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Neural basis of approximate number in congenital blindness

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ABSTRACT

Although humans are unique among animals in their ability to manipulate symbolic numbers, we share with other species an approximate number sense that allows us to estimate and compare the number of objects or events in a set, such as the number of apples in a tree. Our ability to discriminate the numerosity of two sets decreases as the ratio between them becomes smaller (e.g., 8 vs 16 items is harder to discriminate than 8 vs 32 items). The intraparietal sulcus (IPS) plays a key role in this numerical approximation. Neuronal populations within the IPS code for numerosity, with stimuli of different numerosities eliciting discriminable spatial patterns of activity. The developmental origins of these IPS number representations are not known. Here, we tested the hypothesis that representations of number in the IPS require visual experience with object sets, by working with individuals blind from birth. While undergoing fMRI, congenitally blind ($n = 17$) and blindfolded sighted ($n = 25$) participants judged which of two sequences of beeps was more numerous. In both sighted and blind individuals, patterns of activity in the IPS discriminated among different numerosities (4, 8, 16 vs 32), with better discrimination in the IPS of the blind group. In both groups, decoding performance decreased as the ratio between numerosities decreased (e.g., 8 vs 16 was less discriminable than 8 vs 32). These findings suggest that number representations in the IPS either have innate precursors, or that auditory or tactile experience with sets is sufficient for typical development.

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1. Introduction

Human adults possess the unique ability to perform mathematical operations over numerical symbols, but also share with other species and preverbal infants an evolutionarily ancient intuitive number sense (Agrillo, Dadda, & Bisazza,

2007; Brannon & Merritt, 2011; Dehaene, 2009; Dehaene & Cohen, 2007; Dehaene, Piazza, Pinel, & Cohen, 2003; Feigenson, Dehaene, & Spelke, 2004; Izard, Sann, Spelke, & Streri, 2009; Krusche, Uller, & Dicke, 2010; Nieder & Dehaene, 2009; Uller & Lewis, 2009; Viswanathan & Nieder, 2013; Xu & Spelke, 2000). Without counting, humans can estimate the approximate number of apples on a tree or geese in a flock.

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Crucially, numerical approximation is ratio-dependent—we are less accurate at discriminating 10 vs 12 (ratio 1.2) than 10 vs 20 (ratio 2) items, but similarly accurate at discriminating 10 vs 20 and 20 vs 40 items (both ratio 2) (Barth, Kanwisher, & Spelke, 2003; Feigenson et al., 2004; Huntley-Fenner & Cannon, 2000; Whalen, Gallistel, & Gelman, 1999; Xu & Spelke, 2000). This ratio-dependent signature arises from representations of number that are centered around the set's true cardinality, but whose variance increases with the set's numerosity (Feigenson et al., 2004; Gallistel & Gelman, 2000).

Numerical approximation depends on a fronto-parietal neural network of which the intraparietal sulcus (IPS) is a key node (Piazza, Pinel, Bihan, Dehaene, & Cedex, 2004; Piazza, Pinel, Le Bihan, & Dehaene, 2007). Intracranial recordings from the IPS of monkeys have uncovered neurons that are tuned to specific quantities. Each of these neurons fires most in response to its preferred number of objects (e.g., 4 dots) and fires less as quantities become more distant from its preferred numerosity (e.g., less for 3 or 5 dots and still less for 1 or 6) (Nieder, 2005, 2012; Nieder, Diester, & Tudusciuc, 2006; Nieder, Freedman, & Miller, 2002; Viswanathan & Nieder, 2013). Thus, more similar numerosities are represented by more overlapping neuronal populations (Nieder, 2005, 2012; Nieder et al., 2002, 2006; Viswanathan & Nieder, 2013).

In humans, different numerical magnitudes elicit different spatial patterns of IPS activity (Bluthe, De Smedt, & Op de Beeck, 2015; Cavdaroglu, Katz, & Knops, 2015; Eger et al., 2009; Harvey, Klein, Petridou, & Dumoulin, 2013; Harvey & Dumoulin, 2017; Lyons, Ansari, & Beilock, 2015). For example, sets of 4, 8, 16 or 32 dots evoke different patterns of IPS activity. A trained linear support vector machine (SVM) can use IPS activity patterns to predict which quantity a participant viewed on a given trial (Eger et al., 2009). Furthermore, IPS activity patterns for quantities exhibit ratio-dependency: quantities that differ by a smaller ratio (e.g., 4 and 8) evoke more similar neural patterns in the IPS than quantities that differ by a larger ratio (e.g., 4 and 16) (Eger et al., 2009). Together, these data support the idea that neuronal populations in the IPS code for numerical magnitude.

Open questions remain about the developmental origins of IPS approximate number representations. One possibility is that these representations develop as a result of visual experience with numerical sets. Like early visual features such as color, contrast, and orientation, number induces after-effects, suggesting that numerosity is a salient feature of visual scenes that is extracted early in visual processing (Burr & Ross, 2008; Ross, 2010). The IPS is located along the dorsal visual hierarchy and contains other visuo-spatial representations such as size, luminance, length, and angle (Borghesani et al., 2019; Fias, Lammertyn, Reynvoet, Dupont, & Orban, 2003, pp. 47–56; Pinel, Piazza, Le Bihan, & Dehaene, 2004). Neural networks trained with images of arrays containing different numbers of objects spontaneously develop representations of numerosity: “neurons” in the hidden layer of the neural network develop selectivity to number, akin to number-neurons found in the IPS of monkeys (Stoianov & Zorzi, 2012). According to one hypothesis, neurons in the IPS may analogously develop

representations of quantities as a result of accumulated experience with visual sets.

On the other hand, there are reasons to think that approximate number representations in the IPS may be modality-independent. First, from infancy, humans can extract numerical information from sounds and compare approximate quantities across visual and auditory modalities (Gallace, Tan, & Spence, 2006, 2008; Barth et al., 2003; Barth, La Mont, Lipton, & Spelke, 2005; Feigenson, 2011; Izard et al., 2009; Piazza, Mechelli, Price, & Butterworth, 2006; Riggs et al., 2006; Tokita, Ashitani, & Ishiguchi, 2013). For example, 3-month old infants recognize an equivalence between four tones and four visually presented dots (Izard, Dehaene-Lambertz, & Dehaene, 2008). Second, in adults, the IPS responds not only to visual but also to auditory numerical sets and even to symbolic numbers (Cavdaroglu et al., 2015; Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003; Piazza et al., 2006). Furthermore, the IPS of monkeys contains neurons with tuning to visual, auditory quantities or both (Nieder, 2012). However, it remains possible that visual input “bootstraps” representations of numerosity into the IPS. Once in place, IPS number representations could then become accessible through other sensory modalities.

In the present work, we asked whether visual experience is necessary for the development of approximate number representations in the IPS by investigating the neural basis of numerical approximation in congenitally blind individuals. Recent studies have shown that congenitally blind adults recruit the IPS during symbolic math calculation ($7-2 = X$) and that, as in sighted adults, activity in the IPS scales with equation difficulty (Amalric, Denghien, & Dehaene, 2017; Crollen et al., 2019; Kanjlia, Lane, Feigenson, & Bedny, 2016). However, previous studies suggest that partially non-overlapping neural populations in the IPS respond to approximate and symbolic number (Bluthe et al., 2015; Eger et al., 2009; Lyons et al., 2015). Thus, whether the IPS is also involved in non-symbolic numerical approximation in blind individuals remains unknown. Behaviorally, congenitally blind individuals estimate and discriminate auditory quantities with similar or even better accuracy than sighted individuals, but the neural basis of this ability has not been investigated (Castronovo & Delvenne, 2013; Castronovo & Seron, 2007; Kanjlia, Feigenson, & Bedny, 2018).

The goal of the current study was to test the hypothesis that neural populations in the IPS code for numerosity in individuals who are blind from birth. Congenitally blind and sighted participants listened to sequences of 4, 8, 16, or 32 tones and judged whether a subsequent sequence was more or less numerous. Counting was prevented by jittering the duration of individual tones within each sequence. We then trained a machine-learning classifier on IPS activity patterns elicited by listening to sequences of 4, 8, 16 or 32 tones, and asked whether the classifier could predict the number of tones a participant had heard on a given trial. Furthermore, we investigated whether the IPS represents quantities with similar precision in congenitally blind and sighted individuals by testing whether numerical ratio had a similar effect on classification accuracy across the two groups.

A second goal of the study was to ask whether deafferented ‘visual’ cortices of congenitally blind individuals develop sensitivity to approximate number. Previous studies have found that, in addition to the IPS, congenitally blind individuals recruit parts of dorsal occipital cortex, specifically the right middle occipital gyrus (rMOG), during symbolic math calculation (Amalric et al., 2017; Crollen et al., 2019; Kanjlia et al., 2016). Like the IPS, the math-responsive area of the ‘visual’ cortex in blind participants is sensitive to equation difficulty (Kanjlia et al., 2016). This math-responsive ‘visual’ region has strong functional connectivity with the IPS both in sighted and blind participants, and one hypothesis is that this connectivity enables this part of ‘visual’ cortex to develop numerical representations in blindness (Bedny, 2017; Kanjlia et al., 2016). Whether this part of the ‘visual’ cortex enhances its responses to approximate, as well as to symbolic number in blindness remains an open question.

2. Materials & methods

We report how we determined our sample size, all data exclusions, all exclusion criteria, whether exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. Participants

Seventeen congenitally blind (12 female, mean age 49 years, SD = 16, min = 29, max = 73) and twenty-six age-matched sighted control participants (16 female, mean age 43 years, SD = 16, min = 19, max = 67; $t(40) = -1.18$, $p = .25$) contributed data to the final sample (Table 1). Four additional participants

were tested but excluded from the final sample because further screening revealed a history of some vision (1 blind participant), because they fell asleep during the experiment (2 sighted participants), or because they did not complete the experiment (1 sighted participant). All exclusion criteria were established prior to data analysis. Behavioral accuracy (excluding no-response trials) for the remaining participants was within 3 standard deviations of their group's mean. Our sample size should be sufficient to detect potential differences between blind and sighted groups as prior studies observed group differences in neural responses to numerical information with similar sample sizes (e.g., 17 congenitally blind and 19 sighted participants) (Kanjlia et al., 2016, 2018). Blind participants were blind from birth, had at most minimal light perception, and their blindness was due to pathology of the eyes or optic nerve, not brain damage. All participants reported having no cognitive or neurological disorders. Participants provided written informed consent and were compensated \$30 per hour for their time. All experimental procedures were approved by the Johns Hopkins Medicine Institutional Review Board and are in accordance with the principles stated in the Declaration of Helsinki.

