Natural speech reveals the semantic maps that tile human cerebral cortex. Nature 532, 453–458. https://doi.org/10.1038/nature17637.
Huth, A.G., Nishimoto, S., Vu, A.T., Gallant, J.L., 2012. A continuous semantic space describes the representation of thousands of object and action categories across the human brain. Neuron 76, 1210–1224. https://doi.org/10.1016/j.neuron.2012.10.014.
Hyde, D.C., Boas, D.A., Blair, C., Carey, S., 2010. Near-infrared spectroscopy shows right parietal specialization for number in pre-verbal infants. NeuroImage 53, 647–652. https://doi.org/10.1016/j.neuroimage.2010.06.030.
Ischebeck, A., Zamarian, L., Siedentopf, C., Koppelstätter, F., Benke, T., Felber, S., Delazer, M., 2006. How specifically do we learn? Imaging the learning of multiplication and subtraction. NeuroImage 30, 1365–1375. https://doi.org/10.1016/j.neuroimage.2005.11.016.
Izard, V., Sann, C., Spelke, E.S., Streri, A., 2009. Newborn infants perceive abstract numbers. Proc. Natl. Acad. Sci. Unit. States Am. 106, 10382–10385. https://doi.org/10.1073/pnas.0812142106.
Klein, I., Paradis, A.-L., Poline, J.-B., Kosslyn, S.M., Le Bihan, D., 2006. Transient activity in the human calcarine cortex during visual-mental imagery: an event-related fMRI study.
Klessinger, N., Szczerbinski, M., Varley, R., 2007. Algebra in a man with severe aphasia. Neuropsychologia 45, 1642–1648. https://doi.org/10.1016/j.neuropsychologia.2007.01.005.
Kosslyn, S.M., 2005. Mental images and the brain. Cogn. Neuropsychol. 22, 333–347. https://doi.org/10.1080/02643290442000130.
Mahon, B.Z., Caramazza, A., 2009. Concepts and categories: a cognitive neuropsychological perspective. Annu. Rev. Psychol. 60, 27–51. https://doi.org/10.1146/annurev.psych.60.110707.163532.
Maruyama, M., Pallier, C., Jobert, A., Sigman, M., Dehaene, S., 2012. The cortical representation of simple mathematical expressions. NeuroImage 61, 1444–1460. https://doi.org/10.1016/j.neuroimage.2012.04.020.
McMillan, C.T., Clark, R., Moore, P., Devita, C., Grossman, M., 2005. Neural basis for generalized quantifier comprehension. Neuropsychologia 43, 1729–1737. https://doi.org/10.1016/j.neuropsychologia.2005.02.012.
Monti, M.M., Osherson, D.N., Martinez, M.J., Parsons, L.M., 2007. Functional neuroanatomy of deductive inference: A language-independent distributed network. NeuroImage 37, 1005–1016. https://doi.org/10.1016/j.neuroimage.2007.04.069.
Monti, M.M., Parsons, L.M., Osherson, D.N., 2012. Thought beyond language: neural dissociation of algebra and natural language. Psychol. Sci. 23, 914–922. https://doi.org/10.1177/0956797612437427.
Nieder, A., Dehaene, S., 2009. Representation of number in the brain. Annu. Rev. Neurosci. 32, 185–208. https://doi.org/10.1146/annurev.neuro.051508.135550.
Pallier, C., Devauchelle, A.-D., Dehaene, S., 2011. Cortical representation of the constituent structure of sentences. Proc. Natl. Acad. Sci. Unit. States Am. 108, 2522–2527. https://doi.org/10.1073/pnas.1018711108.
Park, J., Hebrank, A., Polk, T.A., Park, D.C., 2012. Neural dissociation of number from letter recognition and its relationship to parietal numerical processing. J. Cognit. Neurosci. 24, 39–50.
Pica, P., Lemer, C., Izard, V., Dehaene, S., 2004. Exact and approximate arithmetic in an Amazonian indigene group. Science 306, 499–503. https://doi.org/10.1126/science.1102085.
Pinheiro-Chagas, P., Daitch, A., Parvizi, J., Dehaene, S., 2018. Brain Mechanisms of Arithmetic: A Crucial Role for Ventral Temporal Cortex. J. Cogn. Neurosci. 30, 1757–1772. https://doi.org/10.1162/jocn_a_01319.
Price, A.R., Bonner, M.F., Peelle, J.E., Grossman, M., 2015. Converging evidence for the neuroanatomic basis of combinatorial semantics in the Angular Gyrus. J. Neurosci. 35, 3276–3284. https://doi.org/10.1523/JNEUROSCI.3446-14.2015.
Shum, J., Hermes, D., Foster, B.L., Dastjerdi, M., Rangarajan, V., Winawer, J., Miller, K.J., Parvizi, J., 2013. A Brain Area for Visual Numerals. J. Neurosci. 33, 6709–6715. https://doi.org/10.1523/JNEUROSCI.4558-12.2013.
Troiani, V., Peelle, J.E., Clark, R., Grossman, M., 2009. Is it logical to count on quantifiers? Dissociable neural networks underlying numerical and logical quantifiers. Neuropsychologia 47, 104–111. https://doi.org/10.1016/j.neuropsychologia.2008.08.015.
Varley, R.A., Klessinger, N.J., Romanowski, C.A., Siegal, M., 2005. Agrammatic but numerate. Proc. Natl. Acad. Sci. U. S. A. 102, 3519–3524.
Wang, J., Conder, J.A., Blitzer, D.N., Shinkareva, S.V., 2010. Neural representation of abstract and concrete concepts: a meta-analysis of neuroimaging studies. Hum. Brain Mapp. 31, 1459–1468. https://doi.org/10.1002/hbm.20950.
Wei, W., Chen, C., Yang, T., Zhang, H., Zhou, X., 2014. Dissociated neural correlates of quantity processing of quantifiers, numbers, and numerosities: neural correlates of quantity processing. Hum. Brain Mapp. 35, 444–454. https://doi.org/10.1002/hbm.22190.
Xu, J., Moeller, S., Auerbach, E.J., Strupp, J., Smith, S.M., Feinberg, D.A., Yacoub, E., Uğurbil, K., 2013. Evaluation of slice accelerations using multiband echo planar imaging at 3 T. NeuroImage 83, 991–1001. https://doi.org/10.1016/j.neuroimage.2013.07.055.