A fast and child-friendly localizer for the identification of ITG-math based on its preference for mathematical processing

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Abstract

The visual number form area (here referred to as ITG-math) has gained recent attention as a neural substrate of mathematical cognition. However, research on this region has been hindered by difficulties identifying it and its precise function hence remains debated. THere we aimed to: 1) Provide an efficient and child-friendly localizer for the region and 2) explore the impact of different tasks and stimuli on its responses. In the developed localizer, participants are presented with digits and UFOs, while performing a 1-back task either on stimulus numerosity or on stimulus color. We collected two sessions of the localizer from 17 healthy adults. From the localizer data, we could identify ITG-math based on higher responses in the numerosity than the color task in 92% of the participants, whereas contrasting digits with UFOs lead to selective responses in only 32% of the participants. Accordingly, in independent data, ITG-math showed a task preference, but no stimulus preference. Multivariate analyses further revealed task encoding, and a combination of task and stimulus encoding, in the left and right ITG-math, respectively. Our work facilitates further research on ITG-math and suggests that the role of ITG-math in mathematical cognition goes beyond the visual encoding of digits.

Keywords: inferior temporal gyrus, mathematical cognition, numbers, vision, visual number form area

1.Introduction

Mathematical abilities are critical in our daily lives, yet our current understanding of the neural substrates of these abilities is limited. A functional region located in the posterior inferior temporal gyrus (pITG) has gained attention recently for its preference to visually presented digits (i.e. Arabic Numerals) over other visual stimuli (Pinel et al. 1999; Roux et al. 2008; Cui et al. 2013; Shum et al. 2013; Hermes et al. 2015; Amalric and Dehaene 2016; Daitch et al. 2016; M. Grotheer et al. 2016). Applying transcranial magnetic stimulation to this area causes a significant impairment in the identification of digits (Mareike Grotheer et al. 2016), suggesting a causal role in digit processing. Due to its preference for digits over other stimulus categories, this functional region is often referred to as the *Visual Number Form Area* (VNFA) or ITG-numbers.

Importantly, the functional role of ITG-numbers remains debated. While several studies have successfully identified a category-selective region for digits in the pITG (Pinel et al. 1999; Roux et al. 2008; Cui et al. 2013; Shum et al. 2013; Abboud et al. 2015; Mareike Grotheer et al. 2016; M. Grotheer et al. 2016), various others found no category-selectivity (Pinel et al. 2004; Libertus et al. 2009; Cappelletti et al. 2010; Andres et al. 2012; Attout et al. 2014; Carreiras et al. 2015; Cummine et al. 2015; Holloway et al. 2015; Peters et al. 2015; Merkley et al. 2019). Moreover, several studies have reported selective responses not only for digit stimuli, but also for other visual numerosity representations (i.e. dice or hands) during a number task (Grotheer et al. 2018) in the pITG and there is mounting evidence that math-related tasks induce increased neural responses in this part of the cortex (Abboud et al. 2015; Hermes et al. 2015; Amalric and Dehaene 2016; Grotheer et al. 2018). As such, it has been suggested that the pITG might contain two distinct functional subregions (Daitch et al. 2016): a smaller and more anterior

region selective for digits (ITG-numbers), and a larger and more posterior region that is selectively involved in math tasks irrespective of the visual stimulus these tasks are performed on (ITG-math).

The current study had 2 goals: 1) design a child-friendly localizer experiment for the identification of ITG-numbers and/or ITG-math subregions within individuals and 2) use the localizer data to shed light on the debated task and stimulus selectivity in the pITG. To this end, we designed an fMRI experiment in which numerosities between 1 and 5 are presented either as digits or as UFOs while participants perform either a numerosity or color (control) task (Fig. 1). This developed localizer only takes ~20 minutes to collect and is accompanied by a child-friendly narrative of Anton the Alien. In our study we collected two sessions of this experiment from 17 adult participants.

Our analyses reveal 4 important findings: 1) a short localizer experiment is sufficient to identify the ITG-math but not the ITG-numbers subregions bilaterally within individuals, 2) the ITG-math subregions show a preference for the numerosity task in independent data, 3) the spatial location of ITG-math is consistent across session, and 4) distributed responses in ITG-math reveal task encoding in the left hemisphere, and task and stimulus encoding in the right hemisphere. By providing a short and child-friendly localizer for the ITG-math subregions, we hope to facilitate further research on this region, its development, and its role in the human aptitude for mathematical cognition.

2. Materials and Methods

2.1. Participants

Nineteen adult volunteers (12 females, mean age 27.5 ± 4,16 years, 17 right-handed) participated in two separate sessions on different days. Before scanning, participants were instructed on the task they were expected to perform and received a brief training on a laptop. Two participants chose not to continue the study after their first session. No participants were

excluded due to participant motion (head motion between or within runs above 3 voxels in any direction). The final data set was hence composed of 17 participants (11 females, mean age 27 ± 4,15 years, 15 right-handed). Subjects had normal or corrected to normal vision and gave their informed written consent. The procedure was approved by the Philipps-University Marburg's Ethics Committee from the Medicine Faculty.

