Are Numbers Special? Comparing the Generation of Verbal Materials From Ordered Categories (Months) to Numbers and Other Categories (Animals) in an fMRI Study

Anja Ischebeck,^{1*} Stefan Heim,^{2,3} Christian Siedentopf,⁴ Laura Zamarian,^{1,5}
Michael Schocke,⁶ Christian Kremser,⁶ Karl Egger,⁶ Hans Streng,⁷
Filip Scheperjans,^{2,8} and Margarete Delazer¹

¹Clinical Department of Neurology, Innsbruck Medical University, Austria

²Research Centre Jülich, Institute of Medicine, Germany

³Brain Imaging Centre West, Jülich, Germany

⁴Department of Radiology II, Innsbruck Medical University, Austria

⁵Department of Psychology, University of Trieste, Italy

⁶Department of Radiology I, Innsbruck Medical University, Austria

⁷Institute of Medical Psychology, University of Kiel, Germany

⁸C. & O. Vogt Institute for Brain Research, University of Düsseldorf, Germany

Abstract: Months, days of the week, and numbers differ from other verbal concepts because they are ordered in a sequence, whereas no order is imposed on members of other categories, such as animals or tools. Recent studies suggest that numbers activate a representation of their quantity within the intraparietal sulcus (IPS) automatically, that is, in tasks that do not require the processing of quantity. It is unclear, however, whether ordered verbal materials in general and not only numbers activate the IPS in such tasks. In the present functional magnetic resonance imaging study word generation of months, numbers, and animals were compared. Word generation of numbers and nonnumerical materials from an ordered category (months) activated the IPS more strongly than generating items from a not-ordered category such as animals or the verbal control conditions. An ROI analysis of three subregions within the anterior IPS revealed that the most anterior and lateral of these regions, human intraparietal area hIP2, shows a greater sensitivity to ordered materials than the other two areas, hIP1 and hIP3. Interestingly, no difference in activation was observed within the IPS between numbers and months suggesting that the activation of the IPS might not be modulated by the additional quantity information carried by numbers. *Hum Brain Mapp* 29:894–909, 2008. © 2007 Wiley-Liss, Inc.

Key words: number processing; silent articulation; intraparietal sulcus; word generation

Contract grant sponsor: European Community; Contract grant number: MRTN-CT-2003-504927.

*Correspondence to: Anja Ischebeck, PhD, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria.
E-mail: anja.ischebeck@i-med.ac.at

Received for publication 16 October 2006; Revised 6 April 2007; Accepted 4 May 2007

DOI: 10.1002/hbm.20433

Published online 17 August 2007 in Wiley InterScience (www.interscience.wiley.com).

INTRODUCTION

Similar to numbers but different from other verbal materials, such as animals or tools, the months of the year and the days of the week form ordered categories. These temporal sequences help us to keep track of time, an important aspect of daily life. However, different from numbers, sequences such as the days of the week or months of the year do not represent quantity information. They represent only sequence information (Thursday follows Wednesday, April follows March). Many recent imaging studies have identified a pivotal role for the intraparietal sulcus (IPS) in the processing of quantity [e.g., Stanescu-Cosson et al., 2000]. It is unclear, however, whether the IPS plays a similar role in the processing of sequence information. In the present study we compare the processing of months to the processing of numbers and the processing of not ordered verbal materials, especially with regard to the IPS.

Rich evidence has been accumulated in recent years that bilateral parietal areas, especially the IPS, play an important role in number processing. Imaging studies have found the IPS to be activated regularly in a wide range of tasks, such as comparison [Chochon et al., 1999; Cohen-Kadosh et al., 2005; Pinel et al., 2001, 2004], approximation [Stanescu-Cosson et al., 2000; Venkatraman et al., 2005], dot estimation [Piazza et al., 2004], simple calculation [Kazui et al., 2000; Stanescu-Cosson et al., 2000], and complex calculation [Delazer et al., 2005; Ischebeck et al., 2006]. Neuropsychological evidence is in line with these results as patients with difficulties in number processing typically have lesions in parietal areas [Cipolotti et al., 1991; Delazer and Benke, 1997; Delazer et al., 2006; Henschen, 1919; Hécaen et al., 1961].

However, comparatively little is known about order or sequence processing. Recent behavioral studies yielded evidence that the processing of numbers is similar to non-numerical ordered stimulus materials. The distance effect (i.e., the time to compare two numbers decreases as their numerical distance increases) observed for numbers [Moyer and Landauer, 1967] has also been found for other ordered stimuli, such as letters of the alphabet [Hamilton and Sanford, 1978; Taylor et al., 1984], months [Gevers et al., 2003], and the days of the week [Gevers et al., 2004]. The SNARC effect [SNARC = spatial numerical association of response codes, i.e. smaller numbers are responded to faster with the left than with the right hand, while larger numbers are responded to faster with the right hand, Dehaene et al., 1993] has been observed also for letters of the alphabet, months [Gevers et al., 2003] and the days of the week [Gevers et al., 2004]. A recent study found that synaesthetes with visuo-spatial forms for numbers often also have visuo-spatial forms for ordered sequences, such as days, months, and letters [Sagiv et al., 2005]. Brain imaging studies observed an activation of the IPS for letters, numbers, or shapes when their order (position in the alphabet, numerical identity, and physical size) had to be verified [Fulbright et al., 2003] compared with

an identification task. Similar to numbers, activation within the IPS was observed to negatively correlate with distance in an order memory task with letters [Marshuetz et al., 2006]. Hence, the IPS seems not only to subserve the processing of numerical or quantity information, but also the processing of order information.

On the other hand, there is a conceptual difference between cardinal and sequence information. Numbers carry cardinal, ordinal,¹ and sequence information, whereas months carry only sequence information. Children learn to recite the counting sequence long before they understand the cardinal meaning of numbers [Fuson, 1988; Wynn, 1990, 1992]. Some processing differences between quantity and order (or sequence) information are reasonable to assume and have been observed. For example, slightly different distance effects were observed for order and comparison judgments in a behavioral study [Turconi et al., 2006] and in ERP components [Turconi et al., 2004]. In patients, access to the cardinal meaning of numbers can be impaired while access to sequence meaning is preserved [Delazer and Butterworth, 1997; Delazer et al., 2006; Turconi and Seron, 2002].

Because the IPS seems to play a crucial role in number processing and in the processing of order and sequence information, it could be hypothesized that this area also plays a role in the retrieval of semantic knowledge related to numbers or order. That different brain areas may be involved in the retrieval of semantic knowledge has been observed in word generation tasks of items of other categories, such as animate and inanimate objects (animals and tools) [see, for reviews, Caramazza and Mahon, 2003; Martin and Chao, 2001]. A similar specialization of the semantic knowledge system might be observed for ordered in contrast to not-ordered verbal materials. Evidence from patients suggests that parietal areas not only subserve numerical processing, such as comparison or calculation, but also the retrieval of semantic knowledge related to numbers. A patient described by Cipolotti et al. [1991] performed in the normal range in a series of tests assessing the comprehension of words and pictures, while she was totally unable to deal with numbers above 4. For example, she was able to understand the Italian noun *venti* [winds], but not the number word *venti* [twenty]. In contrast, Capelletti et al. [2001] reported a patient with left temporal atrophy and a severe deficit in reading and writing non-number words, while reading and writing of number words and numerals was preserved. Zamarian et al. [2006] described a patient with atrophy of the temporal lobes who was unable to understand common animal names, such as *elephant*, but showed good number knowledge and

¹Note that ordinality is not the same as sequence information. Ordinality, but not sequence information, implies the numerosity of predecessors. To determine the number of predecessors requires a starting point. Sequences, however, can be cyclic without a starting point (Monday follows Sunday).

a fully working semantic network for the retrieval of arithmetic facts. These studies suggest that semantic knowledge related to numbers may dissociate from general semantic knowledge.

Two imaging studies addressed the question whether numbers activate the IPS more strongly than other stimulus materials independent of the task. Thioux et al. [2005] used animals and number words in two different tasks, classification (is seven an odd number? is a bear a mammal?) and comparison (is seven larger than five? is a bear more ferocious than a dog?). Independent of the task, numbers activated the IPS bilaterally more than animals, while animals activated the left anterior inferior temporal gyrus more than numbers. Eger et al. [2003] showed that digits and number words elicited stronger activation within the IPS than letters or colors in a simple classification task. This indicates that numbers activate the IPS even when the task does not require more than identity processing. While IPS activation was observed in tasks that explicitly required order judgment, it is unclear whether ordered verbal materials also activate the IPS in other tasks. In the experiment by Eger et al. [2003] only numbers activated the IPS more than colors, but not letters, which also form an ordered category. It is therefore possible that only numerical verbal materials activate the IPS in a word generation task.