2.2. fMRI task

Participants completed an auditory approximate number comparison task that was adapted from a visual approximate number comparison task designed by Eger et al. (2009). On each trial, participants first heard a tap (.1 s) to indicate the trial was starting. This was followed (after .2 s) by a sample sequence of 4, 8, 16, or 32 beeps. After a 6-s delay, they heard a second, test sequence of beeps whose numerosity differed from the first sequence by a ratio of 2 (e.g., sample sequence: 8

Table 1 – Participant demographic information.

Subject Number	Gender	Age	Cause of Blindness	Light Perception	Education
1	M	50	LCA	None	JD
2	F	35	ROP	Minimal	BA
3	F	38	LCA	Minimal	MA
4	M	31	Anophthalmia	None	SC
5	F	42	ROP	None	MA
6	F	67	ROP	None	MA
7	M	47	Unknown	Minimal	BA
8	F	29	ROP	Minimal	MA
9	F	64	ROP	None	HS
10	F	73	ROP	Minimal	HS
11	M	46	Unknown	None	JD
12	M	70	ROP	Minimal	HS
13	F	31	Detached Optic Nerve	None	SC
14	F	65	RP	Minimal	BA
15	F	29	LCA	Minimal	BA
16	F	64	ROP	None	JD
17	F	55	Cataracts, Microphthalmia	None	PhD
Average					
Blind (n=17)	12 F	49 (SD=16)	–	–	BA
Sighted (n=26)	16 F	44 (SD=17)	–	–	BA
LCA = Leber Congenital Amaurosis; ROP = Retinopathy of Prematurity; RP = Retinitis Pigmentosa; BA = Bachelor of Arts; HS = High School; JD = Juris Doctor; MA = Master of Arts; SC = Some College. Bold = group averages.					

beeps; test sequence: 4 or 16 beeps). The test sequence never exceeded 32 beeps and was never smaller than 4 beeps. After a second tap (.1 s; to indicate the end of the second stimulus), participants had 4 s to indicate whether the second sequence was more or less numerous than the first by pressing one of two buttons. Each trial was followed by a 6-s rest period. Participants were instructed to try not to count the beeps but rather to estimate the number of beeps. Individual beep durations and inter-beep intervals were jittered in order to produce less predictable, arrhythmic sequences, and thereby to interfere with counting strategies (Cordes, Gallistel, Gelman, & Latham, 2007; Kanjlia et al., 2018). The audio frequency of each individual beep was 440 Hz.

All analyses focus on neural activity during the first, sample sequence and the subsequent delay period. Activity associated with the sample sequence and delay period were modeled together because participants did not have complete information about the number of beeps in the sequence until the end of the sequence. We therefore reasoned that representations of the sample numerosity would be formed and maintained in memory during the delay period. Test sequences were presented for the purpose of the behavioral task and were not of interest for fMRI analysis (Eger et al., 2009).

To ensure that quantities were not coded on the basis of low-level stimulus features, sample sequences were matched across numerosities either on total sequence duration or individual element duration. In the total-duration matched condition (TM), the sample sequence for every numerosity was 3 s long, with larger numerosities (e.g., 32) playing faster than smaller numerosities (e.g., 4) (see [Supplementary Table 1](#) for detailed timing information). In the element-duration matched condition (EM), each beep in the sample sequence played for ~.2 s, thereby matching numerosities in pacing but not overall duration.

For the first five sighted participants tested, the parameters for controlling stimuli in the total-duration matched condition were slightly differently than the parameters used for the remaining sighted and blind participants. Rather than ensuring that the total sound duration in a trial was matched across trials of the same numerosity, the total sequence duration (sum of beep durations and sum of inter-beep intervals) was matched. Stimuli in the element-matched duration condition were controlled in the same way as the remaining sighted and blind participants. [Supplementary Table 1](#) summarizes the specific timing (e.g., beep durations and inter-beep intervals) used for each number and match condition combination. Results obtained when excluding these participants were found to be indistinguishable from results including them (see [Supplementary Results](#)). Therefore all analysis, except those shown in [Figs. 3–4](#), include the entire sighted group. The analysis in [Fig. 3](#) involved separating trials by match condition (TM vs EM) to compare classifier performance when total-sound duration was correlated with numerosity versus when it was matched across quantities (see [Decoding Procedure](#)). The analyses in [Fig. 4](#) involved training a classifier on quantities that were correlated with total-sound duration (EM) and testing on quantities that were matched on total-sound duration (TM), and vice versa (see [Decoding Procedure](#)). The first 5 sighted participants are excluded from these analyses because the

total-sound duration was correlated with numerosity in both match conditions.

To further discourage participants from using duration as a cue to numerosity, the duration of test sequences was either congruent or incongruent with respect to the numerical ratio between the sample and test sequence. On congruent trials, test sequences that were more numerous than sample sequences played twice as long, and test sequences that were less numerous played half as long (e.g., sample sequence: 8 beeps, 3 s; test sequence: 16 beeps, 6 s), and vice versa on incongruent trials. Note, however, that neural responses to the second, test sequences were not analyzed.

Participants were not informed about the range of stimulus numerosities, the match conditions, or the manipulation of congruence. However, they were told that the speed and duration of the beeps might vary, and were instructed to ignore these features and attend to beep number. Rather than trial-by-trial feedback, participants were given a score (percent correct) at the end of each run of the task.

The experiment was comprised of 8 runs containing 32 trials each. Each of the 8 sample conditions (4 numerosities by 2 match conditions) appeared on 4 trials per run. The 8 sample conditions were arranged in a Latin Square design such that each condition followed and preceded every other condition an equal number of times over the course of the experiment.

Both blind and sighted participants were blind-folded throughout. Code for the behavioral task as well as anonymized behavioral data can be found on Github (https://github.com/NPDL/ANS_MVPA). None of the study procedures or analyses were pre-registered.

2.3. Data acquisition and univariate analysis

MRI data were collected using a 3T Phillips scanner. Structural images were T1-weighted and were collected in 150 axial slices (1-mm isotropic voxels). Functional data sensitive to BOLD contrast were collected in 36 axial slices (340 volumes; $2.4 \times 2.4 \times 3$ mm voxels; FOV $192 \times 107.5 \times 171.79$ mm; repetition time 2 s). Six dummy scans were conducted at the beginning of each run but were not saved. MRI data were analyzed using *Freesurfer*, *FSL*, *HCP* workbench and custom in-house software (Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012; Marcus et al., 2013; Smith et al., 2004; Tange, 2011).

fMRI data were motion corrected, high-pass filtered (128 sec) and mapped to the cortical surface using the standard *Freesurfer* pipeline (normalized to fsaverage). fMRI data were then smoothed with a 6 mm FWHM Gaussian kernel on the surface and prewhitened to remove temporal autocorrelation.

Data were then analyzed using a general linear model, which included eight regressors of interest—one for each sample condition (4 numerosities (4, 8, 16, 32) by 2 duration matching conditions (total-duration matched and element-duration matched)) that modeled the first stimulus and delay periods together. Resulting z-statistic maps for each of the 8 regressors of interest for each run were used for MVPA. Z-statistic maps were computed by *FSL* and represent the parameter estimate (i.e., beta) scaled by the error in the estimate (Misaki, Kim, Bandettini, & Kriegeskorte, 2010;

Pollmann, Zinke, Baumgartner, Geringswald, & Hanke, 2014). The test sequence, response period, and the instruction taps (prior to first stimulus and prior to second stimulus) were modeled separately and were not included in any of the reported analyses. We also separately modeled and excluded trials in which the participant failed to respond.

Code for fMRI analyses can be found on Github (<https://github.com/NPDL/NPDL-scripts> and https://github.com/NPDL/ANS_MVPA). fMRI data are not currently permitted to be shared under the study protocol registered with the Johns Hopkins University Institutional Review Board. Please contact the corresponding author to inquire about data availability. Data will be shared if IRB permission has been obtained and the participants have consented to have their data shared.

2.4. Multi-voxel pattern analysis (MVPA)

2.4.1. ROI definition

We used MVPA to ask whether the following regions of interest (ROIs) contained a spatial code for auditory numerosities: left and right IPS, right middle occipital gyrus (rMOG) within visual cortex, and left and right early auditory cortex (A1) (see [Supplementary Fig. 1](#) for ROI images and sizes). Group-specific IPS ROIs were defined based on a math equations > sentences contrast from a separate published dataset (see [Kanjlia et al., 2016](#) for details). Briefly, in that experiment, participants heard pairs of math equations each with a variable x , and had to judge whether x had the same value in two equations. In the control condition, they judged whether a pair of sentences, one in the passive voice and one in the active voice, had the same meaning. The math > sentences contrast in this experiment identified bilateral math-responsive IPS ROIs in both sighted and blind individuals. Since feature number can affect MVPA results, thresholds were set to define ROIs of approximately equal size across groups ($p < .01$, uncorrected for sighted and $p < .001$, uncorrected for congenitally blind) (see [Supplementary Fig. 1](#) for ROI images and sizes). To ensure that the ROI selection procedure did not affect results, we also conducted the same analysis in independent anatomically-defined IPS parcels ([Destrieux, Fischl, Dale, & Halgren, 2010](#)) ([Supplementary Fig. 1](#)). The results of these analyses did not differ, and are reported in the Supplementary Materials.

Additionally, responses to symbolic math equations were previously observed in the rMOG of the ‘visual’ cortex in the blind group only ([Kanjlia et al., 2016](#)). The math-responsive ‘visual’ cortex ROI (rMOG) was defined as the cluster within the right visual cortex that responded more to math equations than sentences in congenitally blind > sighted individuals in the previous study described above (right middle occipital gyrus, rMOG; $p < .01$, uncorrected) ([Kanjlia et al., 2016](#)) ([Supplementary Fig. 1](#)). To ask whether the auditory cortex was sensitive to numerosity, we used a previously published auditory cortex ROI that includes anatomically defined posteromedial, middle, and anterolateral Heschl’s gyrus ([Norman-Haignere, Kanwisher, & McDermott, 2013](#)) ([Supplementary Fig. 1](#)).

