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Functionally distinct contributions of parietal cortex to a numerical landmark task: an fMRI study

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Abstract

This study aimed at establishing the neural basis of magnitude processing of multiple numbers from working memory. We designed a numerical landmark task and embedded it in a fragmented trial event-related fMRI design, allowing to separate encoding from decision processing. An attentional localiser task not involving numbers allowed further functional specification. The results show that in a numerical landmark task the right anterior intraparietal sulcus is involved in number encoding while more posterior parietal regions, bilateral superior parietal lobule and right inferior parietal lobule, provide domain-general support in the form of constructing a working memory representation or orienting spatial attention within that mental representation during number comparison. The results are in line with earlier studies reporting a functional distinction between anterior and posterior parietal contributions to number processing and further specify their role at a functional level.

Keywords: number processing, intraparietal sulcus, inferior parietal lobule, superior parietal lobule, working memory, spatial attention, landmark task

1. Introduction

The neurocognitive architecture of number processing has received much attention in the last two decades (Dehaene, Piazza, Pinel, & Cohen, 2003; Hubbard, Piazza, Pinel, & Dehaene, 2005; Nieder, 2005). Considerable advancements have been made and the characteristics of the neural coding of numbers have been specified in detail in monkeys (Nieder, Friedman & Miller, 2002; Nieder & Miller, 2004) and in humans (Piazza, Izard, Pinel, Le Bihan & Dehaene, 2004; Piazza, Pinel, Le Bihan & Dehaene, 2007; Roggeman, Santens, Fias & Verguts, 2011; Santens, Roggeman, Fias & Verguts, 2010). Monkey single cell recordings demonstrated neurons in intraparietal sulcus (IPS) and in prefrontal cortex to be selectively tuned to number (Nieder et al., 2002, 2004). These neurons are typically tuned to a preferred number and to its close neighbors but not to numbers farther away from the preferred one. Using fMRI adaptation in humans Piazza et al. (2004, 2007) confirmed the presence of the same type of neural coding in humans in the anterior part of the bilateral IPS. This number-tuned neural coding is thought to provide the number representations that are essential for number tasks, as it can account for important behavioural phenomena like the behavioural distance effect observed in number tasks like number comparison: Numerically close numbers are more difficult to compare than numerically distant numbers because the neural codes are less distinguishable for close numbers than for far numbers.

Apart from very simple and rather exceptional situations (like numbers used in a nominal context or when having to decide on the parity of a given number), numbers are used typically in contexts in which numbers have to be related to one another. In fact, this is the essence of most numerical or mathematical tasks. For instance, in number comparison tasks, the magnitude-based relation between the

two numbers has to be established. Or, in mental arithmetic a number has to be produced as a function of the operation performed on these two numbers, for instance the product.

An important hypothesis is that determining the relation between different numbers is mediated by a spatial representation. This hypothesis is supported by a number of observations, the most prototypical and illustrative are the following. First, patients suffering from spatial neglect establish a systematic bisection bias when they have to determine the midpoint between two numbers (Zorzi, Priftis & Umilta, 2002). Specifically, they exhibit a bias towards larger numbers when having to produce the number that lies in the middle between provided numbers. This bias relates to the rightward bias observed in their performance in physical line bisection, and is highly indicative of a spatial representation underlying the process of relating different numbers. Further studies indicated that the numerical bias of neglect patients also expresses in number comparison and arithmetic tasks, in a way that is relative to the neglected side and to the relation position of numbers to each other (Vuilleumier, Ortigue & Brugger, 2004; Dormal, Schuller, Nihoul, Pesenti & Andres, 2014; Masson, Pesenti, Coyette, Andres & Dormal, 2017). Second, when numbers have to be responded to in a binary manual response task small numbers are responded to faster with the left hand than with the right hand. For large numbers the opposite is true. This spatial numerical association of response codes, or SNARC effect, as this phenomenon is called (Dehaene, Bossini & Giraux, 1993) is dependent on how small and large is defined in relation to other numbers. The nature of the spatial association for a given number depends on the context of other numbers in which the number occurs. For instance, the number 5 receives faster right hand than left hand responses in the context of numbers ranging from 0 to 5,

but it receives faster left than right hand responses when numbers range from 4 tot 9 (Dehaene et al., 1993; Fias, Brysbaert, Geypens & d'Ydewalle, 1995). The spatial association can also depend on the immediate context of another number within a single trial. For instance, in a comparison task, whether a number is responded to preferentially with the left or the right hand depends on the number to which the target number has to be compared.

Third, based on fMRI multivariate pattern analyses techniques, Knops, Thirion, Hubbard, Michel and Dehaene (2009) were able to show that the pattern of neural activity over posterior IPS voxels that distinguishes between left and right saccadic eye-movements is able to also distinguish between addition and subtraction, with addition being associated with rightward shifts. This strongly suggests that determining the arithmetic relation between two numbers engages spatial coding.

A currently widely used task that explicitly addresses the spatial mediation of relating different numbers to each other is the number line estimation task. In this task a line is presented that is flanked by two landmark numbers, one at each end of the line (e.g. 0 and 100) and participants are required to indicate a position on a line that corresponds with the value of a target number. There are a number of reasons why this task is so popular. First, performance on this task developmentally follows a trajectory from non-linear compressed mapping towards linear mapping (Siegler & Opfer, 2003; Thompson & Opfer, 2010). When young children map numbers to a line, they use proportionally more space for the small numbers compared to the large numbers. With ageing, however, performance evolves towards equidistance. Second, accuracy of the mapping correlates with mathematical achievement,

indicating that it taps on spatial processes which form building blocks of

mathematical tasks (e.g. Booth & Siegler, 2006).

Some recent fMRI studies aimed at establishing the neural regions that are

engaged in this task. Vogel, Grabner, Schneider, Siegler and Ansari (2013)

investigated the neural activity elicited by performing a number line estimation task

and compared it to a brightness estimation task (in which the brightness of a target

stimulus had to be indicated on a line flanked by a brighter and a darker landmark

stimulus flanking the ends of the line). The estimated position of the target on the line

had to be produced by means of a trackball. The results revealed an anterior part of

the IPS to be recruited by the number line estimation task only (with the activation

being related to the distance with respect to the landmark numbers) and a posterior

parietal region being involved in both the number and brightness estimation task.

Kanayet et al. (2017) used a similar paradigm. By asking participants to

execute their mapping response only after a cue was presented, Kanayet et al.

(2017) were able to separate the cognitive aspects of the preparation phase from the

somatosensory and motor processing of the execution. Again they found a functional

dissociation between anterior IPS and regions around posterior IPS. The right

anterior IPS activation was found to be related to the numerical distance from the

closest landmark, independent of position. The posterior IPS on the other hand

showed a different pattern. It was activated contralaterally to the spatial position of

the landmark that was closest to the target number.

These results add to a previous meta-analysis suggesting that the anterior

and posterior regions of the IPS play a distinct role in numerical cognition (Dehaene

et al., 2003). The anterior segment was hypothesised to play a number-specific role

by providing the neural resources to represent magnitude of the numbers. The

posterior part was hypothesised to engage general-support functions. Although the nature of the general-support functions has not been specified, mechanisms of spatial attention are plausible candidates. The number bisection bias in attentional neglect patients (Zorzi et al., 2002) and the observations that areas involved in the planning of saccades are also involved in addition and subtraction (Knops et al., 2009) as discussed before.

However, the proposed distinction between the contribution of anterior and posterior parietal regions awaits further validation. The experiment here presented addresses four issues raised by the above studies, which have remained unanswered so far. First, both Vogel et al. (2013) and Kanayet et al. (2017) used an explicit mapping task in the context of production. The landmarks were presented flanking a physically presented line to which a target number had to be mapped by positioning a marker on the corresponding position on the line. It is clear that the spatial mediation that is hypothesised to be recruited when numbers have to be related to each other, was explicitly elicited by the task. The number line estimation task is frequently used and performance of this task is a predictor of math achievement, and therefore, understanding its neural basis is intrinsically interesting. Yet, one can wonder to what extent it can be considered to tap the prototypical number processing mechanisms, given that in most situations number processing tasks are not performed through externally available lines and number landmarks. In the present experiment we used briefly presented number landmarks (one presented in the left visual field and one in the right visual field), without a line being presented. After the landmarks had disappeared and a retention interval had passed, participants received a target number for which they had to indicate whether it was numerically closer to the left or to the right landmark by pressing the left or right

response key. In this way we created a purely internal numerical landmark task. In addition to the numerical landmark task we also used a colour landmark task in which participants had to locate a colour target stimulus with respect to two landmarks of the same colour but differing in brightness. In this way, we tried to verify the extent to which activations were specifically related to number processing as opposed to colour processing.

Second, Dehaene et al. (2003) proposed that the contribution of the posterior parietal cortex could consist of spatial attentional processing. This is indeed a viable hypothesis if one assumes that the relationship between different numbers is established through spatial mediation. Yet, neither the study of Vogel et al. (2013), nor the study of Kanayet et al. (2017) was designed to empirically verify the involvement of the neural mechanisms for spatial attention while performing the number line estimation tasks. In order to judge a possible involvement of internal shifts of spatial attention we included a functional localiser task based on a retro-cueing spatial attention task developed by Lepsien and Nobre (2006).

