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Research Report

Exact and approximate judgements of visual and auditory numerosity: An fMRI study

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ARTICLE INFO
Article history:

Accepted 22 May 2006

Available online 7 July 2006

Keywords:

Estimation

Counting

Number

Right hemisphere

Laterality

Parietal cortex

ABSTRACT

Human adults can assess the number of objects in a set (numerosity) by approximate estimation or by exact counting. There is evidence suggesting that numerosity estimation depends on a dedicated mechanism that is a-modal and non-verbal. By contrast, counting requires the coordination between the pre-existing numerosity estimation abilities with language and one-to-one correspondence principles. In this paper we investigate with fMRI the neural correlates of numerosity estimation and counting in human adults, using both visual and auditory stimuli. Results show that attending to approximate numerosity correlates with increased activity of a right lateralized fronto-parietal cortical network, and that this activity is independent of the stimuli presentation's modality. Counting activates additional left prefrontal, parietal, and bilateral premotor areas, again independently from stimulus modality. These results dissociate two neuronal systems that underlie different numerosity judgements.

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1. Introduction

The human understanding of numbers is rooted in our ability to make judgements about numerosity. Numerosity is an abstract property of a set, since it is independent of the sensory attributes of its members and of the physical parameters of the set, such as shape, luminance, density, duration or frequency, even if it often co-varies with these parameters. Despite its abstractness, the ability to make approximate judgements on numerosity (estimation) does not depend on learning a symbolic system, as it spontaneously emerges in pre-linguistic

infants (Antell and Keating, 1983; Starkey and Cooper, 1980; Xu and Spelke, 2000), and is observable in non-human species (Brannon and Terrace, 2000; Church and Meck, 1984; Davis and Pérusse, 1988).¹ When a symbolic system – such as counting words – becomes available, exact numerosity judgements can extend to numerosities larger than those correctly estimated by infants and other species. It is held that counting develops initially by mapping the pre-verbal representations of numbers to a set of number words, according to certain rules (Gallistel and Gelman, 2000; Gelman and Gallistel, 1978). This mapping from numerosities to number words produces the symmetric

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¹ Particularly convincing are those studies that show cross modal transfer of numerosity and generalization of numerically relevant behavior to novel, non differentially reinforced stimuli (Brannon and Terrace, 2000; Church and Meck, 1984).

mapping from number words to numerosities, which allows the meaning of words as symbols for numerosity to emerge (Butterworth, 1999; Gallistel and Gelman, 1992; Wynn, 1996, 1998). Numerosity estimation and counting are therefore highly interdependent in the numerate adult and constitute the two most basic quantification processes that appear to ground all symbolic numerical thinking (however, see Simon, 1997, and Carey, 1998, for a different view on the development of counting). Nevertheless, while the neural correlates of symbolic numerical thinking such as calculation have been extensively explored, the functional neuroanatomy of quantification processes has seldom been previously investigated.

In this paper we present a functional imaging study that attempts to answer the following questions: which cerebral structures are involved in number estimation and which in counting? To what extent are these structures specific to certain physical attributes of stimuli such as the modality of presentation?

1.1. Estimation

Models of the cognitive processes involved in comparative numerosity estimation are inspired by the scalar timing theory first proposed to account for time estimation (Gibbon and Church, 1981). These models hypothesize the existence of an internal numerosity-accumulator system (Dehaene and Changeux, 1993; Meck and Church, 1983), which transforms objects and/or events into “abstract” items to be accumulated, irrespective of modality (visual, auditory, motor), mode (simultaneous or sequential), and physical characteristics (shape, position in space, duration, etc). The outputs of the accumulator are magnitudes that represent numerosity. While these models are successful in predicting behavior, they do not provide information with respect to the implementation of these mechanisms in the human (or animal) brain. However, recent electrophysiological studies have considerably improved our understanding of the neural bases of number sense, demonstrating the existence of cells that show preferential responses to a given numerosity (number coding cells) located both in the fundus of the intraparietal sulcus and in the lateral pre-frontal cortex between inferior arcuate sulcus and the principal sulcus (Nieder et al., 2002; Sawamura et al., 2002; Thompson et al., 1970). In particular, Nieder and Miller (2004) showed that neurons in the intraparietal sulcus responded to and conveyed numerosity information earlier than prefrontal neurons, suggesting that numerosity information is primarily extracted in the posterior cortex and only successively transmitted to the frontal cortex.

In humans much more data are available on the neural basis of number cognition, and it points to a crucial role for the parietal regions. However, the majority of the studies have been concerned with mental arithmetic or other tasks that depend on interpreting conventional symbols for numbers (numerals or number words) (Dehaene et al., 2003 for a review), while investigations into numerosity estimation are very sparse. Initially, neuropsychological studies showed that impairments in numerosity estimation are more likely to occur after right than left hemisphere damage (Kimura, 1996; McFie et al., 1950). Later it was shown that the right parietal lobe was the only locus relevant for estimation performance

(Warrington and James, 1967), since, out of a pool of subjects with lesions in the three lobes of the two hemispheres, only the group with lesions in the right parietal was impaired at numerosity estimation. Indeed, a right hemisphere superiority in quantity estimation was replicated using unilateral tachistoscopic presentation of stimuli to normal subjects (Kosslyn et al., 1989a; McGlone and Davidson, 1973; Young and Bion, 1979).

However, in all the aforementioned experiments stimuli consisted of simultaneous, very brief, visually presented items; no other modality (auditory, or motor) or mode (sequential) of presentation was tested. This prevents any conclusion being drawn that numerosity estimation is a modality independent process. Second, tasks involved the production of a number word. This could be problematic for investigations of non-verbal estimation because it is possible that subjects, having to generate an exact numerical result, may have used arithmetical strategies that depended on number symbols (such as counting by groups). In this sense, this procedure is not comparable with other studies in animals and infants in which no symbolic output is required, and where estimation is often tested by means of comparison between numerosities. Using fMRI, recently, two groups have independently demonstrated that certain regions in the intraparietal sulci of both hemispheres respond to approximate visual numerosity while subjects are simply passively exposed to arrays of stimuli (Ansari et al., 2006; Piazza et al., 2004, recently replicated by Cantlon et al., 2006). This suggests that both hemispheres possess approximate representations of numerosity. Even if these studies have the merit of not requiring the production of a number word, they do not directly investigate the cerebral correlates of explicit numerosity estimation, on which we are particularly interested here. Moreover, no other modality (auditory, or motor) or mode (sequential) of presentation was tested.