2.4.2. Decoding procedure

We used a linear support vector machine (LinearCSVMC in pyMVPA) to decode numerosity (4 vs 8, 4 vs 16, 4 vs 32, 8 vs 16, 8

vs 32, 16 vs 32) based on patterns of activity within each ROI using a leave-one-run-out cross-validation procedure, in which the classifier was trained on data from all but one run and then tested on data from the left-out run (pyMVPA toolbox, [Hanke et al., 2009](#)). Prior to training, activity in each voxel was z-scored across all 8 conditions within a run. The procedure was repeated iteratively until every run was left out, and classification accuracy was averaged over cross-validation folds. For the primary analyses, we used a two-way classification procedure in which the classifier was trained and tested on one pair of quantities at a time (e.g., 4 vs 8). This process was repeated for every pair of quantities. To evaluate overall classification performance, we averaged classification accuracy over all 6 numerosity pairs. To verify that results did not depend on classification procedure, we repeated all analyses using a 4-way decoding procedure in which a classifier was trained and tested on all four quantities at once. Two-way and 4-way classification produced similar results. The results of 4-way classification were also used to generate confusion matrices that depict patterns of misclassification in each ROI. One-sample Welch’s t -tests were used to test the statistical significance of classification accuracy against chance (chance = .50 for two-way classification and chance = .25 for four-way classification) within each ROI. In the two-way classification analysis, we corrected for multiple comparisons across the 3 ROIs (IPS, A1 and rMOG) and 2 groups (blind and sighted) using a Bonferroni correction (α of .05/6 tests = Bonferroni-adjusted $\alpha_{(.05)}$ of .008). Repeated-measures ANOVAs were used to compare classification accuracy across groups and hemispheres.

For the first analysis, the classifier was trained on data from both match conditions from all but one run (for 2-way analysis: 2 quantities $\times$ 2 match conditions $\times$ 7 runs = 28 vectors of neural activity; for 4-way analysis: 4 quantities $\times$ 2 match conditions $\times$ 7 runs = 56 vectors) and tested on data from both match conditions from the left-out run (for 2-way analysis: 2 quantities $\times$ 2 match conditions $\times$ 1 run = 4 vectors; for 4-way analysis: 4 quantities $\times$ 2 match conditions $\times$ 1 run = 8 vectors). Results were averaged across match conditions (total- and element-duration matched) in this analysis.

As discussed in the Introduction, quantities that differ by a smaller ratio are known to be harder to distinguish behaviorally, and to activate more overlapping neuronal populations. Thus, we predicted that regions that code for numerosity would demonstrate more overlapping neural patterns (i.e., lower classification accuracy) for quantities that differ by smaller ratios, relative to larger ratios. We compared classification performance across ratios by collapsing over pairs of numerosities that differed by the same ratio (e.g., 4 vs 8 and 8 vs 16 are both ratio 2). Note that ratio was determined between sample quantities from different trials, not between sample and test sequences within the same trial (as the ratio between sample and test in all trials was always 2). For example, if trial 1 consisted of 4 beeps (sample) followed by 8 beeps (test) and trial 2 consisted of 16 beeps (sample) followed by 8 beeps (test), MVPA was conducted on the neural activity associated with the samples 4 and 16, whose ratio would be 4. Ratio effects were statistically tested using a repeated-measures ANOVA with ratio as a covariate and hemisphere and group as categorical factors (hemisphere was not included as a factor in analyses involving the rMOG).

In the analyses described above, we averaged classification accuracy across quantities from both match conditions (total-duration matched and element-duration matched). Next we looked at classification accuracy for each match condition separately, in order to test the hypothesis that decoding performance in the auditory cortex is more sensitive to low-level features than decoding in the IPS or rMOG. Specifically, we predicted that decoding would be better in the auditory cortex on element-duration matched trials, in which numerosity was confounded with total amount of sound. The first five sighted subjects who had slightly different matching parameters were not included in this analysis since the relationship between numerosity and low-level features differed for these participants.

To further test for the presence of abstract numerosity coding in the IPS, auditory cortex and rMOG, we probed the classifier's ability to generalize across match conditions (Harvey, Dumoulin, Fracasso, & Paul, 2020). In the above analyses, the classifier was trained on data from both total- and element-duration matched trials. To test for generalization, we trained a two-way classifier on data from the total-duration matched condition (TM) and tested on element-duration matched (EM) data, and vice versa (Eger et al., 2009). If classifier success depends on tracking low-level features correlated with numerosity, such as total amount of sound or temporal rate, it should fail to generalize when a different set of low-level features correlates with numerosity. For example, if a classifier that is trained on element-duration matched (EM) trials is picking up on neural variation related to total amount of sound, it should fail to classify beep sequences that are different in numerosity but matched on total duration (total-duration matched, TM, trials). By contrast, successful performance would indicate sensitivity to numerosity per se. Note that in this cross-match condition analysis, there are two directions of training and testing—training on element-duration matched and testing on total-duration matched (train-EM, test-TM) and vice versa (train-TM, test-EM). The main analyses report the performance of the classifier averaged across the two directions of training and testing, but for completeness, we also report classification accuracy from the two directions of training and testing separately (in Supplementary Results). As above, since for the first five sighted subjects total-sound duration was correlated with numerosity in both element- and total-duration matched conditions, their data were not included in this cross-match condition decoding analysis.

Finally, we used a searchlight analysis to ask where quantities could be decoded across the entire cortex. For each participant and pair of numerosities, MVPA was conducted within circular searchlight regions of 10 mm radius across the cortical surface (Chen et al., 2011; Cichy, Khosla, Pantazis, Torralba, & Oliva, 2016; Valdés-Sosa et al., 2020). Our searchlight ROIs with 10 mm radii included 150.46 vertices on average, which similar to the number of features (i.e., voxels or vertices) used in prior numerosity decoding studies as well as other MVPA studies (Bulthé, De Smedt, & Op de Beeck, 2014; Chen et al., 2011; Connolly et al., 2016; Eger et al., 2009; Hanke et al., 2009; Long et al., 2015; Pennock, Schmidt, Zorbeck, & Blankenburg, 2021, pp. 1–12). One of the advantages of surface-based analyses is the reduced risk of including non-gray matter voxels, even with a searchlight radius of 10 mm

(Hanke et al., 2009). Classification accuracy across all 6 numerosity pairs was averaged within each searchlight. Accuracy maps were logit-transformed and then statistically compared across participants within a group and across groups using random-effects GLM analyses. Searchlight results were corrected for multiple comparisons using a permutation-based cluster-correction procedure with a cluster-forming threshold of $p < .01$ and an alpha level of .05 (see Kanjlia, Pant, & Bedny, 2018 for details) (Winkler, Ridgway, Webster, Smith, & Nichols, 2014). Searchlight results are presented with a voxel-wise threshold of $p < .001$ (Fig. 5).

3. Results

3.1. Behavioral results

Behaviorally, the sighted and congenitally blind groups performed well above chance and no differently from each other (sighted: 86.38%, $SD = 9.72\%$; congenitally blind: 88.17%, $SD = 1.10\%$; $t(41) = .56$, $p = .58$). Note that although sample quantities 4 and 32 were always paired with 8 and 16, respectively, participants were not more accurate on these trials (Supplementary Table 2).

3.2. Enhanced sensitivity to auditory numerosity in IPS, but not A1 or rMOG, of blind group

In the IPS of congenitally blind and sighted individuals, quantities (i.e., 4, 8, 16 and 32) were decoded above chance (left and right IPS average: blind 63.24% ($SD = 6.68$), one-sample t -test $t(16) = 8.17$, $p < .001$; sighted 56.80% ($SD = 6.50$), one-sample t -test $t(25) = 5.35$, $p < .001$; Bonferroni-adjusted $\alpha_{(.05)} = .008$). Decoding in the IPS was significantly better in the congenitally blind than the sighted group (hemisphere by group repeated-measures ANOVA; main effect of group: $F(1,41) = 9.86$, $p = .003$; main effect of hemisphere: $F(1,41) = 2.23$, $p = .14$; hemisphere by group interaction: $F(1,41) = .22$, $p = .64$) (Fig. 1; classification accuracy for each pair of quantities separately is shown in Supplementary Table 2). The results were unchanged when using an anatomically defined IPS ROI (see Supplementary Materials).

Auditory quantities were also discriminable in early auditory cortex (A1) of congenitally blind and sighted adults (left and right A1 average: blind 66.44% ($SD = 4.39$), one-sample t -test: $t(16) = 15.43$, $p < .001$; sighted 66.29% ($SD = 5.34$), one-sample t -test: $t(25) = 15.55$, $p < .001$; Bonferroni-adjusted $\alpha_{(.05)} = .008$). There was no difference between groups in A1 (hemisphere by group repeated-measures ANOVA; main effect of group: $F(1,41) = .01$, $p = .92$; main effect of hemisphere: $F(1,41) = .004$, $p = .95$; hemisphere by group interaction: $F(1,41) = .13$, $p = .72$) (Fig. 1; classification accuracy for each pair separately shown in Supplementary Table 3).