Third, the earlier studies used only a restricted set of landmarks. In fact, Vogel et al. (2013) used the numbers 0 and 100 as landmarks. Kanayet et al. (2017) used 0 and 100 in one condition and -100 and 100 in another condition. This may have induced an atypical way of processing. The involvement of some brain regions, like those related to the encoding and processing of the landmarks, may have been reduced, whereas the involvement of other brain regions related to specific strategies may have been amplified. Hence it is not clear to what extent the results of Vogel et al. (2013) and of Kanayet et al. (2017) generalise to situations in which more flexibility is required. In our study we varied the landmarks from trial to trial thereby guaranteeing extensive landmark processing throughout the experiment.

Fourth, the procedures used by Vogel et al. (2013) and by Kanayet et al. (2017), allowed to separate out the sensorimotor aspects of positioning the landmark, but no distinction could be made between the cognitive substages of solving the landmark task. We adopted a fragmented trial design in which we presented first the landmarks and then, after a jittered interval, the target. This allows to separate the stage of encoding the landmarks in working memory from the response-related processes that are used to relate the numerical value of the target to the numerical value of the landmarks and to give a response. This fragmentation of task performance represents an important step in the investigation of the deployment of domain-general resources, such as working memory, for number processing. Indeed, the encoding stage requires the numbers and their position to be stored in working memory during the retention interval, until the moment that the target is presented and a response decision can be made.

If the results of Vogel et al. (2013) and of Kanayet et al. (2017) generalise to the internal version of the landmark task, we expect to observe differential contributions of the anterior and posterior parts of the parietal cortex. Based on these findings and based on the model of Dehaene et al. (2003) we predict that (1) the anterior IPS will be activated as soon as the landmark numbers are presented, (2) the posterior parietal areas will become active only when the probe number is presented and the comparison process can start, (3) the colour stimuli, in the colour landmark task but also in the localiser task, will not elicit any activation in anterior IPS as this area is assumed to be number-specific. Finally, to the extent that the comparison process of both stimulus types recruits posterior parietal areas, we predict (4) the activation in posterior parietal areas to overlap with the areas related

to orienting of spatial attention in the localiser task.

2. Material and methods

2.1. *Participants*

Twenty-four healthy right-handed volunteers (16 males; 21.8 ± 1.3 years) participated after having given written informed consent. The study was approved by the Ethics Committee of the Medical Department of Ghent University. Six participants (4 males) were omitted from analysis because they failed to reach a minimum accuracy of 66.67% in each condition. One participant was omitted because of a data management error.

2.2. *Stimuli and materials*

There were two experimental conditions: a numerical landmark task and a colour landmark task. Each of these experimental conditions was controlled by a low-level ellipse discrimination condition, resulting in 4 conditions organised in a 2 (task: landmark vs ellipse) x 2 (type: number vs colour) factorial design. In the landmark tasks participants had to indicate with a key press of the index or middle finger of the right hand whether the target was closer, in numerical magnitude or in colour saturation, to the left or to the right landmark that was presented just before (see figure 1). In the numerical landmark task, the landmarks and target were two-digit numbers and the relevant dimension was numerical magnitude. In the colour landmark task, the landmarks and target were the coloured double paragraph symbol (§§) and the relevant dimension was saturation. In the ellipse discrimination control task, subjects had to indicate with a similar key press whether a grey ellipsoid shape around the number or colour target was a circle (diameter 3-6°) or an ellipse.

To discourage the use of strategies other than magnitude-based landmarking, number stimuli (white, 1.2° × 1.5°) were selected taking into account the following

criteria: (1) all numbers were two-digit integers that never contained a 0, (2) the landmark numbers ranged from 21 to 99 with the distance between them varying from 17 to 35 in incremental steps of 2, (3) the value of the target number was always situated between the two landmarks and was never dividable by 5, and (4) to make difficulty comparable across trials, the distance between the target and the mean of the reference numbers was fixed at 20, 25, 30 or 35% of the difference between the two reference numbers.

For the coloured §§-symbol stimuli (1.5° × 1.5°), the landmark and target stimulus had the same hue (red, blue, green, yellow, magenta or cyan), but differed in saturation on the Hue-Saturation-Brightness scale (H-S-B). The saturation levels of the coloured stimuli and the corresponding brightness levels (S-B correlation: > +0.90) were selected based on pilot data to reach a difficulty level comparable to the numerical landmark task. On a scale of 1 to 100, the saturation difference between the landmarks ranged from 75 to 90. The saturation of the target was always situated between the saturation levels of the two landmarks. Furthermore, the distance between the saturation level of the target and the mean of the landmark colours was systematically varied in steps similar to the number stimuli (see above).

In half the trials the ellipsoid around the target number was a circle. To create sufficient variability in the ellipse discrimination control task, the ellipsoid varied both in diameter (3, 3.75, 4.5, or 5.25°) and shape. The latter was defined by the ratio between the minor and major axis, 1 being a perfect circle and 0.88, 0.89 or 0.90 reflecting an ellipse.
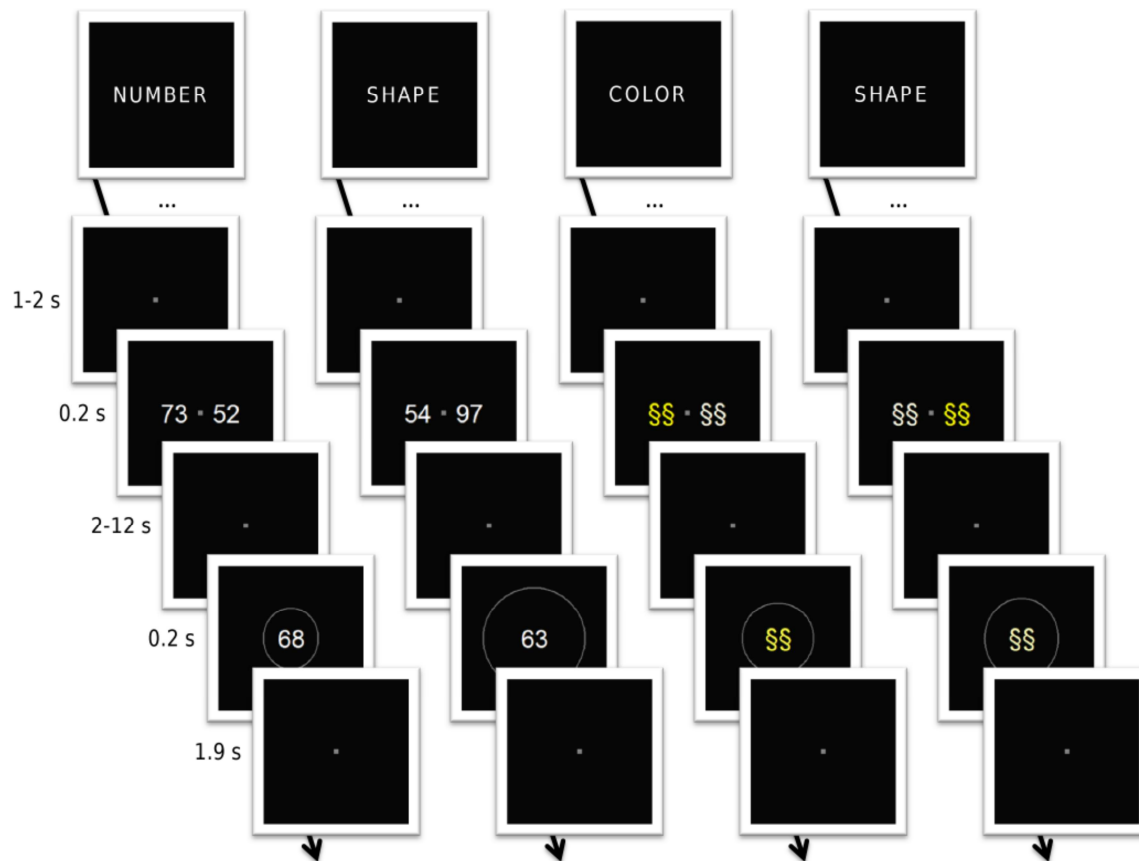
Figure 1. Overview of the experimental paradigm with the possible instructions followed by an example of a trial, resulting from left to right in four different conditions: Number_landmark, Number_ellipse, Colour_landmark, Colour_ellipse.