In the present study we compared different conditions of word generation in a visually paced covert articulation task. The conditions were canonical generation of numbers (i.e., counting), canonical generation of months (i.e., reciting the months sequence), random generation of numbers and months, and word generation of animals. Two related research questions were addressed. First, are verbal materials from ordered categories generated differently than verbal materials from categories that are not ordered? As the IPS is involved in the processing ordered materials, especially numbers, it might become more active in word generation tasks of verbal materials from ordered categories than in word generation tasks of verbal materials from other not-ordered semantic categories, such as animals. Alternatively, if order information plays no role in word generation tasks of numbers and months, no difference with regard to the IPS is expected between verbal materials of ordered and not ordered semantic categories. The second research question is, whether the activation within the IPS is modulated by the type of order information carried by months and numbers. While numbers carry quantity and sequence information, months carry only sequence information. Thus, it might be speculated that numbers activate the IPS more strongly than months. Alternatively, no difference might be detected between numbers and months with regard to activation within the IPS. As months are a temporal sequence, the lack of a significant difference between months and numbers could, for example, indicate that time and numbers share a common representation, such as proposed by Walsh [2003]. A further, supplementary, goal of the present study is to investigate

whether a region within the anterior part of the IPS can be identified that reacts specifically on numerical information. The anterior part of the IPS has been reported to be activated in tasks that do not require explicit number processing such as number detection [Eger et al., 2003] and tasks that involve numerosity change detection in a habituation paradigm [Piazza et al., 2004, but see Shuman and Kanwisher, 2004]. It has been suggested that the representation of number quantity might be located in this part of the IPS, while activation in more posterior parts of the IPS is assumed to be related to, for example, attentional mechanisms [Dehaene, 2003; Simon et al., 2004]. It can therefore be hypothesized that the anterior IPS is the most likely candidate to display a specialization for numbers as compared with other verbal materials. In addition, it should show more activation for numbers than for months if the mental representation of order differs from the mental representation of number quantity. To date, three human intraparietal areas, hIP1, hIP2, and hIP3, within the anterior part of the IPS, have been mapped on the basis of cytoarchitectonic analysis of 10 human postmortem brains [Choi et al., 2006; Scheperjans et al., 2005]. It has been shown that differences in cytoarchitecture and transmitter receptor densities of cortical areas covary with functional differences [Zilles et al., 2002]. It can therefore be hypothesized that the three human intraparietal areas mapped on the basis of cytoarchitectonic differences show different degrees of functional specialization for numerical or order information. To gain insight into the functional role of these three areas within the IPS we will compare the activation elicited by each condition in a region of interest (ROI) analysis.

METHODS

Participants

Nineteen healthy young adults (8 male, 11 female, mean age 27.9, SD = 5.80) participated in the functional magnetic resonance imaging (fMRI) experiment. All participants were native speakers of German. They had no history of psychiatric or neurological disorder, with the exception of one male subject (meningitis in childhood), who was excluded from the analysis. All had normal or corrected-to-normal vision. All had given written informed consent and were paid for their participation. The study had been approved by the local ethics committee.

Conditions

Eight conditions were realized in this experiment (canonical numbers, canonical months, random numbers, random months, word repetition (two- and three syllabic), animals, and multiplication). One condition was word generation of animal names with repetitions allowed (animals). Two conditions were counting from 1 to 12 (canonical numbers) and reciting the months of the year from Jan-

Figure 1.
Schematic of the task.

uary to December in their correct order (canonical months). Months and the number words from 1–12 have similar mean frequencies of occurrence in German [263 (range: 197–361) and 251 (range: 16–868) per million, respectively, according to the Celex database: Baayen et al., 1993]. Two conditions were word repetition (two- or three-syllabic). Participants had either to repeat “Zusatz” (word repetition two-syllabic) or “Zusage” (word repetition three-syllabic). Both words are abstract nouns (“Zusatz” meaning supplement, “Zusage” meaning agreement), they consist of similar phonemes and do not differ with regard to word frequency [10 per million, Baayen et al., 1993]. These conditions were added to control for word length effects, as the numbers from 1 to 12 in German have an average length of 1.1 syllables (months: 2.8 syllables). The most frequent animal names in German are mono-syllabic. The recital of months and numbers in their canonical order is overlearned and the sequence might be retrieved as a whole. This makes these conditions very different from the task of generating animal names, where each item has to be retrieved separately. Canonical generation on the other hand might best be compared to word repetition, because minimal retrieval is required in both cases. Two further conditions were random generation of months and numbers (random months, random numbers). Random generation was included to make word generation of numbers and months more similar to the animal condition, because all three conditions require a search process. As a last condition, participants had to recite the multiplication table for 3, from 3 to 36 (multiplication). This condition was entered for exploratory reasons and is not discussed in detail in the present article.

Task and Design

Participants were instructed to silently articulate each item as clearly as possible (“as if they could hear them-

selves speak in their head”) but without moving the lips or opening the mouth. Silent or covert articulation was used here because overt articulation can cause considerable artifactual activation due to motion [Binder, 1995; for a review, see, Birn et al., 2004; Metha et al., 2006]. Silent articulation activates similar brain areas than overt articulation, although to a weaker extent [Palmer et al., 2001]. Participants were instructed to silently articulate each word synchronized with the appearance of a visually presented pacing cue (visually-paced covert articulation), a red circle presented every 1.5 s (500 ms presentation, 1,000 ms blank screen). A short code indicating the condition was presented visually at the beginning of each task block (e.g., “@ numbers” for random generation of numbers). A task block lasted for 30 s and alternated with 30 s of rest during which a fixation cross was presented (Fig. 1). The 8-task conditions were repeated 6 times each, yielding 48-task blocks in total. The functional measurement session had a total duration of 48.5 min.

Apparatus

Visual presentation and scanner triggering was controlled by a laptop computer using in-house software. The stimuli were projected to a screen at the foot end of the scanner table and viewed by the participants via a mirror mounted on the head coil. Small sand bags were used to minimize head motion.

FMRI Data Acquisition

FMRI measurement was performed with a 1.5 T Siemens Symphony scanner. A Siemens-issued bird-cage head-coil was used. For the functional images an EPI-sequence (TE = 60 ms, flip angle = 90°) sensitive to T2* contrast was used. The images had an in-plane spatial resolution of 3 mm (FOV = 192 mm, matrix = 64 × 64). For each image (TR =

3.0 s) 24 axial slices were acquired ascendingly and parallel to the AC-PC line with a thickness of 4 mm and 1-mm gap. Additionally, a T1-weighted anatomical scan (MPRAGE) was performed (TI = 1,000 ms, TE = 3.93 ms, TR = 1670 ms, flip angle = 15°, matrix = 256 × 256, FOV = 220 mm, 120 slices, in plane spatial resolution = 0.9 mm, 1.5 mm thickness).

FMRI Data Analysis

FMRI data analysis was conducted with SPM2 software (Wellcome Department of Cognitive Neurology, London, UK). The functional data of each participant were motion-corrected. The structural image of each participant was registered to the time series of functional images and normalized using the anatomical brain template provided by SPM2. The functional images were normalized using the normalization parameters of the structural image. Finally, the functional images were smoothed in the spatial domain using a Gaussian kernel of 9 mm FWHM. A statistical analysis on the basis of the General linear model as implemented in SPM2 was conducted. The canonical form of the hemodynamic response function convolved with a boxcar function for the length of the block was used to generate the model time courses for the conditions. A high-pass filter (cut-off frequency: 1/500 Hz) was used to remove low frequency drifts. No global normalization was used. Motion parameters were entered into the analysis as parameters of no interest. The group analysis was implemented by computing linear *t*-contrasts for each subject individually that were then entered into a random effects model. For the comparisons between conditions, significantly activated voxels were identified using an initial uncorrected *p*-value threshold of less than 0.001 reporting only clusters with a corrected (FWE) *p*-value of less than 0.05 on cluster level.