Previous work found that regions in the right dorsal 'visual' cortex (e.g., right middle occipital gyrus, rMOG) are recruited during symbolic math calculation in congenitally blind individuals (Amalric et al., 2017; Crollen et al., 2019; Kanjlia et al., 2016). Here we report that in this same 'visual' cortex region (rMOG), non-symbolic auditory numerosities were successfully decoded in both the blind and sighted groups (blind rMOG:

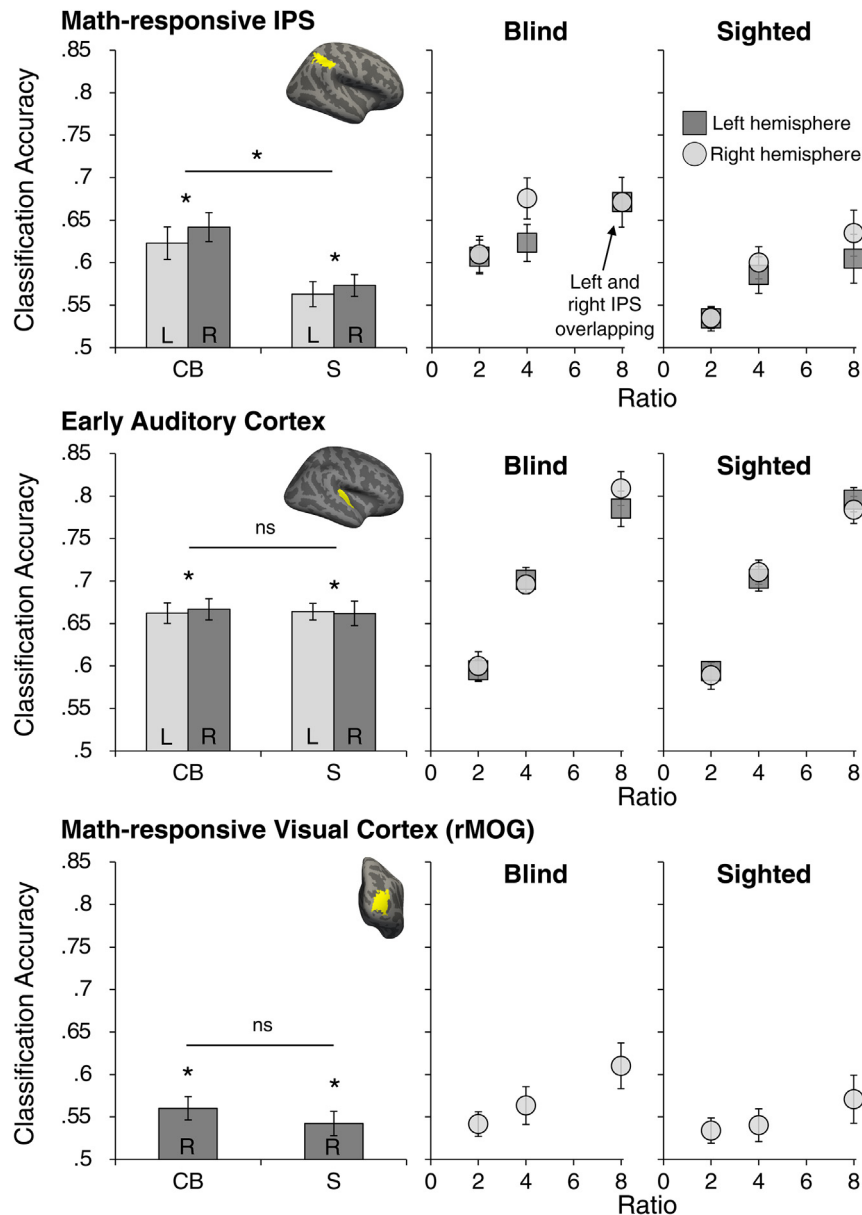


Fig. 1 – MVPA Classification accuracy in IPS, auditory cortex and rMOG. Linear SVM accuracy for classifying neural patterns in the left and right IPS (top panel), auditory cortex (middle panel) and rMOG (bottom panel). Right hemisphere ROIs shown in each panel (ROI shown for IPS is from sighted group; see [Supplementary Fig. 1](#) for IPS ROIs in each group separately). Classification accuracy was averaged across all numerosity pairs in bar graphs and is averaged across all numerosity pairs of the same ratio in scatter plots.

56.04% (SD = 5.66), one-sample t-test: $t(16) = 4.40$, $p < .001$; sighted rMOG: 54.23% (SD = 7.31), one-sample t-test: $t(25) = 2.95$, $p = .007$; Bonferroni-adjusted $\alpha_{(.05)} = .008$. Decoding accuracy in the rMOG was not different across groups (two-sample, two-tailed t-test comparing blind vs sighted: $t(40) = .91$, $p = .37$) ([Fig. 1](#); classification accuracy for each pair separately shown in [Supplementary Table 3](#)).

In the analyses described above, classification accuracy was averaged over match conditions (total-duration matched and element-duration matched). Next, we compared classification accuracy separately for each match condition to test the hypothesis that the auditory cortex is more sensitive than the IPS

and rMOG to the total amount of sound in the stimulus. If so, classification in the auditory cortex should be better on element-duration matched than total-duration matched trials. Consistent with this prediction, in the auditory cortex, classification accuracy was significantly better on element-duration matched trials (match condition by hemisphere by group repeated-measures ANOVA; main effect of match condition: $F(1,36) = 135.68$, $p < .001$; no other significant effects, see [Supplementary Results](#) for details) ([Fig. 2](#)). By contrast, classification accuracy in the IPS and rMOG was not sensitive to match condition (main effect of match condition in IPS: $F(1,36) = 2.04$, $p = .16$; main effect of group in IPS: $F(1,36) = 8.54$, $p = .006$;

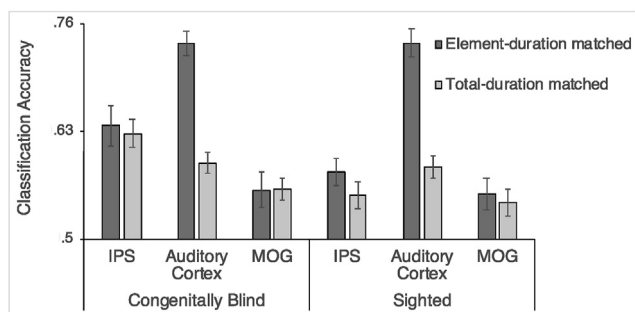


Fig. 2 – Effect of total sound duration on MVPA classification accuracy. Classification accuracy performance shown separately for total-duration and element-duration matched conditions. Classification accuracy is averaged across left and right hemispheres for IPS and auditory cortex ROIs. Error bars represent standard error of the mean.

match condition by group repeated-measures ANOVA in rMOG; main effect of match condition: $F(1,36) = .12$, $p = .74$; no other significant effects, see Supplementary Materials for details) (Fig. 2).

Direct comparison of the auditory cortex to the IPS revealed a significant match condition by ROI interaction (match condition by hemisphere by ROI by group repeated-measures ANOVA; main effect of match condition: $F(1,36) = 104.92$, $p < .001$; match condition by ROI interaction: $F(1,36) = 37.81$, $p < .001$; main effect of ROI: $F(1,36) = 44.60$, $p < .001$; ROI by group interaction: $F(1,36) = 9.68$, $p = .004$; no other significant effects, see Supplementary Results for details) (Fig. 2). Similarly, direct comparison of the right auditory cortex and rMOG revealed a significant match condition by ROI interaction (match condition by ROI by group repeated-measures ANOVA; main effect of match condition: $F(1,36) = 44.75$, $p < .001$; match condition by ROI interaction: $F(1,36) = 47.69$, $p < .001$; main effect of ROI: $F(1,36) = 73.28$, $p < .001$; no other significant effects, see Supplementary Results for details). These results suggest that numerosity coding is more dependent on the total amount of sound in the auditory cortex as compared to IPS and rMOG in blind and sighted adults alike.

All results reported above held when held using 4-way classification (see Fig. 3 and Supplementary Fig. 3 for confusion matrices and Supplementary Results for details). In the IPS, auditory cortex, and rMOG, the classifier performed significantly above chance (higher values along the diagonal than off the diagonal) and was sensitive to match condition in the auditory cortex but not in the IPS or rMOG (see Supplementary Results).

3.3. Ratio dependent sensitivity to numerosity in IPS, A1 and rMOG of sighted and blind adults

A key signature of numerosity estimation is ratio dependent performance—quantities that differ by larger ratios (8 vs 16 as opposed to 8 vs 12) are more discriminable both behaviorally and neurally. Consistent with this idea, we found that

quantities that differed by a larger ratio were discriminated with higher accuracy in the IPS, A1 and rMOG of both groups (ratio by hemisphere by group repeated-measures ANOVAs; main effect of ratio in IPS: $F(1,41) = 15.82$, $p < .001$; A1: $F(1,41) = 489.14$, $p < .001$; ratio by group repeated-measures ANOVA in rMOG; main effect of ratio: $F(1,41) = 5.48$, $p = .02$; see Supplementary Results for details) (Fig. 1). The effect of ratio was similar across groups in all three ROIs (ratio by group interaction in IPS: $F(1,41) = .31$, $p = .58$; A1: $F(1,41) = .06$, $p = .80$; rMOG: $F(1,41) = .49$, $p = .49$; see Supplementary Results for details). Ratio-dependent classification was also observed when the classification procedure was performed using a 4-way classification procedure (see Fig. 3 and Supplementary Results for details).

3.4. Abstract numerosity coding: generalization of classification across match conditions

In the above analyses, the classifier was trained on both element- and total-duration matched quantities. To further test for the presence of abstract numerosity coding, we tested the classifiers ability to generalize across match conditions by training it with quantities from the total-duration matched condition (TM) and testing it on quantities from the element-duration matched (EM) condition (train-TM, test-EM), and vice versa (train-EM, test-TM).

Cross-match condition classification accuracy was significant in the IPS and A1 but not in the rMOG (left and right IPS average; blind: 56.27% (SD = 5.74), one-sample t-test: $t(16) = 4.50$, $p < .001$; sighted: 53.87% (SD = 5.05), $t(20) = 3.51$, $p = .002$; left and right A1 average; blind: 56.80% (SD = 6.49%), $t(16) = 4.32$, $p < .001$; sighted: 56.91% (SD = 4.69), $t(20) = 6.75$, $p < .001$; right MOG; blind: 51.38% (SD = 4.97), $t(16) = 1.15$, $p = .27$; sighted: 51.46% (SD = 5.37), $t(20) = 1.25$, $p = .23$; Bonferroni-adjusted $\alpha_{(.05)} = .008$) (Fig. 4). There were no effects of group or hemisphere in any of the ROIs (see Supplementary Results). These results suggest that both the IPS and A1 code for numerosity above and beyond low-level auditory features.

Interestingly, classification accuracy was better when training on total-duration matched trials and testing on element-duration matched trials than vice versa and this effect of training/testing direction was larger in A1 than in the other ROIs (see Supplementary Fig. 4 and Supplementary Results for details). Finally, four-way cross-match condition classification produced similar results (see Supplementary Results).

3.5. Whole-cortex searchlight analyses of auditory numerosity decoding

We conducted MVPA in 10-mm searchlights across the entire cortex. In addition to the IPS and auditory cortex, searchlight analyses revealed successful decoding of auditory quantities in bilateral dorsolateral and medial prefrontal cortices in both congenitally blind and sighted groups (Fig. 5). Direct comparison of searchlight results across congenitally blind and sighted groups did not yield any significant differences (Fig. 5; Supplementary Table 4).