2.3. *Procedure*

Each trial started with the presentation of a grey fixation square (0.4° × 0.4°) on a black background for a variable duration (between 1000 and 2000 ms). Next, the two landmarks were shown for 200 ms left and right of the fixation square at an eccentricity of 0.8°. In half of the trials, the largest number or brightest §§-symbol was presented left of the fixation square. This was followed by the presentation of the fixation square during a maintenance interval ranging from 2000-12000 ms following a skewed distribution (2000-4000 ms: 50%, 4000-8000 ms: 32.5% and 8000-12000 ms: 17.5%). Subsequently, the target was presented centrally within a grey ellipsoid during 200 milliseconds. Finally, the fixation square was presented again for 1900 ms, followed by a blank of 100 ms to announce the next trial. Forty

trials were presented for each condition. Trials were presented in blocks of eight trials of the same condition. Each block was preceded by an instruction ("number", "colour" or "shape") during 3 seconds to inform the subject which task to execute (numerical landmark, colour landmark or ellipse discrimination respectively) and was followed by an additional fixation square of 15 seconds. Finally, these blocks were distributed across 5 runs, with a block for each condition per run. The order of the blocks and runs was counterbalanced across subjects. Prior to scanning, subjects were familiarised with the tasks and executed a practice block for each condition. Participants were explicitly instructed not to perform any mental calculation on the two landmark numbers during the maintenance interval. During anatomical scanning, subjects performed another practice run. Stimulus presentation and response collection were controlled using Presentation (Neurobehavioral Systems, Albany, California).

Additional localiser task

To evaluate if orienting spatial attention within mental representations is involved in number comparison, subjects performed an additional localiser task based on a retro-cueing paradigm (Lepsien & Nobre, 2006) at the end of the scanning session. Each trial started with a fixation square (0.5° × 0.5°) (1500-2500 ms), followed by the short presentation (200 ms) of an array of four X's (1° × 1°), each in a different colour, positioned in the corners of a virtual square (2.8° × 2.5°). This was followed by a pre-cue interval with the fixation square on screen. Next, the fixation square briefly changed into a cue (100 ms) and transformed back into the fixation square for a post-cue interval. There were two cue types: (1) a neutral cue (with all the sides of the fixation square increasing in line thickness) and (2) an informative cue (with two sides increasing in thickness and forming an arrow to the

position of one of the X's in the previously presented array). Both pre-cue and post-cue intervals were drawn from the same distribution (50% 2100-4000 ms, 37.5% 4100-8000 ms, 12.5% 8100-11000 ms) and orthogonalised with respect to each other. Next, a coloured X was presented as a probe (200 ms) and subjects had to indicate whether or not the probe belonged to the previously presented array (during a response window of 1700 ms displaying the fixation square) by pressing the left or the right button. Response mappings were counterbalanced across subjects. Each trial ended with a blank of 700 ms to announce the next trial (see Figure 2 for trial examples). Probes were present in half of the informative and neutral cues. When the probe was present, the informative cue always predicted its position. A total of 64 trials were presented with 32 trials of each type.
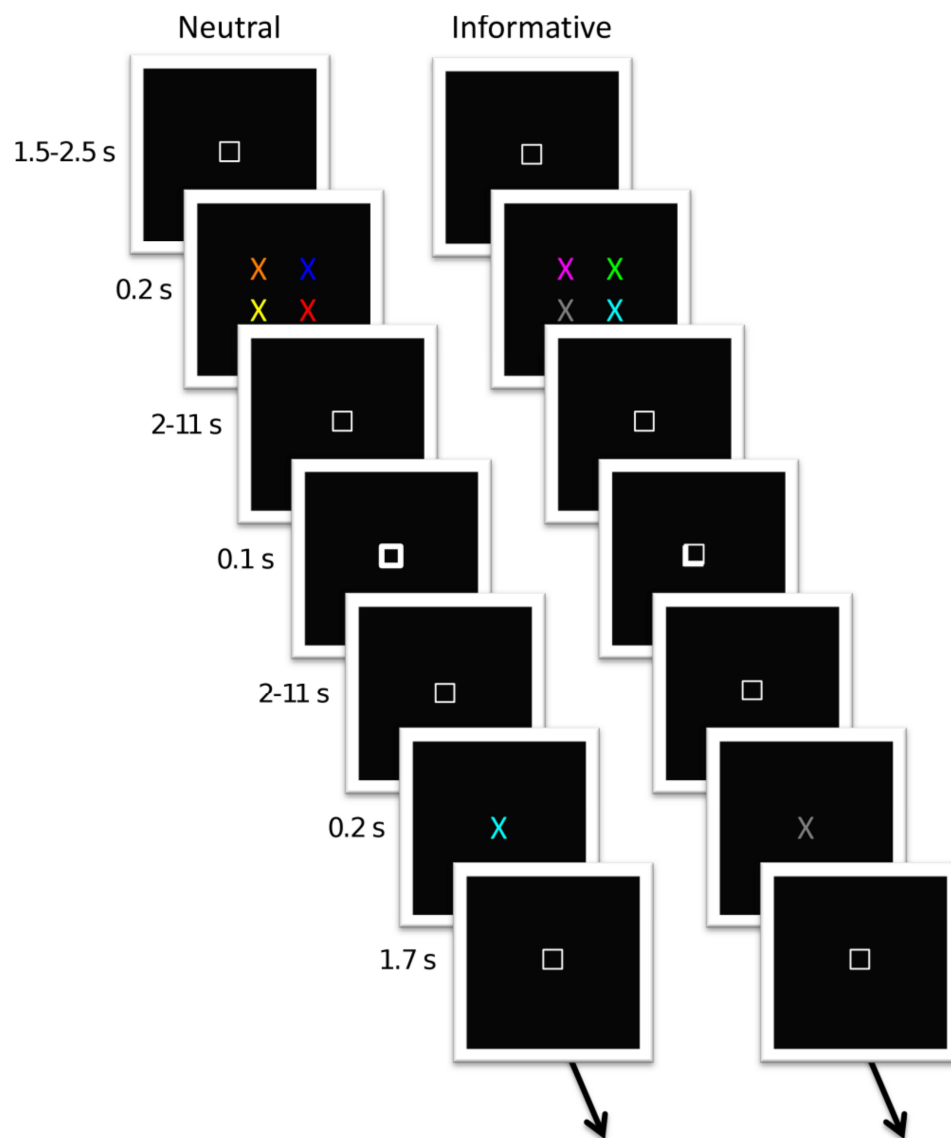
Figure 2. Overview of the experimental paradigm of the localiser task based on Lepsien and Nobre (2006) with an example of a neutral trial (left) and an informative trial (right).

Scanning procedure

Scanning was performed at 3T (Magnetom TRIO, Siemens, Erlangen, Germany), using an eight-channel head coil. First, a 3-D high-resolution T1-anatomical image of the whole brain was acquired with 3-D MPRAGE (TR = 1550ms, TE = 2.39ms, TI = 900ms, 176 sagittal slices, acquisition matrix = 256 x 256, FOV = 220 mm, flip angle = 9°, voxel size = 0.9 x 0.9 x 0.9 mm). Next, 960

whole brain functional images were acquired using a T2*-weighted sequence sensitive to BOLD contrast (EPI: TR = 2000ms, TE = 35ms, 30 axial slices, image matrix = 64 x 64, FOV=224 mm, flip angle = 80°, slice thickness = 3.0 mm with a distance factor of 17%, resulting in an isotropic voxel size of 3.5 x 3.5 x 3.5 mm).

2.4. *Image analysis*

2.4.1. Pre-processing

The fMRI data were analysed with statistical parametric mapping (SPM12; www.fil.ion.ucl.ac.uk/spm). The first three volumes of each EPI series were included to allow magnetic saturation and were removed from the analysis. All functional images were spatially realigned to the mean image and were then temporally realigned to the middle slice. Next, the segment toolbox was used to segment structural images into grey matter (GM), white matter (WM), cerebrospinal fluid (CFS), bone, fat and air by registering tissue types to tissue probability template maps (Ashburner & Friston, 2005). Bias corrected skull-stripped anatomical images were then generated to which the functional images were coregistered. These functional images were normalized to a standard EPI template in Montreal Neurological Institute (MNI) stereotaxic space and resampled at an isotropic voxel size of 2 mm by applying the forward deformation parameters that were obtained from the segmentation procedure. The normalised images were smoothed with a spatial filter of 8 mm full-width at half maximum. Finally, the high resolution anatomical scan of each participant was spatially normalised using the same parameters that were applied for the normalisation of the functional images.

2.4.2. Analysis of the main experiment

We performed a general linear model (GLM) at the first level for each

participant on a trial-by-trial basis with separate events for the encoding (starting at

landmark presentation) and the decision phase (starting at target presentation)

leading to a model with three orthogonal dimensions: stimulus type (number or

colour), task (landmark or ellipse) and phase (encoding or decision) creating a total

of eight conditions of interest (Number_landmark$_{encoding}$, Number_landmark$_{decision}$,

Number_ellipse$_{encoding}$, Number_ellipse$_{decision}$, Colour_landmark$_{encoding}$,

Colour_landmark$_{decision}$ and Colour_ellipse$_{encoding}$, Colour_ellipse$_{decision}$). To model the

hemodynamic response for each event, a stick function time-locked to its occurrence

was convolved with a canonical hemodynamic response function to form covariates

in a general linear model (Friston et al., 1994). An additional diagnostic (variance

inflation factor < 10) revealed no multicollinearity between the regressors for the

encoding and decision events. An exploratory analysis of the RTs revealed that

subjects decided slower during the numerical landmark task than during the other

three tasks (see behavioural results). To avoid that any of the ensuing differential

brain activation patterns during the decision phase could be attributed to RT

differences, we included the trial-by-trial RTs as a separate regressor to the model.