1.2. Counting

Cognitive models of counting (Gelman and Gallistel, 1978) propose that it relies on three crucial mechanisms: the individuation² of every single element of the set, the attribution of attentional “indexes” to already counted items to keep track of the previously explored spatial location and to avoid counting items twice (this only applies when items are simultaneously presented), and the use of articulatory and phonological codes in order to update the running total in the verbal short term storage (Logie and Baddeley, 1987).

Investigations of the neural implementation of this multi-stage attentional and linguistic process have shown a crucial role of both posterior parietal and prefrontal regions (Piazza et al., 2002, 2003; Sathian et al., 1999). However, as in the case of estimation, most studies on counting used simultaneously presented visual items, and this prevents interpretation in terms of a modality independent mechanism.

² Individuation is defined as an operation of selective attention that isolates items by “gluing” their features to particular points in space and/or time (Burkell and Pylyshyn, 1997; Intriligator and Cavanagh, 2001). When the items are less than three or four, in the putative “subitizing range”, individuation does not seem to be necessary.

1.3. The present study

In the present study, we used fMRI to investigate and directly compare brain responses to a numerosity estimation task, and to an exact counting task, using both visual and auditory stimuli. First, we wanted to segregate the functional structures involved in estimation and counting. While the counting task required an exact answer, we used a comparative estimation task (like the one used in infant or animal studies), in order to prevent subjects from counting and/or using arithmetical strategies. Moreover, we kept the stimuli constant across tasks in order to make sure that differences in cerebral activation were not due to differences in the sensory stimulation. The second goal was to investigate to what extent the brain structures involved in estimation and counting are specific to the modality of stimuli presentation, and therefore we used both visual and auditory stimuli.

Stimuli consisted of temporal sequences of alternating items (presented at a high rate of approximately 1 every 3 s) (see Fig. 1 and Experimental procedures). There were two different categories per modality: red and green lights for the visual presentation, and high and low tones for the auditory presentation. The numerosity estimation task consisted of deciding which category contained more items, and the counting task consisted of reporting the number of alternations between the two categories (e.g., the number of switches from a high tone to a low tone, and vice-versa). We also introduced a baseline perceptual task which consisted of

deciding if the last item in the sequence was identical to the first one. This was included in order to control for attention to the whole stimulus sequence, holding some information in working memory for the whole stimulus sequence, and a final two-choice button-press response.

2. Results

2.1. Behavioral data

Responses for the counting and the matching tasks were analysed in terms of accuracy. For the counting task, the mean percentage correct was 78% in the auditory and 79% in the visual modality. For the color (or pitch) matching task, performance was 77% correct in the auditory modality and 80% in the visual modality. A 2×2 (task \times modality) analysis of variance showed no main effect of task, nor of modality, and no interaction between task and modality, confirming that, for both tasks, there was no difference in difficulty between the auditory and visual stimuli.

In the case of the estimation task, where there was no absolute correct answer (as the number of events were the same for the two categories), in order to confirm that subjects cautiously performed the task in the scanner as they were largely trained to do before the scanning session, performance was analyzed in terms of the percentage of responses that could be predicted by the clustering manipulation (see Tasks session).

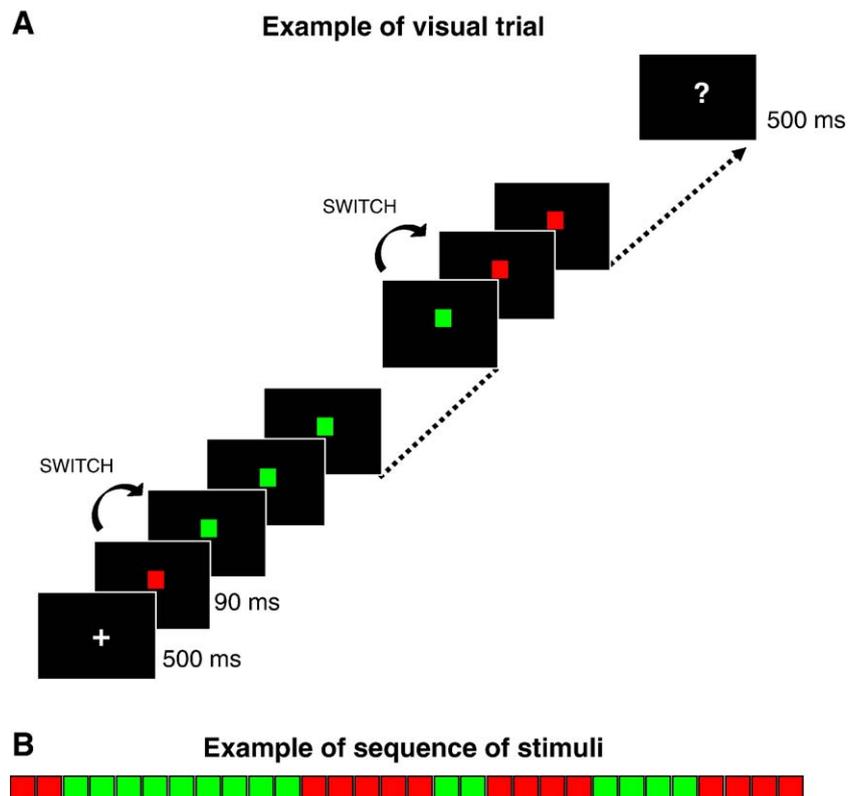


Fig. 1 – Schematic representations of visual sequence. (A) Schematic representation of a trial in the visual modality. Each trial started with a fixation point that lasted for 500 ms, followed by the stimuli (a sequence of 30 visual or auditory events), that lasted for about 6.5 s, and ended with a question mark, after which subjects could give their answer, within 1.5 s, via key pressing. (B) One exemplar sequence of stimuli in the visual modality (30 stimuli grouped in 7 clusters).

As shown initially by Erlick such clustering manipulations minimally but significantly alter the subjects' response distributions, so we expected a small but significant deviation from chance for all subjects (Erlick, 1963). This prediction was confirmed, in that all subjects performed above chance in the direction accounted for the clustering manipulation. Overall, performance on the estimation task was predictable for an average of 62% of the trials in the auditory modality, and 65% in the visual modality. Crucially, such effect did not significantly differ between modalities, and, in both cases, differed from chance ($\chi^2 P < 0.001$). Such results also confirm that subjects were not using a counting strategy: if they had been, their answers would have been at chance level because the number of items was the same in the two categories.