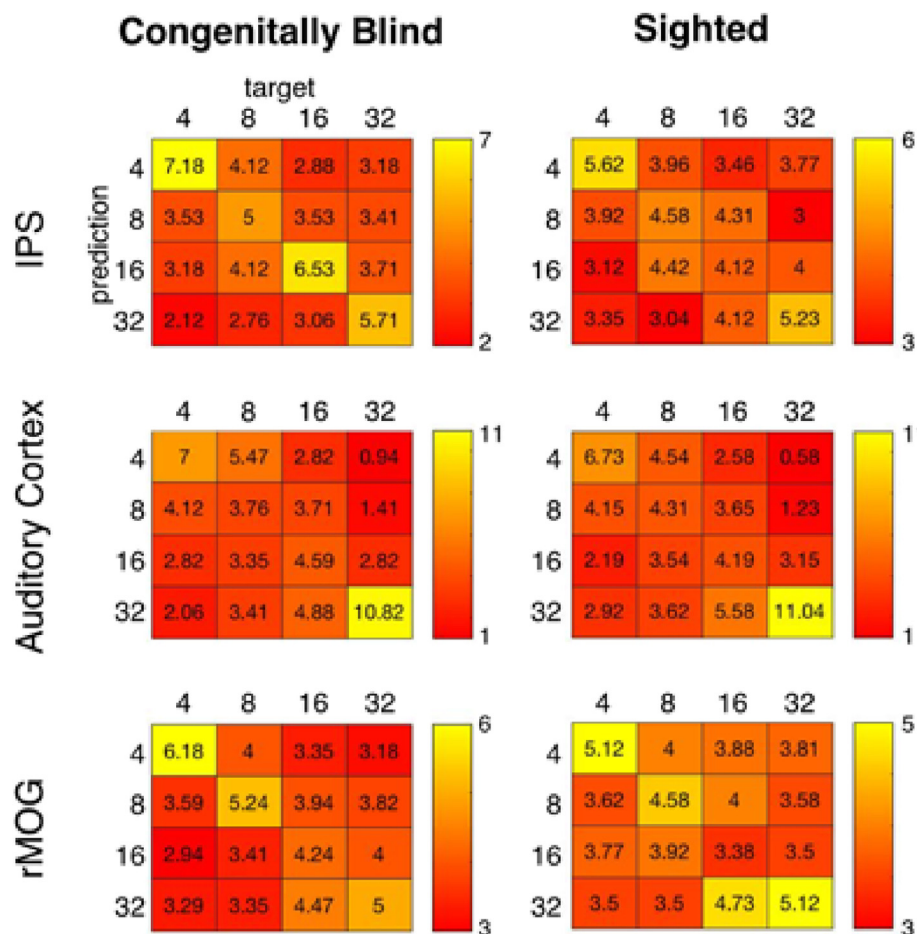


Fig. 3 – Confusion matrices from 4-way MVPA classification. Results of MVPA when the classifier was trained and tested on all four quantities at once. In each matrix, columns represent targets and rows represent classifier predictions. Numbers inside cells indicate number of trials (averaged across participants and hemispheres) classified as each quantity. Confusion matrices for each match condition separately are shown in [Supplementary Fig. 3](#).

4. Discussion

4.1. Preserved ratio-dependent cortical representation of auditory numerosity in blindness

Sensitivity to ratio is a key signature of quantity discrimination behavior. The larger the ratio between two quantities, whether represented by sets of dots or sequences of tones, the better they are discriminated (Barth et al., 2003; Eger et al., 2009; Feigenson et al., 2004; Huntley-Fenner & Cannon, 2000; Odic, Libertus, Feigenson, & Halberda, 2013; Piazza et al., 2007; Tokita et al., 2013; Whalen et al., 1999; Xu & Spelke, 2000). Previous studies have found that the IPS of monkeys and humans likewise codes visual numerosity in a ratio-dependent manner that parallels performance (Nieder & Miller, 2004; Piazza et al., 2007; Pinel et al., 2004).

Here we report that quantities of auditory tones can also be decoded from spatial patterns of activity within the human IPS in a ratio-dependent manner: sequences of tones differing by a larger ratio (e.g., 8 vs 16 as opposed to 8 vs 12) elicited more non-overlapping neural patterns in the IPS. Moreover, the IPS was sensitive to numerosity, even when low-level

auditory features, such as average rate of beeps and duration were controlled. The IPS displayed a similar neural signature of a given quantity (e.g., 8), whether that quantity was correlated with the overall amount of sound in the sequence or the rate of individual tones within it.

Importantly, we find that ratio-dependent IPS responses to auditory quantities are present in people who are blind from birth as well as those who are sighted. This finding is consistent with behavioral studies that show preserved signatures of numerical reasoning, such as ratio-dependent quantity discrimination, in congenital blindness (Castronovo & Delvenne, 2013; Castronovo & Seron, 2007; Kanjlia et al., 2018). Together these studies suggest that visual experience is not required to establish approximate number representations in the IPS.

The early emergence of approximate number representations in children also suggests that experience is not required to establish representations of approximate number. Infants are able to estimate quantities just hours after birth (Izard et al., 2009). Studies using functional Near-Infrared Spectroscopy (fNIRS) observe parietal responses to numerosity as early as 6 months of age, and fMRI studies have identified IPS responses to numerosity in 3–4 year-old-children (Cantlon, Brannon, Carter, & Pelphrey, 2006; Hyde, Boas, Blair, &

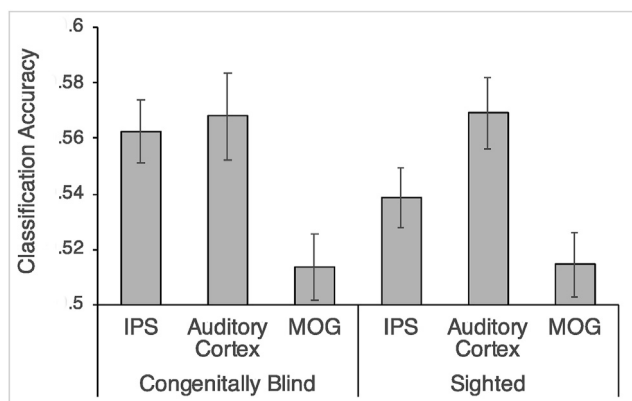


Fig. 4 – Cross-match condition MVPA classification accuracy. Classification accuracy in IPS, auditory cortex and rMOG after training on quantities from total-duration matched (TM) condition and testing on quantities from element-duration matched (EM) condition (train-TM, test-EM) and vice versa (train-EM, test-TM). Classification accuracy is averaged across left and right hemispheres and direction of training/testing (train-EM-test-TM and train-TM-test-EM). Error bars represent standard error of the mean.

Carey, 2010; Kersey & Cantlon, 2017). These studies suggest that representations of quantity in the IPS are established very early in development. One possibility is that these representations are innately specified (Feigenson et al., 2004). Alternatively, either visual or auditory experience with sets may be sufficient to establish IPS representations of number.

4.2. Enhanced decoding of auditory numerosity in IPS of blind adults

In blind as compared to sighted people, different auditory quantities produced more distinctive neural patterns in the

IPS. In the current study, enhanced numerosity decoding in the IPS was not accompanied by better behavioral numerosity discrimination in the blind group. However, the behavioral task in the current study was very easy (i.e., quantities always differed by a ratio of 2) and therefore might not have been sensitive to group differences. Previous behavioral studies have found better performance in congenitally blind than sighted individuals on some estimation tasks but not others, such as when producing specific numbers of tones, footsteps, or finger taps (Castronovo & Delvenne, 2013; Castronovo & Seron, 2007; Kanjlia et al., 2018). One study found that blind individuals were particularly better than sighted individuals at approximating larger quantities (Castronovo & Seron, 2007). In future work, it would be interesting to explore the precise differences in neural numerosity coding between blind and sighted groups by testing a wider range of quantities and ratios. In addition, the behavioral consequences of enhanced neural numerosity coding in blindness should also be investigated in future studies.

Blindness-related enhancements have been observed on other high-level auditory tasks, such as sound localization and pitch discrimination (Lessard, Paré, Lepore, & Lassonde, 1998; Röder et al., 1999; Voss et al., 2004; Wan, Wood, Reutens, & Wilson, 2010; Watkins et al., 2013). In addition, experiences other than blindness, such as the acquisition of number words and experience with math education, have been shown to improve the precision of approximate number representations (Elliott, Feigenson, Halberda, & Libertus, 2019; Lindskog, Winman, & Juslin, 2014; Piazza, Pica, Izard, Spelke, & Dehaene, 2013; Pica, Lemer, Izard, & Dehaene, 2004). These findings suggest that it is possible that better numerosity coding in the IPS of blind individuals is associated with enhancements or changes in some aspects of numerical approximation.

Better numerosity decoding in the IPS of blind individuals could result from the IPS becoming more tuned to sequential auditory quantities. Electrophysiological studies in monkeys suggest that the IPS contains both modality-specific and modality-invariant number neurons. The majority of IPS

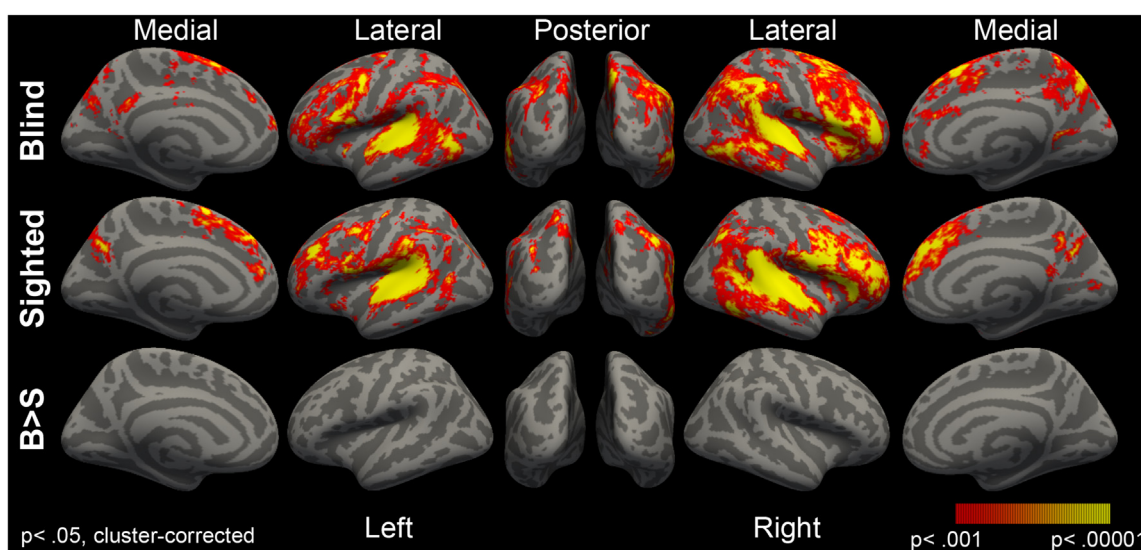


Fig. 5 – Whole-cortex searchlight results. MVPA classification conducted in searchlights of 10 mm radius across entire cortex ($p < .01$ cluster-forming threshold, cluster-corrected $p < .05$, vertex-wise threshold $p < .001$).

number neurons preferentially respond to numerosity in one modality (auditory or visual) or format (sequential or simultaneous), although some IPS neurons are tuned to a specific number of events regardless of format (Nieder, 2012; Nieder et al., 2006). Blindness might increase the proportion of number-responsive neurons in the IPS preferring auditory or sequentially presented input or may selectively improve the tuning of these neurons as a result of habitual reliance on audition for numerical information. In other words, experience may tune the IPS to represent the types of stimuli that are most frequently used to extract numerical information, such as auditory input in the case of blindness.