Additionally, instructions, movement-related effects (3 translational and 3 rotational),

and trials on which participants responded incorrectly were included as covariates of

no interest. All of these regressors were included in the model for each of the five

runs separately. Finally, high-pass filtering at a cutoff of 128Hz and a first-order

autoregressive (AR(1)) serial correlation correction were also included in the

analysis. The eight conditions of interest were then contrasted against the implicit

baseline across scanning sessions yielding eight contrast images. These first level

contrast images were then entered into the second level by using a 2 x 2 x 2 factorial

design with subjects as a random variable (Friston, Holmes, Price, Buchel, & Worsley, 1999). To achieve a corrected extent threshold of $p < 0.05$ at the cluster level (voxel level $p < 0.001$, uncorrected), a minimum cluster size of 54 voxels was used based on Monte Carlo simulations (http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html).

To investigate the specificity of the activations obtained from one contrast with respect to activations from another contrast, we exclusively masked the first contrast with the second contrast at a threshold of $p < 0.05$ uncorrected.

2.4.3. Region-of-interest (ROI) analysis of the localiser task

Our main interest in administering the localiser task was to further specify the function subserved by the regions obtained from the analyses of the main task. For this purpose, we extracted the time course of neural data within the functionally defined parietal regions of the landmark task and averaged across all voxels within these regions. Then, we fitted a GLM to this averaged time course data for each subject by convolving a canonical hemodynamic response function to the onsets of the memory array, informative cue, neutral cue and probe stimulus. Movement-related effects (3 translational and 3 rotational), and trials on which participants responded incorrectly were included as covariates of no interest. High-pass filtering at a cutoff of 128Hz and a first-order autoregressive (AR(1)) serial correlation correction were also included in the analysis as in the first level analysis of the number landmark task.

3. Results

3.1. *Behavioural performance*

An overview of the results is shown in table 1. In the main experiment, RTs and error rates were first averaged per condition and per subject and were then independently subjected to a repeated-measures analysis of variance with task (landmark vs ellipse) and stimulus type (number vs colour) as within-subject factors. Paired *t*-tests were then applied as post-hoc tests comparing the different conditions.

The RTs showed a main effect of stimulus type [$F(1,16)=90.15$, $p<0.001$, $\eta^2=0.85$] and task [$F(1,16)=39.22$, $p<.001.$, $\eta^2=0.71$]. Furthermore, the task by stimulus type interaction was also significant [$F(1,16)=37.94$, $p<0.001$, $\eta^2<0.70$] . Post-hoc comparisons revealed that these effects were driven by the Number_landmark task which had significantly longer RTs compared to the other three tasks [all *t*s> 7]. Based on these results, we wanted to eliminate reaction time differences from subsequent imaging analyses at the decision phase for which we included the trial-by-trial RTs as an additional regressor.

Error rates showed no main effect of stimulus type [$F(1,16)=2.14$, $p=0.16$, $\eta^2=0.118$] or task [$F(1,16)=0.17$, $p=0.682$, $\eta^2=0.011$], but an interaction between these factors [$F(1,16)=34.11$, $p<0.001$, $\eta^2=0.68$]. Subjects were more accurate during the Colour_ellipse condition than during the Number_ellipse condition [$t(16)=4.98$, $p<0.001$] and the Colour_landmark condition [$t(16)=3.63$, $p=0.012$]. This can be explained by a low-level visual effect at the decision phase of the ellipse discrimination task. The same symbols were used (§§) throughout the colour condition. This may have served as an easier visual reference that allowed subjects to more easily distinguish a circle from an ellipse compared to the Number_ellipse condition where the visual appearance of the stimulus was less homogenous (different digits) and varied from trial to trial due to the variability of the number stimuli. Furthermore, subjects were also more accurate during the Number_landmark

condition than during the Number_ellipse condition [t(16)=-2.96, p=0.009] and Colour_landmark condition [t(16)=-2.41, p=0.028]. These accuracy measures suggest that in combination with the RT measures subjects put more effort in the number landmark task for which they spent more time in order to perform well.

Finally in the localiser task, informative trials led to faster RTs compared to neutral trials [neutral: $M = 929.87$ ms, $SE = 35.57$; informative: $M = 820.45$, $SE = 42.96$; t(16)=-3.35, p=0.0041], indicating that participants processed and employed the cues to direct their attention, however, without having an impact on accuracy. Accuracy was equal in the two conditions [neutral: M=73.7%, $SE = 1.9$; informative: $M = 76.7$%, $SE = 1.7$; t(16)=1.35, p=0.20].

Table 1. Behavioural Results Main Experiment

	Numbers		Colours	
	Landmark	Ellipse	Landmark	Ellipse
Error Rate	10.88 (1.17)	18.97 (2.56)	15.88 (2.13)	9.41 (1.49)
RTs	864.26 (32.74)	707.01 (23.41)	703.44 (26.95)	693.54 (23.70)

Note: Error rates in percentages and RTs in milliseconds with standard errors between brackets.

3.2. *Imaging results*

3.2.1 Main experiment

In a first contrast, we identified the number network used to solve the numerical landmark task [(Number_landmark$_{encoding}$+Number_landmark$_{decision}$)> (Number_ellipse$_{encoding}$+ Number_ellipse$_{decision}$)]. This revealed an extensive bilateral parietofrontal network with parietal regions ranging from posterior to anterior parietal

cortex (see Table 2). There was also an involvement of the left inferior temporal

cortex, probably corresponding to the visual number form (Arsalidou & Taylor, 2011).

Similarly, we tried to identify the colour network, but we did not find any supra-

threshold difference [(Colour_landmark$_{encoding}$+Colour_landmark$_{decision}$)>

(Colour_ellipse$_{encoding}$+ Colour_ellipse$_{decision}$)]. This failure in identifying the colour

network could be explained by a strong heterogeneity in how participants solved the

task. This is supported by anecdotal evidence from participants reporting a mixture

of visual and verbal strategies. Therefore, we decided to discard the colour tasks

from further analyses and interpretation.

To get a better understanding of the specific functional contributions of the

regions in the number network to the number landmark task, we tested which

parietal nodes were involved in the encoding of numbers

(Number_landmark$_{encoding}$>Number_ellipse$_{encoding}$) using the number decision

contrast (Number_landmark$_{decision}$>Number_ellipse$_{decision}$) as an exclusive mask

(p<0.05, uncorrected). This revealed a right lateralized activation in the anterior part

of the intraparietal sulcus (anterior IPS, which we will further refer to as aIPS when

abbreviations are used; Choi et al., 2006; Scheperjans et al., 2007, 2008), extending

towards the postcentral gyrus and the supramarginal gyrus, as well as, more

posteriorly, in the bilateral superior parietal lobule (SPL; Scheperjans et al., 2007,

2008) (see Table 3A and Figure 3A).

Conversely, to test which parietal nodes were involved in the comparison of

numbers (Number_landmark$_{decision}$>Number_ellipse$_{decision}$) we used the number

encoding contrast (Number_landmark$_{encoding}$>Number_ellipse$_{encoding}$) as an exclusive

mask (p<0.05, uncorrected). This revealed a contribution of the right inferior parietal

lobule (R IPL) corresponding to the angular gyrus, with three neighbouring peaks

(PGp, PGa and PFm; Capsers et al., 2006, 2008) (see Table 3B and Figure 3A).

Table 2. Number network

Anatomical Region	Hemisphere	Cluster size	Z score	MNI coordinates		
				x	y	z
Number Network						
Posterior-Medial Frontal	L	1682	5.77	-6	8	52
Precentral Gyrus	L	830	5.04	-46	4	38
Inferior Frontal Gyrus (p. Opercularis)	R	250	4.28	42	8	40
Middle Frontal Gyrus	R	712	4.64	36	46	22
Inferior Parietal Lobule (Supra Marginal Gyrus)	**R**	**1482**	**4.78**	**50**	**-34**	**44**
Intraparietal sulcus (hIP2/Area2)	**R**		**4.54**	**42**	**-40**	**50**
Inferior Parietal Lobule	**R**		**4.36**	**26**	**-62**	**36**
Intraparietal sulcus (Area 2)	**L**	**383**	**4.08**	**-42**	**-36**	**42**
Intraparietal sulcus (hIP3)	**L**		**3.89**	**-32**	**-42**	**44**
Superior Parietal Lobule (7A/hIP3)	**L**	**524**	**4.34**	**-22**	**-58**	**52**
Superior Parietal Lobule(7A/7PC)	**L**		**3.47**	**-36**	**-52**	**62**
Superior Parietal Lobule (7A)	**L**		**3.46**	**-24**	**-70**	**40**
Insula lobe	R	1226	4.17	32	20	0
Insula lobe	L	306	4.02	-24	32	0
Inferior Temporal Gyrus	L	111	4.01	-46	-60	-8

Note: List of main peaks that showed a significant activation during the number landmark task relative to the number ellipse condition at a threshold level of *p*<0.001 (0.05 corrected at cluster level). For parietal regions, subpeaks within the main cluster are also reported. The anatomical labels for the MNI coordinates were obtained from the SPM Anatomy Toolbox (Eickhoff et al., 2005).