2.2. Activation data

2.2.1. Effects that are common for visual and auditory modalities

2.2.1.1. Estimation. Activation for estimation relative to matching was fully right lateralized (see Table 1 and Fig. 2A). It included a fronto/parietal network comprising a large part of the right intra-parietal sulcus, along the horizontal segment, the right precentral and inferior frontal cortices, the right dorsolateral prefrontal cortex extending rostrally to anterior middle frontal gyrus, and the medial superior frontal gyrus. No left hemisphere activation could be detected even when the threshold was as low as $P < 0.05$ uncorrected at the cluster level. Moreover, analysis at the individual subject level showed that indeed the right hemisphere superiority for estimation was highly reproducible across subjects: all ten subjects showed activation of the right parietal circuit described above. In addition, one subject (out of ten) showed symmetric activation in the left hemisphere, two showed some activation in different regions of the left parietal cortex (one in posterior parietal and one in the supramarginal gyrus), and a fourth subject activated a very anterior site of the dorsolateral prefrontal cortex.

Interestingly, some of the peaks of increased activation for estimation relative to the matching were also more active for estimation relative to counting (see plots in Fig. 2A). However, the random effect analysis directly comparing estimation and counting did not reveal any significant voxel.

2.2.1.2. Counting. Activation for counting relative to matching comprised all the regions involved in estimation. In

addition, there was increased activation in symmetric regions of the left hemisphere (inferior frontal gyrus, lateral precentral gyrus, and anterior intraparietal sulcus), and bilaterally in the dorsal and medial precentral gyrus. Some of these effects were confirmed in the contrast of counting > estimation. In particular, regions of higher activation for counting > estimation were located in the bilateral dorsal and medial precentral gyri (see Tables 2 and 3, and Figs. 2B and 3).

2.2.1.3. Task-related hemispheric differences. In order to study the possible task-related hemispheric asymmetries, and therefore to better distinguish counting from estimation, for each subject and each hemisphere we then extracted a standard measure of the intensity of the activation (the regression coefficient between the activity and the canonical HRF at the peaks identified in the random effect analysis) of the two regions showing bilateral symmetrical activation in counting and that were also activated in the right hemisphere for estimation, namely the anterior intraparietal (IP) and the lateral precentral cortex (see Fig. 4).

The data for each region in each hemisphere was then entered into an ANOVA, investigating the main effects of task and hemisphere, and possible task by hemisphere interactions. This analysis showed a reversed hemispheric pattern: for estimation the right hemisphere was more active than the left hemisphere, while the reverse was true for counting.

Overall, activity in the IP (see Fig. 4 top) was higher in the right than in the left hemisphere (main effect of hemisphere, $F(1,9) = 16.87$, $P = 0.003$), and higher for counting than for estimation (main effect of task, $F(1,9) = 96.82$, $P = 0.000$). However, crucially, there was a reversed pattern of activation of the left and right (IP) as a function of the task (hemisphere by task interaction, $F(1,9) = 190.69$, $P = 0.000$). Activation in the right IP cortex was higher for estimation than for counting ($t(9) = 6.79$, $P = 0.000$), while in the left IP it was higher for counting than for estimation ($t(9) = 13.66$, $P = 0.000$). Fig. 4 top right shows the individual subjects' data, from which it is evident that the reversed effect is present in each end every subject, and is therefore highly significant even if it is small in size. As for the precentral cortex (see Fig. 4 bottom), overall, its activation was higher for counting than for estimation (main effects of task ($F(1,9) = 9.51$, $P = 0.013$). However, a significant task by hemisphere interaction ($F(1,9) = 16.35$, $p.0.003$), indicated that higher activation for counting was present in the left hemisphere only ($t(9) = 4.37$, $P = 0.002$, and $t(9) < 1$, for the left and right hemisphere respectively).

2.2.2. Effects that are specific for each modality

There were no brain regions that were activated by one modality more than the other in our contrasts of interest (estimation > matching; counting > matching, estimation > counting, or counting > estimation).

3. Discussion

We collected fMRI brain activations while 10 subjects performed three tasks: approximate number estimation, exact counting, and perceptual matching over exactly the same temporal sequences of visual and auditory stimuli.

Table 1 – Estimation > matching

P (cluster)	Z	x	y	z	Cerebral region
0.000	(6.31)	48	42	14	Right Middle Frontal Gyrus (1)
	(5.60)	50	8	34	Right Lateral Precentral Gyrus (2)
	(4.84)	54	14	12	
0.000	(4.90)	52	-48	50	Right Intraparietal Cortex (3)
	(4.57)	54	-36	50	
	(4.52)	50	-56	54	
0.004	(4.25)	0	24	48	Medial Precentral Gyrus (4)
	(3.97)	-2	30	42	
	(3.96)	4	14	54	