A ROI analysis of three cytoarchitecturally defined subregions of the anterior IPS was performed for all tasks to investigate possible functional differences between these regions. The anatomical data were part of a probabilistic atlas on the basis of cytoarchitectural analysis in 10 human brains [Amunts et al., 1999; Zilles et al., 2002]. This approach is preferable to other brain mapping methods that are based on the analysis or visual inspection of one individual's brain [Brodmann, 1909; Talairach and Tournoux, 1988]. This is especially important in the case of the IPS, a brain area with a very high interindividual anatomical variability. For the analysis of the relation between structure and function, the three-dimensional probabilistic maps of this atlas can be combined with fMRI data analysis using the Anatomy toolbox [Eickhoff et al., 2005, 2006]. To date, three distinct areas within the IPS have been mapped, the human intraparietal areas hIP1, hIP2, and hIP3 [Choi et al., 2006; Scheperjans et al., 2005]. Whereas hIP1 and hIP2 are located within the lateral wall and fundus of the IPS, hIP3 is located mostly in the medial wall of the IPS. The area hIP2 is the most anterior and lateral of

these region. The areas hIP1 and hIP3 are located more posterior, with hIP1 lateral to hIP3 (see Fig. 3, top, for a visualization of the three IPS ROIs). For each ROI, effect-sizes (contrast estimates) for the comparisons between task conditions and fixation were averaged over all voxels separately for each hemisphere (see Fig. 3, bottom).

Behavioral Experiment

Because of the covert articulation task, participants' performances within the scanner could not be monitored. It is therefore difficult to assess whether the participants performed as intended with the tasks. It is possible, for example, that participants deviated from some of the tasks to render them less demanding. To have some means of control for possible behavioral differences between the conditions, an additional behavioral study using overt articulation was conducted outside the scanner. Ten healthy volunteers (7 male, 3 female, mean age 27.6, SD = 6.22) who had not participated in the fMRI study took part. All were native speakers of German. Similar to the fMRI study, a red dot was presented 20 times every 1.5 s (visually-paced articulation). A verbal cue indicating the condition (months, numbers, and animals) was shown for 7 s between blocks. Only the three most difficult conditions of the fMRI experiment were tested, random generation of months and numbers, and generation of animals. The same instruction was used as in the fMRI experiment. Participants were asked to randomly generate numbers and months, and to generate animal names, with repetitions allowed. As in the fMRI experiment, the three conditions were presented in blocks and repeated six times each, yielding 18 blocks in total. The experiment lasted for 10 min. The responses of the participants were recorded and analyzed.

RESULTS

Behavioral Experiment

The behavioral experiment had been undertaken to investigate performance in the three most difficult conditions, random generation of months and numbers, and generation of animals. All participants were able to perform all tasks without errors in the random generation conditions of numbers and months. In the animal generation condition there were two naming errors (production of foreign language items). The average word length of the animals produced in the animal generation task was 1.85 syllables, indicating that this condition should be compared to the two-syllabic word generation condition. Humans typically deviate from a random sequence when asked to randomize numbers. Fewer direct repetitions and more instances of producing the direct successor or predecessor of an item (counting bias) are observed than expected in a 'true' random sequence [Wiegersma, 1982]. The counting bias has been shown to increase sharply

when the production rate is raised to one item per second [Jahanshahi et al., 2000]. To assess differences with regard to difficulty or strategy, the behavioral data were analyzed with regard to trial-to-trial repetitions (i.e. repetitions of the immediately preceding word) and trial-to-trial counting (forward and backward). In total, 31 immediate repetitions of the same item were observed, 20 for numbers, 6 for months, and 5 for animals. Numbers were repeated more often than months ($t(9) = -2.49, P < 0.05$), and than animals ($t(9) = -2.49, P < 0.05$). With regard to counting, there were in total 171 cases of forward counting (136 backward counting) in random generation of numbers, and 195 cases in total of forward counting (130 backward counting) in random generation of months. The counting data were entered into a repeated measures analysis of variance with the factors Counting Direction (forward/backward) and Material Type (numbers/months). No significant effects were obtained in this analysis.

FMRI Data

Comparisons to fixation

Conditions that did not yield any significant clusters in the whole brain analysis in the comparison against the word repetition condition (canonical months, canonical numbers), and the word repetition conditions themselves were compared with fixation (Table I). This allows an assessment of the overall stability of the activation pattern observed in these different silent articulation tasks. All other conditions were compared to the two or three-syllabic word repetition conditions depending on their word lengths, that is, numbers and animals to the two-syllabic word repetition condition, months to the three-syllabic condition. Compared with fixation, activations were observed within the supplementary motor area (SMA), the left postcentral gyrus, the right inferior and middle frontal gyrus, the right middle and superior temporal gyrus, as well as within IPS, bilaterally, for both canonical conditions (months and numbers, respectively). Additional activations were observed for the canonical months condition compared with fixation within the left inferior frontal gyrus (IFG), the left putamen and insula, as well as in the left supramarginal gyrus. Comparing the two word repetition conditions with fixation yielded frontal activations within the pre- and postcentral gyri, bilaterally, within the left middle frontal gyrus (three-syllabic only) and within the SMA, as well as within temporo-parietal areas, but not within the IPS. The other three conditions (random months, random numbers, animals) yielded significant activations compared to word repetition. The comparison of these conditions against fixation is therefore not reported here to avoid redundancy.

Comparisons with word repetition

Comparing random generation of numbers and months with the two- and three-syllabic word repetition conditions,

respectively, yielded activations within the SMA, the middle and superior frontal gyrus, bilaterally, the left IFG, the left precentral gyrus, the IPS and the precuneus, bilaterally. For the condition random months, additional activations were observed in the left insula and in the right IFG. Word generation of animals compared to word repetition activated the IFG and insula, bilaterally, the SMA, the left superior frontal gyrus, the left precentral gyrus and the posterior part of the left IPS. No significant activations were observed when the three- and two-syllabic word repetition conditions are compared (three > two). Comparing the two- with the three-syllabic condition (two > three) yielded an activation within the right middle frontal gyrus.

Comparisons between ordered and not ordered verbal materials

Though canonical months and numbers did not significantly activate the IPS more than word repetition in the whole brain analysis, a significant difference between these conditions was observed in the ROI analysis (see below). When random generation of months and numbers was each compared to word generation of animals, stronger activation for months and numbers was observed within fronto-parietal areas, bilaterally, that is, within the IPS and precuneus, and the inferior and superior frontal gyrus, as well as the right middle and inferior temporal gyrus. When word generation of animals was compared to random generation of numbers and months, respectively, stronger activations for animals were observed within the left inferior frontal gyrus and the left inferior temporal gyrus/fusiform gyrus (Table II, Fig. 2).

Comparisons between months and numbers

Comparing canonical generation of months with numbers did not yield significant activation. In random generation, numbers did not yield stronger activations than months. Stronger activations for months than for numbers were observed frontal areas, such as the SMA, the insula and the inferior and middle frontal gyrus (Table II, Fig. 2).

Comparing random generation to canonical recital

Random generation yielded stronger activations than canonical recital, for months and numbers, respectively, within bilateral fronto-parietal regions, such as the SMA, the inferior, middle and superior frontal gyri, the prefrontal gyrus, in the caudate nucleus, and the IPS. Comparing the canonical recital conditions with their corresponding random generation conditions did not yield any supra-threshold clusters.

ROI analysis of the IPS

The effect sizes of all task conditions compared to fixation were entered into an analysis of variance with the

TABLE I. Contrasts of the task conditions to fixation and word repetition (threshold: $P < 0.001$ uncorrected, $P < 0.05$ corrected on cluster level)