Table 3

Anatomical Region	Hemisphere	Cluster size	Z score	MNI coordinates		
				x	y	z
A. Number Landmark Encoding						
Precentral Gyrus	L	614	5.18	-48	-2	54
Posterior-Medial Frontal	L	620	5.04	-4	2	60
Inferior Temporal Gyrus	L	329	4.19	-46	-64	-8
Inferior Temporal Gyrus	R	69	4.01	54	-54	-6
Superior Parietal Lobule (7A)	**L**	**137**	**4.08**	**-18**	**-58**	**56**
Superior Parietal Lobule (7A)	**L**		**3.81**	**-18**	**-66**	**54**
Superior Parietal Lobule (hIP3)	**L**		**3.69**	**-18**	**-60**	**46**
Superior Parietal Lobule (hIP3)	**R**	**170**	**3.98**	**26**	**-58**	**58**
Superior Parietal Lobule (7PC)	**R**		**3.62**	**30**	**-54**	**68**
Superior Parietal Lobule	**R**		**3.54**	**22**	**-54**	**48**
Anterior Intraparietal sulcus (hIP2)	**R**	**178**	**3.91**	**44**	**-34**	**34**
Inferior Parietal lobule (PFt; postcentral gyrus)	**R**		**3.8**	**46**	**-24**	**32**
Inferior Parietal lobule (Area 2; supramarginal gyrus)	**R**		**3.67**	**42**	**-32**	**42**
Postcentral Gyrus	L	62	3.8	-64	-16	22
Area hOc4la	L	56	3.74	-48	-84	4
Superior Occipital Gyrus	R	63	3.58	24	-96	10
Caudate Nucleus	L	3424	5.37	-22	30	4
Cerebellar Vermis (4/5)		194	3.99	0	-50	-2
B. Number Landmark Decision						
Middle Frontal Gyrus	R	197	4.02	28	12	50
IFG (p. Triangularis)	L	519	4.24	-42	34	20
Inferior Parietal Lobule (PGp)	**R**	**79**	**4.19**	**44**	**-74**	**36**
Inferior Parietal Lobule (PGa)	**R**	**73**	**3.61**	**34**	**-58**	**40**
Inferior Parietal Lobule (PFm)	**R**	**55**	**3.79**	**48**	**-52**	**56**
Insula Lobe	R	269	4.17	34	28	0
Insula Lobe	L	131	3.73	-34	22	0
Superior Medial Gyrus	R	59	3.51	4	24	50

Note: (A) Number Encoding. List of areas that showed a significant activation during the encoding of the number landmark task [(Number_landmark$_{encoding}$ > Number_ellipse$_{encoding}$) exclusively masked by number landmark decision (Number_landmark$_{decision}$ >

Number_ellipse$_{decision}$)]. (B) Number Decision. List of areas that showed a significant activation during the decision of the number landmark task [(Number_landmark$_{decision}$ > Number_ellipse$_{decision}$) exclusively masked by number landmark encoding (Number_landmark$_{encoding}$ > Number_ellipse$_{encoding}$)]. Threshold level was set at p<0.001 (0.05 corrected at cluster level) for the main contrast and at p<0.05 for the exclusive mask. For parietal regions, subpeaks within the main cluster are also reported. The anatomical labels for the MNI coordinates were obtained from the SPM Anatomy Toolbox (Eickhoff et al., 2005).

3.2.1 Localiser task

  To further specify the functional characteristics of the four parietal regions that we identified through the whole brain analysis (encoding: bilateral SPL and R aIPS; decision: R IPL; see figure 3A), we inspected how these regions behaved in the attentional localiser task by means of ROI analyses in which each of the four regions was taken as a separate functionally defined ROI. Note that we clustered the PGa, PGp and PFm regions into one larger IPL cluster (Choi et al., 2006; Scheperjans et al., 2007, 2008). We did this for the following reasons: First, the neural responses in these smaller regions were similar when the ROI analyses were performed on them separately. Second, lowering the statistical threshold to (<.005) at the whole-brain level showed that these three subpeaks belonged to the same cluster in the IPL.

  In a first ROI analysis (see figure 3B), we tested whether the parietal nodes of the landmark task were also involved in the encoding of information in working memory. Specifically, for each of the four parietal regions we compared the estimates of the encoding phase of the localiser task (in which 4 coloured crosses and their position had to be encoded) to the estimates of the attentional cueing phase in which a cue was presented (defined as the average of the informative and neutral cue estimates).

  Paired t-tests were performed in each ROI analysis that were then Bonferroni-corrected (p<.05) for the number of ROIs. While the encoding and cueing

stages of the landmark task were indiscriminable in the right anterior IPS [$t(16)$=1.67, p=0.45], bilateral pSPL [left: $t(16)$= 3,57, p=0.01; right: $t(16)$=4.05, p=0.004] showed a stronger response in the encoding phase than in the cueing phase, indicating that SPL plays a general role in working memory encoding, as it is involved in both the encoding phase of the number information in the landmark task and the coloured crosses in the localiser task. Right IPL [$t(16)$=-2.98, p=0.04] showed the opposite profile: activity was stronger in the cueing phase than in the encoding phase.

In a second ROI analysis (see figure 3C), we further inspected the activity of

the ROIs during the cueing phase. In particular, we tested which of the ROIs were

sensitive to attentional shifts in working memory by comparing the model estimates

related to the condition with informative cues to the condition with neutral cues. Only

the right IPL showed a significant difference between the informative and neutral cue

trials [$t(16)=3.57$, $p=0.01$], while the other parietal nodes were not responsive to this

difference [L SPL: $t(16)=2.11$, $p>0.05$; R SPL: $t(16)=0.78$, $p>0.05$;R aIPS $t(16)=$

$t(16)=-0.92$, $p>0.05$]. This is in line with the first ROI analyses that showed right IPL
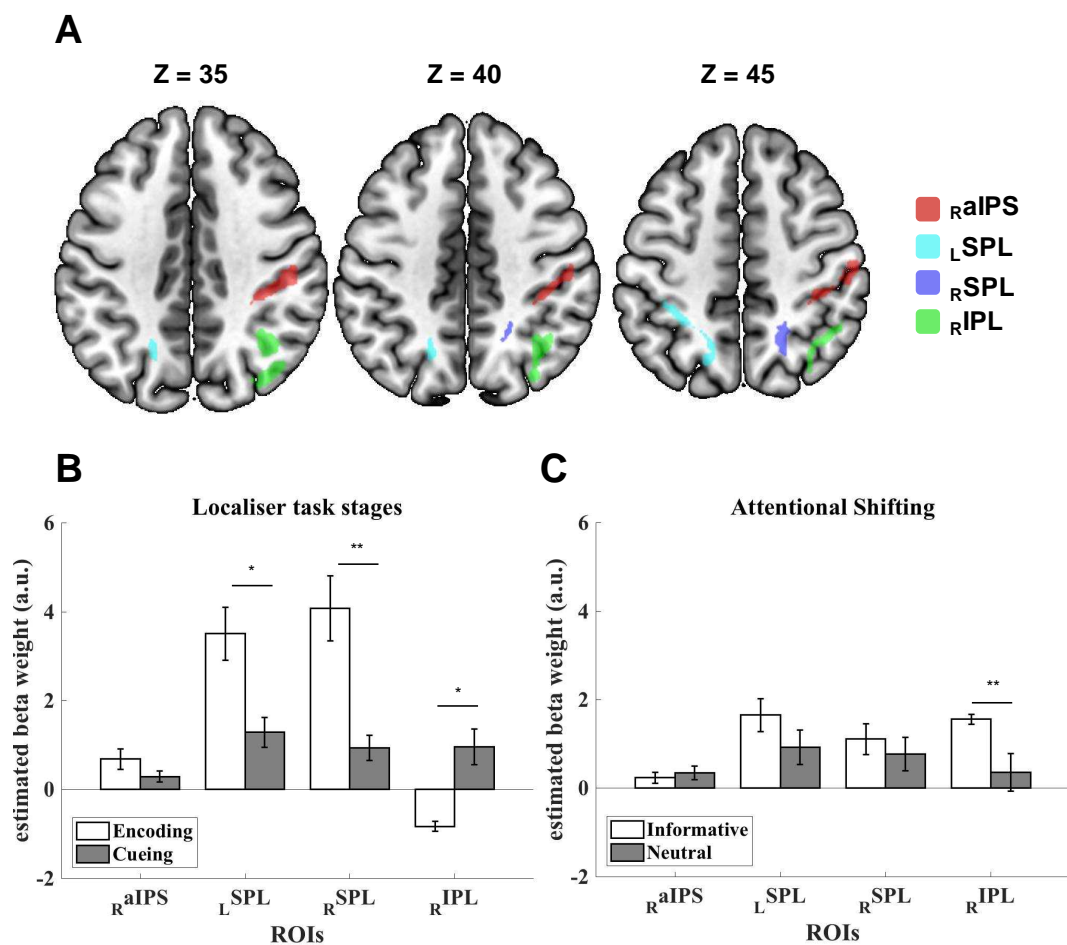
involvement in the cueing phase.