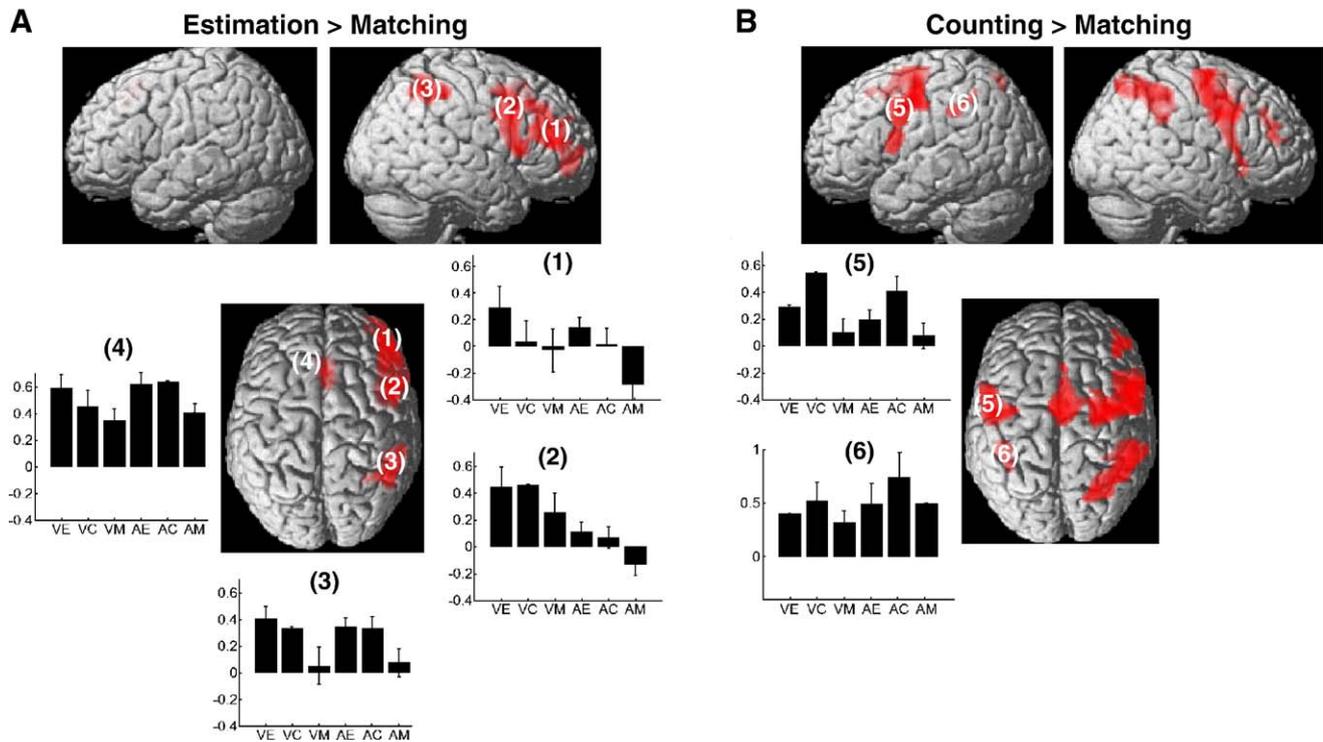


Fig. 2 – Cortical regions of increased activation common to visual and auditory modality for estimation and counting. Group results ($n = 10$, $P < 0.05$ corrected at the cluster level) are visualized on a three-dimensional rendering showing the left, right, and top views of the hemispheres. Plots show the activation of the (1) right middle frontal gyrus, (2 and 5), right and left precentral gyrus, (3 and 6) right and left anterior intraparietal cortex, (4) medial precentral gyrus peaks of the random effect analysis as a function of the 6 different experimental conditions (visual (V) and auditory (A) estimation (E), counting (C), and matching (M) tasks). Error bars represent standard errors of the mean (SEM). See Tables 1 and 2 for the co-ordinates of the clusters.

3.1. An a-modal right hemisphere superiority for approximate numerosity judgements

We identified a strictly right lateralized modality invariant fronto-parietal circuit, comprising intraparietal, pre-motor and dorso-lateral prefrontal cortex, which, given temporal sequences of visual and auditory items, is more activated when subjects estimate the number of items than when they attend to their color or pitch. This group result was confirmed at the single subject level, where all ten subjects participating in the study showed activation in those regions, and only four out of ten showed some activated voxels in the left hemisphere, all in small clusters inconsistently located even within these four subjects. The identification of such right lateralized circuit confirms previous behavioral studies that used tachistoscopic presentation and neuropsychological reports suggesting a right hemisphere superiority for numerosity estimation (Kimura, 1996; Kosslyn et al., 1989b; McGlone and Davidson, 1973; Warrington and James, 1967; Young and Bion, 1979). Our results also revealed that the activation of the right lateralized circuit involved in estimation was not modulated by the modality (visual or auditory) in which stimuli were presented. Even if such modality invariance has to be taken with the care generally devoted to null effects, it is to be noted that it comes as a confirmation of several previous observations and is predicted by a computational model of number processing. For

example, previous behavioral studies showed identical performance and cost-free transfer of numerosity across modalities of stimulus presentation, both in adults and in infants (Barth et al., 2003, 2005; Church and Meck, 1984; Starkey et al., 1990). Such modality-invariance is in line with a model of number processing that postulates an abstract supramodal internal representation of numerical quantity (Dehaene and Changeux, 1993). Finally, the absence of increased activation in the left hemisphere linguistic perisylvian areas for numerosity estimation, with respect to perceptual matching, indicates the relatively low involvement of linguistic operations in numerosity estimation, in line with the fact that non-human animals as well as pre-verbal infants are able to perform similar numerosity estimation tasks (Davis and Pérusse, 1988; Gallistel and Gelman, 1992; Starkey and Cooper, 1980). What is the nature of the computations performed by the frontal and parietal areas of the right hemisphere? One speculative interpretation is that it reflects the functional implementation of the numerosity-accumulation mechanism previously sketched in Introduction (Meck and Church, 1983). This mechanism consists of an initial transformation into abstract “oneness” (normalization), where each stimulus is transformed into abstract “oneness” by discarding irrelevant physical information like shape, color, intensity, position in space, duration in time, and so on (Dehaene and Changeux, 1993), and a subsequent accumulation of items in memory.

Table 2 – Counting > matching

P (cluster)	Z	x	y	z	Cerebral region
0.000	(7.28)	-54	4	38	Left Lateral Precentral Gyrus (5)
	(7.09)	-52	-8	46	
	(4.55)	-60	6	16	
0.000	(6.64)	32	-10	56	Right Lateral Precentral Gyrus (2)
	(6.62)	52	4	34	
0.000	(6.54)	6	-8	66	Medial Precentral Gyrus (4)
	(5.34)	52	-46	48	Right Intraparietal Cortex (3)
	(4.63)	46	-50	52	
0.028	(4.55)	60	-40	32	
	(4.38)	-40	-36	38	Left Intraparietal Sulcus (6)
0.009	(3.75)	-38	-48	46	
	(4.02)	46	42	16	Right Middle Frontal Gyrus (1)
	(3.84)	42	42	26	
	(3.54)	42	34	36	

In our experiment, information with respect to the shape and position in space of the visual stimuli were irrelevant, and so was information with respect to the duration or direction of the auditory stimuli. This kind of normalization process is typical of the computations attributed to parietal cortex, a high order cortex that receives direct and indirect projections from all sensory regions, activated in many tasks that involve attention and coordinates transformation in both spatial and temporal domains (Culham and Kanwisher, 2001; Duhamel et al., 1992). Numerosity sensitive cell assemblies in monkeys and cats have been found by electrophysiological recordings from areas that are homologous to parietal regions (Nieder and Miller, 2004; Sawamura et al., 2002; Thompson et al., 1970). According to the present proposal, then, the process of abstraction of numerosity could primarily be a function of the parietal cortex. After the initial normalization stage, the second stage consists of continuously accumulating the items in working memory and comparing them. These operations could be seen as emergent properties of the functional connections between parietal and frontal pre-motor and DLPF regions. Fronto-parietal functional loops are common to a wide range of cognitive operations where the active maintenance of information on line is necessary (Coull and Nobre, 1998; Jonides et al., 1998; Mccarthy et al., 1994). However, interestingly, the pattern of activation typically associated to generic mechanisms of temporal attention (i.e., attention to stimuli presented in different moment in time vs. in different spatial locations) tend to be left lateralized (Coull and Nobre, 1998), while attention to spatial positions or stimulus features is classically associated to bilateral activation (Corbetta and Shulman, 2002; Nobre, 2001; Wojciulik and Kanwisher, 1999). In the present study, stimuli were presented in temporal sequences in a fixed spatial position therefore the strictly right lateralized fronto-parietal activation associated to estimation seems to be unlikely to reflect a generic attention mechanism. Moreover, crucially, we observe a reversed hemispheric dominance as a function of the task: counting showed more activity in the left hemisphere while estimation showed more activity in the right hemisphere. Therefore, even if it can be argued that our perceptual matching baseline task was less attentional demanding than both our number-related tasks, it is difficult to maintain that the hemispheric dissociations that we observe between counting and matching are