Side		<i>x</i>	<i>y</i>	<i>z</i>	<i>k</i>	<i>Z</i>		<i>x</i>	<i>y</i>	<i>z</i>	<i>k</i>	<i>Z</i>
Canonical number > Fix							Canonical month > Fix					
<i>Frontal</i>												
Left	SMA ^a	−6	−9	63	1184	4.48	SMA	−9	−6	63	379	5.53
Left	PreG, PostG ^a	−57	3	21	1184	4.50	IFG	−54	15	−3	80	4.70
Left							Putamen, Insula	−21	12	3	221	4.12
Left							MFG, IFG	−36	39	30	95	4.30
Right	PreG, MFG	33	−6	39	1184	4.61	SFG, MFG	24	6	51	127	3.97
Right	MFG ^a	27	9	45	1184	4.58	IFG	57	18	24	262	3.90
Right	IFG ^a	48	27	18	1184	4.15	MFG, IFG	48	33	21	149	3.81
Right	MFG ^a	42	30	30	1184	4.11	MFG ^a	54	−9	51	713	4.79
<i>Temporal</i>												
Right	STG	57	−39	18	279	4.33	MTG, STG	57	−39	6	177	3.99
Right	MTG ^a	45	−63	9	1184	4.09						
<i>Parietal</i>												
Left	IPS	−33	−48	51	471	4.90	IPS	−36	−48	48	547	4.48
Left	PostG	−48	−12	48	592	4.82	PostG, PreG	−51	−12	51	621	5.29
Left							supramG, STG ^a	−51	−39	24	547	4.06
Right	IPS, supramG	42	−42	48	357	4.76	IPS	51	−39	48	713	4.92
Two-syllabic control > fix							Three-syllabic control > fix					
<i>Frontal</i>												
Left	SMA	−9	−9	63	233	4.56	SMA	−3	−6	66	66	3.93
Left	PostG, PreG	−51	−15	51	484	5.07	PostG, PreG	−48	−15	48	276	4.52
Right	PreG, PostG	54	−12	48	505	4.73	MFG, PreG	51	−9	51	132	4.24
Right							PostG, PreG	60	0	18	65	3.82
<i>Temporal</i>												
Left							MTG	−42	−66	6	97	4.06
Left							STG, supramG	−51	−42	18	74	3.69
Right	STG, MTG	54	−39	9	258	4.16						
RG number > two-syllabic word repetition							RG month > three-syllabic word repetition					
<i>Frontal</i>												
Left	SMA ^a	−3	15	48	509	4.30	SFG, PreG, SMA	−24	−6	57	2072	5.45
Left	SFG, MFG	−24	−6	54	509	5.52	Insula, IFG	−30	27	0	253	4.57
Left	PreG, IFG	−48	6	33	58	4.40	MFG, IFG ^a	−39	33	30	2072	4.37
Left	MFG, IFG	−39	39	21	49	3.81						
Right	SFG, MFG	27	−6	57	227	4.83	SFG ^a	27	−9	63	2072	5.06
Right							MFG	36	36	30	182	4.45
Right							IFG, Insula	51	15	3	233	4.91
<i>Parietal</i>												
Left	IPS ^a	−36	−39	39	549	4.70	IPS	−42	−42	42	1332	5.85
Left	Precuneus	−15	−69	60	549	5.46	SPL, Precuneus ^a	−12	−69	54	1332	4.28
Right	IPS, supramG	42	−39	45	186	4.80	IPS, supramG ^a	42	−42	45	1332	5.25
Right	Precuneus, SPL	12	−66	57	83	4.35	Precuneus, SPL ^a	9	−72	54	1332	4.81
							AngG ^a	27	−63	48	1332	4.02
Animals > two-syllabic word repetition							Two-syllabic > three-syllabic word repetition					
<i>Frontal</i>												
Left	SMA	−3	12	54	1763	5.72	MFG, SFG	27	51	30	42	3.68
Left	IFG, Insula ^a	−36	27	0	1763	5.25						
Left	SFG, PreG, MFG ^a	−33	0	66	1763	4.91						
Left	MFG, SFG ^a	−30	−60	18	1763	4.74	Three syllabic > two-syllabic word repetition					
Right	IFG, Insula	42	15	6	153	4.47	ns					
<i>Parietal</i>												
	SPL	−27	−69	45	53	4.18						

Coordinates (*x*, *y*, *z* column headers) of peak activation within a cluster are reported as given by SPM2 (MNI space), corresponding only approximately to Talairach Turnoux space (Talairach and Tournoux, 1988; Brett et al., 2001). Anatomical labels are given on the basis of the classification of the AAL (automated anatomical labeling) atlas (Tzourio-Mazoyer et al., 2002). The first label denotes the location of the maximum, the following labels denote further areas containing a majority of voxels of the activated cluster. Column headers: *k*, number of voxels contained within a cluster; *Z*, statistical *Z*-value at coordinates.

IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus; SMA, supplemental motor area; MTG, middle temporal gyrus; STG, superior temporal gyrus; IPS, intraparietal sulcus; PrecG, precentral gyrus; PostG, postcentral gyrus; supramG, supramarginal gyrus; AngG, angular gyrus.

^a Activation is part of a bigger cluster. IPS is not an AAL label, it is used here to denote activations which are predominantly within the intraparietal sulcus rather than on the surface of the parietal gyri.

TABLE II. Contrasts between task conditions (threshold: $P < 0.001$ uncorrected, $P < 0.05$ corrected on cluster level)

Side		<i>x</i>	<i>y</i>	<i>z</i>	<i>k</i>	<i>Z</i>		<i>x</i>	<i>y</i>	<i>z</i>	<i>k</i>	<i>Z</i>
Ordered vs. not ordered verbal materials												
RG numbers > animals							RG months > animals					
Frontal												
Left	SFG	−24	−9	51	85	4.32	PreG, SFG	−27	−15	51	127	4.07
Right	IFG	57	12	21	79	4.27	IFG ^a	54	12	21	800	4.39
Right	SFG, PreG	30	−6	57	217	5.08	SFG, MFG	30	−6	57	800	5.42
Right							MFG ^a	27	12	42	800	4.13
Temporal												
Right	MTG, ITG	57	−54	0	77	4.36	MTG, ITG	57	−51	−3	49	4.09
Parietal												
Left	IPS	−42	−39	42	392	5.69	IPS, Precuneus ^a	−45	−36	42	3406	5.85
Left	Precuneus	−15	−69	48	2014	4.79						
Right	IPS, Precuneus	39	−39	45	2014	5.96	IPS, Precuneus	36	−39	48	3406	5.87
Right	MOG ^a	39	−78	33	2014	4.41						
Animals > RG numbers							Animals > RG months					
Frontal												
Left	SMA	−6	15	57	324	4.85						
Left	IFG	−33	30	3	907	5.53	IFG	−33	30	−15	303	4.86
Right	Insula, IFG	39	21	3	109	4.38						
Temporal												
Left	FusiG, ITG	−39	−33	−18	315	4.87	ITG, FusiG	−42	−33	−15	79	3.86
Left	LingG	−6	−36	3	44	3.95						
Sequence (months) vs. quantity (numbers) - commonalities ^b												
Canonical months/numbers > Fix							RG numbers/months > control					
Frontal												
Left	SMA	−6	−6	63	454	5.29	SFG, SMA	−24	−6	57	496	6.43
Left	IFG	−54	12	0	28	4.04	MFG	−39	39	21	33	3.64
Left	MFG	−39	39	27	35	3.81						
Left	SFG	−12	12	36	26	3.85						
Left	Putamen	−21	6	3	54	3.76						
Right	MFG, PreG	51	−9	51	596	4.74	SFG	27	−6	57	267	5.25
Temporal												
Left	MTG	−42	−66	6	30	3.61						
Right	STG, MTG	57	−39	9	214	4.43						
Right	MTG	45	−63	9	28	4.12						
Parietal												
Left	PostG, PreG	−48	−12	51	581	5.54	PreG, IFG	−45	3	33	66	4.28
Left	IPS	−33	−48	48	492	5.08	IPS	−39	−39	39	500	6.03
Right	IPS	51	−36	48	377	5.27	IPS	42	−39	45	181	5.22
Right							Precuneus, SPL	12	−69	54	80	4.08
Sequence (months) vs. quantity (numbers) – differences ^c												
RG months > RG numbers							RG numbers > RG months					
Frontal												
Left	SMA	−6	15	51	55	3.61	ns					
Left	IFG	−45	15	27	42	3.54						
Left	PreG	−42	3	36	55	4.14						
Right	IFG, Insula	39	21	30	102	3.94						
Right	IFG	54	18	12	17	3.78						
Right	SPL	30	−63	51	15	3.76						
Canonical months > Canonical numbers							Canonical numbers > Canonical months					
ns							ns					
Random generation vs. canonical generation												
RG numbers > Canonical numbers							RG months > Canonical months					
Frontal												
Left	SMA, SFG	−12	0	69	665	5.52	SMA, PreG, SFG	−3	9	48	3012	5.79
Left	IFG, Insula	−51	18	−6	140	5.05	MFG	−45	30	30	3012	4.67
Left	PreG, IFG	−51	9	30	133	4.23	Putamen, Caudate	−24	6	18	3012	4.27
Left	Putamen, Caudate	−21	3	15	41	4.24						
Right	MFG, SFG	33	−3	57	285	5.32	Insula, IFG	30	33	6	457	4.81
Right	Caudate, IFG	24	18	9	86	4.15	Caudate	21	−6	27	60	4.05
Right							PreG, SFG	27	−6	54	3012	5.48
Right							IFG	54	6	24	3012	4.21
Right							MFG	36	33	33	3012	4.39

TABLE II. (continued)

Side		x	y	z	k	Z		x	y	z	k	Z
<i>Parietal</i>												
Left	SPL, IPS, Precuneus	-15	-72	54	424	5.57	IPS, supramG ^a	-39	-42	42	1389	5.50
Left							SPL, Precuneus ^a	-24	-63	60	1389	5.01
Right	SPL, Precuneus	15	-66	60	161	4.84	IPS, supramG	39	-36	45	1389	5.88
Right	IPS	39	-39	45	140	4.30	Precuneus ^a	15	-66	54	1389	4.72
Canonical numbers > RG numbers ^d							Canonical months > RG months ^e					
ns							ns					

IFG, inferior frontal gyrus; MFG, middle frontal gyrus; SFG, superior frontal gyrus; SMA, supplemental motor area; ITG, inferior temporal gyrus; MTG, middle temporal gyrus; STG, superior temporal gyrus; IPS, intraparietal sulcus; PrecG, precentral gyrus; MOG, middle occipital gyrus; FusiG, fusiform gyrus; LingG, lingual gyrus.