Figure 3. (A) Regions that were activated during the encoding and decision of the numbers in the number landmark task. The parietal nodes that were involved in the encoding stage constituting the ROIs for the subsequent ROI analyses were: $_L$SPL = Left Superior Parietal

Lobule (Scheperjans et al., 2007, 2008), $_R$SPL = Right Superior Parietal Lobule (Scheperjans et al., 2007, 2008) and $_R$aIPS = Right anterior Intraparietal Sulcus (Choi et al., 2006; Scheperjans et al., 2007, 2008). The parietal ROI that was involved in the decision stage was the $_R$IPL = Right Inferior Parietal Lobule (Caspers et al., 2006, 2008). Note that we lowered the statistical threshold to (<.005) at the whole-brain level for visualisation purposes. (B) Localiser task stages. ROI analyses comparing the encoding and cueing stages of the localiser task. (C) Attentional Shifting. ROI analyses pertaining to the attentional shifting in working memory by comparing the informative cue condition to the neutral cue condition. Significant differences between the different stages and cue conditions of the localiser task are indicated by the asterisks (* = p<0.05; ** = p<0.01, Bonferroni corrected).

4. Discussion

This study was designed to explore the neural basis of number processing in the context of a numerical landmark task that requires the storage and processing of multiple numerical magnitudes in symbolic notation in working memory with the aim of validating the functional interpretation of parietal activations observed in previous studies and of further refining the purported functions. More specifically, we wanted to evaluate to what extent the regions that were identified by earlier studies during the execution of a numerical landmark task depend on the explicit display of landmark labels flanking a visual line (the so-called number line estimation task). To do so, we used a fragmented landmark task where the two number landmarks were held in working memory, without any visual aid on the screen, until the target was presented to be mentally compared to the memorised landmarks. Previous studies revealed a functional distinction between anterior and posterior parietal regions (Kanayet et al., 2017; Vogel et al., 2013). In the study of Kanayet et al. (2017), anterior IPS was activated in the number line estimation task but not in the non-numerical control tasks and its activity depended on the numerical magnitude relationships between the landmarks and target number, suggesting a specific involvement in number processing. The posterior regions did not specifically depend on the processing of numerical magnitude, suggesting that they serve domain-

general functions. This interpretation also fits the results of a meta-analysis that has led to the proposal of distinct roles in numerical cognition for the anterior and posterior regions of the parietal cortex (Dehaene et al. 2003).

The results of the present study show that, indeed, the numerical landmark task elicits a similar pattern of activations as those observed in the number line estimation task in earlier studies. This suggests that the activations of Vogel et al. (2013) and Kanayet et al. (2017) are not restricted to explicit mapping in situations where the number line is visually available. This has also implications for studies relating the performance of the number line estimation task to mathematical achievement. Our results indicate that this relationship might be mediated by regions coding number magnitude but also by regions supporting more general functions.

The results of the present study show that the numerical landmark task engages an extensive parietofrontal network. The use of a fragmented trial design allowed us to determine specific regions that distinctively contributed to the encoding or decision stages of the landmark task: Three parietal regions in the right hemisphere and one in the left hemisphere. Comparison of these regions to the activations elicited by a non-numerical attentional localiser task allowed to further specify the functional contribution of these regions.

An anterior part of the right intraparietal sulcus was activated while encoding the numerical landmarks, but not at the time the target was presented and a response decision had to be made. This region overlapped with or was very close to the anterior parietal regions reported in Vogel et al. (2013) and Kanayet et al. (2017) as well as in another numerical landmark study (Koten, Lonnemann, Willmes & Knops, 2011). Taking this anterior IPS area as a region of interest for the analyses

of the attentional localiser showed that this area was not involved when the array of memory items (coloured crosses) had to be encoded. This indicates that the contribution of this region to encoding in working memory is not general but specific to the numerical landmark task. Of course, based on the current study specificity can only be defined relative to the stimuli and processes in the localiser task. Yet a broader sense of specificity is suggested by the fact that this region was also activated in the studies of Kanayet et al. (2017) and Vogel et al. (2013). In the first study, the activity of this region was determined by the numerical distance of the target number with respect to the landmark during the planning phase of the number line estimation task. In the second study, this region was activated during the mapping of numerical magnitudes on a line but not during the mapping of non-numerical magnitudes. Our design does not allow to determine the exact nature of the representations and/or processes during number encoding. There are a number of possibilities. First, the fact that our anterior parietal region overlaps with or is in the close proximity of clear magnitude-based neural activations in other studies (for meta-analyses, see Dehaene, et al., 2003; Sokolowski, Fias, Mousa & Ansari, 2017; Sokolowski, Fias, Bosah Ononye & Ansari, 2017) suggests the involvement of a representation of number magnitude. A critical question that arises in this respect is whether, if numerical, these regions are reflecting calculation processes during the retention interval. Indeed, in principle participants could have calculated the numerical midpoint between the two numbers which could then be used as a reference for situating the target number. However, it is unlikely that this strategy was employed by the subjects. Not only did we instruct the participants not to do so, the procedure discouraged them from doing so. The numbers were selected in such a way that easy calculations were avoided. Landmarks were always two-digit

numbers avoiding the easy numbers below 20, with distances of 17 to 35 units between them. Also, targets were close to the mean of the two numbers, so that approximate calculations would not be sufficient.

Apart from specific magnitude-related number representations or processes, a second possibility to consider is that this anterior IPS region reflects working memory-related processing, given that the anterior IPS regions were active during the number encoding stage, which has a clear maintenance component to keep the numbers active during the retention interval. Interestingly, the same anterior IPS regions have been shown active in working memory tasks (Majerus et al., 2010). The involvement is most pronounced when the serial order of information in working memory has to be maintained or recognised (Majerus et al., 2006, 2007, 2010; Marshuetz, Smith, Jonides, DeGutis, & Chenevert, 2000). Order is a property shared by numbers and several other series, such as letters of the alphabet, that were also found to activate the anterior IPS areas (Fias, Lammertyn, Caessens & Orban, 2007). Attout, Fias, Salmon and Majerus (2014) demonstrated an explicit neural overlap between number and order processing in working memory. It has also been demonstrated that serial order in verbal working memory is spatially coded, with initial items on the left and items towards the end of the sequence on the right leading to SNARC-like effects, not on the basis of number magnitude but on the basis of serial position in working memory (van Dijck & Fias, 2011; van Dijck, Abrahamse, Majerus & Fias, 2013).

Hence, it is possible that the anterior IPS regions that are activated during the maintenance interval provide the spatially coded order working memory frame on which the selection mechanisms operate during the number landmark task. Interestingly, a study of Koten et al. (2011) showed that a right anterior IPS, also

extending to the postcentral gyrus like in the present study, was involved in the integration of numerical and spatial information in a numerical landmark task in which the physical position of the target to the closest landmark was manipulated such that it could be congruent or incongruent with the numerical distance. The right anterior IPS region was shown to be sensitive to this congruency of spatial and numerical information.

Such a spatially coded order working memory frame may be constructed and used in contexts that might be then recruited when an unequivocal mapping to serial position in working memory is possible (as is the case for instance with information stored in long-term memory that is organised based on serial order [e.g. alphabetical order, Fias et al., 2007]) or is needed (as is the case for order working memory tasks). However, when there is no intrinsic order in long term memory and there is no need to order information, no such spatially coded order working memory frame will be constructed, and no involvement of the anterior IPS is expected. This is confirmed by the absence of activation during the encoding phase of the localiser task. Similarly, a study looking at the parietal involvement of the anterior IPS (at a similar location as our region) during the generation of words from ordered (numbers and months) versus non-ordered (animals) semantic categories revealed anterior IPS activation for the ordered but not for the non-ordered categories (Ischebeck et al., 2008).

Interestingly, the use of a spatially coded order working memory frame might also be the underlying explanatory factor for the fact that individual differences in tasks requiring the processing of the order of numbers, rather than their magnitude, are predictive of mathematical skill (Lyons & Beilock, 2011). Along the same lines, but at a neural level, Knops and Willmes (2014) recently found that a right anterior

parietal region, very similar to the parietal region that we observe in the present study, is not only involved in numerical ordering but also plays a role in symbolic arithmetic tasks, especially when order is important, as is the case for subtraction (Knops & Willmes, 2014).

Encoding in the numerical landmark task not only recruited the right anterior parietal region but also the more posteriorly located superior parietal lobule (SPL), bilaterally. However, when looking at the involvement of this region in the attentional localiser task, this SPL region shows a different profile, because it is clearly recruited during the encoding of the coloured stimuli. This suggests that this region plays a role in encoding information in working memory that is of a more general nature than the processes that are specifically involved in number representation or order working memory.