attributable to some generic attentional mechanisms. Instead, the hemispheric dissociation can be seen in light of a previously suggested hemispheric specialization for global and local processing: previous imaging and neuropsychological studies, in fact, suggested a relative advantage of the right hemisphere for global processing (i.e. perception of and attention to the whole) and a left hemisphere bias for local processing (i.e. perception of and attention to the focal aspects of a complex stimulus) (Fink et al., 1997; Hellige et al., 1984; Robertson and Lamb, 1991; Robertson et al., 1988). In our study, estimation required more attention to the global numerosity while counting required more attention to the focal changes.

The right hemisphere superiority observed in the present study might seem to be in contradiction with the recent work of Piazza et al. (2004) and (Ansari et al., 2006) which show that both hemispheres respond to the number of objects in a visual array. However, a number of tentative arguments can be used to resolve such apparent discrepancy: first, as suggested by the fact that the Weber fraction of the number-coding voxels of the right hemisphere was larger than that in the left hemisphere, it is possible that there is a differential precision of number coding in the two hemispheres, perhaps due to interactions with an exact verbal code for number within the language-dominant left hemisphere (Dehaene and Cohen, 1997). In the present study, the subjects were explicitly instructed to perform a comparative judgement relying exclusively on their feeling of numerosity, and therefore it is possible that this has amplified the activation of the more approximate representation of the right hemisphere. On the contrary, in both previous studies on numerosity (Piazza et al., 2004; Ansari et al., 2006) subjects were not involved in an active task on numerosity, but simply requested to observe the stimuli, and therefore it is possible that they had nevertheless tried to determine the exact number of elements, therefore recruiting also the more exact representation of numerosity of the left hemisphere. Second, in both studies stimuli were presented in a visual array, while in the present study they were presented in temporal sequences. While behavioral data do not seem to suggest a difference in performance between these two modes of presentation in numerosity judgements, it is possible that the relative neural substrates are quite different. This is a probable but still open hypothesis which deserves future investigation.

3.2. Numerosity estimation and time estimation

Influential models of timekeeping and numerosity keeping are very similar, and this is because the psychophysics of

Table 3 – Counting > estimation

P (cluster)	Z	x	y	z	Cerebral region
0.001	(5.52)	8	-8	66	Medial Precentral Gyrus (7)
	(4.78)	-6	-4	62	
0.009	(4.99)	-50	-10	48	Left Superior Precentral Gyrus (8)
	(3.36)	-36	-10	42	
0.012	(4.59)	26	-12	58	Right Superior Precentral Gyrus (9)
	(4.05)	28	-14	48	
	(4.03)	40	-12	48	

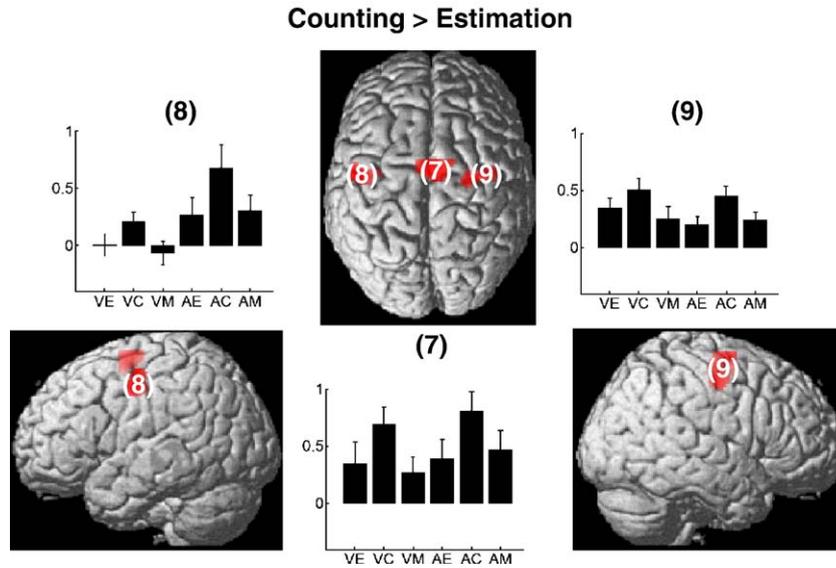


Fig. 3 – Cortical regions of increased activation common to visual and auditory modality for counting with respect to estimation. Group results ($n = 10$, $P < 0.05$ corrected at the cluster level) are visualized on a three-dimensional rendering showing the left, right, and top views of the hemispheres. Plots show activation of the (7) medial precentral gyrus and (8 and 9) left and right precentral gyri as a function of the 6 different experimental conditions (visual (V) and auditory (A) estimation (E), counting (C)),