^a Activation is part of a bigger cluster.

^b Assessed using conjunction analysis.

^c Interaction contrast: [months-3-syll. control] vs. [number-2-syll. control].

^d Masked with canonical numbers versus fixation.

^e Masked with canonical months versus fixation.

Figure 2.

Visualization of the activations for numbers (left side) and months (right side) in different contrasts. Threshold $P < 0.001$ uncorrected, minimum cluster size = 40 voxel, corresponding to a $P < 0.05$ corrected on cluster-level.

Figure 3.

Visualization and ROI-analysis of three human intraparietal areas within the IPS (hIP1, hIP2, and hIP3). Visualization: hIP1 is given in red, hIP2 in green and hIP3 in blue. ROI-Analysis: Bar graphs of averaged effect sizes for all tasks compared to fixation, for hIP1, hIP2, and hIP3. Error bars denote the standard error of the mean (averaged over all conditions). Abbreviations: CN = canon-

ical numbers (counting), CM = canonical months (recitation Jan-Dec), 2S = two-syllabic word repetition, 3S = three-syllabic word repetition, RN = random generation of numbers, RM = random generation of months, A = generation of animals. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

factors HEMISPHERE (left, right), ROI (hIP1, hIP2, hIP3) and TASK (canonical numbers, canonical months, random numbers, random months, two-syllabic word repetition, three-syllabic word repetition, animals). The different activation strengths within the IPS-ROIs for the different tasks are reflected in a main effect of TASK ($F[6,102] = 17.37$, $MSE = 0.092$, $P < 0.001$). The left IPS was more strongly activated than the right yielding a main effect of HEMISPHERE ($F[1,17] = 4.71$, $MSE = 0.106$, $P < 0.05$). On average, hIP2 was more strongly activated than hIP3 and hIP1 yielding a main effect of ROI ($F[2,34] = 24.87$, $MSE = 0.033$, $P < 0.001$). The areas hIP1 and hIP3 were more strongly left lateralized than hIP2, indicated by a significant interaction of ROI $\times$ HEMISPHERE ($F[2,34] = 3.81$, $MSE = 0.024$, $P < 0.05$). Some tasks were more left lateralized (animals) than others, which is reflected in a significant interaction between

TASK and HEMISPHERE ($F[6,102] = 10.19$, $MSE = 0.012$, $P < 0.001$). The different tasks activated the three ROIs differently, yielding a significant interaction of ROI $\times$ TASK ($F[12,204] = 14.33$, $MSE = 0.006$, $P < 0.001$). The triple interaction was also significant ($F[12,204] = 4.89$, $MSE = 0.003$, $P < 0.001$). The averaged effect sizes for the separate conditions and ROIs are given in Figure 3.

Comparing the canonical months and numbers with word repetition yielded significantly stronger IPS activation in all three ROIs for months and numbers ($P < 0.05$, Newman-Keuls post-hoc tests, ROI $\times$ TASK). Comparing random months and numbers with animals yielded significantly stronger IPS activation for months and numbers than for animals in all three ROIs ($P < 0.001$, Newman-Keuls post-hoc tests). The differences between months and numbers, in random or canonical generation, respectively,

were not significant with one exception. There was stronger activation for random generation of months than for random generation of numbers in hIP3 ($P < 0.05$, Newman-Keuls post-hoc tests). Random generation of months and numbers activated all three ROIs more than word generation of animals ($P < 0.001$, Newman-Keuls post-hoc tests). The differences between animals and two-syllabic word repetition were not significant in any of the three ROIs when averaged over both hemispheres. Of all seven word generation tasks only word generation of animals was significantly left-lateralized ($P < 0.001$, Newman-Keuls post-hoc tests, $SIDE \times TASK$).

The difference between canonical months and numbers to verbal control, as well as the differences between random generation of months and numbers to generation of animals was greater in hIP2 than in hIP1 and hIP3 (planned comparisons, $P < 0.005$ and $P < 0.001$). The tasks random generation of months, random generation of numbers and generation of animals were more strongly left lateralized in hIP1 and hIP3 than in hIP2 (planned comparisons, $P < 0.05$).

DISCUSSION

In this study, we investigated possible differences between the generation of words from ordered categories such as months and numbers with the generation of other verbal materials (animals and word repetition conditions). The significant and meaningful differences between these conditions indicate that participants behaved according to the instruction within the scanner. Behavioral results gathered outside the scanner indicate that participants were able to generate animals and to randomize months and numbers at the rate required by the experiment. In the following we will give a short discussion of our results with regard to our two main goals and hypotheses.

Ordered Vs. Not Ordered Verbal Materials

The first aim of this study was to determine whether generating verbal materials from ordered categories involves different brain areas than generating verbal materials that are not ordered. We had hypothesized that the IPS, an area involved in quantity and order processing, might also play a role in the retrieval of semantic knowledge related to numbers and maybe other verbal materials from ordered categories. If this is the case then it should be more strongly activated by months and numbers than by animals or the word repetition conditions. Alternatively, if there is a specialization within the semantic system for numbers alone [e.g., Eger et al., 2003] but not for non-numerical ordered verbal materials, months should be processed similar to animals and only numbers should activate the IPS. Our results indicate that numerical and nonnumerical ordered materials activate the IPS more strongly than other verbal materials. In all three ROIs investigated in the ROI-analysis, generating numbers, and months in their canonical order activates the IPS more

than the respective word repetition conditions. Stronger activations were also observed within the IPS for random generation of numbers and months than for animals, in the whole brain analysis as well as in the ROI-analysis. Our results therefore show that not only numerical materials but also nonnumerical ordered materials (months) activate the IPS in a word generation task. The IPS is therefore likely to be involved not only in the retrieval of semantic knowledge related to numbers or quantity but also in the retrieval of semantic knowledge related to order.

It could be argued that it is problematic to compare random generation of numbers or months to the generation of animals. A greater activation of the IPS in random generation could be due, for example, to random generation being more demanding than animal generation [Collette et al., 2005]. It is unlikely, however, that this is the case. The rate used in the present study (1.5 s) was adequate for random generation [Jahanshahi et al., 2000], but twice as high as the rate for spontaneous production of animal names [Tombaugh et al., 1999, see also, Aschenbrenner et al., 2001, for German norms, with no repetitions allowed]. Word generation of animals therefore is likely to be the more difficult task. As repetitions were allowed in the present study, participants might have repeated animals more often to reduce processing load. We had conducted an off-line behavioral experiment to investigate this possible confound but found that participants repeated animals and months less often than numbers. The greater activation within the IPS for random generation compared with animal generation is thus not likely to be due to task difficulty. It should be noted, however, that both tasks are quite different from each other and remain difficult to compare. Nevertheless, random generation of items from a limited set is the only possibility to implement a rough equivalent to the lexical search required in word generation tasks of verbal materials from not-ordered semantic categories. In several aspects, however, both tasks are similar. Random generation of numbers and word generation of items from a semantic category exert strong demands on executive functions. The ability to simultaneously engage in other tasks is limited, for random number generation [Baddeley et al., 1998] as well as for word generation tasks [Bowers et al., 1978]. Moreover, patients with dysexecutive syndrome have difficulties, with random number generation [Spatt and Goldenberg, 1993] as well as with semantically based word generation [Baldo and Shimamura, 1998; Reverberi et al., 2006; Troyer et al., 1998].