More lateral and posterior from these bilateral SPL regions, activation was observed in the right IPL during the numerical landmark task. Unlike the anterior IPS and the SPL regions that were engaged in the encoding phase, this right lateralised IPL region was active during the decision phase. Activity in this region was also observed in the Vogel et al. (2013) and Kanayet et al. (2017) studies. However, in contrast to these previous studies we were able to evaluate the underlying function of this domain-general contribution. The right IPL region, as opposed to the IPS and SPL regions, shows systematic activity during the localiser task: it shows greater activity when an informative cue is presented compared to when a non-informative cue is presented, confining its functional contribution to the landmark task as cue-based shifts of spatial attention in representational space. Together with the fact that the localiser task involved non-numerical stimuli, this suggests that the decision comprises domain-general attentional mechanisms to situate the probe with respect

to the landmarks. The fact that this region was involved in the present study with memorised landmarks and in the Vogel et al. (2013) and Kanayet et al. (2017) studies which used visually available landmarks, indicates that the attentional mechanism subserved by this area operates both in mental and physical space. Such a functional interpretation is in line with the hypothesis proposed by Dehaene et al. (2003) and is consistent with behavioural indications that domain-general mechanisms of spatial attention are closely related to number processing as a means to orient attention in representational space (Hubbard, Piazza, Pinel & Dehaene, 2005), as is evident by the fact that numbers can act as spatial cues in a Posner cueing paradigm as a function of their numerical value (Fischer, Castel, Dodd & Pratt, 2003). Small numbers can cue attention to the left, large numbers to the right. Also the bisection bias towards larger number produced by spatial neglect patients in the numerical bisection task (Zorzi et al., 2012) is indicative in this respect. At the neural level, the systematic involvement of saccade-related areas during addition and subtraction (Knops et al., 2009) similarly points to an involvement of spatial attention in numerical processing. At the behavioural level a number of studies have shown that shifts of spatial attention have an impact on arithmetic problem solving (Masson & Pesenti, 2015; Masson, Letesson & Pesenti, 2017; Liu, Cai, Verguts & Chen, 2017).

Interestingly, mechanisms of spatial attention have also been implicated in the processing of serial position in working memory (van Dijck, et al., 2013; De Belder, Abrahamse, Kerckhof, Fias & van Dijck, 2015). Analogously to Fischer et al. (2003) shifts of spatial attention in a Posner cueing paradigm could be evoked by cues retrieved from working memory: the more the cue was positioned towards the end of a working memory sequence, the more the detection of a right target was facilitated

compared to the detection of a left target (van Dijck et al., 2013). Vice versa, an attention shift towards the left facilitated retrieving information from the beginning of a memorised sequence, while an attention shift towards the right facilitated retrieval of information from the end of the sequence (De Belder et al., 2015).

It is hard to determine whether the anterior IPS and posterior parietal circuits that were observed in the present study build on long-term spatial number representations or, alternatively, on flexible spatially defined working memory representations. A flexible working memory representation is in line with recent studies that have shown that the pattern of activation of multiple voxels in regions corresponding to the present anterior IPS regions reflects the semantic relations between object names or pictures that were presented to the participants (Devereux, Clarke, Marouchos & Tyler, 2013; Neyens et al., 2017). This was interpreted in terms of the long-term semantic representations of the objects being mapped to working memory structures in the anterior IPS. In this respect, both possibilities (number vs working memory representations) do not have to exclude each other. The long-term number semantic information can be mapped to spatially coded working memory for efficient processing (Abrahamse, van Dijck & Fias, 2017). Another possibility is that serial order information is encoded using long-term numerical rank order representations (Marshuetz et al., 2000; Marshuetz, 2005), the computational possibility of which has recently been demonstrated in a modelling study (Botvinick & Watanabe, 2007).

In conclusion, our results show that in a numerical landmark task the right anterior IPS is involved in number coding while more posterior parietal regions, namely right IPL and bilateral SPL, provide domain-general support in the form of constructing a working memory representation or orienting spatial attention within

that mental representation during number comparison. These parietal regions largely

correspond to the activations observed in the number line estimation task,

suggesting that both tasks tap on the same neurocognitive circuitry. Further studies

should clarify whether these circuits support a long-term spatial representation of

numbers or general working memory frames that are spatially coded, and how the

interplay between these two putative systems is implemented at a neural level.

5. Acknowledgments

6. References

Abrahamse, E, van Dijck, J-P, & Fias, W. (2017). Grounding verbal working memory: The case of serial order. *Current Directions in Psychological Science, 26(5),* 429-433.

Arsalidou, M., & Taylor, M. J. (2011). Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage*, *54*(3), 2382–93. http://doi.org/10.1016/j.neuroimage.2010.10.009

Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *Neuroimage*, *26*(3), 839-851.

Attout, L., Fias, W., Salmon, E., & Majerus, S. (2014). Common neural substrates for ordinal representation in short-term memory, numerical and alphabetical cognition. *PloS One, 9(3)*, e92049. http://doi.org/10.1371/journal.pone.0092049

Booth, J. L., & Siegler, R. S. (2006). Developmental and individual differences in pure numerical estimation. *Developmental Psychology, 42(1)*, 189–201. http://doi.org/10.1037/0012-1649.41.6.189

Botvinick, M., & Watanabe, T. (2007). From numerosity to ordinal rank: a gain-field model of serial order representation in cortical working memory. The Journal of Neuroscience : *The Official Journal of the Society for Neuroscience, 27(32)*, 8636–42. http://doi.org/10.1523/JNEUROSCI.2110-07.2007

Caspers, S., Eickhoff, S. B., Geyer, S., Scheperjans, F., Mohlberg, H., Zilles, K., & Amunts, K. (2008). The human inferior parietal lobule in stereotaxic space. *Brain Structure and Function*, *212*(6), 481-495.

Caspers, S., Geyer, S., Schleicher, A., Mohlberg, H., Amunts, K., & Zilles, K. (2006). The human inferior parietal cortex: cytoarchitectonic parcellation and interindividual variability. *Neuroimage*, *33*(2), 430-448.

Choi, H. J., Zilles, K., Mohlberg, H., Schleicher, A., Fink, G. R., Armstrong, E., & Amunts, K. (2006). Cytoarchitectonic identification and probabilistic mapping of two distinct areas within the anterior ventral bank of the human intraparietal sulcus. *Journal of Comparative Neurology*, *495*(1), 53-69.

De Belder, M., Abrahamse, E., Kerckhof, E., Fias, W., & Dijck, J. Van. (2015). Serial Position Markers in Space : Visuospatial Priming of Serial Order Working Memory Retrieval. *PloS One, 1–10*. http://doi.org/10.1371/journal.pone.0116469

Dehaene, S., Bossini, S., & Giraux, P. (1993). The mental representation of parity and number magnitude. *Journal of Experimental Psychology: General*, *122*(3), 371.

Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology, 20(3)*, 487–506. http://doi.org/10.1080/02643290244000239

Devereux, B. J., Clarke, A., Marouchos, A., & Tyler, L. K. (2013). Representational Similarity Analysis Reveals Commonalities and Differences in the Semantic Processing of Words and Objects. *Journal of Neuroscience, 33(48)*, 18906–18916. http://doi.org/10.1523/JNEUROSCI.3809-13.2013

Dormal, V., Schuller, A.-M., Nihoul, J., Pesenti, M., & Andres, M. (2014). Causal role of spatial attention in arithmetic problem solving: Evidence from left unilateral

neglect. *Neuropsychologia, 60*, 1–9.

Eickhoff S, Stephan KE, Mohlberg H, Grefkes C, Fink GR, Amunts K, Zilles K: A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage* 25(4), 1325-1335, 2005

Fias, W., Brysbaert, M., Geypens, F., & d'Ydewalle, G. (1996). The importance of magnitude information in numerical processing: Evidence from the SNARC effect. *Mathematical Cognition, 2*, 95-110.

Fias, W., Lammertyn, J., Caessens, B., & Orban, G. a. (2007). Processing of abstract ordinal knowledge in the horizontal segment of the intraparietal sulcus. The Journal of Neuroscience : *The Official Journal of the Society for Neuroscience, 27(33)*, 8952–6. http://doi.org/10.1523/JNEUROSCI.2076-07.2007

Fischer, M. H., Castel, A. D., Dodd, M. D., & Pratt, J. (2003). Perceiving numbers causes spatial shifts of attention. *Nature Neuroscience, 6(6)*, 555–6. http://doi.org/10.1038/nn1066

Friston, K. J., Holmes, A. P., Price, C. J., Büchel, C., & Worsley, K. J. (1999). Multisubject fMRI studies and conjunction analyses. *Neuroimage, 10*(4), 385-396.

Friston, K. J., Rotshtein, P., Geng, J. J., Sterzer, P., & Henson, R. N. (2006). A critique of functional localisers. *Neuroimage, 30(4)*, 1077-1087.

Hubbard, E. M., Piazza, M., Pinel, P., & Dehaene, S. (2005). Interactions between number and space in parietal cortex. *Nature Reviews. Neuroscience, 6(6)*, 435–48. http://doi.org/10.1038/nrn1684

Ischebeck, A., Heim, S., Siedentopf, C., Zamarian, L., Schocke, M., Kremser, C., & Delazer, M. (2008). Are numbers special? Comparing the generation of verbal materials from ordered categories (months) to numbers and other categories (animals) in an fMRI study. *Human brain mapping*, *29*(8), 894-909.