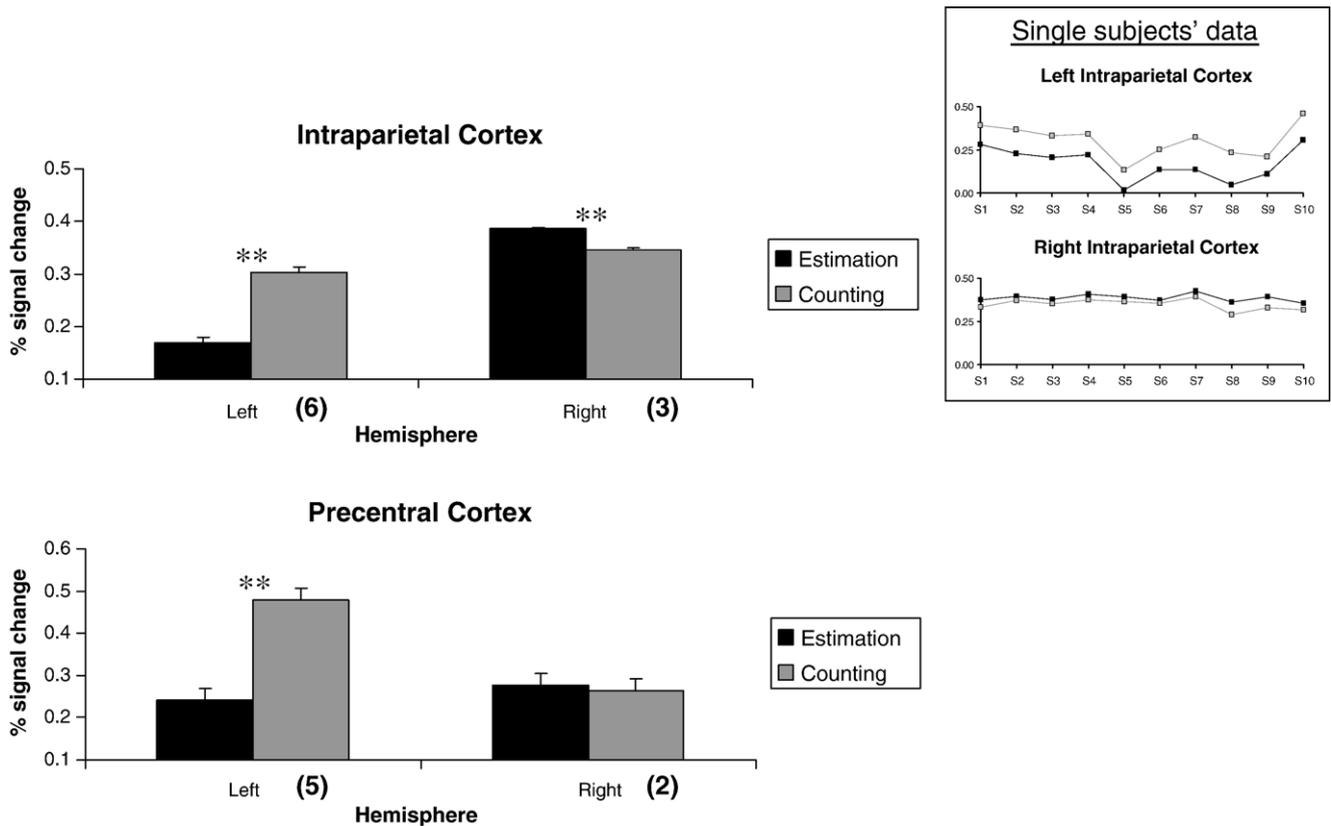


Fig. 4 – Plots of the task-related hemispheric dissociation. Top left is the mean activation level across subjects for the peak of the random effect analysis of the anterior intraparietal cortex as a function of the task and the hemisphere. Top right is the mean activation for each of the ten participants. Bottom is the mean activation across subjects for the precentral cortex peak. Error bars represent SEM. Numbers next to the x-axes indicates the regions labeled in Fig. 2 (co-ordinates in Tables 1 and 2).

numerosity and duration discrimination are themselves very similar (Meck and Church, 1983). Indeed, models of numerosity estimation and their version in the timing domain differ only in that the variable to be represented is numerosity in one case, and time in the other. Many experiments have previously been performed on time estimation: typically, they require subjects to compare and match time intervals. These experiments converge in highlighting the crucial role of subcortical structures like the basal ganglia and the cerebellum in the representation of time, together with a fronto-parietal system attributed to subsidiary functions of the process of accumulation and comparison (Malapani et al., 2002; Maquet et al., 1996; Rao et al., 2001; Tracy et al., 2000) (Coull et al., 2004). In the present experiment we did not observe activation in either the basal ganglia nor in the cerebellum (the cerebellum was not completely included in the data acquisition field). Does this result imply that representation of time and representation of numerosity rely on different brain systems? This is a plausible possibility that will require further direct investigation. For example, this idea would predict that patients with lesions in the cerebellum and/or basal ganglia that show impaired performance in time estimation should be perfectly normal in numerosity estimation tasks. To our knowledge, this comparison has not been performed yet. As we proposed earlier, it is possible that the abstraction of numerosity would be a function implemented in intraparietal regions of the right hemisphere. Whether there are specific sub-sets of neurons that are involved in numerosity estimation but not in time estimation is not known. This was not tested in the present experiment, but would be easily testable, for example by directly comparing brain activity during time and numerosity estimation.

3.3. Counting

The brain regions that showed increased activation in counting with respect to matching comprised the right fronto-parietal network that was also involved in estimation, with additional activation in superior lateral and medial precentral regions bilaterally, in the premotor and supplementary motor cortices.

This motor/attentional related system is likely to reflect sub vocal articulation during counting but may also reflect finger movement during counting which occurs as a vestige of the learning process, even when no real movement is actually performed, or explicitly imaged. In fact the dorsal prefrontal (pre-motor) peaks showing increased activation for counting with respect to estimation in the present study correspond to peaks previously associated to movements of the hand (while more ventral regions are associated with movements of the mouth, congruently with the classical motor organization of the region (Buccino et al., 2001).

The historical basis of number words in many languages, including English, lies in body-part names, in particular in the names for finger and hand (Menninger, 1969), and it is also a near universal feature to use one's fingers when learning both counting and simple arithmetic (Butterworth, 1999; Jeannerod et al., 1995). This hypothesis is also supported by the existence of a neuropsychological syndrome that Gerstmann first described at the beginning of the century (Gerstmann, 1940) in which trouble with numbers co-occur with trouble in representing fingers (finger agnosia). Indeed, a recent rTMS study showed that

stimulation over the left angular gyrus that selectively affected a finger gnosis task, also affected a numerical task that required consideration of number magnitudes (Rusconi et al., 2005). Interestingly, activity in most of the regions involved more in counting than in the perceptual baseline, were modulated by the number of items to be counted in displays of simultaneously presented dots in a previous study (Piazza et al., 2003). This suggests that the same cortical mechanisms are recruited when subjects count arrays, irrespective of whether the stimuli are presented sequentially or simultaneously, and, as shown here, in the visual or the auditory modality.

If we think of the numerosity estimation system as representing approximate numerosities, it could also be activated in symbolic number processing, especially in tasks that put great emphasis on numerical quantity, as numerals are symbols for numerosity. Indeed, a recent review on different neuroimaging studies of number processes reported that regions of the horizontal segment of the intraparietal sulcus, especially of the right hemisphere, are systematically activated whenever numbers are manipulated, independently of number notation, and with increasing activation as the task puts greater emphasis on quantity processing (Dehaene et al., 2003). Alone, at present, such results from functional imaging seem to be discrepant with lesion studies of symbolic number processing: in fact, acquired acalculias (resulting in different types of deficits of symbolic calculation) normally result from unilateral parietal lesions to the left hemisphere only (Cipolotti and van Harskamp, 2001). However, our admittedly speculative hypothesis that the left lateralized symbolic number system, in normal subjects, works in complete synergy with a right lateralized non-symbolic numerosity system, would resolve such apparent discrepancy. Our hypothesis therefore needs further testing, for example using within-subject fMRI experiments with high spatial resolution, where each subject performs both a non symbolic numerosity estimation task and a symbolic number manipulation task like number comparison or calculation. This would allow us to directly compare regions of increased activation in both processes, and to confirm or disconfirm our hypothesized common, abstract, number system.