2.2. Data acquisition and preprocessing

Acquisition: Data was collected using a Siemens 3 tesla Magnetom Prisma scanner with a 64-channel head coil. We acquired 42 slices covering the whole brain using two T2*-sensitive gradient echo-planar sequences. One for the main experiment (voxel size: 2.5 mm x 2.5 mm x 2.5 mm, TR: 1500 ms, TE: 30 ms, FoV: 192 mm, flip angle: 71°, slice thickness: 2.5 mm, acceleration factor of 2) and another for the localizer (voxel size: 2.5 mm x 2.5 mm x 2.5 mm, TR: 1000 ms, TE: 30 ms, FoV: 192 mm, flip angle: 59°, slice thickness: 2.5 mm, acceleration factor of 3). Additionally, a whole-brain, anatomical volume was collected once for each participant using a T1-weighted BRAVO pulse sequence (Voxel size: 0.9 mm x 0.9 mm x 0.9 mm, TI: 949 ms, FoV: 240 mm, flip angle: 8°, slice thickness: 0.94 mm).

Processing: The anatomical brain volume of each subject was segmented into gray and white matter using FreeSurfer 7.3.2 (https://surfer.nmr.mgh.harvard.edu/), with manual corrections using ITKGray (https://github.com/vistalab/itkgray), and each participant's cortical surface was reconstructed. Functional data was analyzed using the mrVista toolbox (https://github.com/vistalab) for Matlab (R2021b). fMRI data from each experiment was motion-corrected within and between runs, and then aligned to the T1-weighted anatomical volume. We did not apply any spatial smoothing. In each experiment, a separate design matrix was created and convolved with a hemodynamic response function in Matlab to generate predictors for each experimental condition. We estimated regularized response coefficients

(betas) for each voxel and each predictor using a general linear model (GLM) indicating the magnitude of response for that condition.

2.3. Experimental design

Main experiment (UFO-paradigm)

Stimuli and tasks: We presented images of digits or UFOs during either a numerosity or a color task. Stimulus numerosities ranged from 1 to 5, and stimuli were depicted in one of five possible hues of blue. Behavioral pilots were used to select color hues in such a way that task difficulties in the numerosity and color task were matched as closely as possible. Three different types of UFOs and three different fonts for the digit images were used, resulting in a total of 75 unique images per stimulus category. Participants performed two different 1-back tasks on the same stimuli: Numerosity: Participants were instructed to press a button whenever two consecutive images within a block depicted the same numerosity. Color: Participants had to press a button whenever two consecutive images repeated the same hue of blue. A cue presented prior to each block indicated the participant's task. For the numerosity task, the cue image displayed three alien hands indicating different numerosities, whereas a painter's palette was used for the color task (Fig. 1A).

Trial structure: The experiment was a mixed design with four experimental conditions: UFO-numerosity, digit-numerosity, UFO-color, and digit-color. Four ~5 min long runs were collected in each session with each run containing 28 blocks from a single condition (Fig. 1B). Cues lasted 1500 ms and were followed by a blank period of either 0, 1500 or 3000 ms. In each block, four images were presented for 1500 ms each, with an inter-stimulus interval (ISI) of 0s. To isolate and remove activations induced by the cues, four "blank blocks" were included in which only the cues were presented. All stimuli covered a visual angle of ~2.5°. The

experimental conditions were pseudo-randomized so that each condition appeared six times per run.

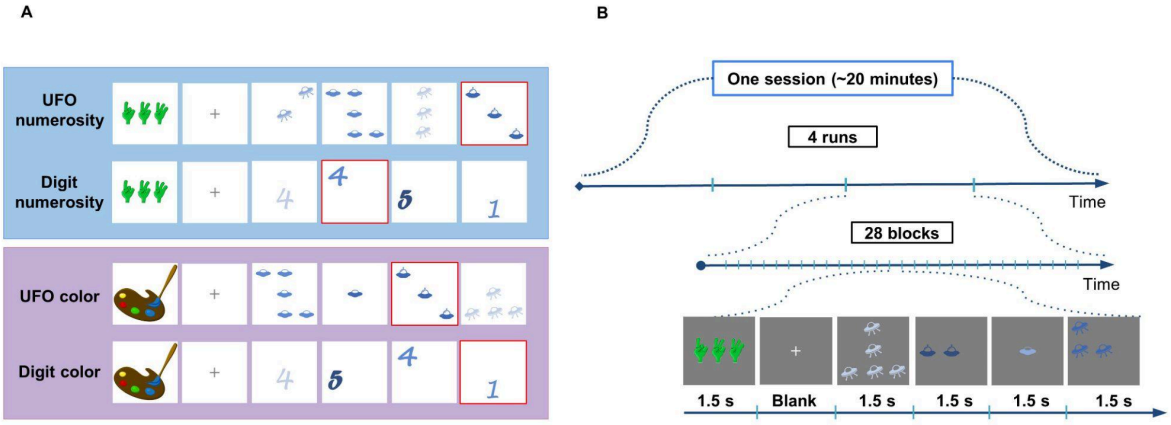

Fig. 1. Experimental design. A. Overview of the experimental conditions. Subjects viewed UFOs or digits (Arabic numerals) on a gray background while performing a 1-back task attending either to the numerosity or the color of the stimuli. B. Overview of the block structure. The experiment comprised four runs, each containing 28 blocks. At the beginning of each block, a cue indicating the task was presented for 1.5 seconds. This was followed by a blank period of 0, 1.5 or 3 seconds. Immediately after, four images of a single experimental condition were presented for 1.5 seconds each.