Word Generation Tasks and the IPS

Though some of the conditions used in the present investigation have been used before in brain imaging experiments, our study is the first to realize these conditions, among others, in one experiment and to compare them jointly, focussing on possible activation differences within the IPS. The results for those conditions in our experiment that were used in earlier studies agree well with the results reported previously. In word generation of

animals, activations within the left inferior frontal gyrus have been interpreted as being due to lexical retrieval and verbal working memory, whereas activations within inferior temporal and occipital areas was associated with visualization employed as a search strategy [see, for a review, Vitali et al., 2005]. The stronger activations in fronto-parietal regions for random number generation compared to counting also replicate well previous results [Daniels et al., 2005; Jahanshahi et al., 2000]. Different from Jahanshahi et al. [2000], no activations were observed in the present study in the reverse contrast (counting > random), since we had masked this contrast with counting > fixation to exclude baseline deactivations. Usually, imaging experiments using word generation tasks [Gaillard et al., 2003; Vitali et al., 2005; see, for a review, Costafreda et al., in press] focus on left inferior frontal and temporal brain areas involved in lexical retrieval, articulation and visual imagery. Activation in parietal areas, such as the precuneus, was interpreted as being due to mental imagery. As far as we know, none of these studies considered a possible special role of the IPS in word generation tasks of ordered verbal materials. Ordered verbal materials were used rarely in word generation tasks and then only as a control or baseline condition.

To our knowledge, just two studies used and analyzed recital of overlearned sequences such as months of the year and days of the week. One study compared semantic word generation with the recital of overlearned sequences such as months of the year and days of the week [Gurd et al., 2002; for reanalyses of the same data, Gurd et al., 2003; Amunts et al., 2004]. While left-lateralized frontal areas were more strongly activated for semantic word generation than for overlearned sequences, no brain area was significantly activated in the reverse contrast. Another imaging study using the recital of months as a control condition was conducted by Riecker et al. [2000] investigating brain areas related to singing. However, no activation within the IPS was reported for the recital of months compared to singing. Some studies used counting as a low-level verbal control condition [Blank et al., 2002; Kazui et al., 2000; Schlösser et al., 1998], but did not report comparisons between counting and a low level control condition such as fixation. When counting dots aloud was compared with a baseline condition [Piazza et al., 2002, 2003], activation was observed within the IPS bilaterally that increased with the number of the dots. In these two latter studies, however, the activation of the IPS can be due to the active counting process (counting a set of dots) itself and not only to the retrieval of the counting sequence. It therefore cannot inform about a possible involvement of the IPS for ordered verbal materials in word generation tasks.

Numbers Vs. Months

A second goal of our study was to investigate whether the activation within the IPS was modulated by the number of properties carried by the stimuli that are potentially pro-

essed or represented within the IPS. While months carry only sequence information, numbers additionally carry quantity information. As these properties are assumed to be processed within the IPS, it could be speculated that the activation within this area might increase with the number of such properties carried by the stimulus. Then, stronger activation would be expected for numbers than for months. If, alternatively, the number of properties carried by the stimulus does not play a role, no activation difference might be expected between numbers and months. In the present study no differences were observed between months and numbers in canonical and random generation with regard to the IPS, on the level of the whole brain analysis as well as the ROI-analysis. Our observation of similar rather than different activation levels for months and numbers indicates that the greater number of properties carried by numbers does not activate the IPS more strongly than months. One possibility to account for this finding is to assume that the representation of one property dominates the processing within the IPS in a given task. We will discuss this interpretation in more detail below.

Differences were observed between randomizing months and numbers in the frontal lobe, such as the inferior and middle frontal gyrus as well as in the insula and in the SMA. It is not likely that the activation differences in frontal areas are due to differences in word length. The three-syllabic word repetition condition did not activate any brain region more strongly than the two-syllabic word repetition condition. It could be speculated that the stronger frontal activations for months are due to a greater degree of unfamiliarity with the task. While randomizing numbers is sometimes required in games or when selecting numbers for the lottery, it is unlikely that participants ever had to randomize months prior to their participation in this experiment. The results of the behavioral experiment are compatible with this view. When humans are asked to randomize numbers, they deviate in specific ways from a truly random sequence. They generally produce fewer direct repetitions than could be expected and they have a tendency to produce more forward and backward counting sequences [Wiegiersma, 1982]. The counting bias has been shown to increase sharply when the production rate is raised to one item per second [Jahanshahi et al., 2000]. In the results of the behavioral study random generation of numbers did not differ from months with regard to the counting bias. This indicates comparable levels of difficulty. Participants showed, however, greater repetition avoidance in the case of months. We would interpret this as a lack of awareness that trial-to-trial repetitions of months are part of a 'true' random sequence due to the conceptual unfamiliarity of months as materials for randomization.

The Role of the IPS in the Processing of Ordered Verbal Materials and Numbers

To provide a context for the interpretation of our results, we propose that the IPS not only hosts a representation of

quantity but also a representation of an element's position within a sequence. In the case of numbers, the representation is also referred to as the 'mental number line' [Dehaene and Cohen, 1995]. On the mental number line numbers are imagined to be represented in an orderly fashion from small to large. We suggest that verbal materials from ordered categories are similarly represented. Adjacent elements within a sequence will activate adjacent elements of the sequence representation within the IPS. Note that this assumption does not imply a spatially oriented line.

We had hypothesized that numbers would activate the IPS more than months because numbers carry cardinal and ordinal information, whereas months only carry sequence information. Our results show, however, that both types of stimuli activate the IPS to the same degree. One possibility to account for this result is to reject the assumption that the processing of individual properties can add up if they are processed within the same brain area. If this assumption is not rejected, one possibility to account for the data is to conclude that only select properties become active in a given task and that the task determines the type of representation invoked. In the word generation tasks of numbers used here only the representation of sequence information might become activated because this task does not require quantity processing. This account could also explain the task-dependent differences observed by Turconi et al. [2004] who found a different distance effect for the same stimuli (numbers) in a numerical comparison task as compared to an order judgement task. From this account it follows that the activation within the IPS observed for numbers in some studies is possibly not due to the quantity representation of numbers but rather to the representation of order information about the number sequence. The results from the present study could therefore enrich current models of number representation in the IPS that, at present, emphasize the quantity represented by numbers [Dehaene et al., 2004; Verguts and Fias, 2004], rather than their sequential nature. Although the absence of a significant difference between months and numbers cannot be taken as a proof of its absence in reality, the results of the present study agree well with other studies showing functional similarities for order and number processing. Behavioral effects previously interpreted as being indicative of numerical processing have also been observed for ordered materials, such as the SNARC-effect for months and days of the week [Gevers et al., 2003, 2004]. These findings and the results of the present study indicate that order information plays a more significant role in number processing than previously thought. It is possible, for example, that the order rather than the quantity representation of numbers determines behavioral as well as imaging results in a numerical comparison task. It should be mentioned, however, that it could finally be speculated that the processing similarities between months and numbers also originate from a different source. It has been proposed that the IPS also subserves the processing of time. Stronger activation for months than for other

verbal materials would then be expected within the IPS because months are concepts related to time.

A second purpose of the ROI-analysis was to investigate whether different subregions of the IPS have a different functional profile. On the one hand, functional behavior of all three IPS ROIs is similar. First, all three show a greater sensitivity for ordered than for not ordered verbal materials. Significantly stronger activation has been observed in all three ROIs for canonical generation of months and numbers compared to the respective verbal control conditions, as well as for random generation of months and numbers compared to generation of animals. Second, no ROI showed a preference for numerical compared to ordered material, as no greater activation was observed for numbers than for months. On the other hand, some functional differences were also observed between the three ROIs. For example, the activation differences between ordered and not ordered verbal materials was greater in hIP2 than in hIP1 and hIP3. This indicates that hIP2 shows a greater functional specialization for ordered materials than hIP1 and hIP3. It is possible, for example, that this area hosts a larger proportion of neurons coding order or quantity information. Furthermore, hIP3 and hIP1 show a greater left-hemispheric dominance than hIP2 for the random and animal generation tasks. This left lateralization suggests that hIP1 and hIP3 subserve general attentional and language processes to a greater degree than hIP2.