Kanayet, F. J., Mattarella-Micke, A., Kohler, P. J., Norcia, A. M., Mccandliss, B. D., & Mcclelland, J. L. (2017). Distinct Representations of Magnitude and Spatial Position within Parietal Cortex during Number–Space Mapping. *Journal of Cognitive Neuroscience.* http://doi.org/10.1162/jocn_a_01199

Knops, A., Thirion, B., Hubbard, E. M., Michel, V., & Dehaene, S. (2009). Recruitment of an Area Involved in Eye Movements During Mental Arithmetic. *Science, 324(5934)*, 1583–1585. http://doi.org/10.1126/science.1171599

Knops, A., & Willmes, K. (2014). Numerical ordering and symbolic arithmetic share frontal and parietal circuits in the right hemisphere. *Neuroimage*, *84*, 786-795.

Koten Jr, J. W., Lonnemann, J., Willmes, K., & Knops, A. (2011). Micro and macro pattern analyses of fMRI data support both early and late interaction of numerical and spatial information. *Frontiers in human neuroscience*, *5*, 115.

Lepsien, J., & Nobre, A. C. (2006). Cognitive control of attention in the human brain: Insights from orienting attention to mental representations. *Brain Research, 1105*, 20-31.

Lyons, I. M., & Beilock, S. L. (2011). Numerical ordering ability mediates the relation between number-sense and arithmetic competence. *Cognition*, *121*(2), 256-261.

Liu, D., Cai, D., Verguts, T., & Chen, Q. (2017). The Time Course of Spatial Attention

Shifts in Elementary Arithmetic. *Scientific Reports, 1–8.*

Majerus, S., Bastin, C., Poncelet, M., Van der Linden, M., Salmon, E., Collette, F., & Maquet, P. (2007). Short-term memory and the left intraparietal sulcus: focus of attention? Further evidence from a face short-term memory paradigm. *NeuroImage, 35(1)*, 353–67. http://doi.org/10.1016/j.neuroimage.2006.12.008

Majerus, S., D'Argembeau, A., Martinez Perez, T., Belayachi, S., Van der Linden, M., Collette, F., & Maquet, P. (2010). The commonality of neural networks for verbal and visual short-term memory. *Journal of Cognitive Neuroscience, 22(11)*, 2570–93. http://doi.org/10.1162/jocn.2009.21378

Majerus, S., Péters, F., Bouffier, M., Cowan, N., & Phillips, C. (in press). The dorsal attention network reflects both encoding load and top-down control during working memory. *Journal of Cognitive Neuroscience.* http://doi.org/10.1162/jocn

Majerus, S., Poncelet, M., Van der Linden, M., Albouy, G., Salmon, E., Sterpenich, V., & Maquet, P. (2006). The left intraparietal sulcus and verbal short-term memory: focus of attention or serial order? *NeuroImage, 32(2)*, 880–91. http://doi.org/10.1016/j.neuroimage.2006.03.048

Marshuetz, C. (2005). Order information in working memory: an integrative review of evidence from brain and behavior. *Psychological Bulletin, 131(3)*, 323–339. http://doi.org/10.1037/0033-2909.131.3.323

Marshuetz, C., Smith, E. E., Jonides, J., DeGutis, J., & Chenevert, T. L. (2000). Order information in working memory: fMRI evidence for parietal and prefrontal mechanisms. *Journal of Cognitive Neuroscience, 12 Suppl 2*, 130–44. http://doi.org/10.1162/08989290051137459

Masson, N., Letesson, C., & Pesenti, M. (2017). Time course of overt attentional shifts in mental arithmetic: Evidence from gaze metrics. *The Quarterly Journal of Experimental Psychology*, 1–39.

Masson, N., & Pesenti, M. (2015). Interference of lateralized distractors on arithmetic problem solving: a functional role for attention shifts in mental calculation. *Psychological Research*, 1–12.

Masson, N., Pesenti, M., Coyette, F., Andres, M., & Dormal, V. (2017). Shifts of spatial attention underlie numerical comparison and mental arithmetic: Evidence from a patient with right unilateral neglect. *Neuropsychology, 31*, 822-833.

Neyens, V., Bruffaerts, R., Liuzzi, A. G., Kalfas, I., Peeters, R., Keuleers, E., … Vandenberghe, R. (2017). Representation of Semantic Similarity in the Left Intraparietal Sulcus: Functional Magnetic Resonance Imaging Evidence. *Frontiers in Human Neuroscience, 11(August)*, 1–18. http://doi.org/10.3389/fnhum.2017.00402

Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage, 25(3)*, 653-660. doi: 10.1016/j.neuroimage.2004.12.005

Nieder, A. (2005). Counting on neurons: the neurobiology of numerical competence. Nature Reviews. *Neuroscience, 6(3)*, 177–90. http://doi.org/10.1038/nrn1626

Nieder, A., Freedman, D. J., & Miller, E. K. (2002). Representation of the quantity of visual items in the primate prefrontal cortex. *Science (New York, N.Y.), 297(5587)*, 1708–11. http://doi.org/10.1126/science.1072493

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)*, 7457–62. http://doi.org/10.1073/pnas.0402239101

Piazza, M., Izard, V., Pinel, P., Le Bihan, D., & Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron, 44(3)*, 547–55. http://doi.org/10.1016/j.neuron.2004.10.014

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. http://doi.org/10.1016/j.neuron.2006.11.022

Roggeman, C., Santens, S., Fias, W., & Verguts, T. (2011). Stages of nonsymbolic number processing in occipitoparietal cortex disentangled by FMRI adaptation. *The Journal of Neuroscience, 31(19)*, 7168–73. http://doi.org/10.1523/JNEUROSCI.4503-10.2011

Santens, S., Roggeman, C., Fias, W., & Verguts, T. (2010). Number processing pathways in human parietal cortex. *Cerebral Cortex (New York, N.Y. : 1991), 20(1)*, 77–88. http://doi.org/10.1093/cercor/bhp080

Scheperjans, F., Eickhoff, S. B., Hömke, L., Mohlberg, H., Hermann, K., Amunts, K., & Zilles, K. (2008). Probabilistic maps, morphometry, and variability of cytoarchitectonic areas in the human superior parietal cortex. *Cerebral cortex*, *18*(9), 2141-2157.

Scheperjans, F., Hermann, K., Eickhoff, S. B., Amunts, K., Schleicher, A., & Zilles, K. (2007). Observer-independent cytoarchitectonic mapping of the human superior parietal cortex. *Cerebral Cortex*, *18*(4), 846-867.

Siegler, R. S., & Opfer, J. E. (2003). The Development of Numerical Estimation: Evidence for Multiple Representations of Numerical Quantity. *Psychological Science, 14(3)*, 237–250. http://doi.org/10.1111/1467-9280.02438

Sokolowski, H. M., Fias, W., Bosah Ononye, C., & Ansari, D. (2017). Are numbers grounded in a general magnitude processing system? A functional neuroimaging meta-analysis. *Neuropsychologia, 105*, 50–69. http://doi.org/10.1016/j.neuropsychologia.2017.01.019

Sokolowski, H. M., Fias, W., Mousa, A., & Ansari, D. (2017). Common and distinct brain regions in both parietal and frontal cortex support symbolic and nonsymbolic number processing in humans: A functional neuroimaging meta-analysis. *NeuroImage, 146(October 2016)*, 376–394. http://doi.org/10.1016/j.neuroimage.2016.10.028

Thompson, C. A., & Opfer, J. E. (2010). How 15 hundred is like 15 cherries: Effect of progressive alignment on representational changes in numerical cognition. *Child Development*, *81*(6), 1768-1786.

van Dijck, J.-P., Abrahamse, E. L., Majerus, S., & Fias, W. (2013). Spatial attention interacts with serial-order retrieval from verbal working memory. *Psychological Science, 24(9)*, 1854–9. http://doi.org/10.1177/0956797613479610

van Dijck, J.-P., & Fias, W. (2011). A working memory account for spatial-numerical associations. *Cognition, 119(1)*, 114–9. http://doi.org/10.1016/j.cognition.2010.12.013

Van Essen, D.C., Drury, H.A., Dickson, J., Harwell, J., Hanlon, D., & Anderson, C.H. (2001) An integrated software suite for surface-based analyses of cerebral cortex. *Journal of the American Medical Informatics Association, 8(5)*, 443–459.

Vuilleumier, P., Ortigue, S., & Brugger, P. (2004). The number space and neglect. *Cortex, 40(2)*, 399–410.

Vogel, S. E., Grabner, R. H., Schneider, M., Siegler, R. S., & Ansari, D. (2013). Overlapping and distinct brain regions involved in estimating the spatial position of numerical and non-numerical magnitudes: An fMRI study. *Neuropsychologia, 51(5)*, 979–89. http://doi.org/10.1016/j.neuropsychologia.2013.02.001

Worsley, K. J., Marrett, S., Neelin, P., Vandal, A. C., Friston, K. J., & Evans, A. C. (1996). A unified statistical approach for determining significant signals in images of cerebral activation. *Human Brain Mapping, 4(1)*, 58-73.

Zorzi, M., Priftis, K., & Umiltà, C. (2002). Neglect disrupts the mental number line. *Nature, 417(May)*, 138–139.