Color Localizer

Color-selective control regions in the ventrotemporal cortex (VTC) were identified via a visual localizer experiment designed in previous work (Stigliani et al. 2015; Grotheer et al. 2018; Dalski et al. 2024). In this localizer, five visual stimulus categories were presented either in color or in grayscale: faces, houses, limbs, text, and objects. Each stimulus was presented for 500 ms, with an ISI of 0 s, in blocks of 8 stimuli. Each participant completed 4 runs that were ~5 min long and included 10 repetitions of each stimulus category. All stimuli subtended a visual angle of ~8°. The task was to fixate the center of the screen and to press a button when only the background without any image was presented (oddball task). 3% of all stimuli were oddballs.

2.4. Regions-of-interest definition

Functional regions of interest (fROIs) were defined in the native brain space of each participant, using both functional and anatomical criteria. The first session of the main experiment and the color localizer data were used to define the fROIs. These were then used to evaluate responses in the second session ensuring independence between fROI definition and data analysis.

ITG-math and ITG-numbers: The current literature indicates a preference for number stimuli (Roux et al. 2008; Shum et al. 2013; Mareike Grotheer et al. 2016) and mathematical processing (Hermes et al. 2015; Amalric and Dehaene 2016; Daitch et al. 2016; Grotheer et al. 2018) in the posterior ITG. Thus, we aimed to define fROIs for both selectivities using data from the main experiment (T=3, voxel level, uncorrected). First, we contrasted the digit with the UFO stimuli, to identify regions selective for digit stimuli (ITG-numbers). ITG-numbers (average size: left hemisphere: 198.86 (±22.24) mm^3, right hemisphere: 124.40 (±32.27) mm^3) was found in 7 (41.18%) participants in the left and 5 (29.41%) participants in the right hemisphere. Next, we contrasted responses to the numerosity with the color task, to identify regions selective for mathematical processing (ITG-math). ITG-math was identified in 16 participants in the left and 15 participants in the right hemisphere. On average, the size of left and right ITG-math was 303 (±48.89) mm^3 and 380 (±73.25) mm^3, respectively. As ITG-math regions were more reliably identifiable than ITG-numbers regions, we focused on ITG-math for most analyses. Additionally, a second ITG-math was defined using responses to the numerosity task in the second session, in order to calculate the spatial consistency across sessions (average size: left hemisphere: 434.93 (±93.30) mm^3, right hemisphere: 432.23 (±107.20) mm^3).

Color-sensitive region: We contrasted responses to colored and gray-scale images in the color localizer data to define three color-sensitive patches in the medial fusiform gyrus (Lafer-Sousa et al. 2016). We identified the anterior (Ac-color), central (Cc-color), and posterior color regions (Pc-color) in 15, 17, and 17 participants in the left hemisphere, and in 16, 17, and 16 participants, respectively in the right hemisphere (average size Ac-color: left hemisphere:

414.67 (±61.87) mm^3, right hemisphere: 457.37 (±90.45) mm^3; Cc-color: left hemisphere: 755.23 (±149.37) mm^3, right hemisphere: 754.23 (±116.82) mm^3; and Pc-color: left hemisphere: 753.94 (±141.84) mm^3, right hemisphere: 936.62 (±156.86) mm^3).

2.5. Statistical analysis

Behavioral responses: We assessed subjects' performance (measured in % correct) as well as reaction times (RTs, measured in ms) with repeated measures ANOVAs (rmANOVAs). In the main experiment we used task, stimulus, and session as factors. In the color localizer, we used stimulus and color as factors. Tukey-Kramer post-hoc tests were applied when the rmANOVAs revealed significant main effects or interaction effects.

Univariate analysis: For both the main experiment and the color localizer, the average time course in percentage signal change (PSC) was extracted for each condition from each fROI. Then we applied GLMs to estimate betas (measured in units of PSC±SEM; Fig. 2; Supplementary Fig. 1), which indicate the magnitude of the response for each condition. Crucially, we used independent data for fROI definition (main experiment session 1 for ITG-math, color localizer for color regions) and signal extraction (main experiment session 2). We analysed univariate responses in the main experiment with rmANOVAs that used hemisphere, task, stimulus, and session as factors.