Interestingly, although we also found sensitivity to numerosities in early auditory cortex and a dorsal visual region (rMOG) (discussed in detail below), there were no differences between the blind and sighted groups in either of these other cortical areas. Enhanced auditory numerosity coding in the IPS of blind individuals in the absence of changes in the auditory cortex and rMOG suggests that plasticity for auditory estimation in blindness 1) occurs at higher levels of processing than early sensory regions and 2) is not related to reorganization of deafferented visual cortices.

4.3. Numerosity decoding in prefrontal and inferior temporal cortices

Searchlight analyses revealed that, in addition to the IPS and auditory cortex, numerosities could be decoded in dorsolateral and medial prefrontal cortices as well as inferior temporal/lateral occipital cortices, in both blind and sighted individuals. These regions have previously been implicated in numerical thinking (Amalric & Dehaene, 2016, 2019; Cavdaroglu et al., 2015; Kawashima et al., 2004; Kersey & Cantlon, 2017; Zago et al., 2008). For instance, quantity coding has previously been observed in prefrontal cortices in both humans and monkeys (Nieder et al., 2002; Piazza et al., 2007). The present results suggest that the involvement of these regions is modality-independent and does not require vision.

The present findings are particularly interesting in the case of the inferior temporal cortex—the locus of the putative, modality-specific “visual number form area” (Hermes et al., 2017; Shum et al., 2013; Yeo, Pollack, Merkley, Ansari, & Price, 2020). While this functional region was originally thought to respond selectively to visual numerals, recent evidence implicates it in numerical processing more generally (Grotheer, Jeska, & Grill-Spector, 2018; Hermes et al., 2017). The present data support this account and suggest that regions in inferior temporal cortex may be involved in encoding non-visual, non-symbolic numerosities independent of visual experience.

4.4. Numerosity coding in the auditory cortex

We found that neural patterns in the early auditory cortex of both sighted and congenitally blind people were sensitive to numerosity. This finding is consistent with a prior study showing auditory quantity decoding in auditory cortices of

sighted individuals (Cavdaroglu et al., 2015). We found that, relative to the IPS, auditory cortex activity during a number estimation task was more influenced by low-level auditory features. When trained on neural patterns from both total-duration and element-duration matched quantities, the classifier was significantly better at discriminating quantities that were correlated with total amount of sound (element-duration matched quantities) in the auditory cortex but not in the IPS. This result suggests that, when trained on auditory quantities with a mixture of low-level features (total-sound duration and average rate), the auditory cortex is more likely to hone in on total sound duration as a cue for quantity.

Nevertheless, even in early auditory cortex, representations of numerosity were present above and beyond sensitivity to low-level auditory features correlated with numerosity. A classifier was able to generalize neural patterns associated with numerosities with one set of low-level features to quantities with a different set of low-level features. This finding is consistent with a growing body of work suggesting that numerical information is present in early sensory and sensorimotor cortices (Anobile, Arrighi, Castaldi, & Burr, 2020; Castaldi, Piazza, Dehaene, Vignaud, & Eger, 2019). Visual quantities are coded throughout the dorsal visual pathway, from V1 to the IPS, even when controlling for correlated visual features, such as density and total surface area (Castaldi et al., 2019). In the sensorimotor domain, neurons in early somatosensory cortices of monkeys selectively respond to a particular number of movements in a sequence of motor actions (Sawamura, Shima, & Tanji, 2010). Together with the present findings, these results suggest that representations of numerosity are present not only in higher-level cortices such as the IPS, but in early sensory cortices as well.

4.5. Numerosity coding in dorsal ‘visual’ cortices

We find that the approximate number of auditory tones can be decoded based on patterns of activity in the right middle occipital gyrus (rMOG), a region in the dorsal visual pathway, in both congenitally blind and blindfolded sighted individuals. Decoding in the rMOG was ratio-dependent and, like the IPS and unlike the auditory cortex, the rMOG showed little sensitivity to low-level auditory features. The rMOG is functionally and anatomically connected with the IPS, in both sighted and blind people (Bray, Almas, Arnold, Iaria, & MacQueen, 2015; Bray, Arnold, Iaria, & MacQueen, 2013; Caspers & Zilles, 2018; Greenberg et al., 2012; Kanjlia et al., 2018; Richter et al., 2019; Tong, 2003; Uddin et al., 2010; Vinette & Bray, 2015). This connectivity could convey number-related information to the rMOG, even during a purely auditory task. The sighted participants in the current study were blindfolded, reducing the influence of bottom-up visual input on the rMOG and likely enhancing top-down influence.

Previous studies have found that dorsal occipital cortex, and the rMOG in particular, responds to symbolic number in blind but not sighted individuals (Amalric et al., 2017; Crollen et al., 2019; Kanjlia et al., 2016). By contrast, in the current study, we did not observe enhanced numerosity decoding in

blind relative to sighted participants in the rMOG. This is particularly interesting since auditory numerosity decoding was enhanced in blind participants in the IPS. Although, notably, the rMOG ROI was smaller than the IPS ROI and numerosity decoding was generally weaker in the rMOG than the IPS, potentially giving us less power to detect group differences in this region.

Setting potential issues of power aside, why blindness enhances ‘visual’ cortex responses to symbolic number more so than approximate number remains an open question. Prior studies of symbolic number used univariate methods, and it is possible that blindness has a greater effect on univariate responses than multivariate patterns. An alternative intriguing but speculative hypothesis is that functional plasticity is more pronounced for evolutionarily modern cognitive functions, such as math and language, than for evolutionarily ancient functions, such as non-symbolic numerical approximation that may have more evolutionarily entrenched neuroanatomical specifications. According to this view, higher-level cognitive functions that are more evolutionarily and ontogenetically recent are more apt to take over deafferented cortices that have not evolved for the invading cognitive domain. Finally, in addition to numerical estimation, mathematical reasoning involves many other cognitive processes, including spatial reasoning, working memory and attention, that are supported by the IPS, as well as other cortical structures (Anobile, Stievano, & Burr, 2013; Blair & Razza, 2007; Dehaene et al., 2003; Kong et al., 2005; Menon, Rivera, White, Glover, & Reiss, 2000; Skudlarek & Brannon, 2017; Wilkey & Price, 2019; Zago et al., 2001, 2008; Zhou et al., 2007). Visual cortex recruitment during mathematical reasoning in blind individuals may well reflect these other processes rather than uniquely number-related processes. Whatever the reason, it is interesting that not all ‘cross-modal’ responses observed in sighted participants are enhanced in blindness.

In summary, our results suggest that visual experience is not required to establish typical, ratio-dependent neural representations of approximate number. In blind and sighted adults alike, a fronto-parietal network, that includes the IPS, as well as early auditory cortices and parts of the dorsal visual network, encodes auditory quantities in a ratio-dependent manner. Numerosity is represented above and beyond low-level auditory features, although activity in early auditory cortex is more influenced by these features. Interestingly, blindness appears to heighten sensitivity to auditory numerical information in the IPS, but not in the early auditory cortex or dorsal visual areas (i.e., rMOG). This finding suggests that, in the absence of vision, the parietal cortex may become more specialized for processing approximate numerical information derived from auditory input.

Open practices

The study in this article earned an Open Materials badge for transparent practices. Materials for this study can be found at <https://github.com/NPDL/NPDL-scripts> and https://github.com/NPDL/ANS_MVPA.

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Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2021.06.004>.

REFERENCES

- Agrillo, C., Dadda, M., & Bisazza, A. (2007). Quantity discrimination in female mosquitofish. *Animal Cognition*, 10, 63–70.
- Amalric, M., & Dehaene, S. (2016). Origins of the brain networks for advanced mathematics in expert mathematicians. *Proceedings of the National Academy of Sciences*, 113(18), 4909–4917.
- Amalric, M., & Dehaene, S. (2019). A distinct cortical network for mathematical knowledge in the human brain. *Neuroimage*, 189(January), 19–31.
- Amalric, M., Denghien, I., & Dehaene, S. (2017). On the role of visual experience in mathematical development: Evidence from blind mathematicians. *Developmental Cognitive Neuroscience*, 30, 314–323.
- Anobile, G., Arrighi, R., Castaldi, E., & Burr, D. C. (2020). A sensorimotor numerosity system. *Trends in Cognitive Sciences*, 2105(xx), 1–13.
- Anobile, G., Stievano, P., & Burr, D. C. (2013). Visual sustained attention and numerosity sensitivity correlate with math achievement in children. *Journal of Experimental Child Psychology*, 116(2), 380–391.
- Barth, H., Kanwisher, N., & Spelke, E. (2003). The construction of large number representations in adults. *Cognition*, 86(3), 201–221.
- Barth, H., La Mont, K., Lipton, J., & Spelke, E. S. (2005). Abstract number and arithmetic in preschool children. *Proceedings of the National Academy of Sciences*, 102(39), 14116–14121.
- Bedny, M. (2017). Evidence from blindness for a cognitively pluripotent cortex. *Trends in Cognitive Sciences*, 21(9), 637–648.
- Blair, C., & Razza, R. P. (2007). Relating effortful control, executive function, and false belief understanding to emerging math and literacy ability in kindergarten. *Child Development*, 78(2), 647–663.
- Bluthe, J., De Smedt, B., & Op de Beeck, H. P. (2015). Visual number beats abstract numerical magnitude: Format-dependent representation of Arabic digits and dot patterns in human parietal cortex. *Journal of Cognitive Neuroscience*, 27(7), 1376–1387.