Of the three human intraparietal areas, hIP2 is located anterior and lateral with regard to hIP1 and hIP3. A greater functional specialization for numerical or ordered materials of hIP2 agrees well with the findings by Simon et al. [2004] who also identified a functionally specialized area for calculation rather than other tasks not involving numbers within the anterior part of the IPS. Although it is difficult to assess the relation between the mapped human intraparietal areas hIP1, hIP2, and hIP3 relate to areas mapped within the macaque brain, it has been suggested, among other possibilities, that hIP1 and hIP2 correspond to VIP and AIP of the macaque brain, respectively, or that these two areas correspond to the medial and lateral part of VIP [Choi et al., 2006]. If this interpretation is correct, the greater sensitivity of hIP2 observed here for numbers and months might agree well with the assumption that the human homologue of macaque VIP plays a prominent role in number processing [for a review, see, Hubbard et al., 2005]. To date, only three regions of the IPS have been cytoarchitecturally mapped and it is unclear, whether more posterior regions of the IPS show a similar affinity to number or order processing. Future imaging studies of number and order processing might give a more complete picture of functional specialization within the IPS once the mapping of the IPS is completed.

CONCLUSION

The months of the year and days of the week share with numbers their ordering within a sequence. It was the aim of

the present study to investigate whether the IPS that plays a prominent role in the retrieval from semantic memory of numbers, also plays a role in the retrieval of non-numerical ordered verbal materials, such as the months of the year. We observed a stronger activation of the IPS for months and numbers in word generation compared to the word repetition conditions and word generation of items from a non-numerical not-ordered verbal category (animals). This confirms our hypothesis that the IPS is involved not only in the retrieval of semantic knowledge related to numbers but also in the retrieval of sequences. As a second goal, we had hypothesized that numbers might activate the IPS more strongly than sequences (months), as numbers contain also cardinal and ordinal information. However, no such difference was observed indicating that the activation of the IPS does not depend on the number of properties carried by stimuli. Finally, an analysis of three regions within the anterior IPS revealed that the most anterior and lateral of these regions (human intraparietal area hIP2) showed greater sensitivity to numbers and ordered verbal materials than the other two areas (hIP1 and hIP3). This indicates that the most anterior and lateral part of the IPS might host a greater number of neurons that code order or number quantity than other parts of the IPS.

REFERENCES

- Amunts K, Schleicher A, Bürgel U, Mohlberg H, Uylings HBM, Zilles K (1999): Broca's regions revisited: Cytoarchitecture and intersubject variability. *J Comp Neurol* 412:319–341.
- Amunts K, Weiss PH, Mohlberg H, Pieperhoff P, Eickhoff S, Gurd JM, Marshall JC, Shah NJ, Fink GR, Zilles K (2004): Analysis of neural mechanisms underlying verbal fluency in cytoarchitectonically defined stereotaxic space—The roles of Brodmann areas 44 and 45. *Neuroimage* 22:42–56.
- Aschenbrenner S, Tucha O, Lange KW (2001): Regensburger Wort-flüssigkeitstest. Göttingen: Hogrefe Verlag für Psychologie.
- Baayen RH, Piepenbrock R, van Rijn H (1993): The Celex Lexical Database [CD-ROM] Philadelphia: University of Pennsylvania Linguistic Data Consortium.
- Baddeley A, Emslie H, Kolodny J, Duncan J (1998): Random generation and the executive control of working memory. *Q J Exp Psychol A* 51:819–852.
- Baldo JV, Shimamura AP (1998): Letter and category fluency in patients with frontal lobe lesions. *Neuropsychology* 12:259–267.
- Binder J (1995): Functional magnetic resonance imaging of language cortex. *Int J Imaging Syst Technol* 6:280–288.
- Birn RM, Cox RW, Bandettini PA (2004): Experimental designs and processing strategies for fMRI studies involving overt verbal responses. *Neuroimage* 23:1046–1058.
- Blank SC, Scott SK, Murphy K, Warburton E, Wise RJS (2002): Speech production: Wernicke Broca and beyond. *Brain* 125:1829–1838.
- Bowers D, Heilman KM, Satz P, Altman A (1978): Simultaneous performance on verbal nonverbal and motor tasks by right-handed adults. *Cortex* 14:540–556.
- Brett M, Christoff K, Cusack R, Lancaster J (2001): Using the Talairach atlas with the MNI template. *Neuroimage* 13:S85.
- Brodman K (1909): Vergleichende Lokalisationslehre der Großhirnrinde—In ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig: Verlag von Johann Ambrosius Barth.
- Cappelletti M, Butterworth B, Kopelman MD (2001): Spared numerical abilities in a case of semantic dementia. *Neuropsychologia* 39:1224–1239.
- Caramazza A, Mahon B (2003): The organization of conceptual knowledge: The evidence from category-specific semantic deficits. *Trends Cogn Sci* 7:354–361.
- Chochon F, Cohen L, van De Moortele PF, Dehaene S (1999): Differential contributions of the left and right inferior parietal lobules to number processing. *J Cogn Neurosci* 11:617–630.
- Choi HJ, Zilles K, Mohlberg H, Schleicher A, Fink GR, Armstrong E, Amunts K (2006): Cytoarchitectonic identification and probabilistic mapping of two distinct areas within the anterior ventral bank of the human intraparietal sulcus. *J Comp Neurol* 495:53–69.
- Cipolotti L, Butterworth B, Denes G (1991): A specific deficit for numbers in a case of dense acalculia. *Brain* 114:2619–2637.
- Cohen-Kadosh R, Henik A, Rubinsten O, Mohr H, Dori H, van de Ven V, Zorzi M, Hendler T, Goebel R, Linden DE (2005): Are numbers special? The comparison systems of the human brain investigated by fMRI. *Neuropsychologia* 43:1238–1248.
- Collette F, Van der Linden M, Laureys S, Delfiore G, Degueldre C, Luxen A, Salmon E (2005): Exploring the unity and diversity of the neural substrates of executive functioning. *Hum Brain Mapp* 25:409–423.
- Costafreda SG, Fu CH, Lee L, Everitt B, Brammer MJ, David AS (2006): A systematic review and quantitative appraisal of fMRI studies of verbal fluency: Role of the left inferior frontal gyrus. *Hum Brain Mapp* 27:799–810.
- Daniels C, Witt K, Wolff S, Jansen O, Deuschl G (2005): Rate dependency of the human cortical network subserving executive functions during generation of random number series—A functional magnetic resonance imaging study. *Neurosci Lett* 345:25–28.
- Dehaene S, Cohen L (1995): Towards an anatomical and functional model of number processing. *Math Cogn* 1:83–120.
- Dehaene S, Bossin S, Giraux SP (1993): The mental representation of parity and number magnitude. *J Exp Psychol Gen* 122:371–396.
- Dehaene S, Molko N, Cohen L, Wilson AJ (2004): Arithmetic and the brain. *Curr Opin Neurobiol* 14:218–224.
- Delazer M, Benke T (1997): Arithmetic facts without meaning. *Cortex* 33:697–710.
- Delazer M, Butterworth B (1997): Dissociation of number meanings. *Cogn Neuropsychol* 14:613–636.
- Delazer M, Ischebeck AK, Domahs F, Zamarian L, Koppenstaetter F, Siedentopf C, Kaufmann L, Benke T, Felber S (2005): Learning by strategies and learning by drill—Evidence from an fMRI study. *Neuroimage* 25:838–849.
- Delazer M, Karner E, Zamarian L, Donnemiller E, Benke T (2006): Number processing in posterior cortical atrophy—A neuropsychological case study. *Neuropsychologia* 44:36–51.
- Eger E, Sterzer P, Russ MO, Giraud A-L, Kleinschmidt A (2003): A supramodal number representation in human intraparietal cortex. *Neuron* 37:719–725.
- Eickhoff SB, Klaas ES, Mohlberg H, Grefkes C, Fink G, Amunts K, Zilles K (2005): A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage* 25:1325–1335.