Dice coefficient (DC): To evaluate the spatial reliability of ITG-math across sessions, we first defined the anatomical boundaries of the posterior ITG, i.e. the area of cortex in which ITG-match could fall: anteriorly: the posterior hippocampus; inferiorly: the occipito-temporal sulcus (OTS); superiorly: the middle temporal gyrus (MTG); and posteriorly: the anterior occipital sulcus (AOS)). We then evaluated the spatial overlap of ITG-math defined in the two sessions within these boundaries and quantified it with the Dice coefficient $DC = \frac{2|A \cap B|}{|A|+|B|}$, where |A| and |B| are ITG-math from session 1 and session 2 data, respectively, and $|A \cap B|$ is the intersection between them. The DC quantifies the similarity of two samples from 0 to 1,

indicating none or a complete overlap, respectively (Dice 1945). To assess if the measured DC was above chance, we generated a chance level by randomly positioned 2 disk ROIs, matched in size to ITG-math from session 1 and 2, within a square matching the size of the combined anatomical ITG and quantified the DC. This process was repeated 10000 times within each subject, and the average DC was defined as the chance level DC. We then used paired t-tests to evaluate if the measured DC was different from chance (Fig. 3B).

Multivoxel pattern analysis: Disk fROIs, centered on their respective fROI, but with constant radii that matched the average fROI sizes across participants (ITG-math: left hemisphere: 7.14 mm; right hemisphere: 7.80 mm; right Ac-color: 8.10 mm) were used for the multivoxel pattern analyses (MVPAs, Fig. 4). First, the responses to each experimental condition were computed for each voxel with a GLM. Responses were then normalized and z-transformed. Subsequently, we used a leave-one-run-out procedure to calculate correlations between pairs of multivoxel patterns (MVPs), and summarized them in representation similarity matrices (RSMs), which were first calculated at subject level and then averaged across subjects (Fig. 4A, B). Additionally, winner-takes-all (WTA) classifiers, with a leave-one-run-out procedure, determined in each subject and experiment, whether stimulus and/or task information can be decoded from MVPs in the fROIs. Paired t-tests were used to evaluate if WTA classifier performance exceeded 50% chance level (Fig. 4C, D). Additionally, differences in classification performance across conditions were tested with rmANOVAs with hemisphere, task and stimulus as factors.

Group-level whole brain analysis: We also evaluated whole brain responses in the main experiment by combining the contrast maps of interest (numerosity vs color task, and digit vs UFO stimuli) from both sessions at subject-level. The combined contrast maps of all subjects were mapped to the FreeSurfer average brain (T≥1 at voxel level, uncorrected) for visual inspection (Fig. 5, Supplementary Fig. 2).

Code and data availability: Experimental and analysis code can be found in GitHub: https://github.com/EduNeuroLab/ITG-math_localizer.git MRI data will be made available by the corresponding author upon reasonable request.

3. Results

3.1. All tasks were performed with high accuracy

Here we tested whether a numerosity task and/or digit stimuli can be used to identify functional subregions in the ITG that are involved in mathematical processing across individuals in a fast and reliable manner. Seventeen healthy adults were presented with UFOs and digits, while they performed either a numerosity or a color task. We employed rmANOVAs to compare performance and reaction times (RTs) across conditions and sessions. In performance, these rmANOVAs revealed a task effect ($F(1,16)=4.76$, $p=0.04$) with higher performance in the numerosity task 95.23% (±0.02%) than the color task 91.73% (±0.02%). There was no significant stimulus ($F(1,16)=1.45$, $p=0.24$) or session effect ($F(1,16)=0.53$, $p=0.47$), but an interaction effect of task and stimulus was found ($F(1,16)=6.56$, $p=0.02$), with highest accuracies for digits in the numerosity task (97.55±2.11%). In the RTs, rmANOVAs revealed significantly shorter RTs in the color task than the numerosity task ($F(1,16)=14.10$, $p=0.002$; color: 702 (±27) ms; numerosity: 760 (±26) ms). There was no significant stimulus ($F(1,16)=1.06$, $p=0.32$) or session effect ($F(1,16)=2.79$, $p=0.11$). An interaction effect of task and stimulus ($F(1,16)=13.21$, $p=0.002$) was found for RTs; in the numerosity task, RTs were shorter for numbers (730 (±26) ms) than UFOs (790 (±26) ms) ($p=0.03$), whereas the opposite was found for the color task ($p=0.03$, numbers: 717 (±28) ms, UFOs: 688 (±27) ms).

In addition to the main experiment, we also collected a color localizer to identify color-sensitive regions in the medial fusiform gyrus that were used as control ROIs. In this localizer, rmANOVAs revealed no effects of color or stimulus and no interaction effect between color and stimulus in either performance (color: $F(1,16)=3.21$, $p=0.09$; stimulus: $F(4,64)=2.08$, $p=0.09$,

interaction: $F(4,64)=0.54$, $p=0.71$) or RTs (color: $F(1,16)=2.13$, $p=0.16$; stimulus: $F(4,64)=0.74$, $p=0.57$, interaction: $F(4,64)=0.74$, $p=0.57$).