- Borghesani, V., de Hevia, M. D., Viarouge, A., Pinheiro-Chagas, P., Eger, E., & Piazza, M. (2019). Processing number and length in the parietal cortex: Sharing resources, not a common code. *Cortex*, 114, 17–27.
- Brannon, E. M., & Merritt, D. J. (2011). Evolutionary foundations of the approximate number system. In *Space, Time and Number in the Brain*, 207–224.
- Bray, S., Almas, R., Arnold, A. E. G. F., Iaria, G., & MacQueen, G. (2015). Intraparietal sulcus activity and functional connectivity supporting spatial working memory manipulation. *Cerebral Cortex*, 25(5), 1252–1264.
- Bray, S., Arnold, A. E. G. F., Iaria, G., & MacQueen, G. (2013). Structural connectivity of visuotopic intraparietal sulcus. *Neuroimage*, 82, 137–145.
- Bulthé, J., De Smedt, B., & Op de Beeck, H. P. (2014). Format-dependent representations of symbolic and non-symbolic numbers in the human cortex as revealed by multi-voxel pattern analyses. *Neuroimage*, 87, 311–322.
- Burr, D., & Ross, J. (2008). A visual sense of number. *Current Biology*, 18(6), 425–428.
- Cantlon, J. F., Brannon, E. M., Carter, E. J., & Pelphrey, K. A. (2006). Functional imaging of numerical processing in adults and 4-year-old children. *Plos Biology*, 4(5), e125.
- Caspers, S., & Zilles, K. (2018). Microarchitecture and connectivity of the parietal lobe. In *Handbook of clinical neurology* (1st ed., Vol. 151). Elsevier B.V.
- Castaldi, E., Piazza, M., Dehaene, S., Vignaud, A., & Eger, E. (2019). Attentional amplification of neural codes for number independent of other quantities along the dorsal visual stream. *ELife*, 8, 1–26.
- Castronovo, J., & Delvenne, J. F. (2013). Superior numerical abilities following early visual deprivation. *Cortex*, 49(5), 1435–1440.
- Castronovo, J., & Seron, X. (2007). Numerical estimation in blind subjects: Evidence of the impact of blindness and its following experience. *Journal of Experimental Psychology. Human Perception and Performance*, 33(5), 1089–1106.
- Cavdaroglu, S., Katz, C., & Knops, A. (2015). Dissociating estimation from comparison and response eliminates parietal involvement in sequential numerosity perception. *Neuroimage*, 116, 135–148.
- Chen, Y., Namburi, P., Elliott, L. T., Heinze, J., Soon, C. S., Chee, M. W. L., et al. (2011). Cortical surface-based searchlight decoding. *Neuroimage*, 56(2), 582–592.
- Gichy, R. M., Khosla, A., Pantazis, D., Torralba, A., & Oliva, A. (2016). Comparison of deep neural networks to spatio-temporal cortical dynamics of human visual object recognition reveals hierarchical correspondence. *Scientific Reports*, 6(June), 1–13.
- Connolly, A. C., Sha, L., Guntupalli, J. S., Oosterhof, N., Halchenko, Y. O., Nastase, S. A., et al. (2016). How the human brain represents perceived dangerousness or “predacity” of animals. *The Journal of Neuroscience*, 36(19), 5373–5384.
- Cordes, S., Gallistel, C. R., Gelman, R., & Latham, P. (2007). Nonverbal arithmetic in humans: Light from noise. *Perception & Psychophysics*, 69(7), 1185–1203.
- Crollen, V., Lazzouni, L., Rezk, M., Bellemare, A., Lepore, F., Noël, M. P., et al. (2019). Recruitment of the occipital cortex by arithmetic processing follows computational bias in the congenitally blind. *Neuroimage*, 186, 549–556.
- Dale, A. M., Fischl, B., & Sereno, M. I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage*, 9(2), 179–194.
- Dehaene, S. (2009). Origins of mathematical intuitions: The case of arithmetic. *Annals of the New York Academy of Sciences*, 1156, 232–259.
- Dehaene, S., & Cohen, L. (2007). Cultural recycling of cortical maps. *Neuron*, 56(2), 384–398.
- Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology*, 20(3–6), 487–506.
- Destrieux, C., Fischl, B., Dale, A., & Halgren, E. (2010). Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *Neuroimage*, 53(1), 1–15.
- Eger, E., Michel, V., Thirion, B., Amadon, A., Dehaene, S., & Kleinschmidt, A. (2009). Deciphering cortical number coding from human brain activity patterns. *Current Biology*, 19(19), 1608–1615.
- Eger, E., Sterzer, P., Russ, M. O., Giraud, A., & Kleinschmidt, A. (2003). A supramodal number representation in human intraparietal cortex. *Neuron*, 37(4), 719–725.
- Elliott, L., Feigenson, L., Halberda, J., & Libertus, M. E. (2019). Bidirectional, longitudinal associations between math ability and approximate number system precision in childhood. *Journal of Cognition and Development*, 20(1), 56–74.
- Feigenson, L. (2011). Predicting sights from sounds: 6-month-olds’ intermodal numerical abilities. *Journal of Experimental Child Psychology*, 110(3), 347–361.
- Feigenson, L., Dehaene, S., & Spelke, E. (2004). Core systems of number. *Trends in Cognitive Sciences*, 8(7), 307–314.
- Fias, W., Lammertyn, J., Reynvoet, B., Dupont, P., & Orban, G. A. (2003). Parietal representation of symbolic and nonsymbolic magnitude.
- Fischl, B., Sereno, M. I., & Dale, A. M. (1999). Cortical surface-based analysis II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage*, 9(2), 195–207.
- Gallace, A., Tan, H. Z., & Spence, C. (2006). Numerosity judgments for tactile stimuli distributed over the body surface. *Perception*, 35(2), 247–266.
- Gallace, A., Tan, H. Z., & Spence, C. (2008). Can tactile stimuli be subitised? An unresolved controversy within the literature on numerosity judgments. *Perception*, 37(5), 782–800.
- Gallistel, C. R., & Gelman, R. (2000). Non-verbal numerical cognition: From reals to integers. *Trends in Cognitive Sciences*, 4(2), 59–65.
- Greenberg, A. S., Verstynen, T., Chiu, Y. C., Yantis, S., Schneider, W., & Behrmann, M. (2012). Visuotopic cortical connectivity underlying attention revealed with white-matter tractography. *Journal of Neuroscience*, 32(8), 2773–2782.
- Grotheer, M., Jeska, B., & Grill-Spector, K. (2018). A preference for mathematical processing outweighs the selectivity for Arabic numbers in the inferior temporal gyrus. *Neuroimage*, 175(March), 188–200.
- Hanke, M., Halchenko, Y. O., Sederberg, P. B., Hanson, S. J., Haxby, J. V., & Pollmann, S. (2009). PyMVPA: A python toolbox for multivariate pattern analysis of fMRI data. *Neuroinformatics*, 7(1), 37–53.
- Harvey, B. M., & Dumoulin, S. O. (2017). A network of topographic numerosity maps in human association cortex. *Nature Human Behaviour*, 1(2), Article 0036.
- Harvey, B. M., Dumoulin, S. O., Fracasso, A., & Paul, J. M. (2020). A network of topographic maps in human association cortex hierarchically transforms visual timing-selective responses. *Current Biology*, 30(8), 1424–1434. e6.
- Harvey, B. M., Klein, B. P., Petridou, N., & Dumoulin, S. O. (2013). Topographic representation of numerosity in the human parietal cortex. *Science*, 341(6150), 1123–1126.
- Hermes, D., Rangarajan, V., Foster, B. L., King, J. R., Kasikci, I., Miller, K. J., et al. (2017). Electrophysiological responses in the ventral temporal cortex during reading of numerals and calculation. *Cerebral Cortex*, 27(1), 567–575.
- Huntley-Fenner, G., & Cannon, E. (2000). Preschoolers’ magnitude comparisons are mediated by a preverbal analog mechanism. *Psychological Science*, 11(2), 147–152.