- Eickhoff SB, Heim S, Zilles K, Amunts K (2006): Testing anatomically specified hypotheses in functional imaging using cytoarchitectonic maps. *Neuroimage* 32:570–582.
- Fulbright RK, Manson SC, Skudlarski P, Lacadie CM, Gore JC (2003): Quantity determination and the distance effect with letters numbers and shapes: A functional MR imaging study of number processing. *Am J Neuroradiol* 23:193–200.
- Fuson KC (1988): *Children's Counting and Concepts of Number*. New York: Springer-Verlag.
- Gaillard WD, Sachs BC, Whitnah JR, Ahmad Z, Balsamo LM, Petrella JR, Branietki SH, McKinney CM, Hunter K, Xu B, Grandin CB (2003): Developmental aspects of language processing: fMRI of verbal fluency in children and adults. *Hum Brain Mapp* 18:176–185.
- Gevers W, Reynvoet B, Fias W (2003): The mental representation of ordinal sequences is spatially organised. *Cognition* 87:B87–B95.
- Gevers W, Reynvoet B, Fias W (2004): The mental representation of ordinal sequences is spatially organized: Evidence from days of the week. *Cortex* 40:171–172.
- Gurd JM, Amunts K, Weiss PH, Zafiris O, Zilles K, Marshall J, Fink G (2002): Posterior parietal cortex is implicated in continuous switching between verbal fluency tasks: An fMRI study with clinical implications. *Brain* 125:1024–1038.
- Gurd JM, Weiss PH, Amunts K, Fink GR (2003): Within-task switching in the verbal domain. *Neuroimage* 20:S50–S57.
- Hamilton JME, Sanford AJ (1978): The symbolic distance effect for alphabetic order judgements: A subjective report and reaction time analysis. *Q J Exp Psychol* 30:33–43.
- Hécaen H, Angelergues R, Houillier S (1961): [The clinical varieties of acalculias during retrorolandic lesions: Statistical approach to the problem] *Rev Neurol (Paris)* 105:85–103.
- Henschen SE (1919): Über Sprach- Musik- und Rechenmechanismen und ihre Lokalisationen im Großhirn. *Zeitschrift für die gesamte Neurologie und Psychiatrie* 52:273–298.
- Hubbard EM, Piazza M, Pinel P, Dehaene S (2005): Interactions between numbers and space in parietal cortex. *Nat Neurosci* 8:435–448.
- Ischebeck AK, Zamarian L, Siedentopf C, Koppelstaetter F, Benke T, Felber S, Delazer M (2006): How specifically do we learn? Imaging the learning of multiplication and subtraction. *Neuroimage* 30:1365–1375.
- Jahanshahi M, Dirnberger G, Fuller R, Frith CD (2000): The role of the dorsolateral prefrontal cortex in random number generation: A study with positron emission tomography. *Neuroimage* 12:713–7125.
- Kazui H, Kitagaki H, Mori E (2000): Cortical activation during retrieval of arithmetical facts and actual calculation: A functional magnetic resonance imaging study. *Psychiatry Clin Neurosci* 54:479–485.
- Marshuetz C, Reuter-Lorenz PA, Smith EE, Jonides J, Noll DC (2006): Working memory for order and the parietal cortex: An event-related functional magnetic resonance imaging study. *Neuroscience* 139:311–316.
- Martin A, Chao LL (2001): Semantic memory and the brain: Structures and processes. *Curr Opin Neurobiol* 11:184–201.
- Metha S, Grabowski TJ, Razavi M, Eaton B, Bolinger L (2006): Analysis of speech-related variance in rapid event-related fMRI using a time-aware acquisition system. *Neuroimage* 29:1278–1293.
- Moyer R, Landauer T (1967): Time required for judgements of numerical inequality. *Nature* 215:1519–1520.
- Palmer ED, Rosen HJ, Ojemann JG, Buckner RL, Kelley WM, Petersen SE (2001): An event-related fMRI study of overt and covert word stem completion. *NeuroImage* 14:182–193.
- Piazza M, Mechelli A, Butterworth B, Price C (2002): Are subitizing and counting implemented as separate or functionally overlapping processes? *Neuroimage* 15:435–446.
- Piazza M, Giacomini E, Dehaene S (2003): Single-trial classification and serial attentive magnetic resonance. *Proc R Soc Lond* 270:1237–1245.
- Piazza M, Izard V, Pinel P, Le Bihan D, Dehaene S (2004): Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron* 44:547–555.
- Pinel P, Dehaene S, Riviere D, Le Bihan D (2001): Modulation of parietal activation by semantic distance in a number comparison task. *Neuroimage* 14:1013–1026.
- Pinel P, Piazza M, Le Bihan D, Dehaene S (2004): Distributed and overlapping cerebral representations of number size and luminance during comparative judgements. *Neuron* 41:983–993.
- Reverberi C, Laiacina M, Capitani E (2006): Qualitative features of semantic fluency performance in mesial and lateral frontal patients. *Neuropsychologia* 44:469–478.
- Riecker A, Ackermann H, Wildgruber D, Dogil G, Grodd W (2000): Opposite hemispheric lateralization effects during speaking and singing at motor cortex insula and cerebellum. *Neuroreport* 11:1997–2000.
- Sagiv N, Simner J, Collins J, Butterworth B, Ward J (2005): What is the relationship between synaesthesia and visuo-spatial number forms? *Cognition* 101:114–128.
- Scheperjans F, Mohlberg H, Amunts K, Zilles K (2005): Observer-independent cytoarchitectonic mapping of human superior parietal lobule and anterior medial intraparietal sulcus. *Neuroimage* 26:S23.
- Schlösser R, Hutchinson M, Joseffer S, Rusinek H, Saarimaki A, Stevenson J, Dewey SL, Brodie JD (1998): Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *J Neurol Neurosurg Psychiatry* 64:492–498.
- Shuman M, Kanwisher N (2004): Numerical magnitude in the human parietal lobe: Tests of representational generality and domain specificity. *Neuron* 44:557–569.
- Simon O, Kherif F, Flandin G, Poline J-B, Riviere D, Mangin J-F, Le Bihan D, Dehaene S (2004): Automated clustering and functional geometry of human parietofrontal networks for language space and number. *Neuroimage* 23:1192–1202.
- Spatt J, Goldenberg G (1993): Components of random generation by normal subjects and patients with dysexecutive syndrome. *Brain Cogn* 23:231–242.
- Stanescu-Cosson R, Pinel P, van De Moortele PF, Le Bihan D, Cohen L, Dehaene S (2000): Understanding dissociations in dyscalculia: A brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation. *Brain* 123:2240–2255.
- Talairach J, Tournoux P (1988): *Co-Planar Stereotaxic Atlas of the Human Brain*. New York: Thieme Medical.
- Taylor DA, Kim JO, Sudevan P (1984): Representation of linear orders. *J Exp Psychol Learn Mem Cogn* 10:61–71.
- Thioux M, Pesenti M, Costes N, De Volder A, Seron X (2005): Task-independent semantic activation for numbers and animals. *Brain Res Cogn Brain Res* 24:284–290.
- Tombaugh TN, Kozak J, Rees L (1999): Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Arch Clin Neuropsychol* 14:167–177.
- Troyer AK, Moscovitch M, Winocur G, Alexander MP, Stuss D (1998): Clustering and switching on verbal fluency: The effects of focal frontal- and temporal-lobe lesions. *Neuropsychologia* 36:499–504.

- Turconi E, Seron X (2002): Dissociation between order and quantity meanings in a patient with Gerstmann Syndrome. *Cortex* 38:911–914.
- Turconi E, Jemel B, Rossion B, Seron X (2004): Electrophysiological evidence for differential processing of numerical quantity and order in humans. *Brain Res Cogn Brain Res* 21: 22–38.
- Turconi E, Campbell JID, Seron X (2006): Numerical order and quantity processing in number comparison. *Cognition* 98:273–285.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labelling of activations in spm using a macroscopic anatomical parcellation of the MNI MRI single subject brain. *Neuroimage* 15:273–289.
- Venkatraman V, Ansari D, Chee MWL (2005): Neural correlates of symbolic and non-symbolic arithmetic. *Neuropsychologia* 43: 744–753.
- Verguts T, Fias W (2004): Representation of number in animals and humans. A neural model. *J Cogn Neurosci* 16:1493–1504.
- Vitali P, Abutalebi J, Tettamanti M, Rowe J, Scifo P, Fazio F, Cappa SF, Perani D (2005): Generating animal and tool names: An fMRI study of effective connectivity. *Brain Lang* 93:32–45.
- Walsh V (2003): Time: The backdoor of perception. *Trends Cogn Sci* 7:335–338.
- Wiegersma S (1982): Sequential response bias in randomized-response sequences: A computer simulation. *Acta Psychol* 52: 249–256.
- Wynn K (1990): Children’s understanding of counting. *Cognition* 36:155–193.
- Wynn K (1992): Children’s acquisition of the number words and the counting system. *Cogn Psychol* 24:220–251.
- Zamarian L, Karner E, Benke T, Donnemiller E, Delazer M (2006): Knowing 7×8 but not the meaning of ‘elephant’: Evidence for the dissociation between numerical and non-numerical semantic knowledge. *Neuropsychologia* 44:1708–1723.
- Zilles K, Schleicher A, Palomero-Gallagher N, Amunts K (2002): Quantitative analysis of cyto- and receptor architecture of the human brain. In: Toga A, Mazziotta J, editors. *Brain Mapping: The Methods*, 2nd ed. San Diego: Academic Press. pp 573–602.