3.2. ITG-math shows stronger activations in the numerosity than the color task

We started by contrasting the numerosity and color tasks, and the digit and UFO stimuli using only session 1 data ($T\geq3$ voxel-level, uncorrected). When contrasting tasks, 16 and 15 of the subjects (total N=17) showed selective activations for the numerosity task in the left and right posterior ITG, respectively (for example subject see Fig. 2A, B). In contrast, when comparing responses to different stimuli, only 7 and 5 of the subjects showed a preference for digits in the left and right posterior ITG, respectively. As reliable activations across subjects were only found for the task contrast, we focus on the fROIs defined by their task preference and refer to these fROIs as ITG-math. Across participants, ITG-math was located posterior to the fMRI signal dropout zone near the ear canal (Supplementary Fig. 3, 4). Within each participant, we extracted ITG-math responses in the second session (i.e. independent data) and assessed its response profile using rmANOVAs with task, stimulus, and hemisphere as factors. We found a main effect of task ($F(1,13)=33.30$, $p<0.0001$), with higher responses in the numerosity task, as well as a main effect of stimulus ($F(1,13)=13.33$, $p=0.003$), with higher responses for the UFO stimuli. We also found an interaction effect between hemisphere and stimulus ($F(1,13)=13.11$, $p=0.003$). Subsequent post-hoc tests revealed significantly higher responses to UFOs than digits in the right hemisphere ($p=0.0002$; Fig. 2B) but not the left hemisphere ($p=0.50$). No other main effects or interaction effects were found.

In our main control region Ac-color, we found a main effect of task ($F(1,14)=4.99$, $p=0.04$) with higher responses in the color task, as well as a main effect of stimulus ($F(1,14)=12.15$, $p=0.004$), with higher responses for UFO stimuli. No main effect of hemisphere or interaction effects were found. For results of additional control regions Cc-color and Pc-color please see Supplementary Figure 1.

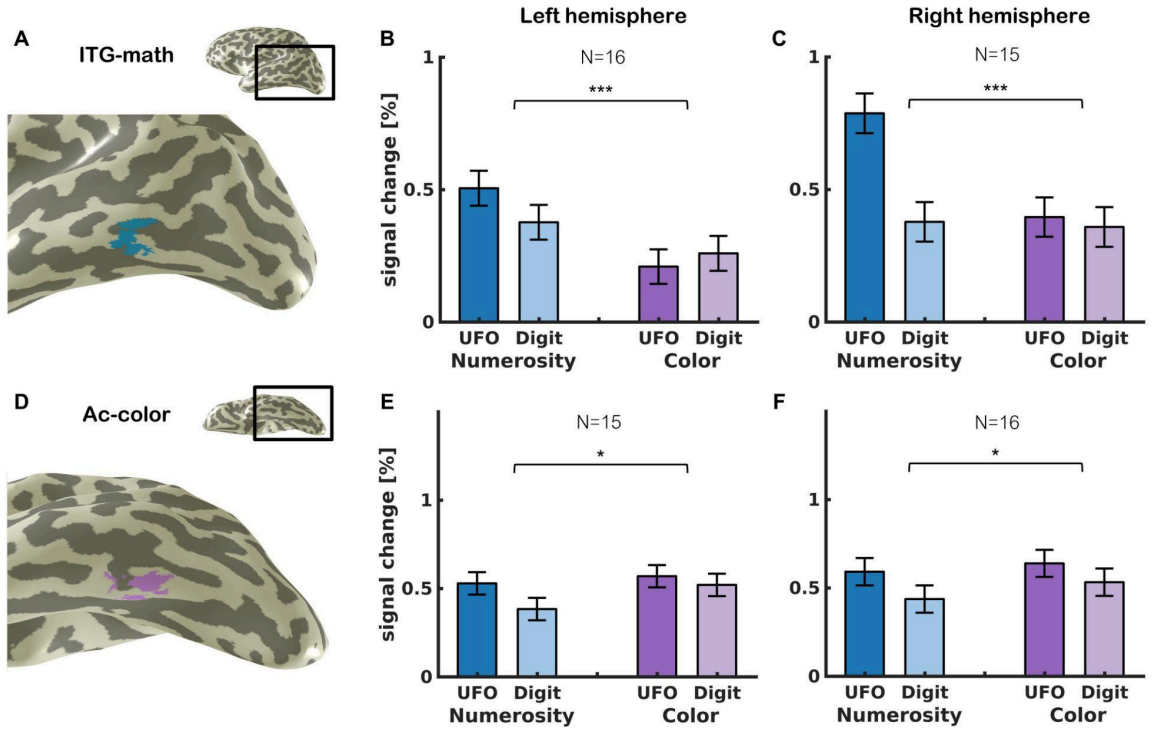

Fig. 2. ITG-math shows a preference for the numerosity task. A. ITG-math: voxels in the ITG/ITS that showed significantly higher responses during the numerosity than the color task (T=3, voxel level, uncorrected). Data is shown in the inflated left hemispheres of a representative subject. B. Mean responses ± SEM across 16 subjects in the left ITG-math from independent data. C. Mean responses ± SEM across 15 subjects in the right ITG-math from independent data. D. Ac-color: voxels in the median fusiform gyrus (FG) that showed significantly higher responses for colored than gray-scale images in the color localizer (T=3, voxel level, uncorrected).. E. Mean responses ± SEM across 15 subjects in the left Ac-color. F. Mean responses ± SEM across 16 subjects from the right Ac-color. Asterisks indicate main effect of task across hemispheres, *p<0.05, ***p<0.001