- 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(2), 647–652.
- Izard, V., Dehaene-Lambertz, G., & Dehaene, S. (2008). Distinct cerebral pathways for object identity and number in human infants. *Plos Biology*, 6(2), e11.
- Izard, V., Sann, C., Spelke, E. S., & Streri, A. (2009). Newborn infants perceive abstract numbers. *Proceedings of the National Academy of Sciences*, 106(25), 10382–10385.
- Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., & Smith, S. M. (2012). Fsl. *NeuroImage*, 62(2), 782–790.
- Kanjlia, S., Lane, C., Feigenson, L., & Bedny, M. (2016). Absence of visual experience modifies the neural basis of numerical thinking. *Proceedings of the National Academy of Sciences*, 113(40), 11172–11177.
- Kanjlia, S., Feigenson, L., & Bedny, M. (2018). Numerical cognition is resilient to dramatic changes in early sensory experience. *Cognition*, 179, 111–120.
- Kanjlia, S., Pant, R., & Bedny, M. (2018). Sensitive period for cognitive repurposing of human visual cortex. *Cerebral Cortex*, bhy280.
- Kawashima, R., Taira, M., Okita, K., Inoue, K., Tajima, N., Yoshida, H., et al. (2004). A functional MRI study of simple arithmetic - a comparison between children and adults. *Cognitive Brain Research*, 18, 225–231.
- Kersey, A. J., & Cantlon, J. F. (2017). Neural tuning to numerosity relates to perceptual tuning in 3- to 6-year-old children. *Journal of Neuroscience*, 37(3), 512–522.
- Kong, J., Wang, C., Kwong, K., Vangel, M., Chua, E., & Gollub, R. (2005). The neural substrate of arithmetic operations and procedure complexity. *Cognitive Brain Research*, 22, 397–405.
- Krusche, P., Uller, C., & Dicke, U. (2010). Quantity discrimination in salamanders. *The Journal of Experimental Biology*, 213(11), 1822–1828.
- Lessard, N., Paré, M., Lepore, F., & Lassonde, M. (1998). Early-blind human subjects localize sound sources better than sighted subjects. *Nature*, 395(6699), 278–280.
- Lindskog, M., Winman, A., & Juslin, P. (2014). The association between higher education and approximate number system acuity. *Frontiers in Psychology*, 5(MAY), 1–10.
- Long, S., Haxby, J. V., Abdi, H., Guntupalli, J. S., Oosterhof, N. N., Halchenko, Y. O., et al. (2015). The animacy continuum in the human ventral vision pathway. *Journal of Cognitive Neuroscience*, 27(4), 665–678.
- Lyons, I. M., Ansari, D., & Beilock, S. L. (2015). Qualitatively different coding of symbolic and nonsymbolic numbers in the human brain. *Human Brain Mapping*, 36(2), 475–488.
- Marcus, D. S., Harms, M. P., Snyder, A. Z., Jenkinson, M., Wilson, J. A., Glasser, M. F., et al. (2013). Human Connectome Project informatics: Quality control, database services, and data visualization. *Neuroimage*, 80, 202–219.
- Menon, V., Rivera, S. M., White, C. D., Glover, G. H., & Reiss, A. L. (2000). Dissociating prefrontal and parietal cortex activation during arithmetic processing. *Neuroimage*, 12(4), 357–365.
- Misaki, M., Kim, Y., Bandettini, P. a., & Kriegeskorte, N. (2010). Comparison of multivariate classifiers and response normalizations for pattern-information fMRI. *Neuroimage*, 53(1), 103–118.
- Nieder, A. (2005). Counting on neurons: The neurobiology of numerical competence. *Nature Reviews. Neuroscience*, 6(3), 177–190.
- Nieder, A. (2012). Supramodal numerosity selectivity of neurons in primate prefrontal and posterior parietal cortices. *Proceedings of the National Academy of Sciences*, 109(29), 11860–11865.
- Nieder, A., & Dehaene, S. (2009). Representation of number in the brain. *Annual Review of Neuroscience*, 32, 185–208.
- Nieder, A., Diester, I., & Tudusciuc, O. (2006). Temporal and spatial enumeration processes in the primate parietal cortex. *Science*, 313(5792), 1431–1435.
- Nieder, A., Freedman, D. J., & Miller, E. K. (2002). Representation of the quantity of visual items in the primate prefrontal cortex. *Science*, 297(5587), 1708–1711.
- Nieder, A., & Miller, E. K. (2004). A parieto-frontal network for visual numerical information in the monkey. *Proceedings of the National Academy of Sciences of the United States of America*, 101(19), 7457–7462.
- Norman-Haignere, S., Kanwisher, N., & McDermott, J. H. (2013). Cortical pitch regions in humans respond primarily to resolved harmonics and are located in specific tonotopic regions of anterior auditory cortex. *Journal of Neuroscience*, 33(50), 19451–19469.
- Odic, D., Libertus, M. E., Feigenson, L., & Halberda, J. (2013). Developmental change in the acuity of approximate number and area representations. *Developmental Psychology*, 49(6), 1103–1112.
- Pennock, I. M. L., Schmidt, T. T., Zorbek, D., & Blankenburg, F. (2021). Representation of visual numerosity information during working memory in humans : An fMRI decoding study, (February).
- Piazza, M., Mechelli, A., Price, C. J., & Butterworth, B. (2006). Exact and approximate judgements of visual and auditory numerosity: An fMRI study. *Brain Research*, 1106(1), 177–188.
- Piazza, M., Pica, P., Izard, V., Spelke, E. S., & Dehaene, S. (2013). Education enhances the acuity of the nonverbal approximate number system. *Psychological Science*, 24(6), 1037–1043.
- Piazza, M., Pinel, P., Le Bihan, D., Dehaene, S., & Cedex, O. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron*, 44(3), 547–555.
- Piazza, M., Pinel, P., Le Bihan, D., & Dehaene, S. (2007). A magnitude code common to numerosities and number symbols in human intraparietal cortex. *Neuron*, 53(2), 293–305.
- Pica, P., Lemer, C., Izard, V., & Dehaene, S. (2004). Exact and approximate arithmetic in an Amazonian indigene group. *Science*, 306(5695), 499–503.
- Pinel, P., Piazza, M., Le Bihan, D., & Dehaene, S. (2004). Distributed and overlapping cerebral representations of number, size, and luminance during comparative judgments. *Neuron*, 41(6), 983–993.
- Pollmann, S., Zinke, W., Baumgartner, F., Geringswald, F., & Hanke, M. (2014). The right temporo-parietal junction contributes to visual feature binding. *Neuroimage*, 101, 289–297.
- Richter, M., Amunts, K., Mohlberg, H., Bludau, S., Eickhoff, S. B., Zilles, K., et al. (2019). Cytoarchitectonic segregation of human posterior intraparietal and adjacent parieto-occipital sulcus and its relation to visuomotor and cognitive functions. *Cerebral Cortex*, 29(3), 1305–1327.
- Riggs, K. J., Ferrand, L., Lancelin, D., Fryziel, L., Simpson, A., Xii, P., et al. (2006). Subitizing in Tactile Perception, 17(4), 271–272.
- Röder, B., Teder-Sälejärvi, W., Sterr, A., Rösler, F., Hillyard, S. A., & Neville, H. J. (1999). Improved auditory spatial tuning in blind humans. *Nature*, 400(6740), 162–166.
- Ross, J. (2010). Vision senses number directly. *Journal of Vision*, 10(2), 1–8.
- Sawamura, H., Shima, K., & Tanji, J. (2010). Deficits in action selection based on numerical information after inactivation of the posterior parietal cortex in monkeys. *Journal of Neurophysiology*, 104(2), 902–910.
- Shum, J., Hermes, D., Foster, B. L., Dastjerdi, M., Rangarajan, V., Winawer, J., et al. (2013). A brain area for visual numerals. *The Journal of Neuroscience*, 33(16), 6709–6715.
- Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage*, 23, S208–S219.

- Stoianov, I., & Zorzi, M. (2012). Emergence of a “visual number sense” in hierarchical generative models. *Nature Neuroscience*, 15(2), 194–196.
- Szkudlarek, E., & Brannon, E. M. (2017). Does the approximate number system serve as a foundation for symbolic mathematics? *Language Learning and Development*, 13(2), 171–190.
- Tange, O. (2011). Gnu parallel—the command-line power tool. *The USENIX Magazine*, 36(1), 42–47.
- Tokita, M., Ashitani, Y., & Ishiguchi, A. (2013). Is approximate numerical judgment truly modality-independent? Visual, auditory, and cross-modal comparisons. *Attention, Perception & Psychophysics*, 75(8), 1852–1861.
- Tong, F. (2003). Primary visual cortex and visual awareness. *Nature Reviews. Neuroscience*, 4(3), 219–229.
- Uddin, L. Q., Supekar, K., Amin, H., Rykhlevskaia, E., Nguyen, D. A., Greicius, M. D., et al. (2010). Dissociable connectivity within human angular gyrus and intraparietal sulcus: Evidence from functional and structural connectivity. *Cerebral Cortex*, 20(11), 2636–2646.
- Uller, C., & Lewis, J. (2009). Horses (*Equus caballus*) select the greater of two quantities in small numerical contrasts. *Animal Cognition*, 12, 733–738.
- Valdés-Sosa, M., Ontivero-Ortega, M., Iglesias-Fuster, J., Lage-Castellanos, A., Gong, J., Luo, C., et al. (2020). Objects seen as scenes: Neural circuitry for attending whole or parts. *Neuroimage*, 210(December 2019).
- Vinette, S. A., & Bray, S. (2015). Variation in functional connectivity along anterior-to-posterior intraparietal sulcus, and relationship with age across late childhood and adolescence. *Developmental Cognitive Neuroscience*, 13, 32–42.
- Viswanathan, P., & Nieder, A. (2013). Neuronal correlates of a visual “sense of number” in primate parietal and prefrontal cortices. *Proceedings of the National Academy of Sciences*, 110(27), 11187–11192.
- Voss, P., Lassonde, M., Gougoux, F., Fortin, M., Guillemot, J.-P., & Lepore, F. (2004). Early- and late-onset blind individuals show supra-normal auditory abilities in far-space. *Current Biology*, 14(19), 1734–1738.
- Wan, C. Y., Wood, A. G., Reutens, D. C., & Wilson, S. J. (2010). Early but not late-blindness leads to enhanced auditory perception. *Neuropsychologia*, 48(1), 344–348.
- Watkins, K. E., Shakespeare, T. J., O'Donoghue, M. C., Alexander, I., Ragge, N., Cowey, A., et al. (2013). Early auditory processing in area V5/MT+ of the congenitally blind brain. *The Journal of Neuroscience*, 33(46), 18242–18246.
- Whalen, J., Gallistel, C. R., & Gelman, R. (1999). Nonverbal counting in humans: The psychophysics of number representation. *Psychological Science*, 10(2), 130–137.
- Wilkey, E. D., & Price, G. R. (2019). Attention to number: The convergence of numerical magnitude processing, attention, and mathematics in the inferior frontal gyrus. *Human Brain Mapping*, 40(3), 928–943.
- Winkler, A. M., Ridgway, G. R., Webster, M. A., Smith, S. M., & Nichols, T. E. (2014). Permutation inference for the general linear model. *Neuroimage*, 92, 381–397.
- Xu, F., & Spelke, E. S. (2000). Large number discrimination in 6-month-old infants. *Cognition*, 74(1), B1–B11.
- Yeo, D. J., Pollack, C., Merkley, R., Ansari, D., & Price, G. R. (2020). The “inferior temporal numeral area” distinguishes numerals from other character categories during passive viewing: A representational similarity analysis. *Neuroimage*, 214(March), 116716.
- Zago, L., Pesenti, M., Mellet, E., Crivello, F., Mazoyer, B., & Tzourio-Mazoyer, N. (2001). Neural correlates of simple and complex mental calculation. *Neuroimage*, 13(2), 314–327.
- Zago, L., Petit, L., Turbelin, M. R., Andersson, F., Vigneau, M., & Tzourio-Mazoyer, N. (2008). How verbal and spatial manipulation networks contribute to calculation: An fMRI study. *Neuropsychologia*, 46, 2403–2414.
- Zhou, X., Chen, C., Zang, Y., Dong, Q., Chen, C., Qiao, S., et al. (2007). Dissociated brain organization for single-digit addition and multiplication. *Neuroimage*, 35(2), 871–880.