In conclusion, in this study we used fMRI to isolate a right lateralized fronto-parietal network of increased activation for numerosity estimation which is independent from the modality (visual or auditory) of stimulus presentation. This result is in agreement with previous neuropsychological results suggesting a right hemisphere superiority for numerosity estimation and reinforces the assumption of an a-modal and non-verbal system for numerosity judgements. Results also revealed that counting recruited additional activity in pre-motor cortices, suggesting the attentional and/or sensorimotor nature of counting.

4. Experimental procedures

4.1. Subjects

Ten, healthy, right-handed volunteers (age 23 to 31, seven males, and three females), with normal or corrected-to-normal sight gave written consent.

4.2. Design

We used a 2×3 factorial design, with two input modalities (auditory and visual), and three tasks (estimation, counting, and matching). The 25-min single session experiment was organized into 4 modality specific blocks, presented in a counterbalanced order (Visual–Auditory–Auditory–Visual for 5 subjects and Auditory–Visual–Visual–Auditory for the other 5 subjects). Within each modality block, the three tasks were each repeated three times, and presented in alternating blocks of 4 trials each (see Fig. 1). Each task block was preceded by short instructions, consisting in one word written on the screen: “estimate”, “count”, or “match”, presented on the screen for 3 s. Between each modality block, subjects had a blank screen for 10 s, followed by a word (“visual”, “auditory”) announcing the modality of the following block. Overall, subjects performed 24 trials for each of the 3 tasks in each input modality, making a total of 144 trials ($24 \times 2 \times 3$) (see Fig. 5).

4.3. Stimuli

Stimulation consisted of temporal sequences of two distinct categories of very rapidly presented visual and auditory stimuli. For the visual modality, the stimuli were green and red filled squares (subtending a visual angle of 1.5°) presented one at a time on the center of a black computer screen. The luminance of the two colors was assigned by averaging subjective equi-luminance values from five volunteers. For the auditory modality, the stimuli were high and low tones (1200 Hz and 400 Hz, respectively) presented binaurally through headphones. The intensity of the two tones was assigned by averaging subjective equi-loudness values (tested over the scanner noise) from five volunteers. The temporal structures of the visual and auditory stimulus sequences were identical. Each stimulus (colored square or tone) lasted for 90 ms, and the interval between stimuli varied randomly between 90 and 180 ms, so that they were not presented at a constant rhythm (see Fig. 1A). Each trial started with a fixation point that lasted for 500 ms, followed by the stimuli (a sequence of 30 events), that lasted for about 6.5 s, and ended with a question mark, after which subjects could give their answer, within 1.5 s, via key pressing. Overall, each trial lasted for about 9 s. All sequences consisted of 30 stimuli overall, half from each category (i.e., 15 green and 15 red squares for the visual; 15 high and 15 low tones for the auditory modality). The relative clustering of stimuli was manipulated so that 9 stimuli from one category appeared in a single “cluster” (i.e., a sequence of 9 identical stimuli), while the remaining 6 stimuli alternated with

the 15 stimuli of the other category, grouped in smaller clusters of 2 to 6 items each, appearing in the sequence in an alternating and random order. Overall, each sequence was made of either 7 or 8 alternated clusters of stimuli. The long cluster of 9 stimuli of one category could appear at random times along the sequence. Fig. 1B shows one exemplar sequence of 30 stimuli, made of 7 clusters, and with the green stimuli forming the longer “cluster”, presented at the beginning of the sequence.

4.4. Tasks

For each of the two modalities there were three tasks, all requiring a two-choice button-press decision with the stimulus sequence held constant across tasks:

Estimation: subjects were asked to decide which of the two categories was the more numerous (the green or the red square for the visual modality; the high or the low tone for the auditory modality). Since the number of stimuli from the two categories was always the same (15) in each sequence, subjects could not base their judgement on the total time taken by each stimulus type nor on the relative frequency of the different stimulus types. In fact, these two variables naturally co-vary with numerosity. However, as previous studies on temporal numerosity judgements have shown, we expected the subjects’ numerosity judgements to be slightly but significantly biased towards the category that show the higher degree of clustering (Erlick, 1963). In the 1960s and 1970s temporal numerosity judgments were extensively studied (Erlick, 1959; Erlick, 1961; Erlick, 1962; Erlick, 1963; Viviani, 1979). In particular, using in settings identical to the one we used in our experiment (where visual or auditory stimuli are presented sequentially and at high rates) Erlick and Viviani described three important phenomena:

1. subjects underestimate numerosity (the same is true for displays in which items are presented simultaneously, and is consistent with a leaky and approximate accumulator system).
2. Accuracy increases as a function of increasing duration of observation.
3. When both categories are equal in number, the category having the higher degree of clustering (or repetitiveness) is judged more numerous.

Observation 3 directly follows observations 1 and 2: if subjects tend to underestimate, and the underestimation is less important for longer sequences, it follows that the category where the stimuli are grouped in long chunks is

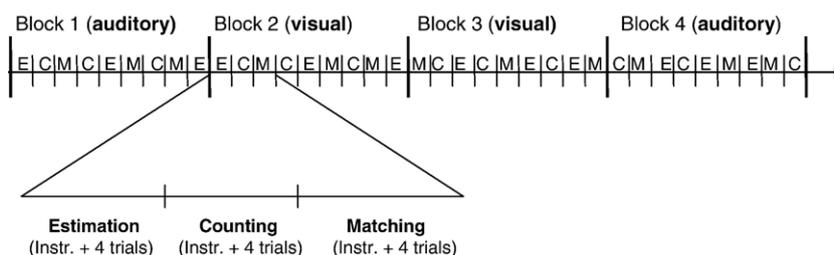


Fig. 5 – Schematic representation of the temporal structure of the experiment.

judged more numerous than the one where the stimuli are presented in multiple short chunks.

We therefore exploit this phenomenon and arrange the stimuli so that, in every trial, one of the two categories had a higher degree of clustering (see Stimuli for a detailed description of this clustering manipulation).