3.3. ITG-math shows a consistent spatial location within individuals across sessions

To determine if ITG-math's spatial location is consistent across sessions, next, we also defined ITG-math by contrasting the numerosity and color tasks in session 2 data (T≥3 voxel-level, uncorrected). We could define an ITG-math fROI in most of the participants (left hemisphere: N=14; right hemisphere: N=13). Across sessions, ITG-math fROIs overlapped in 12 of the subjects in both hemispheres. The average DCs (mean across subjects ± standard

error (SE): left hemisphere: 0.17 (±0.05), right hemisphere: 0.31 (±0.05)) were significantly above chance in both hemispheres (left: p=0.02; right: p=0.0007; Fig. 3B). An additional independent t-test across hemispheres revealed significantly higher DCs in the right hemisphere (p=0.04).

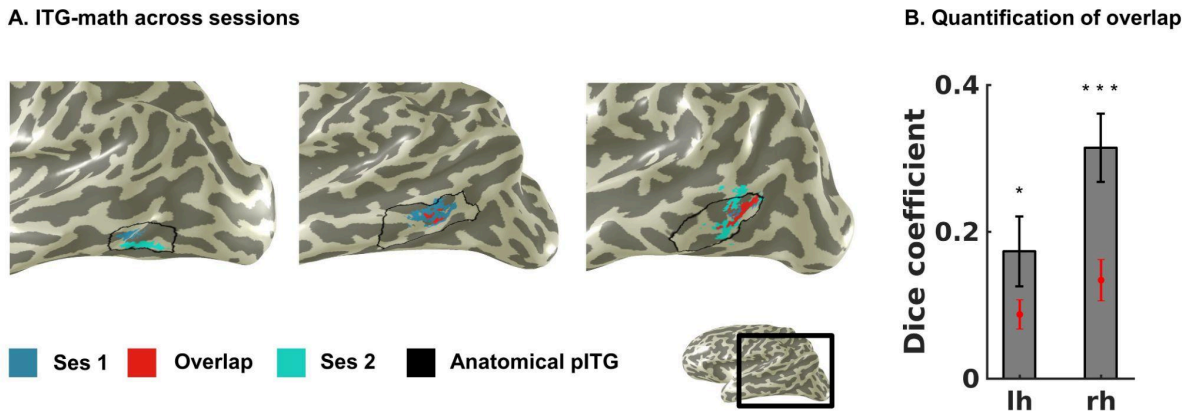

Fig. 3. ITG-math fROIs show consistent localization across sessions. A. Figure shows the inflated cortical surface of three participants representing examples of low (left), medial (middle), and high (right) spatial overlap in ITG-math fROIs across sessions. B. Quantification of the overlap between fROIs across sessions using the dice coefficient (DC), mean across subjects ± SEM. Red dots indicate chance level. Star indicates DCs is significantly higher than chance, *p<0.05, ***p<0.001.

3.4. Distributed responses in ITG-math differ across hemispheres

To determine what kind of information is encoded within ITG-math, we also conducted MVPAs in session 2 data using constant size disk ROIs centered on session 1 fROIs. We computed RSMs using a leave-one-run out procedure. Visual inspection of the RSMs reveals interhemispheric differences. While the RSM from the left ITG-math shows positive correlations for different stimuli under the same task (N=16, Fig 4A), the RSM from the right ITG-math shows positive correlation for all stimuli and task combinations except for UFOs during the numerosity task (N=15, Fig 4B). We used winner-takes-all (WTA) classifiers, with a leave-one-run out procedure, to quantify what types of information can be decoded from ITG-math. In the left ITG-math, the classifier could decode task and stimulus with accuracies

of 63.09% (±5.53%) and 53.32% (±4.95%), respectively. In the right ITG-math task and stimulus decoding accuracies were 58.96% (±4.65%) and 64.79% (±4.93%), respectively. One-tailed t-tests against chance level (50%) and with a Bonferroni-corrected threshold of p=0.01 showed significantly above-chance decoding for task (p=0.009; Fig. 4C) but not for stimulus (p=0.015) in the left hemisphere. In the right hemisphere, decoding accuracy was significantly above chance level for both stimulus and task (stimulus: p=0.002, task: p=0.01; Fig. 4D). We directly compared WTA decoding accuracy across experimental conditions using rmANOVAs with decoding type (task or stimulus) and hemisphere as factors. No significant main effects of hemisphere (F(1,13)=2.03, p=0.18) or decoding type (F(1,13)=0.16, p=0.70) were observed. However, an interaction effect was found (F(1,13)=7.75, p=0.01), which was driven by higher performances for stimulus in the right hemisphere (p=0.01).

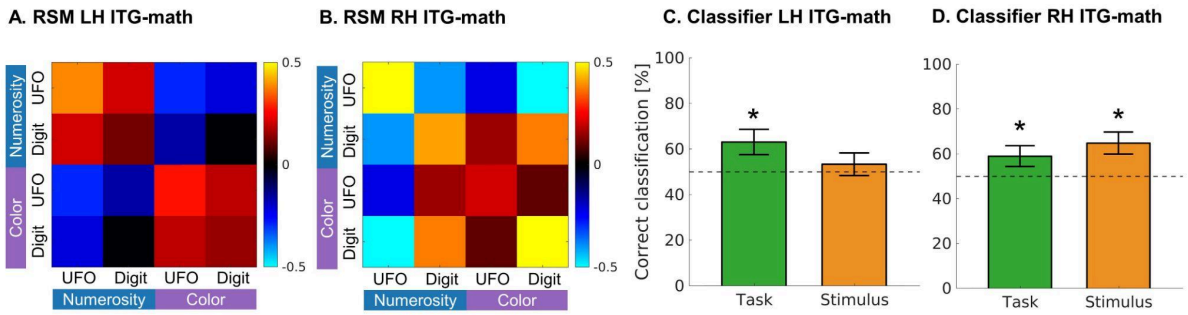

Fig. 4. Distributed responses in ITG-math vary across hemispheres. A-B. RSM from ITG-math in the left (A. N=16) and right (B, N=15) hemispheres. Conditions are arranged by stimulus (UFO vs. digit) and grouped by task (numerosity vs.color). C-D**.** Mean ± SEM winner-takes-all (WTA) classification performance for task and stimulus in left (C) and right (D) ITG-math. Star indicates that classifier performance is significantly above chance level (p<0.01 with Bonferroni-corrected threshold). Abbreviations: RSM, representational similarity matrix; WTA, winner-takes-all.

3.5. ITG-math is part of a network of brain regions that prefer the numerosity task

Here we found a reliable preference for the numerosity task in the posterior ITG, which raises the question if other regions of the brain may also show such a preference. To test this, we

averaged individual subjects' contrast maps comparing the numerosity and color tasks and evaluated the resulting group-average activation maps. As expected, visual inspection of the group maps revealed a preference for the numerosity task in the pITG bilaterally. In addition, in the left hemisphere, a preference for the numerosity task was observed in the intraparietal sulcus (IPS), the supramarginal gyrus (SMG), and the precentral sulcus (PCS) (Fig. 5A, B), while in the right hemisphere, the preference for the numerosity task was largely limited to the pITG and the IPS (Fig. 5B, C). A group average map contrasting responses to digits and UFOs is presented in Supplementary Fig. 2.

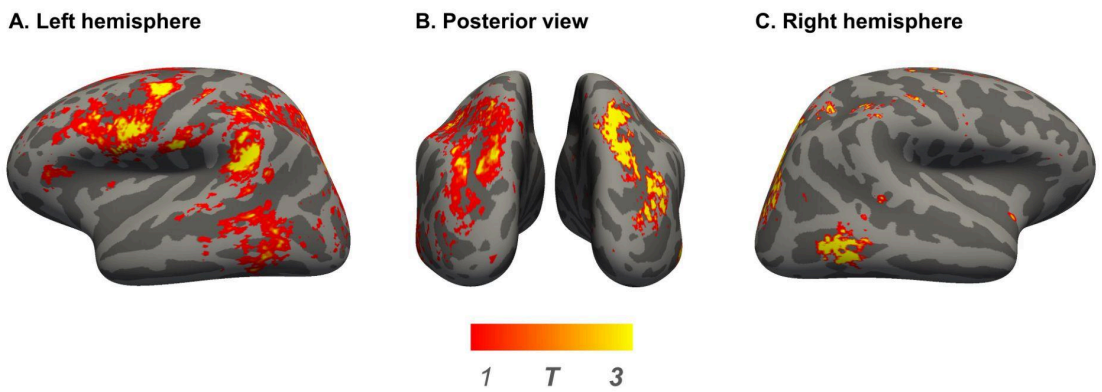

Fig. 5. Whole-brain analysis contrasting the numerosity and color tasks across participants. Responses elicited by contrasting the numerosity with the color task in both sessions were averaged across participants and are presented on the inflated cortical surface of the Freesurfer average brain.

4. Discussion

In this study, we aimed to 1) design a child-friendly localizer experiment for the identification of ITG-numbers and/or ITG-math subregions within individuals and 2) use the localizer data to shed further light on task and stimulus preferences within these regions. Our results revealed four key findings: 1) contrasting a numerosity with a color task allowed the identification of an ITG-math subregion in individual subjects bilaterally, 2) contrasting digit and UFO stimuli did not allow for the identification of an ITG-numbers subregion across individuals, 3) ITG-math shows

spatial consistency across sessions, and 4) ITG-math encodes task information and both stimulus and task information in the left and right hemisphere, respectively.