Using this phenomenon, we could therefore manipulate subject's feeling of numerosity without having to control/decouple numerosity with its co-varying physical variables of time or frequency. Therefore, behavioral measures allowed us to determine that subjects were actually paying attention to numerosity, and carrying out the estimation task conscientiously if the pattern of judgements could be predicted by the degree of clustering. Moreover, given the type of sequences of stimuli used, where the elements of the two categories alternated several times, it was virtually impossible to count each element of each category to then finally compare their relative number: this would require switching between 2 counting sequences (one for category) several times and very quickly, stopping and restarting each counting sequence several times (in order to get a feeling of what this would mean, see Fig. 2B and try to imagine such stimuli presented very fast [with a mean of 1/235 ms] in temporal sequence, and then try to count the total number of green and red items. The resulting sequence that you should say in your head should be something like: 1 2–1 2 3 4 5 6 7 8 9–3 4 5 6 7–10 11–8 9 10 11–12 13 14 15–12 13 14 15). In any case, should some subjects managed to do so, their performance should be at chance, as the exact number of elements is identical in the two categories. On the contrary, should the subjects rely on a non verbal feeling of numerosity, their performance should be biased towards one response according to the clustering manipulation.

Counting: subjects were asked to count (silently, “in their head”) and then decide if there were 6 or 7 switches between the category clusters in each sequence (a switch was defined as a change in color in the visual sequences, and in tone in the auditory sequence).

Matching: subjects were asked to decide whether the last stimulus in the sequence was identical to the first one. This baseline task was designed to control for sensory stimulation, holding some information in working memory for the whole stimulus period, and producing a two-choice button-press final response.

All subjects were substantially trained on all three tasks immediately prior to the scanning session outside the scanner. In particular, for the estimation task, subjects were encouraged to rely solely on their feeling of numerosity without trying to deploy any other conscious strategy in order to perform the task. Moreover, after the experimenter checked that their performance was modulated by the clustering manipulation, subjects were given a feedback on their performance, and reassured that their feeling of numerosity was adequate, and their answers correct.

4.5. fMRI scanning technique

A 2 T Siemens VISION system (Siemens, Erlangen, Germany) was used to acquire both T1 anatomical volume images (1 × 1 × 1.5 mm voxels) and T2*-weighted echoplanar images

(64 × 64, 3 × 3 mm pixels, TE = 40 ms) with BOLD contrast. Each echoplanar image comprised 32 axial slices (2.0 mm with a 0.5 mm slice interval, giving a resolution of 2.5 mm). A total of 518 volume images were taken continuously with a repetition time (TR) of 2.974 s/volume, the first six volumes being discarded to allow for T1 equilibration effects.

4.6. Image processing

Data were analysed with statistical parametrical mapping (SPM99: Wellcome Department of Cognitive Neurology, London, 1999). All volumes from each subject were realigned using the first as reference and re-sliced using sinc interpolation methods, adjusting for residual motion-related signal changes. A mean image was created using the realigned volumes and the anatomical MRI was co-registered to this mean image. This ensured that the structural and the functional images were spatially aligned. The functional images were spatially normalized (Friston et al., 1996) to a standard T2* template using non-linear-basis functions. This transformation was also applied to structural T1 volume. Data were then spatially smoothed with a 6 mm full width at half maximum isotropic Gaussian kernel, to compensate for residual variability after spatial normalization and to permit application of Gaussian random field theory to provide for corrected statistical inference (Friston et al., 1995). A boxcar waveform convolved with a synthetic hemodynamic response function (HRF) was used as the reference waveform for each condition. Differences in global flow within subjects were removed using proportional scaling. The data were high-pass filtered using a set of discrete cosine basis functions with a cut-off period of 512 s. To condition temporal autocorrelation in the data, the time series were low-pass filtered using a symmetric HRF as the smoothing kernel. All activations were identified both at the single subject level, and at the group level. For the group analysis, we used a random effect analysis of individual contrasts modeled in an ANOVA with 4 conditions (estimation > matching and counting > matching in each stimulus modality separately).

4.7. Statistical analysis

Data were analysed in order to address:

4.8. Modality independent effects (common for auditory and visual modality)

4.8.1. For estimation

Areas that were activated by estimation more than the matching baseline (hereafter E and b respectively) were identified by the main effect of E > b. In addition, to ensure that the areas identified corresponded to increased activation in each modality separately, the main effect was inclusively masked ($P < 0.05$ uncorrected) with the E > b contrasts for each modality separately. The inclusive masking option identifies the voxels significant in the main contrast that are also significant in each of the contrasts specified as a mask.

Areas that were activated by estimation more than counting (hereafter C) were identified by the main effect of

($E > b$) > ($C > b$) summed over both modalities and inclusively masked ($P < 0.05$) with the same contrast ($E > b$) > ($C > b$) for each modality separately.

4.8.2. For counting

The same procedure was used to identify the areas involved in counting. Areas that were activated by counting more than the matching baseline were identified by the main effect of $C > b$, inclusively masked ($P < 0.05$) with the $C > b$ contrasts for each modality separately. Areas that activated by counting more than estimation were identified by the main effect of ($C > b$) > ($E > b$) summed over both modalities and inclusively masked ($P < 0.05$) with the same contrast ($C > b$) > ($E > b$) for each modality separately.

4.9. Modality specific effects: effects that are bigger in the auditory than visual modality

4.9.1. For estimation

Areas that were activated by estimation more than the matching baseline in the auditory modality only, were identified by the modality (auditory vs. visual) by task ($E > b$) interaction, inclusively masked ($P < 0.05$) with $E > b$ in the auditory modality. Areas that were activated by estimation more than counting in the auditory modality only were identified by the modality (auditory vs. visual) by task ($E > C$) interaction, inclusively masked ($P < 0.05$) with $E > C$ in the auditory modality.

4.9.2. For counting

Areas that were activated by counting more than the matching baseline in the auditory modality only were identified by inclusively masking ($P < 0.05$) the modality (auditory vs. visual) by task ($C > b$) interaction with $C > b$ in the auditory modality. Areas that were activated by estimation more than counting in the auditory modality only were identified by inclusively masking ($P < 0.05$) the modality (auditory vs. visual) by task ($C > E$) interaction with $C > E$ in the auditory modality.

4.10. Modality specific effects: effects that are bigger in the visual than auditory modality

With the same procedures as in 2, we also identified effects for estimation and for counting that were seen in the visual modality only.

Inferences were made at $P < 0.05$, corrected for multiple comparisons at the cluster level, $P < 0.001$ uncorrected at the voxel level.

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