We could successfully identify ITG-math in ~91% of the participants by contrasting responses in the numerosity and color tasks. These results are consistent with previous studies finding a format-invariant selectivity for mathematical tasks in the pITG (Coderre et al. 2009; Cui et al. 2013; Grotheer et al. 2018; Cai et al. 2021; Cai et al. 2023). Importantly, ITG-math displayed reproducible localization, as measured with DCs, which is also considered an indicator of specialisation (Cohen and Dehaene 2004). Interestingly, responses to UFOs were higher than to digits across hemispheres during the numerosity task. We hypothesize that these differences could be driven by the more resource-demanding nature of non-symbolic numerosities (Skagenholt et al. 2018; Sokolowski et al. 2022), which is consistent with the higher RTs observed for UFOs in the numerosity task. Altogether, these findings indicate that the pITG contains a functional subregion engaged in numerosity tasks (ITG-math), which may support mathematical cognition irrespective of the stimulus. As indicated by our whole-brain analyses, ITG-math is part of a larger network of brain regions involved in numerosity processing which includes the bilateral IPS, and left SMG and PCS, i.e. regions which have consistently been associated with mathematical cognition in prior work (Menon et al. 2000; Daitch et al. 2016; Damarla et al. 2016; Nakai and Nishimoto 2023).

We also aimed to identify a subregion selective to digits (ITG-numbers) in pITG by contrasting responses to digit against UFO stimuli. However, such a stimulus preference was found only in ~35% of the participants in the left and right hemisphere, respectively. These results are in contrast with previous work successfully identifying ITG-numbers (Pinel et al. 1999; Roux et al. 2008; Cui et al. 2013; Shum et al. 2013; Hermes et al. 2015; Amalric and Dehaene 2016; Daitch et al. 2016; M. Grotheer et al. 2016; Mareike Grotheer et al. 2016). However, not all prior studies were able to identify such a region (Pinel et al. 2004; Libertus et al. 2009; Cappelletti et al. 2010; Andres et al. 2012; Attout et al. 2014; Carreiras et al. 2015; Cummine et al. 2015; Holloway et al.

2015; Peters et al. 2015; Merkley et al. 2019) (for a meta-analysis see Yeo et al., 2017) and several potential explanations about these differential results have been provided, including: 1) the number stimuli used (single digits, multiple digits, strings of digits etc.) and the stimuli numbers are contrasted with (faces, dot clouds, fourier noise, dice, etc.) vary drastically across experiments (Yeo et al. 2017), 2) the location of ITG-numbers is relatively close to the fMRI signal dropout zone of the ear canal, and specialized imaging acquisition parameters may be needed in this part of the brain (Shum et al. 2013; M. Grotheer et al. 2016), and 3) the task participants are performing vary drastically across studies and passive tasks in particular have been suggested to fail to elicit significant responses to digits in the pITG (Liu et al. 2025). Here we are using active tasks, and were able to successfully identify another subregion in the pITG based on its task preference which was located posterior to the signal drop-out zone (Supplementary Figure 3, 4). As such, we propose that the relatively strict stimulus contrast, in which we compared digits to other numerical stimuli, may contribute to the absence of a reliable ITG-numbers subregion.

Interestingly, within ITG-math, we found differential sensitivities to stimulus features across hemispheres with larger overall responses to UFOs than digits in the univariate data as well as significant stimulus encoding in the multivariate analyses found only in the right hemisphere. These findings align with prior research showing subtle differences in the response profile of function regions in pITGacross hemispheres. First, prior work found a positive correlation between age and neural responses for arithmetic only in the left but not in the right pITG (Rivera et al. 2005). Furthermore, EEG research suggests a dynamical interplay between the bilateral pITG during numerosity tasks, where the right pITG attributes numerical meaning at early stages, then passes it on to the left hemisphere for information integration, and finally the operational momentum is supported by the bilateral pITG (Jang and Hyde 2020). Indeed, our observed stimulus sensitivity of the right ITG-math might reflect remnants of an initial right-lateralization for non-symbolic numerosities similar to the right IPS (for a meta-analysis

see: Faye et al., 2019). However, others did not find such hemispheric asymmetries in pITG functional subregion (Hermes et al. 2015; Amalric and Dehaene 2016; Daitch et al. 2016; Grotheer et al. 2018) and further research investigating the division of labor of ITG-math across hemispheres is needed.

There are several limitations of the current study that should be considered. First, sample size might have played a role in us not being able to identify ITG-numbers. However, it is important to note that here we aimed to identify the subregions in individual subjects and the relative proportion of identified ITG-numbers to ITG-math fROIs in this study, which was roughly 1:2 and 1:3 in the left and right hemispheres, respectively, is unlikely to change in a larger sample. Further, our results are limited to a numerosity task, which raises the question if ITG-math engages in other more complex mathematical tasks (e.g. addition, multiplication, subtraction and division). Prior work using arithmetical equations including addition and multiplication, as well as formulas (i.e. Zeta function) (Hermes et al. 2015; Amalric and Dehaene 2016; Amalric and Cantlon 2022) found increased activity in the pITG, thus suggesting that ITG-math may be engaged in various mathematical tasks. Similarly, here we used only two types of stimuli, digits and UFOs, yet numerosities can be represented by various other stimulus categories as well (Grotheer et al. 2018). As such, future work employing a larger variety of stimuli including e.g. number words or Roman numerals is needed to fully grasp the stimulus preferences of functional subregions in pITG.

We conclude that the bilateral ITG-math, which can be consistently found across individuals, is involved in numerosity processing independent of the visual features of the presented stimulus. Crucially, these results were obtained by employing a fast, child-friendly, and open-source localizer, which we hope will promote future research on the development and functional specificity of ITG-math.

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